

THE
NATURE OF DISEASE

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THE NATURE OF DISEASE

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PART III—SECTION I



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GENERAL INTRODUCTION

THE first two volumes of "The Nature of Disease" were published in 1924 and 1927 respectively. It was the author's aim to bring his research and clinical work up to date in a third volume, but owing to the immensity of the material in hand and to the expense of issuing another volume before the first two are out of print, he has decided to publish his future work in sections. This section includes a General Introduction, with chapters on Mal-co-ordination and Disease, Disease and the Nervous System, and Chronic Intestinal Intoxication. The main theme pervading the author's work is that there is only one disease, that the so-called "diseases" are but the signs and symptoms of this one disease and that disease is the result of the defeat of the body's resistance by the invader. Similarly there is only one invader; that is to say, the manner in which the host's resistance is damaged is the same whether the invader be a physical agent, a chemical agent or a micro-organism. In spite of the fact that this concept of the existence of only one disease simplifies medicine, it has, nevertheless, proved difficult of acceptance. A few words of explanation are necessary, therefore, to trace the reason for this difficulty before drawing the reader's attention to what constitutes the body's resistance.

Medicine is the outcome of magic, with which it is still pervaded, and the difficulties which have continued to multiply throughout the ages have all been due to the age-old error of scratching on the surface instead of penetrating to the depths. The principle of magic rests, as Dewey aptly puts it, in hoping to get results without the intelligent control of means. Consequently end-gaining entails, as it always must, a scratching on the surface only. Man's first thought when he fell sick was doubtless how to get rid of the sickness—not of how he came by it. In endeavouring to get rid of the sickness it is reasonable to suppose he either sought advice from another or made for himself a herbal decoction. If the sickness disappeared after taking the advice, one of these methods would be adopted by others similarly unfortunate, and if it was followed by similarly successful results the adviser would be raised to the position of doctor. But, no account would ever be taken of the mode of action of the advice. If the sickness disappeared after taking the decoction, the herb or herbs from which it was made would be used in future for this and similar complaints. If success followed the use

of particular herbs in particular complaints the time would come when their action would be regarded as specific, although there had been no attempt to unravel the mode of action. That this is what most probably occurred is suggested by the fact that the fundamental error with which medicine began and which still persists, was the raising of symptoms to the lofty position of diseases. This has led to differentiation as against correlation, and to-day it is impossible to see the truth through the difficulties which the former has brought in its wake. The modern physician acts just as did his earliest predecessor in that he aims at reaching the end, which must necessitate a neglect of the means. Even the drugs in daily use have come into favour through trial and error and not as a result of logical sequence of thought in action. The action of digitalis being a direct one upon the heart, of adrenalin upon the sympathetic nervous system, of atropine upon the vagus, of arseno-benzene upon spirilla, are still referred to as truths in spite of the fact that they are not so, because not one of these preparations acts directly upon the structure mentioned. Had attention not been directed on the end, but on the immediate means whereby, medicine would not have become in course of time the mass of empiricism which it is to-day, so-called "discoveries" would not be labelled with that blessed hyphenated word "epoch-making," and imitation would not take the place of originality. The persistence of empiricism leads not only to the treatment of symptoms as if they were diseases, but also to the still more serious error of thinking that a disappearance of a symptom is synonymous with a cure of disease. A symptom can be no more than palliated, and its palliation throws no light on its causation. Find the cause of any symptom and the origin of disease is exposed. Once this is done, there would be no use for the word "cure"—which has misled men for centuries—as it would be seen that disease must be prevented to be rendered non-existent, and that any attempt to rectify the damage done can be no more than palliation.

The author is of the opinion that disease is largely the product of civilisation, and if this be so it must inevitably increase as civilisation advances. This view can neither be affirmed nor denied unless it is understood what disease really is. That the nature of disease is not comprehended is proved by the fact that committees and councils are formed to investigate symptoms. Committees and councils are often the outcome of ignorance; they denote an *impasse*, or, in other words, that another cul-de-sac has been reached. On looking around to-day nothing but cul-de-sacs meet the eye, and the greater the attempt made to let in light the more loculated the sac becomes. In spite of this

man cannot learn that the only way to get out of a cul-de-sac is to retrace his steps. Once this were done and the nature of disease thus discovered, medicine could be utilised to the advantage of civilisation and employed as the means whereby its other faults could be corrected. The mere formation of a committee or council is an end in itself and therefore no great truth can emerge from it. How then is it conceivably possible to throw light on the nature of disease when a gathering is formed to investigate a symptom? Not only is no light thrown upon medicine, but progress is, unfortunately, actually impeded in addition. Most, if not all, the present-day discoveries in medicine which have been hailed as "epoch-making" have arisen through accident, and no better example could be given than that of insulin. Diabetes, thought to be a disease, although no more than a symptom, may be produced by extirpation of the pancreas, and in fatal cases the islet cells of Langerhans are often found to have undergone degeneration. An extract of the islet cells is made, its administration lowers the percentage of the blood-sugar, and "insulin," the name given to the product, is hailed as curing diabetes. When used in overdose, insulin causes certain signs and symptoms considered to be brought about by too great a lowering of the percentage of the blood-sugar. Therefore, sugar is prescribed to make good the loss insulin has occasioned, and the signs and symptoms vanish. Diabetes is a symptom of disease and occurs when the host's resistance is subjected to chronic dehydration by the invader. In the end, the islet cells of Langerhans may suffer destruction, but this is by no means invariable and the converse is equally true—namely, that the destruction of the cells does not necessarily result in diabetes. Insulin lowers the percentage of the blood-sugar because it corrects the dehydration, but it does not cure diabetes. Shock, which follows an overdose of insulin, is due to excessive hydration of the host's resistance, and hypoglycæmia is no more than one of the signs of this chemico-physical change. The clinical manifestations are not the result of the hypo-glycæmia and they do not vanish when glucose is prescribed because sugar is restored to the blood, but because glucose causes dehydration of the hydrated protein particles.

There is just as much sugar in the blood after as before a dose of insulin, only it is in another form, and there are hosts of dehydrators as efficient as glucose. Even assuming that insulin is a great discovery it can never reduce the incidence of diabetes, and it throws not one ray of light upon the cause of the condition.

The shock occurring after the use of insulin differs in no wise from the clinical signs and symptoms produced by the protein particles undergoing

sudden hydration at the hands of invaders having no connection whatever with insulin. The shock produced by histamine and called "anaphylaxis" is of the same nature, and so likewise is the shock encountered in the last stage of an acute illness. Anaphylactic shock can be prevented and overcome with Sup. 36, as well as with glucose and other dehydrators, and Sup. 36 is equally useful in preventing and overcoming insulin hypo-glycæmia, although the drug is in no way chemically related to glucose. It has become customary to prescribe calcium in severe forms of shock on the ground that there is a hypo-calcæmia. Whenever the protein particles undergo hydration the calcium, like the sugar, cannot be detected because a colloid adsorption complex is made with the protein, but both become evident when the hydrated protein particles are dispersed. Dispersion is occasioned by Sup. 36, certain compounds of calcium and strontium and hosts of other substances. In the chronic stage of an infection, for example, strontium aspartate raises the percentage of the calcium in the blood more efficiently than the corresponding calcium salt, and the drug is equally useful in preventing and overcoming shock occasioned by insulin, histamine, etc. The patient does not recover because calcium restores what is lost to the blood—in fact, hypo-calcæmia means an altered physical state and not a loss of calcium—but because the protein particles previously too big have been broken up into several smaller particles.

It is difficult to force acceptance of new and radical ideas, because man is essentially conservative and imitative. It is largely the fault of education that imitation has usurped originality. Education is in the hands of those who have power and authority, and therefore what is taught tends to be that which does not disturb the conditions by which the teacher profits. It has thus come about that the discoveries which coincide with accepted teaching are labelled as "epoch-making," while those the result of independent thought on the part of others are regarded as anarchical. Science would be better served by pointing out the errors of its great men than by dwelling upon and continually re-iterating the steps they advanced. The latter can never be more than stepping-stones for those who come after and such landmarks are always self-evident, while mention of the former would prevent the same mistakes from being continually repeated. True discoveries are not ends, but merely means towards an end which can never be reached and to which attention should never be directed. Education as applied to-day can only lead to conventions and to the worship of institutions and personages, themselves lacking in imagination, observation and liberal thought. No better example of this could be given than the side-chain theory of immunity.

The side-chain theory of immunity is really nothing more than an attempt to fill lacunæ with coined words which merely blind the issue the more. Being fundamentally unsound, it was always therefore incapable of comprehension, in spite of which the theory has been and is still being taught to thousands, and already innumerable volumes have been written upon it. The theory has put back the clock of progress many years, and has led to abysses into which medicine has fallen and from which it will be difficult to extricate it.

The whole idea of immunity can be put into one sentence : " a phenomenon brought about by causing the host's resistance to turn the tables on the invader," and immunity is achieved in the following simple way : When an invader attacks the host's resistance, some of the protein particles are subjected to dehydration, and as a result others undergo hydration. Hydration is a sequence of dehydration, consequently when an infection, for example, has been overcome hydrated protein particles are left behind which undergo dispersion, should any renewal of activity of the infective agent take place. The hydrated protein particles are split up into myriads of tiny particles, and the dispersion is greatest when caused by the agent which set in motion the hydration in the first instance. To this phenomenon the term " specificity " has been applied. When the enlarged or hydrated protein particles are dispersed their area of resistance is enormously increased, their Brownian movements become more active and their negative electric charge is enhanced. The result is that they occasion dehydration ending in destruction of the micro-organisms renewing the attack, consequently a fresh infection or a recurrence cannot take place.

These examples of insulin and immunity show that medicine cannot be advanced unless conservatism and tradition, products of end-gaining, are made to give way to renewal, the product of making the means the immediate end. These explanations of the mode of action of insulin and of the rationale of immunity, should (or will) serve to draw the reader's attention to the fact that health and disease are entirely a question of the body's resistance. Health is the maintenance of this resistance and disease is its breakdown. There can be only one disease, and all the clinical signs and symptoms presented are but manifestations of the breakdown of the body's resistance. As the breakdown is caused by the resistance being subjected to altered chemico-physical changes, it follows that there can be but only one invader.

It now remains to introduce the last fact, namely, that the resistance of the host resides in the chemico-physical architecture of the cells of the body,

but particularly of the protein particles in the plasma and of the protein particles constituting the protoplasm of the leucocytes. The former constitute what may be termed best "the dynamic resistance," and the latter "the static resistance"—dynamic because each protein particle is able to circulate independently all over the body, and static because many protein particles are confined to a special area by the so-called "cell membrane." Many find this description of the body's resistance difficult to understand because the belief has been general that the protein in the plasma is in solution and not in the form of particles having an infinite instead of a finite surface area. Similarly, a cell is regarded as a unit and not as a composite structure made up of particles limited to an area by a few particles having a different chemico-physical architecture (cell-membrane), which may undergo a still different chemico-physical change enabling the particles enclosed within to escape outside. Disease in the main is but an expression of the altered chemico-physical changes undergone by the host's dynamic resistance at the hands of the invader. This and other sections deal with how these chemico-physical changes are brought about; light is thrown upon the actions of the invader, and an attempt is made to show how the cells of the body are affected by these alterations, giving rise to the signs and symptoms of disease.

Not only is the protein in the serum in the form of particles, but also each particle is a system best likened to a solar system in which there is a part corresponding to the sun, with other parts taking the place of the planets. The former is the protein nucleus and the latter the adsorbed constituents, such as amino acids, fats, urea and uric acid, carbohydrates, salts and electricity. The planets of the solar system are kept in constant relationship to the sun by gravity and the adsorbed constituents to the protein nucleus by water. Owing to the extreme condensation the solar system has undergone, there is no interchange between the planets and the sun, and gravity is not heavily pervaded with the various forms of matter of which the sun and its various planets are composed. Indeed gravity would appear to be remarkably pure, and although its nature is unknown it is probably a manifestation of matter too small to be ponderable, a something more minute and a possible constituent of an electron. In the case of the protein particles the adsorbed constituents are in an ever-varying relationship with the protein nucleus forming at one time a colloid complex and at another time an intermediate and less complex combination, according to the concentration of the water in the particle. The protein particles are what are called "emulsoid particles," that is to say,

they both contain and are in water. Moreover, the water which surrounds them contains in true solution every adsorbed constituent of which the particles are made up and even some protein itself. The adsorbed constituents in true solution are in the form of ions, and between the ionic state and the colloid state, which is sufficiently colloid to allow of the word "particle" being used, there is an intermediate state which is neither wholly ionic nor wholly colloid. In other words, not only are the various adsorbed constituents of the protein particles in varying combination with the protein sun or nucleus, but also they are in varying combination with those which are in true solution in the liquid portion of the plasma.

Water is the medium common to the two phases of the plasma (the colloid phase, dispersed phase or particle, and the liquid phase or dispersion medium), as is gravity the medium common to the two phases of the solar system. But, here the analogy fails, because the concentration of the water within and outside the protein particles varies according to altered conditions. The protein particles may lose water, in which case the adsorbed constituents previously in a colloid complex with the protein nucleus sever their connection, break away from the protein sun, to become more and more ionic, until they reach the stage of true solution. To this stage the term "dehydration" is best applied. The protein particles may take up water, in which case the particles become richer in constituents because they acquire the simple colloids and ions the water held. The adsorbed constituents form colloid complexes with the protein nucleus or sun, and the combination becomes the more complex the greater the quantity of the water taken up. To this change the term "hydration" is best applied.* The more ionic the various constituents become the more they regain their individuality, while the more colloid they grow the more they lose their individuality, till they cease to be detected by the means generally employed.

To take the carbohydrate constituent as an illustration. When the carbohydrate constituent is in an ionic form it gives the tests for glucose, but these fail the more adsorbed to the protein nucleus the sugar becomes. Consequently, when the protein particles undergo dehydration the percentage of the blood-sugar is raised, and *vice versa* when the protein particles undergo hydration. The fall in the percentage of the blood-sugar after insulin is due to the action this drug has in increasing the size of the protein particles and in rendering more complex the adsorption between the protein sun and some

* The more hydrated the protein particles become, the more the liquid part of the plasma approaches that of true water. This results in the water invading the tissues and producing oedema.

of its adsorbed constituents. Similarly the rise in the percentage of the blood-sugar after glucose is due to the liberation of the carbohydrate planet from the protein sun, or, in other words, to the dehydrator action of the drug. That the rise is not due to the addition of glucose is proved by the fact that if too much glucose is injected the percentage of the blood-sugar falls, because all dehydrators in overdose occasion hydration. In the solar system some of the planets are more distant from the sun than other planets, and this is likewise the case with the adsorbed constituents in the protein particles. The further the adsorbed constituent is removed from the protein sun the less complex can become its colloid combination with the nucleus in hydration, and the more readily it is detached in dehydration. When the protein particles undergo dehydration the planets lose their connection with the protein sun in this order—electricity, salts, sugar, urea, and so on. The electricity which is liberated first becomes ionic; heat is evolved and fever is the consequence. When the salts become ionic they are voided in the urine at the moment the liquid portion of the plasma can hold no more in solution. This happens also with the sugar and the other planets. But, with those planets which are near to the protein sun and which form enormously complex colloid combinations with the protein sun in hydration, the distance to travel before the ionic state is reached is so great that intermediate compounds are formed which, owing to the retention of their colloid characteristics, cannot readily pass through the glomerular membranes into the urine. These intermediate substances are retained in the body and deposited as a rule in the mesenchymatous tissues. As examples may be mentioned the uric acid deposits in gout and the cholesterol ester deposits in xanthoma. Although the chief constituents of tophi are urates the substances deposited are not in this simple form but in a much more complex form, from which urates arise as a result of analysis. Some adsorbed constituents are more closely related not only to the protein sun than others, but also to each other. For example, there is a certain relationship between sugar and fat, so that, as the dehydration which causes hyper-glycæmia proceeds, the percentage of the fat in the blood rises. In these cases of lipæmia the fat may diminish if sugar is prescribed—a phenomenon referred to as “the burning of fat in the carbohydrate furnace.” The fat is not burnt, it is merely enabled to renew its allegiance with the protein nucleus, which it can do only so long as sugar is present. Another excellent example is the disappearance of uræmia in diabetes following the administration of glucose. The planet urea is nearer to the protein sun than the planet sugar. Diabetes is a clinical manifestation of

chronic dehydration and, as the dehydration continues, the time may arrive when after all the sugar has been liberated it is the turn of the urea to be liberated next, a liberation which is checked if sufficient sugar is available. Although insulin will save the life of a patient when he is dying with—but not from—a hyper-glycæmia, the drug will kill him if the planet urea is being liberated in any large quantity. This is because the very first action of insulin is one of dehydration and because, when dehydration has advanced so far as to cause in such a case a hyper-uræmia, other protein particles undergo hydration to avoid the same fate, and the hydration of these may be so augmented by insulin for fatal shock to result. In practically every case of dehydration some of the particles undergo hydration, and it is to these hydrated protein particles that death is due. It is due in part to the dehydration of these hydrated protein particles following the administration of glucose in lipæmic and uræmic diabetic coma that recovery ensues. Nevertheless, it is a fact that when a planet is being detached from the protein sun the administration of the one or more of the planets more distant to it checks the dehydration. The restoration of electrons to protein particles losing the adsorbed constituent calcium may result in the percentage of the blood-calcium being reduced to the normal, just as the restoration of sugar may cause a hyper-uræmia to vanish. When a planet has been separated off from the protein particles and has disappeared in the urine, the percentage of this planet in the blood tends to reach its normal level, then the dehydration affects the next planet in sequence. The planet chlorine is external to the planet calcium, calcium to the planet sugar, sugar to the planet urea, and so on. Consequently, when the stage of hyper-calcæmia is reached the percentage of the blood-chlorine tends to be normal and so on. As the dehydration in disease may vary not only in degree but also in the manner in which the protein particles are affected thereby, it follows that no clinical manifestation has its specific blood-picture.

Speaking generally, the first action of every invader is a dehydration of the dynamic resistance. The effect of this dehydration is to cause a disruption of the protein particles, which leads at first to a numerical increase of the particles. So long as this pertains, the clotting time of the plasma is hastened because clotting is primarily dependent upon the number of the protein particles. Protein particles when they break up into more and smaller particles tend to become more negatively charged. Therefore, provided the dehydration has not resulted in a great loss of electrons, there may be a temporary "alkalosis." But, more often the loss of electrons is great, with

the result that the hydrated protein particles formed as a sequence of dehydration are less negatively charged than normal particles. Protein particles are never acid ; they are either more or less negatively charged ; consequently although the term "alkalosis" may be permissible, "acidosis" never is, and as explained in the previous volume "alkalosis" is really a misnomer.

If the dehydration is general and severe there occurs a numerical increase of particles, with feeble Brownian movements, occasioned by the loss of electrons and of particles which have the chemico-physical characteristics of albumin. The former is revealed in the ultra-microscopic picture, and the latter by the fall in the refractive index of the serum. When the protein particles suffer a great loss of electrons the red blood-corpuscles go into *rouleaux* formation, become heavier, and sink in a column of citrated blood more rapidly. Indeed, the suspension stability of the red blood-corpuscles runs *pari passu* with the loss of electrons sustained by the protein particles in the plasma, being reduced when the loss is great and *vice versa*. It is unusual for the dehydration to be general, because as some protein particles are split up others adsorb the parts, increase in size and agglutinate. In other words, a dehydration of some protein particles leads to a hydration of other protein particles, and it is due to this concomitant dehydration and hydration that no clinical condition has a specific blood-picture. Moreover, it often makes the interpretation of a blood-picture a difficult matter, and it is only by experience that it is possible to tell whether dehydration exceeds hydration or the reverse. But, when it comes to treatment the matter is simplified, because there is always a greater need to correct hydration than dehydration owing to the fact that most of the signs and symptoms of disease are the direct result of hydration of the protein particles. Hydrated protein particles give the chemico-physical characteristics of globulin, which is detected by a rise in the refractive index of the serum. The terms "fibrinogen," "pseudo-globulin" and "eu-globulin" apply to the stages from general dehydration to hydration and are unnecessary. Hydrated protein particles tend to become self-reliant and to work out their metabolism independently of the particles around. In the ultra-microscopic picture this is characterised by a halo surrounding the large and refractile giant particles. A sort of "no-man's-land" is formed between these and neighbouring particles, and the halo corresponds to the capsule possessed by certain bacilli and to the unstained space which occurs between the phases of the *Leucocytozoon syphilidis* and the surrounding cells.*

* The halo, capsule, etc., probably represent activity, the something smaller than an electron and possessed by all chemical substances.

It thus comes about that hydrated protein particles are always at the least potentially foreign bodies. Indeed, the author holds the view that most of the changes undergone by the tissues in disease are due to the hydrated particles collecting in and passing through the walls of the peri-capillary lymphatic vessels and capillaries, rather than to the actual invader which occasioned the hydration in the first instance. It is not certain whether the hydrated protein particle itself or a particulate form of it passes through the vessel wall.* Hydrated protein particles cause not only dilatation, but also increase the permeability of the vessels in which they collect. Hydrated protein particles tend naturally to stagnate in the circulation because of their large size and because as a rule they are less negatively charged. Electrons are needed for metabolism, and as hydrated protein particles require many for their needs they develop their fat moiety, hence the meaning of so-called "lipoid-globulin."

Hydration is a sequence of condensation, and should the condensation increase one large particle gives rise to several smaller particles, all of which retain certain of the characteristics of hydration. When this change affects the nucleolus of a cell the cell becomes what is termed "malignant." Indeed, the author holds that cancer is merely an altered chemico-physical change occurring in the vital part of a cell whereby many smaller cells are formed, each generation behaving more as a foreign body or invader than did the first aberrant cell. Herein lies the explanation as to why cancer is more common in the old than the young. Age is synonymous with progressive dehydration, and whenever there is dehydration there is a varying amount of hydration. In fact, hydration occurs more commonly as a sequence of dehydration than *de novo*. The sub-particulate formation of hydrated protein particles in the plasma is in some instances a true example of malignancy of the dynamic resistance, and this formation is characterised in the ultra-microscopic picture by ringed protein particles.

All chemico-physical changes tend to be cyclical, and instead of the process described above taking place hydrated protein particles may break up into more or less normally behaving particles. The cyclical change is always one of breaking up. The break up may be into particles fully negatively charged, in which case the term "dispersion" is used. More often the break up is into particles with a feeble negative charge, when the term "gelation" is used.

Hydrated protein particles are most likely to undergo gelation when they become arrested in veins, to occasion venous thrombosis. *Phlegmasia alba*

* It is probable that in some cases at least only the activity passes through the vessel wall.

dolens, pulmonary thrombosis (post-operative pneumonia) and pulmonary embolism are clinical examples of gelation occurring as a cyclical change of hydration. The cyclical change need not be general—that is to say, only some of the protein particles may become dehydrated. When this occurs the liberated planets find their way into the urine more readily than usual. This is because in chronic hydration the concentration of the adsorbed constituents in solution in the aqueous phase of the plasma is altered.* The result of this phenomenon is that sugar, for example, may be found in the urine without its percentage in the blood reaching the so-called “threshold concentration.”

After anæsthesia, a clinical manifestation of hydration, an uneven cyclical dehydration, may result in a ketonuria, glycosuria, etc., without a corresponding ketonæmia and hyper-glycæmia. According to the relationship existing between the protein particles undergoing the cyclical change and the protein particles remaining hydrated, there may occur (taking the carbohydrate planet as an illustration again) a hyper-glycæmia with no glycosuria and a glycosuria with a normal blood-sugar or hypo-glycæmia. In all three instances the protein particles remaining in the hydrated state may be giving rise to clinical signs and symptoms which fail to disappear until they are broken up by nature or by the administration of dehydrators, of which the favourite is glucose. In other words, post-operative shock may occur with the percentage of the blood-sugar raised above normal or lowered, and whichever happens to occur, glucose is indicated. In hydration the number of the protein particles as viewed with a dark-ground condenser is reduced, and consequently the coagulation time of the plasma is lengthened. Hydration may be brought about *de novo*, not necessarily as a sequence of dehydration, and any invader can achieve this provided it is able to lower the surface tension of the protein particles sufficiently. Proofs for the various statements made in this introduction are given in the earlier parts of this work.

To sum up : The protein particles in the plasma in disease undergo either dehydration or hydration. The dehydration may be pure, as in streptococcal septicæmia, for example, but more often there occurs with it a varying degree of hydration. As every invader causes dehydration when it first attacks, it comes to pass that dehydration is the prevailing abnormal chemico-physical change in the acute stage of disease and hydration in the chronic stage. Hydrated protein particles undergo three cyclical changes : (1) dispersion, represented by immunity ; (2) gelation, which causes venous thrombosis ; (3) uneven dehydration, giving rise to what has been called “acidosis.” In

* As stated above, the aqueous phase becomes more and more like pure water.

dehydration the urine contains in solution an excess of the adsorbed constituents liberated from the protein particles in the plasma. In hydration the urine contains less of these constituents than normal in true solution, but more in colloid form. It is due to the breaking up of these colloid complexes that the addition of fuming nitric acid gives rise to a nuance of colours and of the hydrochloride of di-methyl-*para*-amino-benzaldehyde to a range of colours spreading from pale pink to purple. When the hydrated protein particles undergo their cyclical changes sugar may appear in the urine without the percentage of the sugar in the blood being raised. Naturally what gets into the urine is regulated in part by the changes occurring in the kidneys, but whatever may be their nature these are secondary to the blood changes. Below are some blood-pictures illustrating the abnormal chemico-physical changes the dynamic resistance of the blood undergoes.

Moderate Dehydration

The blood is dark, the plasma is pale, and the clotting time is shortened.

Suspension stability of the red blood-corpuscles	= 2.0 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.168 grm.
Percentage of the blood-urea	= 25 mgrm.
Ultra-microscopic picture	= Fair number of particles moving, with some giant particles and giant-particled clumps. There were more particles precipitated, and these were mainly giant particles and giant-particled clumps.

This specimen of blood was taken from a patient suffering from influenza with a temperature of 105° F.

Severe Dehydration

The blood is dark, the plasma is pale, and the clotting time is considerably shortened.

Suspension stability of the red blood-corpuscles	= 5.3 c.c.
Refractive index of the serum	= 1.3457.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 120 mgrm.
Ultra-microscopic picture	= Myriads of tiny gray particles. A few giant particles moving and some giant-particled clumps and agglutinations precipitated. There was some sheet-like precipitation and evidence of secondary coagulation.

This specimen of blood was taken from a patient suffering from streptococcal septicæmia. When serum contains an enormous number of small particles it may undergo coagulation again while being examined with a dark-ground condenser, presumably due to an evaporation of part of the water. It is possible also that the bright light and heat from the arc lamp help in the phenomenon. The occurrence of secondary coagulation and the fact that citrated plasma clots in the presence of certain conductors and in the absence of blood-platelets shows that clotting is not of ferment action and that blood-platelets are not essential. Blood-platelets are probably nothing more nor less than agglutinated protein particles.

Acute Concomitant Dehydration and Hydration

The colour of the blood is either dark or unaltered, that of the plasma may be deep yellow and the clotting time is shortened.

Suspension stability of the red blood-corpuscles	= 3·0 c.c.
Refractive index of the serum	= 1·3505.
Percentage of the blood-sugar	= 0·143 grm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture	= Few particles moving and most of those were giant particles, with a halo around. There were many more particles precipitated <i>en masse</i> as separate particles, giant particles, ringed particles and giant-particled clumps. The Brownian movements of the particles were very sluggish.

This specimen of blood was taken from a patient suffering from early generalised syphilis.

Chronic Concomitant Dehydration and Hydration

The colour of the blood is unaltered, but that of the plasma is usually deepened and the clotting time tends to be lengthened.

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3488.
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood-urea	= 68 mgrm.
Ultra-microscopic picture	= Normal number of particles moving with many clumps. There were a fair number of particles precipitated, with one or two agglutina- tions.

This specimen of blood was taken from a patient, a typical example of familial chronic intestinal intoxication, who sought advice for chronic indigestion.

Hydration

The blood may be brighter red than normal, the normal colour of the plasma is deepened and the clotting time is lengthened.*

Suspension stability of the red blood-corpuscles	= 0.01 c.c.
Refractive index of the serum	= 1.3520.
Percentage of the blood-sugar	= 0.068 grm.
Percentage of the blood-urea	= 8 mgrm.
Ultra-microscopic picture	= Very few particles moving or precipitated and those visible were for the most part giant particles, ringed particles and clumps. All the particles were very refractile.

This specimen of blood was taken from a patient suffering from *Acne vulgaris* and neurasthenia.

Gelation

The blood is dark red, the plasma is usually pale and the clotting time is shortened.

Suspension stability of the red blood-corpuscles	= 5.8 c.c.
Refractive index of the serum	= 1.3489.
Percentage of the blood-sugar	= 0.137 grm.
Percentage of the blood-urea	= 30 mgrm.
Ultra-microscopic picture	= Myriads of particles moving. The Brownian movements became sluggish and precipitation followed rapidly.

This specimen of blood was taken from a patient suffering from widespread post-operative venous thrombosis.

Glycosuria *sine* Hyper-glycaemia

The blood is as a rule dark red, the colour of the plasma is unaltered and the clotting time remains normal.

Suspension stability of the red blood-corpuscles	= 2.1 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 28 mgrm.

* In these cases the red blood-corpuscles do not form a conical clot, but sink as a whole.

Ultra-microscopic picture = Very many particles
moving with a few clumps, and all were very refractile.
There were a few giant-particled clumps and agglutinations
precipitated.

This specimen of blood was taken from a patient who on the third day following an operation was found to have sugar in the urine.

CHAPTER I

MAL-CO-ORDINATION AND DISEASE

Introduction

IN the epilogue to the second part of "The Nature of Disease," the author announced his intention to correlate with medicine Mr. F. M. Alexander's work on the conscious control of the individual. The announcement was made because it became apparent to the author after meeting Mr. Alexander and watching his technique, that the wrong use of the body plays an important rôle in disease. Now that the time has come to fulfil the promise, the author is less sanguine of success. This is partly because Alexander's view is possibly even more fundamental than the author's view that there is only one disease, partly because the written word can neither convey the whole idea nor satisfactorily describe the technique, and partly because to link any subject with medicine it is necessary to commit the basic error of practising differentiation instead of correlation. Put succinctly, Alexander's view is that in a rapidly changing environment man's instinctive guidance is likely to be wrong, and therefore conscious control is needed, his response to stimulus generally being unreliable. When the response first became unreliable, how long it has continued to be unreliable, and whether the unreliability has progressed throughout each succeeding generation need not be dealt with for the moment. At this juncture it is only necessary to realise that if it is a fact that the response is unreliable, it means that there is not an action performed by man to-day which may not be mis-directed. This is sufficiently fundamental in itself, but when to this is added the statement that the response to the stimulus or stimuli is one of the body as a whole and not of a part, the reader will appreciate the author's difficulty in attempting to link up the work with medicine. In place of the word "body" Alexander substitutes the term "psycho-physical mechanism." By this Alexander wishes to imply that there is no separation of the mental from the physical activity, and that any expression of activity, be it correct or incorrect, is one of the whole being and not of the brain, lungs, heart, liver, kidneys, endocrine glands, muscles, skin, etc., as separate therefrom. In view of these difficulties the author proposes in this chapter to give an outline of Mr. F. M. Alexander's work, and in the next chapter to link it up with medicine as far as possible.

Although it may not have been brought to the reader's notice, through the innate egotism which characterises man, that man has been found wanting in the forward march of civilisation, the idea is not a novel one. The reason why special attention is paid to Alexander's work, which emphasises the fact once more, is because, in contra-distinction to his predecessors, he has evolved a technique capable both of preventing and correcting the mis-directed activities. Despite the vaunted optimism widely expressed that civilisation as it advances necessarily progresses, there is not a single problem facing mankind to-day with which he is able to grapple. Instead conferences, committees, councils, etc., are formed which only make confusion worse confounded. What could prove this better than the recent war through which the world has just passed, and the widely divergent, but equally dogmatic, opinions held regarding religion and medicine? Both religion and medicine have focused man's attention on parts to the neglect of the whole; the former on the soul, about which nothing is really known, and the latter on various organs in turn, according to the fashion existing at the time.

Medicine to-day is more or less limited to the internal organs, and it usually carries the word "internal" as a prefix; moreover, the subject excites little interest. The muscles have been given over to the physical culturist, who only succeeds in aggravating the mal-co-ordination. The ductless glands are now in the care of the endocrinologist, who holds that the secretions manufactured, and about which he knows next to nothing, are responsible for the conduct and personality of the individual. The mind has been wrested from the body by the psychologist, who traces all ills to repressions which he thinks he discovers by psycho-analysis and gets rid of by psycho-therapy.

The latest advent to the popular vernacular, to add still more confusion, is the vitamin, the unknown chemico-physical body existing in infinitesimal amounts but nevertheless held to be responsible for keeping the whole mechanism in proper action.

Even these few remarks show that man has developed a mania for differentiation, and the results prove that this is the outcome of mis-directed activity. No good can ever result from being unable to see the wood for the trees, and it is certain that the adoption of such a policy can lead to one end only—destruction, a falling to pieces of the whole mechanism.

As mentioned above, there are many who realise the evil of differentiation, but few who can see how it is possible to correlate and co-ordinate the real advances which have attended the march of civilisation. From the amount of unhappiness extant it is perfectly obvious that the activity regulating human

conduct and behaviour has been unreliable and mis-directed for many generations. This being the case, it is becoming ever increasingly difficult to render activity co-ordinated. Indeed, there is even the possibility that rational thinking, unprejudiced action and, in short, co-ordinated activity are unattainable. It is easier to point out faults than to remedy them, and although destructive criticism is often a tonic, it can never be more than palliative, and to remedy the whole construction is the only solution. Alexander's two books, "Man's Supreme Inheritance" ¹ and "Constructive Conscious Control of the Individual," ² differ from all others in that they indicate not only the tonic but the actual remedial and preventive measures. Alexander has been working for many years evolving a technique for the control of human conduct on a conscious basis, and although the technique, when put into practice, is able to remedy defects resulting from wrong use, its main aim is to prevent misuse. As Arthur J. Busch puts it in "The Brooklyn Citizen," ³ "Alexander perceived that in the evolutionary process the instincts which once were capable of guiding man in an efficient functioning of his whole organism have become so debauched by his civilising environment as to have been rendered unreliable. Where once a man, like an animal, could safely rely upon these instincts to undertake the relatively simple exigencies of his existence, he can no longer do so with safety and efficiency. Civilisation has made man rely less and less upon physical labour to maintain his subsistence, and this has rendered instincts once all-important no longer useful." It has resulted in the misuse of the psycho-physical mechanism. As the passage from the instinctive guidance to the conscious control has resulted in mal-co-ordination, it stands to reason that the development of a faulty carriage feels right to the individual. This has naturally entailed a lack of knowledge concerning the correct sensory experience associated with normal carriage. Taken still further, this means that man in accomplishing his ends does so with a sensory guidance which may be wholly unreliable. The result is a blundering through with no certainty of success, which makes for lack of confidence, worry, nervousness, despondency, etc. Therefore, it is not surprising to find a steady rise in the incidence of melancholia and neurasthenia, which only too often end in mania and insanity.

It is this restoration of the sensory apparatus which Alexander's technique is able to accomplish, and the basis of the technique is the complete interdependence between the mind and the body, without which there can be no co-ordination of the whole organism named "man." Although the technique brings the requisite sensory material under definite and usable control, the

written word cannot satisfactorily detail the technique, and the reader must see it in action before being able to grasp it.

The principles of the psycho-physical control must not be considered to be in any sense concerned with therapeutics. Although primarily preventive they are also remedial, and this introduction cannot be closed better than by quoting Dewey,² who writes the introduction to "Constructive Conscious Control of the Individual": "The method is not one of remedy: it is one of constructive education. Its proper field of application is with the young, with the growing generation, in order that they may come to possess as early as possible in life a correct standard of sensory appreciation and self-judgment. When once a reasonably adequate part of a new generation has become properly co-ordinated, we shall have assurance for the first time that men and women in the future will be able to stand on their own feet, equipped with satisfactory psycho-physical equilibrium to meet with readiness, confidence and happiness, instead of with fear, confusion and discontent, the buffetings and contingencies of their surroundings." After studying Alexander's work for himself, the reader should peruse Professor John Dewey's fascinating little book, "Human Nature and Conduct."⁶

In describing Alexander's work in more detail, the reader should realise that the author can write only what he himself has gained from actual experience of the work. Although the following may fail to do justice to Alexander's work, the author after many attempts has come to the conclusion that it is the easiest way in which the work can be conveyed to one who has had no practical experience.

First, simple examples of man's mal-co-ordination are afforded, with a brief discussion dealing with the main cause; next come a few remarks concerning the technique devised to render man co-ordinated, in which the responsibility of mal-co-ordination for disease is mentioned. Finally, a brief outline is given showing how the adoption of the end-gaining principle, the main source of mal-co-ordination, has adversely affected the evolution of medicine as a science.

Simple Examples of Mal-co-ordination

One of the simplest examples of mal-co-ordination encountered every day by medical men is the passing on of a prescription to a mere acquaintance by one who has the idea that it helped a friend. There is the example mentioned by Alexander of Carlyle giving his friend, Henry Taylor, Mrs. Carlyle's medicine, without consideration of the friend's trouble or even a knowledge of the con-

tents of the bottle. If the response to a sudden stimulus could be so unreliable in a person with Carlyle's attainments, it is not surprising to find mankind searching for "cures" and physicians labelling them as specific. It is also not to be wondered at that clinics are established at an enormous cost to treat symptoms, and it probably has not occurred to one of those associated with the latest clinics for the treatment of rheumatism that their activities are mis-directed. Be this as it may, it is perfectly certain that not one of the patients will be instructed in the right use of the psycho-physical mechanism, the wrong use of which is such an important factor in the ever-increasing incidence of rheumatism. Another example of "mind-wandering" is the almost complete inability of the average individual to understand aright what is new to him. It is necessary to have the stimulus to understand first, and it is mainly the want of this which results in the good being classed as incomprehensible or rubbish.

Even when the stimulus is present, understanding does not come, because the attempt is made to adapt the new to the old, instead of discarding the old and enquiring into the means whereby the new was reached. No better illustration can be given than the response to the lectures delivered on "The Nature of Disease." The question is almost invariably the same: What would you do in such and such a case? This is a typical example of visualising the end and neglecting the means.

The reader can test the ubiquity of mis-directed activity by showing the following sentence to his friends: "The federal fuses are the ultimate result of scientific investigation combined with the fruits of long experience," and asking how many "f's" there are, when the answer is almost invariably four instead of six, due to the missing out of the letters in the two words "of". The author tried this on fifty consecutive patients and not one gave the correct answer. The most mal-co-ordinated did not even read the sentence, and merely guessed.

To test the wrong use of the psycho-physical mechanism, laying emphasis on the word "physical," the reader should ask his friend to lean the head forward while keeping the shoulders still. Should the head come forward, the shoulders are almost bound to follow. If the shoulders are fixed, the head will go back before going forward. Indeed, in practically every movement executed by the individual in response to a stimulus, the first is a retraction of the head, because the muscles in the posterior part of the neck are in a constant state of tension. Note the drooping of the head in cases of Parkinsonism, the result of fatigue occasioned by years of unnoticed muscle tension.

From the manner in which the body adjusts itself to this undue muscle tension, it is not difficult to see how Sherrington³ and Magnus⁴ came to recognise that the mechanism of the main control of the whole body's co-ordination lies in the head and neck. If the pupil who habitually throws his head back when he should put it forward is asked to stand up, he will be found, when he has taken up his position, to have the chest fixed, the back arched, and the abdomen protruded.

When the examiner's hands are passed over the pupil the latter will be found to be rigid from head to foot, that is to say, in a general condition of exaggerated muscle tension. On further examination the neck will be found to be shortened and taut—shortened because the shoulders are raised and taut owing to the contraction of the neck muscles. The observer will be able to see at a glance that this cervical mal-co-ordination must necessarily fix the larynx and interfere with the blood-supply to the brain. An examination of the chest will show that the ribs are fixed, a mal-co-ordination which obviously must interfere with the proper functioning of the thoracic viscera. Coming to the abdomen the anterior abdominal wall will be found to be hard and protruded at its base, a mal-co-ordination which by itself can only lead to stasis and, associated with the mal-co-ordinations described above, to a dropping of the viscera. The fixing of the chest renders movements of the arms ungainly, while the sinking of the trunk into the pelvis puts a limitation on the movements of the legs, and the general wrong position taken up tends to the formation of flat-foot.

Three lessons are to be learned from this simple examination: (1) that the main control governing mal-co-ordination lies in the head and neck; (2) that this single mal-co-ordination causes the wrong functioning of the body as a whole; (3) that (1) and (2) indicate over-excitation or a lack of inhibition. The significance of these three lessons will be appreciated later.

A Cause of Mal-co-ordination

The simplest method of observing a cause, possibly the main cause, of mal-co-ordination, wrong functioning, undue muscle tension, over-excitation, or lack of inhibition is to study the response of a mal-co-ordinated seated person to the order given to stand. A mal-co-ordinated person answers to the order to stand *by an expression of the will to stand*. In other words, so long as no gross lesion is present which makes standing impossible, the pupil assumes that correct standing or standing to best advantage cannot fail to be accom-

plished. The *means whereby* he is able to stand correctly are taken for granted, the *means whereby* correct standing is accomplished do not enter into his realm of established habit—in short, *the end, or the goal, is the sole point considered*. From this it follows that a man who habitually stands properly is the only one who can stand properly, all others must stand improperly. In the former case a will or wish is unnecessary, and in the latter useless. In the latter case it is useless because a man who stands improperly does so by habit, with the result that each and every time he wills or wishes to stand he will execute the action wrongly. Furthermore, no rectification of the bad posture can be accomplished by will or wish, and such a man can stand properly only so long as he changes the objective conditions. The objective conditions can be changed only so long as an intelligent control of the *means whereby* correct standing is accomplished is employed. The proof of this point lies in the fact that if a man who is asked to stand stands badly and the fact is pointed out to him, although he will immediately stand differently, it is only a *different kind of badly* ! Moreover, the different kind of badly will be persisted in until the individual realises a return of the feeling that he has hitherto associated with his ordinary habit of standing. Since his habit of standing is the wrong habit he immediately relapses into his original position of assuming to be right that which has always been wrong. Further, since practically every individual is mal-co-ordinated it is not to be wondered at that mal-co-ordination as a *fons et origo mali* has been missed—a point which proves the truth of the adage, that it is unreasonable to expect to discern the discrepancies in another until one has fully found out those present in oneself. Putting the matter succinctly, *the main cause of mal-co-ordination is the belief that an end can be reached by neglecting the intelligent control of the means*. How our progenitors came to neglect the intelligent control of the means and became “end-gainers,” and the fact that mal-co-ordination thereby became hereditary, is probably due, as Alexander points out in his books, to the changes in man’s environment over-balancing or out-racing the development of his “mental” activity. Man’s reasoning powers in the past were, as now, probably unable to cope with the frequent occurrence of the many new and untried situations which demanded an ever rapidly increasing development of his “mental” activity.

The lesson to be learnt from this paragraph is that man’s response to stimulus has become unreliable, and that this has been in the main due to over-excitation or lack of inhibition.

Technique to Correct Mal-co-ordination

Since mal-co-ordination is the result of precipitous and excessive action, the first and main point to be borne continuously in mind is *the necessity for inhibition*, because muscular relaxation cannot be brought about till the desire to execute a muscular action is inhibited. Naturally no manipulations, whatever they may be or however employed, to bring about the necessary co-ordinations can achieve anything until the individual is completely relaxed, or, rather, in a state of perfect reciprocal muscle tension, since complete relaxation is only possible in death. When the necessary co-ordinations have been made the patient usually exclaims that his new stance feels awkward; indeed, the degree of awkwardness is generally in direct ratio to the mal-co-ordination. Having expressed the sensation of awkwardness, the pupil should be shown himself in a glass and a comparison should be made with his habitual, or what has always been his wrong stance. Every individual can help himself by watching the movements of animals. A cat, in jumping from the floor on to a table, usually alights just where it is necessary, with no force, and with no more expenditure of energy than is actually required to execute the act. Before jumping the muscles are relaxed and the neck is out-stretched. No act illustrates better the forward projection of the head and the out-stretching of the neck than that of a swan on the water preparatory to flying. Neither the cat nor the swan wills or consciously wishes to co-ordinate the head and neck prior to executing the desired action, and it is in this fact that a human being fails in trying to emulate the smooth and graceful movements of the lower animals—he fails even when he knows that projection is the right movement because he tries to relax his neck and to put his head forward and up. This brings the reader back once more to the salient point—*inhibition*; it shows further that there lies in the head and neck the mechanism of the main control, a conclusion to which both Sherrington³ and Magnus⁴ arrived from their experimental work on the reflexes in animals. No technique devised to correct mal-co-ordination can succeed *until the neck is relaxed and the head is projected forward and up*. Once this co-ordination is perfected the muscles of the back become relaxed, the spine is lengthened, free movements of the chest are rendered possible and the manipulator is able to make the abdominal viscera fall into place. The premier co-ordination results also in the arms and legs becoming flaccid, which renders it possible for the manipulator to raise the individual and correct *Pes planus* when this deformity is present. As there is not a single physical exercise, drill, etc., which is based on inhibition or takes into account the main control, or premier co-ordination,

there is only one logical conclusion which it is possible to arrive at—viz., that they are one and all actually harmful. If proof be needed that physical exercises and drill aggravate an already existing mal-co-ordination, it is only necessary to call the reader's attention to the mental and physical disabilities of men who have left the Services, to the high incidence of physical defects in those still in the Services, to the ever-increasing incidence of disease in schools, and to the very high percentage of flat-foot in the boys and youths of to-day.

How Mal-co-ordination can Cause Disease

Mal-co-ordination is the result of the expression of a will or wish. A will or a wish cannot be translated into action without an output of energy. Mal-co-ordination implies mis-directed activity, and as a rule the result of an excessive expenditure of energy is shown by undue muscle tension being the most obvious manifestation. As muscular contraction is the outcome of a discharge of energy from the central nervous system, it follows that when there is over muscular contraction there is an excessive outpouring of this energy. If this is the case when the mis-directed activity is mainly physical, then it must be similarly the case when the mis-directed activity is mainly psychic. In order to make the subject-matter clear, it is necessary to separate the physical from the psychic activity, and the words "corporal" and "mental" are sometimes used in their place.

No cells can liberate excessive energy indefinitely, and as mis-directed activity usually implies excessive expenditure of energy, it follows that mal-co-ordination must result sooner or later in hypo-activity consequent upon cell degeneration.

Before mentioning a few of the manifestations of disease resulting from a hyper-activity of the psycho-physical mechanism under the headings of psychic and physical respectively, it is necessary to refer to energy and activity—synonymous terms—in more detail.

Through man's innate egotism, perhaps the greatest, and probably the earliest, of his mis-directed mental activities, he has attached a something to his cerebral activity which he has denied to all more lowly evolved forms of life. He has coined such words as "supernatural" and "metaphysical," which have no meaning; he has invented the soul, which has caused infinitely more misery, and has evolved more discussion, than any material invention, and he has sub-divided the psychic activity into intelligence, mind, consciousness, sub-consciousness, conscience, etc., all of which have led him into cul-de-sacs from which he can find no escape. For the sake of description, it is immaterial

whether the activity of the cerebral cortex is referred to as "cerebral," "mental," "psychic" or "neuronic," because there is nothing peculiar in the activity, and the activity does not and cannot differ fundamentally from the activity of the rest of the brain or from any other cellular activity. Although the development of the cerebral hemispheres has enabled man to reach the highest rung of the evolutionary ladder, it does not follow as yet that they should be placed upon a higher plane, in the fullest sense of the term, than were the lungs, liver, etc., when they became more highly developed structures. The cerebral cortex is only an outgrowth from the brain, as were the lungs, liver, etc., from the intestinal tract. Not only does the activity of the cerebral cortex not differ fundamentally from the activity of the brain-stem, but also it is the same activity as that directing falling bodies to move in straight lines, and sodium and chlorine to form sodium chloride. Animals have nerve cells like human beings, hence there can be no difference in the nature of the energy liberated and no starting-point for such conditions as are understood by such words as "mind," "soul," "consciousness," or "conscience"—all words the deletion of which would be to man's advantage.

It is not a difference of energy which separates the neuronic activity in man and animals, but solely a difference in the manner in which the energy functions. The different ways in which the energy functions are well illustrated in tracing their growth from plants to man, but it is illogical to conclude that their high functioning in man is extraordinary or still less that it must always progress to man's advantage. On the contrary, the more complicated a function becomes the more its instability increases, and there is certainly ample evidence to-day of the instability of man's nerve mechanism.

In plants and the lowest animals the organic or body mechanism has a greater control than the nerve mechanism, while in man the position is reversed—with what result? Each piece of a plant cut into pieces is able to grow into a new plant, a worm can grow a new end when one has been severed, a starfish or a crab acquires a new limb when one has been lost, but man cannot replace any organ. Midway between the lowest animals and man the body and nerve mechanisms work in perfect harmony in their customary environment, and the word "instinct" is applied to their activity. In man on the other hand the nerve mechanism is controlling the body mechanism, and as the activity resulting from the former is being mis-directed it is not surprising that the activity resulting from the latter is seriously interfered with or that man is more readily affected by disease than animals. It is obvious that the more mis-directed the activity of man's nerve mechanism

becomes the more generally will he become diseased, and it is just possible that disease will in the end cause man's disappearance.

There does not seem, from the above, much justification for assuming a design in nature or purposeful existence for man, and still less for an immortality which man regards as his natural heritage. If the fundamental beliefs of man are the products of mis-directed psychic activity, it is not surprising that there are spiritualists and individuals who become labelled with "melancholia," "neurasthenia," "mania" and "insanity." Leaving the cerebral cortex and passing through the tegmentum, the seat of the pyramidal reflex circuit is brought into view. It is to the hyper-activity of this area that undue muscle tension is in no small measure due. This explains why the end result of mal-co-ordination in the clinical expression of hypo-activity is so frequently what is known as "Parkinson's disease."

Passing still further down the brain, the centre of the vagus is reached and hyper-activity of the vegetative nervous system is one of the most potent factors in the causation of chronic intestinal intoxication, which in turn causes or aggravates existing mal-co-ordination.

The undue muscle tension, the most obvious manifestation of mal-co-ordination, causes serious symptoms of disease to follow in its wake, and this is why in every instance of disease it is necessary to render the patient co-ordinated if the best results are to be obtained. Throwing the head back and contracting the neck lead to venous congestion, a condition which deprives the brain of the supply of arterial blood it needs. Whenever there is venous congestion there is a local collection of hydrated protein particles. As hydrated protein particles are more particularly concerned with their own metabolism and carry it out at the expense of the cells around, they develop certain of the characteristics of parasites. One of the effects of this acquired parasitism is to cause dehydration of the protein particles constituting the cytoplasm of the cells in their neighbourhood. The first effect of dehydration of the cells concerned is hyper-activity, consequently the mis-directed activity already present becomes still more mis-directed. In addition to accentuating the mis-directed activity of the psychic mechanism, mal-co-ordination may cause and aggravate chronic nasal catarrh—the commonest symptom of inherited and congenital disease—with resulting middle-ear complications, hay-fever, pharyngitis and laryngitis. This being the case, how glaringly futile it is to treat these conditions by local applications alone, when all that may be required is to correct the wrong functioning. The effect of mal-co-ordination upon the chest, leading as it does to a lowered respiratory response, is to

render the lungs less resistant to the activity of micro-organisms and tends to stagnation, the primary cause of asthma. The heart is affected likewise, and the functions of both these organs are altered still further by the hyper- or hypo-activity of the vegetative nervous system. The main evil effect of mal-co-ordination upon the abdominal viscera is what is referred to in this volume as a chronic intestinal intoxication. The reason why a chronic intestinal intoxication looms so large as a cause of disease is because the trouble begun by the mal-co-ordination is continued, and often in an ever-increasing degree, by wrong food and insufficient elimination. Various structural defects are embraced in the term "chronic intestinal intoxication," such as dropping of the viscera, a lengthening of the duodenum and colon, diverticulitis, ulcer formation, with polypi and malignancy. Chronic intestinal intoxication being caused in the way it is and being continually aggravated by wrong acting, the reader must see how useless it is to order patients abdominal supports. A support can only aggravate the trouble, and the abdominal wall reacts to the support as do a certain class of able-bodied men to the dole. The shortening of the spine presses the vertebræ together and narrows the inter-vertebral foramina, giving rise to sciatica. The inter-vertebral foramina most affected are those between the fourth and fifth lumbar and first sacral vertebræ. The narrowing is still further accentuated by the facets of the articulations growing into different planes, as pointed out by Putti.⁵ The biggest root of the sacral plexus comes through the smallest foramen, *i.e.* between the fifth lumbar and the first sacral vertebræ, another reason for sciatica being so common. The alteration in the position of the facets of the articulations leads to the formation of osteo-arthritic changes, hence it is not surprising to find so many cases of sacro-iliac disease and of osteo-arthritis of the hip-joints amongst the grossly mal-co-ordinated. No condition shows so much as sciatica how a mal-co-ordination may be aggravated by one of its own results. Most patients with sciatica develop, through muscular over-contraction, a forward and lateral curvature of the spine, which may lead to changes occurring in the vertebral column, unless the mal-co-ordination is corrected in time. Patients with rheumatism tend to become more mal-co-ordinated than ever. The additional mal-co-ordination leads to the continuance of the pain caused by the sciatica and the rheumatism in the first instance long after the actual neuritis and arthritis have vanished. Both the patient and the physician are apt to mistake the persistence of the pain for the continued activity of the inflammation and, if this mistake is made, the mal-co-ordination which is the real cause is missed and the patient is harmed by the further treatment prescribed.

The temporary success achieved by the osteopath is due to his manipulations to lengthen the whole of the vertebral column, and there is no gainsaying the fact that an improvement in the general condition is experienced thereafter. The amelioration is caused by the venous congestion giving place to an improvement in the arterial circulation, which means an increased conduction of electrons to the protein particles, the essence of health and well-being. The success is temporary, and cannot become permanent until the patient learns how to keep himself continuously co-ordinated, and this the osteopath cannot and does not teach him, since he is himself unaware of its importance and is obviously also an "end-gainer."

As flat-foot is a result of general mal-co-ordination it can be appreciated how senseless must be exercises and supports, and no condition in medicine illustrates better than *Pes planus* the evils which follow the adoption of the end-gaining principle. Last, but not least, must be borne in mind the effect of mal-co-ordination upon the protein particles, in the plasma, which form the host's main pillar of protection against any invasion, both from without and from within. The venous congestion resulting from mal-co-ordination causes first dehydration of the protein particles, and later hydration owing to the adsorption by the protein particles in the colloid state of the parts of those particles being driven from the colloid state into the state of true solution. The protein particles in the plasma bathe every cell in the body, indeed the activity of every cell is influenced by the chemico-physical state in which the protein particles in the plasma happen to be. This is why the point has always been stressed by the author that there is only one disease and that this results from the worsening of the host's main protective substance by an invader—using the word "invader" in its broadest sense. There is not a sign or symptom produced by mal-co-ordination which cannot be produced by the protein particles in the plasma subjected to abnormal chemico-physical changes. Hence it comes about that a vicious circle is formed, and as it came into operation generations back, it is useless to argue whether it was mal-co-ordination or abnormal protein particles which started the ball rolling. Both produce disease, one aggravates the other, and both require adjusting before health is fully restored. The protein particles in the plasma are rendered abnormal in the present generation most frequently by intoxicants which reach the blood-stream, presumably *via* the lymphatics from the large intestine. Chronic intestinal intoxication is playing a larger part than ever before in the causation of disease to-day, and it would seem destined to play an even greater *rôle* in the future. Indeed, civilisation might easily be brought

to nought by a chronic intestinal intoxication, and in the author's opinion it is thus that civilisation may meet its end. A chronic intestinal intoxication can cause all the signs and symptoms resulting from mal-co-ordination and even produce mal-co-ordination itself. Therefore, in the treatment of disease, the adoption of the principle of intelligent control of the *means whereby* as opposed to the principle of *end-gaining*, which aims at merely palliating symptoms, three points and three points only require consideration: (1) ridding the patient of his chronic intestinal intoxication; (2) correcting the abnormal chemico-physical changes to which the protein particles in the plasma have been subjected; (3) correcting the mal-co-ordination. So long have these three factors in the causation of disease been extant that all can be transmitted by both parents to their offspring. Consequently, if the incidence of disease is ever to be checked, each and every individual will have to be particular, not only in the choice of his mother and father, but also of his great-great-grandparents!

As there are three statements made in the above which go far beyond what Alexander writes in his books, and as they are no *ipse dixit* statements, the author deems it advisable to say a few more words about them. (1) "There is not a sign or symptom produced by mal-co-ordination which cannot be produced by the protein particles in the plasma subjected to abnormal chemico-physical changes." The outcome of protein particles in the plasma subjected to abnormal chemico-physical changes is disease. Disease in animals perfectly co-ordinated rapidly causes them to become mal-co-ordinated and in man it aggravates an already present mis-directed activity. It is difficult to judge aright the psychic activity in animals and almost impossible to discern when it becomes mis-directed; hence, main attention has to be directed to their physical activity. The intravenous injection of toxic drugs into animals which act first upon the protein particles in the plasma, may cause gross mal-co-ordination, and here again the first mis-directed activity is a retraction of the head and neck. This is evidenced most readily when drugs which produce sudden hydration such as histamine, coniine, arecoline, cardiazol, etc., are injected intra-venously. Altering the normal food of an animal, which rapidly causes changes in the blood, may render it mal-co-ordinated and, curiously enough, if manifestations of disease are caused, sufficiently pronounced to be observed, the most common is rheumatism, and the most constant and perhaps the first pathological change is aortitis. Feeding an animal on wrong food readily causes a chronic intestinal intoxication and alters the bacterial flora of the intestinal contents, potent factors in the ætiology of both disease and

mal-co-ordination. To the observant eye it is readily noticeable in man that abnormal changes affecting the protein particles in the plasma bring about and aggravate an already existing mal-co-ordination. This may be emphasised to a marked degree when a patient first goes under an anæsthetic. The production of anæsthesia is such an everyday occurrence that sight has been lost of the fact that all anæsthetic preparations are toxic drugs and act first upon the protein particles in the plasma. Conversely, correcting the mal-co-ordination may cause the protein particles in the plasma previously abnormal to become normal. (2) "A vicious circle is formed, which came into operation generations back." This statement suggests that mal-co-ordination may be inherited and congenital. If this be true, the possibility arises of man's response to stimuli becoming so faulty in the course of time as to bring about his downfall. There are plenty of signs of man's devolution having been in progress for some time, and considering the manner in which he is becoming mechanised, growing ever more and more artificial, more steeped in subterfuge and bent on destroying nature, perhaps the sooner the end comes the better. The author is firmly of the opinion that disease is both inherited and congenital, and this opinion is supported by the cases reported below. As mal-co-ordination is only a part of the vicious circle, it is reasonable to suppose that if the whole is inherited, mis-directed activity is inherited as well.

Although this subject is dealt with in the next chapter it is of such importance that the author proposes to bring forward a point here which has not been stressed before, and which he ventures to think proves that mal-co-ordination is not solely an after-birth manifestation. Mal-co-ordination came into being when instinctive guidance became replaced by conscious control, and it is the result of a faulty response to stimuli of the latter, or to be more specific, of the neurones in the cerebral cortex. For the sake of description the brain can be divided into two parts, the cerebral hemispheres and the brain-stem. Excluding lesions caused by trauma and micro-organisms it may be said, likewise for the sake of description, that lesions of these two parts are either innate or secondary to the abnormal chemico-physical changes the protein particles in the plasma undergo. Innate lesions are almost invariably lesions of the cortex, while those secondary to the changed protein particles occur for the most part in the brain-stem, and particularly in the lowest part of the brain-stem, namely, in the regions of the centres of the vagus. In other words, there are no lesions in the brain-stem comparable to such inborn lesions attacking the cerebral hemispheres as amaurotic family

idiocy, spastic diplegia, oto-sclerosis, etc. Mal-co-ordination in its worst form is to be encountered in patients the victims of these and other congenital defects of the cerebral hemispheres, and it is evident as soon as the child comes into the world. The mal-co-ordination is much more pronounced than in those cases where it makes its appearance after birth, or occurs as a result of a hyper-activity of the neurones in the brain-stem caused by the precipitation of hydrated protein particles either before birth or after in the vessels of the area involved. It comes to pass that the worst form of mal-co-ordination is met with in inborn lesions of the latest, most highly developed and most vulnerable portion of the psycho-physical mechanism, and the mal-co-ordination is evident before environmental stimuli begin to trouble the conscious control. These inborn lesions are both inherited and congenital, and can be traced either to the paternal or maternal side of the family, or to both sides. As there are plenty of milder cases where the defect is not sufficiently pronounced to be called a lesion, and where the mal-co-ordination is gross it would appear that the activity of the nerve mechanism may be inherently and congenitally mis-directed. It is probable that the centres of the vagus are the oldest parts of the brain, and represent the œsophageal ganglia which make their first appearance in the rotifers.

(3) "A chronic intestinal intoxication can cause all the signs and symptoms resulting from mal-co-ordination, and even produce mal-co-ordination itself." A chronic intestinal intoxication is caused in two ways, either by a stimulation of the centres of the vagus or by a stimulation of Auerbach's plexus. Hyper-activity of the vagus may occur either before or after birth, and in both instances the hyper-activity is most usually occasioned by the precipitation of hydrated protein particles in the vessels in the neighbourhood of the third and fourth ventricles. Protein particles are most readily hydrated before birth by syphilis. The author brought forward evidence in the first part of this work to the effect that a positive Wassermann reaction is in a large measure due to the hydration the protein particles in the plasma undergo at the hands of the *Leucocytozoonsyphilidis*. In practically all cases of congenital syphilis one or more of the signs and symptoms of vagotonia are pronounced and mal-co-ordination is never absent. Stimulation of the centres of the vagus after birth invariably causes or accentuates an already existing mal-co-ordination, as evidenced in cases of infantile convulsions, particularly when *Laryngismus stridulus* is a symptom, epilepsy, migraine, asthma, etc. Stimulation of Auerbach's plexus to cause achalasia, pyloric hypertrophy, colonic spasm, etc., is invariably associated with mal-co-ordination. When the intestinal

trouble is at its worst the mal-co-ordination is most pronounced. Correcting the intestinal trouble may correct the mal-co-ordination, but rendering the patient co-ordinated does not correct the intestinal trouble. In whatever way a chronic intestinal trouble is caused the results are the same. The most important result, so far as it concerns this discussion, is the formation of hydrated protein particles in the plasma occasioned by the entrance into the bloodstream of abnormal metabolites formed from faulty articles of diet by pathogenic mutative forms of the *Bacillus coli communis*. These hydrated protein particles are particularly liable to become arrested in the cerebral circulation where they interfere with the normal activity of the neurones.

Even these few remarks show that from whatever angle the subject is discussed a vicious circle is traced, and like most vicious circles, it is difficult or impossible to mark the beginning. Summing up the subject, it may be said that mal-co-ordination is inherited and congenital, that it is in the main the result of mis-directed activity of the cerebral mechanism, that the activity of the neurones in the cerebral cortex rules the activity of all the other cells in the body, and that acquired mal-co-ordination is more a result of the mis-directed activity of the brain-stem than of the cerebral cortex and that attempts made to correct mal-co-ordination are more readily followed by success in the acquired than in the congenital form.

How the Adoption of the End-Gaining Principle has adversely affected the Evolution of Medical Science

This part of the subject is opened by assuming that ills became prevalent when man left the state, characterised by instinctive guidance and control and by co-ordination, to enter the civilised state, characterised by an ever-increasing lowering of the standard of sensory appreciation. There are three facts in support of this assumption : (1) The greater number of ills among civilized than uncivilized people ; (2) the low incidence of disease in animals as compared with man ; (3) the higher incidence of disease in animals under domestication than in animals living in their natural wild state. With his lowered standard of sensory appreciation, man's response to ills would be to seek a remedy for them with the logical sequence that no enquiry would be made into their causation. If the ill vanished after the application of the remedy, the latter naturally would come to be regarded as a "cure." The very word "cure" is the essence of end-gaining ; its introduction has done an incalculable amount of harm to medicine, and it is a word which should vanish from the medical vocabulary. In time certain remedies would be found to be

more useful in some ills than in others, with the inevitable result that cures came to be regarded as specific and ills as diseases. Later, a progressively sharper differentiation was made between the various diseases, and the art of finding specific remedies for them increased gradually. So great has become this differentiation that man has found himself capable of mastering the science of a few ills only, hence the growth and spread of specialism. Aiming at results without the intelligent control of means is Dewey's⁶ definition of magic. Therefore not only did medicine evolve out of magic, but its evolution is still proceeding along the lines of magic. Had man adopted an intelligent control of the means, the science of medicine to-day would be more simple than it is and the whole would be well within the grasp of those who devote their lives to it.

It would be useless to discuss the activities or behaviour of man without considering at the same time his environment, yet in medicine it has been assumed that an organ and even certain cells can function abnormally without affecting adversely the rest of the body. Perhaps the greatest division of man's activities is the one separating the mental from the physical. This separation has led to the sub-division of the mental activities, so that now such hypotheses as the "conscious mind," the "sub-conscious mind" and the "unconscious mind" are seriously discussed. In the first place mental activity is merely an expression of the energy evolved and liberated from the protein particles constituting the cytoplasm of nerve cells. The energy is the same as that liberated from the protein particles constituting the cytoplasm of any other cells as already stated above. The energy liberated by nerve cells may differ in quantity and quality; in fact, the amount and kind of energy liberated are determined by the chemico-physical state in which the protein particles constituting the cytoplasm of the nerve cells happen to be, but it is unnecessary to give special names to the different exhibitions of this energy and logically unsound to base a special kind of therapy (psychotherapy) upon one or more of them. Although it is true that "consciousness" has reached a very high level in man and its growth has run *pari passu* with the development of the cerebral cortex, there never was any justification for assuming that "consciousness" in its widest sense was an attribute peculiar to man or an expression of cerebral activity alone. Even an amœba has "consciousness," and there is no fundamental difference between the "consciousness" of a uni-cellular organism and the "consciousness" of man. It was due to regarding the "consciousness" of man as something distinct that led to the coinage of the word "soul," and it is only in com-

paratively recent times that the idea of the soul having a material basis—of being an entity—was discarded. “Consciousness” is not an activity peculiar to the cerebral cortex; indeed, many of the different expressions of “consciousness” are determined by changes which take place in the brain-stem. In fact, it would be better to drop the word “consciousness” and use the word “intelligence” to denote the activity of the cerebral cortex.

Too sharp a differentiation has been made between the cerebral cortex and the brain-stem and too much importance has been placed by neurologists on the activities of the former so far as their *rôle* in disease is concerned. This being the case, it is hardly logical to assume that the sharp differentiation of certain cells covering a tiny area in the brain-stem, for example, can be correct or even advantageous. Indeed, recent work shows that the sharp division made between the autonomic and the sympathetic halves of the vegetative nervous system is not entirely justifiable. As is shown in the next chapter, the vegetative nervous system is but a part of a whole in which the autonomic nervous system is the exciter part and the sympathetic nervous system the inhibitor part. In support of this reasoning is the interesting fact that, of all branches of medicine, the prize for diagnostic acumen has to be given to neurology. On the other hand, it is the branch which shows the greatest inability to rectify the damage detected. Ophthalmology and otology are two branches of medicine which should never have been separated from neurology. There is a much more intimate connection between the eyes and ears and the brain than is generally believed, and both these sense organs are organs *whereby* man sees and hears, not *with which* he sees and hears. Once the connection is re-established, it will probably be found that the common condition “oto-sclerosis” is primarily a lesion of the brain and not of the ears. In fact, Gray⁷ in his “Oto-sclerosis” suggested this in 1917.

Turning attention to the internist, it is found that the more he tracks down disease to an organ or to a part of an organ the less he is able to suggest a treatment which will benefit the patient. Although there are elaborate tests which are supposed to measure the damage sustained by such organs as the liver and kidneys, it is well-nigh impossible to correct the damage detected. The author holds the opinion, and it was expressed in the previous volume, that the foundation upon which the hepatic and renal tests are founded is unsound. In the case of the liver all tests may be positive, pointing to a hepatitis and cholecystitis when the liver and gall-bladder are normal. In the case of the kidneys, although the condition in which the glomerular or filtering membrane happens to be may influence what passes through it,

the factor possessing much greater influence is the constitution of the blood on the far side of the membrane. The internist has had part of his realm stolen from him by the pharmacologist, who still believes that certain drugs can correct the damage sustained by certain organs. The primary action of choline is not upon the autonomic nervous system, nor of adrenalin upon the sympathetic nervous system; neither digitalis nor strophanthus has a direct action upon the heart, and no so-called "parasiticide" directly kills micro-organisms in the body. The primary action of drugs is upon the host's main protective substance, and when benefit follows their use it is due to the correction of the chemico-physical changes rendered abnormal by the invader.

The principle underlying the treatment of the manifestations of disease with drugs adopted to-day shows that magic still pervades medicine, because the principle does not differ fundamentally from that adopted by the ancients when they used decoctions of certain plants to reduce fever, etc. There is no fundamental difference between what was understood by the febrifugal action of centaury and what is meant now by the spirillocidal action of arseno-benzene. Pharmacology has been deprived of some of its territory by the immunologist, who is the offspring of the bacteriologist. The bacteriologist and the pathologist are the offshoots of the physician's branch of the medical tree.

Immunology, although it has been productive of enormous benefits to mankind in preventing infections, has probably done more than any other branch of medicine to make the science unnecessarily incomprehensible. The coinage of a verbiage is always a cloak to cover ignorance, and although the author has been accused of floundering in the side-chain theory maze, he has nevertheless succeeded in demonstrating that immunity is nothing more nor less than an exhibition of dispersion of hydrated protein particles in the plasma, or, in other words, a turning of the tables by the host's resistance upon the invader. Had man not inherited disease by fault, there would not have been the need for many of the preventive measures now in force against disease.

Many of the infections considered to-day to be specific are caused by micro-organisms ordinarily saprophytic becoming pathogenic because the patient's resistance has been lowered by inherited disease. The future will probably show that some of the manifestations of disease thought to be caused by micro-organisms are not so caused, and that some of the micro-organisms thought to be distinct are in reality related.

Internal medicine has been robbed of another portion of its territory by

the endocrinologist, who considers that all the activities of the body are regulated by the secretions of the ductless glands. In the first place, he does not know how the glands secrete, in what form the chemical substance is secreted, whether there are one or more chemical substances secreted, or the exact nature of the substance which reaches the blood-stream. He assumes the glands are interdependent, and glibly talks about the quantities of this and that secretion circulating in the blood-stream in divers conditions, having at his command no means for directly testing the chemical compound in question. For example, clinical conditions are described as being due to an excess of histamine, thyroxin, adrenalin, and guanidin circulating in the blood-stream and labelled as shock, exophthalmic goitre, fear and spasmophilia respectively when no tests exist by means of which an excess or absence of the chemical products can be determined.

The branch of medicine to which the prefix "internal" cannot be applied has long since passed into the hands of the dermatologist, physical culturist, electro-therapist, balneologist, etc. The dermatologist is an arch-offender because he gives wonderful names to conditions he knows nothing about. The physical culturist, by failing to use the mechanism of the main control, usually adds to the mal-co-ordination already existing. The electro-therapist plays the rôle of the last treater of symptoms, and generally has to deal with cases which the rest of the profession has thrown over in disgust. The balneologist may, by enforcing a *régime*, temporarily benefit his patient, but as most of his cases are cases of rheumatism, the most serious manifestation of familial disease to-day because of its high incidence, he does more harm by neglecting causes than any of his *confrères*. The world could be rid of rheumatism if familial chronic intestinal intoxication was prevented and treated, and at much less cost than is being expended on clinics where merely the symptom is treated. Not only would this manœuvre get rid of rheumatism, but also it would abolish many other manifestations of inherited and congenital disease. The last branch of medicine to stir the public mind is that dealing with the vitamins, about which as much nonsense is being talked as occurred when the hormones saw daylight. The true nature of vitamins can never be determined, as they are chemico-physical bodies whose nature is altered whenever an attempt is made to extract them from the bodies of which they are actually part. Vitamins did not trouble man's forefathers, and their expanded use will be employed as a pretext and excuse to render food more unnatural than ever. Had man not forsaken the land for the lure of the towns and had he not accepted imported, artificial and wrongly

handled foodstuffs, there would have been no necessity for the vitamins, which are never going to replace natural and wholesome food.

Turning attention to surgery, it is found that most of the operations performed remove symptoms only, to the neglect of causes. How many surgeons before removing the appendix, for example, ask themselves why the patient has appendicitis? If the reason why was probed in every case, fully three-quarters of the operations now performed would never be performed. The combat between allopathy and homœopathy has been recently renewed, but on scrutinising the situation, it is clear the division should never have occurred. Had neither adopted the principle of end-gaining, there would not have been allopaths or homœopaths. Both palliate symptoms and leave disease untouched. The homœopath, by employing infinitesimal doses of preparations which, employed in larger doses in healthy individuals, would give rise to the symptoms, causes no more than dispersion of the hydrated protein particles in the plasma, an effect aimed at by every rational treatment with drugs. Disease is caused in the main by the protein particles in the plasma undergoing hydration, and treatment, when successful, counteracts disease by subjecting the hydrated protein particles to dispersion. Further, even the allopath treats certain intoxications with drugs having a similar action to those causing the intoxication. For example, the use of sulphur, oxygen, and iodine in overcoming intoxication caused by nitrogen, which has a greater negative valence than the other three metalloids, is essentially a homœopathic manœuvre. Even the research conducted to-day is conducted on the end-gaining principle, and this explains why the results are neither commensurate with the work done nor with the money expended. Let the reader divert his attention to one of the most recent discoveries, namely insulin. *Diabetes mellitus*, characterised by a rise in the percentage of the blood-sugar and by the passage of sugar into the urine, is regarded as a disease brought about by the destruction of the island cells of Langerhans in the pancreas. Once this view was accepted it was logical to suppose that an extract of the island cells would cure diabetes. Great credit is due to Banting and his co-workers⁸ for the introduction of insulin, but because insulin causes the glycosuria to vanish and the percentage of the blood-sugar to fall, no justification exists for acknowledging that insulin cures diabetes. Indeed, it is known only too well that insulin once prescribed has to be continued, in the majority of instances, throughout the patient's lifetime, and even then that the mortality of the condition in certain decades of life has not diminished. In actual fact, diabetes is on the increase, supporting the view expressed above that familial chronic intestinal intoxication is becoming

more prevalent, diabetes being merely a symptom of this condition. The introduction of insulin does not explain why diabetes can occur without a total destruction of the acinous cells, nor why complete destruction can take place in the absence of diabetes. Finally, in spite of the work done, no answer has been given to the question—where does the blood-sugar go in the presence of insulin? To assume that a vacuum is formed in the muscles does not answer the question. The action of insulin is exhibited by certain organic preparations containing sulphur or positively charged nitrogen atoms. The effect of such drugs is to cause hydration of the protein particles in the plasma, in the course of which the planet sugar is drawn more closely to the protein sun. The sugar enters into a complex colloid combination with the protein sun and its other planets, whereby it ceases to be detected as sugar. Therefore the sugar, supposed to rush into the muscles when insulin is prescribed, never leaves the blood-stream. The percentage of the blood-sugar is raised by all drugs causing dehydration of the protein particles in the plasma. When the percentage of the sugar in true solution reaches a certain level the blood gets rid of it through the kidneys. If the dehydrator process is continued over a long period of time it may result in the destruction of the acinous cells of the pancreas. The dehydrators most capable of acting in this way are those which reach the blood-stream from the large intestine. Diabetes, therefore, is an external manifestation of a chronic intestinal intoxication in which in the end stage the island cells of Langerhans may suffer destruction. Ridding humanity of a chronic intestinal intoxication would prevent diabetes and render insulin superfluous.

Medicine cannot advance by referring to the results of research which become most fashionable as "epoch-making." The advance is to be made by future generations, and it depends upon the tuition given. Such teaching can never be sound which ignores or glosses over the omissions of past generations, and it is the author's opinion that the exchange from adopting the principle of end-gaining to the intelligent control of the means can be perfected only by realising and avoiding the omissions and commissions made by the scientists of the past. No good can result from the establishment of committees to investigate this or that subject, a statement confirmed by history, but in spite of this new committees are continually being formed and money is wasted on the work done.

Even when dealing with medicine as a whole it is often difficult to avoid falling into the same error as that which caused the physicians of bygone days to divide and sub-divide medicine into diseases. For example, the treatment

of ills when they first arose was only one way of counteracting the ills. Although the occurrence of ills led men to search for cures, they were accompanied by fear, for which relief was sought in other directions. It is not within the province of this volume to trace the means employed to mitigate fear, and all that need be said is that they are represented by religion and law to-day as medicine represents the counteracting of ills by means of cures, and they are merely mentioned to show that not even medicine itself is a subject within strict confines. To what does all this lead? To the one inevitable conclusion that no gain will accrue from substituting a new institution for an old. To gain liberty of thought and action and thereby happiness, man must forsake conventions and respond correctly to the stimuli arising from his environment. This would seem to be the sole way in which it is possible for man to advance untrammelled. A glimpse at freedom is afforded by every revolution, but no more than a glimpse is allowed because all revolutions are based upon the fundamental error of substituting one form of slavery for another. That this idea cannot be so far removed from the true one is afforded by the fact that the men who have made the greatest advances, in the various sciences, for example, have been those who had no early training in these sciences, and that these men have usually been the most unpopular of their time. The moral of which is that conventions imprison the individual, a state of affairs which cannot but fail to curb and mis-direct his activities, and that academical training is the greatest obstacle to the advancement of science, and of medical science in particular.

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CHAPTER II

DISEASE AND THE NERVOUS SYSTEM

Introduction

It is proposed in this chapter to discuss the relationship between mal-co-ordination and the nervous system, to explain how a chronic intestinal intoxication can be responsible for nervous manifestations and to demonstrate how nerve tissue is damaged by the abnormal protein particles in the plasma.

These three divisions of the subject form a vicious circle, and, as pointed out in the previous chapter, it is impossible to mark the point at which the circle commences. The difficulty is rendered still greater by the fact that the vicious circle is initiated in the child *in utero*. In other words, the elements of the vicious circle are congenital. This being the case the chapter is opened with a discussion upon the hereditary factor and disease, and attention is drawn to the intimate relationship between the familial lesions of the central nervous system and the acquired lesions. Although it has been customary to regard epilepsy, migraine, etc., occurring in adult life as acquired lesions and distinct from such familial lesions as amaurotic idiocy, Little's disease, the convulsions of childhood, etc., they have, in the author's opinion, the same fundamental origin, and the seeds of all are sown and take root in the embryo. The difference in the lesion produced and the time of life at which it appears are influenced by the quantity of the seed sown, the damage done to the tissues by its taking root, and whether the soil is such as to enable the seed to bear fruit. For example, amaurotic idiocy is a result of the sowing of much seed and of its taking root firm enough to damage the host beyond repair. Migraine occurring in adult life is an instance where the seed sown is too little or too widespread and too insufficiently rooted to bear fruit unless some extraneous influence or precipitant appears, such as a chronic intestinal intoxication, to act as a stimulus. The discussion upon the relationship between mal-co-ordination and the nervous system brings into prominence the pyramidal reflex circuit, through which the primitive brain is connected to the cerebrum. The primitive brain, the seat of instinct, has its executive machinery stored for the most part in the grey matter around the third ventricle and that which constitutes the centre of the vagus. From the great *rôle* played in disease by the vagal grey matter in the brain it is

tempting to hazard the opinion that this marks the seat of the earliest brain. The cerebrum, which has reached to such a high pitch of development in man, is but an outgrowth of the primitive brain, and the main connecting link is the pyramidal reflex circuit. The development of the cerebrum has resulted in certain differences of activity not generated by the primitive brain, differences which account for man's unique position in the universe. Although these differences have brought man to where he is, it does not necessarily follow that they have been, are and will be properly directed. Indeed, there is evidence that these differences are being mis-directed, and mal-co-ordination, the outstanding feature of so-called civilisation, is an excellent example of such. Continued mis-direction may result in the devolution of man, and he is faced with the possible outlook that the enormous development of the cerebrum may ultimately lead to his destruction, as did a similar development of skeletal structure in his forerunners, the great Saurians. Although mal-co-ordination occurs when there is a lesion in both the primitive brain and the cerebrum, it is brought into greatest prominence when the connecting link between the two is affected—viz., the pyramidal reflex circuit. This is illustrated clinically in what is usually referred to as "Parkinsonism." Parkinsonism occurs as a sequel of encephalitis and of cerebral arterio-sclerosis and is, in the main, the result of damage done to the pyramidal reflex circuit. The pyramidal reflex circuit consists of the pyramidal tract, the exciter arc and of the extra-pyramidal tract, the inhibitor arc. Damage sustained by this circuit results either in a hyper-activity or hypo-activity of the exciter arc. Hyper-activity may be associated with and aggravated by a lack of inhibition, but hypo-activity does not, as might be expected, mean an excess of inhibition. It is doubtful if an excess of inhibition as a primary condition can exist. Mal-co-ordination, the prominent feature of damage done to the pyramidal circuit, is due either to a hyper-activity of the exciter arc, to a hypo-activity of the inhibitor arc, or to both.

The pyramidal reflex circuit is involved in most lesions of the central nervous system, and the various pathways are damaged either by micro-organisms or by the collection of hydrated protein particles around them. There is no difference in the result produced, and this explains why it is impossible at present to be certain, whether the various forms of encephalitis are due to ultra-microscopic micro-organisms or to ultra-microscopic particles derived from the host's own hydrated protein particles. When the excitant arrives at the scene of action it causes stimulation or increased activity of the exciter arc of the pyramidal reflex circuit. Should the excitant be particularly

active the result is paralysis, and the invariable sequence of this, should recovery ensue; is a loss of balance between the exciter and the inhibitor arcs, or in other words uncontrolled excitation. What this all comes to is that any interference with the proper activity of the central nervous system results in over-excitation, insufficient inhibition, or both.

The relationship between a chronic intestinal intoxication and disease of the nervous system is approached from three different angles : (1) the effect upon the alimentary tract of damage sustained by the vegetative nervous system ; (2) the rôle played by a chronic intestinal intoxication in the invasion of the nervous system by micro-organisms ; (3) the effect upon nerve tissue exercised by protein particles in the plasma, which have been subjected to abnormal chemico-physical changes by the entrance into the blood-stream of toxic metabolic products formed in the large intestine. Owing to the brain being the latest and most highly developed structure in man it is the most vulnerable, and, therefore, the part of the body most readily attacked by congenital disease. It would appear from the evidence available that congenital disease acts in the *fœtus* primarily by subjecting to abnormal chemico-physical changes the protein particles in the fluid (blood) which bathes and by means of which nourishment is carried to all the tissues and cells of the developing body. The main abnormal chemico-physical change is the one termed "hydration," and this change has various untoward effects upon the proper development of the *fœtus*. When protein particles become hydrated their surface area is diminished, and this means a lessening of their power to carry nourishment. This loss of nourishment is further accentuated by the fact that hydrated protein particles are more concerned with their own metabolism than with the metabolism of the tissues and cells around them. Indeed, the change may become so pronounced as to make the particles become actually parasitic upon the tissues and cells over whom their primary function was to watch. Further, hydrated protein particles move more slowly—and when the hydration results in an enormous increase in size the particles become too large to circulate. As by this time they have generally developed parasitic properties it is not surprising that the tissues and cells where the hydrated protein particles become precipitated either fail to develop or undergo degeneration. In ordinary cases where the degree of hydration reached falls far short of parasitism, their arrest in the circulation causes first a stimulation of the activity of the cells around. As this arrest occurs in every case in the brain and invariably in the most primitive parts of the brain, the reader will understand why congenital disease always shows itself in a stimulus of the vagus or in what is usually referred to as

“vagotonia.” The vagus is the exciter arc of the vegetative nervous system and the sympathetic the inhibitor arc. In the vegetative reflex circuit, as in the pyramidal reflex circuit, a lesion results either in a hyper- or a hypo-activity of the exciter arc, and in the former there may be in addition a hypo-activity of the inhibitor arc. On the other hand, when a lesion is present suggestive of a stimulation of the sympathetic nervous system, it is usually the result of a paralysis of the autonomic nervous system (*vagus*).

Irritation of the *vagus* occurring in the *fœtus* is kept up and aggravated after the birth of the child by faulty feeding and insufficient elimination of the waste products of the food. This is why in every case of congenital disease a chronic intestinal intoxication looms largest in the clinical picture.

A chronic intestinal intoxication, first of nervous origin and then kept up by faulty local conditions, results in abnormal metabolic products being formed from the food by mutation forms of the normal *flora* of the intestines. It would seem to be the case that the *Bacillus coli communis* develops into various mutative pathogenic forms which are usually classed as “non-lactose fermenting micro-organisms.” The toxic metabolic products cause the protein particles in the plasma to undergo abnormal chemico-physical changes which so lessen the resistance of the host as to enable micro-organisms ordinarily saprophytic to become pathogenic. If the central nervous system has suffered damage already at the hands of congenital disease it is not to be wondered at that it is picked out later in life either by these micro-organisms, by a particulate form of them, or by a particulate form of the protein particles in the plasma hydrated by the toxic products. The effect which hydrated protein particles have upon the cells of the central nervous system depends naturally upon the degree of the hydration. If the hydration is sudden and severe the cells are paralysed and destroyed, and the clinical picture presented is that of shock. When the hydration is slight the cells are stimulated. Should the hydration be continuous and increase in severity the initial stimulation is followed by abnormal activity and finally by hypo-activity or degeneration.

Heredity and Disease

GENERAL

Many of the signs and symptoms of an involvement of the nervous system which cause or aggravate mal-co-ordination in a child or adult may also lead to gross mal-co-ordination in a newly-born infant, strongly suggesting that the nerve lesion has its inception *in utero*. The various forms of amaurotic idiocy exemplify this statement. There is evidence that the vegetative nervous

system may be attacked *in utero*, because, apart from the various signs characterising familial chronic intestinal intoxication, such conditions as hypertrophic stenosis of the pylorus and intussusception occur in new-born infants, and the former of these may exist *in utero*. Furthermore, in infants who succumb to the clinical manifestations of a chronic intestinal intoxication the terminal parts of the ileum and of its mesentery are found to be inflamed and often thickened. This area may be regarded as the seat of election of later trouble in the colon. The evidence is even stronger that the blood of the child may be rendered abnormal before it is born, because it is possible to measure the abnormal chemico-physical changes affecting the protein particles in the plasma in blood withdrawn the moment the infant comes into the world. There is, moreover, the additional information afforded by the fact that the blood of an infant born of a woman who contracted syphilis two months previous to the birth gives a positive Wassermann reaction, although the child is non-syphilitic. As it is not generally known that a woman who contracts syphilis during the last two months of pregnancy does not infect her unborn infant, the author would remind the reader that infection contracted during the sixth and seventh months may cause congenital syphilis, and that infection contracted during the first five months always does. Protein particles give a positive Wassermann reaction when they have been subjected to a certain degree of hydration as explained in the first part of "The Nature of Disease." Owing to hydrated protein particles becoming independent they tend to behave as foreign bodies, which enables them to pass through colloid membranes more readily than other and smaller particles. The permeability of colloid membranes is influenced less by the size and more by the electro-physical characteristics of the colloid particles passing through than is generally thought. Indeed, the more alike are the membrane and the particles, the less does size play a part in the permeability. In a very large number of cases of proteinuria, for example, the protein in the urine represents such hydrated protein particles, which have passed from the blood through the glomerular membranes. Similarly hydrated protein particles can readily pass through the placenta, and, as disease is caused in the main by hydrated protein particles, it is not to be wondered at that mothers who are the victims of a chronic intestinal intoxication readily pass on the condition to their offspring. Since the father is almost as important a factor as the mother in causing familial chronic intestinal intoxication, judging from the family history obtainable, it would appear that some of the changes which start the vicious circle in the embryo are present in the sperm.

Having paid particular attention to the family history in all the cases of disease examined, the author has formed the opinion that familial chronic intestinal intoxication is on the increase, and this opinion would seem to be confirmed by the undoubted increase in the incidence of disease in schools to-day. Although statistics may be produced to show that the longevity of life is increasing and that infant mortality is decreasing, it cannot logically be inferred that the individual is healthier. Moreover, in medicine particularly, it is common knowledge how untrustworthy statistics are apt to be. It is idle to enquire into the nature of the determinant of congenital disease, as it is doubtful if it will ever be possible to throw light upon its true nature.

Although Weismann's view of the physical basis of inheritance has had many adherents, one is no nearer to the solution of the nature of the determinants supposed to reside in the chromosomes by referring to them as "germinules," "idants," "ids," "biophores," etc.

Once the glamour occasioned by the coinage of a special jargon (nomenclature) is removed the fact is laid bare that the manoeuvre impedes rather than advances knowledge. Whatever views may be held regarding the nature of congenital disease (and no view is ever likely to contain the whole truth), there can be no two opinions about the wisdom of preventing it. Prevention can be achieved only so long as individuals who show signs of mal-co-ordination or chronic intestinal intoxication, and whose blood gives a grossly abnormal picture, are precluded from having children.

How far the correction of these abnormalities would prevent disease in the children the future alone can determine. Be that as it may, these are the only three points which the author holds require to be taken into consideration, and if correct it would appear to be useless to rely upon the selective breeding advocated by the Eugenists. If the Eugenists' principles were sound, then one or more of Shakespeare's immediate descendants should have had equal poetic genius. It is not improbable that Shakespeare's genius was a product of inherited disease; indeed, this is a possible explanation of the origin of genius, but it does not necessarily follow that always the same product is passed on from one generation to another. If history be probed it is found more often than not that the biggest human figures have been sick men and women, and the offsprings of neuropathic parents. To mention a few—Saint Paul suffered from manic depressive psychosis, Julius Cæsar was an epileptic and Napoleon was a most perfect example of familial chronic intestinal intoxication. The last-mentioned was grossly mal-co-ordinated both physically and intellectually, his protein particles must have been in a perpetual state of hydration, as through-

out his life he presented signs and symptoms of irritation of the autonomic nervous system, such as bradycardia, hypertrophy of the pylorus, piles, pronounced sexual activity, etc. Napoleon's family history is also unique. His father most probably died of cancer of the stomach, his brother Joseph had paralysis, Lucien was myopic, Louis was an invalid, Caroline had gastric cancer, Pauline died of consumption, and Jerome alone lived to old age. All Napoleon's nephews and nieces were neurotic. The King of Rome was a profound neurasthenic and died of what is described as premature decay (says Nisbet¹). The point the author wishes to emphasise here, is that the protein particles in the blood of the child *in utero* may be in a state of hydration capable of producing disease, and inherited from either the father, the mother, or both.

The Congenital Lesions

Strictly speaking, most of the lesions of the brain, excluding those caused by micro-organisms and new growths, are familial in that they have their origin *in utero*. But under this heading it is intended to refer to those lesions which manifest themselves when the child is born, and to draw attention to their milder forms, forming as they do the connecting links between amaurotic family idiocy on the one hand and neurasthenia in the adult on the other hand, for example. Although for the sake of description it is necessary to divide the lesions into three classes: (1) those affecting the cortex; (2) those affecting the pyramidal circuit; (3) those affecting the vegetative nervous system, the author wishes the reader to realise that a lesion of the brain affects the central nervous system as a whole, and the body in addition, that no lesion is really specific, and that connecting links exist between the clinical manifestations appearing in the child on the one hand and in the adult on the other hand. The most important familial lesion affecting the cortex is amaurotic family idiocy linked to anencephaly on the one side and to colour-blindness on the other side.

Amaurotic family idiocy often goes by the name of "Waren Tay and Sach's disease." The condition is, on the whole, more common in Jews; it seldom affects the first-born, but when it makes its appearance the subsequent children rarely escape. This greater frequency amongst Jews has some significance. Inherited disease or familial chronic intestinal intoxication, the main symptom of it, is definitely more pronounced in Jews than in other peoples, most probably because the former is the older civilisation. In this connection it is interesting to note, not only the greater frequency, but also the

occurrence at an earlier age amongst Jews of hyperpiesia, *Diabetes mellitus*, *Thrombo-angitis obliterans*, etc., all manifestations of a familial chronic intestinal intoxication. The author has gained the impression that these conditions are beginning to occur more commonly and at a later age in non-Jewish races, and in the case of amaurotic family idiocy it is to be noted, that there is a post-infantile form which attacks them in preference to Jews. The common form of amaurotic family idiocy is characterised by progressive mental impairment, spastic paralysis and loss of vision, but in the post-infantile form the lesion tends to be limited to the cortical visual centre. Although the post-infantile form is the milder of the two, there are many variations, which account for the mention in the literature of "Batten-Mayou's disease," "Jansky-Bielschowsky's disease" and "Spielmeyers-Vogt's disease."

If such extreme differentiation has been made in variations of a condition exceedingly rare, it is not surprising that the more remote links in the chain have been missed. In these conditions the eye changes encountered may be those of *Retinitis pigmentosa*, which is after all only a degenerative change. In all cases of the post-infantile form the patient is grossly mal-co-ordinated, and presents one or more of the common signs and symptoms of familial chronic intestinal intoxication. This being the case, the author has made ophthalmoscopic examination a routine with his patients, and has found fundus changes in all who are grossly mal-co-ordinated and obviously the victims of familial chronic intoxication. The most common change is an accentuation of the cupping and pallor of the optic discs, nearly always more pronounced on the left side. Occasionally the optic discs are obliquely oval instead of being circular, and are definitely under- or mal-developed. Blindness in one eye with or without nystagmus has been encountered, and when a great error of refraction is present it is usually myopic astigmatism. Some degree of colour-blindness is not at all uncommon. It is probable that the lesion responsible for these changes lies in the visual cortical centres in the occipital lobes, because colour-blindness would seem to be due to the mal- or non-development of certain nerve fibres in the centre for the *macula*. The visual cortical centres are far from being the only cortical centres involved; indeed, it is probable that the auditory cortical centres are as frequently selected for attack, and when this occurs oto-sclerosis is the most common clinical manifestation presented. To the same category belong the cases of word-blindness, word-deafness, aphia and agraphia. The cerebral cortex may be damaged where there are no centres, in which case mental deterioration looms largest

in the picture. When the damage sustained is severe, Mongolian idiocy is produced, and when mild merely a retardation in the development of the patient's mental activity.

Mongolism is most likely to affect the last-born of a family where the conception and birth take place at or about the menopause, the time when women who are the victims of a chronic intestinal intoxication are particularly prone to develop external manifestations. The author agrees with those who hold that Mongolism is not the result of syphilis. Mongolian idiots bear out the statement made above that lesions of the central nervous system are not limited thereto, but affect the body as a whole, because there is generally some abnormality in the secretion of the thyroid gland. There is not such a very wide gap between a Mongolian idiot and a cretin. Allied also to Mongolism is the condition which manifests itself in adult life under the name of *Dementia præcox*. In this condition there is usually an abnormal change affecting the internal secretion of the sexual glands. In the second class of case to be discussed the pyramidal arc is damaged most, and the patient presents spastic paralysis. In the bad cases of spastic paralysis there is always some mental deterioration, with the presence or absence of an ocular lesion. In the milder cases, where there is no ocular lesion and where the pyramidal circuit bears the main brunt of the attack, the condition has suffered differentiation, as mentioned above, as occurring in the post-infantile form of family idiocy, because mention is made in the literature of "Little's disease," "Merzbacher-Pelizæus's disease," "Friedreich's disease" and "Schilder's disease." Schilder's disease, often labelled *Encephalitis peri-axialis diffusa*, may, as a matter of fact, be associated with optic atrophy and oto-sclerosis. There is an acquired form of Schilder's disease caused either by micro-organisms or by ultra-microscopic particles of the host's own hydrated protein particles. This acquired condition is closely allied to the post-vaccinal and post-measles encephalo-myelitis and to disseminated sclerosis. The more remote links in the chain are made up of mal-co-ordination, restlessness, irritability, nail-biting, etc., all of which are but external manifestations of damage sustained by the pyramidal circuit. This discussion shows the connection between amaurotic family idiocy and spastic paralysis on the one hand, and between the post-infantile form of amaurotic family idiocy and Schilder's disease on the other hand. Further, it shows that the mildest forms of both are characterised by eye and ear troubles and by mal-co-ordination, all demonstrating that in every case the whole and not merely a small defined area is attacked. The picture is made still more complete by bringing into the discussion the involvement of

the vegetative nervous system, but before doing so several cases must be given to illustrate the points that have been raised.

Case 1

A boy, aged fourteen months, had had fits for the past six months. The mother used to suffer from chilblains and had a nervous breakdown when aged twenty-nine. The illness lasted one year and began with *Tinnitus aurium* and deafness. The mother's brother was a martyr to asthma. Her first child developed a prolapsed bowel and a hernia soon after birth, and the testicles had not descended. The infant never cried, it had a bilateral squint and nystagmus, and was both blind and deaf. The anterior fontanelle closed when the baby was ten months old, and at about this time a pigmented patch appeared in the small of the back, which lasted only two to three weeks.

An example of amaurotic family idiocy, but the parents were not Jewish.

Case 2

A girl, aged eight, and looking four, was the first-born of parents who were typical examples of familial chronic intestinal intoxication. The child was an obvious cretin. The first sign of trouble was persistent diarrhoea at the age of three months. This was followed by chronic constipation, and when the patient was aged two she developed broncho-pneumonia. The child was mentally deficient, was always sucking her fingers, and was very heavy to lift. The teeth were irregular, not developed and decayed, and the child had megalo-colon. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3492
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 34 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, and some giant particles. There were many particles and giant particles precipitated, as well as a few giant-particled clumps.
Wassermann reaction	= Positive + ± —

This case is of particular interest, because neither the father nor the mother had had syphilis, and the Wassermann reaction of their blood and of the blood of two younger children was completely negative. As a positive Wassermann reaction is primarily dependent upon hydration of the protein particles in the plasma, this case shows that there is nothing specific in the hydration caused by the *Leucocytozoon syphilidis*.

Case 3

A girl, aged 10, was a typical Mongolian idiot. The patient was the fifth and last of the family ; she was conceived when the mother was passing through the climacteric at the early age of forty, and when the first-born was eighteen years of age. Both the father and mother were typical examples of familial chronic intestinal intoxication. The patient was grossly mal-co-ordinated and had passed mucus *per anum* on several occasions. The pathogenic* micro-organism found in the excreta was the *Bacillus proteus valeriei* (25 per cent.) and the blood picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.4 c.c.
Refractive index of the serum	= 1.3477.
Percentage of the blood-sugar	= 0.086 grm.
Percentage of the blood-urea	= 35 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a fair percentage of giant particles and ringed particles. There were many particles, giant particles, ringed particles and clumps precipitated with one or two agglutinated masses.

The serum was remarkably light-coloured.

Wassermann reaction = Negative.

Case 4

A boy, aged fifteen, overgrown, extremely mal-co-ordinated and mentally deficient, was brought for advice because he also had fits. The patient's father was grossly mal-co-ordinated and suffered from psoriasis, and his younger brother bit his nails. The patient had convulsions as an infant and these developed into epileptiform attacks. He had had his tonsils and adenoids removed and had been troubled with nocturnal enuresis. He was tall and had a vacant expression ; the ears protruded, the mouth gaped, saliva poured out over thickened lips, and excessive secretion came from the nose. The head was thrown back, the abdomen was protruded, and there was a hollow in the small of the back. The patient could hardly walk, and threw himself into a chair when he was asked to sit down. He could scarcely speak, was unable to keep still for a moment, and the movements of his extremities were most ungainly. The patient suffered from *Acne vulgaris* and seborrhœa, and had marked acro-asphyxia and hyperidrosis. The pulse was 100 and the blood-pressures registered 105 and 70 mm. of Hg. respectively. Large quantities of

* The word " pathogenic " is used solely for convenience, as the micro-organism may or may not have been pathogenic at the time.

protein were passed in the urine. The colon was particularly tender in the regions of the splenic and hepatic flexures, and where it is joined by the ileum. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 14 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but all were larger than normal. There were some giant particles and clumps precipitated. The Brownian move- ments of the particles were sluggish.

The patient was dieted, his bowels were opened two to three times a day, and when not successful a treacle enema was given. The colon was washed out and various injections of an autogenous fæcal vaccine (atypical *Bacillus coli communis* 10 per cent.) and of contramine were prescribed. In addition Alexander's re-educational methods were adopted. Previously the patient had been found by skin tests to be hyper-sensitive to egg-albumin, but cutting out eggs alone from the diet left the clinical condition unchanged. In course of time the patient improved sufficiently to do some manual work in the garden and fields.

Had the patient ever been normal the diagnosis of post-encephalitic Parkinsonism would have been made the moment he was seen. The mental deterioration, the mal-co-ordination, *Seborrhœa faciei* (Krestin³⁰), sialorrhœa, excessive nasal secretion, hyperidrosis and acro-asphyxia are the predominant symptoms of post-encephalitic Parkinsonism, and arise through damage done to the pyramidal circuit and the grey matter in the region of the third and fourth ventricles. The reader should pay particular attention to the connection between the congenital cerebral lesion and the acquired, because it shows that the paths along which the hydrated protein particles travel in the embryo *in utero* are the same as those along which micro-organisms appear to travel in the child and adult.

The protein in the urine was mainly globulin, and due to the passage through the glomeruli of hydrated protein particles from the plasma.

Case 5

A girl, aged sixteen, mentally deficient and an epileptic, was brought to seek relief from persistent "night-terrors." The patient was grossly mal-

co-ordinated, blind in the left eye and myopic in the right. She suffered badly from chilblains, all her teeth showed evidence of decay, and the tongue was furred and deeply fissured. Menstruation began at the age of fourteen, but since then there had been only two or three periods. The pulse was 88, and the blood-pressures registered 100 and 30 mm. of Hg. respectively. An examination of the abdomen revealed definite evidence of a chronic intestinal intoxication in contraction of the left colon, marked dilatation of the right colon and cæcum and a thickening in the ileo-cæcal region. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (100 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3489.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 34 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few giant particles and a fair number of giant- particled clumps, both moving and precipitated.
Wassermann reaction	= Negative.

Both the patient's parents were unintelligent and refused to allow the girl to be treated. Curiously enough the father and his father had a high degree of myopic astigmatism. The case is of particular interest because no *Bacillus coli communis* was grown from the excreta.

Another interesting feature is the more or less normal condition of the blood, showing the capacity of the blood to right itself, in spite of the continued activity of the intoxication. The reader's attention is drawn here to this point, because he will doubtless be struck by the constancy of the blood-picture in the cases mentioned below despite disease being active. There are several explanations for this which should always be borne in mind whenever a blood-picture is examined. Blood has an extraordinary capacity for righting itself. Disease is in the main the result of the protein particles in the plasma undergoing hydration. Hydrated protein particles are particularly stable and the chemico-physical reactions do not differ very much from the normal, hence the reason why the author called this in his first volume "the stable form of condensation." For disease to occur it is necessary for only comparatively few protein particles to become hydrated, and those responsible for the damage leave the peripheral circulation from which blood is withdrawn to be tested, to become arrested in the area involved. Added to

all this is the fact that all blood-tests are crude, and have to be done on the blood *in vitro*. Whenever gross changes are found in the blood-picture it usually means that active dehydration is going on at the time of examination, and this has always to be checked before it is possible to cause dispersion of the hydrated protein particles, the main aim of treatment. The reason why treatment is sometimes unavailing, is partly because the damage done may be irreparable and partly because the stable form of condensation is so stable that even if dispersion can be achieved it is quickly succeeded by the old hydration.

Case 6

A man, aged forty-four, sought advice for asthenia. The patient had a twin brother who also suffered from asthenia, with asthma in addition. Both used to have eczema in the same places and at the same time and both suffered from migraine. The twins and their father and mother were blind in the right eye from astigmatism. The patient had been operated upon for hernia, all his molars had been stopped, he was mal-co-ordinated, nervy and introspective. The pulse was 104 and the blood-pressures registered 100 and 65 mm. of Hg. respectively. The urine gave a very strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and an examination of the abdomen revealed definite evidence of chronic colitis. Both twins had been married some years without children. The pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligenes* (10 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3502.
Percentage of the blood-sugar	= 0.106 gm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving with a few giant-particled clumps. There were a few giant particles and giant-particled clumps precipitated.

This patient did not undergo the treatment advised. The interesting feature in the case is the hereditary history of blindness in one eye from myopic astigmatism.

Case 7

A girl, aged twelve, sought advice for chronic constipation, and in the course of the examination it was found that she had word-blindness and tone-deafness. The patient was grossly mal-co-ordinated, and extremely

clumsy and fidgety. There was marked central cupping of both optic discs, the patient was left-handed and had pronounced acro-asphyxia. The tongue was fissured, the blood-pressures registered 95 and 60 mm. of Hg. respectively, and an examination of the abdomen revealed a contracted left colon and a dilated ascending colon and cæcum. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes*, the same micro-organism as was infesting the father's stools. The father and his brother were typical examples of familial chronic intestinal intoxication. Both were thin, with bad circulation, winged ears, fissured tongue, and had suffered from rheumatic fever in the past. Both were still troubled with hay-fever, and the father complained of recurrent aphthous ulceration of the mouth. All three were treated by dieting, colonic lavage and injections of Sup. 468 and of the autogenous vaccine with considerable benefit :—

Through the kindness of Macleod Yearsley the author has been enabled to make clinical and blood-examinations of a large number of cases of oto-sclerosis, and the following reports have been selected from the number as illustrating the main features of the condition :—

Case 8

A boy, aged nine, had suffered from increasing deafness since the age of three. The patient could not talk till he was three years of age, and his teeth erupted late. The boy suffered from chilblains and *Lichen urticatus*. He always had a cold in the head and presented most of the signs of familial chronic intestinal intoxication. The pathogenic micro-organism found in the excreta was the *Bacillus pyocyaneus* (10 per cent. atypical).*

The boy was dieted, the colon was washed out, he received injections of his fæcal vaccine and had two courses of Zünd-Burguet's treatment with considerable improvement to the hearing. The patient improved in every way and the *Lichen urticatus* completely vanished.

In another boy, aged eight and a half, who presented all the signs and symptoms of familial chronic intestinal intoxication and suffered from tinnitus and deafness for over four years, the pathogenic micro-organism found in the excreta was the *Bacillus asiaticus* (80 per cent.).

Case 9

A woman, aged nineteen, was completely deaf from oto-sclerosis, which began when she was aged seven. The patient's father was deaf, as were the paternal grandmother, three of the father's sisters and two of the father's

* The name given to the pathogenic micro-organism is the nearest possible. Many of the micro-organisms are atypical in one or more respects, but it must be remembered that the tests used to differentiate them are purely arbitrary.

brothers. The patient's brother and sister were both deaf. The patient suffered badly from chilblains and chronic nasal catarrh. Menstruation started at the age of fifteen, and there had always been menorrhagia. The patient had pronounced acro-asphyxia; she could not stand with her knees and feet together at the same time, the elbows were wide-angled and hyper-extended, there was marked central cupping of both optic discs, and one central incisor in the lower jaw still belonged to the first dentition. The pulse was 118 and the blood-pressures read 115 and 55 mm. of Hg. respectively. An examination of the abdomen revealed a hard, contracted and tender left colon; the cæcum was dilated and there was tenderness over the appendix area. The pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici* (50 per cent.) and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.75 c.c.
Refractive index of the serum	= 1.3487.
Percentage of the blood-sugar	= 0.081 grm.
Percentage of the blood-urea	= 22 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a few ringed particles. A fair number of giant particles, ringed particles and small giant-particled clumps precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, she had the whole of the colon washed out by the siphon method, she took iodine, ichthyol and thyroid extract internally, she received several injections of contramine and four injections of her faecal vaccine and had two courses of Zünd-Burguet's treatment. The patient's general condition improved enormously, and it was thought that the ear trouble had been arrested.

Case 10

A man, aged twenty, had complained of increasing tinnitus and deafness in both ears for five years. The patient's father died of cerebral hæmorrhage, aged fifty-five. The mother had oto-sclerosis and had been operated on twelve years previously for gastric ulcer. One brother died of phthisis, aged twenty-three. The patient was always tired; he could not stand with his knees and feet together, most of his teeth had been removed or stopped, the tongue was furred and there was acro-asphyxia. The heart was dropped, elongated and narrowed, the pulse was 88 and the blood-pressures read 150 and 90 mm. of Hg. respectively. The patient had hypospadias, and an

examination of the abdomen revealed definite evidence of chronic colitis. The urine contained protein and gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus pyocyaneus* (75 per cent. atypical) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3497.
Percentage of the blood-sugar	= 0.086 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but they were mostly larger than normal and there were a few ringed particles. There was an occasional giant particle and giant-particled clump precipitated.

This patient's general condition was improved by treatment, but the tinnitus and deafness were not benefited.

Case 11

A woman, aged twenty-four, had complained of deafness and noises in the head, which had been getting much worse for six years. The mother and father were deaf and a sister was going deaf. The patient had suffered from migraine, chronic nasal catarrh, chronic gastritis and constipation for many years. The lips were always dry and sore, the tongue and teeth were bad, the patient could not stand with her knees and feet together at the same time, the elbows were wide-angled and hyper-extended and there was acro-asphyxia. The patient had a vacant expression and she was extremely forgetful. The left colon was contracted, the ascending colon and cæcum were dilated and the patient was very tender in the regions of the splenic flexure, hepatic flexure and appendix ; the pathogenic micro-organism in the excreta was the bacillus of epidemic jaundice (50 per cent.), and an examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0.9 c.c.
Refractive index of the serum	= 1.3504.
Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 41 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving and all were giant particles. There were more particles precipitated with some big agglutinations.

The patient was dieted, subjected to colonic lavage, had a course of injections of contramine followed by Sup. 36 and then four injections of the vaccine. As regards her general condition the patient improved enormously, but as regards the tinnitus and deafness it could only be said that the progress of the trouble had been arrested.

Case 12

A woman, aged twenty-nine, sought advice for *Tinnitus aurium* and deafness. The tinnitus had been present for many years, but the deafness had been precipitated by a pregnancy, which had occurred five years previously. The patient had a brother, a Mongolian idiot, who died of convulsions at the age of three. The patient suffered severely from chilblains, had bad nightmares and was a somnambulist. She had been pregnant twice and had had hay-fever only when in this state. The patient used to have severe fits of depression as a girl, she had had frequent attacks of mucous colitis and her appendix, a supernumerary breast and most of her teeth had been removed. The patient showed the cardinal signs of familial chronic intestinal intoxication. The pulse was 92 and the blood-pressures registered 100 and 60 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (25 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuseles	= 0.3 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.137 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a few giant particles and ringed particles. There were a few giant particles, ringed particles and giant-particled clumps precipitated.

The patient was dieted, the colon was washed out, strychnine, iron and arsenic were prescribed internally and three injections of the faecal vaccine were made. The patient improved both generally and in hearing.

Case 13

A woman, aged thirty-two, had suffered from *Tinnitus aurium* and oto-sclerosis for several years, a condition she had inherited from her father, who died following an operation for appendicitis, aged fifty-four. The

patient was the only child, she suffered from chilblains on both heels and from menorrhagia and metrorrhagia. The tonsils and adenoids had been removed before the deafness started. The patient could not stand with her knees and feet together, the teeth were small, mal-formed, irregular and widely spaced, and there was marked central cupping of both optic discs. The pulse was 90 and the blood-pressures registered 100 and 55 mm. of Hg. respectively. An examination of the abdomen revealed marked tenderness in the regions of the splenic and hepatic flexures of the colon and in the ileo-cæcal area. The pathogenic micro-organism found in the excreta was the *Bacillus fecælis alkaligenes* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.35 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.118 grm.
Percentage of the blood-urea	= 82 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some giant particles, ringed particles and a few giant-particled clumps. There were a few giant particles and giant-particled clumps precipitated.

The patient's general condition improved enormously under treatment, but the tinnitus and deafness remained *in statu quo*.

A study of these six cases shows quite clearly that oto-sclerosis is not a disease, but merely one of many associated manifestations of inherited disease, aggravated and maintained by a chronic intestinal intoxication. Having treated several cases, the author is in a position to say that when an attempt is made to remove the chronic intestinal intoxication and one or more courses of the electrophonoid treatment are prescribed, the hearing is definitely improved in a few cases, and prevented from getting worse in some of the remainder, but in most it remains unaltered.

The ear lesion in oto-sclerosis would appear, from a recent discussion opened by Mayer² at the Otological Section of the Royal Society of Medicine, to be an ankylosis of the stapes caused by changes in the bone of the labyrinth capsules. The changes the bone undergoes are of the nature of both hyper- and hypo-plasia. Hyper-plasia of mesenchymatous tissues is the result of dehydration of the protein particles in the plasma, and hypo-plasia of hydration. The changes of dehydration and hydration occur concomitantly, and at one time the former prevails and at another time the latter. This point is brought out in the blood-pictures portrayed above. Although most of the

lesions encountered in disease are secondary to the dynamic resistance, the host's protein particles in the plasma undergoing hydration, and this is particularly true of congenital lesions, nevertheless there are congenital lesions caused by chronic dehydration, and one of them, neuro-fibromatosis, may be met with in cases of oto-sclerosis. It is interesting to note that pregnancy characterised by an initial dehydration and a later hydration of the protein particles in the plasma is one of the most potent factors aggravating oto-sclerosis. In pregnancy both osteophytes, the product of dehydration, and osteomalacia, the product of hydration, may be encountered.

Some authors have laid stress upon a faulty calcium metabolism as being a factor in the causation of oto-sclerosis. In some cases of oto-sclerosis the calcium content of the blood is raised, but in others there is a definite hypo-calcæmia. The percentage of the blood-calcium is influenced by the chemico-physical state in which the protein particles in the plasma happen to be, and it has nothing to do with the ear trouble. Because in some cases of oto-sclerosis a hyper-calcæmia has been encountered a connection has been assumed to exist between the condition and *Osteitis fibrosa*, in which the percentage of the calcium in the blood is usually raised. *Osteitis fibrosa* is merely an organic lesion resulting from chronic dehydration, and it does not differ from those trophic lesions met with in bones in cases of syphilitic degenerative myelitis, where there may also be a hyper-calcæmia.

To illustrate these points two cases of *Osteitis fibrosa* and one of Charcot's arthritis are reported below.

Case 14

A woman, aged seventy, had an incomplete fracture of the middle third of the left femur. The patient's father was a martyr to gout and succumbed to pulmonary fibrosis, aged sixty-nine; the mother died of erysipelas, aged forty-four, and one sister of phthisis, aged eleven. The patient used to have bad chilblains, she had been anæmic all her life, and her hair went white in the early thirties. The patient was bow-legged, she had hyper-extended and wide-angled elbows, Heberden's nodes, all her teeth had been removed and she had been operated upon for piles. The pulse was 94 and the blood-pressures registered 140 and 90 mm. of Hg. respectively. An examination of the abdomen revealed evidence of chronic colitis, and the urine gave a reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and contained a trace of protein. The blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.8 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-calcium	= 9 mgrm.
Percentage of the blood-sugar	= 0.093 gm.
Percentage of the blood-urea	= 38 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles. There were a few giant particles and a fair number of giant-particled clumps precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of treacle enemata, took iodine, ichthyol and thyroid internally and had six intra-muscular injections of contramine each of 0.125 gm. The patient improved considerably and the condition of the bones had not progressed, but a few weeks later the patient was awakened every morning at 3 a.m. with an attack of asthma. The asthma was most probably produced by the iodine, ichthyol, thyroid and contramine providing a toxic degree of hydration, because it vanished when 0.002 gm. doses of Sup. 468 were prescribed. This case is particularly interesting because it shows that drugs having ordinarily a dehydrator action may exhibit on occasions a hydrator effect, substantiating what the author has always maintained, namely, that a drug has no specific action and that its action is regulated by the state in which the protein particles in the plasma happen to be when it is prescribed.

Case 15

A man, aged forty-six, sought advice for repeated spontaneous fractures of bones. The first bone to fracture was the right patella when the patient was aged thirty-two, and since then the left patella and both femora had fractured. The bone condition was one of *Osteitis fibrosa*. The patient's father was a dipsomaniac and died aged fifty-five, and the mother succumbed to a hemiplegia, aged sixty-two. The patient had convulsions as a child, had been very "nervy" all his life and had had several nervous breakdowns, and was in the habit of frequently bursting out crying for no reason. He had never been able to earn his livelihood and had threatened suicide on more than one occasion. He had been troubled with severe neuritic pains and insomnia for about twelve years. He had suffered from indigestion and constipation all his life with periodic attacks of diarrhoea, and presented the usual signs of familial chronic intestinal intoxication. All the teeth had been removed,

the pupils were pin-point and failed to react to light. Rhomberg's sign was present and the reflexes, except the abdominal, were absent. There were several sub-cutaneous rheumatic nodules, arthritis of the right ankle and cutaneous anæsthesia. The patient had never had syphilis; he had generalised arterio-sclerosis, aortitis and interstitial myocarditis. The cerebro-spinal fluid was normal and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·6 c.c.
Refractive index of the serum	= 1·3478.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 30 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with many giant particles and a few clumps. There were some giant particles and giant-particled clumps precipitated.
Wassermann reaction	= Negative.

The patient was dieted, he had a course of colonic lavage, took internally iodine, thiol-amino-methyl-glyoxaline and thyroid and received intra-muscular injections of contramine with a certain amount of benefit.

Case 16

A man, aged forty-six, sought advice for swellings of the left hip and foot which turned out to be a Charcot's arthritis and a spontaneous fracture of a metatarsal bone respectively. The syphilitic infection had been contracted fifteen years previously, and when signs of posterior column degeneration appeared nine years later he was thoroughly treated with repeated drainage of the cerebro-spinal fluid. Prior to the onset of the troubles above-mentioned the patient had an œdema of the left leg, a condition the author has noted frequently in cases of syphilitic degeneration of the central nervous system. The patient was a typical example of familial chronic intoxication and the pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilis* (20 per cent.). But, before the intestinal condition was dealt with the blood was examined with the following result, and the patient received 20 ten-unit doses of insulin, which caused the hip and foot troubles to vanish as if they had never existed.

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3490.
Percentage of the blood-calcium	= 16 mgrm.

Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 37 mgrm.
Ultra-microscopic picture of the serum	= Myriads of particles moving. There were a few giant-particled clumps and one or two agglutinations precipitated.
Wassermann reaction	= Negative.

Later the patient was dieted, he had his colon washed out and received injections of the fæcal vaccine. For the past two years the patient has had no further trouble, and he has never had better health.

This case shows that symptoms usually thought to be due to syphilis may arise as a result of the infection in the same way as *Osteitis fibrosa* may be a result of a chronic intestinal intoxication. Indeed, a familial chronic intestinal intoxication plays an important rôle both in the symptoms produced by and in *sequelæ* of a syphilitic infection. It shows also that the use of a drug aimed at correcting the blood-change detected improved the symptoms presented. As the blood-change was one of dehydration, as evidenced by the rise in the percentage of the blood-calcium and by the ultra-microscopic picture, insulin was prescribed. Insulin has an equally good effect upon those interesting cases of *Osteitis fibrosa* associated with an adenoma of the parathyroid glands, showing that there is no specific relationship between diabetes, pancreas and insulin.

The discussion passes at this point to certain of the definitely familial lesions affecting in the main the vegetative nervous system. When the vegetative nervous system bears the brunt of the attack it is due to the precipitation of the hydrated protein particles in the peri-capillary lymphatic vessels mainly in the regions of the third and fourth ventricles. The former is considered to contain the cerebral centre of the sympathetic nervous system, and the latter the centre of the para-sympathetic nervous system or vagus. The sympathetic nervous system is the inhibitory arc of the vegetative nervous system. It probably has no cerebral centre and the signs and symptoms which are labelled as sympathetic-tonia of central origin are more probably produced by paralysis or degeneration of some of the cells of the vagal centre, rather than by a stimulation of the cells in the *Corpus Luysii*, thought by some to mark the cerebral centre of the sympathetic nervous system.

Precipitation of hydrated particles in the regions of the third and fourth ventricles causes, when not too severe and sudden, stimulation of the nerve cells; the signs and symptoms produced are definitely vagotonic, and when a lesion occurs in the *Corpus Luysii* chorea is the result. Stimulation of the

cells in the neighbourhood of the third ventricle may be responsible for dilatation of the pupils, tonic muscular contractions, pallor, *Keratitis pilaris*, sialorrhœa, hyperidrosis, enuresis, *Petit mal*, epilepsy, narcolepsy, migraine, etc., all signs and symptoms encountered so commonly in cases of familial chronic intestinal intoxication.

In *Petit mal*, but more particularly in epilepsy, discussion has been rife for years concerning the part of the brain involved. Opinion is still and always will be divided, so long as it is thought that the manifestations of disease are the result of damage sustained by certain areas to the exclusion of other parts of the brain. Although this section deals with the vegetative nervous system in particular, the reader must realise that this system cannot be attacked to the exclusion of other systems, and further that a definite involvement of organs other than the central nervous system may be involved as well and damaged by the precipitation of the hydrated protein particles therein. This is emphasised particularly in the case of epilepsy. The main area involved in epilepsy is the grey matter in the neighbourhood of the third ventricle, but the precipitation of the hydrated protein particles responsible for the attack may occur in the cerebrum, in any part of the brain and even in the thoracic and abdominal viscera.

Müller³ drew attention to the fact that in cases of epilepsy the pressure in the third ventricle is raised, and that hæmorrhages into the ventricle not infrequently occur. The optical *auræ*, sialorrhœa and hyperidrosis, common accompaniments of epilepsy, all point to a stimulation of the hypothalamic region. The fever which invariably occurs in *Status epilepticus* is probably in part due to a stimulation of the *Tuber cinereum*. The fever is caused also by the active dehydration the protein particles themselves undergo, and as acetone is to be found in the cerebro-spinal fluid it would appear to be the case that the dehydration is rather a cyclical change to the hydration than a concomitant chemico-physical change caused by the invader. Acetone may be encountered in the cerebro-spinal fluid during the seizures of syphilitic degenerative encephalitis, where some of the hydrated protein particles primarily responsible for the lesion undergo the cyclical change of dehydration. In fatal cases of *Status epilepticus* hæmorrhages are not limited to the third ventricle but occur in the brain-stem and in the cerebrum, as they do in fatal cases of syphilitic degenerative encephalitis, heat-stroke, eclampsia, insulin hypo-glycæmia, post-anæsthetic cerebral shock, arsenical and alcoholic encephalitis, etc. Furthermore, in all these conditions the temperature rises to a great height just before death, and *post-*

mortem there is always to be found a varying degree of fatty degeneration of the myocardium, some degeneration of the parenchyma of the liver and kidneys and an alteration of the mucous membrane of the large intestine. This shows that epilepsy is closely allied to other cerebral conditions, and that the hydrated protein particles responsible for the attack may be precipitated in other organs of the body at the same time, to cause stimulation or degeneration of the parenchymatous cells according to the degree of the hydration.

A fact of more interest which proves that epilepsy is primarily the result of the protein particles in the plasma undergoing hydration was the great rise in the incidence of the condition amongst the peasantry of Russia when sugar was unobtainable. In these cases a hypo-glycæmia was frequently encountered prior to the crisis. Speaking generally, carbohydrates are powerful dehydrators. Diet plays an important rôle in disease, and by no means the least in epilepsy; indeed, a special diet has been advised of late, known as the "ketogenic diet." Geyelin⁴ made the observation in 1921 that fasting for ten to twelve days stopped epilepsy, and it was on the assumption that the good results were due to the associated ketonæmia that Wilder,⁵ Peterman⁶ and others advised the ketogenic or high fat diet. These observers thought that the aceto-acetic acid acted as an anæsthetic and reduced the activity of the nerve cells.

The effect of starvation is to cause hydration of the protein particles in the plasma, and this is why athletes who have over-trained readily pass into a state of shock (relieved at once by glucose, the dehydrator *par excellence*) when their supreme effort is required. In disease where the protein particles are already hydrated starvation may either add to the hydration or cause dispersion. An augmentation of the hydration may make the patient worse, but the change is merely temporary because dehydration as a cyclical change soon follows to give rise to acetonæmia and ketonuria. When dispersion occurs almost at once the patient is benefited, and acetonæmia does not necessarily follow. The almost immediate occurrence of dispersion is an excellent example of the truth of treating like with like, the doctrine of the homœopathist. When fits abate under the ketogenic diet it is due to the precipitated protein particles in the brain undergoing either dehydration or dispersion, and not to any possible anæsthetic action exhibited by the di-acetic acid. In the author's experience the ketogenic diet has not proved very satisfactory. Benefit has resulted when there has been no acetonæmia, and the patient has been made worse when there has been acetonæmia.

Indeed, where the fits have been lessened the greatest abatement has occurred during the period when carbohydrate was prescribed to correct the acetonæmia. As carbohydrates have a dehydrator action it is logical to infer that the benefit is due to the dispersion of the protein particles left hydrated, because acetonæmia occurs only when some of the hydrated protein particles undergo dehydration. Narcolepsy and migraine do not differ from epilepsy except in minor details, and a few case reports of these clinical manifestations of inherited disease render further discussion unnecessary.

Case 17

A boy, aged five and a half, had an attack of what was diagnosed as paratyphoid one year previously, and since had been subject to *Petit mal*. The boy was an only child, a typical example of inherited disease, his father having been an epileptic at puberty and a martyr to angio-neurotic œdema since. Migraine occurred in most of the members of the father's family and for the past nine years the father had had two yearly attacks of cheiro-pomphylox. The pathogenic micro-organisms found in the father's excreta were the *Bacillus Gärtner* (50 per cent.), and in the patient's, *Bacillus Morgan* and *Bacillus pyocyaneous* (10 per cent.).

The patient was dieted, he had treacle enemata regularly and received injections of his faecal vaccine in doses of 1,000, 10,000 and 100,000 respectively on three days in succession. Three months later the injections were repeated in 100,000, 250,000 and 500,000 doses, with the result that the patient had no more fits and he has been free now for over two years. The association of the son's *Petit mal* with his father's manifestations of inherited disease makes the case a particularly interesting one.

Case 18

A boy, aged eleven, grossly mal-co-ordinated, very fidgety and a nail-biter, was brought for advice because he was developing *Petit mal*. The boy's parents were first cousins; the father had had rheumatic fever, followed by attacks of rheumatism at irregular intervals, and the mother had oto-sclerosis. Oto-sclerosis was marked on the maternal side of the family. The patient presented most of the signs of familial chronic intestinal intoxication; he was pale and freckled. The pulse was 118, the blood-pressures registered 100 and 50 mm. of Hg. respectively, the left colon was contracted and the urine contained a trace of protein and gave a very strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found

in the excreta was the *Bacillus proteus hydrophilus* (25 per cent. atypical), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·4 c.c.
Refractive index of the serum	= 1·3498.
Percentage of the blood-sugar	= 0·075 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= M a n y p a r t i c l e s moving with many giant particles, some ringed particles and giant-particled clumps. A fair number of giant particles, ringed particles and giant-particled clumps pre- cipitated with one or two agglutinations.

Case 19

A boy, aged twelve, suffered from epilepsy. As a baby the patient was a victim of the so-called "cyclical vomiting of infants," a condition which was followed by convulsions and later by *Petit mal*. At the time of examination the boy was mentally deficient, he had hallucinations, sialorrhœa and polyuria. The boy's father, the father's two sisters and aunt had oto-sclerosis. The father's appendix had been removed and for the past three years he had been crippled with rheumatism. The patient had two brothers, aged fourteen and nine respectively ; the former had been operated upon for tonsils and adenoids, the latter for appendicitis. The patient was grossly mal-co-ordinated and very fidgety. The palate was high-arched and narrow, the optic discs were deeply cupped and the nails were ridged and had lost their gloss. The pulse was 92 and the blood-pressures registered 100 and 50 mm. of Hg. respectively. The urine gave a very strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde ; an examination of the abdomen showed the colon in the left iliac fossa to be contracted, the splenic flexure to be tender and the cæcum to be dilated. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (10 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3491.
Percentage of the blood-sugar	= 0·137 grm.
Percentage of the blood-urea	= 17 mgrm.
Ultra-microscopic picture of the serum	= S c a r c e l y a p a r t i c l e moving. Practically all the particles were precipitated in the form of large and refractile giant particles, ringed particles, giant-particled clumps and agglutinations.

The treatment advised in this case was not properly carried out and no improvement was registered. The case is of interest, first as showing that epilepsy is merely a manifestation of a chronic intestinal intoxication and, secondly, that the chronic intestinal intoxication was familial. In other words, there was a close connection between the family oto-sclerosis and the patient's epilepsy. The signs and symptoms produced by the epilepsy pointed to involvement of the cortex, mid-brain and hind-brain.

Case 20

A youth, aged fifteen, had suffered from epilepsy, with fits every two days for three years. Between the ages of ten months and three years the patient had convulsions. The maternal grandmother died of diabetes, aged sixty-four, the patient's mother had been operated upon for appendicitis and the father had had frequent attacks of furunculosis. The patient's tonsils and adenoids were removed when he was eleven years of age. He suffered from nocturnal enuresis, he was grossly mal-co-ordinated and very awkward and clumsy. The ears stood out, the patient had *Acne vulgaris*, he salivated and had dilated pupils. The tongue was quite smooth, the arms were long, the elbows were hyper-extended and the fingers long and tapering. The pulse was 100 and the blood-pressures read 105 and 70 mm. of Hg. respectively. An examination of the abdomen revealed an extremely bad form of chronic colitis. The urine contained much protein and gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The boy was supposed to be sensitive to egg-albumin, but depriving him of eggs in no wise benefited his condition. The pathogenic micro-organism found in the excreta proved to be an atypical *Bacillus coli communis*. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3491.
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood-urea	= 14 mgrm.
Ultra-microscopic picture of the serum	= M a n y p a r t i c l e s moving but all were larger than normal and the Brownian movements were very sluggish. There were some giant particles and clumps precipitated.

The patient was dieted, his colon was washed out, he received a few injections of his faecal vaccine and 0·05 grm. contramine weekly for over a

year, with the result that he improved enormously and only had an occasional *Petit mal* attack. Both in this and the last case note should be made of the low percentage of the blood-urea, a phenomenon significant of protein hydration. The success following the use of contramine and the faecal vaccine was due to the drugs occasioning dispersion of the hydrated particles, which, collecting in the vessels of the brain, were subjecting the neurones to dehydration and then to true solution. The dehydration is evidenced by neuronal hyper-activity and the conversion into true solution by neuronal degeneration. The protein passed in the urine was mainly globulin and caused by the passage through the glomeruli of protein particles which had become so hydrated as to behave as foreign bodies.

Case 21

A youth, aged eighteen, had had epilepsy for six years. When first seen the attacks, accompanied with vomiting and intense thirst, were becoming more frequent and more severe. The patient stammered, he had had attacks of mucous colitis and every attack was characterised by fits of *Petit mal*. The patient was a very typical case of chronic intestinal intoxication, and his father had been under the author's treatment for lumbago and sciatica. The pathogenic micro-organism found in the excreta was the *Bacillus pyocyaneus* and an examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3513.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 19 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving and most of them were giant particles. There were many giant particles precipitated. The Brownian movements were sluggish.

The patient became a strict vegetarian, the colon was washed out, the hydrated protein particles were dispersed with choline and Sup. 36 and injections of the faecal vaccine were made over a space of two years. The patient was freed of his fits for a time, but they recurred later, although in a less severe form.

In this case the hydration is evidenced by the high refractive index of the serum and by the ultra-microscopic picture.

Case 22

A woman, aged twenty-three, had suffered from epilepsy for eleven years. The fits occurred on rising in the morning. The patient's mother had been operated upon for gall-stones and the father suffered badly from rheumatism. The patient still had chilblains and her tonsils and adenoids had been removed ten years previously. She could not stand with her knees and feet together at the same time. She had prominent upper central incisors and all the molars had been stopped. The tongue was furred and fissured, the elbows were wide-angled and hyper-extended and there was acro-asphyxia. There was cupping of both optic discs and the retinal veins showed congestion. All the reflexes had vanished. The pulse was 78 and the blood-pressures registered 105 and 65 mm. of Hg. respectively. The left colon was contracted and the right dilated ; the cæcum was distended and there was tenderness in the ileo-cæcal region, the terminal portion of the ileum on palpation was contracted and thickened. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (25 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3471.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 36 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, with many giant particles and ringed particles. There were more particles precipitated <i>en masse</i> .

The patient avoided butcher's meat, eggs and milk, the colon was washed out as far back as the ileo-cæcal valve, collosol ferromalt and lacto-dextrin were prescribed internally and intra-muscular injections of Sup. 468 and of the autogenous vaccine were made. The patient did well up to a point, but every injection of the vaccine, if the dose exceeded a quarter of a million, precipitated a fit on the morning following. This phenomenon would seem to point to a connection between the clinical condition and the activity of the patient's *Bacillus proteus hydrophilus*. The fits never entirely disappeared, and a re-examination of the excreta made one year later revealed the same micro-organism in company with the *Bacillus pyocyaneus*.

Case 23

A woman, aged twenty-nine, suffered from epilepsy and *Acne vulgaris*. She was a typical case of familial chronic intestinal intoxication. The patho-

genic micro-organism found in the excreta was the *Bacillus pyocyaneus* (25 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3503.
Percentage of the blood-sugar	= 0.118 grm.
Percentage of the blood-urea	= 67 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving. There were a few giant particles and many agglutinations precipitated.

The patient was dieted, the colon was washed out and three injections of the fæcal vaccine were made. The first vaccine (1 million) precipitated four fits the following day, but after that they remained absent for several months and the acne completely disappeared.

This case is reported first to emphasise the connection between *Acne vulgaris* and epilepsy and, secondly, to emphasise that, in spite of the hydration, certain of the protein particles were being subjected to severe dehydration as evidenced by the rise in the percentage of the blood-urea when the blood was withdrawn. Regarding the first point, the author has been particularly struck by the fact that in practically every case of *Acne vulgaris* he has examined some cerebral lesion coexisted, such as neurasthenia, *Petit mal*, epilepsy and insanity. It is interesting to note how many epileptics develop a *Seborrhœa faciei* when they are about to have an attack and how common is this condition in post-encephalitic Parkinsonism.

Case 24

A woman, aged thirty-five, had suffered from migraine with vomiting since a child. The patient's father died of phthisis, aged thirty-four, and she had a brother living who had generalised *Lichen planus* and toxic myocarditis. Menstruation started at fourteen, periods of amenorrhœa occurred frequently, lasting six or more months, during which vicarious menstruation occurred in the form of epistaxis. The patient had one child, and while carrying it suffered from *Hyperemesis gravidarum*. Recently the vomiting had become so incessant as to be at times hæmorrhagic and to cause a loss of 12 lb. in weight in two months.

The patient was very "nervy," she was a typical example of familial chronic intestinal intoxication, the pulse was 116 and the blood-pressures registered 115 and 80 mm. of Hg. respectively. The urine was loaded

with indican and ketone bodies. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 4.3 c.c.
Refractive index of the serum	= 1.3508.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Hardly a particle moving and those seen were either giant particles or clumps.
There was some precipitation <i>en masse</i> .	

The patient refused all treatment, went to a spa, and died shortly after her return.

Apart from the clinical condition, the severity of the case is emphasised by the enormous reduction in the suspension of the red blood-corpuscles. The blood-picture shows active dehydration and hydration. The dehydration attacked in the main the fat planet, as evidenced by the ketonuria, and the hydration occurred both in the brain and in the splanchnic area, affecting the stomach in particular. The patient had the clinical signs and symptoms of the cyclical vomiting of infants and spasmophilia, and this case shows all three conditions to be of the same nature.

Case 25

A woman, aged forty-two, had complained of migraine since a child. Both the father and mother suffered from asthma. The attacks of migraine occurred roughly every three weeks, and on over forty different occasions they had been accompanied by a unilateral ophthalmoplegia. Ordinarily an attack of migraine would last two days, but when an attack was accompanied by paresis of the right oculomotor nerve, the paresis started with ptosis on the fourth day and lasted from two to seven weeks. The patient was a very typical instance of familial chronic intestinal intoxication, the abdomen was one of the worst it was possible to feel, the pulse was 89 and arrhythmic, and the blood-pressures read 145 and 80 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.1 c.c.
Refractive index of the serum	= 1.3489.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 20 mgrm.

Ultra-microscopic picture of the serum = Very few particles moving with some giant particles and ringed particles. There were some giant particles, ringed particles and clumps precipitated. The Brownian movements were sluggish.

The patient was dieted, subjected to colonic lavage and had a course of injections of choline and Sup. 36, followed by the fæcal vaccine, with the result that she improved considerably and had no further attack of ophthalmoplegia.

This case is reported because some of the migraine attacks were accompanied by a paresis of the third nerve, showing that universal as the precipitation of the hydrated particles in the brain may have been, they nevertheless tended to select a special area, namely, in the region of the nucleus of the oculomotor nerve.

Case 26

A man, aged forty-one, had had very severe migraine with fits of crying since a child. Some attacks were accompanied by shivering fits and vomiting. The patient was a very typical example of familial chronic intestinal intoxication. He had an acute attack of migraine when the blood was withdrawn.

Suspension stability of the red blood-corpuscles = 0.01 c.c.
 Refractive index of the serum = 1.3481
 Percentage of the blood-sugar = 0.175 grm.
 Percentage of the blood-urea = 51 mgrm.
 Ultra-microscopic picture of the serum = Few particles moving with some giant particles and one or two small clumps. There were some giant particles and giant-particled clumps precipitated with one or two agglutinations.

The pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici*.

The patient was dieted, he had his colon washed out, took iodine, thio-amino-methyl-glyoxaline and thyroid substance internally, and had intramuscular injections of his fæcal vaccine and contramine, with the result that the attacks entirely disappeared.

This case shows again active dehydration and hydration occurring synchronously, but the dehydration is of a different type, affecting the sugar and urea planets instead of the fat planet.

A stimulation of the cells in the neighbourhood of the fourth ventricle causes circulatory, respiratory and intestinal troubles. It is by no means always easy to determine how far the lesion presented is due to cerebral changes

and how far it is caused by local changes. Taking the various forms of acro-asphyxia as representing the circulatory troubles, it would seem that the factors playing the greatest aetiological rôle are the altered chemico-physical changes undergone by the protein particles in the vessels involved. Hydration leads to vascular dilatation. When most pronounced, the precipitated protein particles collect in the peri-capillary lymphatic vessels, constrict the capillaries, render the area bloodless and cause the Raynaud phenomenon. When the precipitation takes place in the capillaries the vessels become filled with red blood-corpuscles and the hands are bright red. When the hydrated protein particles collect in the veins chilblains are liable to arise, and ulceration is apt to occur should the cyclical change of gelation occur. That these lesions arise more from the altered chemico-physical changes the protein particles undergo locally than from a precipitation in the brain, is suggested by the effect ultra-violet radiation and rubbing the hands with colloid silver have in ridding the patient of chilblains. Another reason why the circulatory disturbances are more probably of local than of central nerve origin is the prevalence of tachycardia over bradycardia. Bradycardia is the text-book circulatory vagotonic symptom, but it is seldom encountered, tachycardia being infinitely more common in cases of familial chronic intestinal intoxication. In practically every case of familial disease the heart is attacked, and it would appear to be the case that the tachycardia is occasioned by the precipitation of hydrated protein particles in the heart muscle, paralysing or causing degeneration of the nerve endings of the vagus. The respiratory troubles, of which asthma is the most common, are certainly due primarily to the arrest of hydrated protein particles in the peribronchial and peri-capillary lymphatic vessels and capillaries of the lungs. It may be that the central trouble occurred before, *in utero*, and determined which organ was to bear the brunt of the attack after birth. This would explain why one person has a cardiac lesion and another a pulmonary lesion. It is tolerably certain that the intestinal troubles are primarily central in origin, because hypertrophic stenosis of the pylorus can occur *in utero*. But, it is also equally certain that stimulation and paralysis of the intestinal tract can be produced by the local precipitation of hydrated protein particles, this being evidenced by the inflammatory changes occurring in and by the degeneration of Auerbach's plexus in such conditions as œsophageal achalasia, Hirschsprung's disease, etc. The local precipitation of hydrated protein particles in the walls of the intestinal tract shows why chronic intestinal intoxication looms largest in the picture of disease, the precipitation being caused both by a faulty dietary and by an inefficient elimination. These few words explain the relationship between

chronic intestinal intoxication, mal-co-ordination and mental disorientation. The autonomic nervous system may be involved in its sacral portion to cause that prevalent condition, "nocturnal enuresis." In bad cases involuntary micturition occurs during the day as well as during the night. The reason why the prefix nocturnal is required is simply because the protein particles in the plasma are more hydrated during the night than during the day. Proper dieting, efficient elimination and colonic lavage get rid of enuresis at once. There is no need to prescribe belladonna, and its use in the condition is based upon entirely false premises. When belladonna does good, and this is seldom, it acts by causing dehydration of the hydrated protein particles and not by paralysing the vagus, upon which it has no direct action.

Case 27

A woman, now aged twenty-seven, used to suffer as a child from giant urticaria and nocturnal enuresis. Later she developed very bad chilblains and a chronic nasal catarrh. When twenty-five years of age she acquired dysentery and jaundice, and since then her periods had been scanty and she had become "nervy." During these two years she lost approximately three stone in weight. Her teeth were bad, the tongue was furred and fissured, she had hyper-extended and wide-angled elbows and acro-asphyxia. The patient could not stand with her knees and feet together at the same time, she had central cupping of both optic discs, she complained of hyperidrosis, the pulse was 128, and the blood-pressures registered 120 and 65 mm. of Hg. respectively. An examination of the abdomen revealed definite evidence of chronic colitis and the blood-picture was as follows :--

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3490.
Percentage of the blood-sugar	= 0.168 grm.
Percentage of the blood-urea	= 61 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving. There were some giant particles, ringed particles, giant-particled clumps and agglutinations precipitated. The Brownian movements were very sluggish.

The patient became a vegetarian. She had a course of colonic lavage and of injections of Sup. 468, with the result that she improved enormously in health and had no more chilblains.

Case 28

A boy, aged ten, complained of nocturnal enuresis. The boy was pale, his ears stood out, he had hyper-extended elbows, a furred tongue, cupping of both optic discs and many of his teeth had been stopped. The pulse was 92 and the blood-pressures registered 95 and 40 mm. of Hg. respectively. The patient had an abdomen typical of chronic colitis and he was particularly tender over the appendix area. A bacteriological examination of the excreta revealed 75 per cent. atypical *Bacillus coli communis*. The boy was dieted (vegetarian), made to have his bowels opened two or three times a day, and received three injections of the fæcal vaccine. Within a space of two months the enuresis had completely disappeared.

Nocturnal enuresis may last into adult life, as depicted in the following case :—

Case 29

A man, aged twenty-four, had had nocturnal enuresis for over twenty years. He lost a sister from appendicitis when aged six. The patient suffered from chilblains and angio-neurotic œdema. His tonsils and adenoids were removed at six and both *antra* drained at fifteen. The patient was grossly mal-co-ordinated, his ears projected, he picked his nails, and could not stand with his knees and feet together. He had hyper-extended elbows and fingers. The palms were clammy, all the molars had been stopped, and the blood-pressures registered 90 and 60 mm. of Hg. respectively. The urine gave a violet colour with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. An examination of the abdomen showed the right colon and cæcum to be dilated and the left colon to be contracted. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (25 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3483.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 27 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with a fair number of giant particles and small giant-particled clumps. There was much precipitation, and in a minute or two complete precipitation <i>en masse</i> .

The patient was dieted, had a course of colonic lavage and injections of

Sup. 468 and of his own faecal vaccine. The nocturnal enuresis disappeared completely.

Enuresis strictly means "to make water in," but the word has acquired the significance that the act is involuntary. Although, when the trouble is pronounced and occurs in children, the act is generally involuntary, this is by no means so in milder cases affecting adults, as the two following reports show :—

Case 30

A woman, aged twenty-four, had suffered for some years from chronic constipation and recurrent attacks of *Herpes oris*. She had to get up three to four times at night to pass water. The patient's father and mother were rheumatic. The patient had suffered from chilblains affecting her heels since childhood, had had rheumatic fever twice, and bronchitis, furunculosis and *Acne vulgaris*. Her tonsils, adenoids and appendix had been removed. She presented the cardinal features of inherited disease, and an examination of the abdomen revealed tenderness in the four usual areas: sigmoid, splenic flexure, hepatic flexure and ileo-cæcal region. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkahigenes* (30 per cent.), while the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3502.
Percentage of the blood-sugar	= 100 grm.
Percentage of the blood-urea	= 42 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, with a fair number of clumps. There were some giant particles and giant-particled clumps precipitated.

The patient became a vegetarian; she had a course of colonic lavage and injections of contramine and of the faecal vaccine, and took lacto-dextrin and an emulsion of *Bacillus acidophilus* internally. She recovered completely, and was able to sleep through the night without being disturbed.

Case 31

A woman, aged fifty-seven, had suffered from having to get up four to five times at night to pass water for over thirty years, for which she had had innumerable operations without relief. She had been troubled also with leucorrhœa. The patient had threadworms for several years; she had had chronic indigestion and constipation all her life, had suffered from chronic nasal catarrh, jaundice and mucous colitis, and her appendix had been removed,

the operation being followed by widespread venous thrombosis (post-operative gelation). For the past nine years she had been troubled with sialorrhœa, dryness of the skin and pruritus. The patient presented most of the cardinal signs of inherited disease. Two of her sisters had oto-sclerosis. She had generalised arterio-sclerosis, and an examination of the abdomen showed the left colon to be contracted and the right colon and cæcum to be dilated. The patient was tender in the region of the flexures, the transverse colon was dropped and there were numbers of small diverticula. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.7 c.c.
Refractive index of the serum	= 1.3482.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 34 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a fair number of giant particles, both moving and precipitated.

The patient avoided butchers' meat, eggs and milk in large quantities. She had a course of colonic lavage, injections of Sup. 468 and of the fæcal vaccine and took hexyl-resorcinol internally. For the leucorrhœa contramine pessaries were prescribed. Within a space of three months the urinary trouble and leucorrhœa had much improved.

The following case is of considerable interest because it depicts an actual lesion of the *Cauda equina*.

Case 32

A woman, aged thirty-four, sought advice for inability to walk and for discomfort in the perineum. The patient was a typical example of chronic intestinal intoxication, and both she and her mother had had rheumatic fever. She had suffered so severely from menorrhagia and metrorrhagia for sixteen years that a pan-hysterectomy was performed, after which she developed incontinence of fæces and urine and wasted almost to a shadow. The operation did not improve the nerve condition, and when she was examined six weeks later she presented what was obviously a lesion of the *Cauda equina*, occasioned by an ascending infection of the nerve roots. The left leg was paretic and much wasted, the patient complained of pain in the back of the left leg and of numbness of the left buttock, posterior part of the right thigh and left foot. Both knee-jerks were present, the right being more active than the

left. The right ankle-jerk was present, but the left had vanished, and there were no abdominal reflexes. The patient was completely anæsthetic over the left buttock and the posterior part of the right thigh. She was unaware when urine passed, and her habitual constipation was aggravated by the fact that she had lost the sensation caused by the bowels wanting to work. The pathogenic micro-organism found in the excreta proved to be the *Bacillus acidi lactici* (20 per cent.). An examination of the blood showed the following :—

Suspension stability of the red blood-corpuscles	= 0·65 c.c.
Refractive index of the serum	= 1·3488.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 31 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but all were larger than normal and there were some giant-particled clumps. There were a fair number of giant particles and giant-particled clumps precipitated and the precipitation increased with time.

The patient was dieted, she had her colon thoroughly washed out, she received five injections of contramine (0·05 grm.), two of Sup. 36 (0·01 grm.) and three doses of the fæcal vaccine. When examined nine months later, the patient was found to have improved enormously in health. She had put on over a stone in weight, she could walk perfectly, but, of course, many of the signs and symptoms of the caudal lesion still remained. It is inconceivable that a micro-organism such as the *Bacillus acidi lactici* could possibly itself have ascended the nerve roots to cause the lesion in the *Cauda equina*. It is possible that the *Bacillus coli communis*, of which the *Bacillus acidi lactici* is possibly a mutation form, was the micro-organism responsible. But, it is more probable that the lesion was produced by the protein particles in the plasma which had been subjected to hydration by the toxic chemical substances reaching the blood-stream from the large intestine, and which had collected in the veins, causing venous congestion of the *Cauda equina*.

Cases illustrating such conditions as Raynaud's phenomenon, bradycardia and asthma are reported in the chapters dealing with disease and the skin, the circulatory system and the lungs respectively.

Inherited disease of the nervous system may attack the ventral horn cells and their nerve roots giving rise to a progressive spinal muscular atrophy (Werdnig-Hoffmann paralysis) and to a hypertrophic muscular paralysis (Leyden-Möbius's pseudo-muscular hypertrophy). The latter is illustrated by the following case, which is particularly interesting, in view of the discussion

above on nocturnal enuresis and because the patient's condition appeared to be aided by paying attention to the chronic intestinal intoxication.

Case 33

A boy, aged eight, was found four years ago to be unable to walk upstairs, and when placed upon the ground he was unable to get up without assistance. The patient's sister, aged eleven, suffered from nocturnal enuresis. The father was a victim of recurrent fever, and had periodic attacks of lumbago and sciatica, while the mother suffered from menorrhagia and metrorrhagia associated with migraine. Since six the patient had developed a progressive mental deterioration and become clumsy and fidgety. His face had many milia, most of the molars had been stopped, the scapulæ were winged and the elbows were hyper-extended. All the reflexes were absent, the pulse was 112 and the maximum blood-pressure measured 80 mm. of Hg. An examination of the abdomen showed that the boy had chronic colitis, and the pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (90 per cent.). It is interesting to note that the pathogenic micro-organism found in the father's excreta was the *Bacillus fæcalis alkaligenes* (80 per cent.), that a pure culture of the coccoid form of the same micro-organism was obtained from the blood, and was doubtless responsible for the recurrent fever. The father was a veterinary surgeon.

The patient was dieted, had a treacle enema at night-time when the bowels failed to be opened at least twice in the day, took lacto-dextrin with an emulsion of *Bacillus acidophilus* internally, and had injections of his fæcal vaccine, with the result as stated above.

Allied to the atrophic form of muscular paralysis is the peroneal atrophy (Charcot-Marie-Tooth paralysis) and to the hypertrophic form myotonia (Thomsen's disease). The author has seen a marked case of the former, in which the pathogenic micro-organism in the fæces proved to be the *Bacillus coli anaerogenes* (30 per cent.).*

The discussion up to this point has been confined to lesions more or less localised to the central nervous system, but it is incomplete unless mention is made of the nervous manifestations which occur merely as a portion of a general attack upon the whole body. This part of the subject embraces such clinical conditions as infantile convulsions, progressive lenticular degeneration, chorea and Huntington's chorea.

* Treatment aimed at relieving the chronic intestinal intoxication definitely arrested the condition.

Infantile convulsions, often labelled "spasmophilia" or "tetany," are common, and are caused, judged from experimental work on animals, by the precipitation of hydrated protein particles in the cerebral pericapillary lymphatic vessels and capillaries. The particles are hydrated in the first instance by the entrance into the blood-stream of poisonous substances from the large intestine, because the convulsions cease when the patient is dieted properly and when it is seen that the bowels are opened two or three times a day. Although the precipitation may occur in any part of the brain, the site of predilection is the grey matter around the fourth ventricle, the centre of the vagus, because *Laryngismus stridulus*, or croup, is the most common localising symptom. Spasmophilia is considered by many to be caused by rickets, but it may be encountered in non-rickety children. Moreover, rickets is only an external manifestation of protein hydration, as is the spasmophilia. The condition received the name of "tetany" because the signs and symptoms produced are the same as those occurring after a removal of the parathyroid glands. The increased nerve irritability characteristic of tetany and evidenced by Chvostek's sign and spontaneous contractures of the extremities is a sign of hydration of the dynamic resistance and is by no means peculiar to spasmophilia. Involuntary muscles as well may undergo spasm, and when the intestinal tract is involved the chronic intestinal intoxication, the original cause of the trouble, is accentuated. Spasmophilia may be characterised by cyclical vomiting associated with acetonuria and with œdema of the legs, the back of the hands and the dorsum of the feet. The vomiting is occasioned by the precipitation of the hydrated protein particles in the splanchnic area. The acetonuria is caused by some of the hydrated protein particles undergoing the cyclical change of dehydration whereby the fat planet is separated from the protein particles, being sent into true solution.

There is no fundamental difference between the cyclical vomiting of infants, the recurrent vomiting of adults, victims of a chronic intestinal intoxication, the persistent vomiting of pregnancy, post-operative vomiting, and seasickness. In all there is a varying degree of nerve hyper-excitability and there may be acetonuria. The œdema is caused by the precipitation of the hydrated protein particles in the vessels of the area affected. Œdema occurs because the presence of hydrated protein particles in a vessel causes dilatation and increased permeability of the vessel wall. It is interesting to observe that œdema may be congenital, showing that hydration may be inherited. In cases of congenital œdema, called "Meige's or Milroy's disease," there is always a marked family history of the condition. Children the victims of a chronic

intestinal intoxication are liable to develop spasmophilia after an operation owing to the hydrator action of the anæsthetic. It is these cases which link spasmophilia with heat-stroke and eclampsia. Post-operative spasmophilia is often characterised by a high temperature, cyanosis due to pulmonary congestion, convulsions, coma and death, as occur in heat-stroke. *Post-mortem* there is found to be cerebral degeneration, parenchymatous degeneration of the liver and kidneys, a varying degree of fatty degeneration of the myocardium and a necrosis of the mucous membrane of the colon. No better example of the connection between a lesion in the brain and one in the colon could be given than this. The convulsions in spasmophilia are fundamentally the same as those encountered in cerebral shock, of which eclampsia is one of the forms. Eclampsia occurs most commonly in the later months of pregnancy because the protein particles in the plasma become hydrated at this period. The hydration may be sufficient to make the blood give a positive Wassermann reaction in a non-syphilitic subject, and in such cases an injection of arsenobenzene may aggravate the hydration to produce eclampsia just as the hydrator action of the anæsthetic may precipitate spasmophilia. There is no fundamental difference between spasmophilia and so-called *Status lymphaticus*. *Status lymphaticus* is merely a form of shock occasioned by excessive hydration of the protein particles in the plasma. Cases of spasmophilia are particularly liable to *Status lymphaticus*, and the shock occurs when the anæsthetic increases the hydration sufficiently to cause sudden death. The anæsthetic most liable to act in this way is chloroform, because the hydrator action of the substance is greater than that of other anæsthetics in general use. The patient, always a victim of familial chronic intestinal intoxication, and therefore an individual whose protein particles are already hydrated, is usually being operated upon for tonsils and adenoids, and dies on the operating table with, but not from, a persisting thymus. Chronic hydration of the protein particles in the plasma leads to a hyperplasia of lymphoid tissue, hence the reason for the enlargement of the tonsils and adenoids and for the thymus persisting in certain cases of familial chronic intestinal intoxication, for the general lymphadenitis in syphilis, and for the enlarged spleen in malaria. If young animals are treated continuously with drugs exhibiting an hydrator effect, the thymus can be made to persist indefinitely. Such animals become anæsthetised with doses which fail to cause even sleep in healthy animals and are killed instantaneously with doses which are ordinarily harmless. Death is due not to the persisting thymus, but to the excessive protein hydration occasioning shock. When the protein particles undergo hydration the number of the protein particles in the plasma

is enormously reduced and the body attempts to make good the loss by manufacturing lymphocytes. The protein particles constituting the protoplasm of the lymphocytes enter the blood-stream, and not only add to the number of the protein particles therein, but also help to cause dispersion of the hydrated protein particles. It is due to an aggravation of the existing hydration which causes a seizure in a general paralytic, a condition fundamentally similar to infantile convulsions, and in both conditions acetone may be detected in the cerebro-spinal fluid. Much has been made of the fact that there is usually a hypo-calcaemia in spasmophilia and in tetany following removal of the parathyroid glands. This form of tetany is said to be caused by an excess of compounds of guanidin in the blood. As it vanishes with para-thor-mone and the percentage of the calcium in the blood rises when this compound is administered, the parathyroid glands have come to be regarded as containing the hormone of the calcium metabolism similarly to insulin of the sugar metabolism. There is no hormone for the metabolism of any adsorbed constituent, and this is indeed a blessing, because it would be only logical for those who so regard para-thor-mone and insulin to hunt for ductless glands secreting hormones for the metabolism of urea, uric acid, fat, amino acids, etc. Insulin lowers the percentage of the blood-sugar because it functions as a hydrator, an action exhibited by certain compounds of guanidin. Para-thor-mone prevents insulin and those compounds of guanidin from occasioning hydration, and overcomes the chemico-physical change when it is in being. When the protein particles are hydrated and dehydrated the percentage of the blood-calcium is lowered and raised respectively. The symptoms of tetany vanish when para-thor-mone is administered, and the percentage of the blood-calcium is raised because the hydrated protein particles are dispersed. Certain compounds of calcium act similarly and not because they restore to the blood the calcium it has supposed to have lost, for certain compounds of strontium and Sup. 468 are as effective. On the other hand compounds of barium tend to be harmful because the nucleus of barium is larger than that of strontium and calcium, a fact which imparts to the compounds a hydrator action. Insulin lowers the percentage of blood-calcium in cases of hyper-calcaemia. The whole question is purely one of hydration and dehydration, spasmophilia and tetany are not due to an excess of guanidin products in the blood, and para-thor-mone is effective, not because it acts upon the calcium metabolism, but because it causes dispersion of the hydrated protein particles. All children who develop convulsions are mal-co-ordinated, irritable and fidgety, some have night-terrors and sweat profusely during the night, further external manifestations

of protein hydration, and a few develop *Petit mal*, which may later pass on into epilepsy.

Progressive lenticular degeneration, although a rare condition, is nevertheless a very interesting one, and for most of the knowledge concerning it medicine is indebted to Kinnier Wilson.⁷ The condition is a familial one characterised by a symmetrical degeneration affecting the putamen, *Globus pallidus*, caudate nucleus, and internal capsule, and a sclerosis of the liver. Some of the cases commence with jaundice, and Wilson thinks it probable that the changes in the brain are due to the selective action of a toxine found in the liver. The sclerosis is of the portal type, and in some of the cases the spleen is enlarged, the whole suggesting a form of so-called "Banti's disease." In this form of splenic anæmia hæmorrhages occur, and these are liable to lead to a fatal issue. The actual fibrosis is the result of long-continued dehydration of the protein particles in the plasma, while the hæmorrhages are the result of hydration. Indeed, Banti's syndrome is one of the best clinical examples of concomitant dehydration and hydration or of long-continued dehydration succeeded by hydration. Therefore it is probable that in progressive lenticular degeneration the hepatic sclerosis is the result of dehydration, and the cerebral lesion of hydration. As sclerosis or fibrosis denotes a long-continued dehydration, and as dehydration is occasioned by the entrance into the blood-stream of intoxicants from the large intestine, it would seem to be most probable that progressive lenticular degeneration is merely one of the manifold symptoms of congenital disease. This idea is supported by the fact that degenerative changes affecting the abdominal viscera may be encountered in cases of amaurotic family idiocy and Mongolism. In so-called "Banti's disease," and in cases of progressive lenticular degeneration, the liver may evidence signs of fatty degeneration showing that the effects of protein hydration may make themselves felt in this organ as well.

When protein particles undergo extreme hydration the lipid fraction is strongly developed, and as amaurotic family idiocy is a sequence of pronounced hydration it is not surprising to find that the lesions affecting the abdominal viscera in this condition fall into the category known as "Gaucher's splenomegaly." Although Gaucher's splenomegaly is a rare condition, the author wishes to draw particular attention to it because it shows that nerve lesions are not different from lesions occurring in other parts of the body, and that there is nothing peculiar in the association of liver changes with brain changes in cases of progressive lenticular degeneration. "Gaucher's disease" so-called is a congenital and familial condition characterised by the deposit of

lipoid material in the endothelial cells of the vessels, by an enlargement of the spleen and liver, by a brownish pigmentation of the exposed parts of the skin, by hæmorrhages, by leucopenia, and by delayed clotting of the blood. The Gaucher cells, which are found in the lymphatic glands and bone-marrow as well as in the spleen and liver, are endothelial cells containing lipoid material which Epstein and Lieb showed to be a sphingo-galactoside called "kerasin," and ether-insoluble phosphatides. In the type of splenomegaly found in cases of amaurotic family idiocy, a type known as "Niemann-Pick's disease," the lipoid material is not confined to the endothelial cells but is distributed in all possible cells of the body^{8, 9, 10, 11}.

There seems reason to believe that ordinary chorea is due in the main to damage sustained by the cells in the *Corpora Luysii* between the optic thalamus and the *Substantia nigra*. The association of chorea with rheumatic fever is probably no more than accidental and occurs merely because rheumatic fever is one of the most common infections caused from within, primarily by a chronic intestinal intoxication. In the author's opinion rheumatic fever is an infection occasioned by streptococci and possibly by other micro-organisms ordinarily saprophytic, which become pathogenic in a patient whose resistance has been lowered by a chronic intestinal intoxication. It is possible that rheumatic fever may be caused by the protein particles in the plasma rendered abnormal by poisonous chemical substances reaching it from the large intestine, without the intervention of micro-organisms. The author feels most strongly that rheumatic fever is not a specific infection, that in some instances it is merely an intoxication, a view supported by three significant facts: (1) that the family history of rheumatic fever is strong; (2) that rheumatic fever tends to recur; (3) that it is frequently followed by myositis, fibrositis and neuritis and by such common clinical conditions as lumbago and sciatica, which are definitely non-bacterial in origin. Chorea may appear as one of the rarer complications of pregnancy, when it is most prone to affect *primiparæ*. *Chorea gravidarum* is probably the result of an infection occurring in a woman whose resistance is being lowered by the chemico-physical changes the dynamic resistance undergoes as the result of the pregnancy.

Chorea is not an uncommon sequence of canine distemper, and like its less severe sister symptom hysteria, it is most likely to be precipitated by undue muscular exertion before the animal has sufficiently recovered from the distemper. This post-infective chorea is of very great interest, as it would seem to be most likely due to altered chemico-physical changes affecting the

protein particles in the blood-stream. After a fever there are always some hydrated protein particles left behind. These hydrated protein particles are liable to collect in veins where they may undergo gelation, and the thrombosis resulting may occasion chorea. But, chorea is more likely to be precipitated by the hydration being augmented, as occurs in excessive muscular exertion, which in a weak animal causes shock. In shock the blood collects in the big vessels, the peripheral circulation is depleted and the hydrated protein particles in the plasma are liable to become precipitated in the peri-capillary lymphatic vessels and capillaries of the brain, to produce chorea as one of manifold symptoms. It has often occurred to the author that the so-called post-influenzal, post-vaccinal, post-measles, etc., encephalitis is due, not to ultra-microscopic micro-organisms, but to the collection of hydrated protein particles in the brain causing dehydration of the nerve cells. There is no fundamental difference between cerebral shock, various nerve lesions and encephalitis, and owing to the seeming ubiquity of the ultra-microscopic viruses, it is possible that some of the supposed cases of infective encephalitis are due not to specific micro-organisms but to hydrated protein particles splitting up the protoplasm of the nerve cells, or to ultra-microscopic particles being broken off from the hydrated protein particles and acting as foreign bodies.

Concerning Huntington's chorea little is known except that it is an hereditary condition and follows the Mendelian law of hybrids. A recent paper was published by Worster-Drought and Allen¹² with a report of two cases. The condition is characterised by chorea, grimaces, explosive speech, a grotesque gait and later by dementia. The succeeding dementia is not invariable. Most patients show a marked tendency to repeat phrases and sentences. The following cases illustrate the points raised above.

Case 34

A woman, aged thirty, complained of rheumatism of two years' duration. The patient's mother was rheumatic and her father succumbed to cholecystectomy at the age of sixty ; one brother died of convulsions, aged eighteen months, one brother of a cerebral tumour, aged sixteen, having had severe convulsions as a child, and one sister of phthisis, aged twenty-three. The patient had convulsions and croup as a child, she suffered much from chilblains and had frequent attacks of depression. Menstruation began at the age of fifteen, and the periods never lasted for more than two days. The patient presented many signs of inherited disease, the pulse was 64 and the blood-

pressures registered 140 and 100 mm. of Hg. respectively. The patient was very tender in both hypochondria and in both iliac fossæ. The pathogenic micro-organisms found in the excreta were the *Bacillus coli anaerogenes* and the *Bacillus fecalis alkaligenes*.

This case illustrates the after-history of a patient who had been a victim of convulsions as a child.

Case 35

A woman, aged twenty-five, suffered from chorea when aged nine, and again when she contracted syphilis about two years before being admitted into hospital suffering from eclampsia. The patient's mother died of cerebral hæmorrhage at the age of fifty-four and her father of Bright's disease at the age of fifty-six. She was a typical example of familial chronic intestinal intoxication, but had never had rheumatic fever or rheumatism. Menstruation began at the age of sixteen. She was seven months pregnant when admitted and had had three previous miscarriages. On November 10th she was recognised to have a syphilitic lesion of the tongue, and an intravenous injection of novarseno-benzene was made. This was repeated on the 17th and 24th. Two days later the patient complained of severe headaches and vomiting, and was admitted into the hospital on the 27th more or less unconscious. On admission the urine was found to be loaded with protein and the blood-pressures registered 195 and 130 mm. of Hg. respectively. On the following day she miscarried a macerated seven-months *fœtus* (female). The blood-picture on November 30th was as follows :—

Suspension stability of the red blood-corpuscles	= 5·5 c.c.
Refractive index of the serum	= 1·3490.
Percentage of the blood-sugar	= 0·118 grm.
Percentage of the blood-urea	= 35 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some refractile giant particles, ringed particles and giant-particled clumps. There were a few giant particles and ring particles precipitated.
Wassermann reaction	= Positive (+ + +)

An uneventful recovery was recorded.

This case is of particular interest, first because the chorea relapsed when the patient contracted syphilis, the infection *par excellence* for occasioning protein hydration; secondly, because the injections of arseno-benzene augmented an already existing hydration sufficiently to cause eclampsia. The

blood-picture shows the benefit which was wrought by the mis-carriage—hydration giving place to the cyclical change of dehydration, as evidenced by the great reduction in the suspension stability of the red blood-corpuscles and by the ultra-microscopic appearance of the protein particles.

Case 36

A girl, aged thirteen, sought advice for rheumatism. The patient's mother suffered from rheumatism, and had had typhoid fever, followed by pleurisy and phlebitis. The patient had been operated upon three times for tonsils and adenoids, and had had chorea seven years previously. The patient was a brunette, pale and mal-co-ordinated. Many of her molars had been stopped, she had hyper-extended and wide-angled elbows and acro-asphyxia. The reflexes were sluggish, the pulse was 79, and the blood-pressures registered 105 and 60 mm. of Hg. respectively.

The patient was always getting a "stitch," and she was definitely tender in both iliac fossæ. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.7 c.c.
Refractive index of the serum	= 1.3495.
Percentage of the blood-sugar	= 0.166 gm.
Percentage of the blood-urea	= 23 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving and all were larger than normal. There were many giant particles, ringed particles, and giant-particled clumps precipitated as well as some precipitation <i>en masse</i> .

The patient did not undergo the treatment advised, and the case is reported merely to emphasise the fact that the chorea pre-dated the rheumatism by some years.

Case 37

A man, aged forty, sought advice for abdominal pain due to colitis, which had been present for over a year. He had had rheumatic fever, with chorea, and lumbago and sciatica since. He had also had scarlet fever and typhoid fever. The patient was grossly mal-co-ordinated, both mentally and physically. He could not stand with his knees and feet together at the same time. The teeth were decayed, the tongue was furred and fissured, and the left eye was a blind one as a result of a squint. The pulse was 70 and the blood-pressures registered 85 and 50 mm. of Hg. respectively. The urine gave a marked reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde

and contained a trace of protein. The colon was tender, particularly in the region of the flexures. The patient had a boy aged eight, who suffered from glandular fever and cyclical vomiting with ketonuria. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (10 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.25 c.c.
Refractive index of the serum	= 1.3492.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 15 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some refractile giant particles and ringed particles. There were some large and refractile giant particles and ringed particles precipitated.

The patient was dieted ; he had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and had injections of contramine and of his fæcal vaccine. The patient improved enormously.

The case is one of long-continued hydration, evidenced clinically in the main by the sub-normal blood-pressures and hæmatologically by the low percentage of the blood-urea. It is interesting to note that the rheumatic fever and chorea were followed by other rheumatic manifestations.

A series of cases are reported below illustrating the link between the definitely familial lesions of the central nervous system and the lesions more truly acquired.

Case 38

A girl, aged twelve, sought advice for severe asthma, of which one of the worst features were fainting attacks. The trouble began about four years previously with a typical nervous breakdown, necessitating a stay in bed for over three months. For the first week of the attack the child was unconscious. The patient was a typical example of familial chronic intestinal intoxication ; she suffered from a chronic nasal catarrh, for which she had had three operations upon the tonsils without benefit ; she had acro-asphyxia and well-marked *Keratosis pilaris*. The pulse was 119 and slightly arrhythmic, the blood-pressures registering 110 and 60 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus coli anaerogenes* (80 per cent.) and in the excreta of the patient's sister, who was constituted somewhat similarly, the *Bacillus proteus hydrophilis* (25 per cent.). An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·6 c.c.
Refractive index of the serum	= 1·3489.
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood-urea	= 38 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some giant particles and a few ringed particles. There were some giant particles and giant-particled clumps pre- cipitated, with a tendency towards general precipitation.

The patient and her sister were placed upon a vegetarian diet, the colon was washed out and the bowels were opened two to three times a day, colossal ferromalt was prescribed internally and a few injections of the fæcal vaccine were made, with an excellent result in both cases.

Case 39

A girl, aged eighteen, had had severe asthenia since childhood and suffered in addition from chilblains and hay-fever. The patient was thin and had a sallow complexion. She squinted and was blind in the squinting eye. There was a bilateral nystagmus, the optic cups were developmentally defective, being very depressed and very white. The teeth were badly developed and had spaces between them. The scapulæ were winged and the elbows were wide-angled and hyper-extended. The hands were very cold and the fingers long, tapering and hyper-extended. The patient was grossly mal-co-ordinated, very fidgety, and mentally deficient. The pulse was 112 and slightly irregular, and the blood-pressures read 145 and 50 mm. of Hg. respectively. The patient had *Acne vulgaris*. An examination of the abdomen revealed tenderness in the usual four places, both iliac fossæ and both hypochondria.

An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3500.
Percentage of the blood-sugar	= 0·093 grm.
Percentage of the blood-urea	= 20 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and these were either giant particles or ringed particles. There were more particles precipitated in the form of giant particles, ringed particles, clumps and small agglutinations. The Brownian movements were very sluggish.

All treatment was refused.

Case 40

A woman, aged twenty-eight, an only child, suffered from manic depressive psychosis. The patient's mother suffered from migraine. The patient used to have chilblains and hay-fever; menstruation began at the age of twelve and was normal for five years, when amenorrhœa occurred, lasting for eight months, the time the patient was in an asylum for her first attack. When the second attack occurred the periods ceased. The patient had mal-developed, irregular and widely-spaced teeth; *Keratosis pilaris* was marked on the extensor surfaces of the arms and acro-asphyxia was pronounced. The pulse was 78 and the blood-pressures registered 90 and 70 mm. of Hg. respectively. An examination of the abdomen revealed definite evidence of chronic colitis and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3496.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 25 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving but they were mostly giant particles, ringed particles and giant-particled clumps. There were some giant particles, ringed particles, clumps and a few agglutinations precipitated. The Brownian movements of the particles were sluggish.

Unfortunately the patient did not undergo the treatment advised.

Case 41

A woman, aged thirty-four, while always mentally deficient, had been acutely insane for six weeks before she was examined. The patient's father was peculiar mentally and her mother was a dipsomaniac. The paternal grandfather and the mother's brother committed suicide, the latter having spoken to nobody for over twenty years. The patient was a very typical example of familial chronic intestinal intoxication. The tonsils and teeth had been removed without benefiting the clinical condition. The patient was in the habit of biting her nails. The pulse was 86 and the blood-pressures registered 115 and 60 mm. of Hg. respectively. An examination of the abdomen revealed tenderness in both hypochondria and in the right iliac region. The pathogenic micro-organism found in the excreta was the *Bacillus coli anaerogenes* (20 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.45 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 30 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving with some giant particles and ringed particles. There were more particles precipitated as giant particles, ringed particles and giant-particled clumps. The Brownian movements were very sluggish.

The patient became a vegetarian, the colon was washed out and she received several injections of Sup. 468, para-thor-mone, choline and of her own fæcal vaccine, with the result that she improved sufficiently to be able to go about and enjoy herself.

Case 42

A man, aged thirty-three, had a mental aberration concerning sex matters and suffered from a non-specific urethritis. His father was a chronic alcoholic and the mother a pronounced neurasthenic. The patient looked wild, his facial expression was fixed, he could not stand with his knees and feet together at the same time, the elbows were wide-angled and hyper-extended, and there was acro-asphyxia. The patient had had his teeth, tonsils and appendix removed without benefit. He was backward at school, had no memory, could not concentrate, and was liable to fits of melancholia. The pulse was 72 and the blood-pressures read 115 and 75 mm. of Hg. respectively. The left colon was contracted, there was tenderness in both hypochondria and the ascending colon and cæcum were dilated. The urine gave a most intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (80 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3492.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 34 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving and these were either giant particles or ringed particles. There were more particles precipitated as giant particles, ringed particles and giant-particled clumps. The Brownian movements were sluggish.

The patient was dieted, his colon was washed out and he received a course of injections of para-thor-mone and of his own fæcal vaccine. He improved immensely, and his non-specific urethritis completely disappeared.

Case 43

A man, aged thirty-eight, had severe habit spasms of the facial muscles and a lowered mentality, which prevented his following an occupation. The patient's mother died of gastric ulcer at the age of sixty-one, and the father as the result of prostatectomy at seventy-five. The patient suffered from rheumatism and had a chronic nasal catarrh, for which he had been operated upon without success. The teeth and tongue were bad, there was pronounced *Arcus senilis*, central cupping of both optic discs and acro-asphyxia. He perspired profusely, was very "nervy" and had a dropped, elongated and narrowed heart. The pulse was 116 and the blood-pressures registered 150 and 75 mm. of Hg. respectively. An examination of the abdomen revealed definite evidence of chronic colitis. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* and the blood-picture was as follows:—

Suspended stability of the red blood-corpuscles	= 0.4 c.c.
Refractive index of the serum	= 1.3507.
Percentage of the blood-sugar	= 0.175 gm.
Percentage of the blood-urea	= 25 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving with some ringed particles. An occasional giant particle precipitated.

The author has no record of the effect of treatment upon this patient.

Case 44

A woman, aged thirty-five, but looking fifty-five, was one of the worst cases of asthenia the author has seen. The patient was tall, thin, of sallow complexion and presented almost every sign of inherited disease. The patient was the only one of five children to reach adult life, the other four having succumbed to infantile convulsions. No further family history was available. She harboured every ailment imaginable. She had had numerous nasal operations for sinus trouble and her abdomen had been opened six times for appendicitis and tube trouble with enteroptosis, uteropexy, etc. Menstruation began at the age of twenty and the periods were irregular, scanty and painful. The whole of the colon was very painful and appeared to be contracted.

The pathogenic micro-organism found in the excreta was the *Bacillus pyocyaneus* (10 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 70 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving and these were giant particles and clumps whose Brownian movements were very sluggish. There were many more very refractile giant particles, ringed particles and clumps precipitated.

The author has no record of the effect of treatment upon this case, and the case is reported to show the futility of surgery in inherited disease.

Case 45

A man, aged twenty-eight, had been a chronic alcoholic for eight years. The patient's father had a nervous breakdown when the boy was three years of age, and had been hopelessly neurasthenic since.

The patient's sister was in an asylum, and a brother was a confirmed drunkard.

The patient was mal-co-ordinated, he presented most of the signs of inherited disease, was marked by bygone *Acne vulgaris*, the terminal phalanges of the fingers were slightly clubbed, and the heart was elongated, dropped and narrowed. The pulse was 92 and the blood-pressures registered 120 and 85 mm. of Hg. respectively.

An examination of the abdomen revealed definite evidence of chronic colitis.

The pathogenic micro-organism found in the excreta was the *Bacillus fœcalis alkaligenes* (15 per cent.), and the blood-picture was as follows, no alcohol having been consumed for six weeks:—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 18 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few giant particles and giant-particled clumps moving and precipitated. There were one or two agglutinations precipitated.

The author has no record of the effect of treatment in this case, but reports it as showing the influence of inherited disease in causing dipsomania.

Case 46

A girl, aged eighteen, grossly mal-co-ordinated, moody and quite unmanageable, was brought to the author because she suffered from chilblains in the summer as well as in the winter. The patient had had her tonsils, adenoids, appendix and many teeth removed. She used to suffer from winter bronchitis as a child, and menstruation began at the age of seventeen and had been characterised since by amenorrhœa. The pulse was 96 and the blood-pressures registered 95 and 60 mm. of Hg. respectively. The patient was terribly constipated, which rendered a satisfactory examination of the abdomen impossible. The pathogenic micro-organism found in the excreta was the *Bacillus fœcalis alkaligenes* (25 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3472.
Percentage of the blood-sugar	= 0.075 gm.
Percentage of the blood-urea	= 15 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving but all were larger than normal and very refractile. There were some giant-particled clumps moving. There were some large giant-particled clumps precipitated and a tendency to form precipitation <i>en masse</i> .

The patient was dieted, had the colon washed out, took colloid ferromalt and lacto-dextrin internally and received injections of Sup. 468 and of the fœcal vaccine. The hands were rubbed with colloid silver and iodine alternately and exposed to ultra-violet rays. The patient recovered completely and became a useful member of society.

Case 47

A woman, aged twenty-five, sought advice for asthenia. The patient's father died of disseminated sclerosis, her mother was crippled with rheumatism, and a sister suffered from wide-spread vitiligo. The patient suffered from chilblains, hay-fever, migraine and was a homo-sexualist. She had had two attacks of rheumatic fever. Menstruation began at the age of fifteen and the periods were irregular and either profuse or scanty. The patient had a sallow

and pigmented complexion. She had many tricho-epitheliomatous growths on the lower eyelids and she presented most of the classical signs of inherited disease. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·5 c.c.
Refractive index of the serum	= 1·3490.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a fair number of giant particles. There were a few giant particles and ringed particles precipitated, with one or two clumps.

The patient refused to undergo treatment.

Case 48

A man, aged forty-seven, sought advice for neurasthenia which appeared to be aggravated by a non-specific urethritis. The patient had insomnia, was at times acutely depressed and had frequently talked of suicide. He was troubled with a chronic nasal catarrh, pharyngitis, rheumatism and chronic indigestion and constipation. He had had several nasal operations, most of his teeth had been removed and he had been operated upon for hernia and undescended testicle. He had been advised to have his appendix removed and to be short-circuited for what had been diagnosed as a duodenal ulcer, as melæna had occurred on more than one occasion. The patient had a vacant expression ; he was quite bald and presented most of the classical signs of inherited disease. Both optic discs were deeply cupped. He was becoming increasingly deaf and the blood-pressures were sub-normal. The whole of the colon was tender on palpation and the pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (15 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3501.
Percentage of the blood-sugar	= 0·068 grm.
Percentage of the blood-urea	= 30 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving and these were either giant particles or ringed particles. There were some very refractile giant particles, ringed particles and giant-particled clumps precipitated, as well as several tiny particles precipitated <i>en masse</i> .

One of the greatest points of interest in this case is the reduction in the percentage of the blood-sugar. Had this case been examined from a different angle and the hypo-glycæmia detected, the whole of the nervous condition would have been ascribed to the low blood-sugar and glucose would have been prescribed. Needless to say, the hypo-glycæmia was, like the neurasthenia, dependent upon the protein hydration. Treatment which aimed at removing the cause and did not contain glucose, raised the blood-sugar to 0.112 grm. per cent., and improved the neurasthenia.

Summary

Familial disease can be caused both by the mother and by the father. Disease is brought about mainly by hydrated protein particles in the plasma subjecting the protein particles which constitute the cytoplasm of cells to abnormal chemico-physical changes. The fact that the father can be responsible for disease in his children suggests that certain chemico-physical changes occur in his sperm which have the effect of either directly damaging the organs in the embryo, or indirectly by subjecting the protein particles in the plasma of the embryo to hydration. It is highly improbable that the exact nature of the chemico-physical changes occurring in the sperm will ever be known, and it is equally highly probable that the chemico-physical changes affect the spermatozoon as a whole and not solely its chromosomes.

Inherited disease may be so marked as to prevent the cerebral cortex from developing, and when this occurs anencephaly is the result. When it is less marked, certain of the cortical cells are prevented from developing, or are so damaged as to produce such conditions as amaurotic family idiocy, idiocy with or without blindness and spastic paralysis, deaf-mutism, oto-sclerosis, mal-co-ordination, errors of refraction, colour blindness, etc. In other cases the damage done may be more marked in the brain-stem than in the cortex, and the clinical signs and symptoms produced depend first upon whether the mid-brain or the hind-brain bears the brunt of the attack, and secondly, whether the attack causes stimulation or degeneration of the nerve cells. When the mid-brain suffers most the main sign produced is mal-co-ordination, caused by interference with the extra-pyramidal system, and to this are added other and various signs which give rise to such clinical conditions as tetany, *Petit mal*, epilepsy, migraine, etc. When the hind-brain suffers most the patient presents one or more of the signs and symptoms commonly referred to as vagotonia.

It is a significant point that over-muscular activity and signs and symptoms

referable to stimulation of the vagus exceed muscular palsies and signs and symptoms referable to stimulation of the sympathetic nervous system. This is possibly to be explained by the pyramidal and extra-pyramidal systems and the autonomic or para-sympathetic (vagus) and sympathetic systems each constituting a whole or a complete reflex circuit. So far as the extra-pyramidal and pyramidal systems are concerned the former deals with posture, the static arc of the reflex circuit, and the latter with muscular activity, the dynamic arc. So far as the vegetative nervous system is concerned the autonomic nervous system represents the dynamic arc and the sympathetic nervous system the static arc. Even when the cord bears the brunt of the attack the clinical signs and symptoms most frequently presented are those produced by stimulation of the sacral autonomic nervous system, as evidenced by the ubiquity of enuresis. When actual muscular inactivity occurs it is found to be due rather to local damage sustained by the muscles themselves than to actual lesions in the central nervous system, as evidenced by the muscular atrophies and pseudo-muscular hypertrophies. When the clinical signs and symptoms produced point to the stagnation of hydrated protein particles in the brain, the stagnation is more frequently general than local, in spite of the fact that the clinical examination points to a definite and small area being involved. This accounts for the fact that in every case of familial disease affecting the central nervous system, whether the case be labelled as one of idiocy, spastic paralysis, epilepsy, etc., the patient presents one or more of the general manifestations such as neurasthenia, asthenia, mal-co-ordination, cerebral disorientation, etc. The still more important fact is accounted for, namely, that in every case of familial disease affecting the central nervous system the whole body is affected and not the central nervous system only. *Hence there is only one disease.*

Mal-Co-ordination and the Nervous System

Under this heading an attempt is made to correlate Alexander's work with medicine. The author considers the best way to do this is to draw attention to certain widespread examples of mis-directed activity which receive scant recognition at the hands of medical men, but which are often the forerunners of serious and irremediable manifestations of disease.

The reason for coupling mal-co-ordination with the nervous system is because a mis-directed activity of the physical mechanism is due, in most instances, to a mis-directed activity of the nervous mechanism. To facilitate description further, it is necessary to sub-divide the brain into three parts : (1) the cerebral

cortex ; (2) the pyramidal reflex circuit ; (3) the centres of the vegetative nervous system.

As a special section is devoted to discussing the rôle played by the vegetative nervous system in disease, it is not considered here, although a remark or two in passing is desirable. The centres of the vagus, the exciter arc of the vegetative nervous system, most probably represent the primitive brain, since they watch over the two main functions of animal life ; namely, feeding and reproduction, and control later functions such as breathing and blood-circulation. It is probable also that these centres have their origin in the œsophageal ganglia, which make their first appearance in the rotifers. The rôle these centres play in mal-co-ordination of the nervous mechanism is quite a subsidiary one compared with that of the cerebral cortex, and is of even less importance than that of the pyramidal reflex circuit. Indeed, it may be said that mis-directed activity of the centres of the vagus is much more frequently due to a mis-directed activity of the conscious control than *vice versa*. The cerebral hemispheres, the main seat of the conscious control, may suffer serious congenital defects, such as do not occur in the base of the brain-stem. This is likewise true of the pyramidal reflex circuit in the upper part of the brain-stem, the main seat of the instinctive guidance.

The greater importance of the mis-directed activity of the cerebral cortex in the production of mal-co-ordination than of the other two parts of the brain probably accounts for two important facts : (1) the absence of a mal-co-ordination in animals in the wild state except when disease has attacked them ; (2) the greater frequency of mal-co-ordination in animals under domestication. These two facts lend further support to the view that mal-co-ordination in man may be both hereditary and congenital. It is interesting to note that when mal-co-ordination and disease are encountered in animals the most common manifestation of the latter is rheumatism, and one, if not the earliest, pathological change is found to occur in the heart and aorta.

Although a mis-directed activity of the neurones in the cerebral cortex more or less controls a mis-directed activity of the pyramidal reflex circuit, the manifestations of the mal-co-ordination resulting are more pronounced in the latter because a physical deformity strikes the eye more than a mental aberration. It is for this reason that the upper part of the brain-stem is considered before the cerebral hemispheres. Moreover, it is only by an extension of the pyramidal reflex circuit through the tegmentum that the cerebral hemispheres came into being. The pyramidal reflex circuit is made up of the pyramidal system, the exciter arc, and the extra-pyramidal or proprioceptive system, the

inhibitor arc. Mal-co-ordination, expressed as undue muscle tension, may be said to result when the balance between the two arcs of the pyramidal reflex circuit is unequal. An upset of the normal equilibrium may be caused or augmented by the mis-directed activity of the other two parts of the brain, but much more so by that of the cerebral cortex than by that of the vegetative nervous system. This point emphasises again the generalship of the cerebral cortex over the rest of the central nervous system.

Although the pyramidal reflex circuit is a whole, the extra-pyramidal arc is more concerned with posture, while the pyramidal arc is more responsible for the muscular movements which enable the posture to be assumed or changed; the extra-pyramidal arc is perhaps the more important of the two, and thus differs from the inhibitory or sympathetic arc of the vegetative nervous system. While the mis-directed activity of the vegetative nervous system is the result of either a hyper- or a hypo-activity of the vagus, the exciter arc, the position is reversed in the case of the pyramidal nervous system. This is possibly due to the fact that the sympathetic nervous system has no centre in the brain. Many text-books state that the centre of the sympathetic nervous system is situated in the region of the *Corpus Luysii*, but the experimental evidence upon which this is based is slender. The clinical manifestations resulting from interference with the normal activity of the vegetative nervous system are far more frequently vagotonic than sympathetico-tonic, and this point again stresses the importance of the brain in disease. Furthermore, any interference with the normal activity of the cerebral cortex affects the exciter more than the inhibitor arc of the vegetative reflex circuit. This is because the cerebral centres of the vagus are connected with the cerebral cortex, and there is no evidence that there is a similar connection between the cerebral cortex and the sympathetic nervous system.

As many, if not most, of the clinical signs and symptoms of disease of the brain result from damage sustained by areas with which the extra-pyramidal system is intimately connected and through which extensions are carried to the cerebral cortex, it is necessary to trace in brief the course taken by the proprioceptive fibres. In the spinal cord the proprioceptive fibres take different courses according to whether they are directed to the cerebellum or to the brain-stem, from which they are projected to the cerebral cortex. Some of the fibres end in the *Nucleus dorsalis* of Clarke, whence they are carried to the cerebellum in the dorsal and ventral spino-cerebellar tracts. The other proprioceptive fibres are conveyed upwards in the *Fasciculus gracilis* and *Fasciculus cuneatus*. These fibres cross in the *Medulla oblongata*,

and are conveyed to the thalamus *via* the medial lemniscus or fillet. After another synapse they are projected to the cerebral cortex. In the brain-stem the extra-pyramidal system has various centres such as the *Corpus striatum*, *Globus pallidus*, *Corpus Luysii* and the *Substantia nigra*, one or more of which are damaged in most cases of disease affecting the central nervous system. Indeed the damage sustained by the cells marking the centres in the brain-stem plays a greater rôle in acquired disease of the nervous system than the damage sustained by the cells in the cerebral cortex, a view contrary to the one usually expressed.

Another important area in the mid-brain which helps to regulate posture is the *Nucleus ruber*. This area of grey matter is connected with the extra-pyramidal system mainly with the *Corpus Luysii* and the *Substantia nigra* and also with the cerebellum. It is partly through the *Nucleus ruber* that the extra-pyramidal system is brought into connection with the frontal lobes of the cerebral hemispheres. Fibres of the extra-pyramidal system are projected directly to the cerebral cortex mainly through the thalamus and in part through the *Substantia nigra*. It is probable that fibres from the area of the *Corpus Luysii* are also projected directly to the cerebral cortex; the great interest of this structure lies in the fact that it is situated in the sub-thalamic portion of the mid-brain, a part of the brain where hydrated protein particles become precipitated to produce sleep, fits, etc. The reason why the mid-brain is one of the main areas picked out in acquired disease is probably because it is the least modified part of the embryonic neural tube, the part containing centres of the vegetative nervous system, and the part having the richest blood-supply.

If, as stated above, the cerebral cortex is the most vulnerable part of the cerebrum, why should this be so? The explanation is to be found by drawing a distinction between acquired and congenital disease. Acquired disease is due to the altered chemicophysical changes the protein particles in the plasma undergo. Consequently, the areas affected thereby depend largely on the blood-supply. In congenital disease, on the other hand, the tissues are involved before there is a blood-supply, and so far as the central nervous system is concerned, when it is damaged, the cerebral cortex is damaged most. For example, there is no lesion in the brain-stem comparable to anencephaly, amaurotic family idiocy, Little's disease, oto-sclerosis, etc.¹

The clinical example depicting best the features presented when acquired

¹ So far as it concerns evolution, the fact that the most vulnerable and highest developed part of the body is damaged *in utero* cannot be over-emphasised.

damage is sustained by the pyramidal reflex circuit is *Paralysis agitans*, or so-called "Parkinson's disease."

In the first place, the main damage is sustained by the extra-pyramidal arc. In the second place, the lesion is primarily vascular. In the third place, it is merely an end-stage of mal-co-ordination. A victim of *Paralysis agitans* is a candidate for the condition years before the signs and symptoms are sufficiently pronounced to be labelled, and he presents the features of mal-co-ordination years in advance, so much so that a true observer can foretell the advent of the Parkinsonism. If the mal-co-ordination is corrected the progress of the condition can be checked, a manoeuvre, helped by ridding the patient of his chronic intestinal intoxication and by correcting the abnormal chemico-physical changes presented by the protein particles in the plasma. *Paralysis agitans* is an ideal condition to study, not only because of what has been stated above, but also because it is often a sequel to encephalitis and because of its frequent association with rheumatism, the commonest manifestation of disease.

Post-encephalitic Parkinsonism is an excellent example of extreme acquired mal-co-ordination, and if the condition was viewed from the mis-directed activity standpoint much could be done to prevent the infirmity, and even when well established the application of Alexander's technique to correct mal-co-ordination is more productive of benefit than prescribing hyosine, pilocarpine, strychnine, etc. Rheumatism occurs more commonly in mal-co-ordinated than in co-ordinated patients; indeed, it is highly probable that mal-co-ordination is in part responsible for rheumatism being the commonest manifestation of disease. Furthermore, rheumatism accentuates and may even cause mal-co-ordination.

It is a fact that the persistence of pain following rheumatism is more frequently the result of over-muscular contraction, the expression of the mal-co-ordination, than of the continued activity of the arthritis, myositis, fibrositis, neuritis, etc., the undue muscle tension being brought about in the first instance as an attempt to protect the inflamed area. The continuance of the pain leads the unwary physician to prescribe treatment for the rheumatism which no longer exists, whilst his attention should be centred on correcting the habitual wrong use of the whole body.

Still more important are the interesting facts that the deformity may lead to disease of healthy bones and to an alteration of psyche where there is no realisation of the deformity. The fact that mal-co-ordination may produce actual osteo-arthritic changes in previously healthy bones is of some significance, but of how much greater significance is the fact that a patient grossly

deformed may be unaware of his deformity ? The latter shows that a patient, through mis-directed activity, can confuse wrong with right, and become accustomed to consider right what is wrong. The author has seen cases bent almost double as a sequel to sciatica not know they were stooping. It stands to reason that if the patient's sensory appreciation is so unreliable no good can be expected from applying plaster jackets, irons, etc.

This is equally true of the common condition labelled "scoliosis." Scoliosis is often a result of mal-co-ordination, and the interest of the condition lies in the fact that it is particularly common in patients who are victims of congenital disease.

Another common expression of mal-co-ordination is lordosis, and the main interest of this condition is the not infrequently associated proteinuria. It is thought that the kidneys suffer damage as a result of the lordosis, but this is not the case. The proteinuria is merely a sign, like the lordosis, of congenital disease, and is due to hydrated protein particles in the plasma escaping through slightly damaged glomerular membranes.

Needless to say, the only reliable treatment in these and hosts of other allied conditions is re-educational training, aimed at teaching the patient to inhibit.

Orthopædy as a branch of surgery and psycho-analysis, a branch of medicine, stand out as the two biggest failures of medical science. This is not surprising, seeing that both result from the failure to appreciate the true significance of mal-co-ordination, and the failure could only have come about as a result of the mis-directed activity of the mind (cerebral cortex) of medical men throughout many generations.

Mal-co-ordination, caused by an inequality of the balance between the two arcs of the pyramidal reflex circuit, is exhibited first by over-muscular contraction or what Alexander refers to as undue muscle tension, lack of inhibition, etc. From the nervous standpoint this is most probably to be explained by the damage done to the extra-pyramidal system causing a hyper-activity of the pyramidal system. This is tantamount to saying that the pyramidal system or exciter arc gets out of control. In course of time the excursion of the muscular movements is shortened, the muscles tire easily, because long-continued hyper-activity always tends towards hypo-activity, and finally to no-activity or paralysis. When the damage sustained by the extra-pyramidal system is maintained over a long period of years, the facial features tend to vanish, the eyelids fail to blink, and the patient develops what has been so aptly termed a "poker face." Then follow the tremors so characteristic of *Paralysis agitans*, and these may be either choreatic or athetotic, depending upon the main site of the attack upon the extra-pyramidal system in the

brain-stem. To illustrate some of the points raised a few cases of *Paralysis agitans* are reported below.

Case 49

A man, aged fifty-six, was a typical example of *Paralysis agitans*. His mother died of cancer, aged seventy-seven, one brother died in a lunatic asylum, aged sixty-two (admitted when aged twenty-six), one brother died of cancer of the colon, aged fifty-eight, one brother of phthisis, aged forty-one, and a sister of convulsions in infancy. Early canities and *Arcus senilis* were family characteristics. The patient was a medical man, and was of the opinion that his trouble began when he was about twenty years of age. He was childless, a typical example of familial chronic intestinal intoxication, the pulse was 80 and the blood-pressures registered 145 and 85 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligenes* (10 per cent.), and the blood-picture was as follows :

Suspension stability of the red blood-corpuscles	= 0.4 c.c.
Refractive index of the serum	= 1.3490.
Percentage of the blood-sugar	= 0.118 grm.
Percentage of the blood-urea	= 27 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a high percentage of large and refractile giant particles. There were some giant particles, giant-particled clumps and one or two agglutinations precipitated.

The patient was dieted, subjected to colonic lavage, took iodine, thiol-amino-methyl-glyoxaline and thyroid substance internally, was injected with contramine and the fæcal vaccine, with the result that the general condition improved considerably.

The interest of this case lies in the strong family history of chronic intestinal intoxication, and this points strongly to the *Paralysis agitans* as being merely a manifestation of this fundamental condition.

Case 50

A man, aged sixty-one, was a typical case of *Paralysis agitans*. The condition appeared to begin after an attack of influenza, five years previously. The patient had projecting ears, he could not stand with his knees and feet together at the same time, he had wide-angled elbows, and had worn dental plates for over forty years. The tongue was glazed and fissured, the pupils reacted sluggishly to light, and the vessels of the fundi showed arterio-sclerotic changes.

The patient had generalised arterio-sclerosis, the heart was enlarged, the pulse was 126, and the blood-pressures registered 150 and 80 mm. of Hg. respectively. The patient had a bilateral Dupuytren's contraction affecting the ring and little fingers of the left hand and the ring finger of the right hand. He had had several attacks of mucous colitis, and an examination of the abdomen revealed definite evidence of chronic colitis. The urine gave a strongly positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, but contained no protein or sugar. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (10 per cent.), and an examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3492.
Percentage of the blood-sugar	= 0·206 grm.
Percentage of the blood-urea	= 116 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with many giant particles and ringed particles. There were a few giant particles precipitated, and the Brownian move- ments were sluggish.

This case is reported, first to show a variety of manifestations of a chronic intestinal intoxication, and secondly to emphasise the rise in the percentages of the blood-sugar and blood-urea. It has been the author's experience to find the percentage of the blood-sugar raised in many cases of *Paralysis agitans*; indeed more regularly than in cases of *Thrombo-angiitis obliterans*, but, as stated above, the phenomenon is of no particular significance, and shows no more than that some of the protein particles in the blood-stream are being subjected to dehydration.

Case 51

A man, aged sixty-seven, a typical example of *Paralysis agitans*, sought advice for chronic indigestion, which had been getting progressively worse for about thirty years. The patient used to have chilblains; he was very thin and grossly mal-co-ordinated. All the teeth had been removed; there was bilateral *Arcus senilis* and the vessels of the fundi evidenced arterio-sclerotic changes. He had varicose veins; the pulse was 60 and the blood-pressures registered 105 and 70 mm. of Hg. respectively. The heart was dilated, and there was generalised arterio-sclerosis. The urine gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The

left colon was contracted and the right dilated. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3485.
Percentage of the blood-sugar	= 0·168 grm.
Percentage of the blood-urea	= 37 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a high percentage of giant particles and some ringed particles. There were few giant particles and clumps precipitated. All the particles were very refractile.

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and had injections of contramine and of the fæcal vaccine. The general condition improved considerably and the indigestion vanished completely. After a single course of treatment the percentage of the blood-sugar fell to 0·100 grm. This was a patient who had obviously had a chronic intestinal intoxication all his life. The intoxicants had presumably subjected the protein particles in the plasma to one continuous dehydration, as evidenced by both the clinical picture (thin, general senile change, arterio-sclerosis) and the blood-report (rise in the percentage of the blood-sugar).

Case 52

A woman, aged fifty-eight, with the typical Parkinsonian syndrome, sought advice for giddiness. The patient's father died of pernicious anæmia, her mother of phthisis, and one sister in an asylum of religious mania. There was one brother living who had phthisis. The patient used to have chilblains; she had been subject to migraine and various forms of rheumatism all her life, and she had a severe form of anæmia when aged nineteen. Menstruation began at the age of twelve; it was always irregular and profuse, and ceased when the patient was forty-four years of age. She had never been pregnant. She had had all her teeth removed for the rheumatism, without benefit, and had been operated upon for a supposed floating kidney. There was central cupping of both optic discs, and the fundi showed arterio-sclerotic changes. There were Heberden's nodes on the fingers; the pulse was 90, and the blood-pressures registered 110 and 70 mm. of Hg. respectively. An examination of the abdomen revealed definite evidence of chronic colitis. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.8 c.c.
Refractive index of the serum	= 1.3489.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 20 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and these were mostly giant particles and ringed particles. There were as many particles precipitated as giant particles, ringed particles and giant-particled clumps. The Brownian movements were sluggish.

The patient was dieted, had a course of colonic lavage, took iodine, thio-amino-methyl-glyoxaline and thyroid internally, and had several injections of contramine. The general condition improved considerably, but the Parkinsonian syndrome remained unaltered. This case illustrates the significance of inherited disease, and brings out the association of rheumatism with *Paralysis agitans*, an association more frequently present than absent.

Case 53

A woman, aged sixty-six, had had *Paralysis agitans* for over seven years, and was in a very advanced stage when examined. The patient's father and mother succumbed to apoplexy, aged seventy and sixty-one respectively. The patient had suffered from various manifestations of rheumatism all her life and had been much troubled with repeated attacks of tachycardia. She had suffered from insomnia since the age of twenty; she had *Arcus senilis*, affecting the left eye only; the tongue was very fissured, and indigestion and constipation were habitual. Many of the cardinal signs of inherited disease were present, there was generalised arterio-sclerosis, the pulse was 96, and there were many extra-systoles; the blood-pressures registered 160 and 95 mm. of Hg. respectively. An examination of the abdomen revealed a contracted and painful left colon and an atonic right colon, and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 14 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving with some giant particles and ringed particles. There were some giant particles, ringed particles, clumps, and one or two agglutinations precipitated.

The patient did not undergo any treatment, and died not long afterwards from a cerebral hæmorrhage. The interesting feature in this case is the clinical picture of progressive dehydration, and the blood-picture of hydration. The latter was doubtless a cyclical change.

Case 54

A man, aged fifty-nine, was in the most advanced stage of *Paralysis agitans*. His cerebration was exceedingly slow and all his tissues showed evidence of interstitial changes. The skin was dry, thin and pruritic, the nails were dry and cracked easily. The tongue was glazed, fissured and atrophic. The pulse was 82 and the blood-pressures registered 130 and 85 mm. of Hg. respectively. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. An examination of the abdomen revealed definite evidence of chronic colitis. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (50 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3483.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 25 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a high percentage of giant particles and a few clumps. The Brownian movements were sluggish and there was a tendency to the formation of precipitation <i>en masse</i> of masses of giant particles.

The patient found it practically impossible to carry out the treatment, and he quickly progressed into a state of senile dementia.

The main interest of the case lies in the fact that the patient was at work as a solicitor three years before he was required to seek advice.

It is interesting to note that in all the cases of *Paralysis agitans* examined by the author, the pathogenic micro-organism found in the excreta has been the *Bacillus fæcalis alkaligenes*. This is the micro-organism found most frequently in what may be termed the dry form of rheumatism, the form which is associated with *Paralysis agitans*, and which is due in part to a hardening of the mesenchymatous tissue. Whether this is pure coincidence or is connected with the strong alkali-producing properties of the micro-organism in question future research alone can show.

The cerebral cortex is but a prolongation of the brain-stem where the centres or generators of the activities known as instinct have their seat. The development of the cerebral cortex has meant the transference of the generalship of the central nervous system from the brain-stem to this area, and although the change has resulted in a complexity of activities the actual activity is the same as it has always been. It is not difficult to describe some of the normal and mis-directed activities of the brain-stem, because they run in more or less definite channels, but when it comes to describe those of the cerebral cortex manifold difficulties arise. This is due partly to the fact that those activities which run in definite channels travel along paths too freely intercommunicating to be accurately charted, and partly to the fact that many of the activities run along no definite paths. Although the whole of the brain-stem is represented in the cortex owing to the enormous development of the association centres and tracts, no prolongation can be sharply or accurately delineated. Even the pyramidal or motor-sensory nervous system is far from being limited to the pre- and post-central gyri respectively, as is usually thought.

The development of the association centres and tracts, which are probably prolongations of the reticular formation, bring every channel into intimate relationship with every other channel. It is due to the enormous development of these centres and tracts that man has been enabled to reach the position he holds to-day. It is entirely due to their manifold intricacies that conscious control is possible. But, because this name has been given to their activities it does not signify that the activities are any different to what they were when they had their origin in the brain-stem. This is clearly proved by the fact that Pavlov's so-called "conditioned responses," definitely of cortical origin, can be elicited in animals which either have no cerebral cortex or have been deprived of what they had. Apart from the association centres and tracts the cerebral cortex is characterised by the layers of cells constituting the grey matter. Although man differs from the other mammals in having the supra-granular layers more richly developed, for which reason these layers are supposed to form the main seat of intelligence, there is no true line of demarcation between the various layers or even a functional difference.

Pharmacologists have gone so far as to suggest that drugs have a special affinity for the various layers. Caffeine, for example, is considered by many to check the activity of the supra-granular layers and to stimulate that of the infra-granular layers. Special attention is paid below to the action of drugs upon the central nervous system, so it is not necessary to say more here than

that although dehydrators tend to pick out the cortex and hydrators the brain-stem, no one part of the brain is attacked to the exclusion of other parts and there is no selection of one or more of the neuronics layers.

The infra-granular layers mature earlier in the development of the brain, and they are the last to suffer degeneration in the neuronics destruction which occurs in the acute dementias. But, this means no more than that the supra-granular layers have developed latest, are the most vulnerable, and exhibit the most complex activities. The activities of the supra-granular layers are no more than the most highly developed and therefore complicated activities of the brain-stem, as proved by the fact that all congenital lesions of the cerebral cortex and the acquired acute dementias, may damage both conscious control and instinct without causing any ascertainable lesion in the brain-stem. The word "instinct" in the above applies to the activities of the brain-stem. This fact would seem to make it unnecessary to regard variable and modifiable functions and acquired automatisms as being solely cortical activities and impossible to differentiate what activities are and are not capable of being transmitted in heredity.

That congenital lesions of the central nervous system should show preference for the cerebral cortex is of the greatest significance. It emphasises the point above mentioned that the grey matter of the cerebrum is the most vulnerable structure in the body, and being so it stands the risk of becoming over-developed. It is a biological fact that whenever the over-development of a structure takes place, there is always the danger of this structure losing its connection with the whole, growing aberrantly, and ultimately destroying the body. It is not at all improbable that gigantism led to the ultimate demise of the pre-historic Saurians. This biological change may occur acutely in a short space of time, and in the actual life of the individual when it causes a condition known as "cancer." This idea regarding the origin of malignant disease is ably put by Morley Roberts¹⁴ in his book on "Malignancy and Evolution." Should the view be correct, the possibility of the highly-developed brain in man bringing about his ultimate destruction becomes a plausible hypothesis. To make the hypothesis still more plausible it is necessary to show, taking the analogy of the malignant process, that the development is proceeding aberrantly.

It is not a difficult matter to bring forward evidence to show that the activities of the cerebral cortex are mis-directed, and that the mis-direction is both congenital and acquired, and this is done in this section. But, it is well-nigh impossible to be certain whether the continuance of the congenital form

is the result or the cause of the development of the neuron layers becoming aberrant.

Although several observers have attempted to compare the cerebral capacity of man to-day with that of his ancestors, the result is not satisfactory, particularly where it concerns lack of intelligence. There are many reasons for this. In the first place, it takes several generations for the smallest change to take place ; secondly, no one observer lives long enough, and, if he did, there is no guarantee that his observation would be reliable ; and, thirdly, man to-day is so egotistical that he must needs think, say and write what is flattering or at least agreeable. Of all the mis-directed activities covered by the terms "intellectual," "mental," etc., egotism is probably the greatest and the one which has caused man most harm.

When the other side of the picture is viewed and the highest intellects of to-day are compared with those of thousands of years ago, it cannot honestly be said that the former are any greater. Even when due consideration is given to the modern advantage accruing from the vast accumulation of facts unknown to the ancients, it is doubtful if there has been a greater intelligence than that exhibited by Aristotle, who was born in 384 B.C. It is true that 2,300 years is as nothing in the space of time, but it is doubtful if there were the unreliable beings, the neurotics, the psychotics and the demented *per* population even in the age of the Greek philosophers as there are to-day. An answer to this question would help in the solution of the problem as to whether the activities of the cerebral hemispheres were becoming more mis-directed or not.

When all is said and done, and discussions on points which never can be settled run rife, there stands out the most fundamental point of all, which is that correlation is the essence of cortical function. In spite of this, man has persistently practised differentiation, and in no science is this fault more emphasised than in medicine. After egotism the practice of differentiation is easily the most mis-directed activity of so-called civilisation. Differentiation has resulted in the separation of nations, in different religions, in diverse laws, etc., all of which rob man of his rightful heritage of the world and prevent him and his goods from being free to roam where they will. Differentiation has made it impossible for man to-day to give a really sound judgment on any large problem, and it has made practically every individual regard as right what is actually wrong. Bolshevism is an attempt to reverse things, and it is a curious fact that all revolutions contain the seeds of what ultimately become recognised as truths. That truths should require revolutions to bring them into prominence shows the chaos to which man has been brought. The fundamental

tenet of Bolshevism is correlation, and as it seems to be more durable than most revolutions, it is possible that this now considered hideous menace may save egotism and differentiation from destroying mankind.

Passing by the commissions of egotism and differentiation, it is not difficult to find other evidences of mis-directed activity which are not generally considered such. Even the foundation upon which intelligence, one of the most important of the activities of the cerebral cortex, is based, viz., education, is unsound. The greatest proof that education as conducted to-day is stultifying rather than stimulating efficiency is the fact that the most important advances made in the various sciences have come from uneducated men. While men of letters were teaching their pupils, Stephenson was working in a coal pit and Edison was selling newspapers in the streets. It is well known that academicians form the greatest bulwarks against knowledge, but no attempt is made to rectify the pernicious check which they exert against advancement. Another glaring example of mis-directed intelligence is spiritualism, which has taken hold of so many "intellectual" people to-day. Even the very words "intelligent" and "intellectual" are capable of multi-definition, a sure sign of mis-directed activity. The conditions accompanying the evolution and devolution of the body exclude the possibility of there being any "spirit" of an individual organism existing after death. Whatever may happen at spiritualistic *séances* can be readily explained, and an attempt is made here to do so, because the explanation is one which throws the required light upon what is known as "psychology," a branch of medicine which had better never have seen daylight. A medium when functioning falls into an abnormal condition and the protein particles in the plasma undergo a degree of hydration which increases as the success becomes more marked. The clinical manifestations of this hydration are cold extremities, a sub-normal temperature, a fall of blood-pressures and an increase of perspiration. These statements, and others made below, are based upon personal examinations and inferences drawn from a study of allied states. Owing to the difficulties attending such examinations they are not sufficiently complete to warrant description in detail. The human body is mostly water; indeed, the chemico-physical changes undergone by the protein particles depend in the main upon whether they lose, or retain and increase, their water content, hence the reason why the author uses the words "dehydration" and "hydration." Protein particles when they lose their water content, or undergo dehydration, pass from the colloid state into true solution, where they can function only as ions and not as particles liberating or acquiring electrons. Protein particles when

they undergo hydration increase their water content. As Dawson¹⁵ points out, an ordinary individual has about 100 lb. of water in his system. Water has a greater amount of specific heat than any other known substance. The amount of heat necessary to raise the temperature of 1 lb. one degree is sufficient to raise the temperature of more than 30 lb. of lead to the same extent. An individual losing 1 degree of temperature (Fahrenheit) has radiated away as much energy as would be sufficient to raise 100 lb. in weight to a height of 772 feet. This is sufficient energy to lift a large circle of sitters and all the furniture in the room to the ceiling. A successful medium is able to cause the liberation of energy from sympathetic sitters, as he, or she, was able to effect personally in the first instance, hence the reason why a sympathetic sitter feels cold at a *séance*. The protein particles in the plasma of a sympathetic sitter undergo hydration, as do those in the plasma of a successful medium. It is much easier to subject protein particles to hydration in a person whose protein particles have already undergone some degree of hydration at the hands of disease than in a normal person. This explains why mediums and sympathetic sitters are diseased individuals. Women make more successful spiritualists than men, because their protein particles tend to be more hydrated than those in men. For a *séance* to be successful the room needs to be dark, cold and airless, three conditions favouring hydration.

Case 55

A woman, aged thirty-five, was considered to be psychic and a successful medium. Her father died of cancer of the rectum, aged sixty-three, and he had had three attacks of rheumatic fever. Her mother was a profound neurasthenic and suffered from rheumatism. The patient used to suffer from chilblains and she had rheumatic fever when aged twelve, which left a cardiac lesion. A nervous breakdown occurred four years before the patient came under observation. For the past two years she had suffered from giant urticaria. Menstruation started at the age of fourteen and there had been many periods of amenorrhœa since. Most of the teeth had been removed, most of the signs of familial chronic intestinal intoxication were present, the pulse was 76 and the blood-pressures registered 120 and 70 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus*, and the blood-picture was as follows after a certain amount of treatment had been prescribed :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3495.

Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 32 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with many large and refractile giant particles, ringed particles and giant-particled clumps. There were a fair number of refractile giant particles, with a halo around, precipitated with some ringed particles and giant-particled clumps. The Brownian movements were very sluggish.

The first injection of the faecal vaccine aggravated the urticaria and occasioned angio-neurotic oedema of the face. The treatment was continued until the patient was perfectly well, at the end of which time most of her psychic power had vanished.

It is easy to understand from the above why a physician with experience and one who has his whole heart and soul in his work has his patient summed up at sight. A really able physician should be able to sum up his patient thoroughly after being closeted an hour with him. Such knowledge, the value of which is immeasurable, can never be gained in a laboratory. This explains why drugs used by a physician of this kind benefit a patient, whilst the same drugs in another physician's hands prove valueless. The author knew of a physician who could diagnose diphtheria by the odour the patient emitted immediately he entered the room or approached the bedside, and he never failed, although his colleagues who examined the throat and took swabs frequently failed to make a correct diagnosis. A diagnostician who has no medical knowledge can often locate the diseased area in a patient and bring benefit where a physician has failed. An inflamed area in the body loses more electrical energy than any other area, hence the *rationale* of covering such areas with paraffin, a substance which shows no affinity for electrons (hence its name *parum affinitatis*). Successful lay diagnosticians are themselves sick people, their protein particles are hydrated and therefore in a condition where they are anxious to adsorb electrons. The adsorption of electrons causes the hydrated particles to undergo dispersion, a change the individual recognises immediately. A person who can diagnose by this means is not always an equally successful healer. To heal, it is necessary for the healer to give up electrical energy to the patient, and this can be observed with the naked eye by the swelling which the hands of a successful healer undergo after treatment. The hands swell because the lymphatics and capillaries, or the veins,

depending upon the degree of hydration the protein particles undergo, become filled with protein particles which have undergone hydration.

The neuronic activity varies in different individuals, so much so that the electrical energy liberated by one person may control that to be liberated by another person. The control may be enhanced further by the controller increasing his output of energy by an effort of will. One individual may increase, or check, the electrical energy liberated by the neurones in himself or in another individual, and this forms the basis of auto-suggestion, hypnotism, etc. But, the effort made is not upon the "sub-conscious mind," as this has no existence.

If these and other mis-directed activities to which attention could be drawn *ad libitum* pass as normal activities, it is not surprising to find that medical men dare not make a diagnosis of neurasthenia and that the laity regard such a diagnosis as an insult. Neurasthenia and melancholia as examples of the mis-directed activity of the cerebral cortex bear an analogy to scoliosis, lordosis and *Pes planus* exhibitions of the mis-directed activity of the pyramidal system. They remain unrecognised, fail to excite interest and to be regarded as manifestations of disease because no pathological changes can be detected.

When two conditions like neurasthenia and melancholia, which only too often end in insanity, mania and suicide, have no pathological characteristics, it is obvious that medicine has not advanced very far, and that when pathological changes are discernible it is tantamount to saying that the cells concerned are dead. This is certainly true of central nerve lesions showing pathological changes. Although it is difficult, and sometimes impossible, to draw a distinction between neurasthenia and melancholia, the clinical course run by both is more or less definite.

A neurasthenic recovers, although he may relapse and ultimately become insane. A melancholic may have respites, but he invariably relapses, and each relapse is usually more severe than the preceding one. Melancholics have the desire to commit suicide, although they do not necessarily express it, and many succeed. Neurasthenics, on the other hand, often say they will commit suicide, and never do. Melancholia is very liable to develop into manic depressive psychosis, a condition which frequently goes by the name of "cyclothymia." Even when the realm of insanity is reached, the ground trodden is no firmer.

Certain names have been given for various conditions which may differ clinically, such as "paraphrenia," "schizophrenia," etc. But, very little light has been thrown upon their pathology, still less upon their cause, and none at all upon their treatment. There is no concord to-day as to where insanity

begins, and the position is likely to become still more confused in the future. In reality this is not surprising when it is remembered that some of the oldest and most revered tenets, particularly those bearing a religious aspect, are the outcome of the mis-directed mental activities of mentally abnormal idealists. The whole of civilisation has been formed far more by the mis-directed activities of mentally abnormal men than by the co-ordinated activities of mentally normal men.

While on the subject of mental conditions, it is interesting to note that while homœopaths pay premier attention to what they call "mentals," allopaths do not. The allopath misses a great deal by neglecting the mental picture which every patient is anxious to draw. If he would only follow the homœopaths in this respect he would achieve infinitely more than by suggesting tests which are supposed to, but do not, estimate the functional activity of this or that organ. After all, the patient's main response to disease is the mental one, and once this is corrected when wrong, the rest follows. The author is not prepared to state at present how and why homœopathy often succeeds where allopathy fails, because his work on the action of homœopathic remedies is still in the experimental stage. But, he has seen enough to satisfy himself that listening to every word the patient has to say and trying to probe his mentality play no small part in his treatment and whether it is successful or not.

When all this is taken into consideration it is not surprising to find that quacks are so frequently successful. There is much outside academical medicine a doctor can learn, as is proved by the fact that, the more academical he is, the worse physician he makes. As the most academical men take up the ancillary branches of medicine, and as these are being developed at the expense of clinical medicine, there is a grave danger of medical science falling into disrepute. Indeed, there is evidence of this happening now. Below are reported a few cases of neurasthenia, melancholia and insanity.

Case 56

A girl, aged eleven, was very backward, almost like a cretin in her behaviour, and had had oto-sclerosis for two years. The patient's maternal grandmother had oto-sclerosis and suffered from asthma. The patient was slightly asthmatic, and had a chronic nasal catarrh; she was grossly mal-co-ordinated, had epicanthus, wide-angled elbows, hyper-extended fingers, and acro-asphyxia; she bit her nails and had marked central cupping of both discs. The pulse was 96 and slightly arrhythmic, and the blood-pressures registered 90 and 60 mm. of Hg. respectively. The left colon was contracted and the ascending colon

and cæcum were dilated, and there were tender areas in both iliac fossæ and both hypochondria.

Five years before she sought advice the patient was supposed to have had an attack of typhoid fever. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3473
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, many of which were giant particles. There were some giant-particled clumps moving. There were many giant particles and giant-particled clumps precipitated with some precipitation <i>en masse</i> , which evidenced signs of re-clotting.

The patient did not undergo the treatment advised.

Case 57

A woman, aged twenty-one, had been suffering from a condition akin to *Dementia præcox* for three months. The patient's father and mother were mentally abnormal, and typical examples of familial chronic intestinal intoxication, as were an elder brother and sister. The brother had had his tonsils and adenoids removed, and the sister developed delusions later.

The patient used to have chilblains, she had suffered from chronic indigestion and constipation all her life, and was badly scarred from *Acne vulgaris*. Menstruation began at the age of fourteen, since when there had been periods of amenorrhœa, and the patient had not been unwell for six months before the dementia was noticed. The patient was short, had a dark and oily complexion, perspired profusely, and had bromidrosis. She looked younger than she was, her legs were bowed and the elbows wide-angled and hyper-extended. The pulse was 90, and the blood-pressures registered 120 and 80 mm. of Hg. respectively. The whole of the colon was too tender to allow of a proper examination. The pathogenic micro-organism was the *Bacillus proteus hydrophilis*, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3497

Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 34 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with some giant particles. There were a fair number of particles, giant particles and ringed particles precipitated with a tendency towards the formation of precipitation <i>en masse</i> . The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of colonic lavage which failed to get the colon clean, took iodine, ichthyol and thyroid internally, and received injections of ovarian extract, emetine hydrochloride and the fæcal vaccine.

The patient did not appear to be materially benefited by the treatment, and continued as before, fooling all those whom she knew she could.

The case emphasises the almost ever-present occurrence of amenorrhœa preceding and accompanying severe mental disturbance. The treatment did not succeed in bringing on a period.

Case 58

A woman, aged thirty-four, sought advice for nervousness, lack of energy, disturbing dreams and claustrophobia. It transpired also that the patient was a homo-sexualist. The patient's father died of cancer of the stomach, aged forty-six, and her mother and brother were profound neurasthenics.

The patient had suffered from chronic indigestion and constipation more or less all her life, as well as from psoriasis and migraine. Up till the age of sixteen she had had recurrent attacks of vomiting with acetonuria, and since then glycosuria had been found from time to time. As a child she stammered and bit her nails. At the time of examination she had an attack of *Lichen planus* and *Herpes febrilis*. She could not stand with her knees and feet together at the same time, she had gingivitis and a furred and fissured tongue, the elbows were hyperextended and wide-angled, and she had acro-asphyxia. The optic discs were very small. The pulse was 110, and the blood-pressures registered 115 and 80 mm. of Hg. respectively. The colon was full of fæces, as the patient frequently went a week or more without having the bowels open. Menstruation began at the age of seventeen, there was amenorrhœa till nineteen, and since then the periods have never lasted for more than two days. The pathogenic micro-organism in the excreta of the patient, her mother and brother, was

the *Bacillus faecalis alkaligenes* (75 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.1 c.c.
Refractive index of the serum	= 1.3499
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 16 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and these were mostly giant particles and ringed particles. There were more particles precipitated in the form of giant particles, ringed particles and clumps. The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of colonic lavage, took radiostoleum internally, and had injections of Sup. 468 and of the fæcal vaccine.

The patient recovered completely, but it is not known whether she became normal sexually.

The author has had a case of homo-sexuality in a man where two years after treatment the patient married a woman and later had a child, a girl. Although the suspension stability of the red blood-corpuscles is reduced, the refractive index of the serum is normal and the percentages of the blood-sugar and blood-urea are slightly reduced, showing a degree of hydration which is confirmed by the ultra-microscopic picture. Hydration is, as a rule, well to the fore in mental conditions, and this explains why disordered mental activities in women are so frequently associated with scanty menstruation and amenorrhœa.

Case 59

A man, aged thirty-five, sought advice because "his nerves were too bad to let him work." He suffered severely from night terrors as a child, and was now a somnambulist. During his walks at night-time he frequently smashed windows, and on one occasion nearly succeeded in throwing himself out.

The patient's father and mother were both nervy, and the former committed suicide when aged forty-eight. The patient was grossly mal-co-ordinated and generally "double-jointed," which made him an excellent dancer. He suffered from hay-fever, seborrhœic eczema, and had been operated upon for appendicitis and duodenal ulcer. He could not stand with his knees and feet together at the same time, he had hyper-extended and wide-angled elbows, gingivitis, a furred and fissured tongue, and an elongated, dropped and narrowed heart. The pulse was 60 and the blood-pressures registered 100 and 75 mm. of Hg.

respectively. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, contained a little protein and reduced Nylander's reagent.

An examination of the abdomen showed marked evidence of chronic colitis. The pathogenic micro-organisms found in the excreta were the *Bacillus fæcalis alkaligenes* (50 per cent.), the enterococcus (40 per cent.) and late lactose fermenters (5 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3486
Percentage of the blood-sugar	= 0.086 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving, with many giant particles, ringed particles and giant-particled clumps. There were a few giant particles and giant-particled clumps precipitated.

The patient was dieted, had a course of colonic lavage, took strychnine, iron and arsenic internally, and received injections of Sup. 468 and of the mixed fæcal vaccine.

The patient recovered, lost his nocturnal trouble, and was able to take up his work as a professional dancer.

It is interesting to note the low percentage of the blood-sugar associated with glycosuria. The condition is quite a common one; it is found in cases mentally sound; it has nothing to do with so-called "leaky kidney," but merely denotes that some of the hydrated particles are undergoing the cyclical change of dehydration.

Case 60

A Russian Jew, aged thirty-eight, sought advice for periodic attacks of acute asthenia and depression. The patient's father died of intestinal trouble (? nature) aged seventy, and a sister succumbed to appendicitis aged twenty-two. There were two brothers and four sisters alive, all of whom were more or less invalids and had had abdominal operations.

The patient had been short-circuited and had had his appendix removed. The patient was mal-co-ordinated and anæmic, he had been grey and bald since the age of nineteen, he had widespread *Acne vulgaris*, his pulse was 76, and his blood-pressures registered 100 and 70 mm. of Hg. respectively. There were no abdominal reflexes, the left colon was contracted, and the patient was very tender in the ileo-cæcal area. The urine gave an intense reaction with the

hydrochloride of di-methyl-*para*-amino-benzaldehyde and contained a trace of protein. The pathogenic micro-organisms found in the excreta were the *Bacillus Aertrycke* (6 per cent.) and another non-lactose fermenter which failed to ferment dulcitate. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·5 c.c.
Refractive index of the serum	= 1·3495
Percentage of the blood-sugar	= 0·075 grm.
Percentage of the blood-urea	= 32 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with some giant particles. There were some giant particles and giant-particled clumps precipitated.

The patient did not undergo the treatment advised, and the case is reported because of the rarity in finding the *Bacillus Aertrycke* in the excreta.

Case 61

A man, aged fifty-seven, had had several nervous breakdowns, and at the time of examination he had had severe neurasthenia for over two years because of which he had had to give up his work. The patient used to suffer from chilblains, bronchitis, and had had indigestion and constipation more or less all his life. The patient was grossly mal-co-ordinated both mentally and physically ; he could not straighten his elbows, and his back muscles were as hard as iron. The pupils were dilated and reacted briskly, there was central cupping of both discs, the tongue was furred and fissured, and all the teeth had been removed. The pulse was 76 and the blood-pressures registered 105 and 75 mm. of Hg. respectively. The sigmoid was contracted, there was tenderness in the regions of the flexures, and the ascending colon and cæcum were dilated. The urine gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (25 per cent.), and the blood-picture was as follows :

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3483
Percentage of blood-sugar	= 0·150 grm.
Percentage of blood-urea	= 36 mgrm.
Ultra-microscopic picture of the serum	Many particles moving, all of which were larger than normal. There were a few small giant-particled clumps moving. There were a fair number of particles, giant particles and giant-particled clumps precipitated.

The patient cut out butcher's meat, eggs and milk from his diet, he had a course of colonic lavage, four injections of Sup. 468, and two of the fæcal vaccine.

The patient recovered sufficiently to be able to return to work.

Case 62

A woman, aged forty-three, was brought to the author because for the past two years she had become mentally unstable and subject to hallucinations. The patient used to suffer from chilblains, she had had migraine and a nervous breakdown with insomnia, between the ages of eighteen and twenty. During the breakdown her hair went grey. The patient had been operated upon for lymphadenitis (axilla) and appendicitis. Menstruation began at the age of eighteen, and the periods tended to be scanty. The patient had a vacant look, an anæmic and greasy complexion, and could not keep her head still. All the reflexes were exaggerated, with the exception of the abdominal, which were absent. The pulse was 82, and the blood-pressures registered 110 and 65 mm. of Hg. respectively. The whole of the colon was dilated (megalo-colon), and there was tenderness in the ileo-cæcal area. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (100 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·6 c.c.
Refractive index of the serum	= 1·3480
Percentage of the blood-sugar	= 0·125 grm.
Percentage of the blood-urea	= 37 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and these were all giant particles. There were more particles precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of colonic lavage, took strychnine, iron, arsenic and calcium internally, and had injections of Sup. 468 and of the fæcal vaccine.

The result was most satisfactory, as the patient was able to take up work six months later. The author is of the opinion that if the patient had not been treated she would have to have been removed to a mental home or lunatic asylum.

Case 63

A man, aged fifty, had suffered from *Petit mal* and epilepsy for sixteen years, and was gradually becoming demented. Six months before the author

saw the patient he had had an acute fever, which annulled the epileptic attacks for the time being. The patient's father died of phthisis aged fifty-three, and his only sister was in a lunatic asylum. The patient had three children, all boys; the first died with a congenital heart aged six months, the second died of nephritis aged three years, and he was mentally deficient, and the third was alive and also mentally deficient.

The patient was nearly bald, he had suffered from rheumatism, and had been operated upon for varicocele, strangulated hernia and appendicitis. He could not stand with his knees and feet together at the same time, he had bilateral *Arcus senilis*, all the teeth had been removed, the tongue was furred and fissured, and the fundi showed arterio-sclerotic changes. The pulse was 92, and the blood-pressures registered 105 and 50 mm. of Hg. respectively. The left colon was contracted, and the right colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkali-genes* (100 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3500
Percentage of the blood-sugar	= 0.150 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Many tiny grey particles moving with some giant particles and ringed particles.
	There were many giant particles and small giant-particled clumps precipitated.

The patient was transferred to a mental home and had no treatment. The case is mentioned to illustrate the heredity of mental instability.

Case 64

A man, aged fifty-two, had suffered from melancholia for some months, and had attempted suicide once. The patient was obsessed with the idea that he had had syphilis and had infected his wife and children. Every test possible had been done over and over again, a number of provocative injections had been made, and a lumbar puncture had been performed five times, always with negative results. The patient had been troubled with insomnia for years, and had had several attacks of iritis and furunculosis. He had had his tonsils and teeth removed without deriving any benefit.

The patient was stout, he had been bald since the age of twenty-two, he had myopic astigmatism, the pupils reacted sluggishly to light, the tongue was

furred and fissured, and showed patches of leucoplakia. All the reflexes had vanished, and both testicles had atrophied. The pulse was 84 and the blood-pressures registered 125 and 80 mm. of Hg. respectively. The abdomen was too fat to permit of a proper examination. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligenes* (20 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.0 c.c.
Refractive index of the serum	= 1.3508
Percentage of the blood-sugar	= 0.187 grm.
Percentage of the blood-urea	= 20 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving, all of which were larger than normal, and very refractile. There was an occasional giant particle precipitated.

The patient had thirteen wash-outs, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the fæcal vaccine.

The patient recovered sufficiently to go back to work in his shop, but relapsed a year later, when he had to be put into a mental home, as he attempted suicide again. When the blood was re-examined the picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.6 c.c.
Refractive index of the serum	= 1.3506
Percentage of the blood-sugar	= 0.137 grm.
Percentage of the blood-urea	= 27 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with a few giant particles. There were some giant particles precipitated with one or two agglutinations.

The patient had another course of colonic lavage and received twelve injections of acetyl-choline (0.1 grm.) and two of the fæcal vaccine. He recovered sufficiently to leave the home, but he is sure to commit suicide sooner or later.

When the melancholia returned the patient developed œdema of the left foot and ankle. Such œdema is due to a local precipitation of hydrated protein particles ; it vanishes as a rule under intra-muscular injections of contramine, and it is not infrequently encountered in cases of general paralysis and disease of the anterior cerebral arteries. There is a type of œdema affecting one or both

feet, ankles or legs occurring in young women as the only sign of hydration, the result of chronic intestinal intoxication. In these two types, as well as the one due to *Thrombo-angiitis obliterans* and venous thrombosis, there is no proteinuria and no nephritis.

The following two cases are of particular interest because the patients were brothers. One had acute melancholia when examined, and the other was in a lunatic asylum labelled with "paraphrenia."

Case 65

A man, aged sixty, had been in bed with acute melancholia for some months. Both parents died of phthisis, one sister succumbed to pernicious anæmia aged sixty-three, and another sister had been in an asylum and was at the time a chronic neurasthenic. The patient had always been strange, and had never been able to attend seriously to anything. He had had hay-fever and asthma when a youth, and typhoid fever with costal periostitis when thirty-five years of age. The pupils reacted sluggishly to light, both optic discs were cupped, and all the teeth had been removed for a previous attack of melancholia. The tongue was furred, the nails were ridged, the pulse was 90, and the blood-pressures registered 100 and 65 mm. of Hg. respectively. The skin of the trunk was covered with vascular nævi, the ascending colon and cæcum were dilated, and the urine contained protein and gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligenes* (10 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 1.1 c.c.
Refractive index of the serum	= 1.3502
Percentage of the blood-sugar	= 0.150 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, most of which were giant particles, ringed particles and giant-particled clumps. There were many giant particles and giant-particled clumps precipitated. All the particles were very refractile.

The patient was dieted, had a course, first of treacle enemata, then of colonic lavage, took iodine, thyroid and potassium permanganate internally, and received four injections of Sup. 468, followed by two injections of the fæcal vaccine, with another two three months later.

The patient lost his melancholia, but remained peculiar mentally. After the treatment the suspension stability of the red blood-corpuscles returned to 0·2 c.c. and the blood-sugar fell to 0·093 grm. per cent.

Case 66

A man, aged sixty-five, had been strange all his life and had been in a lunatic asylum for seven years because voices tormented him for having seduced his mother, sisters and sundry other women. He threw things about to drive them away. The patient had never had any sexual connection. He had suffered from asthma as a youth and had had chronic bronchitis and pulmonary fibrosis more or less since. All the teeth had been removed, the tongue was furred and fissured, the left colon was contracted, and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (25 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1·2 c.c.
Refractive index of the serum	= 1·3507
Percentage of the blood-sugar	= 0·093 grm.
Percentage of the blood-urea	= 22 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a few giant particles, ringed particles and small clumps. There were a few particles and giant particles precipitated with some giant-particled clumps and agglutinations. The Brownian movements of the particles were sluggish.

Treatment could not be carried out properly, and the patient showed no signs of improvement.

Summary

Mal-co-ordination is mis-directed activity, and there is no fundamental difference between the activity of neurones and the activity of other cells.

Mal-co-ordination may show itself as over-muscular activity produced in the brain by stimulation of the pyramidal nervous system, as vagotonia produced by stimulation of the autonomic or para-sympathetic nervous system, and as an alteration of psyche produced by stimulation of the cerebral cortex. Although these three types of mal-co-ordination are to a certain extent distinct they are at the same time interdependent, because when one occurs all occur, although in varying degrees, showing that disease affects the central nervous

system as a whole and not in parts as differentiated by the anatomists and physiologists. Mal-co-ordination, and likewise disease, are more common in man than in animals, partly because there has developed a lack of harmony between neuronie and corporal activity. In man neuronie activity far outweighs corporal activity, and as neuronie activity has, on account of what is termed "civilisation," become mis-directed, it would seem probable that as both advance the end must be the disappearance of man, just as the giant Saurians vanished in the past when their corporal activity became mis-directed.

The Vegetative Nervous System and the Alimentary Tract

The first evidence of a relationship between the vegetative nervous system and the alimentary tract is the occurrence of hypertrophic stenosis of the pylorus and of intussusception in new-born infants. Both are the result of over-muscular contraction and insufficient inhibition, brought about either by stimulation of the vagal nucleus or of Auerbach's plexus between the muscular coats of the gut. It is more probable that the lesions are of central than of peripheral origin, because other children in the same family or children with less severe intestinal spasm are so liable to present later spasmophilia, *Petit mal* or epilepsy, three conditions which are caused almost certainly by precipitation of hydrated protein particles in the peri-capillary lymphatics, capillaries, or veins of the mid-brain. Therefore, severe intestinal spasm is probably largely brought about by the precipitation of protein particles (which have become hydrated *in utero*), in the region of the vagal nucleus in the *Medulla oblongata*.

Later in life, after wrong food has been taken and adequate elimination has been disregarded, local inflammation is produced, which must of course have a direct effect upon the endings of the autonomic nerve fibres. The sympathetic nerve fibres end under the lining mucous membrane in the sub-mucous or Meissner's plexus, and the autonomic nerve fibres end between the muscular coats in the myenteric or Auerbach's plexus. The endings of the autonomic nerve fibres are simple terminals in the visceral muscles, those of the sympathetic nerve fibres being free arborisations in or under the mucous membrane. There are no specialised end-organs, as are formed in the skin, muscles, tendons, etc. Is it possible that this difference accounts for the fact that, generally speaking, muscular tissue innervated by the vegetative nervous system is unstriated, while that innervated by the cerebro-spinal nervous system is striated? There must be some connection between the type of muscle and the kind of nerve-ending therein, because in the involuntary,

though striated, muscle cells of the heart the fibres of the nerve-endings have expanded tips. The histological picture certainly suggests that unstriated muscular tissue and the vegetative nervous system are primitive types of the tissues they represent. In every case of chronic intestinal intoxication toxic substances reach the blood-stream *via* the large intestine, being formed by non-lactose fermenters from animal food in particular. The toxic substances are not chemical products as is usually thought, such as indol, phenol, cresol, the hydroxy-phenols, *para*-oxy-phenyl-acetic and proprionic acid, etc., but ordinary products of digestive metabolism which differ from the normal physically rather than chemically. The primary action of these products is one of dehydration. The hydration, the chemico-physical change responsible for most of the clinical signs and symptoms, is secondary to the initial dehydration.

The protein particles hydrated collect in the walls of the intestines first to stimulate, and later to paralyse, the endings of the vagus in Auerbach's plexus, and also in the brain to irritate the centres of the vagus with the result that a familial chronic intestinal intoxication already present is aggravated.

In practically every case of familial chronic intestinal intoxication the victim presents other clinical signs and symptoms of an involvement of the vegetative nervous system. Although the clinical signs and symptoms are produced by hydrated protein particles, it is not always possible to say, whether any particular sign or symptom is due to a central or to a local dehydrator effect of these hydrated particles.

Clinical signs and symptoms are caused in the main by protein particles in the plasma which have been subjected to hydration, and they are actually produced by the hydrated particles occasioning the protein particles, which constitute the cytoplasm of the cells around them to undergo dehydration (hyper-activity). It thus comes about that the lesion produced is the positive of the negative or stands to the invader (hydrated protein particles) as does a photograph to its plate (negative).

Should the hydrator effect of the invader be excessive, then paralysis or hypo-activity of the cells around results, and it is for this reason that in certain cases it is difficult to determine, whether the condition is the result of paralysis of the sympathetic nervous system or of stimulation of the autonomic nervous system and *vice versa*. In most instances the latter may be assumed because in practically every case where the clinical signs and symptoms are the result of stimulation it is the autonomic nervous system which has been stimulated. This is only what might be expected when it is realised that the autonomic

nervous system is the exciter or dynamic part of the vegetative nervous system, and the sympathetic nervous system is the inhibitory or static part of the reflex circuit. This explains why the other clinical signs and symptoms presented are much more frequently vagotonic than sympathetico-tonic in nature.

From this the reader will be able to understand why victims of a familial chronic intestinal intoxication tend to present contracted pupils, enophthalmos, vaso-dilatation, chilblain circulation, chronic nasal catarrh and hay-fever, bronchial catarrh, achalasia, gastric catarrh, pyloric hypertrophy, duodenal catarrh, intussusception, hypertrophic ilial obstruction, spasm of the colon, enuresis, menstrual trouble, abortion, and pronounced sexual activity with a tendency to perversion.

When a patient in addition to the above presents one or more clinical signs and symptoms suggesting hyper-activity of the sympathetic nervous system, it is more probable that the same points to a paresis or paralysis of some of the central cells or nerve-endings of the autonomic nervous system, for instance, when patients have dilated pupils, *Keratitis pilaris*, tachycardia, etc.

Vagotonic individuals should according to plan have a slow pulse, but in the author's experience bradycardia is a rare clinical manifestation of familial chronic intestinal intoxication; tachycardia is infinitely more common. Tachycardia is perhaps the most common clinical manifestation suggesting hyper-activity of the sympathetic nervous system met with in familial chronic intestinal intoxication, and the author is prompted to think that it is caused by the collection in the heart muscle of hydrated protein particles which are sufficiently hydrated to paralyse the autonomic nerve endings. Although the heart can sustain life in spite of repeated and continued battering, it is nevertheless the fact that wherever chronic dehydration or hydration occur in the body the heart is never spared. This point deserves further illustration owing to the great importance of that organ.

In many cases of familial chronic intestinal intoxication the heart is dropped, elongated and narrowed. The two most common valvular lesions are mitral stenosis and aortic regurgitation. Mitral stenosis is to be found predominantly in the young, affecting females more frequently than males. Mitral stenosis, although most probably of infective origin and most commonly the result of acute rheumatism, may occur independently of either. Rheumatic fever is not a specific fever, but an infection caused by ordinarily saprophytic micro-organisms becoming pathogenic in an individual whose

resistance has been lowered by a chronic intestinal intoxication. In acute rheumatic fever large cells, first described by Aschoff,¹⁸ are to be found in the heart particularly. In the last volume the opinion was hazarded that these cells were lymphocyte-producing endothelial cells of lymphatic vessels, which never develop in the way mentioned unless severely taxed by the invader. In other words, they are cells the host never brings to the front till his resistance has been severely strained. As a matter of fact, these cells may be found in other organs, and in conditions unconnected with rheumatism. Aortic regurgitation occurs comparatively early in life and affects men more frequently than women. This lesion is definitely not necessarily of infective origin. Even mitral regurgitation may be caused by a chronic intestinal intoxication in the absence of rheumatic fever, a fact which suggests that cardiac lesions may result from chemical intoxication and are not invariably of microbic origin, as is the general opinion. It is probable that the damage done is actually caused by the hydrated protein particles precipitated in the structure involved. In a very large number of cases of familial chronic intestinal intoxication the heart-beats are arrhythmic, and the arrhythmia is most frequently produced by extra-systoles. In every case where there is a chronic dehydration there is a varying degree of interstitial myocarditis, and in every case where there is hydration the cardiac muscle cells evidence signs of degeneration. Indeed, in acute conditions fatty degeneration may be found in the cardiac muscle cells and in no other organ. Lastly, it is a failing heart which so often terminates fatal hydration. The following cases illustrate some of these points.

Case 67

A man, aged forty-seven, suffered from rheumatism, hay-fever and eczema. He had had rheumatic fever three times and rheumatism in most of its forms since. The patient had a nervous breakdown in 1917. He was troubled with *Pruritus ani*, varicose veins and furunculosis, the last having been present for over three years. All the teeth had been removed ; the tongue was furred and fissured ; the optic fundi showed arterio-sclerotic changes ; all the reflexes had vanished ; the pulse was 52 and the blood-pressures registered 170 and 110 mm. of Hg. respectively. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and contained some protein. An examination of the abdomen revealed a contracted left colon and a dilated ascending colon and cæcum, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3500.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 31 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a high percentage of large and refractile giant particles. There were many large and refractile giant particles precipitated, as well as some ringed particles and giant-particled clumps. The Brownian movements were sluggish.

The patient had no treatment, and did not return. The case is full of interest, particularly the association of bradycardia with hyperpiesis.

Case 68

A woman, aged sixty-eight, sought advice for chronic indigestion, recurrent *Herpes febrilis*, affecting the buttocks only, and frequency of micturition, with occasional inability to hold her water. The patient had lost three brothers, one from phthisis, aged forty-five, one from Bright's disease, aged forty-eight, and one from rectal carcinoma, aged fifty. The patient had had rheumatic fever, with rheumatism off and on since; she had had several attacks of mucous colitis; she had been operated upon for piles and had had bouts of bradycardia when the pulse rate did not exceed 28 per minute. Menstruation began at the age of seventeen, and the climacteric occurred at the age of forty-five. The patient was tall and thin; she could not stand with knees and feet together, and she had wide-angled elbows and acro-asphyxia. The pupils reacted sluggishly to light and the optic fundi showed arterio-sclerotic changes; the pulse was 50 and the blood-pressures registered 85 and 70 mm. of Hg. respectively. The patient had active colitis at the time of examination. The pathogenic micro-organism found in the excreta was an atypical *Bacillus proteus hydrophilus* (30 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-sugar	= 0.118 grm.
Percentage of the blood-urea	= 67 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some giant particles, ringed particles, and a fair number of giant-particled clumps. There were some particles and giant particles precipitated, and all the particles were very refractile.

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and had five injections of contramine and two of the faecal vaccine, each of 0.5 million. A year later the patient had much improved; the pulse rate was 70, and the blood-pressures registered 135 and 85 mm. of Hg. respectively. Although some active dehydration was going on, as evidenced by the rise in the percentage of the blood-urea, the main feature was hydration, the chemico-physical change responsible for the low blood-pressures. The dehydration characterised by a rise in the percentage of the blood-urea is usually of a severe type, hence the reason why there is always hydration of other particles occurring concomitantly.

Case 69

A man, aged sixty-three, sought advice for asthenia and heart attacks, which had worried him for about fifteen years. When the patient was thirty-six years of age he developed phthisis, which incapacitated him for four years; a year later he was troubled with an ischio-rectal abscess, six years later with appendicitis, and seven years later with renal calculus. He began to go bald and white at the age of twenty-two, and could not stand with his knees and feet together at the same time. His pupils were miotic, and reacted sluggishly to light. He had bilateral *Arcus senilis*, the teeth were bad, and the tongue was very furred. An ophthalmoscopic examination revealed arterio-sclerotic changes. The pulse was 32 and there were a few extra-systoles, and the blood-pressures registered 190 and 90 mm. of Hg. respectively. The patient said that his pulse rate had never exceeded 40 per minute. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (90 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.7 c.c.
Refractive index of the serum	= 1.3508.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, most of which were larger than normal, with some giant particles and ringed particles. There were as many particles, giant particles, ringed particles and giant-particled clumps precipitated. The Brownian movements of the particles were sluggish, and there was a tendency towards the formation of precipitation <i>en masse</i> .

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the fæcal vaccine. The patient improved in every way, and some months later the pulse rate was 62, and the blood-pressures 140 and 80 mm. of Hg. respectively.

This case is particularly interesting because of the pronounced bradycardia, and of the length of time it had obviously been present.

Case 70

A man, aged forty-five, sought advice for neurasthenia, which showed itself mainly as an inability to sign his name in the presence of people. The patient lost two brothers of convulsions in infancy. He had chilblains and migraine as a boy, and had been "nervy" since. He suffered all his life from chronic indigestion and constipation; he had piles and two attacks of jaundice when aged sixteen and thirty-eight respectively. The patient was grossly mal-coordinated and anæmic. All his teeth had been removed, to no purpose; the tongue was fissured; the elbows were hyper-extended; there was central cupping of both optic discs; the pulse was 92, and the blood-pressures registered 100 and 65 mm. of Hg. respectively. There was marked evidence of aortic regurgitation, which had obviously been present for many years. Although the patient had had lumbago, he had never had rheumatic fever. An examination of the abdomen revealed definite evidence of chronic colitis. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and contained a trace of protein. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (40 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuseles	= 0.1 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-sugar	= 0.093.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with many giant particles, with a halo around them, and ringed particles. There were many particles, giant particles, ringed particles and clumps precipitated, almost amounting to precipitation <i>en masse</i> . The Brownian movements were very sluggish.

The patient was dieted, had a course of colonic lavage, took lacto-dextrin and *Bacillus acidophilus* emulsion internally, and received injections of Sup. 468

and of the faecal vaccine. The patient improved, but never quite lost his neurasthenia. The patient had never had syphilis, and in the author's opinion this infection is not the chief cause of aortic regurgitation, although that opinion is held by many.

Case 71

A man, aged forty-five, in the absence of any rheumatism, was found to have a double mitral murmur when he was twenty-seven years of age ; five years later a double aortic murmur. The patient's father and mother had been martyrs to rheumatism ; one brother had been short-circuited for a duodenal ulcer and was a chronic invalid ; another brother was a profound neurasthenic, and the only sister suffered from ulcerative colitis. The patient suffered from hay-fever, asthma and a chronic nasal catarrh, and he had had several attacks of mucous colitis. He presented most of the cardinal signs of inherited disease ; the pulse was 84 and the blood-pressures registered 145 and 90 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (20 per cent.), and the blood-picture was as follows :

Suspension stability of the red blood-corpuscles	= 0.05 c.c.
Refractive index of the serum	= 1.3502.
Percentage of the blood-sugar	= 0.156 grm.
Percentage of the blood-urea	= 18 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, with a few giant particles, ringed particles and small clumps. There were a few giant particles, ringed particles and small clumps precipitated.

The patient cut out meat, eggs and milk from his diet, he took iodine, ichthyol and thiol-amino-methyl-glyoxaline internally, he had treacle enemata twice a week for several weeks, and four injections of the faecal vaccines in doses of half a million, with three months' interval between each two injected on two successive days. Six months later the patient took lacto-dextrin internally for two months. Two years later the patient was much better but still had some active colitis, so a course of colonic lavage was prescribed, and then two more injections of the faecal vaccine in doses of a half and one million respectively on two days in succession. The improvement was great enough to allow the patient to take exercise again, and the cardiac murmurs became almost inaudible. In addition, the patient lost his hay-fever, asthma and nasal catarrh.

Angina pectoris is caused in most instances by the collection of hydrated

protein particles in the coronary arteries and peri-capillary lymphatic vessels and capillaries in the myocardium and a consequent collection of fluid in the pericardial sac. This view is confirmed by the readiness with which the pain vanishes with drugs exhibiting an initial hydrator action and a later dehydrator action, to mention nitrites, *penta*-methylene-tetrazol, choline, acetyl-choline, etc. These drugs, in virtue of one or more positively charged nitrogen atoms, occasion an initial hydration which causes a dilatation of the vessels in the periphery. Although the initial action is one of hydration it does not add to the trouble already present, because the peripheral dilatation relieves the congestion in the heart. The later action of dehydration is due to negatively charged groups which cause dispersion of the hydrated protein particles.

The collection of fluid or œdema which occurs in areas where hydrated protein particles are precipitated plays an important rôle in the signs and symptoms produced. Cerebral hydration increases the amount of cerebro-spinal fluid, thereby raising the pressure. Glaucoma is of like origin. The excess of fluid in the pericardial sac seriously impedes the action of the heart, etc., etc.

Angina pectoris is occasionally due to gelation occurring in the cardiac arteries, causing arterial thrombosis, a condition beautifully illustrated in the following case :—

Case 72

A man, aged forty-four, was sitting up in bed, having difficulty of breathing and acute anginal attacks every hour or so. The patient had been in this condition for about three years, and had been an inmate of several hospitals without deriving any benefit. His last treatment had been injections of acetyl-choline, which did him more harm than good. The patient lost a brother from cancer of the colon, aged fifty-five, and a sister from cancer of the stomach, aged forty-five. A brother living, aged fifty-three, had a stroke when only thirty-five years of age. The patient was a Jew ; he had suffered from chronic indigestion, constipation and migraine all his life, and had had a gastric ulcer. All the teeth had been removed and the tongue was furred. The pulse was 132, and the blood-pressures registered 160 and 100 mm. of Hg. respectively. The heart was enlarged, the sounds were normal, and the patient could hardly bear the skin over the heart being touched. He was worried with cramps in both calves, which were doubtless caused by *Thrombo-angiitis obliterans*, as there was no pulsation in the *Dorsalis pedis* on either side. He had also recurrent *Herpes febrilis* affecting the right foot. The urine contained no sugar. An examination of the abdomen revealed definite evidence of chronic colitis, and the

pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligines* (75 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.85 c.c.
Refractive index of the serum	= 1.3512.
Percentage of blood-sugar	= 0.200 grm.
Percentage of the blood-urea	= 53 mgrm.
Ultra-microscopic picture of the serum	= Myriads of particles moving with a few ringed particles. There were a few giant particles and small clumps precipitated.

The patient was dieted and cut down his smoking, he had three treacle enemata a week for several weeks, took iodine, ichthyol and thyroid internally, and had 350 units of insulin in ten-unit doses five days a week. The patient improved at once, and later returned to work. Three months later the blood was re-examined with the following result :—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3493.
Percentage of blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 43 mgrm.
Ultra-microscopic picture of the serum	= Not many particles moving, and amongst them were some giant particles and ringed particles. There were as many particles precipitated in the form of giant particles, ringed particles and giant-particled clumps. The Brownian movements were sluggish.

The patient continued to take iodine, ichthyol and thyroid internally, he had five intra-muscular injections of contramine, and a course of colonic lavage followed by two injections of the faecal vaccine.

After the treatment the patient felt better than he had ever been, he lost his anginal pain and cramps in the calves, the heart was reduced to its normal size, but pulsation did not re-appear in the *Dorsalis pedis* arteries.

No case could show better than this the value of the routine examination of the blood, because the moment the gelation process was checked with insulin the patient began to have relief.

In chronic intestinal intoxication the pupils are found to be more often contracted than dilated. Both eyes need not necessarily be affected to the same degree. An irregularity of contour seems to be the initial sign of any permanent damage being sustained by the nerve tissue. Later the pupil fails

to remain contracted in the presence of a strong light. As time progresses the light reflex vanishes, then the accommodation reflex, and when both have vanished the pupils remain miotic. There may be a stage during which one or both pupils present the Argyll-Robertson phenomenon in the absence of a syphilitic infection, and occasionally the pupils are found to be unequal. Finally, the pupils are liable to become dilated if the patient succumbs to a cerebral lesion. The primary contraction would appear to be due to the precipitation of hydrated protein particles in the peri-capillary lymphatics, capillaries, or veins of the mid-brain. The intermediate phenomena probably result from stimulation of the exciter arc of the vegetative nervous system, namely, the autonomic nervous system. The final dilatation is caused by the precipitation of hydrated protein particles in the hind-brain sufficient to cause cerebral shock and hence paralysis of the dynamic arc of the vegetative nervous system. Moderately severe changes affecting the protein particles appear to influence the mid-brain in particular, while very severe changes appear to damage the hind-brain most.¹

It is interesting to observe that in the most severe forms of chronic intestinal intoxication where there is mental instability, the patient presents dilated pupils, an oily skin and *Acne vulgaris*.

While the pupil phenomena are to be particularly observed in cases of syphilitic degenerative myelitis, this is not because of the activity of the *Leucocytozoon syphilidis*, but because of the arterio-sclerotic changes and hydration that syphilis causes to appear early and leaves in its wake. By the time patients seek advice, more of the clinical signs and symptoms of syphilitic degenerative myelitis are the result of damage actually accomplished, of arterio-sclerotic changes, rather than of actual degeneration brought about by the causative micro-organism. Hence the explanation of the fact that anti-syphilitic treatment in tabes is of so little value. In addition, hydration is the sequence and is kept going by a chronic intestinal intoxication, hence the reason why it is advisable to pay more attention to the large intestine than to the syphilis. It has been the author's experience to find that patients with deep sunken eyes are the victims of a severe form of chronic intestinal intoxication. The victims are invariably mal-co-ordinated and not infrequently exhibit a mis-directed intelligence. Hot-headed extremists, deeply religious people and sexual perverts tend to have pronounced enophthalmos, as evidenced by the following case :—

¹ Many of these pupil changes may be congenital, and a unilateral Argyll-Robertson pupil may occur in this manner in the absence of syphilis. In such cases the deep reflexes are generally absent.

Case 73

A man, aged twenty-five, sought advice for asthenia. The patient was tall and thin, he had pronounced enophthalmos ; he was brilliant in many ways, though it was all mis-directed, and he was a homo-sexualist, having never been any different. The patient's mother and sister were hopelessly neurasthenic. The patient had had several operations without benefit for chronic nasal catarrh, one testicle had been brought down and the other had been removed for a tumour (? nature).¹ He had experienced two attacks of jaundice, all his molars had been stopped, his tongue was dirty, his ears outstanding, he could not stand with his knees and feet together at the same time, the elbows were hyper-extended and wide-angled, the fingers were long, tapering and bent back easily, and the optic discs were small and not fully developed. The pulse was 86, the blood-pressures registered 110 and 70 mm. of Hg. respectively, and the heart was elongated, dropped and narrowed, so there was only a tiny area of superficial cardiac dullness. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and contained some protein. The left colon was hypertonic, the flexures were tender, the ascending colon and cæcum were atonic, and the ileo-cæcal region was thickened and tender.

The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (75 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 20 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with a few giant particles and ringed particles. There were a fair number of giant particles, ringed particles and giant-particled clumps precipitated.

The patient could not be persuaded to undergo treatment.

Patients presenting dilated pupils and exophthalmos usually have the thyroid gland enlarged. The triad is more common in women than in men, because pregnancy plays a causative part, as does early syphilis. Both pregnancy and early syphilis have this action only in women the victims of inherited chronic intestinal intoxication, and they act by augmenting the hydration already present. In the author's opinion the enlargement of the thyroid gland in so-called " Graves' disease " is due to the precipitation of

¹ Death occurred some months later from generalised sarcoma.

hydrated protein particles therein and some of the other signs and symptoms are brought about by the precipitation of hydrated protein particles in the hind-brain causing degeneration of some of the cells in the centre of the autonomic nervous system. This explanation seems to be a more rational one than the view that the signs and symptoms of "Graves' disease" are wholly due to a stimulation of the sympathetic nervous system. Iodine is beneficial in this condition because it causes dispersion of the hydrated protein particles, but there are hosts of other dehydrator substances which have as good an action, although, naturally, none of them should be regarded as other than palliative. The treatment of "Graves' disease," as in other cases of enlargement of the thyroid gland (new growth excluded), not associated necessarily with pupil and heart changes, rests in correcting the chronic intestinal intoxication. *Keratitis pilaris* appears on the extensor surfaces of the arms and sometimes of the legs, and the victim is usually fat and presents a varying degree of acro-asphyxia. Catarrh of some part of the respiratory tract is found in practically every case of chronic intestinal intoxication, and it ranges from colds in the head to hay-fever, chronic pharyngitis and laryngitis, bronchorrhœa and pulmonary catarrh. The discharge is mucous at first; it may be so profuse as to drench the pillow-case at night-time. There is danger of its later becoming purulent, when an infection of the air sinuses is liable to occur, and also such conditions as pneumonia and bronchiectasis. The pulmonary catarrh is most frequently apical, and it allows of the implantation of the tubercle bacillus. An infection of the air-sinuses is seldom primary and experience would seem to point to the tubercle bacillus as being rather a saprophytic than a pathogenic micro-organism.

Over-muscular contraction of the alimentary tract is liable to lead to hypertrophy, then to lengthening, and to the formation of diverticula, the parts most affected being the œsophagus, duodenum and colon. The stomach may present signs and symptoms of either hyper- or hypo-secretion. In the former instance the secretion may be profuse (water-brash), comparable to so-called "vaso-motor rhinorrhœa" and "bronchorrhœa." Patients with gastric hyper-secretion usually present neurasthenia as well, suggesting cerebral hydration, but the local collection of hydrated protein particles also causes hyper-secretion, and this is probably how histamine and phenyl-hydro-chinazolin or orexin—drugs which are sometimes used as appetisers—function. In both histamine and orexin there are positively charged nitrogen atoms which cause the preparations to produce a hydrator effect. Several cases are on record of marasmus with gastric hypo-secretion

being benefited by insulin. In view of the above facts this is explainable; marasmus is a sign of progressive dehydration; another sign is hypo-secretion. Insulin, most probably, in virtue of one or more positively charged nitrogen atoms, causes hydration, the antidote to dehydration. In the first volume attention was drawn to the similarity of action of histamine and insulin. Local hydration, particularly if the hydrated protein particles lodge in veins, is liable to be followed by necrosis, and this is the most probable explanation of the ulcers met with in chilblains, *Pernio*, *Erythema induratum* and of gastric and duodenal ulcers. It is a significant fact that gastric and duodenal ulceration are preceded by hyper-secretion and that they occur only in hydration.

The gastric and other crises met with in cases of syphilitic degenerative myelitis are doubtless caused by irritation of the vegetative nervous system. The so-called *Anorexia nervosa*, with vomiting, is merely a form of splanchnic shock, and the vomiting occurs because the hydrated protein particles become precipitated in the gastric capillaries and veins.

Achylia, representing a total lack of digestive ferments and of free or combined hydrochloric acid in the gastric juice, is always secondary to a chronic intestinal intoxication, and its presence denotes that the protein particles in the plasma are being subjected to active dehydration. This explains why achylia is so prominent a feature of pernicious anæmia. The achylia occurs presumably because the protein particles constituting the cytoplasm of the gastric cells undergo hydration. The fact that achylia and gastroptosis go hand in hand supports this view—hydration always causes a softening, loosening and stretching of the supporting tissues. The advantage to the patient which follows the internal administration of dilute hydrochloric acid is not solely due, as is usually thought, to the supply of a need, but also to the conic action, which causes dispersion of the hydrated protein particles. Ptosis of the stomach cannot be remedied either by operation or by belts. Indeed, surgical treatment is contra-indicated, first, because "neurasthenic" patients are always made worse thereby, secondly, because ptosis of other organs usually accompanies gastroptosis, viz., heart, intestines and kidneys, and thirdly, because ptosis becomes symptomless the moment the chronic intestinal intoxication is treated and the patient's mal-co-ordination is corrected by re-education.

Finally, account has to be taken of the action of drugs upon the vegetative nervous system, because it was mainly due to Langley's¹⁸ work that the vegetative nervous system came to be divided into its two parts.

Drugs have been separated into those stimulating the autonomic nervous system, those stimulating the sympathetic nervous system, and those paralysing the autonomic nervous system. The action of drugs upon the vegetative nervous system is by no means so clear as the text-books state. For one thing it is often difficult to decide, even when the drug seems to affect the vegetative nervous system, whether the action is upon the centres or upon the nerve endings. All drugs have to circulate in the blood-stream before they can reach either the centres or the nerve endings; therefore the primary action of drugs must be upon the protein particles in the plasma. Finally, if mention be made of drugs acting upon the vegetative nervous system, why is it that medical literature contains no reference to drugs acting upon the pyramidal system? The obvious answer is that drugs have no selective action upon any part of the central nervous system. It has been shown conclusively in the previous parts of "The Nature of Disease"^{20, 21} that the action of drugs is influenced by the chemico-physical state in which the protein particles in the plasma happen to be at the time. In this section it is shown that, so far as the cells of organs are concerned, in drug intoxication as much if not more damage is done by the hydrated protein particles in the blood-stream passing through the walls of the lymphatics and capillaries than by the actual drug itself.

Finally, it is inconceivable to think that a drug injected anywhere in the body is able to pick out so tiny an area as the cerebral centre of the sympathetic nervous system must be, and wait till it has reached this area before it commences to act. Moreover, as stated above, it is improbable that the sympathetic nervous system has a centre in the brain. Following Langley's nomenclature, it is found that drugs exhibiting a conductor-dehydrator action are sympathetico-tonic, that drugs exhibiting a hydrator-dehydrator action are vagotonic and that drugs exhibiting a hydrator action only paralyse the autonomic nervous system. Note that no mention is ever made of drugs paralysing the sympathetic nervous system. There must be a very much simpler reason for this anomaly than the one usually given, and it is practically certain that no drug has a direct action upon the vegetative nervous system, or even has a predilection for any part of the central nervous system. The protein particles in the plasma are not restricted to a specified area by a cell membrane as are the protein particles constituting the cytoplasm of cells; the former may be referred to as dynamic and the latter as static. It is because of this difference that the chemico-physical changes wrought in the latter by the former stand in the same relationship to one another as does a

photograph to its negative. Drugs exhibiting a combined conductor-dehydrator effect subject the protein particles in the plasma to chemico-physical changes which affect but little the static protein particles ; if any change is produced it is one of hydration. Drugs exhibiting a hydrator-dehydrator effect subject the protein particles in the plasma to chemico-physical changes which have a dehydrator effect upon the static protein particles. Drugs exhibiting a hydrator effect subject the protein particles in the plasma to chemico-physical changes which cause so much dehydration of the static protein particles as to send them into solution or to cause what is known as "degeneration." The initial result of hydration of the static protein particles is inertia, of dehydration, increased activity and of degeneration, paralysis. The exciter part of the vegetative nervous system is the autonomic nervous system, and the inhibitor part the sympathetic nervous system. Therefore it is only natural to expect conductor-dehydrators to produce signs and symptoms as if they stimulated the sympathetic nervous system, hydrator-dehydrators to act similarly upon the autonomic nervous system, and hydrators to cause paresis or paralysis of the autonomic nervous system. In support of this line of reasoning are the two most interesting facts : (1) that vagotonia is more commonly met with in disease than sympathetico-tonia ; (2) that over-excitation and insufficient inhibition are the chief characteristic features of disease—*vide* mal-co-ordination.

Drugs are not referred to as stimulating the pyramidal and extra-pyramidal nervous systems ; it is known, however, although no cognisance is taken of its significance, that cerebral shock is occasioned by hydrators and that before paralysis ensues over-muscular activity is experienced. The significance of these excessive muscular contractions has doubtless been clouded by the names given to them, as if they were several distinct conditions, viz., fits, convulsions, eclampsia, tetany, spasmophilia, uræmia, insulin intoxication, etc.

Before dealing with the various drugs it is necessary to point out the chemico-physical changes suffered by the static protein particles under the long-continued influence of the dynamic protein particles. Continued dehydration of the dynamic protein particles—most conductors come to behave as dehydrators when injected at frequent intervals over a long period of time—causes a hardening of the mesenchymatous tissue and a combined hypertrophy (hydration) and atrophy of the parenchymatous tissue. Continued hydration causes degeneration of the static protein particles, and continued gelato-hydration (a combination of dehydration and hydration) inflammation.

Inflammation is characterised by the endothelial cells of the peri-vascular lymphatics manufacturing leucocytes. Adrenalin and pituitrin are the drugs usually cited as being stimulants of the sympathetic nervous system, choline and pilocarpine of the autonomic nervous system and atropine as having a paralysing effect upon the autonomic nervous system. Adrenalin has a combined conductor-dehydrator action, the former being executed by the negatively charged phenolic hydroxyl group and the latter by the negatively charged methyl group. The negatively charged methyl group may have a slight conductor effect, particularly if the chemico-physical state in which the protein particles happen to be is suitable. The same is the case with ephedrin, which has two negatively charged methyl groups, but no phenolic hydroxyl group. When protein particles undergo pure dehydration and no hydration occurs the blood-vessels contract, and if a large capillary network, particularly in the brain, is put out of action, the blood-pressures are raised. But, these phenomena result from a direct action of the drug upon the protein particles in the plasma and not upon the endings of the sympathetic nerves or the hypothetical centre in the brain. Adrenalin stimulates inhibition, which in turn detracts from the excitation of the autonomic nervous system, hence the pupils are dilated, the heart's action is accelerated, the *Arrectores pilorum* are stimulated, and the stomach, intestines, bladder and uterus are relaxed and their secretions diminished. Adrenalin is supposed to relax the bronchial muscles, and it is thought to be due to this action that the drug is useful in asthma. In the first place asthma is not due to the contraction of the bronchial muscles, it is due to the precipitation of hydrated protein particles in the peri-vascular lymphatic vessels and capillaries of the lung in the course of which the bronchial muscles may become contracted. Adrenalin is of benefit in asthma only so long as it is able to cause dispersion of the hydrated protein particles, and this it often fails to do because, owing to the dilatation of the lymphatic vessels, the capillaries may be contracted and rendered impervious to the protein particles which have been already subjected to dehydration by adrenalin. Ephedrin and ephetonin are in certain cases more useful than adrenalin because they act more slowly and over a longer period of time; they cause less vascular constriction and function more as pure dehydrators. In cases where the patient has knowledge of an impending attack of asthma or if the attack has not been present too long no drug is so beneficial as Sup. 36, which acts solely as a conductor. The author has had several cases in which a single injection freed the victim of asthma for months and even years. Once the attack has fully developed a

drug exhibiting a dehydrator effect is essential. Sup. 36 is useful because the hydration causing the asthma is preceded by dehydration occasioned most frequently by intoxicants reaching the blood-stream from the large intestine, and when electrons are conducted to such particles hydration does not ensue. Repeated injections of adrenalin may cause contraction of the bronchial muscles ; drugs supposed to stimulate the vagus do not necessarily contract the bronchial muscles, and when hydrated protein particles have been precipitated in the lungs for any length of time the bronchial muscles may undergo relaxation—indeed, in cases of pulmonary shock the bronchial muscles are not contracted. Finally in certain chronic cases of asthma, choline, or better still acetyl-choline, may be the drug best suited to cut short an attack, in spite of its being supposed to stimulate the vagus and to cause the bronchial muscles to contract. These small points are stressed because too much importance has been placed upon the changes met with in the static tissues in disease and too little importance upon the chemico-physical changes to which the dynamic tissue has been subjected. The long-continued use of adrenalin leads to dehydration of the mesenchymatous tissue, and when this occurs there is a danger of hæmorrhage arising, as illustrated by the following case :—

Case 74

A man, aged thirty-three, had had asthma more or less continuously for thirteen years. The paternal grandfather was a chronic asthmatic and so was the patient's brother. The patient had been treated throughout with injections of adrenalin and had already had paraplegia with incontinence and a right-sided hemiplegia. When he was examined he was found to have well-marked arterio-sclerosis and pulmonary fibrosis, but the blood-pressures were not raised owing to the insufficiency of the protein particles in the plasma, most having been driven into true solution by the repeated injections of adrenalin. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 5·2 c.c.
Refractive index of the serum	= 1·3492.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 38 mgrm.
Ultra-microscopic picture of the serum	= Hardly a particle to be seen moving. There were a few more precipitated, but they were either giant particles or clumps.

This blood-picture shows that adrenalin had not only sent many of the

protein particles into solution, but also had caused hydration of those left in the colloid state. The hydration is vouched for, apart from the ultra-microscopic picture, by the relatively high refractive index and by there being no rise in the percentage of the blood-sugar and the blood-urea. The great reduction in the suspension stability of the red blood-corpuscles shows that the hydrated particles were very poor in electrons.

The emotions of fear and rage are said to liberate an excess of adrenalin into the blood-stream. The liberated adrenalin is then supposed to free sugar from the liver-cells, hence explaining the transient glycosuria which may supervene. The sugar set free is then supposed to supply the muscles which have been exhausted with the energy they require. The first effect of fear and rage is to cause dehydration of the protein particles in the blood-stream and the dehydration may go so far as to cause hyper-glycæmia and glycosuria. But, excessive fear causes protein hydration severe enough to occasion shock and parenchymatous degeneration of one or more of the viscera, the liver in particular. The dehydration occurs independently of adrenalin, and adrenalin prevents shock, two facts which negate the current view regarding the action of fear.

The supposed outpouring of adrenalin into the circulation in fear and other conditions has received so much publicity in medical circles that the author feels compelled to dwell longer on the subject. In the first place it is not known how a ductless gland pours its product into the blood-stream. In the second place it is not known whether the product poured out is the actual substance found afterwards and synthesised in the laboratory. In the third place the presence of the product in the blood-stream is determined by indirect means and not by direct means, as there are no specific tests for adrenalin, etc., in the blood. The indirect means draw attention to the altered chemico-physical changes undergone by the protein particles in the plasma and do not lay bare any one or more chemical substances. If adrenalin is increased in the blood in fear, it should be found in excessive quantities in shock, the further stage of fear. But, shock is the result of hydration, for which adrenalin is an antidote. All drugs able to produce shock usually cause fear first.

Take histamine as an example. Histamine produces shock or hydration in virtue of its positively charged nitrogen atoms, but owing to the comparatively small size of its nucleus the initial action is one of dehydration. An animal injected with histamine runs about the room before shock appears to find a dark place in which to hide. So long as it is able to hide

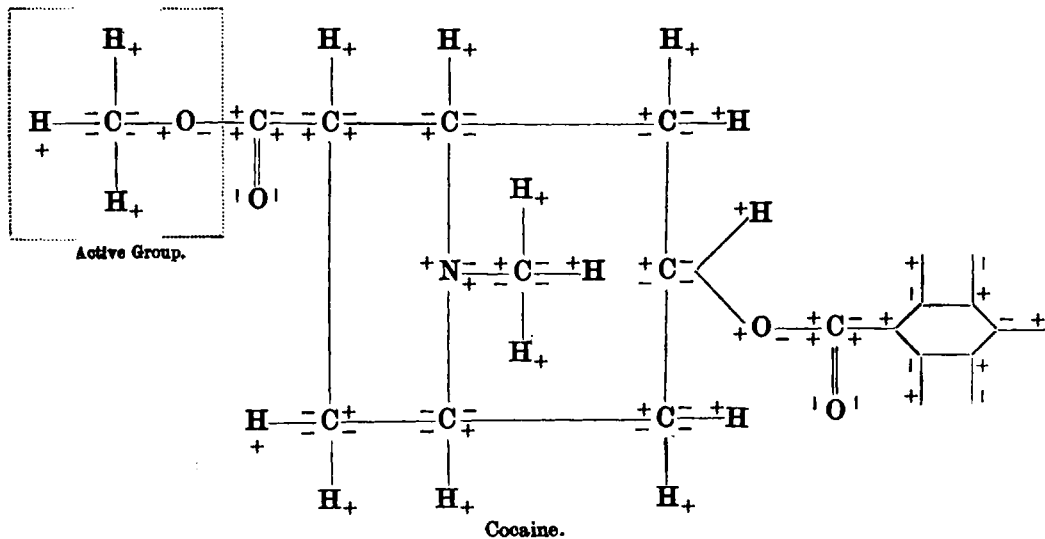
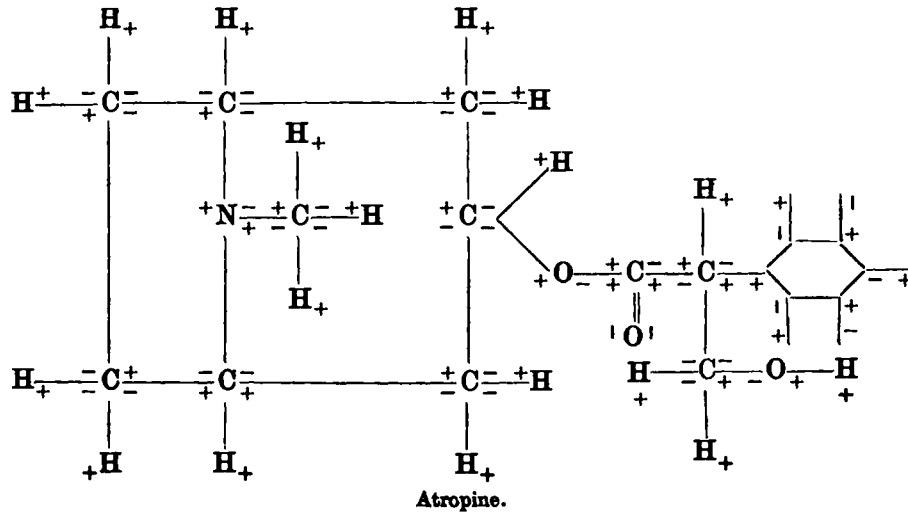
shock may not ensue, but should the animal be handled and frightened, further shock sets in at once. The same occurs with insulin; that is to say, an animal may fail to develop fits, convulsions and shock unless frightened in some way. This explains the peculiar psychic and paralytic phenomena occurring in man towards the end of an acute infection, and in dogs as a sequel to distemper. Acute infections give rise first to dehydration and then to hydration, and alternately the protein particles may become so hydrated as to undergo precipitation in the brain, thus to cause excitation and then degeneration. The author has often wondered whether the encephalitis following measles, vaccination, etc., may not be due to the poorly hydrated protein particles, which have undergone this change as a sequence of the dehydration occasioned by the primary invading micro-organism. Note also the neurasthenia which occurs in the wake of influenza, and the same condition, hysteria, chorea, paralysis, etc., which occur in dogs after an attack of distemper. Following the train of thought even further, the author is reminded of the seborrhœic *facies* found so commonly in post-encephalitic cases, and of the close association of bad *Acne vulgaris* and seborrhœa with mental instability amounting in some cases to insanity.

Choline is a drug consisting of a positively charged *penta*-valent nitrogen atom which functions as the vehicle and hydrator portion, and five negatively charged active groups which function as dehydrators. When the vehicle is positively charged, has a large nucleus or a small nucleus which is naked so to speak, as in choline, it has an initial hydrator action. Hydration causes vascular dilatation, a change which increases the permeability of the vessel wall, thereby allowing hydrated protein particles to pass through and cause dehydration of the static protein particles. This dehydration means increased activity, hence it comes about that the early action is one of excitation and not of inhibition. Excitation of the vegetative nervous system causes contracted pupils, bradycardia, muscular contraction of the alimentary canal with increased secretion, and contraction of the bladder and uterus. Choline has no specific action because practically speaking every compound with a vehicle containing a positively charged nitrogen atom behaves similarly, so long as the active group or groups are negatively charged.

Examples are nitrites, *penta*-methylene-tetrazol (cardiazol), muscarine, pilocarpine, physostigmine, nicotine, arecoline, etc.

A similar effect, though not so strong, is produced if the positively charged nitrogen atom is replaced by a positively charged sulphur, oxygen or phosphorus atom. If too large doses are used there may be intense salivation,

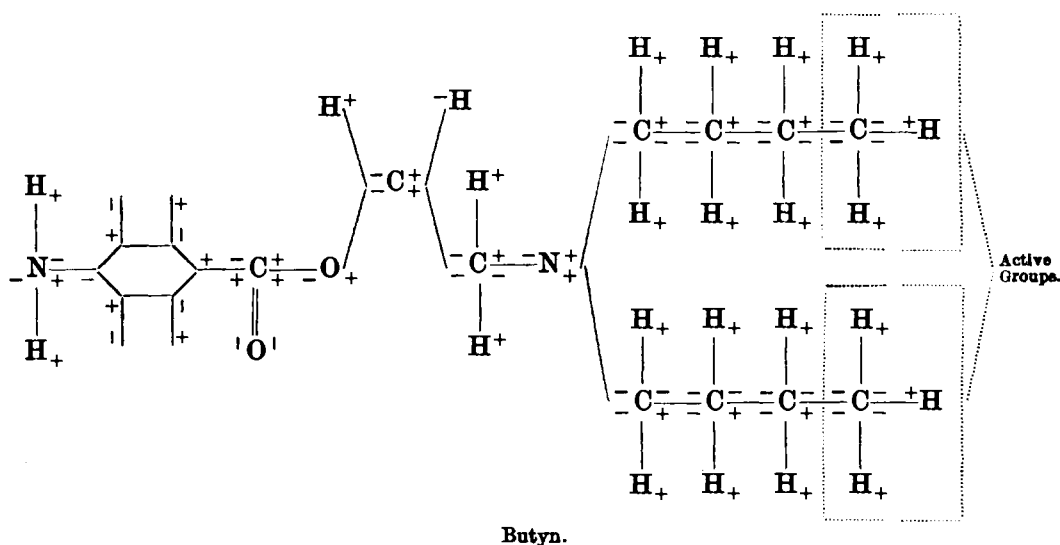
powerful muscular contractions, diarrhoea, paralysis, difficulty of breathing and death from shock. These clinical manifestations arise *de novo* when drugs are employed possessing a similar vehicle but no active groups, drugs



which are regarded as paralysing the autonomic nervous system, such as histamine, coniine, atropine, etc. It is not absolutely essential for the vehicle to contain a positively charged nitrogen, sulphur, oxygen or phosphorus atom because camphor, hexeton, etc., behave somewhat similarly to the choline-like compounds.

There is another group of compounds which has an action akin to choline and its allied preparations, but the relationship has not been recognised, because it has been overshadowed by the peculiar action of these substances—viz., anæsthetic action. Drugs producing anæsthesia do so in virtue of a positively charged vehicle having one or more negatively charged active groups.

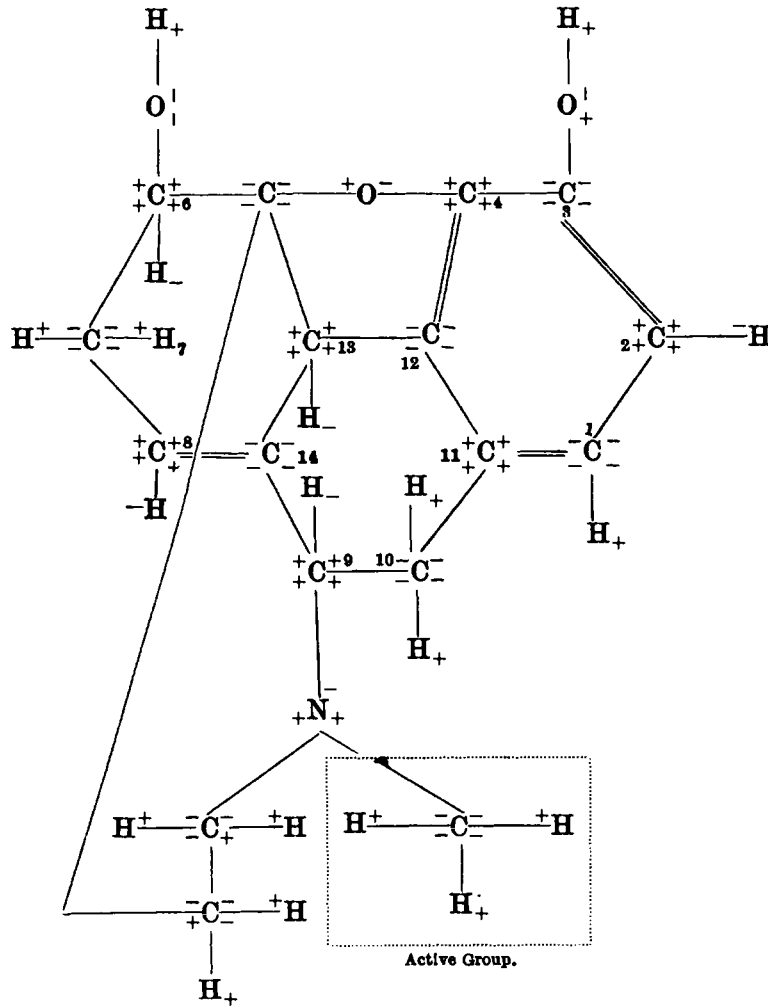
In carbon *tetra*-chloride the vehicle or carbon atom has all its valencies positively charged and the active groups are the negatively charged chlorine groups. In cocaine the active group is the negatively charged ester group, and in the derivatives of cocaine the active groups are the negatively charged



alkyl groups attached to the positively charged nitrogen atom. The altered electronic formulæ of cocaine and butyn which are appended here are probably more correct than those depicted in Part II, "The Nature of Disease," because atropine, which merely paralyses and has no anæsthetic action, would appear to be constituted in the way now illustrated. In morphine the active or dehydrator group is the negatively charged methyl group attached to the positively charged nitrogen atom. Apomorphine has no narcotic action and functions merely as a hydrator, presumably because the positively charged nitrogen is in the ring. Even when a negatively charged methyl group is attached to a positively charged nitrogen atom in a ring no dehydrator effect is produced, as evidenced by the N-propyl-piperidine producing more hydration than piperidine. Papaverine and narcotine doubtless owe their narcotic

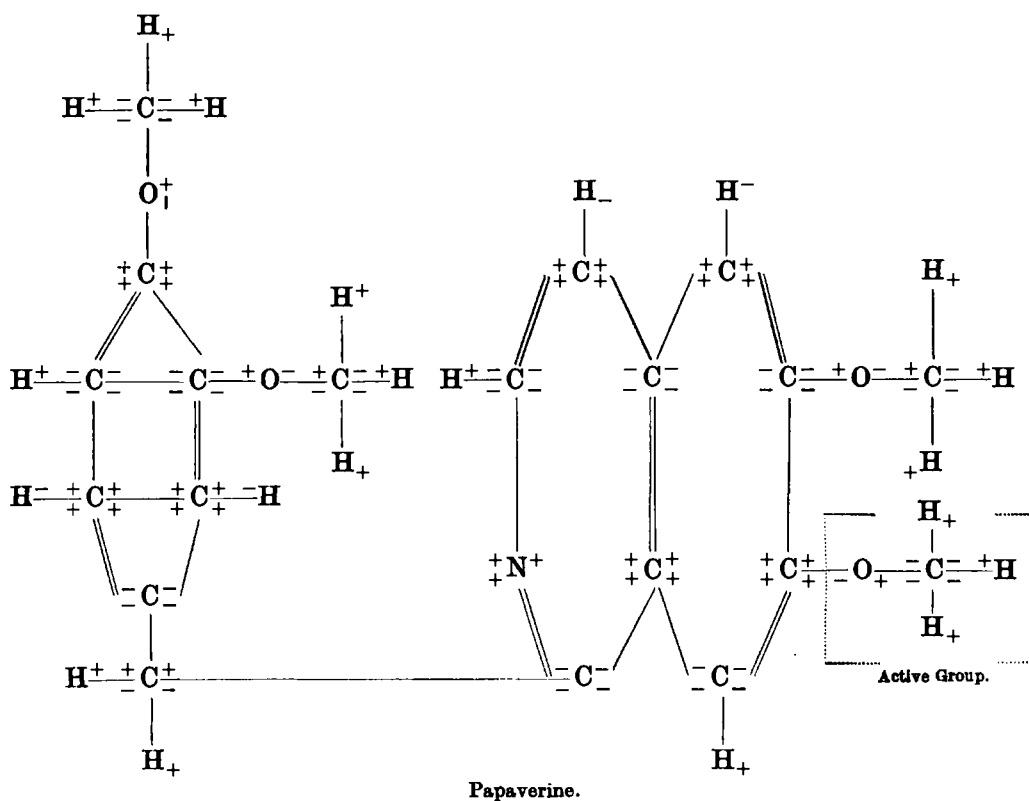
properties to the negatively charged methoxy group in the naphthalene ring, and hydrastine fails to act in a like manner because this group is not present.

Anæsthetic drugs produce sleep owing to the collection of hydrated protein particles in the brain, a condition which causes a varying degree of cerebral



œdema. The hydrated protein particles do not become precipitated in any one part of the brain because, when animals are killed with toxic doses of anæsthetic drugs injected intravenously, the whole of the brain may be œdematous and bloodless and the peri-capillary and peri-neuronic spaces are dilated in the cortex as well as in the brain-stem. During sleep the pupils are contracted,

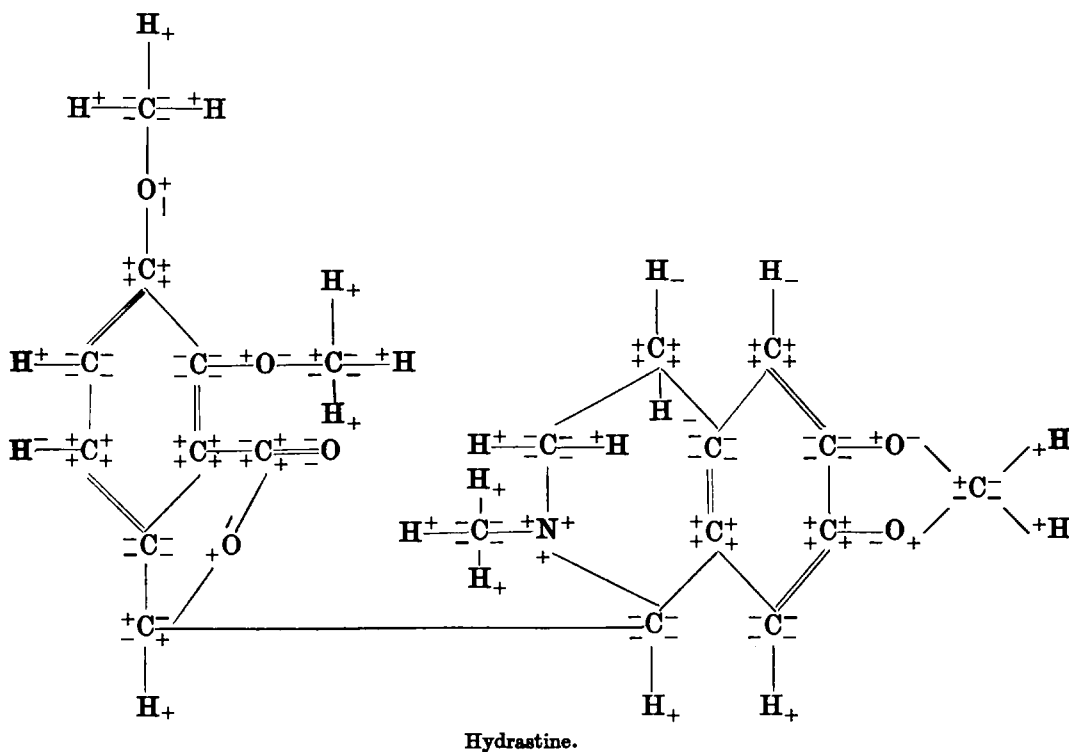
suggesting the collection of the hydrated particles in the mid-brain, and, as anæsthesia progresses, signs as if the vagal nucleus had been stimulated may arise. When toxic manifestations occur they do not differ from those met with in uræmia, eclampsia, insulin intoxication, spasmophilia, etc. A patient dying under an anæsthetic dies of cerebral hydration, œdema or shock as a result of the precipitation of hydrated protein particles in any part of the brain, although in the region of the vagal nucleus particularly. It is obvious



that if the protein particles are hydrated before the anæsthetic is administered the risk of death is enhanced, but it is not necessary to coin the name "*Status lymphaticus*" to describe such a condition.

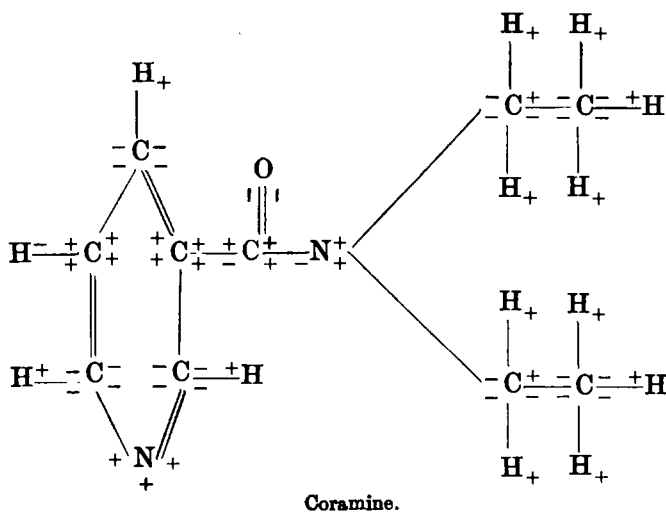
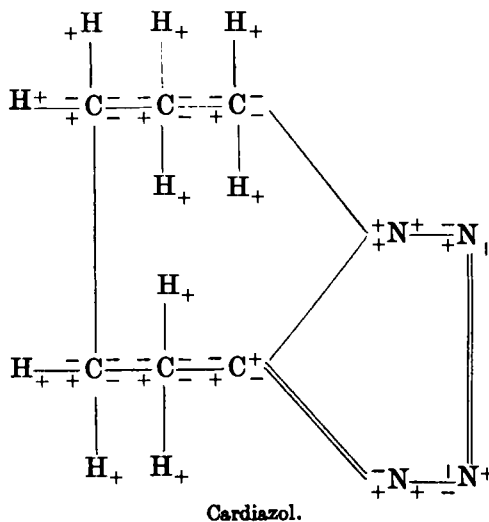
Many hydrators causing cerebral shock occasion before the fatal issue excessive muscular contractions referred to as convulsions and fits, as if some of the hydrated protein particles were stimulating the pyramidal system. Anæsthetic substances may act similarly, and there is no difference in the fits occurring during anæsthesia from those caused by such drugs as histamine,

insulin, etc. Anæsthetic preparations, in virtue of their dehydrator groups, overcome the hydration produced by the vehicle and the hydrated particles become dispersed. If the dispersion is excessive gelation occurs, and this may give rise to various conditions ranging from pulmonary embolism to simple venous thrombosis. On the other hand, some particles may remain hydrated while others are sent rapidly into solution, and when this occurs the patient may present glycosuria, ketonuria, albuminuria, etc.



Choline and the other so-called "vagotonic" preparations have a late action, as do anæsthetic drugs; indeed, many used therapeutically owe their success to this late action, which, in virtue of the negatively charged active groups, causes dispersion of hydrated protein particles. Nitrites, cardiazol and coramine, for example, slow the pulse, stop auricular fibrillation, check extrasystoles and cause the pain of *Angina pectoris* to vanish—first, because they cause a dilatation of the peripheral blood-vessels which relieves the congestion in the heart and aorta, and secondly because they cause dispersion of the hydrated particles which rendered the congestion possible. The first action is

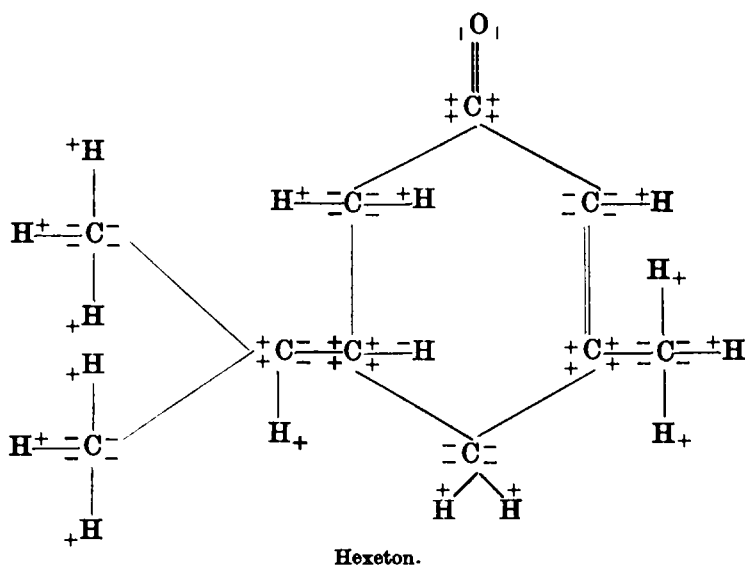
one of hydration occasioned by the positively charged nitrogen atom, and the second action is one of dehydration occasioned by the negatively charged oxygen, nitrogen, and alkyl groups respectively. From this it would appear that



the following electronic formulæ for cardiazol, coramine and hexeton are more correct than those depicted in the previous volume.

Choline in virtue of its positively charged *penta*-valent nitrogen atom causes an initial hydration which quickly wears off and is succeeded by a

combination of dehydration and conduction. The negatively charged alcoholic group causes dehydration and the negatively charged methyl and hydroxy groups tend to cause a slight degree of conduction. Naturally the conductor effect is very slight because the vehicle contains such a small nucleus, but nevertheless it is exhibited particularly if the protein particles have been subjected to hydration beforehand. It is for this reason that the author has used choline on quite a large scale, especially in cases of cerebral hydration causing mental aberration, epilepsy, migraine, etc. Before Villaret and Justin-Besançon²² introduced acetyl-choline into clinical medicine, the author was experimenting with this and other derivatives of choline, and has since



employed the acetyl body in place of the parent substance. The acetyl body is more active because one of the negatively charged active groups forms a terminal link in a chain instead of being attached directly to the positively charged vehicle. The clinical conditions mentioned above are caused by hydrated protein particles becoming precipitated in the peri-capillary lymphatics and capillaries of the cerebral cortex, base of the third ventricle and optic thalamus respectively. The precipitation may and does take place in other parts of the brain, but it is mainly to the precipitation in the areas named that the cardinal clinical manifestations are due. Choline, in virtue of its hydrator action, produces first a peripheral vaso-dilatation, which helps to relieve the cerebral oedema. Later, the dehydrator and conductor groups

come into action and cause dispersion of the hydrated particles, with the result that the clinical signs and symptoms vanish. The following three cases illustrate the therapeutic effect of choline :—

Case 75

A woman, aged forty-four, had had delusional insanity for three months. The patient was a typical example of familial chronic intestinal intoxication ; she was fat, had septic teeth, a furred and fissured tongue, and the pupils were dilated. The patient had hyper-extended elbows and could not stand with her knees and feet together at the same time. The pulse was arrhythmic and the blood-pressures registered 110 and 80 mm. of Hg. respectively. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·6 c.c.
Refractive index of the serum	= 1·3498
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 39 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a high percentage of very refractile giant particles and ringed particles. There were a fair number of very refractile giant particles (with a halo) and ringed particles precipitated with one or two clumps and agglutinations. The particles were extremely refractile and difficult to focus.

The patient received daily injections of choline, each of 0·2 grm., till twelve had been made, the number necessary to restore the patient to her normal condition.

Case 76

A boy, aged twelve, began attacks of *Petit mal* when aged five, and when first seen was a definite epileptic with mental deterioration. Oto-sclerosis was well marked on the paternal side of the family, and the boy's father had been operated upon for appendicitis and suffered from rheumatism. As a child the patient suffered from cyclical vomiting, and ever since he had been liable to attacks of migraine associated with vomiting and diarrhoea. An examination of the abdomen revealed a hard and contracted left colon, and the pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (10 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·15 c.c.
Refractive index of the serum	= 1·3491.

Percentage of the blood-sugar	= 0·137 grm.
Percentage of the blood-urea	= 17 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving. There were many particles precipitated <i>en masse</i> consisting of large and refractile giant particles, ringed particles, giant-particled clumps and agglutinations.

As the patient was having several fits a day, daily intra-muscular injections of choline, each of 0·1 grm., were prescribed, while the colonic lavage, etc., were being carried out. The treatment was continued for about a month. The choline gave the boy good nights and stopped the fits for the time being.

Another patient who had been in a condition of *Status epilepticus* for some days recovered completely when acetyl-choline was injected.

Case 77

A woman, aged forty-nine, had been a martyr to migraine for thirty-one years. The attacks came on about every ten days and lasted from two to eight days. The patient's father died of a stroke, aged fifty-four, and had suffered from fainting attacks for some years previously; the mother died following a miscarriage, aged thirty-two, and two step-sisters (same father) of Bright's disease, aged seventeen and fourteen respectively. The patient used to have very bad chilblains, she had suffered from rheumatism, had always had dysmenorrhœa and repeated attacks of acute colitis. The patient had three children, all of whom had a chronic nasal catarrh, one with hay-fever, and two had been operated upon for appendicitis. The patient had had all her teeth out and intra-neural injections of alcohol without benefit. The pulse was 80 and the blood-pressures registered 170 and 100 mm. of Hg. respectively. An examination of the abdomen revealed definite evidence of chronic colitis, the pathogenic micro-organism found in the excreta was the *Bacillus fœcalis alkaligenes* (25 per cent.), and the blood-picture was as follows (during a bad attack) :—

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3480.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 16 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, but they were mostly large and refractile

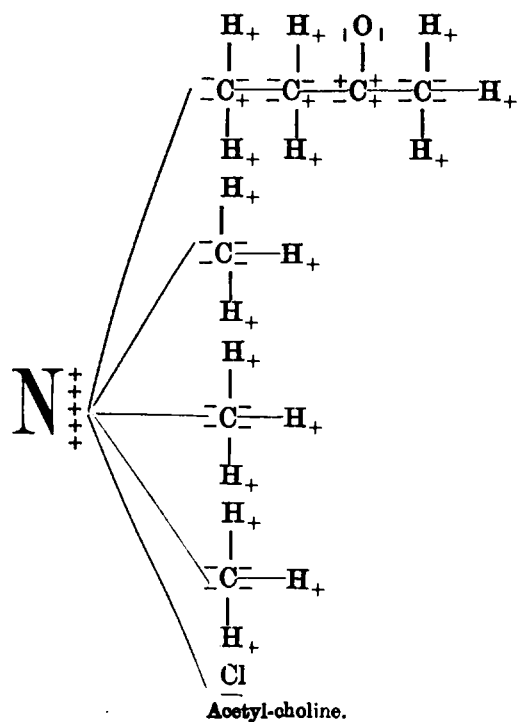
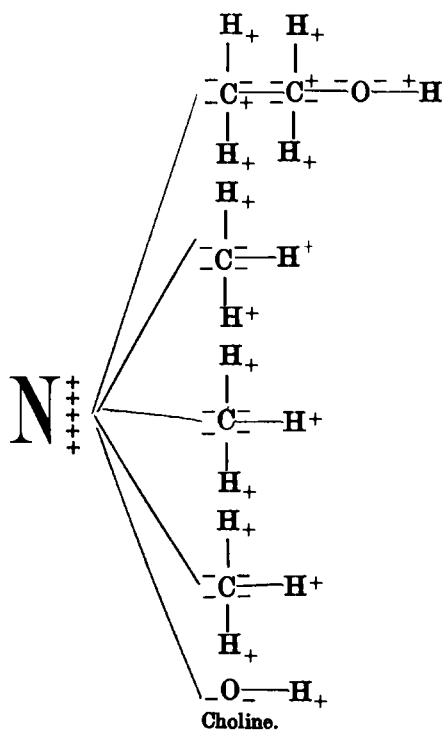
giant particles and ringed particles. There were a fair number of refractile giant particles, ringed particles and giant-particled clumps precipitated with one or two agglutinations. The Brownian movements were sluggish.

The blood-pressures during the attack registered 150 and 85 mm. of Hg. respectively ; 0.2 grm. choline was injected intra-muscularly, with the result that the patient slept all night and woke up the following morning free from pain.

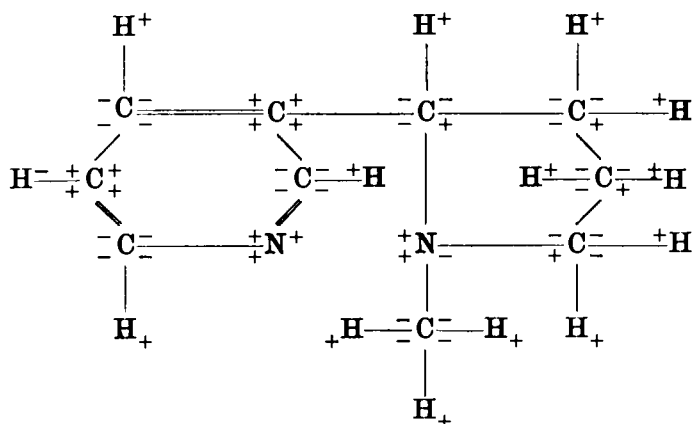
While the chronic intestinal intoxication was being dealt with the patient received about thirty injections of choline with a marked benefit, but the injections had to be stopped as the heart-beat became irregular and the ankles œdematous. The appearance of the arrythmia and œdema showed that the action of the drug was now of an hydrator nature, confirming what has been stated frequently in these volumes, viz., that the late action of a drug tends to be the same as its initial action. To prevent this recurrent hydrator effect of choline it is necessary to intersperse the injections with the conductor-acting symmetrical urea compounds.

These three cases show quite clearly that choline cannot be described as a vagotonic drug. Even its action in overcoming mild cases of ileus does not allow of its being so classified, because cardiazol is equally useful, and both function by subjecting to dispersion the hydrated protein particles which have been precipitated locally. Acetyl-choline, propionyl-choline, neurine and muscarine are all more active than choline. The activity of acetyl-choline is increased as the chain is lengthened up to the valeryl compound. Neurine is more active than choline because of the double bond in the vinyl group. Consequently the compound with the treble bond (acetenyl group) is more active still. If the hydrator effect of the nitrogen group is enhanced as in pyridine-choline, for example, so much hydration occurs as to produce paralysis and death from cerebral shock. The shock effect is diminished in increasing ratio as the nitrogen atom is replaced by sulphur, oxygen and phosphorus, because both the positive and negative valencies of these elements are less than those of nitrogen. Provided sufficiently large doses are used, acetyl-choline, cardiazol, coramine, neurine, muscarine, nicotine, arecoline, etc., cause complete paralysis, and death from cerebral shock occurs, and in such doses these compounds exhibit an action indistinguishable from those of histamine, coniine, apomorphine, etc.

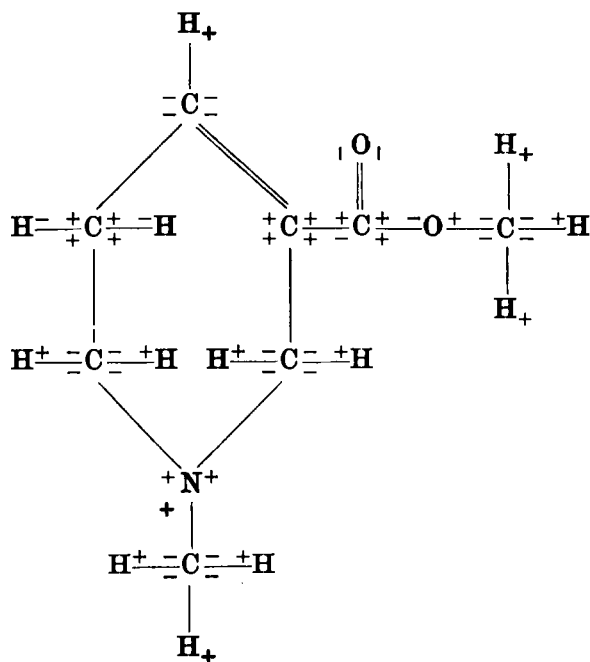
The following diagrams depict the electronic formulæ of choline, acetyl-choline, nicotine and arecoline :—



THE NATURE OF DISEASE



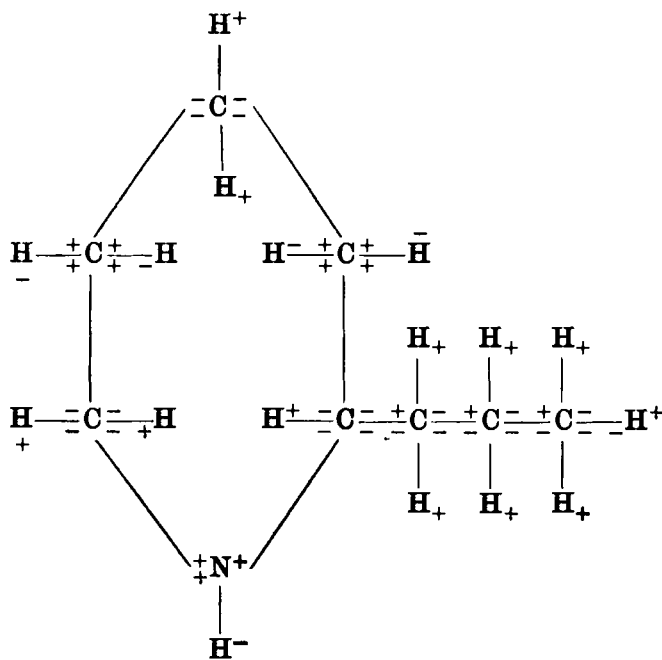
Nicotine.



Arecoline.

It is interesting to compare the action of coniine with the drugs mentioned above, and its electronic formula is depicted on p. 159.

From this formula it is seen that the terminal methyl-link of the alkyl chain is positively charged—in other words there are no active dehydrator groups. Coniine produces complete paralysis and death from cerebral œdema and shock,



Coniine.

as do histamine, atropine, apomorphine and the drugs with dehydrator groups when too large doses are employed. The question might be asked : If anæsthetic drugs and choline function in virtue of their positively and negatively charged groups, why is it that choline does not produce anæsthesia ? The answer is that dehydration is the initial action of anæsthetic substances and hydration the initial action of choline. A few animal experiments are reported below to show the action of some of the drugs mentioned above on the protein particles in the plasma :—

Rabbit 1

This animal, a male, was treated with intra-venous injections of choline.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before 0.001 gm. . . .	Grm. 0.162	1.3477	Many tiny particles moving with some giant particles and a fair number of small clumps. Some giant particles and clumps precipitated with one or two agglutinations.

Rabbit 1—*continued.*

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
One hour later	0·175	1·3485	More particles precipitated.
Before 0·001 grm., a week later .	0·143	1·3491	Very few particles moving with some giant particles, ringed particles and clumps. There was some general precipitation.
Before 0·01 grm., a week later .	0·137	1·3491	Practically no change.
One hour later	0·143	1·3483	General precipitation more marked.
Before 0·01 grm., a week later .	0·150	1·3495	Fair number of particles moving with ringed particles, giant particles and clumps. Some giant particles and clumps precipitated.
Before 0·1 grm., a week later .	0·156	1·3482	Practically no change.
One hour later	0·162	1·3477	More particles precipitated.
One week later	0·156	1·3490	Practically no change.

The first injection of choline raised the refractive index of the serum and increased the precipitation of the protein particles in the plasma, two of the most characteristic features of hydration. The immediate effect of the third injection was to cause some dehydration, as evidenced by the rise in the percentage of the blood-sugar and the fall in the refractive index of the serum. This was still more marked following the fifth injection, although the ultimate effect was hydration, because the refractive index of the serum rose from 1·3477 to 1·3490. First hydration, then progressive dehydration so long as the drug is being prescribed, and finally hydration is the characteristic sequence of events following such a drug as choline. Clinically the initial hydration causes peripheral vascular dilatation, which relieves the congestion of the area involved in the diseased process. The subsequent dehydration breaks up the hydrated particles. The final action may result in the symptoms returning unless in the meantime the cause of the initial hydration has been removed. It follows from this that drugs can never be more than palliatives. It is due to the final hydration that choline and its *confrères* may fail to function on subsequent occasions as on the first.

In order to illustrate the point that choline possesses a dehydrator action, as well as a hydrator action, the rabbit received the week following the fifth injection 0·01 grm. coniine, with the result that it developed a transitory paresis of the hind legs only. Had choline possessed only a hydrator action, the injection of coniine following 0·1 grm. choline would have killed the animal. To show that the dehydrator action of choline is in part dependent upon the

three negatively charged methyl groups, the animal received the following week 0.01 grm. coniine preceded one hour by 0.005 grm. gentian-violet, and no paresis occurred.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before 0.005 grm. gentian-violet	Grm. 0.137	1.3490	Few particles moving with some giant particles, ringed particles and a few clumps. There were some giant particles and giant-particled clumps precipitated.
One hour later, before 0.01 grm. coniine.	0.156	1.3488	More particles precipitated.
One week later	0.168	1.3478	Many particles moving with some giant particles and a few giant-particled clumps. A few giant particles, clumps and one or two agglutinations precipitated. There was also a background of sheet-like precipitation.

To show that coniine was prevented from causing paralysis by the conductor action of gentian-violet, the animal received the following week another injection of coniine, preceded by 10 units of para-thor-mone, the body's own natural conductor, and no paralysis occurred. When coniine alone was injected the following week the animal died. The sex of the animal is given in these experiments because the action of drugs in females is influenced enormously by castration and pregnancy.

Rabbit 2

This animal, a female, received 0.0001 grm. acetyl-choline intra-venously and 0.001 grm. histamine one hour later. The animal became very weak and paretic after the acetyl-choline, but recovered the moment it received benzoyl-*para*-amino-benzoyl-*para*-amino-benzoyl-3-6-8-hydroxy-naphthalene. After the injection of histamine the animal just toppled over and died without exhibiting the violent movements seen in shock.

Acetyl-choline causes marked hydration and dehydration, and the former action is exhibited before the latter. The hydration causes the paralysis and is brought about by the *penta*-valent positively charged nitrogen atom. The naphthalene compound, acting as a conductor, brought the animal round, but not sufficiently to prevent a fatal issue when another drug with positively charged nitrogen was injected. In this case the histamine produced no

initial dehydration, so the animal died as it would have done with a fatal dose of such drugs as coniine, nicotine, arecoline, etc. If a non-toxic dose of acetyl-choline immediately precedes, or follows, a non-toxic dose of coniine, the animal develops complete paralysis. But, if the dose of acetyl-choline is injected some time before that of coniine, even a fatal dose of the latter would prove innocuous. This is because the hydrator action of acetyl-choline is succeeded by one of dehydration.

Rabbit 3

This animal, a male, received eight injections of cardiazol at weekly intervals, three doses of 0.01 gm. and five doses of 0.05 gm.

Injection.	Percentage of the Blood-sugar.		Refractive Index of the Serum.		Ultra-microscopic Picture of the Serum.
Before first .	Grm. 0.112	Difference. —	1.3463	Difference.	Many particles moving with a few giant particles, ringed particles and clumps. Many particles precipitated in the form of giant particles, ringed particles and clumps. There was also some general precipitation. Fewer particles moving and more precipitated. Still fewer particles moving and more precipitated. Fair number of particles moving with some giant particles and small clumps. The Brownian movements were sluggish. Very many particles precipitated in the form of giant particles and clumps. Unchanged.
		+ 0.031 gm.		+ 0.0007	
One hour later	0.143	—	1.3470		
Before second	0.131	—	1.3471		
Before third .	0.150	—	1.3488		
Before fourth.	0.137	—	1.3488		

The blood was very thick and difficult to obtain. The injection of 0.05 gm. caused immediate shock, but the animal recovered the moment 0.002 gm. Sup. 36 was injected. Shock occurred after the injection the following week, and the animal recovered when 0.001 gm. Sup. 468 was injected. The next week shock occurred again and the animal recovered, although 0.0005 gm. digitalin did not hasten its recovery.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before seventh . . .	Grm. 0.125	1.3495	Few particles moving and these were mostly giant particles and clumps. There were many similar particles precipitated, as well as some precipitation <i>en masse</i> .

The animal was badly shocked. Half an hour later another 0.05 gm. dose of cardiazol was administered and the animal recovered more quickly than was the case following the first injection. The following week shock again followed a 0.05 gm. dose of cardiazol and the animal was killed.

From the above it is seen that the action of cardiazol is similar to that of choline. Choline, acetyl-choline, cardiazol, etc., produce shock, as does histamine because of the hydration occasioned by the positively charged nitrogen atoms. But, there are differences in the nature of the shock produced from the type caused by histamine, and it is due to these differences that choline, acetyl-choline, cardiazol, etc., are of value in certain chemical conditions akin to shock. Unless the protein particles are hydrated beforehand, the initial action of histamine is one of dehydration, and this is progressive so long as the injections are made at frequent intervals. The progression is up to a point only because in time hydration must follow upon dehydration, and when this occurs shock supervenes. If an interval of fourteen days is allowed to intervene between the first two injections the second produces fatal shock, and the first injection is referred to as the sensitising dose. Histamine causes a constriction of the peripheral blood-vessels, and the protein particles when hydrated become precipitated in the peri-capillary lymphatic vessels and capillaries of one or more of the vital organs. Choline, acetyl-choline, cardiazol, etc., produce shock with any injection provided the hydration produced is sufficient, and this is uninfluenced by the state in which the protein particles happen to be at the time; consequently no sensitising dose is necessary. Once hydration occurs with histamine it is more or less continuous, but with the other drugs it is fleeting and quickly succeeded by dehydration, with the result that the shock is seldom fatal. The hydration following choline, acetyl-choline, cardiazol, etc., occurs in the peripheral circulation where the vessels are dilated. This relieves the area congested and results in the protein particles precipitated there undergoing dispersion; consequently these preparations are useful in certain clinical conditions allied to shock.

Rabbit 4

This animal, a female, and pregnant at the time, as evidenced by the steady fall in the refractive index of the serum, received intra-venous injections of nicotine in doses of 0.001 grm.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before first	Grm. 0.118	1.3470	Many particles moving with a few giant particles and ringed particles. There were a fair number of particles, giant particles and ringed particles precipitated.
One hour later	0.137	1.3480	Very little change.
Before second, a fortnight later.	0.086	1.3470	Many particles moving with a few giant particles, ringed particles and giant-particled clumps. There were a fair number of refractile giant particles and ringed particles precipitated with a few giant-particled clumps.
One hour later	0.118	1.3460	Very little change.
Before third, one week later	0.086	1.3452	Many particles moving with a fair number of giant particles, ringed particles and giant-particled clumps. There were some giant particles, ringed particles and large giant-particled clumps precipitated.
One hour later	0.118	1.3458	There were a few more particles precipitated.
Before fourth, one week later.	0.156	1.3449	Many particles moving with some refractile giant particles, ringed particles and small clumps. There were a few particles, giant particles, ringed particles and small clumps precipitated.
One hour later	0.150	1.3449	There were more clumps amongst the moving particles.

The animal had severe convulsions immediately following the first injection, then became paralysed and recovered before the blood was taken one hour later.

Paralysis followed the subsequent injections, but on each succeeding occasion it was less marked and recovery ensued more rapidly. The clinical result and the blood-picture show that the initial action of nicotine is one of hydration, but not much more can be gleaned from the latter owing to the complicating factor of the pregnancy.

Rabbit 5

This animal, a female, received four weekly intravenous injections of arecoline hydrobromide.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before first of 0.0001 grm. .	Grm. 0.131	1.3499	Many particles moving with a few giant particles. There were some refractile giant particles, ringed particles and clumps precipitated.
One hour later	0.143	1.3498	Not much change.
Before second of 0.0002 grm.	0.118	1.3480	Fair number of particles moving with some giant particles, ringed particles and small giant-particled clumps. There were a few giant particles, ringed particles, clumps and agglutination precipitated.
One hour later	0.143	1.3482	Not much change.
Before third of 0.0003 grm.	0.131	1.3496	Fair number of particles moving with some refractile giant particles, ringed particles and clumps. Some particles, giant particles and ringed particles precipitated with a few clumps.
One hour later	0.106	1.3496	There was some general precipitation <i>en masse</i> .
Before fourth of 0.0005 grm.	0.131	1.3475	Scarcely a particle moving. There were a fair number of particles, giant particles, ringed particles and giant-particled clumps precipitated.
One hour later	0.137	1.3471	More particles precipitated.

The animal became paretic and had profuse sialorrhœa immediately following the fourth injection. This blood-picture shows evidence of both hydration and dehydration, and the reason why the refractive index is low before and after the fourth injection is because many of the protein particles had left the peripheral circulation and those remaining were poor in electricity.

Rabbit 6

This animal, a female, received intra-venous injections of atropine. A fortnight elapsed between the first two injections, otherwise they were made at weekly intervals.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before first of 0.00001 grm.	Grm. 0.150	1.3483	Very many particles moving with many clumps. There were a few giant particles and small clumps precipitated.
One hour later	0.143	1.3478	More clumps moving and more particles and clumps precipitated.
Before second of 0.00002 grm.	0.131	1.3472	Few particles moving with some giant particles and giant-particled clumps, both moving and precipitated.
One hour later	0.118	1.3472	More particles precipitated.
Before third of 0.0005 grm. .	0.112	1.3452	Fair number of particles moving with a fair number of ringed particles and clumps. There were many more particles precipitated <i>en masse</i> .
One hour later	0.112	1.3457	Fewer particles moving and many more precipitated in large agglutinated masses.
Before fourth of 0.001 grm.	0.112	1.3478	Fair number of particles moving with some giant particles, ringed particles and clumps. There were some particles, giant particles, ringed particles and clumps precipitated. The Brownian movements were sluggish.
One hour later.	0.118	1.3481	The Brownian movements were more sluggish and there was some precipitation.
Before fifth of 0.001 grm. .	0.137	1.3473	Few particles moving with a few refractile giant particles and ringed particles. There were some particles precipitated <i>en masse</i> and the Brownian movements were very sluggish.
One hour later	0.143	1.3500	Many more particles moving with some giant particles, ringed particles and small clumps.
Before sixth of 0.002 grm. .	0.112	1.3474	Fair number of particles moving with some giant particles, ringed particles and small clumps. There were a fair number of particles, giant particles, ringed particles and clumps precipitated with a tendency to form linear precipitation.
One hour later	0.137	1.3490	Many more particles moving.

The general feature of the above picture is hydration as evidenced by the falls in the percentage of the blood-sugar, the rises in the refractive index and the ultra-microscopic appearances. Hydrators of this class frequently cause a temporary fall in the refractive index of the serum. This fall is most marked following the second injection, and it is always greater in does than in bucks; indeed, the author is of the opinion that certain drugs may produce in rabbits a pseudo-pregnancy. This point is dealt with more fully in a later chapter, because oestruation in rabbits seldom occurs in the absence of copulation.

Once the pseudo-pregnancy was over the drug re-exhibited its hydrator action and produced an actual conductor effect, as evidenced by the increase in the number of the moving particles.

Rabbit 7

This animal, a male, received six intra-venous injections of apomorphine.

Injection.	Percentage of the Blood-sugar.	Refractive Index of the Serum.	Ultra-microscopic Picture of the Serum.
Before first of 0.0001 grm. . .	Grm. 0.131	1.3479	Fair number of particles moving with some refractile giant particles, ringed particles and small clumps. There were some very refractile giant particles, ringed particles and small giant-particled clumps precipitated.
One hour later	1.137	1.3477	There were a few more particles moving.
Before second of 0.0005 grm.	0.112	1.3486	Fair number of particles moving with a fair number of giant particles and a few ringed particles. There were a fair number of giant particles, ringed particles and clumps precipitated with much precipitation <i>en masse</i> .
One hour later	0.112	1.3488	Much less precipitation.
One week later	0.112	1.3462	Very many particles moving with a few giant particles. There were some particles, giant particles and ringed particles precipitated with one or two huge agglutinated masses.
A fortnight later and before third of 0.001 grm.	0.112	1.3498	Many particles moving with a fair number of giant particles and clumps. There were some particles, giant particles and clumps precipitated.
One hour later	0.112	1.3480	More particles precipitated.
Before fourth of 0.002 grm. . .	0.156	1.3474	Many particles moving with a few giant particles and large clumps. There were a fair number of large and refractile giant particles precipitated.
One hour later	0.131	1.3478	More particles precipitated.
Before fifth of 0.005 grm. . . .	0.131	1.3468	Many particles moving with some refractile giant particles, ringed particles and giant-particled clumps. There were some giant particles, ringed particles and giant-particled clumps precipitated with one or two huge agglutinated masses.
One hour later	0.131	1.3472	Much more precipitation.
Before sixth of 0.01 grm.	0.131	1.3472	Many particles moving with some giant particles and ringed particles. There were many giant particles precipitated <i>en masse</i> with some linear precipitation.
One hour later and before 0.001 grm. histamine.	0.131	1.3472	There was more precipitation <i>en masse</i> .

The hydrator effect of apomorphine is apparent from the above picture, and it is interesting to note the similar drop in the refractive index of the male occurring after the second injection. The injection of histamine caused the animal to run about violently, to hide itself in a dark corner and to stamp the ground with its feet, which is customary in the wild state as an alarm to the others. The animal then passed its urine and fæces involuntarily and became completely paralysed. There was no shock as usually occurs when histamine produces toxic symptoms, owing to the hydrator influence exerted by the apomorphine upon the protein particles beforehand. Previous hydration produced by a drug causes histamine to carry the hydration a stage further than that necessary to occasion shock, and paralysis is the clinical manifestation.

Summary

The vegetative nervous system is made up of the para-sympathetic or autonomic nervous system and the sympathetic nervous system. The autonomic nervous system is the dynamic arc of the reflex circuit and the sympathetic nervous system the static or inhibitory arc. The autonomic nervous system has its centre partly in the mid-brain and partly in the so-called "sacral" portion of the cord, but mainly in the hind-brain (nucleus of the vagus), and it ends peripherally in the walls of the intestines in Auerbach's plexus. Disease working through hydrated protein particles causes first stimulation and then paralysis of the autonomic nervous system, but it is not always possible to say in any individual case, whether the lesions produced are caused by the collection of the hydrated protein particles centrally, peripherally, or both. Even when the hydrated protein particles collect in the brain, they do not "pick out" the autonomic centres in the mid-brain and hind-brain to the exclusion of the cerebral cortex and the rest of the brain-stem, thereby explaining why lesions of the vegetative nervous system are associated with alterations of psyche and mal-co-ordination. Since disease shows itself first as excitation and then as degeneration, vagotonia is far more common than sympathetico-tonia, although the lesions produced may be referred to as being due to lack of inhibition. Lesions generally considered to be sympathetico-tonic in nature are more probably due to local paralysis of the endings of the vagus than to stimulation of the hypothetical centre or the endings of the sympathetic nervous system. Drugs do not act upon the vegetative nervous system as originally suggested by Langley. Drugs act primarily upon the protein particles in the plasma, and, through the chemico-physical changes wrought, signs and symptoms may be

produced suggestive of a stimulation and paralysis of the autonomic nervous system. Drugs having a conductor action accentuate the state of health or the condition of inhibition, consequently it is not surprising that blood-vessels contract under the influence of adrenalin. But, this action is not due to a stimulation of the sympathetic nervous system, either centrally, peripherally, or both.

The phenomena produced by fear and rage are due to the dehydration and hydration the protein particles in the plasma undergo and not to the pouring of adrenalin into the blood-stream. Drugs having an hydrator action first stimulate and then paralyse nerve centres and endings so long as the hydrator effect is maintained. Hence the reason why such drugs produce alterations of psyche, mal-co-ordination and vagotonia and then loss of consciousness, muscular spasms, and shock. Although some of these drugs may produce signs and symptoms referable to a stimulation and finally a degeneration of the centre and endings of the vagus, other cells in the brain and in the organs where the endings happen to be, suffer stimulation and degeneration as well ; consequently no drug can be spoken of as being vago-tonic. When a drug has a combined hydrator and dehydrator action, sleep, the result of hydration and venous congestion, is enhanced and anæsthesia is produced. Should such drugs be used in toxic doses, hydration is accentuated and loss of consciousness, muscular spasms and shock may be produced.

The relationship between the vegetative nervous system and the alimentary tract comes about in two ways : (1) protein particles in the plasma subjected to hydration by inherited disease stimulating the autonomic nervous system centrally, peripherally, or both ; (2) toxic metabolic substances reaching the blood-stream from the large intestine and subjecting the protein particles in the plasma to hydration, these tend to collect in the brain, where they may stimulate the centres of the autonomic nervous system, and in the splanchnic area where they may stimulate the endings of the autonomic nerve fibres and the cells of the organs.

The *Rôle* Played by a Chronic Intestinal Intoxication in the Invasion of the Nervous System by Micro-Organisms

There is no evidence that the pathogenic micro-organisms found in the excreta, namely, the non-lactose fermenters, ever leave the large intestine as such to invade the central nervous system. Should they gain entrance they are more likely to do so in a morphologically different form. In severe intestinal conditions such as sprue, pernicious anæmia,

intestinal obstruction, etc., the pathogenic micro-organisms are capable of passing from the large intestine through the ileo-cæcal valve into the small intestine. In the conditions named, and particularly in ileus, the result of paralysis, of intestinal obstruction, and of operations upon the intestinal tract, the *Bacillus Welchii* is found in such large numbers as to suggest it has developed pathogenic properties. This view is supported by the success achieved with injections of the anti-serum. On the other hand, these cases do equally well with bile enemata and with intra-muscular injections of choline, acetyl-choline, cardiazol, etc. The author has treated six cases of ileus with these drugs with complete success in five. The benefit resulting from the use of drugs suggests, that the paralysis of the nerve-endings in Auerbach's plexus is caused by the precipitation of hydrated protein particles in the peri-capillary lymphatic vessels and capillaries of the walls of the intestines. Whether the hydration is in any way brought about by the activity of the *Bacillus Welchii* is not easy to determine, but it supports the author's view that disease is occasioned by the changed protein particles rather than by the micro-organisms themselves. The *Bacillus Welchii* is found in the large intestine as well, but it flourishes better in the small intestine, where anaerobic conditions prevail. Bacilli grown under anaerobic conditions are capable of giving rise to particulate forms small enough to pass through filters. Consequently the author has often wondered if it is not possible that the *Bacillus Welchii* is an anaerobic mutation form of the *Bacillus coli communis*, and if some of the so-called ultra-microscopic viruses are not the particulate forms referred to. On the other hand aerobes may at any time develop anaerobic properties, and when they do so particulate forms can be developed therefrom ; therefore, even should the future show that the ultra-microscopic viruses are particulate forms of known micro-organisms, it will be some time before it can be determined whether they originate from the pathogenic micro-organisms in the intestines or from micro-organisms, ordinarily saprophytic, which have developed pathogenic properties in an individual whose resistance has been lowered by a chronic intestinal intoxication.

There is still another possibility to be considered, which is that the so-called ultra-microscopic viruses are not viruses at all, but particulate forms of the host's own protein particles which have been hydrated by an infection or intoxication and made to exist under anaerobic conditions. If this is correct, and likewise the author's view that cancer is due to a particulate body derived from the hydrated protein particles constituting the nucleolus of a cell, then a link is made between what amounts to an infection on the one

hand and to malignant disease on the other hand. In other words, the future may show that *Encephalitis lethargica*, *Herpes febrilis*, disseminated sclerosis, etc., and malignant disease are of the host's own making and manufactured on the same principle. There is a very important fact of which sight should never be lost, and this is that protein particles which reach the cerebro-spinal fluid from the blood, undergo in disease, as a result of the filtration, abnormal chemico-physical changes, whereby their reducing action is increased, or in other words, they acquire the power of subjecting the neurones to dehydration. The ultra-microscopic body formed from an hydrated protein particle cannot develop into a cell because there is no nucleus and nucleolus, and being formed rapidly the conditions are perfect for its behaviour as a parasite. The ultra-microscopic particle formed from a cell can develop into another cell, but it is formed slowly and the conditions are most favourable for its behaviour as a pseudo-parasite. In support of these contentions is the fact that some of the forms of encephalitis occur in the end stage of infections, such as influenza and measles, after vaccination and after the use of anaesthetics and other toxic chemical agents; in short, when protein particles hydrated rapidly are beginning to undergo the cyclical change of dehydration. As the chemico-physical changes most probably take place under anaerobic conditions the particles formed as a result of the cyclical change are ideally constituted to act as parasites. This view is still further confirmed by a study of milk fever in cows, which is considered to be caused by an ultra-microscopic virus. According to Spicer,²³ milk fever is confined to dairy farming; it is never seen in first and second calves, and it is confined to the three days after calving. Domestication of animals raises the incidence of disease in them, or in other words causes protein hydration. Protein hydration occurs naturally towards the end of pregnancy and is apt to be pathological if there was hydration beforehand. After pregnancy the hydrated protein particles are wont to undergo the cyclical change of dehydration, and in certain cases some of the very small particles formed may behave as parasites. If the udder is inflated milk fever does not occur or if already present it disappears at once, because the blood collected there is driven into the general circulation and no hydrated protein particles are able to collect in one area and undergo changes detrimental to the host. If due to an ultra-microscopic virus, milk fever could hardly be prevented and corrected by such a simple manoeuvre as inflation. Sup. 36 and calcium and strontium are also useful.

The nerve tissue infections in man, considered to be due to ultra-microscopic organisms, are *Encephalitis lethargica*, anterior polio-myelitis, *Herpes zoster*

and *Herpes febrilis*. Of these in only the first and the last are recurrences at all frequent. The author has seen cases of recurrent *Herpes zoster*, but relapses or fresh infections are certainly the exception.

From the cases examined the author has been more struck by the resemblances than by the differences between *Encephalitis lethargica* and disseminated sclerosis. Should the future show that these two conditions are related, then evidence will be forthcoming in favour of a link between chronic intestinal intoxication and sleepy sickness, because the cases of disseminated sclerosis have responded much better to treatment aimed at removing the chronic intestinal intoxication than to treatment with arseno-benzene. The following case is a case in point :—

Case 78

A youth, aged nineteen, suffered from disseminated sclerosis, which began three years previously with an inability to hold things in the right hand. The next sign was staggering, then nystagmus, followed by loss of speech and of power of both legs, with numbness affecting the left side of the face. The various clinical signs and symptoms cleared up after they had been present for a short time, to re-appear later in what appeared to be definite attacks. Both the patient and his father were typical examples of familial chronic intestinal intoxication. The patient developed chilblains one year after the nervous trouble began, he could not stand with his knees and feet together at the same time, and all his molars had been either stopped or extracted. He bit his nails, had a congenitally mal-formed left optic disc and was practically blind in this eye. The pulse was 88 and slightly irregular, and the blood-pressures registered 100 and 65 mm. of Hg. respectively. There were no abdominal or cremaster reflexes, an examination revealed a bad form of chronic colitis and the patient was definitely tender over the appendix area. The urine gave a very strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. A bacteriological examination of the fæces showed the pathogenic micro-organism to be the *Bacillus proteus Valeriei* (10 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·8 c.c.
Refractive index of the serum	= 1·3491.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 29 mgrm.

Ultra-microscopic picture of the serum = Fair number of particles moving with many giant particles and a few ringed particles and giant-particled clumps. Some giant particles and giant-particled clumps precipitated. The Brownian movements were sluggish.

The patient was dieted, he had his colon washed out and four injections of the faecal vaccine, since when there has been no relapse. A relapse appeared before the third injection of the vaccine, but it was slighter than usual and vanished immediately after the injection was made.

In another case of disseminated sclerosis affecting a youth in the same school as the above and at the same time, the pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilis* (50 per cent.).

The following case of disseminated sclerosis is an interesting one because it shows that the nerve trouble was only a small part of the clinical picture :

Case 79

A woman, aged thirty-four, had suffered from urticaria all her life, but had been fairly fit until two years previously, when she complained of dimness of vision, numbness of the legs and difficulty in walking. After the nerve trouble began the patient became more and more anæmic and had more or less continuous metrorrhagia. Both arms became involved later. The patient was very anæmic, her hair was almost white, the face was covered with milia, she had bilateral optic atrophy, all the teeth were decayed and the tongue congenitally fissured. The pulse was 86, the blood-pressures registered 105 and 65 mm. of Hg. respectively, and the heart showed signs of toxic myocarditis. The abdomen was tender all over owing to the whole of the colon being inflamed. The pathogenic micro-organism found in the excreta was one of the *Salmonella* group (90 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.6 c.c.
Refractive index of the serum	= 1.3481.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 16 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a fair percentage of giant particles, ringed particles, and small giant-particled clumps. There were a few giant particles, ringed particles, and small clumps precipitated. There were some empty rings moving.

The patient would take nothing internally which was of animal origin,

and she refused all injections. Consequently it was impossible to treat her. Had her urticaria been handled on the lines indicated in this section it is practically certain that disseminated sclerosis would never have supervened.

In view of the discussion above referred to, that the hydrated protein particles of the host cause nerve lesions, two cases are reported below, both of which had been diagnosed as cases of disseminated sclerosis.

Case 80

A woman, aged thirty-seven, complained first of numbness of the left thigh ; this was followed by weakness of the right leg, and later by loss of sensation when passing urine and fæces. The trouble had been present for three years. The patient was fat, she had hair on the upper lip and chin and complained of headaches. She had jaundice when aged twenty-five and had had several attacks of mucous colitis. The patient had oto-sclerosis ; she was never unwell for more than two days ; she had never been pregnant ; her tonsils, teeth and appendix had been removed, and the skin was pigmented as a result of arsenical dermatitis, nov-arseno-benzene having been prescribed without benefit, because the case had been labelled disseminated sclerosis. The patient had bow legs, her elbows were hyper-extended and wide-angled ; she had acro-asphyxia ; all the reflexes were increased except the abdominal, which had vanished ; leucorrhœa was troublesome ; the left colon was contracted ; there was tenderness in the regions of the flexures and ileo-cæcal portion, and the ascending colon and cæcum were dilated. The pulse was 116 and the blood-pressures registered 120 and 80 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (10 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3480.
Percentage of the blood-sugar	= 0·118 grm.
Percentage of the blood-urea	= 21 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few giant particles, ringed particles, and small clumps both moving and precipitated.

The patient was dieted and had a course of colonic lavage ; she took iodine, ichthyol and thyroid internally and received intra-muscular injections of Sup. 468 and of the fæcal vaccine.

The patient improved enormously ; the nervous symptoms abated, the periods lasted four days, and eighteen months later she became pregnant.

The abdominal reflexes are not infrequently absent in bad cases of familial chronic intestinal intoxication, even when there is no ascertainable lesion of the central nervous system.

This case shows the futility of giving a name to part of a clinical picture, because it causes neglect of the patient as a unit, and it makes the unthinking doctor prescribe for that part a treatment, the action of which he does not understand and which may do the patient harm. Disseminated sclerosis is not a clinical entity ; indeed, none of the labelled diseases are. There is no such thing as specific treatment, and in every case the patient as a whole is the premier consideration, not a symptom. Even in classical cases of disseminated sclerosis arsenic is of little or no value, and in the case discussed it did actual harm.

Case 81

A man, aged forty-one, sought advice for impotence, which had been present for about four years. The patient was in the trenches during the war, and after standing for hours in water he suddenly developed an irregular paraplegia. On two separate occasions since the paraplegia had vanished, only to return. Although the sphincters had never been completely paralysed, the control was not perfect and it was becoming less so. The patient used to have chilblains ; he had suffered from asthma and had had bronchial catarrh more or less continuously since. The patient had gingivitis and the teeth required attention ; the tongue was very furred and denuded of papillæ in patches. Acro-asphyxia was marked and Raynaud's phenomenon appeared in the winter. The nails were ridged, cracked and split easily. The patient used to bite his nails, and since he had been treated with nov-arseno-benzene the nails were shed every spring. The patient had central cupping of both optic discs, his pulse was 62 and the blood-pressures registered 120 and 90 mm. of Hg. respectively. There were no abdominal reflexes ; the left colon was contracted and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (50 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.65 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 32 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with some giant particles, ringed particles and giant-particled clumps, both moving and precipitated.

The patient was dieted and gave up smoking ; he had a course of colonic lavage, received injections of Sup. 468 and of the fæcal vaccine, and had his mal-co-ordination corrected. He improved immensely, discarded his irons, and was able to play golf and to dance once more.

In this case also arsenic did the patient more harm than good. Putting the legs into irons made the patient infinitely worse. All appliances, such as abdominal belts to support viscera which have not really dropped, irons which aggravate the mal-co-ordination, foot-pads which destroy the arches and make the feet more flat, etc., should be done away with.

The author has treated seven cases of disseminated sclerosis along the lines adopted to rid the patient of his chronic intestinal intoxication, with the result that all have improved and none have had a recurrence so far. Whether this treatment comes up to the vaccine treatment recently introduced by Sir James Purves Stewart ³² cannot be said, as the author has had no experience of the latter. The vaccine is prepared from what Miss Chevassut ³¹ considers to be the specific micro-organism, another ultra-microscopic virus. After the discovery of the *Spirochaeta pallida* it became fashionable to hunt for spirochaetes in all infections of unknown ætiology, and several observers stated that they found them in disseminated sclerosis, but their work has since been discredited. Since the discovery of an ultra-microscopic virus in distemper the fashion has changed to this realm ; already the infections are legion wherein ultra-microscopic viruses have been found, and disseminated sclerosis is the last to have been added to the list. The ultra-microscopic viruses are thought to be specific, and doubtless a mass of work will be done to differentiate them before any attempt is made to determine their origin. The author, as stated above, holds that the ultra-microscopic viruses are particulate forms either of known bacteria or of the host's own protein particles. Altered conditions favour the formation of these particulate forms, and filtration itself is one of them. Therefore it is possible that in disseminated sclerosis the ultra-microscopic virus is either a particulate form of the non-lactose fermenters which have been able to pass through the choroid plexuses, or a particulate form derived from the host's own damaged protein particles in their passage through the choroid plexuses. When protein particles are subjected to abnormal chemico-physical changes their permeability through colloid membranes may be increased. In filtering such particles ultra-microscopic forms may be manufactured. As the author stated in the first volume of "The Nature of Disease," repeated drainage of the cerebro-spinal fluid increases the permeability of the choroid plexuses and meninges and makes the protein particles which pass through

acquire chemico-physical properties of globulin and precipitate colloid gold. All ultra-microscopic particles appear to be more negatively-charged than normal, they have the chemico-physical characteristics of globulin, and they have the capacity for infinite development. Therefore, it is possible that the body recently discovered in the cerebro-spinal fluid in cases of disseminated sclerosis is derived from the host's protein particles damaged by the activity of the non-lactose fermenters in the large intestine, and thus rendered more able to reach the central nervous system. The reasons why ultra-microscopic particles or viruses show a predilection for nerve tissue are partly because waste products from the central nervous system are not as readily removed as are those from the systemic part of the body, and partly because their reducing action is so pronounced.¹

The waste products from the central nervous system find their way into the venous circulation, while those from the systemic part of the body are voided in the urine. An increase of reducing action means that the particles have a powerful dehydrator effect, and to this the parenchyma of nerve tissue falls a more ready prey than the parenchyma of any other organ. If Chevassut is correct in forming the conclusion that the causal agent in disseminated sclerosis is responsible for the gold-sol reaction, then the view is supported that the causal agent originates from the host's protein particles. Because the precipitation of colloid gold is entirely dependent upon the protein particles in the cerebro-spinal fluid and directly influenced by the abnormal chemico-physical changes to which these particles have been subjected. It does not matter whether the altered protein particles possess the characteristics more of globulin than of albumin, or *vice versa*. Had protein never been divided and sub-divided in the way it has, these and other difficulties would never have originated. The differences are chemico-physical, and are exhibited purely as surface reactions.

The author has seen two cases of *Encephalitis lethargica*, which began between the tenth and twelfth days following an operation for hæmorrhoids and a hernia respectively. Both developed typical post-encephalitic manifestations and both were well-marked cases of familial chronic intestinal intoxication.

Case 82

A man, aged thirty-six, presented himself with marked Parkinsonism which followed an attack of *Encephalitis lethargica* three years previously.

¹ Altered protein particles readily pass through the glomeruli and in their passage have their chemico-physical characteristics changed still further. All such particles which have passed through membranes readily cause dispersion of hydrated protein particles when collected and put into the body again by injection.

The attack appeared on the tenth day following an operation for hæmorrhoids. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3507.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 19 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving and all were either giant particles or ringed particles. There were more particles precipitated in the form of giant particles and giant-particled clumps. The Brownian movements were very sluggish.

Mr. F. M. Alexander had the patient in his care for two months, at the end of which time he was able to leave his chair and walk around a table, having previously been completely bed- and chair-ridden.

A re-examination of the blood made one month after the re-education had been in force revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3495.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few giant particles and clumps, both moving and precipitated.

Comparing these two blood-pictures shows quite definitely that endeavours made to correct the mal-co-ordination resulted in some of the hydrated protein particles undergoing dispersion.

The author has seen five cases of *Encephalitis lethargica* complicating measles, and in all the victims had broncho-pneumonia as well, and suffered from one or more of the signs and symptoms of chronic intestinal intoxication. All the patients were children, two had chronic eczema, two were asthmatic, and one of these had xeroderma in addition, while the fifth child suffered from chilblains and hay-fever.

A milder case of encephalitis which developed Parkinsonism was thoroughly investigated, treated and watched over a long period of time. It is reported below.

Case 83

A man, aged forty-one, developed double vision, lasting one week, three years before he sought advice. Since the double vision the patient developed

a gradually-increasing weakness, loss of energy and a feeling as if his legs would no longer support him. The patient presented all the signs of so-called "Parkinson's disease," the pupils reacted sluggishly to light, and he had most pronounced cupping of both optic discs. He could not stand with his knees and feet together at the same time; he had acro-asphyxia; the pulse was 120 and the blood-pressures read 155 and 96 mm. of Hg. respectively. An examination of the abdomen revealed chronic colitis. The urine contained a trace of protein; it slightly reduced Nylander's reagent and gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta proved to be an atypical *Bacillus coli communis* (10 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.15 c.c.
Refractive index of the serum	= 1.3502.
Percentage of the blood-sugar	= 0.256 gm.
Percentage of the blood-urea	= 35 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but most were giant particles with a halo around. There were a few giant particles and clumps precipitated. The Brownian movements were sluggish.

The patient was dieted; the colon was washed out and he received a course of injections of contramine and three injections of the faecal vaccine. Five months later the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3498.
Percentage of the blood-sugar	= 0.137 gm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Fair number of par- ticles moving, but most were still rather larger than normal. There were many giant particles and clumps precipitated.

The patient improved continuously, and examined frequently over a period of three years, the urine never reduced Nylander's reagent again. The slight reduction with so high a percentage of the blood-sugar is not so unusual, and the author has had a case where the urine was normal and the percentage of the blood-sugar registered 0.256 gm. This and other cases show that there is no fixed renal threshold.¹ The fall in the blood-sugar following treatment shows that treatment aimed at getting the patient well is superior to that aimed at removing a symptom.

¹ The kidneys are not selectors; what passes through is determined by the blood.

The strong connection between a chronic intestinal intoxication and *Herpes febrilis* is well illustrated by the following case :

Case 84

A woman, aged forty, had suffered from severe recurrent *Herpes febrilis* of the mouth for seven years. All the teeth and both tonsils had been removed without benefiting the condition. The patient was a very typical example of chronic intestinal intoxication, and a bacteriological examination of the excreta revealed *Bacillus proteus hydrophilis* (10 per cent.). An examination of the blood showed the following :—

Suspension stability of the red blood-corpuscles	= 0.4 c.c.
Refractive index of the serum	= 1.3490.
Percentage of the blood-sugar	= 0.118 gm.
Percentage of the blood-urea	= Not done.
Ultra-microscopic picture of the serum	= Very many particles moving with a fair number of small clumps. There were a few clumps precipitated. The moving particles showed a marked tendency to become precipitated, and in a minute or two most of them had formed large agglutinated masses.

The patient became a vegetarian ; she had the colon washed out and received two injections of the vaccine, one of one million and one of two million, with two months' interval between. The herpetic lesions vanished and the patient was free of an attack for eight months. She then returned to her usual diet and the lesions re-appeared at once. A third injection of the vaccine was made (dose, three million), and this brought out the worst attack the patient had ever had. The patient became a vegetarian again, and one month later had two injections of the vaccine in doses of half a million. She has been free of an attack for over two years.

The encephalitis of rabbits is another infection which seems to require damage done by another agent before it takes place. The repeated intra-venous injections of drugs, which produce in the end hydration of the protein particles in the plasma render rabbits liable to develop encephalitis and at the same time change the *Bacillus coli communis* into non-lactose fermenters.

Most of the lesions of nerve tissue, secondary to a chronic intestinal intoxication, are caused by the abnormal chemico-physical changes to which the protein particles in the plasma are subjected by the poisonous substances manufactured by the non-lactose fermenters in the large intestine. It would appear

that micro-organisms do not produce disease by the liberation of what are termed "toxines." Micro-organisms act either upon the protein particles (dynamic) in the plasma or upon the protein particles (static), constituting the cytoplasm of cells exactly in the same way as do the altered dynamic particles upon the static particles. Different micro-organisms act in different ways, because the electric charge on their surface varies; indeed, it is due to the surface electric charge that micro-organisms are either Gram-negative or Gram-positive, and that some of the former are able to take up an intracellular habitat, preferably in endothelial cells. Similarly, when micro-organisms are vanquished by treatment their bodies are subjected by the host's resistance to the same chemico-physical changes as those to which they subjected the host's protein particles when they had the upper hand. But, in the process no so-called "endotoxines" are liberated. If any reaction does follow treatment, it is due to the treatment causing a temporary and initial hydration of the host's protein particles. Much stress is laid upon the difference between microbial intoxication and drug intoxication so far as the production of so-called "inflammation" is concerned. In actual fact there is no difference. It is true that inflammation is more an accompaniment of microbial than of drug intoxication, but this is merely because micro-organisms work as a rule more slowly than drugs, and their action is more akin to the action of foreign proteins, because bacteria are protein bodies. It is on account of this fact that a bacterial invasion causes a combination of dehydration and hydration, a chemico-physical change which brings leucocytes to the seat of action and stimulates the endothelial cells of the peri-vascular lymphatic vessels to manufacture leucocytes and lymphocytes in particular.

This explains the cuff-like peri-vascular infiltration met with in most inflammatory lesions of the central nervous system. A chronic intestinal intoxication influences a microbial invasion in two ways: (1) by rendering ordinarily saprophytic micro-organisms pathogenic; (2) by increasing the pathogenicity of micro-organisms which come from without. In the present very imperfect state of medical knowledge, it is impossible to throw any further light upon lesions of the central nervous system caused by micro-organisms from within, that is to say, by micro-organisms ordinarily saprophytic, which become pathogenic owing to the reduction of the patient's resistance. As stated above, such possible lesions are considered to be caused rather by the altered protein particles in the plasma than by the actual micro-organisms themselves. Therefore, a further discussion on this subject is continued under the next sub-heading. The infection from without which is

most liable to attack the central nervous system is syphilis, and the author has been particularly struck by two facts : (1) that syphilitic patients who develop a central nervous lesion are almost invariably well-marked examples of familial chronic intestinal intoxication ; (2) that removal of the intestinal intoxication may benefit the patient more than anti-syphilitic treatment. Congenital syphilis produces lesions in the central nervous system much resembling those found in hereditary disease, and hydration of the protein particles is a marked feature. All cases of congenital syphilis, as might be expected from what has been said above, present the clinical signs and symptoms of chronic intestinal intoxication to a very marked degree, as illustrated by the following cases :

Case 85

A girl, aged sixteen, born of syphilitic parents, and whose father died of general paralysis, sought advice for recurrent attacks of cystitis. The patient suffered from bad chilblains, and bursæ had formed on both heels and underneath both big toes. As a child, the patient had had enuresis and, for some years past, attacks of rheumatism. The patient showed a high degree of myopic astigmatism, she could not stand with her knees and feet together at the same time, and the elbows were wide-angled and hyper-extended. Menstruation began at the age of nine, and was followed by amenorrhœa for two years, since when the periods had been more or less normal. The appendix was removed four years ago, and jaundice developed some days later. An examination of the abdomen revealed a marked form of chronic colitis ; the pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (50 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3495.
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood-urea	= 47 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some small giant-particled clumps.
Wassermann reaction	= Positive (+ + +)

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of Sup. 468 and of the fæcal vaccine. The chilblains were treated with colloid silver and with a mercury vapour lamp. The patient's general condition improved considerably, the chilblains vanished and the Wassermann reaction became negative.

Case 86

A woman, a congenital syphilitic, aged forty-one, had had incessant tinnitus for seven years, but she was not deaf. Her father was a chronic alcoholic and died of sclerosis of the liver, aged fifty-six. Her mother died of cerebral syphilis, aged sixty-six. The patient was the fifth of eleven pregnancies; the first three were born dead, the others lived and were healthy, although a brother, the fourth pregnancy, and a sister, the sixth pregnancy, gave a positive Wassermann reaction. The patient was blind in her right eye from birth (choroiditis), she had had her right kidney removed for calculi three years before the author saw her, and ten years prior to this she is said to have had multiple syphilitic periostitis. The patient had two healthy children. When she was thirty-one years of age she developed interstitial keratitis, first of one eye and then of the other. The right pupil did not react to light and the left pupil was not in the centre of the iris; the tongue was furred and fissured, there was acro-asphyxia, the patient had severe fits of depression, the pulse was 84 and the blood-pressures registered 110 and 80 mm. of Hg. respectively. The left colon was contracted, the ascending colon and cæcum were dilated, the patient was tender in the regions of the flexures; the ileo-cæcal area was tender and thickened, and a barium meal revealed diverticula. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (30 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 19 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving and these were mostly giant particles and ringed particles. There was precipitation <i>en masse</i> of refractile giant particles and giant-particled clumps. The Brownian movements were sluggish.
Wassermann reaction	= Positive (+ + +)

The patient was dieted; she had a course of colonic lavage, took iodine, ichthyol and thyroid internally, received six injections of contramine and four of the fæcal vaccine in two sets of two (dose 0.5 million), with three months' interval between. Nine months later the patient was generally better; the blood-pressures registered 125 and 85 mm. of Hg. respectively, but the tinnitus had not changed.

The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3495.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 30 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few giant particles and ringed particles.
Wassermann reaction	= Practically negative.

It is a renowned fact that anti-syphilitic treatment has no influence in changing the Wassermann reaction in cases of late congenital syphilis. Indeed, the author has advised for many years that these cases should not be treated, not only because of the above, but also because specific treatment does sometimes make the patient definitely worse, and the author has seen it precipitate syphilitic symptoms. These two cases illustrate what can be done by treating the patient and by neglecting the infection, and below other cases are recorded to show that even in acquired syphilis the same manœuvre is more profitable than prescribing arsenic, mercury and bismuth. This is in part due to the fact that many of the signs and symptoms encountered in the late cases of syphilis are the result rather of the infection than caused by the *Leucocytozoon syphilidis*. In short, the reader will realise later that syphilis is not really a specific infection, that it acts no differently than inherited disease, and that many of the signs and symptoms produced would never come into being in the absence of the underlying inherited disease. This, of course, confirms the author's view that there is only one disease and that the action of treatment with drugs is the same whether it be Sup. 36 for influenza or arseno-benzene for syphilis. Once this undoubted truth is universally recognised medicine will become the simplest science imaginable, and there will be no need for specialists and less need for hospitals.¹

The connection between congenital syphilis and inherited disease can be carried still further, because in view of the above it explains also why congenital syphilitic women and women who acquire conceptional syphilis are more liable than non-syphilitic women to develop a toxæmia of pregnancy. It was emphasised in the previous volume that a chronic intestinal intoxication was the fundamental cause of the toxæmias of pregnancy. The following case is of sufficient interest to be reported here, and the reader is referred back to Case 35.

¹ Any country which adopts the method of treating disease as mentioned in these volumes will save millions of pounds *per annum* and will have its industries brought up to the highest level of efficiency.

Case 87

A girl, aged twenty, a congenital syphilitic, with bilateral interstitial keratitis and well-marked chronic intestinal intoxication, was thirty weeks pregnant and complained of œdema of both feet and ankles. The patient was passing not more than twenty ounces of urine a day, the specific gravity was very high, and the urine contained sugar, but no protein.

An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 1.2 c.c.
Refractive index of the serum	= 1.3481.
Percentage of the blood-sugar	= 0.081 grm.
Percentage of the blood-urea	= 17 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few small clumps. There were a few giant particles precipitated as well as some large agglutinations.
Wassermann reaction	= Positive (+ + +).

The patient took glucose internally and received two intra-muscular injections a week of Sup. 468, each of 0.002 grm., until the baby was born, when nov-arseno-benzene was prescribed. The mother and child did splendidly, and all the signs and symptoms of the toxæmia vanished before the child was born.

Although syphilitic patients, the victims of a chronic intestinal intoxication, seem particularly prone to develop a central nervous lesion for reasons which the author will endeavour to explain, it cannot be said that persons suffering from a chronic intestinal intoxication are more prone to develop syphilis or any other infection than others who are not so afflicted. Indeed, the worst cases of a chronic intestinal intoxication have a certain immunity to infections in general, as evidenced by the fact that sufferers from epilepsy, migraine, etc., seldom develop any other illness, and may be relieved of the cerebral trouble by pregnancy. This is because the protein particles in the plasma are already so hydrated as to undergo immediate dispersion on the advent of a new dehydrator. When the hydration is less marked, as in the milder cases, the advent of a new dehydrator increases the hydration, thereby rendering a victim of a mild chronic intestinal intoxication more prone to develop any other illness, and a woman who is pregnant to develop epilepsy, eclampsia, etc. The author was among the first to draw attention to the increased incidence of syphilis of the nervous system which followed the introduction of arseno-benzene, and the opinion was then hazarded that there was a direct relationship between nervous syphilis and treatment.

It was pointed out that the incidence of syphilis of the nervous system increased as the treatment improved, but only so long as it was spasmodic and inadequate. The nervous system in syphilis becomes invaded by the *Leucocytozoon syphilidis* at a very early stage of the infection. If treatment is prescribed sufficient to sterilise temporarily the systemic part of the body, but insufficient to do the same to the nervous part of the body, the latter is deprived of a main pillar of support or resistance and the micro-organisms are stimulated to activity.

In certain cases of chronic intestinal intoxication the systemic part of the body is readily sterilised, because one of the effects of the infection is to cause dispersion of the hydrated protein particles in the plasma, and when this happens the micro-organisms are enabled to multiply in the nervous part where the natural resistance is not as great. The syphilitic lesions of the central nervous system aggravated by a chronic intestinal intoxication can be divided into three groups: (1) those caused by the actual presence of the syphilitic micro-organism; (2) those resulting from the dehydration brought about by the activity of the syphilitic micro-organism; (3) those resulting from the hydration brought about by the activity of the syphilitic micro-organism.

The two most important lesions of the central nervous system caused by the actual presence of the *Leucocytozoon syphilidis* are degenerative encephalitis or general paralysis of the insane and degenerative myelitis or tabes.

Although the subject of syphilis has been worn nearly threadbare, there are still a few new points that the author is able to bring forward. First as regards general paralysis of the insane. There is no absolutely clear-cut clinical or pathological picture of this condition, hence it is better to refer to it as syphilitic degenerative encephalitis. A patient may present the clinical features of G.P.I., and his blood and cerebro-spinal fluid may give the classical tests, and yet, even without treatment, the patient may go on for years and succumb to a hæmorrhagic lesion like a case of senile cerebral softening. On the other hand a patient may be clinically not far removed from the normal, and his blood and cerebro-spinal fluid may be only slightly pathological, but yet in spite of the most up-to-date treatment the patient succumbs in a few months to degenerative encephalitis.

The seizures met with in G.P.I. do not differ in essential details from those clinical conditions encountered in drug encephalitis, *Status epilepticus*, heat-stroke, etc. The clinical picture is the same, the histological picture shows the same punctate hæmorrhages, and the same types of cell degeneration

involving the same areas are to be found. Acetone may appear in the cerebro-spinal fluid, pointing to the cyclical change of dehydration undergone by some of the hydrated particles, and similar pathological changes are to be encountered in the other viscera, such as contraction of the left ventricle, congestion of the liver and lungs, parenchymatous degeneration of the viscera and necrosis of the mucous membrane of the colon. The malarial treatment of syphilitic degenerative encephalitis is without question the best form of treatment to-date, but the effect the induction of the super-infection has upon the blood-picture varies enormously in different individuals. The changes undergone by the cerebro-spinal fluid as the result of the treatment also differ widely, and there appears to be no relationship between these changes and the clinical result. The author has treated twenty-three cases with malaria, and the oldest case, one of the first cases inoculated in this country, is still clinically sound, although his cerebro-spinal fluid is as positive as ever. This patient was a raving lunatic when put under treatment, and now he is a lecturer on surgery and a first-class operator. The patient was treated for two years after the malarial induction, and his only trouble to-day is cutaneous vaso-dilatation, which occurs when chemical substances touch his skin or his skin is in any way roughly handled—for example, a nail brush cannot be used to sterilise the hands, nor strong antiseptics.¹ Below are recorded a few of the cases.

Case 88

A man, aged forty, contracted syphilis fifteen years before malaria was induced. The patient received at the beginning seventeen injections of arseno-benzene and seventeen injections of mercury. Six months before the signs and symptoms of degenerative encephalitis developed, the patient received eighteen intra-venous injections of arseno-benzene. Before the malaria was induced the blood gave a slightly positive Wassermann reaction (+ — —), and an examination of the cerebro-spinal fluid revealed the following :—

Pressure	= Raised.
Cells	= 10 lymphocytes per c.mm.
Globulin	= + + + +.
Gold-Sol	= 2222222000.
Wassermann reaction	= + + +.

The blood was taken again after the third rigor and after the eleventh

¹ The vaso-motor trouble vanished when the chronic intestinal intoxication was dealt with.

before the quinine was prescribed to stop the rigors, with the following results :

After Third Rigor.

Suspension stability of the red blood-corpuses = 1.7 c.c.
 Refractive index of the serum = 1.3506
 Percentage of the blood-sugar = 0.143 grm.
 Percentage of the blood-urea = 26 mgrm.
 Ultra-microscopic picture of the serum =

Fair number of particles moving. All were very refractile, and larger than normal. There were very many giant particles, and giant-particled clumps precipitated. The Brownian movements were sluggish, and the precipitation increased with time.

Wassermann reaction = Positive (+ + -)

After Eleventh Rigor.

Suspension stability of the red blood-corpuses = 4.6 c.c.
 Refractive index of the serum = 1.3470
 Percentage of the blood-sugar = 0.162 grm.
 Percentage of the blood-urea = 34 mgrm.
 Ultra-microscopic picture of the serum =

Myriads of particles moving with a very large number of highly refractile giant particles and giant-particled clumps. There were some giant particles and clumps precipitated. The precipitation increased with time, so that in a few minutes there was general precipitation *en masse*.

Wassermann reaction = Positive (+ + +)

There are several points of interest in this case. The clinical picture is classical, and probably made so by the eighteen injections of arseno-benzene. Syphilologists have yet to learn that treatment does not kill the micro-organisms directly, and when injudiciously prescribed it may even stimulate them into activity. The cerebro-spinal fluid was more pathological than the blood, which is not infrequently the case in degenerative encephalitis. Indeed, the positive Wassermann reaction in the blood may be caused by the passage of hydrated protein particles into the blood-stream from the cerebro-spinal fluid *viâ* the arachnoid villi. The blood-pictures show that the malaria acted by subjecting the hydrated protein particles to dehydration, and this is roughly how all treatment functions when it does good. Gelation was the type of dehydration produced. The rigors ceased after quinine owing to the conductor action of the drug. As considerable conduction is required to correct the gelation it is necessary to carry on with anti-syphilitic treatment for two years or more. The fact that the Wassermann reaction in the blood became more and more positive in spite of the clinical condition improving shows that the reaction is partly dependent upon the protein particles being poor in electricity, and that it bears no relationship to the activity or otherwise of the micro-organisms.

The patient did extraordinarily well and was able to resume his employment as a telephone operator, but he was troubled afterwards with universal formication.

Case 89

A man, aged forty-four, with no history of syphilis, had had degenerative encephalitis for four years. The blood gave a positive Wassermann reaction (+ + -), and an examination of the cerebro-spinal fluid revealed the following :—

Pressure	= Raised.
Cells	= 112 per c.mm., mainly lymphocytes.
Globulin	= + + + +.
Gold-Sol	= 555532200.
Wassermann reaction	= + + +.

The blood was withdrawn after the second rigor, and again after the eighth, when quinine had to be prescribed as the patient was not standing the rigors very well, with these results :—

After Second Rigor.

Suspension stability of the red blood-corpuses	= 2.1 c.c.
Refractive index of the serum	= 1.3512
Percentage of the blood-sugar	= 0.162 grm.
Percentage of the blood-urea	= 27 mgrm.
Ultra-microscopic picture of the serum =	

Few particles moving and these were mostly giant particles and ringed particles. There were some giant particles, ringed particles and agglutinations precipitated on what looked like a sheet of small dull particles.

Wassermann reaction = Positive (+ + -)

After Eighth Rigor.

Suspension stability of the red blood-corpuses	= 2.3 c.c.
Refractive index of the serum	= 1.3471
Percentage of the blood-sugar	= 0.175 grm.
Percentage of the blood urea.	= 26 mgrm.
Ultra-microscopic picture of the serum =	

Myriads of particles moving with a few giant particles and small giant-particled clumps. There were a few satellitic clumps moving. There were some giant particles and small clumps precipitated. The precipitation increased with time and in a few minutes all the moving particles had come to a standstill.

Wassermann reaction = Positive (+ + +)

The outstanding difference, when this case is compared with the former, is the infinitesimal reduction in the suspension stability of the red blood-corpuses. This shows that the induction of malaria did not occasion such a marked degree of dehydration of the hydrated protein particles. It was doubtless due to the persistence of the hydration that the patient could not withstand the rigors. Although the patient did well up to a point, he did not make the complete recovery of the former case; in fact, he relapsed and died about three years later.

Case 90

A man, aged thirty-eight, contracted syphilis six years before he developed signs and symptoms of degenerative encephalitis. He was spasmodically

treated with arseno-benzene. The cerebro-spinal fluid was tested seven months before the malaria was induced, with the following result :—

Pressure	= Raised.
Cells	= 115 per c.mm. Lymphocytes 85 per cent.
	Large mononuclears 10 „
	Polymorphonuclears 5 „
Globulin	= + + + +.
Gold-Sol.	= 4554321000.
Wassermann reaction	= + + +.

The blood was taken at the time of the inoculation and after the ninth rigor, when quinine was prescribed with the following results :—

<i>Before Inoculation.</i>	<i>After Ninth Rigor.</i>
Suspension stability of the red blood-corpuses = 0.5 c.c.	Suspension stability of the red blood-corpuses = 0.7 c.c.
Refractive index of the serum = 1.3476	Refractive index of the serum = 1.3440
Percentage of the blood-sugar = 0.086 grm.	Percentage of the blood-sugar = 0.118 grm.
Percentage of the blood-urea . = 37 mgrm.	Percentage of the blood-urea = 28 mgrm.
Ultra-microscopic picture of the serum = Normal number of particles moving, with a large number of giant particles and a few giant-particled clumps. There were some giant-particled clumps precipitated.	Ultra-microscopic picture of the serum = Very few particles to be seen either moving or precipitated.
Wassermann reaction = Positive (+ + +)	Wassermann reaction = Positive (+ + +)

Here again the induction of malaria had little change on the suspension stability of the red blood-corpuses, showing that the particles had not been robbed of much of their electricity. The refractive index was low to begin with, showing that most of the particles had the physical characteristics of albumin. This was still further accentuated by the malaria and the ultra-microscopic picture showed very few particles, because albumin particles diffract little light and in consequence may not be visible as particles. With subsequent anti-syphilitic treatment this patient recovered sufficiently to take up a big directorship in the city.

Case 91

A man, aged thirty-seven, contracted syphilis twelve years before he developed degenerative encephalitis. He received a full year's treatment with arseno-benzene and mercury when he contracted the infection and this was

repeated three years later. An examination made of the cerebro-spinal fluid two years before malaria was induced revealed the following :—

Pressure	= Raised.
Cells	= 195 per c.mm. Lymphocytes 82 per cent.
	Large mononuclears 8 „
	Polymorphonuclears 10 „
Globulin	= + + + +.
Gold-Sol.	= 1244544421.
Wassermann reaction	= + + +.

The blood was examined at the time of the malarial inoculation with the following result :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3520.
Percentage of the blood-sugar	= 0.118 gm.
Percentage of the blood-urea	= 97 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving with a high percentage of giant particles and giant-particled clumps. There were some giant particles and giant-particled clumps precipitated. All the particles were very refractile.
Wassermann reaction	= Positive (+ + +).

One week after the inoculation the patient developed a big burn on the buttocks and heels, presumably from sitting on a stove. This caused a rise of temperature to 104° F., vomiting, ileus and melæna. Three weeks later the patient died of hæmorrhagic encephalitis. The dura was thickened and there were several soft areas on the surface of the brain. The capillaries and arterioles were dilated, the walls were thickened and invaded with lymphocytes, and there was an infiltration of the peri-capillary lymphatic vessels. Some of the capillaries were filled with red blood-corpuscles, there were many punctate hæmorrhages and granulomatous areas. The nerve cells showed lipid degeneration. There were vegetations on the mitral valve and marked atheroma at the base of the aorta. The heart muscle showed interstitial changes and there was some fatty degeneration. There was some fatty degeneration of the liver parenchyma, and the kidneys evidenced long-standing interstitial nephritis.

The rise in the percentage of the blood-urea showed that the protein

particles were being severely attacked, and it is doubtful if the patient would have withstood the malarial treatment.

Case 92

A man, aged fifty, consulted the author originally for insomnia and attacks of giddiness, lumbago and sciatica. The patient's father died of cancer of the stomach, aged fifty-one, and the mother of apoplexy, aged sixty. The patient used to suffer from chilblains and hay-fever as a boy and had his tonsils removed in 1911. In 1914 the patient contracted syphilis, for which he was treated with mercury internally for two years. The first recurrence occurred in 1916, when the patient had injections of nov-arseno-benzene and mercury, and in 1922 there was definite evidence of posterior column degeneration. But, in addition, the patient had generalised arterio-sclerosis and his blood-pressures registered 190 and 110 mm. of Hg. respectively. An examination of the cerebro-spinal fluid at this time showed the following :—

Pressure	= Raised.
Cells	= 32 lymphocytes per c.mm.
Globulin	= +.
Gold-Sol test	= 111120000.
Wassermann reaction	= + + +.

The patient was treated thoroughly with intra-venous injections and auxiliary tapping of the spinal theca and was not seen again till May 2nd, 1927, when he sought advice for frequency of micturition. The patient's behaviour seemed a little strange, and general paralysis was suspected, but the blood-pressures were the same as before, there was definite evidence of chronic colitis, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3497.
Percentage of the blood-sugar	= 0.118 gm.
Percentage of the blood-urea	= 21 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving and most of them were large. There were some ringed particles and big clumps moving. There were some giant particles and clumps precipitated.
Wassermann reaction	= Negative.

The pathogenic micro-organism found in the excreta was the *Bacillus*

proteus hydrophilis (10 per cent.). The patient was seen again September 15th, 1927, when a clinical examination revealed general paralysis, but as the blood-pressures now registered 210 and 130 mm. of Hg. respectively, eight ounces of blood were withdrawn from a vein and 60.0 c.c. of cerebro-spinal fluid from the spinal canal. Examinations of the blood before and after were as follows :—

Before.

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3489.
Percentage of the blood-sugar	= 0.075 grm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and these were mostly giant particles and ringed particles. There were very few giant-particled clumps. There were a few giant particles and giant-particled clumps precipitated. The Brownian movements were sluggish.
Wassermann reaction	= Positive (+ + +).

After.

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3526.
Percentage of the blood-sugar	= 0.075 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= There were still fewer particles moving and more particles precipitated.
Wassermann reaction	= Positive (+ + +).

The cerebro-spinal fluid was under great pressure and an examination revealed the following :—

Cells	= 36 lymphocytes per c.mm.
Globulin	= + + +.
Refractive index	= 1.3345.
Sugar	= 0.100 grm.
Urea	= 10 mgrm.
Gold-Sol test	= 555555200.
Wassermann reaction	= + + +.
Ultra-microscopic picture of the fluid	= No particles moving, but some very refractile giant particles, ringed particles and giant-particled clumps precipitated <i>en masse</i> .

The patient was inoculated with malaria November 8th, 1927, had ten rigors and then received treatment with acetyl-arsan, mercury and bismuth. The blood-pressures fell to 160 and 95 mm. of Hg. respectively, and the patient improved sufficiently to resume his occupation as a clergyman.

The rigors were stopped with quinine and the patient received anti-syphilitic treatment for two years. The three blood-pictures reported below are of some interest.

<i>Blood taken 22-11-27.</i>	<i>Blood taken 13-6-28.</i>	<i>Blood taken 19-6-29.</i>
Suspension stability of the red blood-corpuses . . . = 0.5 c.c.	= 2.7 c.c.	= 0.5 c.c.
Refractive index of the serum = 1.3493	= 1.3482	= 1.3470
Percentage of the blood-sugar = 0.137 grm.	= 0.075 grm.	= 0.068 grm.
Percentage of the blood-urea = 39 mgrm.	= 39 mgrm.	= 40 mgrm.
Ultra-microscopic picture of the serum =		
Fair number of particles moving with a few giant particles and ringed particles. There was an occasional giant particle and ringed particle precipitated and the Brownian movements of the particles were sluggish.	Fair number of particles moving with some giant particles, ringed particles and giant - particled clumps. There were a fair number of giant particles, ringed particles and clumps precipitated with one or two agglutinations. The Brownian movements of the particles were sluggish.	Many particles moving with an occasional giant particle and agglutination precipitated.
Wassermann reaction = Positive (+ + ±)	= Negative	= Negative

When the patient was last seen (June 19th, 1929) the blood-pressures registered 170 and 110 mm. of Hg. respectively.

There are many points of interest in this case. In the first place there is just the possibility that the injections of the faecal vaccine precipitated the degenerative encephalitis. The sudden rise in the blood-pressures could not have been due to an increase of the dehydration, but was caused by an increase of the hydration as evidenced by the blood-picture and by the cerebro-spinal fluid being under such great pressure. Hydration raises the blood-pressures when the hydrated protein particles become precipitated in the peri-capillary lymphatics because this closes the capillaries. The withdrawal of blood caused the blood-pressures to rise rather than to fall, and the rise in the refractive index of the serum and the ultra-microscopic picture show that the manoeuvre caused hydration. This fits in with the explanation given above.

The nervous symptoms of general paralysis are caused by hydration, as are also those of migraine, epilepsy, eclampsia, spasmophilia, etc. The rise of the blood-pressures in eclampsia is due to the precipitation of the hydrated protein particles in the peri-capillary lymphatics constricting the capillaries, and that the explanation of the rise in this case is correct is confirmed by the fact that a fall occurred after the induction of malaria, a manoeuvre which acts by subjecting hydrated protein particles to dehydration.

The ultimate rise in the blood-pressures again suggests a resumption of dehydration occasioned by the anti-syphilitic treatment. This is confirmed by the blood-pictures and by the clinical picture reverting to that of posterior column degeneration of arterio-sclerotic origin.

Regarding syphilitic degenerative myelitis there is little new to add, although two points certainly do stand out. One is that a chronic intestinal intoxication plays a prominent part in the condition, and the other is that the signs and symptoms produced are more frequently the result of damage done than due to local activity of the *Leucocytozoon syphilidis*. These points are brought out in the cases reported below.

Case 93

A man, aged fifty-one, was in the middle of a nervous breakdown, of which he had had at least two, some years previously. The patient was very thin, and had suffered from bad chilblains as a child. His blood-pressures registered 120 and 80 mm. of Hg. respectively and he presented the signs and symptoms of degenerative myelitis, with bilateral optic atrophy. An examination of the abdomen revealed a marked form of chronic colitis and the *Bacillus fecalis alkaligenes* (10 per cent.) was found in the excreta. The patient had been over-treated with anti-syphilitic remedies, and his condition became more and more aggravated as injections of nov-arseno-benzene and inunctions of mercury were prescribed. The patient was carefully dieted, the colon was washed out and four injections of the faecal vaccine were made, with the result that in a year's time he was able to get about to enjoy himself and thought his vision had improved. An examination of the blood made after the completion of the colonic lavage showed the following :—

Suspension stability of the red blood-corpuscles	= 0.3 c.o.
Refractive index of the serum	= 1.3487.
Percentage of the blood-sugar	= 0.150 grm.
Percentage of the blood-urea	= 23 mgrm.

Ultra-microscopic picture of the serum	= Many particles moving but all were larger than normal and very refractile. There were a few giant-particled clumps moving. There were some giant-particled clumps and a few small agglutinations precipitated.
Wassermann reaction	= Negative.

Case 94

A man, aged forty-eight, contracted syphilis in 1908, and in spite of most vigorous anti-syphilitic treatment almost continuously since had developed degenerative myelitis with diplopia and foot-drop (left foot). The last course of anti-syphilitic treatment at Aachen made the patient definitely worse. The patient was a very typical case of chronic intestinal intoxication and had generalised arterio-sclerosis. The pathogenic micro-organism found in the excreta was an atypical form of the *Bacillus proteus Valeriei*, and an examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0.35 c.c.
Refractive index of the serum	= 1.3489.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a fair number of giant particles and a few ringed particles and small clumps. There were some large giant particles and giant-particled clumps precipitated.
Wassermann reaction	= Positive + — —.

The patient was dieted, subjected to colonic lavage and received four injections of the faecal vaccine, a treatment which wrought an enormous improvement in his condition.

Case 95

A man, aged forty-one, contracted syphilis in 1919 and was put under treatment with "606" and Hg. before signs and symptoms of the generalisation stage had been reached and when the Wassermann reaction was negative. A year later mucous papules appeared in the mouth and a rash on the trunk, for which he received another twelve injections of "606" and took mercury internally for two years, at the end of which time he complained of chronic pharyngitis, lumbago and sciatica. In 1926 the patient complained of giddi-

ness and vomiting. Upon examination he was found to have degenerative myelitis and generalised arterio-sclerosis, and he presented the signs and symptoms of a chronic intestinal intoxication. The patient had been operated upon for hare-lip when aged ten, for varicose veins at thirty-one, and for bilateral inguinal hernia at forty. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (90 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3481.
Percentage of the blood-sugar	= 0·206 grm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with many giant particles, some ringed particles and clumps. There were a fair number of particles and ringed particles precipitated. The Brownian movements were sluggish and the precipitation increased with time.
Wassermann reaction	= Negative.

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the faecal vaccine, with the result that his condition improved enormously.

All pathogenic micro-organisms, when they occasion an infection, subject the protein particles in the plasma to both dehydration and to hydration. Although in the syphilitic infection hydration comes more to the fore than dehydration—indeed, it is the hydrated protein particles which make the blood give a positive Wassermann reaction—the *Leucocytozoon syphilidis* nevertheless causes a considerable degree of dehydration. It is to dehydration that generalised arterio-sclerosis is due, a condition met with frequently in syphilis and equally frequently in cases of chronic intestinal intoxication. Syphilitic arterio-sclerosis is really a misnomer, because the lesion occurs rather as a result of syphilis than as actually caused by the syphilitic micro-organism. An arterio-sclerotic lesion may affect the posterior part of the cord to give rise to clinical signs and symptoms indistinguishable from those met with in degenerative myelitis; in fact the signs and symptoms may be produced by arterio-sclerosis of intestinal origin in the absence of syphilis. Arterio-sclerotic changes may take place in other parts of the cord to produce lateral sclerosis, chronic anterior polio-myelitis, amyotrophic lateral sclerosis

and Erb's syphilitic spinal paralysis. In the brain arterio-sclerotic changes may occur to produce encephalomalacia, a condition apt to be mistaken by the unwary for degenerative encephalitis. The hydration which syphilis causes or leaves in its wake is particularly apt to cause what has often been termed "encephalopathy." The patient is neurasthenic and asthenic; as a rule he complains of being always slack and depressed, he finds it difficult to take an interest in things and to concentrate; insomnia is usually present and the blood-pressures are sub-normal. Sometimes the patient complains of there being a weight on the head, a pain in the nape of the neck and a feeling of oppression in the small of the back. These symptoms occur not infrequently after a prolonged course of intra-venous injections of arseno-benzene because, as has been pointed out before, the late action of this drug is one of hydration. In connection with this, the reader's attention is drawn to Korsakow's psychosis met with in cases of arsenical intoxication. The signs and symptoms just mentioned are met with in many forms of intoxication and particular attention would be drawn to their occurrence when too large doses of insulin are being employed, a point confirming the view expressed some years back that insulin depends for its action upon its hydrator effect. Cerebral hydration is prone to be the most noticeable because once it is in being other factors arise which tend to maintain and even to aggravate it. The moment hydration occurs in the brain, the pressure of the cerebro-fluid becomes raised, more fluid is formed and the ventricles may become dilated. As this process continues, the blood in the great vein of Galen, as pointed out by Stopford,²⁴ becomes congested, resulting in an increased intra-cranial pressure and an over-production of cerebro-spinal fluid. In this way a vicious circle is formed, and the explanation is forthcoming as to why tapping the theca benefits the patient.

Summary

A chronic intestinal intoxication aids a bacterial invasion of the nervous system by depressing the patient's resistance. This enables a microbic invasion from without to produce lesions of the central nervous system, syphilis in particular. But, even in the case of syphilis nervous lesions may be accentuated and even produced more by the changes the protein particles in the plasma undergo than by the *Leucocytozoon syphilidis*. As the changes produced by the syphilitic micro-organism are much the same as those produced by a chronic intestinal intoxication, it comes to pass that in certain cases more benefit results from removing the chronic intestinal intoxication than by prescribing anti-syphilitic treatment. The lowering of the patient's

resistance by a chronic intestinal intoxication enables micro-organisms ordinarily saprophytic to become pathogenic and the pathogenic forms possibly to invade the nervous system. Whether the pathogenic micro-organisms are mutation forms of the *Bacillus coli communis* and the ultra-microscopic viruses are particulate forms of the non-lactose fermenters or of micro-organisms ordinarily saprophytic cannot be answered at present. It is also possible that some of the ultra-microscopic viruses are particulate forms of the host's own protein particles.

The Influence of Altered Protein Particles in the Plasma upon the Nervous System

This part of the subject is divided into two parts : (1) the effect of altered protein particles upon the blood-vessels ; (2) the effect upon the nerve cells. Protein particles subjected to dehydration damage the blood-vessels only so long as the dehydration is chronic. When the dehydration is acute a certain percentage of the protein particles undergo hydration, and if any damage is sustained by the blood-vessels the changes produced are wrought by the hydrated particles and not by the dehydrated particles.

Chronic dehydration leads first to hypertrophy and later to atrophy. Every coat of the vessel may undergo hypertrophy, the changes wrought are most marked in the arterioles, and the lesion produced is referred to generally as "hyperplastic sclerosis." It is impossible to say which part of the vessel is the first to become hypertrophied and it is doubtful whether it is always the same structure in every case. The endothelial cells multiply and become spindle-shaped, but the most noticeable change is the hypertrophy of the elastic and sub-endothelial layers. The sub-endothelial layer becomes more homogeneous, less cellular and studded with elastic tissue elements. Although these changes are hypertrophic in nature they are nevertheless degenerative. The invasion of the sub-endothelial layer with elastic tissue can be independent of the elastic layer, that is to say, the elastin is formed *in situ* as a result of a degenerative change undergone by the fibrous tissue. The degeneration is one where protoplasm becomes broken down into amino acids, and the blue-black colour elastin stains with orcein is due most probably to the formation of a derivative of the amino acid tyrosin.

Hyperplastic sclerosis, the result of pure chronic dehydration, is a degenerative and not an inflammatory lesion in the true sense of the term. When the dehydration is accompanied by hydration inflammatory changes appear upon the scene, and these alter the lesion produced. Hydration results in stimu-

lating the endothelial cells of the lymphatic vessels to manufacture leucocytes which invade the various coats of the vessel. The endothelial cells of the vessel undergo local disintegration, which has a two-fold effect: either a so-called atheromatous ulcer is produced or the hypertrophied sub-endothelial layer projects into the lumen of the vessel. In both cases the defect leads to local arrest of the protein particles in the plasma. The precipitated particles either extend the destruction the tissues have already sustained or undergo the cyclical change of gelation. In the former case the vessel undergoes dilatation, the permeability of its walls is increased and a hæmorrhage may result. This is the *rationale* of sub-arachnoid hæmorrhages, which in the author's opinion occur more frequently than is generally thought. Sub-arachnoid hæmorrhages may occur, as Hall²⁵ pointed out, in the twenties, showing that hyperplastic sclerosis is by no means limited to patients much older in life, and the following is a particularly illustrative case:—

Case 96

A woman, aged twenty-six, suffered from severe attacks of headache. The patient's father died of apoplexy, aged sixty-nine, and the mother of broncho-pneumonia, aged sixty-seven. The mother was crippled with osteo-arthritis for many years before she died. The patient's only sister was an epileptic, but the fits did not begin until she was thirty years of age. The patient suffered from chilblains and rhinitis, which started when the headaches began, three years previously. The headaches were very severe. They were sometimes associated with coloured lights, and two attacks occurred requiring special mention. The first attack was characterised by malaise and, during the day, while putting some coal on the fire, the patient had a sensation as if something had suddenly snapped in her head. This was followed by a severe headache lasting for fourteen days, and for the first twenty-four hours the patient vomited and was temporarily blind. The second attack, which started a month later, began with blindness and vomiting. The patient then became unconscious for three days, and the headache persisted for five weeks. Four months later another attack, even worse than the second, occurred. Three months before the patient sought advice she had put on nearly two stone in weight, and since the attacks had begun the periods had become irregular. The patient had the usual signs of familial chronic intestinal intoxication. She was accustomed to bite her nails, the pulse was 124 and the blood-pressures registered 120 and 60 mm. of Hg. respectively. The colon in the left iliac fossa was contracted, tender areas

were present in the regions of the splenic and hepatic flexures and the cæcum was dilated. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilis* (20 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·6 c.c.
Refractive index of the serum	= 1·3492.
Percentage of the blood-sugar	= 0·137 grm.
Percentage of the blood-urea	= 23 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles and ringed particles.

There were a fair number of giant particles, ringed particles and clumps precipitated and there was a tendency towards precipitation *en masse*.

The cerebro-spinal fluid was examined between the first two attacks. The fluid was xanthochromic, there were twelve cells per c.mm. and almost all were small mononuclears containing hæmosiderin crystals. There was no globulín and the percentage of the sugar was 0·073 grm. The Wassermann reaction in both the blood and cerebro-spinal fluid was negative.

The patient was dieted, her colon was washed out, she had injections of choline and of the fæcal vaccine and had no further attack.

During both the attacks the patient behaved at first as an epileptic, her face was livid, the teeth were clenched, and the temperature rose to 102° F.

Hall²⁵ draws attention to the pyrexia occurring during the attacks, and says that Korsakow's syndrome may be a sequence of the condition. The author observed two other cases affecting men aged twenty-four and twenty-seven respectively, but unfortunately the notes are not sufficiently complete to record, and mention is made of this merely because the elder of the two became insane later. The vessels involved are not limited to those of the meninges; indeed, this type of hyperplastic sclerosis may affect any vessel in the brain. The arterioles in the internal capsule may undergo hyperplastic sclerosis and a hæmorrhage occurring causes hemiplegia. This is doubtless the *rationale* of hemiplegia encountered, particularly in men between the ages of twenty-four and forty. Syphilis is not the cause, as is generally thought, and this is illustrated by the following case :—

Case 97

A man, aged twenty-seven, had had repeated attacks of left hemiplegia during the past eighteen months. The patient's father died of diabetes, aged

fifty-nine, and his mother of chronic pulmonary trouble (? interstitial pneumonitis), aged forty-eight. He had a sister living who suffered from hay-fever and asthma, and two brothers who had had rheumatic fever. The patient had had rheumatic fever himself and had always been subject to tonsillitis. He had been constipated all his life and had suffered from boils and carbuncles. He was tall and thin ; he could not stand with his knees and feet together at the same time ; his elbows were wide-angled and hyper-extended and he had marked acro-asphyxia. The pulse was 72 and the blood-pressures registered 90 and 70 mm. of Hg. respectively. The left colon was tender and the ascending colon and cæcum were dilated. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (40 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and these were mostly giant particles and ringed particles. There were as many particles precipitated with some large agglutinations.

Wassermann reaction = Negative.

The patient was dieted, his colon was washed out, he took iodine, ichthyol and thyroid internally and had injections of contramine and of the faecal vaccine, with the result that he had no further attacks. Some of the previous attacks had undoubtedly been caused by injections of nov-arseno-benzene, which had been prescribed on the assumption that the condition was due to vascular syphilis, because they synchronised. The patient had never had a venereal infection and the Wassermann reaction of the blood and cerebro-spinal fluid had always been negative. The following is an interesting case, possibly of the same nature, because it brings out a feature not previously described, but one the author has noted on several occasions in men with vascular sclerosis, namely, hyperkeratosis of the *Glans penis*.

Case 98

A man, aged forty-five, had complained of headaches and dizziness (loss of equilibrium) for some days and was thrown to the ground while dressing through a hemiplegic attack. The patient had suffered from tonsillitis and

chronic nasal catarrh as long as he could remember, and he had been habitually constipated. He had been operated upon for hernia twenty-five years previously; he had had two attacks of jaundice, but never a venereal infection. The patient presented many of the signs of inherited disease; his pulse was 66, and the blood-pressures registered 90 and 75 mm. of Hg. respectively. The knee jerks, and ankle jerks, and left abdominal reflex had vanished, and the whole of the *Glans penis* and under surface of the prepuce presented the hyperkeratotic appearance met with in cases of *Keratoderma blennorrhagica* and psoriasis. The sigmoid and ileo-cæcal regions were tender on pressure, and the ascending colon and cæcum were dilated. The urine gave a reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus proteus Valeriei* (15 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0·4 c.c.
Refractive index of the serum	= 1·3481.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-urea	= 23 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and amongst them were some giant particles and ringed particles. There were more particles precipitated in the form of giant particles, ringed particles, and agglutinated masses.

Wassermann reaction = Negative.

The patient received first injections of acetyl-choline to overcome the attack, and when he was better he was dieted, had colonic lavage, took iodine, ichthyol and thyroid internally and had injections of contramine and of the fæcal vaccine. The patient went abroad and the author has not heard of him since.

Another interesting condition caused by multiple punctate cerebral hæmorrhages, although not the result of hyperplastic sclerosis, is "punch drunk," called attention to by Martland.³⁷ According to this observer, boxers and men who have concussion without fracture of the skull get punctate hæmorrhages, particularly in the *Corona radiata* of both frontal lobes and in the *Corpora striata*. These hæmorrhages are followed by a varying degree of gliosis, which is apt to cause neuronie degeneration leading to neuroses, psychoses, and Parkinsonism. This explains why pugilists so frequently end their days in an asylum.

When the precipitated protein particles undergo the cyclical change of

gelation a thrombus forms; the fibrin of the thrombus undergoes organisation into fibrous tissue, which in addition to the invasion of the lumen by the hypertrophied sub-endothelial tissue may result in a more or less complete blocking of the vessel. The blocking is seldom complete, because the tissue becomes canalised. One of the best-known clinical examples of the inflammatory type of hyperplastic sclerosis is *Thrombo-angiitis obliterans*, often called "Buerger's disease." *Thrombo-angiitis obliterans* is not a specific condition any more than is hyperplastic sclerosis, because the histological picture presented is influenced by whether hydration wrings a greater change upon the coats of the vessel than dehydration or *vice versa*. *Thrombo-angiitis obliterans* is not a condition encountered solely in Jews, because the author has had many cases affecting other races, one being a man only twenty-six years of age. The author has seen cases in women, and he is convinced that nicotine is not a cause, although it may possibly accentuate the blood-changes rendered abnormal in the first instance by a familial chronic intestinal intoxication. Many observers have stressed the rise in the percentage of the blood-sugar, but this is of course of no significance and is by no means constant. Even when the percentage is raised it shows no more than that some of the protein particles in the plasma are being subjected to dehydration. All patients with *Thrombo-angiitis obliterans* complain of pain in the limb affected, and in the case of the legs the patient generally refers to the pain as cramp in the calves. Since the author has made the rule to interrogate every patient regarding cramp in the calves and to feel for pulsation in the posterior tibial and *Dorsalis pedis* arteries he has come across many cases of *Thrombo-angiitis obliterans* which would have otherwise been missed, and has come to regard the condition as quite a common one irrespective of race. The pain may be worse at night, when it can be severe enough to wake the patient, and it is frequently aggravated by exercise. The pain may be present many years before the condition is recognised clinically, and it is caused by the protein particles which have become arrested locally stimulating the nerves and muscles and occasioning ischæmic contraction of the latter. The superficial veins are liable to become varicose and later the legs swell. The swelling is usually hard, and not œdematous, and the skin is shiny and red. In other cases the various lesions of *Erythema multiforme* may appear on the affected limbs, and some of these lesions may develop into ulcers. The varied local manifestations are occasioned and regulated by the changes the vessels, other than the main arteries, undergo. This explains why dermatomyositis and *Peri-arteritis nodosa* or Kussmaul's disease may be associated with *Thrombo-angiitis obliterans*.

The four following cases illustrate the clinical features of this interesting condition :—

Case 99

A man, aged fifty-eight, and looking seventy-eight, complained of attacks of swelling and ulceration of both legs. The patient's father died of cancer of the colon, aged seventy, and his mother of sprue, aged forty-five. One brother living, aged forty-nine, was in an asylum and four sisters living suffered from rheumatism. The patient used to suffer from chilblains, he had had many attacks of colitis, for which the appendix had been removed, and he was much troubled with nasal catarrh. When the patient was forty-nine years of age he developed what he called "sprue," and was troubled with *Herpes oris* for about four years. When the mouth improved the patient experienced pains in his legs which were aggravated by exercise, he noticed the veins swell and become varicose, he had swellings of the ankles which came and went, and ulcers appeared in quick succession. The legs were deeply pigmented. Exercise caused petechial lesions to appear, which proceeded to form ulcers, and occasionally in the place of petechiæ *Erythema nodosum* lesions occurred. The patient was thin and anæmic, he went grey in the early thirties, he had marked *Arcus senilis* and generalised arterio-sclerosis. The tongue was fissured, all the teeth had been removed, the pulse was 72 and the blood-pressures registered 120 and 75 mm. of Hg. respectively.

The colon was contracted and tender along its whole length, with the exception of the cæcum and part of the ascending colon, which were dilated.

The urine contained a trace of protein and gave a marked reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The patient could not stand with his knees and feet together at the same time, and there was no pulsation to be felt in the arteries of the legs. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 1·2 c.c.
Refractive index of the serum	= 1·3482.
Percentage of the blood-sugar	= 0·068 grm.
Percentage of the blood-urea	= 25 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving, but all were larger than normal and very refractile. There were many giant particles, ringed particles, and giant-particled clumps precipitated and the Brownian movements of the particles were very sluggish.

No pathogenic micro-organisms were discovered in the excreta.

The patient was dieted ; he had his colon washed out, took iodine, ichthyol and thyroid internally, and had two courses of intra-muscular injections of contramine.

The patient improved considerably and had no further ulceration of the legs. There are many significant features in this case. First of all it is seen that *Thrombo-angiitis obliterans* is a manifestation of a familial chronic intestinal intoxication. Secondly, there is the association between excessive pain, swelling, venous engorgement and varicosity. Thirdly, excessive exercise occasioned lesions of the *Erythema nodosum* and purpura (hæmorrhagic) type, which proceeded to ulceration, as the hydration causing them in the first instance went on to produce tissue lesions. In the brain punctate hæmorrhages may occur before the vessel wall is sufficiently recovered to allow a large quantity of blood to escape. Fourthly, the patient was not a Jew. Fifthly, the blood-picture shows dehydration and hydration, the former being evidenced by the reduction in the suspension stability of the red blood-corpuscles and the low refractive index, and the latter by the fall in the percentage of the blood-sugar. Sixthly, no pathogenic micro-organisms were found in the excreta. It not uncommonly happens that in cases of chronic intestinal intoxication the pathogenic mutation forms of the *Bacillus coli communis* vanish as the patient advances in years.

Case 100

A man, aged sixty, sought advice for swelling of both legs of two months' duration. The legs were swollen, the skin over was tense, shiny and red, and scattered about were some purpuric areas ready to proceed to ulceration. The swelling was non-œdematous. There was no pulsation in the posterior tibials or dorsal arteries of the feet. For over fourteen years the patient had had attacks of cramp in the calves, particularly at night time, and on several occasions the pain was severe enough to wake him. His father died of diabetes and two of his sisters from cancer. The patient used to suffer from chilblains, and he had been operated upon for anal fissure, appendicitis and renal calculus. The second operation was followed by a sub-phrenic abscess and venous thrombosis of the left leg. For two years, when aged fifty-five to fifty-seven, he was in a home for delusional insanity. He was short and stout, the pupils reacted sluggishly to light, there was bilateral *Arcus senilis*, all the teeth had been removed and the tongue was furred and fissured. He had acro-asphyxia, the skin of the palms was dry, the nails were ridged, the pulse was 88 and the blood-pressures registered 120 and 80 mm. of Hg.

respectively. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde; the pathogenic micro-organism found in the excreta was the *Bacillus Gärtner* (75 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.0 c.c.
Refractive index of the serum	= 1.3490.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 42 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles, and ringed particles. There were some giant particles, ringed particles, and one or two giant-particled clumps, and agglutinations precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of contramine, and of the faecal vaccine. The swelling of the legs vanished, and the patient improved considerably. This patient was a Jew and had several manifestations of inherited disease. One of the most interesting points in the case is the repetition of the attacks of cramp in the calves for many years before the vascular trouble was diagnosed. The blood-picture shows a combination of dehydration and hydration.

Case 101

A man, aged sixty, sought advice for anæmia and asthenia. The patient's father died of cancer (? sarcoma of jaw), aged twenty-nine, his mother as a result of chronic bronchitis. One brother died with hydrocephalus, aged three, and another of scarlet fever, aged six. The patient used to have chilblains, he had had two attacks of pneumonia and had been operated upon for empyema and appendicitis. He suffered from chronic nasal catarrh and had a troublesome pharyngitis. He had had rheumatic fever and several attacks of lumbago and sciatica since. When he was forty-one years of age he had several boils and carbuncles. The teeth and tonsils had been removed. Eight years previously and several times since, typhoid bacilli were found in the fæces and at the time of this examination they were still present, although Widal's reaction had always been negative. For some considerable time he had had a daily pyrexia. Syphilis was contracted when the patient was eighteen years old. The patient was tall, thin, anæmic and very

weak. He could not stand with his knees and feet together at the same time, he had bilateral *Arcus senilis*, the pupils did not react to light and the tongue was furred and sore in places like a sprue-tongue. The patient was alleged to have had sprue. The nails were dry, cracked easily and were ridged, the pulse was 76 and irregular (extra-systoles), the arteries were hard and tortuous, there was generalised arterio-sclerosis and the blood-pressures read 165 and 80 mm. of Hg. respectively. The veins in both legs were varicose; the skin was deeply pigmented, and no pulsation was to be felt in the posterior tibials or dorsal arteries of the feet. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. An examination of the abdomen revealed an atonic colon. The pathogenic micro-organism found in the excreta was the *Bacillus typhosus*, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.7 c.c.
Refractive index of the serum	= 1.3460.
Percentage of the blood-sugar	= 0.062 grm.
Percentage of the blood-urea	= 33 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles and ringed particles both moving and precipitated. The Brownian movements of the particles were sluggish.
Wassermann reaction	= Negative.
Red blood-corpuscles	= 4,270,000 per c.mm.
White blood-corpuscles	= 12,000 „
Hæmoglobin	= 50 per cent.
Colour index	= 0.6 „
Polymorphonuclear leucocytes	= 81.3 „
Small mononuclear leucocytes	= 10.0 „
Large mononuclear leucocytes	= 7.6 „
Eosinophile leucocytes	= 1.0 „

The red blood-corpuscles showed vacuolation, aniso- and poikilo-cytosis, polychromasia and basophilic stippling.

The patient did not undergo the treatment advised, and died a few months later of degenerative myocarditis. He was not a Jew, and he had never smoked in his life. The pyrexia was of intestinal origin, and there is no doubt it had given rise to a sprue-like condition. Sprue is not a clinical entity, it is merely a more or less acute form of intestinal intoxication caused by a non-lactose fermenting micro-organism, and it is allied to pernicious anæmia, pellagra, etc.

Case 102

A woman, aged sixty, sought advice for what she described as "neuritis" of the legs. The patient was not a Jewess. Her mother died of puerperal fever following her birth, aged twenty-three. She had double pneumonia when aged twenty-five, and phlebitis of both legs following the birth of a child when aged thirty. The patient had had two children and five mis-carriages. Pelvic cellulitis followed one of the mis-carriages, and this led to an emergency intestinal anastomosis having to be made four years previously. She could not stand with her knees and feet together at the same time, she had wide-angled and hyper-extended elbows and acro-asphyxia. All the teeth had been removed, and the tongue was furred and fissured. The pulse was 120, and the blood-pressures registered 200 and 110 mm. of Hg. respectively. One year previously the varicose veins had been blocked with sodium salicylate, and ever since painful and red areas had appeared on both feet. The red patches were signs of impending gangrene, and there was no pulsation to be felt in any of the arteries of the legs. The toe-nails were dry, brown, brittle and hyperkeratotic, as is the rule in cases of *Thrombo-angiitis obliterans*. The arteries elsewhere were also diseased, as the patient had become very intolerant and lost her temper on the slightest provocation. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (75 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.75 c.c.
Refractive index of the serum	= 1.3511.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 41 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, with a fair percentage of giant particles. There were some giant particles and giant-particled clumps precipitated, with one or two agglutinated masses as well as some precipitation <i>en masse</i> .

The patient was dieted, she learned to give herself treacle enemata, she took iodine, ichthyol and thyroid internally, and received injections of contramine and of the fæcal vaccine.

The patient improved, the painful and red patches vanished, but pulsation did not return in any of the leg arteries. This case is of particular interest in that the patient was a woman, and it is curious that in the four cases described the percentage of the blood-sugar was not raised in one. As stated above,

it is just a coincidence whether the percentage of the blood-sugar is raised or not.

There are three clinical conditions which may be caused by vessels undergoing changes akin to those met with in *Thrombo-angiitis obliterans*, namely, transient hemiplegia, Raynaud's syndrome and *Angina pectoris*. Transient hemiplegia is frequently ascribed to vascular spasm, but this is not, strictly speaking, the case. What is meant by vascular spasm most probably occurs in the following way. When protein particles undergo the maximum degree of hydration suddenly and become precipitated in an organ, that organ becomes bloodless and œdematous. The protein particles are precipitated in the peri-vascular lymphatic spaces and the arteries, arterioles, veins and capillaries contain no blood. The vessels are most probably collapsed and not in a state of spasm. When the brain is the organ involved, the peri-vascular lymphatic vessels and peri-neural spaces are found to be dilated, the choroid plexuses present a cystic appearance, and if there has been time for œdema to appear the ventricles are dilated. When the hydration is less severe the capillaries undergo the maximum dilatation and they are filled with red blood-corpuscles in addition to the hydrated protein particles which have been precipitated therein. When the hydration is still less severe the hydrated protein particles collect in the veins, which become filled as well with the red and white blood-corpuscles. Death usually occurs when a vital organ becomes bloodless and œdematous, as in the first instance. In the second case the capillaries undergo marked dilatation, the permeability of their walls is increased and hæmorrhages are liable to occur. In the third case the hydrated protein particles undergo the cyclical change of gelation; inflammation of the polymorphonuclear leucocyte variety results. Should the vessels have undergone changes before hydration occurs, then quite a moderate degree of hydration suffices to produce the bloodless and œdematous picture. The kind of hydration most likely to act in this way is the one occurring as a cyclical change to chronic dehydration when the capillaries evidence fibrosis and the arterioles and arteries hyperplastic sclerosis, of which *Thrombo-angiitis obliterans* may be a type. When the capillaries are fibrosed it requires only a moderate degree of hydration to cause a dilatation of the peri-capillary lymphatic vessels and a precipitation of the hydrated protein particles therein. This results in closing the capillaries still further, and if a large cerebral capillary network suffers this damage the blood-pressures become raised. This is the explanation of the raised blood-pressures in eclampsia, for example. The same sequence of events occurs when the arterioles and arteries have suffered as a result of chronic

dehydration of the protein particles in the plasma, so that when the cyclical change of hydration occurs they undergo collapse the moment the hydrated protein particles become precipitated in the peri-vascular lymphatic vessels and capillaries. Although the peripheral blood-pressures are raised the local blood-pressures are lowered, because the latter is an invariable sequence of hydration. Therefore, when a hæmorrhage occurs it is not because the blood-pressures are raised but because the capillaries are dilated and the permeability of their walls is increased, both of which occur as a result of protein hydration, or in other words when the local blood-pressures are lowered. The shutting off of a cerebral capillary network resulting in an ischæmic condition of the brain causes violent headache, and if the collapse spreads to an important arteriole or artery a transient hemiplegia results. This is also the explanation of temporary amaurosis, which is not infrequently encountered in cases of hyperpiesia. Hæmorrhage does not take place unless the capillaries are dilated and filled with red blood-corpuscles, and this occurs when the hydrated protein particles in the peri-capillary lymphatic vessels begin to undergo their cyclical change or the hydrated protein particles are precipitated in the first instance in the capillaries. Should the capillaries be too fibrosed to undergo dilatation the red blood-corpuscles collect in the arterioles and arteries and the hydrated protein particles collected therein may undergo the cyclical change of dispersion to cause arterial thrombosis. This sequence of events occurs not uncommonly in the central artery of the retina, when it is another cause of amaurosis. The œdema occurring as a sequence of cerebral hydration results in raising the pressure of the cerebro-spinal fluid, and it is for this reason that a lumbar puncture gives relief. Puncturing the theca should always be adopted, because it saves the neurones from being badly damaged. The pressure of the fluid in other spaces may be raised in the vitreous, for example, and when this occurs glaucoma results. It is interesting to note that acute glaucoma occurs most frequently in the early hours of the morning, when hydration is most pronounced. The patient is usually awakened with feverishness, nausea and vomiting, the eye is tender and hard, the conjunctiva is congested and œdematous, the cornea is steamy and insensitive, and the pupil is dilated and fails to react to light.

Some of these signs and symptoms are illustrative rather of dehydration than of hydration, which in fact they are. Indeed, the condition is mentioned to illustrate a point to which the author has frequently drawn notice, namely, that many of the worst and most acute manifestations of disease occur when the altered protein particles undergo their cyclical change, or in other words

when hydration and dehydration occur concomitantly. The explanation given above of transient hemiplegia can be seen with the naked eye in Raynaud's disease and the various forms of gangrene. When the hydration is greatest and occurs suddenly the fingers are white and bloodless owing to the collapse of the vessels occasioned by the precipitation of the hydrated protein particles in the peri-vascular lymphatic spaces. When the hydration is less marked the hands are red, due to the collection of the red blood-corpuscles in the capillaries. When the hydration is least marked the hands are blue, due to the blood collecting in the veins. The local condition passes on to inflammation and ulcer formation, when the hydrated protein particles collected in the veins undergo the cyclical change of gelation. Should the arterioles and arteries evidence the changes of the various forms of hyperplastic sclerosis, hydration occurring locally may result in œdema or in petechial hæmorrhages, etc. If the hydrated protein particles collect in the altered arterioles and arteries and undergo the cyclical change of dispersion, thrombosis with resulting gangrene results. Gangrene can occur, of course, if the area remains ischæmic too long, and whether the gangrene is dry or wet depends upon the absence or presence of inflammation. Inflammation is most prominent when the cyclical change of gelation takes place in the veins, consequently dry gangrene means more arterial thrombosis and wet gangrene more venous thrombosis. *Angina pectoris* is due to the precipitation of hydrated protein particles in the peri-vascular lymphatic vessels of the myocardium. The enclosed capillaries and arterioles, showing varying degrees of fibrous and hyperplastic sclerosis respectively, are collapsed and the heart muscle is ischæmic. The coronary arteries may evidence *Thrombo-angiitis obliterans*, and actual thrombosis may occur in them or they may be normal. In other words, the pain of *Angina pectoris* is directly the result of the myocardial ischæmia. When œdema occurs, which is not infrequent, the fluid collects in the intra-pericardial sac. Should the hydration persist the cardiac muscle cells undergo the various forms of degeneration, ending finally in heart failure, with pulmonary or universal œdema. Since all these vascular conditions result from changes undergone by the protein particles in the plasma, surgical interference can be no more than palliative, and in the author's opinion, many of the operations advised to-day are unjustifiable. In cases of *Thrombo-angiitis obliterans*, Adson and Brown²⁷ advise removal of the second, third and fourth lumbar sympathetic ganglia, the sympathetic trunk and stripping off the peri-vascular tissue from the common iliac arteries to ensure complete removal of the vasomotor fibres. A similar

operation has been advised for Raynaud's disease by Brown²⁸, and for *Angina pectoris* the left cardio-aortic sympathetic trunk and ganglia have been removed by Shaw.²⁹ The main aim of treatment is to cause dispersion of the hydrated protein particles, and this can be achieved with many preparations. In *Thrombo-angiitis obliterans* dehydrators are of most value, such as iodine, ichthyol or thyroid substance taken internally and contramine injected intra-muscularly. In Raynaud's disease conductors are the drugs of choice; colloid silver should be used locally and injections made of strontium aspartate, calcium oleate, para-thor-mone, etc. In *Angina pectoris* recourse is had to dehydrators, of which theophylline is the best, to conductors, of which camphor is a good example, and to drugs which exhibit an initial hydrator and a later dehydrator action. The last are drugs which cause hydration in virtue of a positively charged nitrogen atom and dehydration in virtue of negatively charged active groups. The best examples are amyl-nitrite, erythrol-tetra-nitrate, acetyl-choline, coramine and cardiazol. The initial hydration relieves the local hydration by causing a dilatation of the peripheral vessels, a result which starts the cyclical change of dehydration in the precipitated protein particles.

The following case of *Thrombo-angiitis obliterans* is interesting because it shows the futility of operative measures.

Case 103

A man, aged thirty-seven, had to have a toe removed for gangrene; the wound would not heal, and an ulcer formed and spread along the sole of the foot. Seven months later the sympathetic nerves around the femoral artery were removed, and within a space of three months the ulcer healed. No sooner had this occurred than painful and open cracks appeared under the nails of two toes on the other foot, and painful red swellings came out on both forearms. Similar swellings made repeated appearances on the legs several years before the case was recognised as one of *Thrombo-angiitis obliterans*; indeed, the first appeared when the patient was only seventeen years of age. The swellings were diagnosed as gout, and the patient undoubtedly had lesions on his feet which were indistinguishable from this complaint. The patient's mother died of cancer of the uterus, aged forty-eight, and a brother, aged thirty-six, had been short-circuited for a duodenal ulcer. The patient had a chronic nasal catarrh, and had suffered from chronic indigestion and constipation all his life; he had had an attack of jaundice and three attacks of cystitis. The patient was a Gentile, tall and well built; he could not

stand with his knees and feet together ; all his teeth had been removed ; the tongue was furred, and the elbows were hyper-extended. The pulse was 96 and the blood-pressures registered 125 and 80 mm. of mercury respectively. The patient could not take alcohol, because the red lumps appeared almost immediately afterwards. He was an inveterate smoker. His nails had lost their gloss ; they were ridged and the free ends thickened from hyperkeratosis. The left colon was contracted and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3503.
Percentage of the blood-sugar	= 0·086 grm.
Percentage of the blood-urea	= 27 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, many of which were giant particles and ringed particles. There were a few giant-particled clumps moving. There were a fair number of particles, giant particles, ringed particles and giant-particled clumps precipitated.

The patient did not undergo the treatment advised ; the ulcer on the operated leg broke down again and ulcers appeared on the opposite leg. Both arms also showed evidence of active thrombotic trouble.¹

Hypertrophy of tissue resulting from chronic dehydration tends to change in the course of time into atrophy, and arterio-sclerosis is produced. It is generally thought that arterio-sclerosis and raised blood-pressures go hand in hand and that the primary arterio-sclerotic changes take place in the kidneys. In fact, interstitial nephritis is often regarded as the cause of raised blood-pressures. Arterio-sclerosis and raised blood-pressures do not go hand in hand ; in fact, in the most advanced forms of arterio-sclerosis the blood-pressures may be sub-normal. Arterio-sclerosis is by no means always most marked in the kidneys, and there is no definite relationship between interstitial nephritis and raised blood-pressures. The blood-pressures may be lowered in pronounced cases of interstitial nephritis and raised in cases of parenchymatous nephritis. Blood-pressures are raised when the protein particles are dehydrated, and a large capillary network in the brain is excluded from the circulation. Should the capillary fibrosis be permanent, then the blood-

¹ Since the above was written both legs have been amputated.

pressures may remain raised even should the protein particles undergo hydration. Blood-pressures are lowered when the protein particles are hydrated. The author is gaining the impression that atrophy most readily succeeds hypertrophy when dehydration gives place to hydration, and if this view is correct there is a rational explanation for the association of lowered blood-pressures with arterio-sclerosis. Ordinary dehydration does not provoke the signs of what is called "inflammation." Cellular infiltration occurs only when hydrated protein particles appear upon the scene of action. When dehydration and hydration are acute and occur concomitantly, the walls of the vessels are infiltrated with leucocytes both of the polymorphonuclear and lymphocytic variety, the permeability is increased and multiple hæmorrhagic lesions occur. When the hydration is more pronounced and less acute the walls become infiltrated with lymphocytes and plasma cells and an aneurysm may form. As hydration is more marked in syphilis than in any other infection it explains why most aneurysms are of syphilitic origin.

In considering the effect exercised by altered protein particles in the plasma upon nerve cells, it must be realised firstly that in disease pure dehydration and hydration are seldom encountered. There is usually a simultaneous dehydration and hydration going on, where at one time one chemico-physical change prevails and at another time the other, although it is a general rule for the clinical signs and symptoms to be produced by the protein particles which have been subjected to hydration. Secondly, that the effect of dehydration and hydration upon parenchymatous and mesenchymatous tissue does not run parallel, because dehydration affects mesenchymatous tissue more than parenchymatous tissue and *vice versa*. Thirdly, that the tissue changes are always behind the blood changes, with the result that an examination of the blood does not necessarily give the information required as to what is going on in the organ selected for attack by the altered protein particles—different organs are attacked in different individuals. The effect of dehydration upon the mesenchymatous nerve tissue is to produce first hypertrophy and then atrophy. From the author's experimental work on animals the first cells to undergo hypertrophy would appear to be the ependymal cells of the ventricles. Atrophy of the neuroglial tissue occurs only when the dehydration is prolonged, but when this stage is reached certain of the cells may resist the change and undergo a development resulting in a glioma. Owing to the neurones and neuroglial tissue being affected differently by dehydration and hydration, it comes to pass that neuronie degeneration, the result of hydration, may be encountered alongside with neuroglial hypertrophy,

the result of dehydration—for example, in degenerative encephalitis (G.P.I.). To appreciate the effect altered protein particles have upon the neurones it is necessary to draw attention to the protoplasm of these cells.

The protoplasm of the neuron has two distinguishing features: (1) its fibrillar structure; (2) the chromophilic substance often called the “Nissl or tigroid bodies.” The cytoplasm of the neuron acts presumably like a miniature battery, and as to whether the liberation of electrons therefrom is in excess or not of the normal requirements depends upon the chemico-physical state in which the Nissl bodies happen to be. The Nissl bodies, as seen in stained preparations, are fixation artefacts and *in vivo* the substance is diffused throughout the protoplasm and does not exist in a granular form, although it is made up of distinct particles. The chromophilic substance is usually stated to be a nucleo-protein allied to chromatin, but in the author’s opinion it is a lipid-globulin compound containing both iron and sulphur.

The function of the Nissl bodies is to conduct electrons along the axon and dendrites, and it is probable that this action is executed through positively charged carboxyl groups in the fat moiety of the compound. Conductors increase the electronic activity of the Nissl bodies, which is the reason why they cause increased muscular activity and why when used to excess they occasion tetanic muscular contractions. Conductors used to the point of producing fatal intoxication cause death in *Rigor mortis*. Under the influence of conductors, the Nissl bodies increase in number, diminish in size and develop enhanced reducing properties, tested by their ability to convert certain tri-phenyl-methane dyes into the leuco-base form. Dehydrators may stimulate electronic activity at first, but their action is a variable one depending partly upon the nature of the dehydrator, but more upon the chemico-physical state in which the protein particles in the plasma happen to be when the drug is prescribed. This initial action is quickly succeeded by one of diminished electrical conductivity. Large doses destroy electrical conductivity at once, and this occurs also when dehydrators are used over a long period of time.

The action of increased conductivity is shown by the excitation and increased muscular contraction which occur when a patient is anæsthetised. The diminished conductivity following large doses is evidenced by the loss of consciousness occurring later in anæsthesia. No better example of diminished conductivity following the prolonged use of dehydrators can be given than that of senility. When dehydrators increase electrical conductivity much the same changes are to be noted affecting the Nissl bodies as were seen to occur with conductors, with the exception that the granules do not become so

small and their reducing power is not so great. When the electrical conductivity is diminished the neuron is usually larger than normal, the chromophilic substance is less granular and more homogeneous and it may even stain with methyl-green. Therefore, while conductors cause dispersion of the lipoid-globulin particles, dehydrators cause hydration.

Hydrators tend to diminish electrical conductivity from the start, although in some instances they may increase it, as evidenced by the muscular contractions which occur when toxic doses of cardiazol, nicotine and insulin are injected intra-venously, but the muscular contractions are occasioned by the negatively charged dehydrator-acting groups in the compounds. Hydrators produce dehydration of the chromophilic substance. The Nissl bodies break up and go into true solution and the neuron undergoes what is usually termed "chromatolysis," the change occurring when degeneration follows the cutting of the corresponding axones. As the Nissl bodies go into true solution, they rapidly lose their reducing properties.

Further, when hydration makes itself felt, signs of inflammation appear and neuritis is produced. Hydrated protein particles are dispersed best by condensers or negatively charged drugs, hence the explanation of the benefit following the use of thiol-histamine and contramine in cases of myositis, arthritis, neuritis, etc. Hydrated protein particles tend to become precipitated in the lymphatic vessels and capillaries and are liable, as stated above, to penetrate the walls of the vessels, hence it is not surprising that most of the nerve lesions produced are the result of those protein particles in the plasma which have been subjected to hydration. The lesions produced by the hydrated protein particles are innumerable, but the reader should realise once and for all that all are closely related and that although this or that lesion points to the precipitation of the hydrated protein particles in a special area, this is never the sole area involved. That is to say, if the lesion produced suggests precipitation in the optic thalamus, for example, it may be taken for granted that there is a precipitation also in the cerebral cortex and *vice versa*. Before dealing with the various lesions produced, it is necessary to refer to certain physiological phenomena which are dependent upon a slight degree of protein hydration, which is best referred to as gelato-hydration, because the particles collect in the veins, where dehydration takes place as well.

The most important of these phenomena is sleep. Sleep is due to the collection of gelato-hydrated particles in the veins of the brain, whereby the neuron activity is lessened. The dehydration undergone by the protein particles in the plasma causes just sufficient hydration of the protein particles

constituting the cytoplasm of the neurones as will prevent any liberation of electrons at the bidding of the protein particles in the blood-stream which have been subjected to hydration. That sleep is consequent upon a combination of protein dehydration and hydration is proved by the facts that all anæsthetic drugs act in this way and that the first effect of injecting into animals toxic doses of drugs combining a dehydrator with a hydrator effect, such as cardiazol, coramine, arecoline, nicotine, etc., is to cause the animal to seek out the darkest corner in the room. If the protein particles in the plasma undergo a degree of hydration whereby, in spite of whatever happens, the neurones are robbed of electrons, then cerebral activity is increased.

This explains why insomnia is met with most frequently in patients whose protein particles are abnormally hydrated and why over-physical and over-mental exertion prevent rather than stimulate sleep. The continued action of any stimulation of cerebral activity causes sleep because it leads to cerebral venous congestion and to gelato-hydration of the protein particles which collect in the veins, which explains why monotony, etc., are followed by sleep. But, should the protein particles become so hydrated as to collect in the peri-capillary lymphatics and capillaries, there occurs violent cerebral activity followed by fatal cerebral shock. All these stages can be traced in animals receiving toxic doses of drugs combining a dehydrator with a hydrator action. The violent cerebral activity leads to excessive muscular contractions, pulmonary distress and increased glandular activity, the exact opposite to what occurs in sleep. It is owing to this excessive hydration that anæsthetics produce convulsions and shock (*Status lymphaticus*), and it explains the muscular movements, difficulty of breathing, diarrhœa and death from cerebral shock following toxic doses of histamine, cardiazol and the other drugs mentioned above. Arecoline, in addition, causes excessive salivation, pointing to stimulation of the centre of the vagus nerve. Although the cerebral activity caused by excessive hydration may affect any part of the brain, different areas are picked out in various conditions, but whatever the area may be, one or more signs and symptoms of vagal activity are to be noted.

This point is of some significance as supporting the statements expressed in the discussion on the vegetative nervous system and in explaining some of the characteristics of sleep. In sleep the breathing is slower, deeper and more regular, the heart beats slower and more forcibly and the blood-pressures are lowered. Most of the glands in the body secrete less, with the exception of the sweat glands, which secrete more. The pupils are contracted and not dilated as might on *à priori* grounds be imagined to be the case.

Other characteristics of sleep which have also the characteristics of gelato-hydration are the rise in the carbon-dioxide tension of the alveolar air, the rise in the percentage of the blood-inorganic phosphorus and the increase in the acidity of the urine. Although the volume of the cerebral contents is increased during sleep, this is due in part to the venous congestion and in part to the fact that the rate of flow of the blood through the brain is lowered. These changes are most marked when sleep is deepest, namely, between the hours of 2 and 4 a.m., the time when death is most likely to take place and when a hæmorrhage is most prone to occur, as stated already.

By differentiating the various manifestations of cerebral activity caused by excessive hydration and which may either precede, prevent, or follow sleep, some light will be thrown on conditions thought by many to be distinct clinical entities. Although the part of the brain bearing the brunt of the attack varies in different cases, the gelato-hydration responsible for sleep occurs universally in the brain and there is no special area marking a sleep-centre. It is due to the unequal distribution of the gelato-hydration first that "consciousness" during sleep is never entirely lost and secondly that dreams which invariably occur during sleep are so apt to be distorted. Extra hydration is the cause of talking in one's sleep, somnambulism, waking with a headache, etc.

Excessive hydration may occur mainly in the cerebral cortex, in which case sleep is characterised by a contracted instead of a relaxed musculature, as evidenced by the fact that a sustained acoustic conditioned reflex does not cause sleep in a dog deprived of the cerebral cortex. On the other hand, it is theoretically possible for the same effect to be produced by a collection of hydrated protein particles in the neighbourhood of the *Nucleus ruber*. A collection in the neighbourhood of the grey matter of the third ventricle is the cause of the want of sleep, and of the ptosis and ophthalmoplegia which usher in so many cases of epidemic *Encephalitis lethargica*. The prolonged sleep following these lesions occurs when the hydration severe enough to cause paralysis has given way in part to the cyclical change of dehydration. A collection in the infundibular region gives rise to the condition known as narcolepsy, in which the patient goes to sleep when he is actively engaged, or sleep follows a general relaxation of the muscles, often severe enough to throw him to the ground. In the cases marked by muscular relaxation (catalepsy), the hydration must be severe enough to cause a temporary paresis of the extra-pyramidal system and the collection to take place in that part of the system subjacent to the red nucleus. The following is such a remarkable case of narcolepsy as to demand insertion here :

Case 104

The patient, a man aged twenty-one, had suffered from almost daily attacks of narcolepsy since age sixteen. While some of the attacks were momentary, others lasted all day, and on occasions cataplexy supervened. The patient's father died of phthisis aged thirty-two, and his sister, aged eighteen, had had *Acne vulgaris*. The patient had chilblains as a boy, bronchitis when aged fourteen, and nasal furunculosis when aged nineteen. He was grossly mal-co-ordinated and fidgety, he had gingivitis, a high-arched palate, a furred and fissured tongue, acro-asphyxia and long tapering hyper-extended fingers. There were several warts on the hands, all the reflexes were exaggerated, the pulse was 70, and the blood-pressures registered 90 and 65 mm. of Hg. respectively. The patient was troubled with universal hyperidrosis, the left colon was contracted, and there was tenderness in the ileo-cæcal area and in the regions of the flexures. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (60 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, with a large percentage of giant particles, there were some giant particles and giant-particled clumps precipitated, and the Brownian movements of the particles were sluggish.

The patient cut out butcher's meat, eggs and milk from his diet, had a course of colonic lavage, took strychnine, iron and arsenic internally, and received injections of acetyl-choline (0.1 grm. every other day for twelve doses), and of the fæcal vaccine.

The patient was rid of his attacks and able to take a post six months later. But, for two weeks after the injections of the fæcal vaccine (0.25 and 0.5 million on two successive days) the patient had incessant attacks, which were checked with Sup. 36. Considering how small were the doses of the fæcal vaccine, such a reaction does point to the *Bacillus fæcalis alkaligenes* being the pathogenic micro-organism. The patient had been an inmate of three hospitals for "nervous diseases," where he had received sedatives only, which had aggravated his trouble. When seen a year later the patient complained of feeling sleepy

during the day, but he had had no actual attacks and was able to ride a motorcycle.

Closely allied to narcolepsy are epilepsy and migraine. Epilepsy is not a disease *sui generis*, it does not differ fundamentally from *Petit mal*, spasmodophilia and many other allied conditions. It is due to the precipitation of hydrated protein particles in the peri-capillary lymphatics and capillaries, and although the precipitation may occur in various parts of the brain and in different areas in the same patient, the region most frequently involved would appear to be the between-brain, as suggested first by Müller and Grevnig.² There seems every reason to believe that heat-stroke, a clinical condition closely resembling epilepsy, is due to the precipitation of hydrated protein particles in the between-brain. It is interesting to observe that, even if the hydration be continued, it causes the victim to lie, thieve and to become generally depraved in character, features met with in chronic epileptics following heat-stroke, in morphia addicts, etc.

The reason why a morphomaniac gets respite and a period of exhilaration following each dose is because the active negatively charged group of the compound causes dispersion of the protein particles hydrated by the previous injections. It is due to the hydrated particles becoming broken up, or in other words to hydration being succeeded by dispersion, that sleep is followed by waking. Drugs having a conductor effect, that is to say, being able to give up electrons to protein particles, prevent sleep and likewise narcosis, hypnosis and anæsthesia. Strychnine, para-thor-mone, Sup. 468 and Sup. 36, as examples of conductors, both prevent hydration of the protein particles and overcome it when it is in being.

From this the reader will understand why the author advocates the use of para-thor-mone in place of scopolamine and morphine before an operation, Sup. 36 for acute post-operative manifestations such as venous thrombosis, glycosuria, acetonuria, etc., and strychnine, para-thor-mone and Sup. 468 in place of hyoscine in morphinism.

As the use of conductors in morphinism has not been illustrated in the two previous volumes two cases are cited below, and a study of these shows conductors may be preferred to such drugs as hyoscine, pilocarpine, etc., because both patients had had one or more hyoscine "cures."

Case 105

A woman, aged thirty-three, who had had several abdominal operations, and was a typical example of a chronic intestinal intoxication, had been

accustomed to take about fourteen grains of heroin a day for several years. She had undergone two hyoscine "cures," and was covered from head to foot with lesions resembling deep *Erythema nodosum*.

Several of the lesions had suppurated from time to time, necessitating incision, but the pus was always sterile, although in considerable quantity in some of the lesions. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 4·8 c.c.
Refractive index of the serum	= 1·3502.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving, but all were larger than normal and very refractile. There were a few giant-particled clumps moving and precipitated.

Three injections of Sup. 36 cleared up all the skin lesions, after which the patient received 20–30 units of para-thor-mone, 1/25 grain of strychnine and 0·002 grm. Sum. 468 daily until the heroin could be reduced to 3 grains *per diem* without any withdrawal symptoms appearing. When this stage was reached the patient continued to take 3 grains of heroin a day, but one hour before each injection she injected 10 units of para-thor-mone and in addition she injected strychnine one day and Sup. 468 or Sum. 468 another day. After a period of six months the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·7 c.c.
Refractive index of the serum	= 1·3501.
Percentage of the blood-sugar	= 0·125 grm.
Percentage of the blood-urea	= 27 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but all were larger than normal and very refractile. There were some large and refractile giant particles and a few giant-particled clumps precipitated.

The patient relapsed later and attempted to commit suicide.

Case 106

A man, aged thirty-four, had been accustomed to take about twelve grains of morphine a day for ten years. The patient had had asthma since a child and had lost his father and one brother of the complaint, aged sixty-nine and forty-two respectively. This brother lost a girl child, aged eleven, of

asthma, and another brother, who did not have asthma, lost a boy from the same condition. An examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3504.
Percentage of the blood-sugar	= 0·143 grm.
Percentage of the blood-urea	= 18 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles, ringed particles and large giant-particled clumps. There were some giant particles, ringed particles and giant-particled clumps precipitated. The Brownian movements were very sluggish.

The patient received thirty units of para-thor-mone a day with strychnine and Sup. 468 until he was taking no morphia at all. The narcotic was gradually reduced and withdrawn without any unpleasant symptoms arising. Some time later the asthma returned and morphia was prescribed to relieve the attack, with the result that the patient relapsed again into his old condition. Acting on the supposition that the deleterious action of heroin and morphia might be counteracted by dissolving the drugs in a solution of a condenser, in the first case a single dose of heroin was dissolved in a solution containing 0·0001 grm. benzoyl-benzoic acid 2-chlorine-5-hydroxy, and in the second case a single dose of morphine was dissolved in a solution containing 0·05 grm., the carbon di-sulphide product of di-methyl-amine. In the woman's case several *Erythema nodosum* lesions appeared, while in the man's a bad attack of asthma occurred. In both instances Sup. 36 rectified immediately the damage done, but it is particularly interesting to note how the dehydrator action of the positively charged chlorine atom and of the negatively charged sulphur atom attacked the weak spot. In microbic infections, should a dehydrator be prescribed when a conductor should have been used, it invariably results in an aggravation of the infection and even, in sapræmic conditions, death may result and occur as if an acute septicæmia had suddenly been ushered in.

Summary

The parenchymatous cells of a viscus are more likely to be damaged by protein particles in the plasma which have been subjected to hydration than by micro-organisms or by the chemical intoxicants causing the hydration in the first instance. Neither hydration nor dehydration occur alone. Both exist side by side, for while some of the protein particles are being sent into true solution, others increase in size.

Nevertheless it is the hydrated protein particles which do the most damage to the cells of an organ, because they subject the protein particles constituting the protoplasm of the cells to dehydration. When dehydration occurs first the neuronic activity is increased, but later, as the protein particles go into true solution, degeneration of the cell occurs and the clinical picture presented is one of paralysis.

Dehydrated protein particles, when acting upon the protein particles constituting the protoplasm of cells, cause first hydration and then inflammation, consequently when dehydration synchronises exactly with hydration neuronic activity comes to a standstill and sleep is the result.

Generally speaking, a concomitant dehydration and hydration takes place in the veins and causes venous congestion. Should both the chemico-physical changes of dehydration and hydration take place to excess, hypnosis, narcosis and anæsthesia are produced. When the hydration exceeds the dehydration the hydrated protein particles tend to collect in the peri-capillary lymphatics and capillaries and finally in the arterioles and arteries. This gives rise to excessive neuronic activity, then paralysis, and finally fatal cerebral shock. The clinical conditions produced include neurasthenia, insanity, *Petit mal*, epilepsy, migraine, narcolepsy, eclampsia, tetany, spasmophilia, cerebral shock, as evidenced by diabetic and "uræmic" coma, etc., etc.

Another danger of excessive hydration is hæmorrhage, because hydrated protein particles lower the blood-pressures, dilate the blood-vessels and increase the permeability of their walls, particularly if they have suffered any fibrosis. Acute hydration is very liable to lead to hæmorrhage as evidenced by the *Encephalitis hæmorrhagica* occurring after the first or second dose of arseno-benzene. Chronic dehydration leads particularly to vascular changes and causes first hyperplastic sclerosis and then arterio-sclerosis. These vascular changes tend to result in cellular degeneration, not necessarily due to the vascular changes themselves, but rather to the cyclical change of hydration the protein particles undergo, a change which results in the hydrated protein particles becoming arrested in the damaged vessel. It is in this way that hæmorrhage occurs in hyperpiesia and arterio-sclerosis and that such conditions as *Paralysis agitans*, senile encephalomalacia, locomotor ataxia, amyotrophic lateral sclerosis, Erb's syphilitic spinal paralysis and all cases of chronic anterior polio-myelitis arise.

Hydrated protein particles cause first excitation and then degeneration of the parenchymatous cells, while dehydrated protein particles cause first hypertrophy and then atrophy of the mesenchymatous tissue. Both the

excitation and the hypertrophy are really degenerative changes. Although special areas of the brain may be selected for attack, it may be taken for granted that in every case the brain as a whole is involved. This being the case, it is unnecessary and, indeed, a mistake to talk of neurasthenia and insanity as being lesions of the cerebral cortex, migraine as a lesion of the optic thalamus, epilepsy as a lesion of the mid-brain, and narcolepsy as a lesion of the infundibular region, *Paralysis agitans* as a lesion of the *Substantia nigra*, etc. The clinical conditions referred to are but manifestations of a familial chronic intestinal intoxication, and all are due to the chemico-physical changes to which the protein particles in the plasma are subjected. Consequently, it is futile to expect that any nerve lesion can be benefited by drugs alone, and quite wrong to talk of such drugs as if they influenced the nerve cells directly.

Unless familial disease is prevented, people must become more and more physically and mentally mal-co-ordinated and the increasing demand for mental homes and lunatic asylums, where little or no effort is made to palliate the patient's condition or to find out its fundamental cause, will be ever growing.

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CHAPTER III

CHRONIC INTESTINAL INTOXICATION

Introduction

ALTHOUGH many observers have been struck by the great importance played by chronic intestinal intoxication in disease, few have realised the fact that it is a symptom of congenital disease. It cannot be re-iterated too often, that a chronic intestinal intoxication is present before the patient is born, and that its rôle as a producer of disease is enhanced by faulty feeding and insufficient elimination of the waste products of food after birth.

Disease attacks the intestinal tract from the mouth to the anus *in utero*, mainly through stimulation of the vagus centre occasioned by the precipitation in that area of hydrated protein particles of parental origin. The damage sustained is kept up after birth, and aggravated by the precipitation of hydrated protein particles in the lymphatic vessels and capillaries of the intestinal tract.

Stimulation of the vagus centre causes muscular contraction, terminating mostly in hypertrophy, but occasionally in atrophy, of the walls of the intestine. Local stimulation of the nerve endings of the vagus in Auerbach's plexus causes first muscular contraction and then inflammation. Muscular contraction followed by hypertrophy may result in œsophageal spasm, hypertrophy of the pylorus, intussusception and ileo-cæcal spasm. When followed by atrophy, dilatation of the gut occurs causing such conditions as megalo-colon, duodenal diverticulosis, etc.

Muscular contraction followed by inflammation affects, not only all the coats of the gut, but also its contents and the tissues around. Inflammation results first in hypertrophy and then in atrophy. The layer of the gut which evidences hypertrophy most is the innermost layer, the mucous membrane. The hypertrophied cells are rapidly cast off and form what is known as "mucus." Hypertrophy may be followed by destruction, in which case ulcers are produced, or by atrophy. Although micro-organisms within the gut may play a part in the causation of ulcers, it is generally only a secondary one, because the ulcers are primarily caused by the abnormal chemico-physical changes the protein particles undergo in the vessels of the area affected.

So far as the other layers of the gut are concerned, the results of atrophy, following inflammation, predominate over those of hypertrophy, and thinning of the wall of the gut is a prominent feature. This results in dilatation and diverticulosis and, in the case of the colon, the haustration vanishes, allowing the gut to lengthen, and a redundant loop to form.

Inflammation of the structures around leads most frequently to an involvement of the mesentery, which becomes thickened and contracted. This interferes seriously with the blood-supply to the gut and adds to the mischief already produced.

Inflammation of the walls of the intestines, and of the colon in particular, causes great changes to occur in the bacterial flora within. The most important of these changes would appear to be the mutation of the normal *Bacillus coli communis* into abnormal and mostly non-lactose fermenting micro-organisms.

This is just a brief sketch of the sequence of events as they occur in familial chronic intestinal intoxication, and each is dealt with in more detail in the section to which it belongs. The first section of this chapter deals with the mouth, where the point is stressed that dental sepsis is the result of, and is not caused by, a chronic intestinal intoxication. Neither micro-organisms nor toxins reach the intestines from the mouth to cause trouble in the former, and there is no appearance of the tongue definitely diagnostic of sprue, pernicious anæmia, etc. Indeed, there is no such distinct clinical condition as sprue, it being merely an acute exacerbation of a chronic intestinal intoxication. Pernicious anæmia is only the end stage of a similar sequence of events, and there are no hard and fast lines of demarcation between this form of anæmia and aplastic Addison's anæmia, or the milder, and therefore nameless, varieties of anæmia. Attention is paid to aphthous stomatitis because its origin is never local, which fact explains why local treatment more often aggravates than benefits the condition.

The next section deals with the nose and throat, and it is shown that a chronic nasal catarrh is the most frequent manifestation of a chronic intestinal intoxication. This fact explains why one nasal operation often leads to several, and seldom benefits the individual. The removal of nasal sepsis may cause the disappearance of a clinical symptom, as may removal of septic teeth and tonsils, but the effect is temporary only, because dental, nasal, and tonsillar sepsis are caused by, and are not causes of, a chronic intestinal intoxication. The rôle played by tonsillar infection in disease is considered in some detail because of the part it is thought to play in acute rheumatism and cervical lymphadenitis.

The third section deals with the alimentary canal from the œsophagus to the anus, and with the organs which originated therefrom. Owing to the large size of this section, a division into three sub-sections is necessary. The division is regulated by the blood-supply and not by the part of the tract involved. This is because more lesions are produced by changes the protein particles in the plasma undergo than by infections from within the gut.

The first sub-division is called the "cœliac," and it includes the cardiac end of the œsophagus, the stomach, first part of the duodenum, the liver, spleen and pancreas.

The second sub-division is called the "superior mesenteric," and includes the whole of the small intestine, and the first part of the large intestine.

The third sub-division is called the "inferior mesenteric," and includes the remainder of the large intestine, rectum and anus.

This sub-division was suggested by the study of what the author has termed the "splanchnic" or "portal" form of shock. Shock is the clinical manifestation *κατ' ἐξοχήν* of protein hydration. Most of the lesions discussed in this section are caused by the hydrated protein particles in the plasma, and although precipitation may be general, it tends more often to be localised to one of the three sub-divisions. The part of the œsophagus involved is most commonly the lower end, the lesion most frequently encountered is spasm, and although this may be of central origin, due to precipitation of hydrated protein particles in the vagus centre, it is more frequently due to local precipitation.

Precipitation of hydrated protein particles in the vagus centre causes hypertrophic stenosis of the pylorus, but here again a similar condition may be caused by local precipitation. Precipitation of hydrated particles almost anywhere in the portal area may give rise to vomiting, and vomiting by no means implies a lesion of the stomach.

Local precipitation of hydrated protein particles in the walls of the stomach causes first hyper-activity of the lining cells and later hypo-activity. Hyperchlorhydria is a result of the former and achlorhydria of the latter; otherwise these two states have no special significance, achlorhydria being in no sense a cause of the severe anæmias, as some observers hold.

Ulceration both of the stomach and duodenum is due entirely to the abnormal chemico-physical changes the protein particles in the plasma undergo in the vessels of the area involved. Indeed, it was the not infrequent occurrence of duodenal ulcer in cases of shock which led the author to make this

sub-division. A further study of shock shows that the liver and spleen are involved more frequently, and are attacked more severely, than the other organs in the abdomen, and it is interesting to note that these are the two organs most frequently implicated in so-called "gastric disease."

In a milder form of shock, or what amounts really to intoxication, enteritis may be the most pronounced lesion, and it is interesting to observe that, in the most severe infections of the alimentary canal, the small intestine bears the brunt of the attack. Even in this case, should an organ be attacked, it is most frequently the liver and particularly the gall-bladder, as evidenced by amœbic abscess and typhoid cholecystitis.

So closely allied are the toxic and bacterial forms of enteritis, and so similar are the pathological changes produced as to suggest that, possibly, some of the infections reach the small intestine by the blood-stream, and not by the mouth. In the milder forms of protein hydration, colitis is more frequently encountered than enteritis, and when the colonic infections are considered, it is found that they are occasioned by micro-organisms less pathogenic than those which produce enteritis.

As it would appear that most of the pathogenic micro-organisms in the colon are probably mutation forms of the *Bacillus coli communis*, quite a new vista is opened regarding the origin of the dysentery, typhoid and paratyphoid bacilli.

Light is thrown upon certain problems in connection with food-poisoning which are at present enigmata.

Chronic hydration is much more frequently encountered in disease than acute hydration, hence it is not surprising to find that chronic colitis is ubiquitous. In fact, it might almost be said that acute hydration does not occur in the absence of a chronic colitis. As so many of the lesions mentioned can be prevented by ridding the patient of his colitis, and, as thorough washing out of the colon as far back as the ileo-cæcal valve plays a large part in this treatment, a detailed account is given of the method employed. A few remarks are made concerning the origin and treatment of piles. The fourth section deals with the kidneys which, not belonging to the portal system, do not come under the previous section. Although the kidneys may be attacked in cases of shock, there is not the same relationship existing between the kidneys and the alimentary tract as exists between the liver, spleen or pancreas and the intestines. When the kidneys are attacked, they are usually singled out; if they are damaged in celiac hydration the hydration must be particularly severe. In superior mesenteric hydration, it is rather the tissue around the kidneys

than the organs themselves that are damaged, and the most common lesion is peri-nephritic abscess in para-typhoid entero-colitis. Although the kidneys may suffer damage in chronic colitis, it is more usual for the latter condition to so lower the resistance of the patient as to enable the *Bacillus coli communis* to multiply in the pelves, ureters and bladder, than for the offending micro-organism (non-lactose fermenter) to reach the uro-genital tract. In these cases of pyelitis, which seem to be increasing in number and severity, the *Bacillus coli communis* is at first no more than a harmless saprophyte. It is only by its long continued activity that actual inflammation is produced, and then there is grave danger of a coccogenic infection becoming superadded. Once this occurs the renal tissue becomes liable to be riddled with miliary abscesses.

The Mouth

In congenital disease there is invariably some defect in the mouth. The palate tends to be high arched, and the jaws to be squeezed laterally. The latter causes the teeth, in the lower jaw particularly, to present a convexity inwards and a concavity outwards. One or more teeth may be missing, the molars tend to be more tuberculated than normal, the teeth may be wholly or partly devoid of enamel; micro-dentism, with intervening spaces, is not uncommon, and dental decay is practically a constant feature. The dental decay is never the cause of trouble in the intestinal tract, and it plays no more than the rôle of a precipitant in certain infections. This fact renders total removal of the teeth for rheumatism, for example, a criminal procedure. Even the removal of definitely septic teeth, which is desirable, does no more than cause a temporary alleviation of the patient's symptoms. Gingivitis, which is independent of dental caries, is characterised by a hypertrophy of the mucous membrane showing itself as prominent white folds behind the incisors and canine teeth in the upper jaw. This form of gingivitis is a sign that the protein particles in the plasma are in a state of chronic hydration, a condition which frequently gives rise to the statement that "the blood is too acid." Metallic intoxication is particularly prone to aggravate, and even to cause, a gingivitis, and, should the condition be so severe as to result in ulcer formation, the ulcers almost always make their first appearance behind the last molar teeth of the lower jaw. As the condition proceeds, hypertrophy gives place to atrophy, and the gums recede. The free margin forms a straight line, which is most noticeable along the incisor teeth of the lower jaw. Should the intoxica-

tion be of sufficient severity to occasion a local state of anaerobiosis, Vincent's micro-organisms are liable to gain a foothold, and cause anything from an angina to a noma. The greatest care needs to be taken in handling these conditions ; the simplest and mildest lotions should be used locally ; no more than three injections of arseno-benzene, at the most, should be prescribed ; and the main effort should be directed to improving the intestinal condition. Buccal lesions of this nature are very liable to occur in acute intestinal conditions, and no article of diet is so likely to hasten their progress as milk. If milk were forbidden in a sick room, and its place taken by fruit juice, the mortality from acute infections would be reduced.

In bad cases of congenital disease, the tongue is fissured from birth, and in every case it is more or less coated. In a few cases the papillæ are red and hypertrophied, and, when the latter condition affects the foliate papillæ, the patient is caused considerable annoyance by the rubbing of the painful areas against the teeth. In still fewer cases areas are found denuded of papillæ ; or leucoplakia may occur, this being nothing more or less than a keratinisation and cornification of the mucous membrane. The condition is not caused solely by syphilis as is commonly thought. Definite buccal leucoplakia can occur as a result of a chronic intestinal intoxication. Hutchinsonian teeth can occur, in the absence of syphilis, as a result of inherited disease, and even in syphilis they are more the result of the protein hydration than of the local action of the parasite. *Herpes oris* is one of the most common buccal lesions. It does not differ from *Herpes febrilis* and *Herpes preputialis*. The exact cause is not known, and there seems every reason to suppose that the precipitants may be manifold. Against a micro-organism being the ætiological factor is the fact that a lesion may present itself within a few hours of the precipitant commencing its work. The author is most inclined to take the view that *Herpes oris* is of the host's own making, a lesion resulting from an abnormal chemico-physical change the protein particles in the plasma undergo, such as the formation of sub-particulate or ultra-microscopic forms from particles already hydrated. The vesicles may become ulcers (when they receive the name of "aphthous"), a true stomatitis may be set up and, should anaerobic conditions prevail, a Vincent's infection is prone to supervene. In this way a simple *Herpes oris* may end in a fatal noma. The author is of the opinion that *Herpes oris* is closely allied to acute ulceration of the vulva, *Dermatitis herpetiformis* and *Pemphigus vulgaris*, and that the actual lesion arises in the same way as do the vesicle and bulla in the halogen eruptions.

The Nose, Throat and Ears

If asked to state the most common clinical manifestation of congenital disease, the author would unhesitatingly name "nasal catarrh." As all forms of nasal catarrh are secondary to some other condition, it is not surprising that no cure has been found for a common cold and that one surgical operation is only a prelude to several. The common cold is not caught from another person as is usually thought. It is merely an acute exacerbation of a more or less chronic condition, the acute stage being caused by a further lowering of the victim's general resistance, which was lowered in the first instance by a chronic intestinal intoxication. It is possible for a cold to start, following contact with an individual already a victim, but the cold is caused, not by the micro-organisms passing from A to B, but by these micro-organisms, and the environment, lowering the local and general resistance of B, thereby enabling B's dormant micro-organisms to become active. This explains why the same micro-organisms are not found in the nasal secretions from the affected members of a household and why a heterogeneous vaccine is valueless. Even an auto-genous vaccine is little better, a fact which lends support to the view that nasal catarrh is secondary to a chronic intestinal intoxication. In still further support of this view is the fact that the only reliable method of preventing a nasal catarrh either acute or chronic, is by neglecting the nose and relieving the intestinal condition. The immediate cause of the common cold is the increase in the pathogenicity of one or more of the prevailing pathogenic micro-organisms in the excreta. If a weekly bacteriological examination of a patient's excreta is made a sudden appearance or increase in the percentage of one or more of the pathogenic micro-organisms will be found to precede a cold. Washings made from the micro-organism in question, which is usually the *Bacillus Friedländer* and injected into the patient causes a temporary aggravation of the clinical condition for a day and the disappearance of the cold the following day. Only one injection is necessary, and it causes the pathogenic micro-organism to vanish from the excreta. The most satisfactory method of alleviating a cold is to inject Sup. 36 (0.01 grani.) intra-muscularly, on one or two days in succession, within forty-eight hours of the onset of the trouble. Sup. 36 may be taken internally in homœopathic doses every two hours for six doses. If prescribed in this way on the first or second day of the cold, the results are good, but if later the condition may be aggravated. The 30 C. potency seems to be the best, and it should be taken by "plussing" as follows. Three drops of the potentised product are placed in an ounce of water and well shaken, then two

ounces of water are added, well shaken and taken internally, leaving one ounce behind. The one ounce is made up to three ounces each time, so that every two ounces taken at each dose results in the patient receiving a different potency.

Another form of acute nasal catarrh is hay-fever, a condition which may be alleviated by Sup. 36, calcium and strontium aspartate, etc., and prevented by removal of the chronic intestinal intoxication. Hay-fever is not limited to the young. It may attack the old as well, and may make its first appearance at any age. Although more common in the summer, is not limited to this season, occurring as it does sometimes in the winter. Hay-fever is particularly liable to pass into asthma, but, owing to the importance attaching to the latter because of its increasing frequency, the condition is dealt with fully in the next volume. Below are reported four cases of hay-fever, in all of which the condition cleared up after treatment for the chronic intestinal intoxication.

Case 107

A woman, aged twenty, had suffered from chronic nasal catarrh and hay-fever for many years. The patient had croup and *Lichen urticatus* as a child and had recently begun to suffer from migraine. Her tonsils, adenoids and septic teeth had been removed without benefiting the condition. Various nasal operations had been performed to no purpose, and a vaccine prepared from the micro-organisms found in the nasal secretion proved useless. She exhibited all the signs of familial chronic intestinal intoxication; there was a family history of oto-sclerosis, and one of the patient's brothers suffered from manic depressive psychosis. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (90 per cent.) and an examination of the blood revealed the following:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.086 grm.
Percentage of the blood-urea	= 36 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving with some refractile giant particles, ringed particles and clumps. There were some giant particles, ringed particles and clumps precipitated with one or two agglutinations. The Brownian movements of the particles were sluggish, and there was a tendency for the particles to precipitate <i>en masse</i> .

The patient was dieted, she had a course of colonic lavage, and was given intra-muscular injections of para-thor-mone, and of the fæcal vaccine. Five injections a week, for four weeks, of para-thor-mone in fifteen unit doses were made and, when the colonic lavage was completed, the fæcal vaccine was injected in half million doses on two days in succession. Two further injections of the vaccine were made in half and one million doses on two days in succession, three months later.

Case 108

A woman, aged forty-three, had suffered from hay-fever, without intermission, every summer for eighteen years. Occasionally it was accompanied by asthma. The patient was mentally unstable. She had suffered from migraine, and had had many attacks of lumbago; as a child she had *Lichen urticatus*. For the past three years she had suffered from dysidrosis. She was a typical example of familial chronic intestinal intoxication and had one daughter who suffered severely from chilblains, winter and summer alike. Both mother and daughter had been operated upon for appendicitis; both started to menstruate late (age sixteen), and both at first had amenorrhœa and dysmenorrhœa. The pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici* (20 per cent.) and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3480.
Percentage of the blood-sugar	= 0·086 grm.
Percentage of the blood-urea	= 15 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a high percentage of giant particles, ringed particles and clumps. There were many large and refractile giant particles, ringed particles and clumps precipitated.

Sup. 36 stopped the hay-fever at once. The patient was dieted, she had a course of colonic lavage and had three sets of two vaccines made every three months and injected in doses of a half and one million respectively on two days in succession.

Case 109

A man, aged fifty-one, had suffered from chronic nasal catarrh and hay-fever for thirty odd years. The patient's father, a chronic asthmatic, died of pneumonia, aged forty-four, and his mother of intestinal obstruction, aged

sixty-four. He lost a sister, aged two, from convulsions, and one, aged seven, from diabetes. There was a sister living who suffered from asthma. His three children were all martyrs to hay-fever. The patient had had several attacks of migraine, lumbago and gout. He had had severe *Acne vulgaris*, pneumonia three times, and with the last attack an empyema. He presented the cardinal signs of familiar chronic intestinal intoxication, and had had his teeth, tonsils and appendix removed, in addition to having had several operations upon his nose without benefit. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (15 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1·7 c.c.
Refractive index of the serum	= 1·3482.
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some ringed particles and giant-particled clumps. There were many giant particles, ringed particles and clumps precipitated.

The patient was dieted, had a course of colonic lavage, twelve injections of Sup. 468 in 0·002 grm. doses, and two injections of the fæcal vaccine in half and one million doses respectively on two days in succession.

Case 110

A man, aged seventy, had suffered from hay-fever every May to July since the age of sixteen. His paternal grandfather and his father had suffered from hay-fever, his brother, living, was also a victim, and all the male members of the family had or had had a bilateral Dupuytren's contraction. The patient had suffered from chronic indigestion and constipation all his life and had had attacks of lumbago and sciatica. He had miotic pupils which reacted neither to light nor to accommodation. The optic fundi showed arterio-sclerotic changes, there was evidence of generalised arterio-sclerosis, the deep reflexes were sluggish, the pulse was 78 and arrhythmic, and the blood-pressures registered 160 and 90 mm. of Hg. respectively. The left colon was contracted, the ascending colon and cæcum were dilated. The urine gave a reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and contained some protein. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (30 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.4 c.c.
Refractive index of the serum	= 1.3504.
Percentage of the blood-sugar	= 0.175 grm.
Percentage of the blood-urea	= 19 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, mainly in the form of giant particles with satellitic particles moving rapidly around them. There were about the same number of particles precipitated.

The patient cut out butcher's meat, eggs and milk from his diet, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and had injections of contramine and of the faecal vaccine.

A condition midway between an acute and chronic nasal catarrh is what is known as "vasomotor rhinorrhœa." It is characterised by a profuse nasal discharge which tends to be worse at night-time when the patient is asleep. The author has known cases where the nightdress and pillow have been soaked night after night. The condition is liable, in course of time, to develop into purulent rhinorrhœa or into vasomotor bronchorrhœa. The prefix "vasomotor" is unfortunate as the discharge is no way dependent upon the activity of the vasomotor system. Below are detailed some interesting cases of this condition and, in all, the trouble vanished when the chronic intestinal intoxication had been dealt with.

Case 111

A woman, aged fifty-one, had suffered from purulent rhinorrhœa and bronchorrhœa for many years, and had had the septum, both antra, and both frontal sinuses opened, but without relief. She had had several operations on the neck for adenitis, which was considered to be caused by the tubercle bacillus. An adenoma had been removed from the thyroid and the patient had been operated upon for appendicitis. She looked old for her years, and had begun to go grey at eighteen. She had a high degree of hypermetropic astigmatism, hyper-extended elbows and fingers, and acro-asphyxia. The tongue was furred, an ophthalmoscopic examination revealed arteriosclerotic fundi, the pulse was 100, and the blood-pressures registered 130 and 70 mm. of Hg. respectively. There was marked tenderness over the sigmoid, the splenic flexure, hepatic flexure and ileo-cæcal area, and there had been several attacks of mucous colitis. The pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici* (25 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.3 c.c.
Refractive index of the serum	= 1.3504.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 13 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and they were mostly giant particles and ringed particles. There were a few giant particles and ringed particles with one or two giant-particled clumps precipitated. The Brownian movements were sluggish.

The patient was dieted, had a course of colonic lavage, took iodine, thio-amino-methyl-glyoxaline and thyroid internally, and had injections of contramine, followed by Sup. 36, and the faecal vaccine.

Case 112

A man, aged fifty, sought advice for incessant purulent rhinorrhœa which had been present for nine months. The patient had suffered from rhinorrhœa since youth, and for many years this had developed into hay-fever and asthma during the summer. The discharge became purulent following an attack of influenza. His father died of apoplexy, aged sixty-six, and his mother of cancer, aged sixty-five. One sister, aged fifty-five, was dying of cancer of the womb. He used to suffer from chilblains, had had a long bout of furunculosis, and from December, 1910, to July, 1911, was confined to bed with intermittent pyrexia. He had been bald since the age of twenty-four, he could not stand with his knees and feet together, all his teeth had been removed, and he had had several nasal operations without benefit. He had wide-angled elbows, acro-asphyxia, ridged nails, and venous congestion of the fundi. The pulse was 72, and the blood-pressures registered 105 and 80 mm. of Hg. respectively. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and an examination of the abdomen revealed definite evidence of chronic colitis. Syphilis had been contracted twenty-six years previously. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (30 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 1.6 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 22 mgrm.

Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles and ringed particles. There were some giant particles and giant-particled clumps precipitated. The Brownian movements of the particles were sluggish.
Wassermann reaction	= Negative.

The patient was dieted; he had a course of colonic lavage, twelve intramuscular injections of Sup. 468, each of 0.002 grm., every other day, and then two injections of the faecal vaccine, in doses of a half and one million respectively, on two days in succession.

The purulent discharge was incessant day and night. During the day, the patient had to use several handkerchiefs, and every night the pillow-case had to be protected with jaconet and a towel.

Case 113

A man, aged fifty-four, had suffered from profuse mucous rhinorrhœa over fifteen years, and for the past three years this had developed into bronchorrhœa and asthma. His father died of phthisis, aged fifty-six, and his mother of *Morbus cordis* following rheumatic fever, aged forty-four. Three sisters had succumbed to phthisis, aged forty, twenty-six and twenty-three respectively. The patient had suffered much from rheumatism, and had had syphilis twenty years previously. He was nearly bald, the ears stood out, all the teeth had been removed and several nasal operations had been performed without giving relief. The nails were very ridged, the deep reflexes were absent, and there was generalised arterio-sclerosis which was confirmed by an ophthalmoscopic examination. The pulse was 72 and the blood-pressures registered 105 and 70 mm. of Hg. respectively. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, the left colon was contracted and tender, and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the bacillus of epidemic jaundice (50 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3502.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 25 mgrm.

- Ultra-microscopic picture of the serum = Fair number of particles moving with a fair percentage of very refractile giant particles, ringed particles and small giant-particled clumps. There were some giant particles, ringed particles and small giant-particled clumps precipitated.
- Wassermann reaction = Negative.

The patient cut out butcher's meat, eggs and milk from his diet, he had his colon washed out, took iodine, ichthyol and thyroid internally, had six injections of contramine, each of 0.125 gm., every fifth day, and four injections of the vaccine, with three months' interval between each set of two (1 and 2 million on two successive days).

The nasal discharge in this case was most profuse, and since the onset of the bronchorrhœa the patient had been accustomed to cough up over half a pint of mucus a day.

Before inquiring into the rôle played by tonsillar sepsis in disease it is as well to give an explanation of the frequency with which these glands become septic.

Prior to the tonsils becoming septic they undergo enlargement, and this enlargement is part of the general hypertrophy lymphoid tissue undergoes in congenital disease following hydration of the protein particles in the plasma. This explains why children, whose protein particles are markedly hydrated, have adenoids, cervical adenitis and a persistent thymus, and why any factor accentuating the hydration may precipitate shock, which goes by the name of *Status lymphaticus*. When the hydration is acute, so-called "glandular fever" may result, but it is wrong to regard this as a specific infection. The hydrated protein particles behave in part as foreign bodies, and call forth response on the part of the host, which results in the production of lymphocytes by the endothelial cells of the lymphatic vessels in the organs specially designed for this purpose. In course of time the hypertrophied tissue acquires a lowered resistance and becomes a prey to micro-organisms ordinarily saprophytic, which develop more and more pathogenic properties the more luxuriantly they are able to grow. But the luxuriance of their growth is not solely, or even mainly, dependent upon the conditions existing in the tonsils. It is primarily dependent upon the patient's general resistance which is regulated, in the main, by the conditions existing in the large intestine.

The proof of this contention lies in the facts that removal of the tonsils, when they are enlarged, does not prevent the micro-organisms ordinarily

saprophytic becoming pathogenic and giving rise to symptoms of disease, and, that removal of septic tonsils, when symptoms are present, seldom benefits the condition. It may, indeed, aggravate it, and at the best is no more than palliative.

If septic tonsils need enucleation the operation should be done when the symptoms of disease are quiescent. The best rule to make is not to remove any septic focus which is likely either to augment an existing trouble, or to cause a more serious one, until the patient's resistance has been raised by dealing with the chronic intestinal intoxication.

The saprophytic micro-organisms most likely to develop pathogenic properties in the tonsils are the streptococci, but, contrary to what is generally thought, these streptococci do not develop characteristics which allow them to be separated from other streptococci.

The differences between the various streptococci are occasioned more by the host than by the micro-organisms themselves. This point needs further elaboration. A micro-organism in the blood-stream may grow with, or at the expense of, the protein particles in the plasma. In the first instance it is saprophytic, in the second, pathogenic. Although it may be the same micro-organism in both cases, the chemico-physical properties in one differ materially from those in the other, as do the host's own protein particles. Provided the resistance of the patient is lowered sufficiently, streptococci may enter the blood-stream *via* the tonsils to give rise to such conditions as acute rheumatism, scarlet fever, angina, *Otitis media*, cervical lymphadenitis, etc. But some of these conditions may arise from the mere changes the protein particles in the plasma undergo as the result of an acute exacerbation of the intestinal trouble.

For example, acute rheumatism may arise in this way with exactly the same signs and symptoms as occur when micro-organisms invade the blood-stream. Acute rheumatism is not a specific infection, hence the reason why it is so liable to recur, either in the same form, or in a different and more chronic form. More than one member of the family may be affected; cardiac lesions are common and may occur even in the absence of any signs of rheumatism. The carditis is not specific, because it may also result from the collection of hydrated protein particles in the heart muscle, in the same way as does chorea, when the hydrated protein particles are precipitated in the region of the *Corpus Luysii*.

It is not strictly correct to regard scarlet fever as a specific infective fever because, in the same family, one member may develop scarlet fever and another rheumatic fever,* and, because there are many varieties which are not classified under this head. There are many acute and sub-acute streptococcal infections

* A patient may develop scarlet fever first and rheumatic fever later and *vice versa*.

where it is impossible to be sure whether they are, or are not, cases of scarlet fever and, as the nature of infections varies from year to year, it can be understood how scarlet fever can be prevalent one year and absent another. It is quite true that scarlet fever can be spread from person to person, but this happens in other infections which are certainly not specific—so-called “influenza,” “food-poisoning infections,” for example. When a saprophytic micro-organism develops pathogenic properties in an individual, severe enough to give rise to a more or less definite clinical picture, its pathogenicity can be conveyed to others, who either remain unaffected, or become carriers, or develop the clinical syndrome, according to their powers of resistance. In other words, many of the so-called infective fevers are conveyed from person to person by micro-organisms being able to develop particularly pathogenic properties in an individual with a very low resistance, and these properties enabling them to develop the same clinical condition in other individuals whose resistance is below par.

If the individual responsible for the micro-organisms becoming pathogenic in the first instance could be segregated, there would be less risk of infection spreading, but in most cases the damage is done before the condition is recognised. Segregation later is practically useless, and trying to quarantine carriers is hopeless.

The goal to aim at is to increase the resistance of those not infected and, if this is brought above par, the micro-organisms soon lose their pathogenicity. In all bacterial invasions the fight between the invader and the invaded is merely one for electrical supremacy.* Either the micro-organisms give up electrons to the host's protein particles and vanish, or they acquire electrons from the protein particles and multiply to cause an infection. Enable the host, by increasing the body's resistance, to be the acceptor, and not the donor of electrons and an infection would never occur.

In scarlet fever the kidneys may be attacked, as is the heart in rheumatic fever, and nephritis may occur in the absence of a rash and other signs and symptoms considered to be diagnostic of scarlet fever.

It is quite possible that a form of streptococcus is responsible for measles, because measles and scarlet fever share to some extent the honour of being the more fell infection in turn. A form of *Encephalitis lethargica* follows measles, but rarely scarlet fever, and as there are reasons for suggesting that

* It would be more accurate to replace the word “electrical” by the word “activity.” Activity is something smaller than an electron, a wave upon the characters of which resistance of the host and pathogenicity of the invader depend.

this infection is occasioned by ultra-microscopic particles of a known micro-organism, it is tempting to hazard the opinion that the ætiological factor in measles is a form of streptococcus midway between the known and the particulate form. The growth of streptococci in the tonsils seems to stimulate the growth of diphtheroids in the same site later, and as diphtheria is an infection particularly liable to follow in the wake of scarlet fever, it is possible that the previous activity of streptococci is able to cause harmless diphtheroids to become dangerous diphtheria bacilli. The future might even show that diphtheroids and diphtheria bacilli are bacillary forms of streptococci. Unfortunately, all experiments carried out with micro-organisms *in vitro* tend towards differentiation as against correlation, and what is more unfortunate is the fact that they throw no light whatever upon their behaviour *in vivo*. While mutation in the body would appear to occur with the greatest ease, it cannot be effected in the laboratory. It is to be deplored that bacteriologists are not clinicians as well, because the behaviour of micro-organisms even in laboratory animals is not comparable to their behaviour in the human being.

If medical work was properly apportioned and practised in the simple way now made possible, every physician or group of physicians would have the time to do all their own ancillary work.

The form of angina referred to above is what is sometimes called "Ludwig's angina." It is a widespread infection of the tissues of the neck with streptococci, and is apt to be dangerous, either because of spread into the thorax or because of an involvement of the veins. Once septic venous thrombosis occurs life is seldom saved, because of the rapidity with which septic emboli are carried to the various organs of the body. Pyæmia is undoubtedly the worst form an infection can take, and this is well illustrated by the following case.

Case 114

A woman, aged twenty, had an acute sore throat with fever, April 13th. The temperature rose to 105° F. every night, falling to below normal the following morning. Four days later the whole of the left side of the neck was painful, and both the internal and external jugular veins were thrombosed. Within a week of the onset of the infection septic infarcts had found their way into the lungs, spleen and kidneys. Pericarditis and endocarditis developed May 2nd, and, in spite of all kinds of treatment—Sup. 36, Sum. 468, mercurochrome, anti-streptococcic and anti-scarlet fever serum—the patient died May 15th. She had had scarlet fever and repeated attacks of tonsillitis. She had also had several attacks of bronchitis as a child, and always suffered

from chilblains and chronic nasal catarrh. The excreta contained much mucus, some blood, and large quantities of non-lactose fermenting micro-organisms, which unfortunately were not defined. Blood-examinations made May 2nd were as follows :—

Suspension stability of the red blood-corpuscles	= 3.0 c.c.
Refractive index of the serum	= 1.3469.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 62 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and amongst them were some giant particles with a halo around each. There was a fair amount of precipitation <i>en masse</i> .

The blood was thin and the serum was pale.

The blood-culture was sterile :—

White blood corpuscles	= 6,500 per c.mm.
Hæmoglobin	= 60 per cent.
Polymorphonuclear leucocytes	= 89 „
Lymphocytes	= 9 „
Large mononuclear leucocytes	= 2 „

A study of the blood-picture in these acute cases is always of considerable interest and the above is no exception to the rule. The reduction in the suspension stability of the red blood-corpuscles and the fall in the refractive index are not as great as might have been expected, showing that there was no true septicæmia and that considerable hydration was occurring as a cyclical change to the dehydration. This is confirmed by the ultra-microscopic picture. The rise in the percentage of the blood-urea shows that active and severe dehydration was occurring as well.

Otitis media frequently shows itself at first as an acute tympanitis, and if, in such cases, the drum was trephined, and two injections of Sup. 36, each of 0.01 grm., given on two days in succession, the number of mastoid operations required would be reduced to a minimum. Cervical lymphadenitis is less frequently met with to-day than formerly. At the beginning of this century discussion was rife as to whether the swelling was of a lymphadenomatous nature or due to the invasion of the tubercle bacillus. Although no agreement was come to regarding the ætiology, all were of accord that the glands required removal, and many necks are seen to-day scarred from what was always an unnecessary operation. Many patients lived invalid lives for months and even years in

Margate, and in Switzerland, because a wrong diagnosis of tubercle had been made. The primary swelling is a mere hypertrophy of normal lymphatic gland tissue, in response to the congenital hydration of the protein particles in the plasma. The hypertrophy renders the tissue a *pars minoris resistentiæ*, enabling either streptococci or tubercle bacilli, or both, ordinarily saprophytic micro-organisms, to become pathogenic.

But, generally speaking, the acquired pathogenicity of these micro-organisms is so mild that, even when tubercle bacilli are found, the patient should not be labelled a victim of tuberculosis; because, when treatment aimed at removing the initial cause of the hydration is given, the tubercle bacilli vanish and the swellings disappear.

Needless to add, no operative procedure is required, except an occasional nick to let out pus from a suppurating area. The two cases reported below illustrate these points.

Case 115

A boy, aged eight, was brought to the author, suffering from cervical adenitis. Some of the lymphatic glands had broken down and in removed portions tubercle bacilli had been found. His father's neck was scarred from operations performed for cervical adenitis as a boy, and his younger brother, aged five, had been subjected to operations for the same condition.

The patient suffered from chilblains and hay-fever, and had recently been operated upon for a mastoid. The teeth were small, widely spaced, and evidenced signs of decay, the ears protruded and the elbows were wide-angled. The pulse was 92 and the blood-pressures registered 70 and 50 mm. of Hg. respectively. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The left colon was contracted and tender, the ascending colon and cæcum were dilated, and there was tenderness over the ileo-cæcal area. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (50 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3487.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 23 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with many giant particles and a few clumps. There were a few giant particles and clumps precipitated.

The boy was dieted, he took treacle internally first thing in the morning as an aperient, he had a series of treacle enemata, three injections of Sup. 36 and two courses of injections of the fæcal vaccine in doses of 0·25, 0·25, and 0·5 million on three days in succession with three months' interval between each course.

The cervical lesions vanished and the boy recovered from his hay-fever without having to be sent to the seaside.

Case 118

A boy, aged twelve, had suffered from cervical adenitis for some years and, when he sought advice, three glands were breaking down. The mother suffered from oto-sclerosis. The patient was the only child and an anæmic, undergrown boy. He had suffered from *Lichen urticatus* and cyclical vomiting, and was troubled with indigestion and constipation. The pulse was 104 and arrhythmic, and the blood-pressures registered 130 and 80 mm. of Hg. respectively. The left colon was markedly contracted and tender, the right colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the bacillus of epidemic jaundice, and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3494.
Percentage of the blood-sugar	= 0·143 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but all were very large and refractile. There were a few ringed particles moving. There were several giant particles and small clumps precipitated.

The boy was taken off butcher's meat, eggs and milk, he had a course of colonic lavage, took colloid ferromalt internally, and had injections of Sup 36 and of the fæcal vaccine.

The neck condition cleared up completely, the boy became healthy in every way and, eighteen months later, was able to undertake all the school duties as a boarder.

It is interesting to note, before leaving this subject, that children with tonsillitis and cervical lymph-adenitis are liable to attacks of hæmaturia. The passage of blood is of no real significance, and it is due to the glomerular membranes of the kidneys allowing red blood-corpuscles to pass through

because of the increased permeability resulting from the precipitation of hydrated protein particles in the renal peri-capillary lymphatic spaces.

The Alimentary Canal from the Œsophagus to the Anus

Although, as the result of inherited disease, the alimentary tract may be damaged in any part *in utero*, there are certain areas which are more commonly affected; those are the pylorus, ileo-cæcal region and the colon. Clinical manifestations may not arise for some considerable time after birth.

Damage to the colon looms largest in disease, because it is aggravated by many factors coming into play after birth, which do not affect the other parts of the alimentary canal.

As a chronic colitis is one of the main factors in the causation of disease, it comes to pass that many of the lesions affecting the stomach, duodenum, and small intestine are, in a large part, due to trouble occurring in the large intestine. Although hydration *in utero* may render a portion of the stomach, duodenum, small intestine, etc., *partes minoris resistentiæ*, the hydration usually needs to be augmented before a clinical manifestation is precipitated. In the majority of instances this augmentation is brought about by the entrance into the blood-stream of abnormal metabolites formed from food by the pathogenic non-lactose fermenting micro-organisms in the large intestine. Indeed, the hydration has to be particularly severe if it is to cause a gastric ulcer, a duodenal ulcer or an enteritis in the absence of a chronic intestinal intoxication. This explains why treatment aimed at cleaning the colon may prevent, and get rid of, such lesions as gastric ulcer, duodenal ulcer, enteritis, entero-colitis and appendicitis. As the intestinal lesions mentioned above are due in most instances to protein hydration, and as hydrated protein particles cause damage when they become arrested in the circulation, it follows that the lesions are influenced by the blood-supply. It was owing to this fact, as also to the fact that the splanchnic area is divisible into three great parts, and that precipitation tends to take place in the first, second and third parts according to the degree of the hydration existing, that the author was led to sub-divide this section into cœliac, superior mesenteric and inferior mesenteric respectively. In making this sub-division the reader must understand that it is done primarily to facilitate description, and that the whole of the alimentary tract from mouth to anus may be affected at one and the same time. Indeed, in very severe shock, in addition to the splanchnic area, the cerebral and pulmonary areas may be involved.

Attention was drawn, in the previous chapter, to the connection between

heat-stroke, a form of cerebral shock, and entero-colitis and colitis. In cases of heat-stroke pulmonary œdema may also occur, and in true cases of pulmonary shock, when the lips, tongue, pharynx, etc., swell, and the patient becomes asphyxiated, signs and symptoms of congestion of the liver and the intestinal tract may be present. In milder cases of shock it is not uncommon to find lesions extending along the whole length of the alimentary canal, headed by aphthous stomatitis, and tailed by an ischio-rectal abscess, anal fissure, etc. Sprue falls into this category, as does the so-called "œliac affection of children," which goes by the name of "Gee-Herter's disease." *Pellagra* may also be added to the list. Sprue can occur outside the tropics, and can affect children, and, likewise, the œliac affection is found in adults. Furthermore, certain types of spasmophilia, particularly the so-called "cyclical vomiting of children," link these various conditions together. Although both sprue and œliac disease are characterised by liporrhœa, neither is really a specific entero-colitis, and it is doubtful if the fungus *Monilia psilosis*, described by Kohlbrugge,²⁰ plays any rôle in the ætiology of the former. *Pellagra* can occur in this country, and only differs from its allied conditions in that the skin and central nervous system are attacked as well as the intestinal tract.

The relationship between a pulmonary lesion and an entero-colitis is a closer one than is often supposed. A definite infection of the lung may occur, but in most cases the trouble is due to a scattered œdema. The lesion produced by an infection is more often a broncho-pneumonia than a lobar pneumonia, and the causative micro-organism may be the same as the one responsible for the entero-colitis. The author has had cases where a bacteriological examination of the sputum showed the prevailing micro-organism to be the *Bacillus pyocyaneus*, *Bacillus Gärtner*, *Bacillus fecalis alkaligenes* or Friedländer's bacillus. The last-named bacterium is most probably a mutation form of the *Bacillus coli communis*, and is closely allied to if not the same micro-organism as that considered to be the cause of rhinoscleroma and ozœna. More often the sputum yields streptococci, but occasionally pneumococci prevail, and both are frequently found together.

In these cases the micro-organisms would appear to behave rather in a saprophytic than in a pathogenic capacity. This is because the primary lesion is an œdema, occasioned by the precipitation of hydrated protein in the pulmonary vessels. In the majority of the cases the œdema begins and is most marked at the bases, and in the author's experience the right lung is more frequently involved than the left. The œdema may spread from one area to another in a few hours; cough is not a troublesome symptom, and the

sputum is usually small in quantity until the pulmonary condition begins to resolve, when it may increase and become blood-stained. In some cases there is neither cough nor expectoration. Fever is a prominent sign, ordinary treatment is unavailing, and the death rate is high. The patient is usually more or less delirious, and always feels great exhaustion. The course run by the malady differs from an uncomplicated lobar pneumonia in that the pulmonary condition does not terminate by crisis. In a few cases the pulmonary signs and symptoms may vanish and yet a fatal issue occur, usually as a result of a toxic myocarditis. The fever may last several weeks ; there is nothing peculiar regarding the entero-colitis. The convalescence is slow, and the patient may suffer from depression, or some other manifestation of altered mental activity, for a long time afterwards.

There are two clinical forms of this associated pulmonary cedema and entero-colitis—the acute and the sub-acute. The acute cases either remain unnamed or are diagnosed as influenza, although some have recently received the name of “*Psittacosis*.” The sub-acute cases usually go unnamed unless they become acute, when they are diagnosed as influenza.

The cases are mostly labelled influenza because they occur when influenza epidemics are rife ; but what is influenza ? In the author's opinion, it is not a specific infection, but a febrile condition occurring in individuals whose resistance has been lowered by extraneous factors which allow certain micro-organisms in the intestinal tract to become more active than usual. The extraneous factors lowering the general resistance are, altered climatic conditions, physical and mental overstrain, the ingestion of toxic substances, and insufficient elimination of waste products.

The pathogenic micro-organisms in the intestinal tract are those commonly known as non-lactose fermenters, and most of these the author considers to be mutation forms of the non-pathogenic *Bacillus coli communis*. Although the term “non-lactose fermenter” is frequently employed it is not strictly accurate, because some of the pathogenic forms do ferment lactose. But these, and other points, are considered in more detail below. Suffice it to say here that these pathogenic micro-organisms become more active than usual when the patient's resistance is lowered.

As a result of civilisation, which has entailed an emigration from the land to towns, necessitated the importation of foreign foodstuffs and caused the inadequate elimination of the waste products accumulating in the large intestine, most people to-day have manufactured, and continue to harbour, one or more of the non-lactose fermenters.

These micro-organisms presumably act in a pathogenic fashion by breaking down articles of food, particularly animal protein, in an abnormal way. It has always been thought that toxic chemical compounds are formed, but it seems more reasonable to believe that it is merely a physical change affecting the metabolites which occurs, such, for example, as a difference in the linkage or in the electric charge of one or more of the groups in the proteins, proteoses polypeptides, etc.

These slightly altered metabolites reach the blood-stream where, instead of being absorbed by the protein particles in the plasma, they act as foreign bodies and subject the particles to the abnormal chemico-physical changes of dehydration and hydration which, in turn, give rise to disease. Once the protein particles become sufficiently hydrated to produce disease the activity of the non-lactose fermenters in the intestine is increased, and any factor which adds to the hydration augments the activity still more.

Although the author holds that the signs and symptoms of disease are produced by the host's own damaged protein particles, others maintain that the altered metabolites are the actual cause. Many facts can be arrayed against the latter view. In the first place, the toxic agent or "antigenic substance" as it is often called, is far in excess of any altered metabolite which may reach the blood-stream. In the second place, the amount of the toxic body can be increased to almost any extent by agents which have nothing whatever to do with the metabolic products of food. To give an example: if the protein particles in the plasma of an animal are subjected to a degree of hydration not sufficient to produce the signs and symptoms of shock, any agent capable of augmenting the hydration will precipitate the shock and cause an enormous increase in the amount of the toxic body. As fear may be the precipitant it is clear that the toxic body must be of the host's own making. Still other observers hold that it emanates from the liver, but this cannot be the case, because it is not in every instance of shock that the liver is the organ most damaged. In some cases of shock the brain bears the brunt of the attack, in others the lungs, and in all cases the changes in the parenchymatous cells of the organ attacked are secondary to the changes to which the protein particles in the plasma have undergone. When protein particles are subjected to abnormal chemico-physical changes they act as foreign bodies to the other protein particles and find their way into the urine. The urinary proteoses, to which Oriel and Barber¹ have recently drawn attention, are not true antigenic substances but merely altered or broken down protein particles of hæmic origin. This view is confirmed by the dehydrator and hydrator

effect the urinary particles sometimes have upon the hydrated protein particles in the plasma, when they are collected and re-injected into the blood-stream.

If protein particles are split off from other protein particles and undergo chemico-physical changes, thereby losing connection with their parents, should they meet again, and under slightly altered conditions the maximum shock or repulsion occurs. This is perhaps one of the greatest and most important truths in physico-chemistry.* The repulsion varies in degree, the parent particles may become dehydrated and go into complete solution, or they may undergo hydration. In the former instance the change may stop at dispersion, when the signs and symptoms of disease vanish. In the latter the so-called "negative phase" is produced, when the signs and symptoms of disease are aggravated.

The hydrated protein particles may collect in the pulmonary vessels causing œdema, and when this occurs, micro-organisms, such as pneumococci, streptococci and staphylococci, lying dormant, may be roused to an activity approaching pathogenicity.

Should the *loci minoris resistentiæ* be in other organs, precipitation of the hydrated protein particles takes place therein, but this does not warrant the clinical condition produced being labelled as a different disease.

It is practically certain that the cases discussed under the heading of pulmonary œdema are of the same origin as those labelled "glandular fever," "*Psittacosis*," "P.U.O.," etc.

An increase in the activity of the non-lactose fermenters has various results. It may enable the *Bacillus coli communis* to reach the lungs, but more often this bacillus multiplies in the uro-genital tract, which it reaches *viâ* the lymphatic vessels and capillaries. On the other hand, it occasionally multiplies and circulates in the blood-stream, where it does little or no harm. The pathogenic micro-organism itself may enter the lungs, and those the author has known to act in this way are the *Bacillus Friedländer*, the *Bacillus fœcalis alkaligenes*, the *Bacillus Gärtner*, and the *Bacillus Ærtrycke*. Friedländer's bacillus ferments lactose, but frequently fails to ferment dulcitate. It often goes by the name of *Bacillus mucosus capsulatus*, although in many cases there is no capsule, and in the same strain a capsule may be present on one occasion and absent on another.

The *Bacillus fœcalis alkaligenes* is the most frequently encountered non-lactose fermenter in the excreta at certain times of the year, particularly in the late winter. Whether this micro-organism is a mutative form of the

* It forms practically the whole basis of immunity.

Bacillus coli communis or has some other parent has not been definitely determined.

Although the micro-organism possesses certain characteristics of the coli-group it has others which separate it from the *Bacillus coli communis* more than any other non-lactose fermenter, despite the fact that it is far from being the most pathogenic. It is the strongest alkali-producer of all the non-lactose fermenters; it ferments no sugar, and is at times almost indistinguishable from a spore-bearer. The spore-bearer possesses bacillary and coccoid forms as the *Bacillus fæcalis alkaligenes* may do, and the size of these forms varies enormously. It is possible that the large sized spore-bearing cocco-bacillus so common in the excreta of herbivorous animals is the stock from which the *Bacillus fæcalis alkaligenes* has sprung. It is also equally possible that the *Brucellæ* mutated from the *Bacillus fæcalis alkaligenes* some time back, as they have so many points in common. The *Brucellæ* include the *Micrococcus melitensis*, the *Bacillus abortus* of Bang, the *Bacillus bronchisepticus* and the *Bacterium tularense*. Finally, it is possible that the virus of canine distemper is the ultra-microscopic form of the *Bacillus bronchisepticus*.

The *Bacilli Gärtner* and *Ærtrycke* are closely allied to the para-typhoid and typhoid bacilli, and are included in the *Salmonella* group of bacteria, a group which has almost without doubt mutated in the past from the *Bacillus coli communis*.

The non-lactose fermenter may enter the uro-genital tract, or even the blood-stream, and either lead merely a saprophytic existence or become pathogenic. In the latter case, it may undergo a morphological change, either into a coccoid form, or into a still smaller particulate form sufficiently small to pass through a filter.

The non-lactose fermenter which seems most capable of undergoing these morphological changes is the *Bacillus fæcalis alkaligenes*. The author has had cases of pulmonary œdema, glandular fever, *Psittacosis*, P.U.O., etc., where in the same patient the coccoid form of the *Bacillus fæcalis alkaligenes* was obtained in blood-culture, and the bacilloid form in the excreta.

Other investigations, not yet completed, lead the author to think it possible that the *Brucella* group of micro-organisms are connected in some way with the *Bacillus fæcalis alkaligenes*. The *Brucella* micro-organisms are Gram-negative, non-motile, alkali-producing bacteria, and they do not change any of the sugars. Veterinary surgeons, who have to deal with infected cattle and horses suffering from fistulous withers, are particularly prone to develop what is known as "undulant fever," and in these cases it is not difficult to

isolate one of the *Brucella* micro-organisms. On the other hand, in others, who become ill but do not develop true undulant fever, the coccoid form of the *Bacillus fæcalis alkaligenes* may be recovered from the blood and the bacilloid form from the excreta.

Bedson and Western,^{2, 3, 4, 5} and other observers^{3, 4, 5}, have found an ultra-microscopic virus in *Psittacosis*, but there are cases of *Psittacosis* where no ultra-microscopic virus is obtainable and where only pathogenic non-lactose fermenters are to be found in the excreta. Moreover, Gordon²¹ shows experimentally that filtration diminishes the pathogenic power of the virus, which suggests that not all the virus passes through the filter. There are cases which would not be labelled *Psittacosis* where ultra-microscopic viruses are to be found. There are cases of *Psittacosis* where the victim has had nothing to do with sick birds or with people who, having been in contact with them, were therefore possible carriers.

Glandular fever to which Tidy and Morley,^{6, 7, 8} and others^{7, 8}, have drawn attention is another fever of intestinal origin, and only differs from those described above in that the hydrated protein particles are precipitated in the spleen and lymphatic glands instead of in other organs. The precipitation of the hydrated protein particles in the lymphopoetic system stimulates the production of lymphocytes, but no more importance should be attached to the lymphocytosis in those cases than to the sputum in the pulmonary cases. Two other facts need to be mentioned in connection with fevers of intestinal origin. One of these is that the serum of the patient may give a positive Wassermann reaction. The serum remains positive till after the non-lactose fermenters in the intestinal tract have ceased to be active. The other is that when death occurs in animals, following experimentation with the non-lactose fermenters, enterococci are to be found in the heart's blood.

The acquisition of increased pathogenic properties renders the non-lactose fermenter itself, or one or more of its morphological forms, capable of being conveyed to others. When this occurs, still more factors come into play. The conveyance to another subject, man or animal, may result in the establishment of an infection forthwith, or, in stimulation to increased activity of the non-lactose fermenter already present in that intestinal tract. When a pathogenic non-lactose fermenter gains access to another body and gives rise to an infection, it would appear to reach the intestine *via* the blood-stream, and not to travel the whole length from mouth to anus.

To take the case of *Psittacosis* as an example. Through faulty feeding and other factors, consequent upon captivity, particularly in transit, the

animal's resistance is lowered, and non-lactose fermenting micro-organisms develop in the intestinal tract. These micro-organisms become so pathogenic as to give rise to an infection and the parent micro-organism, or one of its morphological forms, becomes implanted upon another animal or a human being. The implantation may result in a direct infection, or it may do no more than lower the resistance, and thus enable the non-lactose fermenters already present in the intestines to become active. On the other hand, fæcal material from the diseased animal may contaminate the food of a human individual, in which case it is more likely that the infected material acts as an intoxicant rather than as a carrier of the infection. The intoxicant forms faulty metabolites from the victim's food, either before or after it is ingested, and thus renders active the already existing non-lactose fermenters. In this way certain infections of intestinal origin are brought into line with food-poisoning. A few cases to illustrate these points are reported below.

Case 117

A man, aged thirty-five, had felt drowsy, depressed and ill for three days when his temperature suddenly rose to 104° F. It remained at this level for four days before anything definite could be found upon clinical examination, but all the time the patient was slightly delirious. On the fifth day, trouble at the base of the right lung was detected, and diarrhœa developed. A few days later the whole of the lowest lobe of the right lung became consolidated, and some blood-stained sputum was expectorated, but there was little or no cough. The heart was normal and the pulse was not accelerated. The patient would not answer when spoken to, but on examination of the abdomen he made gestures. The abdomen was distended, and obviously tender all over. A bacteriological examination of the sputum revealed a few streptococci and pneumococci and many Friedländer's pneumo-bacillus. A bacteriological examination of the fæces showed the pathogenic micro-organism to be a capsulated Friedländer's bacillus (70 per cent.). The capsules disappeared in sub-culture and in later specimens examined. The blood-cultures were negative, and the serum failed to agglutinate the patient's own pneumo-bacillus. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 2.2 c.c.
Refractive index of the serum	= 1.3467.
Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 43 mgrm.

Ultra-microscopic picture of the serum = Very few particles moving, and these were either giant or ringed particles. There were very many more particles, and giant particles precipitated with some giant-particled clumps and large agglutinations.

The patient was fed on fruit juice, took 1 oz. of glucose a day in imperial drink, and had injections of Sup. 36 and Sup. 468 without any lowering of the temperature. On the nineteenth day of the pyrexia he was given an intramuscular injection (1.0 c.c.) of the washings of 5,000 million of a twenty-four-hour old culture of the Friedländer's bacillus obtained from the excreta. The temperature fell the next day to normal, where it remained, and the patient made an uneventful recovery. A week later a re-examination of the excreta revealed 10 per cent. *Bacillus Friedländer* and two months later still none were grown. Even during the convalescence the patient's serum failed to agglutinate his own bacilli.

This case presents several features of interest. In the first place, and this is typical of the condition, the heart and pulse remained steady. When the former gives way it is owing to a toxic myocarditis, the lesion most frequently responsible for the fatal issue. In the second place, the symmetrical urea compounds were useless, and this is sometimes so in cases of acute pyrexia of intestinal origin. In the third place, despite the absence of agglutination, the Friedländer's pneumo-bacillus was undoubtedly the pathogenic micro-organism, and the author feels that the injection of the washings saved the patient's life. From numerous other agglutination experiments carried out, and the wide experience the author has had in the treatment of chronic intestinal intoxication with preparations made from the non-lactose fermenting micro-organisms found in the excreta, he has come to the conclusion that agglutination tests are of no great value. When the test is positive it is by no means necessarily specific, and when it is negative it by no means indicates that the micro-organism in question is not pathogenic. Positive agglutination seldom occurs with other than the better known non-lactose fermenting micro-organisms, and positive results may be obtained with stock preparations even when none of the micro-organisms are to be found in the excreta. The author has encountered cases where the patient's serum agglutinated typhoid and para-typhoid bacilli when only the *Bacillus fæcalis alkaligenes* was found in the excreta. Agglutination tests should not be relied upon either to detect an infection or a supposed carrier of an infection. In the fourth place, a Friedländer's bacillus can still be a Friedländer's bacillus even in the absence of a

capsule, and there is no necessity to give it a different name when no capsule can be detected. It is highly probable that the capsule has no real existence, it being either an artefact, or a form of activity of the micro-organism—an emanation of the bacillus so to speak, rather than a substance made up of its constituents. The so-called “capsule” would seem to correspond with the halo seen around protozoal bodies and described by the author in the first volume of “The Nature of Disease.”

Finally, the above case occurred during the epidemic of *Psittacosis*, and it could not be ascertained for certain whether the patient had, or had not, been in contact with a sick Amazon parrot. The case was a typical one of pulmonary œdema and could well have been labelled “*Psittacosis*” or “influenzal pneumonia.”

Case 118

A man, aged fifty-six, had been ill and complained of severe headaches for four days, when rigors developed and his temperature rose to 104° F. On the eighth day of the illness scattered œdema of both lungs was noticed, and this developed later into consolidation of both bases. At this time the patient became delirious and remained so until he died on the twenty-second day of the illness. He looked extremely toxic, and his complexion was dusky on a yellowish background. The mouth was foul, and covered with herpetic vesicles and aphthous ulcers; the tongue was very furred. He had no expectoration, the pulse was not accelerated, and the heart beats were normal. The abdomen was distended and abdominal palpation roused the patient, showing that the contents were inflamed. The examination of the blood was made on the eve of death and the picture was as follows:—

Suspension stability of the red blood-corpuscles	= 3.5 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.206 grm.
Percentage of the blood-urea	= 50 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving. There were many particles precipitated <i>en masse</i> with some huge agglutinations.

The blood-culture was sterile.

There is every reason to suppose this was a case of *Psittacosis*, as the patient, at the time of his illness, had an epidemic of enteritis amongst his budgerigars.

Case 119

A man, aged thirty-eight, had been in bed for three months with intermittent pyrexia and scattered œdema in both lungs. The patient had had no cough and no expectoration. He had suffered from chronic nasal catarrh all his life, he had had migraine, and fibrositis, and was invalided out of the Army for dysentery. He was subject to recurrent tonsillitis, and had had an attack of Vincent's angina. He had gingivitis, the teeth needed attention, the tongue was furred, the trunk was covered with big areas of ring-worm, the left colon was tender, the hepatic flexure and ileo-cæcal region even more so, and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the bacillus of epidemic jaundice (5 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·5 c.c.
Refractive index of the serum	= 1·3489.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-urea	= 16 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with many giant particles and ringed particles and a few giant-particled clumps. There were many particles, giant particles and clumps precipitated with some large agglutina- tions.

The patient was fed on fruit juice only, for a time, he took lacto-dextrin and a pill containing thyroid substance and potassium permanganate, had his colon cleaned with treacle enemata and received four injections of Sup. 468 (0·002 grm.). When he was up and about he had a course of colonic lavage and afterwards received two injections of his fæcal vaccine, in doses of 250,000 and 500,000 respectively, on two successive days. The patient made an uneventful recovery.

This case is a typical example of sub-acute pulmonary œdema.

The following case is of particular interest because the pulmonary œdema appeared during the summer as part of a reaction caused by an overdose of the fæcal vaccine :—

Case 120

A woman, aged fifty-four, sought advice for rheumatism and migraine. The rheumatism had been present for fifteen years and had affected the spine and both knees. The patient suffered as a girl from ulcerative chilblains, she

had dysentery in France during the war, and had been operated upon for fibroids three years previously, having always had trouble with her periods. Her hair was quite grey, all teeth had been removed, the tongue was furred and fissured, and the optic discs were mal-developed. The pulse was 86, and the blood-pressures registered 140 and 85 mm. of Hg. respectively. The whole colon was very tender and the passage of mucus was habitual. The pathogenic micro-organisms found in the excreta were the *Bacillus faecalis alkaligenes* (50 per cent.), bacillus of epidemic jaundice (5 per cent.) and *Bacillus proteus Valeriei* (5 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·5 c.c.
Refractive index of the serum	= 1·3500.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with many giant particles and ringed particles.
	As many particles, giant particles and ringed particles precipitated with some giant-particled clumps. The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally and received injections of contramine and of the faecal vaccine.

The faecal vaccine, made from the washings of 5,000 million bacteria, was injected on two successive days in 1·0 c.c. doses. The first injection caused a large patch of erythema around the puncture wound, which should have been a warning not to repeat it. The evening of the second injection the patient did not feel well ; for the next two days she complained of malaise, sickness and headache, and on the fourth day she had rigors, and her temperature rose to 104° F. At this time there were herpetic lesions in the mouth, both tonsils were acutely inflamed (follicular tonsillitis), the tongue was very coated and the abdomen acutely tender. The patient passed large quantities of mucus *per anum* for several days, the temperature continued high for about three weeks, and on the fifth day of the illness œdema of the right lung appeared, which developed later into consolidation of the base. There was no cough and no expectoration. A re-examination of the excreta made when the reaction was passing off showed 1·0 non-lactose fermenters.

A few words are necessary regarding the reaction following injections of the vaccine. An emulsion of 5,000 million of the pathogenic micro-organisms

was prepared, well shaken and centrifuged. The supernatant fluid, completely free of bacteria, was collected, diluted and ampouled in, what were thought to be, doses of 0.25, 0.5, 1.0 and 2.0 million respectively. The two injections given to the patient were the contents of the first two ampoules. As the washings of bacteria contain only their activity it is obvious that a dilution of supernatant fluid to 0.25 million does not represent the activity of 0.25 million micro-organisms. The dilution contains the same activity as the original fluid of the emulsion of the 5,000 million bacteria. This point unfortunately did not occur to the author until the reaction brought it to his notice. Later experience showed that the fault committed in this case was more in making the second injection than in using 5,000 million bacilli. While on the subject, it is well to mention that still more points for discussion are brought out. The activity of pathogenic micro-organisms in an individual varies from time to time, being so low on some occasions as not to warrant the designation "pathogenic" and so high on others as to render the protective mechanism of the patient unable to combat it. There is no means, at present, of measuring activity, consequently experience and time will be required before the author can lay down rules regarding the desirable strength of the original emulsion. The employment of the washings of bacteria as vaccine was introduced by Horder and Ferry¹³. Using the side-chain theory of immunity nomenclature, these two observers referred to the vaccine as "ecto-antigen," but the substitution of the word "activity" describes its action more accurately. In the case of homœopathic remedies mainly the activities of drugs are used, and the present method of preparing the vaccine is fundamentally a homœopathic manoeuvre. It is a great advantage being able to dispense with the vehicle because, in every instance, it causes a varying degree of hydration of the protein particles in the plasma. It is too early to say at present how many injections of the washings should be made, but experience is beginning to show that they need to be injected much in the same way as homœopaths prescribe their remedies—one dose and then wait as long as possible before repeating. Washings taken internally are not so active as when injected intra-muscularly.

Apart from the occurrence of the pulmonary œdema the above case is interesting because it shows that a flare-up of the trouble in the colon can precipitate a tonsillar infection. This point is mentioned because it confirms the author's view that tonsillar, nasal and dental sepsis are secondary to chronic colitis and do no more than precipitate disease.

The following case is one of intermittent pyrexia affecting a veterinary

surgeon, who had had several cases of Bang's infection in cattle and fistulous withers in horses under his care, and who was accustomed to take large quantities of milk :—

Case 121

A man, aged forty, had had his first attack of fever three years previously. It was ushered in with hæmaturia, and lasted fourteen days. There had been five attacks since, and although each lasted a shorter time than the one before, they left him progressively worse and more depressed afterwards. The patient was examined a week after the conclusion of the last attack. He had suffered from lumbago and sciatica, and had been going bald for the past eight years ; he could not stand with his knees and feet together at the same time, the ears stood out, all teeth had been removed, the tongue was fissured and leucoplakic. The pulse was 74, the blood-pressures were 115 and 70 mm. of Hg. respectively ; the abdomen was tender in the region of the flexures and particularly so in the ileo-cæcal area—an operation for appendicitis had been advised thirteen years ago—the urine gave a very strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (80 per cent.) and a coccobacillary form of this was obtained in the blood-culture. The serum did not agglutinate either the patient's, or a stock *Bacillus fæcalis alkaligenes*, or either of the *Brucella* micro-organisms. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3485.
Percentage of the blood-sugar	= 0.151 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a fair number of giant particles and small giant-particled clumps both moving and precipitated.
Wassermann reaction	= Positive (+ + +).

The patient received anti-syphilitic treatment, with the result that his general health improved, the attacks of pyrexia vanished and the *Bacillus fæcalis alkaligenes* disappeared from the blood-stream. From this it might be assumed, without question, that the pyrexia was of syphilitic origin, but how is the presence of the *Bacillus fæcalis alkaligenes* in the blood-stream to be explained ? Furthermore, it is a significant fact that the patient was exposing himself frequently to *Brucella* infections. As a result of experience the author now takes the view that syphilis behaves just as does any other infection or

intoxication. This means that if the patient's resistance is already lowered when he contracts syphilis the infection may still further lower his resistance and precipitate lesions. But they are not necessarily syphilitic, and this is very well illustrated in a case reported below. In the above case the syphilitic infection doubtless stimulated the activity of the *Bacillus fæcalis alkaligenes* and possibly *vice versâ*. As the activity of the *Bacillus fæcalis alkaligenes* attacks the protective mechanism of the host in the same manner as does the activity of the *Leucocytozoon syphilidis*, it is useless to argue about the cause of the pyrexia. Indeed, no argument would arise if the concept of there being only one disease was universally held.

Case 122

A man aged twenty-nine, sought advice for an acute arthritis of one week's duration affecting the left ankle. The father was a chronic asthmatic and died, following an operation for appendicitis, aged fifty. Of the family of eight, six had had the appendix removed. The patient used to suffer from chilblains, he had had bronchitis and double pneumonia, and several attacks of severe migraine. His operation for appendicitis was followed by general *Lichen planus*. He was thin, anæmic and looked very ill, all his teeth had been removed, the tongue was furred, the elbows were wide-angled, and there was acro-asphyxia. The pulse was 110, the blood-pressures registered 110 and 70 mm. of Hg. respectively, and the heart was elongated, dropped and narrowed. The left colon was contracted, the ascending colon and cæcum dilated. There was a papulo-erosive chancre on the corona of the penis, but no evidence of generalised syphilis. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 3·4 c.c.
Refractive index of the serum	= 1·3480.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-urea	= 16 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving.
	There were many more particles and giant particles precipitated <i>en masse</i> with some large giant-particled clumps.
	The Brownian movements of the particles were very sluggish.
Wassermann reaction	= Slightly positive (+ — —).

The patient was a typical example of familial chronic intoxication in whose

case the advent of a syphilitic infection lowered the resistance still further and occasioned an arthritis. It was not a syphilitic arthritis because the infection had not become sufficiently generalised to cause such a lesion. Owing to the readiness with which veterinary surgeons fall victims to a *Brucella* infection and to the occurrence of the *Bacillus fæcalis alkaligenes* in a pathogenic form in those who manage to escape, the author has thought there may be some relation between the two groups of micro-organisms, although there appears to be no proof at present.

It is doubtful whether "undulant fever" should be classed as a specific fever or infection, because there are cases clinically identical caused by other non-lactose fermenters. It is impossible to differentiate clinically between undulant fever caused by the *Brucellæ* and some fevers of intestinal origin. The *Brucellæ* likewise give rise to different kinds of lesions, causing undulant fever in man, abortion in cows, abscesses (fistulous withers) in horses, broncho-pneumonia in dogs, etc.

Another febrile condition allied to those discussed above, and so far unnamed, is one which affects women in preference to men: it is characterised by *Herpes febrilis*, affecting the mouth or vulva or both; treatment is often unavailing and only the mild cases recover.

Case 123

A woman, aged thirty-two, was admitted to hospital with pyrexia, and acute ulceration of the vulva. The patient's mother suffered from rheumatism, and the patient, the youngest of twelve children, had the same condition. Some months previously she had been in another hospital and been treated for gastric ulcer—blood having been found in the vomit and in the stools. There were many aphthous ulcers in the mouth, gingivitis and pyorrhœa were marked, and the tongue was coated and very sore. The thyroid gland was enlarged, the abdomen was too tender to palpate, the urine contained 0·075 per cent. of protein. From the vulval and buccal lesions the *Bacillus crassus* and Vincent's micro-organisms were obtained. The pathogenic micro-organism found in the excreta was the *Bacillus Morgan* (10 per cent.), and the blood-picture was as follows:—

Suspension stability of the red blood-corpuseles	= 5·3 c.c.
Refractive index of the serum	= 1·3488.
Percentage of the blood-sugar	= 0·181 grm.
Percentage of the blood-urea	= 27 mgrm.

Ultra-microscopic picture of the serum = Hardly a particle moving and not many particles precipitated. The precipitated particles were either giant particles or ringed particles.

The patient was fed on fruit juice, took lacto-dextrin internally, and was given injections of para-thor-mone to check the incessant vomiting, which they did successfully. But her condition became worse daily, and she died eighteen days later. Four days before death occurred the blood was re-examined with the following result :—

Suspension stability of the red blood-corpuscles	= 5·0 c.c.
Refractive index of the serum	= 1·3464.
Percentage of the blood-sugar	= 0·287 grm.
Percentage of the blood-urea	= 88 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving with some giant particles, ringed particles and clumps. There were as many particles precipitated in the form of separate particles, giant particles, ringed particles and giant-particled clumps.

On both occasions the blood-cultures were negative and the serum was colourless.

Post-mortem examination revealed pericarditis and myocarditis, generalised pulmonary fibrosis, congenital absence of one kidney and the other reduced to one-third its normal size. There were no signs of gastric or duodenal ulcer, but there was a general entero-colitis.

The *Bacillus crassus*, so named by Lipschütz,⁹ is, in the author's opinion, the same as Döderlein's bacillus, which is probably one of the bacillary forms of spirochæta found in Vincent's angina. The author holds that these micro-organisms are normally saprophytes, which become pathogenic when local anaerobiosis occurs as a result of the patient's resistance being lowered.

In the case reported below the condition was more chronic, and the aphthous ulceration of the vulva and mouth did not begin until a few weeks before the patient died.

Case 124

A woman, aged twenty-eight, suffered from mucous colitis. She had had several attacks of gastritis, and had suffered from migraine and nasal catarrh, more or less, all her life. For the past two years she had been having attacks of pyrexia, during which the abdomen became acutely tender, diarrhœa

appeared, and the passage of mucus with blood occurred. She had a pyrexial attack at the time of examination. The pathogenic micro-organism found in the excreta was the *Bacillus Gärtner* (20 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 4·2 c.c.
Refractive index of the serum	= 1·3490.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 20 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with many giant particles. There was an occasional giant-particled clump both moving and precipitated.

The patient was fed on fruit juice and lacto-dextrin. She received injections of emetine hydrochloride and of the fæcal vaccine in doses of 125,000, 125,000 and 250,000 on three days in succession. Every attempt to clean the colon produced so much reaction as to put this method of treatment out of court. The three injections of vaccine caused an acute flare-up of the mucous colitis, and aphthous ulcers appeared in the mouth. The patient became so emaciated that insulin was prescribed, and she received forty-seven injections each of 20 units, during which course she had no pyrexia. At the end of it, and four months after the first examination of the blood, a re-examination was made with the following result :—

Suspension stability of the red blood-corpuscles	= 1·8 c.c.
Refractive index of the serum	= 1·3456.
Percentage of the blood-sugar	= 0·081 grm.
Percentage of the blood-urea	= 16 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving. There was marked precipitation <i>en masse</i> with massive agglutinations.

Three months later the patient had another pyrexial attack, when she developed vulval and buccal aphthous ulceration and septic peri-onychia.

A re-examination of the excreta showed the pathogenic micro-organism to be the bacillus of epidemic jaundice (20 per cent.). But before any injections of the washings of this bacillus could be made the patient died. *Post-mortem* every organ was found to be riddled with tuberculosis, which doubtless developed in the course of the patient's illness. The author recently saw a case where generalised tuberculosis developed in a case of familial chronic

intestinal intoxication, while the patient was convalescing from an operation performed for an ischio-rectal abscess.

On the second blood examination the serum was colourless, and on both occasions gave a positive (+ + +) Wassermann's reaction, although, as far as could be determined, the patient had never had syphilis. Anti-syphilitic treatment thoroughly tried did no good. The interpretation of the blood-pictures of these two cases, which were clinically as like sprue as can be imagined, is interesting. The first case shows a steadily advancing dehydration attacking the protein particle deeper and deeper, with a feeble attempt at hydration, as evidenced by a reduction in the suspension of the stability of the red blood-corpuscles, and by there being more particles in the ultra-microscopic picture.

In the second case insulin undoubtedly checked the dehydration in one direction, but, on the other hand, it did not stop the change from globulin to albumin, so characteristic of cases going progressively downhill, as evidenced by the great fall in the refractive index of the serum. The fall in the refractive index was due to the advent of a tubercular infection. The last case brings out another interesting point. Following the use of a faecal vaccine it is usual, if the patient does well, for all non-lactose fermenters to vanish from the excreta. If, on the other hand, the patient does not do well and the condition relapses, either the non-lactose fermenter originally present is found again, or, more often, another appears. It may happen that, in the course of time, three or more different non-lactose fermenters are found. It is impossible to make certain whether a fresh mutation occurs or whether all were present throughout, and were prevented from appearing owing to the activity of the one prevailing at the time. It is certain that micro-organisms behave very differently in the body and in the laboratory, mainly because in the former they are subject to variation, and in the latter they remain true to type. This fact alone, if there were no others, must always handicap the bacteriologist, and prevent him drawing either a homology or an analogy between the behaviour of micro-organisms *in vivo* and their behaviour *in vitro*.

The following case of an acute intestinal intoxication causing the appearance of a coccogenic micro-organism in the blood-stream is of some interest :—

Case 125

A man, aged sixty-two, had had a pyrexia with several rigors for three weeks and, for six days, an acute arthritis affecting one shoulder joint. The

patient's mother died of asthma and bronchitis, aged sixty-five. He had chilblains as a boy, and had suffered from chronic nasal catarrh all his life. For this several operations had been performed, with no benefit resulting. He had had attacks of lumbago and sacro-iliac arthritis. Constipation had always troubled him, and on many occasions there had been attacks of pyrexia associated with abdominal tenderness. During one of these the diagnosis of cholecystitis was made, and when the attack had subsided the gall-bladder was removed. Since this operation, which had taken place four years previously, the pyrexial attacks had become more frequent and more severe. The patient had always been a heavy consumer of milk. At the time of the examination his mentality was such as it usually is in cases of intestinal pyrexia—that is to say, he was morose, fault finding and at times slightly delirious. The tongue was covered with a brown fur; there was a severe toxic myocarditis; the whole colon was tender and distended with gas. The urine gave a very strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and contained protein. The pathogenic micro-organisms found in the excreta were the *Bacillus Friedländer* (45 per cent.), and the *Bacillus acidi lactici* (20 per cent.). The blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 4·7 c.c.
Refractive index of the serum	= 1·3470.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-urea	= 36 mgrm.
Ultra-microscopic picture	= Scarcely a particle moving. There was a fair amount of general precipitation <i>en masse</i> .

The blood-culture grew the pneumococcus (type 3).

The myocardial trouble caused so much anxiety as to prevent any treatment other than that aimed at preventing cardiac failure. A vaccine was prepared from the washings (5,000 million) of the pathogenic micro-organisms found in the excreta, but the patient died the day following its injection, which was the twenty-second day of the pyrexia. Although it was practically certain from the beginning that the patient would not recover, it appears equally certain that the washings of the bacilli produced sufficient reaction to hasten the fatal issue. The author is unable to state dogmatically how many bacilli should be used in the emulsion in acute cases. In chronic cases an emulsion of 100 million gives the best results. Washings of 1 million bacilli are apt to produce too much reaction.

The question which arises now is the significance of the micro-organisms in

the blood-stream. If the patient had been a victim to pneumococcal septicæmia the blood-picture would have shown more marked changes of dehydration, *i.e.*, the refractive index of the serum would have been lower, and there would have been a greater rise in the percentage of the blood-sugar or blood-urea. Moreover, it is unlikely that the fæcal vaccine would have produced a reaction. The occurrence of the reaction suggests that the micro-organisms in the excreta played the main pathogenic rôle. Another theory which would fit in with what occurred is that the so-called "pneumococcus (type 3)" was a coccoid form of the Friedländer's bacillus in the intestines. The blood micro-organism was delicate and difficult to keep alive for experimentation. But in view of the close clinical connection between pulmonary lesions and a Friedländer infection of the large intestine, it is worth investigating to see if there is a connection between the two micro-organisms.

I. The Coeliac Division

(a) The Œsophagus

The œsophagus is very seldom involved in congenital disease. The only lesion meriting discussion is that known as "cardiospasm," and this only because it throws light upon the changes the walls of the pylorus and the colon undergo in disease.

The true nature of cardiospasm was revealed by Hurst, who gave the name of "achalasia," a term signifying absence of relaxation, to the condition. Hurst^{10, 11} shows that the primary change is an inflammation of Auerbach's plexus, which in turn results in hypertrophy of the muscular tissue and inflammatory changes in the mucosa. The inflammation in Auerbach's plexus is doubtless caused, in the first instance, by the local arrest of hydrated protein particles. Much the same condition of affairs accounts for hypertrophy of the pylorus, with the difference, in the congenital form, that the hypertrophy and contraction of the muscular tissue are caused by the precipitation of hydrated protein particles in the region of the vagus centre. That this is the most probable explanation is supported by the fact that congenital hypertrophic stenosis of the pylorus most frequently occurs soon after birth, and occasionally even *in utero*. If it is the correct explanation, then operative interference should give way to measures aimed at causing dispersion of the protein particles in the plasma, such as injecting glucose in normal saline containing a trace of adrenalin, ephedrin or ephetonin, into the superior longitudinal sinus *viâ* the anterior fontanelle. The acquired form of hypertrophic stenosis of the pylorus, a condition from which Napoleon probably died, and

one frequently mistaken for malignant disease, arises in the same way as does cardiospasm.

(b) **The Stomach**

The stomach is affected in a variety of ways, but whatever changes occur they are secondary to the abnormal chemico-physical changes undergone by the protein particles in the plasma. It does not necessarily follow because there is vomiting that there is a lesion of the stomach. Vomiting occurs when protein particles become arrested in the portal circulation, particularly in the veins. This explains why examinations of the blood show dehydration and hydration concomitantly, because when this double change takes place it does so most frequently in the veins, where the hydrated protein particles undergo the cyclical change of dehydration. Before this occurs, however, the hydrated protein particles become arrested in the peri-vascular lymphatic vessels, and in the capillaries, but with no symptoms, or only mild ones of splanchnic shock. In course of time the hydrated protein particles become precipitated in the veins, where some immediately undergo dehydration. This is evidenced by the frequent occurrence of acetonæmia and acetonuria, to the clinical significance of which Fawkes¹² has drawn attention. When it occurs, vomiting is frequent, and, as the sequence of events tends to recur at more or less regular intervals, the vomiting develops a cyclical character. Cyclical vomiting does not only occur in children but also in adults, and is relieved by glucose, not because this substance is required for the proper burning of the fat moiety of the protein particles, but because it breaks up the hydrated protein particles into myriads of little particles. If the dehydration exceeds the hydration, then Sup. 36 is called for in preference to glucose. In cases of cyclical vomiting the patient may present one of the manifold forms of *Erythema multiforme* caused by the protein particles undergoing chemico-physical changes in the cutaneous veins. Vomiting occurs, associated with ketonuria, following general anæsthesia, after shock, in sea-sickness, in pregnancy, etc., and in all these conditions the treatment is regulated according to whether dehydration or hydration prevails. Sup. 36 is the drug for choice in the former, and glucose in the latter. If large quantities of glucose are used, it is wise to administer insulin in addition, to prevent the splitting up of the hydrated particles proceeding too far. Insulin is a hydrator and prevents the protein particles being sent into true solution. In really bad cases of post-anæsthetic vomiting where the hydration is producing severe shock, and the patient's life is endangered, blood-transfusion is the best method to adopt. The following case illustrates this well :—

Case 126

A woman, aged thirty-three, had a curettage performed. The day following the operation vomiting began and became incessant till a blood-transfusion and an injection of Sup 36 were made on the twelfth day. The temperature was raised throughout, and red blood-corpuscles, protein and casts were present in the urine. The patient lost much weight, and appeared to be desperately ill. The blood-picture made on the tenth day was as follows :—

Suspension stability of the red blood-corpuscles	= 5·8 c.c.
Refractive index of the serum	= 1·3464.
Percentage of the blood-sugar	= 0·156 grm.
Percentage of the blood-urea	= 93 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving. There was a fair amount of general precipitation <i>en masse</i> .

When the hydrated protein particles undergo a cyclical change spontaneously gelation may occur, and then there is the ever present danger of venous thrombosis supervening. For this condition Sup. 36 is strongly indicated, and glucose contra-indicated.

Gelation occurs most frequently in pregnancy, and is one of the causes of *Hyperemesis gravidarum*. But pernicious vomiting of pregnancy may also occur when the change of hydration is more pronounced than that of dehydration, and in these cases glucose followed by insulin is required.

These points are stressed, because others have not found that Sup. 36 gives as good results in cases of gelation as those described by the author. When detailing the uses of a preparation the author has, unfortunately, to use existing nomenclature, but to him pernicious vomiting of pregnancy means nothing. What he wants to know is why the patient vomits and what chemico-physical changes the protein particles in the plasma have undergone to produce the symptoms complained of. The author does not treat the symptoms, but attempts to correct the altered conditions in the blood. Hence in acute cases, where it is necessary to relieve the patient as soon as possible, it is difficult to know with which drug to strike until an examination of the blood has been made. Medicine can never advance, so long as physicians first give a name to a condition and then prescribe what they have been taught to regard as the specific treatment. The way in which medicine is practised to-day accounts for many really useful drugs falling into disrepute.

The following cases of recurrent vomiting associated with ketonuria are sufficiently interesting to be reported :—

Case 127

A woman, aged thirty-six, sought advice for continuous pain in the occiput, a perforation of the hard palate, and recurrent attacks of vomiting. The patient had contracted syphilis ten years previously, and had been treated for this, with mercury and iodides internally, for two years. Eight years later the tonsils were removed, and the operation precipitated a gumma of the palate which terminated in a perforation. During the last two years the patient had been treated with every form of anti-syphilitic treatment, in spite of which recurrences kept on appearing. Throughout, the Wassermann reaction had been negative. The patient had suffered from chronic indigestion and constipation all her life; she had had chronic nasal catarrh since the age of six, and two attacks of generalised fibrositis. She was a typical example of congenital disease; her thyroid gland was enlarged; she had attacks of giddiness, and frequent bouts of depression, could not sleep and was rapidly losing her memory. The pulse was 120, and the blood-pressures registered 100 and 60 mm. of Hg. respectively. There was marked tenderness in both hypochondria and in the ileo-cæcal area. The urine gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and contained ketone bodies. The pathogenic micro-organism found in the excreta was the *Bacillus coli anaerogenes* (25 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·8 c.c.
Refractive index of the serum	= 1·3498.
Percentage of the blood-sugar	= 0·137 grm.
Percentage of the blood-urea	= 111 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles, ringed particles and small clumps. There were some giant particles, ringed particles, small giant-particled clumps and agglutinations precipitated. The Brownian movements were sluggish.
Wassermann reaction	= Negative.

The patient was dieted, subjected to colonic lavage, took 1 oz. of glucose a day, and received injections of para-thor-mone and of the fæcal vaccine.

She improved considerably, the ketonuria vanished, and two months later a re-examination of the blood revealed the following :—

Suspension stability of the red blood-corpuscles	= 0·25 c.c.
Refractive index of the serum	= 1·3500.

Percentage of the blood-sugar	= 0·150 grm.
Percentage of the blood-urea	= 44 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a few giant particles, ringed particles and clumps.
Wassermann reaction	= Negative.

Because of the high percentage of the blood-urea in the first examination there is no doubt that the patient was very ill. There is also no doubt that the treatment had a marked conductor effect, and a rise in the percentage of the blood-sugar, as shown in the second examination, always occurs when the percentage of the blood-urea falls and the patient improves.

Case 128

A woman, aged thirty-five, sought advice for recurrent attacks of vomiting, with headache, which she had had from childhood. The patient began to menstruate at the age of fourteen, since when she had frequently had periods of amenorrhœa lasting six or even more months. During these periods she had severe epistaxis. She had one child, a girl, and during gestation vomiting had been persistent. Two months previously the patient had had a severe gastric hæmorrhage, followed by persistent vomiting, the sight of food was repulsive to her and she had lost over a stone in weight. She was a typical example of familial chronic intestinal intoxication. Her pulse was 116, the blood-pressures registered 115 and 80 mm. of Hg. respectively, the whole abdomen was tender, the urine contained ketone bodies, and gave the strongest possible reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The patient was on her way to a German spa for treatment, which made it impossible to examine the excreta. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 4·3 c.c.
Refractive index of the serum	= 1·3508.
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Hardly a particle moving, and these were all giant particles and clumps. There was some precipitation <i>en masse</i> .

The blood-picture shows how ill the patient was, and the author learnt that she died four months later, following a severe gastric and intestinal hæmorrhage.

The collection of hydrated protein particles in the portal area, and in the vessels supplying the stomach, causes first a stimulation of the cells of the mucosa. One of the effects of this stimulation is hyperchlorhydria, but the excess of hydrochloric acid means nothing in itself, and the patient is no better off after having been subjected to test-meals to find out this unimportant point. It is likewise equally futile to attach importance to the achlorhydria which occurs as an end result of the hydration.

It is still more senseless to associate achlorhydria with clinical conditions as if it was a salient feature, and to fail to label, if labelling is ever necessary, a condition as one of pernicious anæmia, for example, unless the gastric contents fail to show the presence of free hydrochloric acid. In the first place, patients who are very ill should not be subjected to test-meals. In the second place, achlorhydria may occur in patients who present no clinical symptoms of disease. In the third place, prescribing hydrochloric acid in its natural absence does not supply a want, and in those cases where it does good the benefit is due to its tonic action upon the blood which is achieved by the power acids have to break up certain hydrated protein particles.

The author believes that a gastric ulcer forms in the same way as do ulcers in other parts of the body—for example, ulcerative chilblains, the ulcers of *Erythema induratum* (Bazin's disease), those of *Thrombo-angiitis obliterans*, etc. All these ulcers are produced by the necrosis of tissue lying over veins wherein hydrated protein particles have been precipitated. In favour of this being the sequence of events responsible for gastric ulcer is the fact that around certain ulcers venous thrombosis is the rule. The author does not suggest that all gastric ulcers arise exactly in this way, although he feels confident that all are primarily the result of the local presence of arrested hydrated protein particles. The sites chosen by the ulcers are doubtless regulated by the blood-supply. The same causes are at work in the production and selection of the site of duodenal ulcers, but it is not an easy matter to say why a gastric ulcer so often, and a duodenal ulcer so rarely, becomes malignant. This is a point worthy of serious consideration on the part of those who come across ulcers of the alimentary canal, none of which would ever occur if familial chronic intestinal intoxication was prevented. Their frequency would be much diminished if the intestinal intoxication was dealt with from the beginning, instead of wasting valuable time attempting to palliate the ulcer itself with alkalis in the one case and acids in the other.

The following cases of anæmia illustrate some general points which previously have had no recognition :—

Case 129

A woman, aged fifty-one, had been anæmic all her life. For the past year she had been unable to do any work, and had put on two stone in weight. The patient's father died of cancer of the bladder, aged sixty-seven, her mother was suffering from *Paralysis agitans*, and a brother was in a lunatic asylum. The patient had suffered from chilblains all her life, she was bronchitic, and had had rheumatism and boils. Her tonsils and appendix had been removed. Menstruation began at the age of fourteen and the periods were always accompanied by much pain. The patient was very anæmic, her hair was quite white, all her teeth had been removed, the elbows were wide-angled, there was hyperkeratosis of both palms, and central cupping of both optic discs. The pulse was 78, and the blood-pressures registered 120 and 90 mm. of Hg. respectively. There was marked tenderness in the region of the hepatic flexure of the colon, which had led to the diagnosis of cholecystitis and the advice to have the gall-bladder removed. The pathogenic micro-organism found in the excreta was the *Bacillus Morgan* (15 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 2·2 c.c.
Refractive index of the serum	= 1·3500.
Percentage of the blood-sugar	= 0·150 grm.
Percentage of the blood-urea	= 116 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles, ringed particles and small clumps. There were as many particles precipitated. The Brownian movements of the particles were very sluggish.

The serum was deeply pigmented.

The patient cut out butcher's meat, eggs and milk from her diet, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and was given injections of Sup. 468 and of the fæcal vaccine.

The patient improved enormously, and was able to take up her work again as a restaurant proprietress. She lost two stone in weight, and her blood, when re-examined two years later, was normal.

This patient, when she sought advice, was desperately ill, and was on the point of having her gall-bladder removed. The blood-count did not allow the type of anæmia to be labelled, nor did it throw light upon the case, as did the blood-picture.

Case 130

A woman, aged forty-four, was very anæmic. She had had several spontaneous hæmorrhages, some blood-cysts having been removed, and continuous hæmorrhage from the uterus and large intestine for many years. The patient suffered very much from chilblains, and had had rheumatism and eczema. The present trouble began as bruises, in childhood. Menstruation began at the age of sixteen, then amenorrhœa occurred for two years, since when there had been an almost continuous discharge. The patient could not stand with her knees and feet together, all her teeth had been removed, the tongue was fissured, the hands were red and cold, and the nails ridged. There was central cupping of both optic discs, the pulse was 88, and the blood-pressures registered 160 and 70 mm. Hg. respectively. The temperature was raised a degree or two every night. When the author saw the patient five years previously the spleen and lymphatic glands were enlarged, but this was not the case at the second examination. The abdomen was too tender to palpate, diarrhœa with mucus was constant, and any cleansing of the colon was out of the question. The pathogenic micro-organism found in the excreta was the *Bacillus Morgan* (90 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.4 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 10 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, but these were all giant particles and ringed particles. There were very many giant particles, ringed particles and small clumps precipitated.

The patient was unable to undergo treatment.

There are two points of particular interest in this case. The first is the marked degree of hydration of the protein particles. Hydration and hæmorrhage go hand in hand, and hæmophilia is probably hereditary and congenital hydration, where the protein particles are unable to undergo either dehydration or dispersion. Although treatment in these cases should be aimed at ridding the patient of the chronic intestinal intoxication, much can be done by prescribing dehydrators internally, intra-muscularly and intra-venously, such as calcium oleate, calcium and strontium aspartate, and sodium citrate. The second is that the pathogenic micro-organism found in the excreta belonged to the *Salmonella* group. It is an interesting fact that, in every case of severe

hæmorrhage and anæmia the author has had, the pathogenic micro-organism found in the excreta belonged to the *Salmonella* group. This applies even to pernicious anæmia, which is not to be separated from so-called "Addison's anæmia" and other unnamed anæmias. In the author's experience the *Bacillus Welchii*, although not uncommon in this type of case, does not play the rôle generally assigned to it.

Case 131

A woman, aged thirty-eight, had had anæmia since childhood and had been bed-ridden for over nine months. The patient's father died of chronic bronchitis, and the mother of pernicious anæmia. The patient had always suffered from chilblains, she had had three attacks of pneumonia, one of brachial neuritis, and one of ptomaine poisoning when aged eighteen. The patient was very anæmic, and too weak to get out of bed, she had blue sclerotics, central cupping of both optic discs, and a fissured tongue with hypertrophied papillæ. All the teeth had been removed, as they were lacking enamel. She had hyper-extended and wide-angled elbows; menstruation began at the age of thirteen; for the past eight months she had had only two periods, each lasting for over a fortnight. She had never been pregnant. There was a rise of temperature every night of one to two degrees. The pulse was 114, and the blood-pressures registered 120 and 55 mm. of Hg. respectively. The abdomen was too tender to allow of a proper examination. The pathogenic micro-organism found in the excreta was the *Bacillus Morgan* (90 per cent.) and the blood-count and blood-picture were as follows:—

Red blood-corpuscles	= 2,800,000 per cmm.
White blood-corpuscles	= 4,400 „
Hæmoglobin	= 40 per cent.
Colour index	= 0.7
Polymorphonuclear leucocytes	= 60 per cent.
Lymphocytes	= 27 „
Large mononuclear leucocytes	= 2 „
Eosinophile leucocytes	= 2 „

No nucleated red blood-corpuscles.

Suspension stability of the red blood-corpuscles	= 0.4 c.c.
Refractive index of the serum	= 1.3478.
Percentage of the blood-sugar	= 0.118 grm.
Percentage of the blood-urea	= 35 mgrm.

Ultra-microscopic picture of the serum = Fair number of particles moving with a fair percentage of giant particles, many of which had a halo around. There were some very refractile giant particles, ringed particles and giant-particled clumps precipitated.

The patient was cut off butcher's meat, eggs and milk, she had a series of treacle enemata, took iron and malt internally, and received injections of Sup. 468 and of the fæcal vaccine. Before the injections of the vaccine were made the colon was washed out. The patient improved enormously and was fit enough fourteen months later to do everything she wanted. A re-examination of the blood at this time showed a normal blood-count and blood-picture.

There are many points of interest in this case. First, the patient's mother died of pernicious anæmia. Secondly, the patient had had an attack of ptomaine poisoning, which was undoubtedly an exhibition of the activity of the *Salmonella* in the intestinal tract. Thirdly, all her teeth lacked enamel, an epithelial defect met with in the last-born of a large family, and, in the author's experience, the victim has always been a girl. Fourthly, the rise of temperature was a sign of the continued activity of the *Salmonella*, which once again was the *Bacillus Morgan*. Fifthly, the patient had been in two general hospitals for some weeks at a time, and discharged worse than when she entered, without it being possible to assign a label to her condition. While in the hospitals, test-meals showed the complete absence of hydrochloric acid, but taking this acid internally over a long period of time did not benefit the patient in any way.

Case 132

A man, aged sixty-five, had had pernicious anæmia for two months, during which he had been treated with arsenic, liver and stomach, without benefit. For the past month the temperature had swung between 101° and 102° F., and at the time of examination, three days before he died, he had purpura and ileus, and had lost control of the bladder and rectum. The blood-count and blood-picture were as follows :—

Red blood-corpuscles	= 1,100,000 per cmm.
White blood-corpuscles	= 1,200 „
Hæmoglobin	= 20 per cent.
Colour index	= 1.3
Polymorphonuclear leucocytes	= 51.7 per cent.

Lymphocytes = 40.0 per cent.

Large mononuclear leucocytes . . . = 5.0 „

Eosinophile leucocytes = 3.3 „

Red blood-corpuscles showed a considerable degree of anisocytosis and poikilocytosis. There were a few normoblasts and a little polychromasia.

Suspension stability of the red blood-corpuscles = 8.2 c.c.

Refractive index of the serum = 1.3462.

Percentage of the blood-sugar = 0.162 grm.

Percentage of the blood-urea = 30 mgrm.

Ultra-microscopic picture of the serum = Fair number of tiny dull particles moving with a few giant particles and ringed particles. There was a fair amount of precipitation *en masse* of the tiny particles with some giant particles and ringed particles. The Brownian movements of the particles were sluggish.

Wassermann reaction = Negative.

The patient had contracted syphilis four years previously and was treated thoroughly for two years. The great interest of the case lies in the enormous reduction in the suspension stability of the red blood-corpuscles, the lowest the author has ever experienced.

(c) The Duodenum

There are only two points to which it is necessary to draw attention in this section, the one being ulceration of the gut, and the other diverticulosis. A duodenal or post-pyloric ulcer occurs almost invariably in the first part, which is anatomically and embryologically inseparable from the pyloric portion of the stomach. A duodenal ulcer arises in the same way as a gastric ulcer, that is to say, it is secondary to changes undergone by the protein particles in the vessels supplying the area involved.

In support of this view are the facts that a duodenal ulcer can arise as a result of shock, and that a correction of the abnormal chemico-physical changes relieves the symptoms and renders an operation superfluous, provided there has not been too much delay in putting the patient under treatment. Shock is the clinical manifestation *par excellence* of protein hydration, and an ulcer is formed when the hydrated protein particles are precipitated in the blood-vessels of the area involved, causing dehydration and degeneration of the

protein particles constituting the protoplasm of the cells supplied by these blood-vessels. It depends upon the degree of hydration, where the protein particles in the plasma are precipitated. The precipitation may take place in the peri-capillary lymphatic vessels, in the capillaries, or in the veins. But, in all cases, there is a constriction of the arterioles and arteries, and it is probably to this last change, which means loss of arterial blood to the part, that the necrosis is due. When hydration occurs in the veins, gelation occurs as well, thus accounting for the venous thrombosis which may take place in the tissues surrounding the ulcer. The author has not had sufficient material for examination to enable him to say whether the degree of hydration affects the characteristics of the ulcer. As the changes the protein particles in the plasma undergo to cause an ulcer are the result of congenital disease, the reader will probably not be surprised to learn that a duodenal ulcer is preventable, and can be healed, if caught sufficiently early, by treatment aimed at ridding the patient of his chronic intestinal intoxication. Not only is an operation seldom necessary, but also, in the author's experience, the after results of operating are not as satisfactory as reported. It is not difficult to see why this should be the case when it is realised that short-circuiting never touches the cause and can do no more than palliate the symptoms. The following are a few illustrative cases :—

Case 133

A man, aged thirty, had suffered from severe attacks of abdominal pain eleven years before his duodenal ulcer perforated. He was operated upon, and was relieved for eighteen months, when the pains began again. The patient's maternal grandmother died of intestinal obstruction, his mother was supposed to be suffering from Addison's disease, his father died of carcinoma of the rectum, and two brothers died of phthisis. The patient was a typical example of congenital disease; he had chilblains summer and winter alike, his pulse was 104, and the blood-pressures registered 105 and 55 mm. of Hg. respectively. The abdominal pain was worse than it had ever been, constipation had become most troublesome, and the patient was unable to follow his occupation. The sigmoid colon was contracted, there was marked tenderness in the flexure regions, and the ascending colon and cæcum were dilated. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found both in his and his mother's excreta was the *Bacillus fecalis alkaligenes* (75 and 50 per cent. respectively). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3498.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 31 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some giant particles and a few ringed particles. There were a few giant particles and giant-particled clumps precipitated.

The patient avoided butcher's meat, eggs and milk, his colon was washed out as far back as the ileo-cæcal valve, he took lacto-dextrin internally, and was given injections of the fæcal vaccine. The abdominal pains were first accentuated by the colonic lavage and then disappeared completely. The patient put on nearly two stone in weight, was working as a commercial traveller six months later, and two years later was better than he had ever been. On the return of pain after the operation the patient had been advised to submit himself to operation again.

Case 134

A man, aged forty-five, sought advice about undergoing an operation for duodenal ulcer. The patient's father died of cancer of the stomach, and the mother had been operated upon for carcinoma of the rectum. The patient had had lymphatic glands removed from his neck as a child. He had also had his tonsils and appendix taken out. He suffered from rheumatism, had dental plates in both jaws, the tongue was furred and fissured, the nails were very ridged, and there was marked central cupping of both optic discs, with venous congestion. The pulse was 92, and the blood-pressures registered 115 and 80 mm. of Hg. respectively. The patient complained of depression and insomnia, he had generalised arterio-sclerosis, and the lungs were emphysematous. The left colon was contracted, there was tenderness in both iliac fossæ and both hypochondria, and the ascending colon and cæcum were dilated. The urine gave a positive reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, the pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (75 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·7 c.c.
Refractive index of the serum	= 1·3490.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-uræa	= 21 mgrm.

Ultra-microscopic picture of the serum = Few particles moving with some refractile giant particles, ringed particles and small clumps. There were some refractile giant particles, ringed particles and giant-particled clumps precipitated. The Brownian movements of the particles were sluggish.

The patient hesitated between undergoing the treatment advised and operation. He ultimately chose the latter and died one week later.

Case 135

A man, aged fifty-two, sought advice for a duodenal ulcer. The patient suffered from chilblains and cyclical vomiting as a child, he had had eczema off and on for thirty-one years, had been impotent for over twenty years, and had had rheumatic fever three times. He was tall and thin, and had a sallow complexion, the ears protruded, the elbows were wide-angled and hyper-extended, and he could not stand with his knees and feet together at the same time. All the teeth had been removed, the tongue was furred, the optic discs were small and mal-developed, and he had a high degree of hypermetropic astigmatism. The pulse was 80, and the blood-pressures registered 110 and 90 mm. of Hg. respectively. The left colon was contracted, and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the *Bacillus proteus valeriei* (15 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.15 c.c.
Refractive index of the serum	= 1.3481.
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 38 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving. There were a fair number of giant-particled clumps, both moving and precipitated.

The patient was dieted, had a course of colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of Sup. 468 and of the fæcal vaccine. He improved enormously and all signs and symptoms of the duodenal ulcer disappeared.

Case 136

A man, aged forty-two, had had treatment in a clinic for a gastric ulcer three years previously, and now presented all the signs and symptoms of a duodenal ulcer. The patient lost his mother from Bright's disease, aged

forty-two, a sister from the same condition, aged forty-five, and a brother from cholecystitis, aged forty-six. The patient suffered from chilblains, he had chronic nasal catarrh, and had passed sugar in the urine for over twelve years. The lower jaw was narrowed laterally, all the molars had been either extracted or stopped, the tongue was furred and fissured, there was central cupping of both optic discs and a high degree of myopic astigmatism. The pulse was 78, and the blood-pressures registered 115 and 80 mm. of Hg. respectively. There was evidence of a chronic colitis, and marked tenderness in both iliac fossæ. The pathogenic micro-organism found in the excreta was the *Bacillus acidilactici* (10 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3495.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, with a fair percentage of giant particles, each with a halo around, and some ringed particles. All were very refractile. There were some giant particles and ringed particles pre- cipitated as well as a few giant-particled clumps.

The patient cut out butcher's meat, eggs and milk from his diet, had twelve colon wash-outs, and then two injections of the vaccine in doses of 250,000 and 500,000 on two successive days.

Six months afterwards he was perfectly well and the urine did not reduce Nylander's reagent. Later the patient began to eat the articles of food he had avoided, and allowed himself to become constipated again, with the result that all the symptoms returned, and sugar re-appeared in the urine, although the blood-sugar remained at 0.100 grm. per cent.

Diverticula of the duodenum are of more academic than clinical interest, because they seldom give rise to symptoms and cannot be diagnosed with certainty without an X-ray examination or an operation. The interest lies in the fact that some are definitely congenital, although most are acquired. The congenital diverticula are almost certainly the result of hyper-activity of the vagus, caused most probably by irritation of the vagus centre *in utero*. This form of diverticulum involves all the coats, and is definitely not inflammatory in origin. The acquired form is a bulge of the undamaged layers of the gut through the layers damaged by inflammation occasioned by the precipitation of hydrated protein particles in that part of the intestinal wall where the vessels enter.

(d) The Liver

In this section it is not necessary to make more than a few generalisations, as the changes the liver undergoes by reason of the altered protein particles in the plasma were described in the previous volume. The liver is the largest organ in the body, and although its functions may be legion, they are as simple as they are numerous. The reason why the various activities have always been regarded as puzzles is because they have been viewed as being wholly hepatic and separable from the rest of the body. In experimental work the liver receives much attention, and it is held responsible for many of the phenomena observed for which the experimenter has no rational explanation. Invoking the aid of the liver is merely a manoeuvre, and all it does is to render the problem a little more incomprehensible than it was before. No better example can be given than the current explanation of shock. The intoxicant, or "primary antigen" as it is called, selects the liver and causes this organ to throw into the blood-stream a histamine-like substance or secondary antigen which actually produces the shock. In endeavouring to neutralise the primary antigen the liver uses up its glycogen, and prescribing glucose makes good this loss. In the first place, the intoxicant does not always select the liver, and even should it do so the protein particles in the plasma are damaged long beforehand. In the second place, no cells secrete a histamine-like substance. In the third place, there is just as much glycogen in the liver after as before the intoxicant begins its work. It so happens that when the protein particles are subjected to a profound degree of hydration the protoplasm of the liver cells undergoes a like change. In hydration the carbohydrate planet is drawn nearer to the protein sun or nucleus, where it forms a complex colloid combination whereby its carbohydrate nature cannot be detected. The administration of glucose does not increase the amount of glycogen in the liver, it merely breaks up the hydrated protein particles which produced the shock. In clinical work, attention is seldom focussed on the liver. The signs and symptoms of disease presented are seldom hepatic, a somewhat peculiar fact considering how widespread is chronic intestinal intoxication and how common is the saying "the liver is out of order." Numerous tests have been devised to estimate liver function, but the foundation upon which they are based is false, and none succeed in throwing any light upon what is happening in and to the liver. This is just as well because none but the grossest defects can be confirmed by clinical means, and these require no tests. Also, when the result of the tests points to dysfunction, no suggestions are forthcoming as to how to overcome the same, and the observer finds himself in a position where, in spite of his

action, he has to retreat instead of advancing. No case illustrates the above better than the following :—

Case 137

A man, aged fifty-nine, was knocked down by a motor car and sustained bruises in the right thoracic region. Owing to persistent pain he remained in bed for five days, after which he attended to his duties. Five weeks later he had rigors and a painful cough, with expectoration of rusty sputum, which state of affairs lasted for about a week. But the patient continued to feel ill and the temperature remained high. A clinical examination suggested an abscess at the base of the lung, in the sub-phrenic region, or in the liver, but, as the question of compensation arose, it was necessary to make further examinations. This necessity was increased by the fact that the patient was a chronic alcoholic. He was a typical example of familial chronic intestinal intoxication, he had suffered much from angio-neurotic oedema, he had bilateral *Arcus senilis* and a Dupuytren's contraction affecting the ring finger of the right hand. At the time of examination the temperature was 102.5° F. The pulse was 104, and the blood-pressures registered 105 and 55 mm. of Hg. respectively. The urine contained protein. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 4.7 c.c.
Refractive index of the serum	= 1.3468.
Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 76 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and these were giant particles, ringed particles and giant-particled clumps. There were nearly as many particles precipitated. The Brownian movements were sluggish and the precipitation increased with time.

An X-ray examination merely confirmed the clinical one and threw no further light upon the location of the abscess. Various liver and renal tests were performed with negative results. The blood-picture showed a degree of dehydration such as is encountered in cases of severe sepsis, and consequently it was decided to operate. Operation showed that the accident had caused a rupture of the liver and a contusion of the right kidney. There was a large sub-diaphragmatic blood-clot, and another at the apex of the right kidney. The liver was honeycombed with abscesses. The patient did not survive the operation.

The region from the base of the right lung to the liver is the most confusing

in the body, and all the up-to-date aids to diagnosis usually fail to help the clinician. The following is a case in point, and it, moreover, introduces the subject of intestinal infection and the liver :—

Case 138

A woman, aged fifty-five, was well until six months previously, when she had an attack of fever, which was diagnosed as influenza. It was followed by neuralgia at the back of the neck, which continued until an attack of pleurisy involved the base of the right lung. This was quickly followed by pneumonia, and blood appeared in the sputum and in the stools. A diagnosis of tuberculosis was made, although no tubercle bacilli were to be found in the sputum. At the time of examination the patient looked ill, was slightly jaundiced, and had clubbed fingers. She had lost over two stone in weight. The clinical diagnosis arrived at was an abscess at the base of the lung, in the sub-diaphragmatic area, or in the liver. An examination of the excreta revealed living amœbæ, and a further examination of the sputum showed liver cells, blood, fibrous and elastic tissue. The diagnosis was obviously one of amœbic abscess of the liver, which had penetrated the diaphragm and burst into the base of the right lung. The blood-picture was as follows :—

White blood-corpuses	= 30,000 per cmm.
Polymorphonuclear leucocytes	= 85 per cent.
Lymphocytes	= 10 „
Large mononuclear leucocytes	= 3 „
Eosinophile leucocytes	= 2 „
Suspension stability of the red blood-corpuses		= 2.0 c.c.
Refractive index of the serum		= 1.3478.
Percentage of the blood-sugar		= 0.093 grm.
Percentage of the blood-urea		= 31 mgrm.
Ultra-microscopic picture of the serum		= Very few particles

moving, and these were giant particles, ringed particles and clumps. There were some giant particles, ringed particles and clumps precipitated. The Brownian movements were sluggish and the precipitation increased with time.

The patient was treated with emetine and bismuth iodide internally, and received injections of emetine hydrochloride. She made an uneventful recovery. The patient had lived many years in Chile and had doubtless contracted the infection there, but how did, and do, the amœbæ reach the

liver ? The route by which micro-organisms reach the liver from the intestines is not certain, although evidence is in favour of their travelling *viâ* the blood-stream, and the lymphatic vessels. In support of this view is the not uncommon occurrence of periostitis caused by typhoid bacilli in cases of typhoid cholecystitis, and the fact that micro-organisms which reach the uro-genital tract from the intestines travel *viâ* the circulation, and never from the bladder along the ureters to the pelves of the kidneys.

After the amœbæ, the intestinal micro-organisms showing a preference for the liver, or rather for the gall-bladder, are the typhoid bacilli. Paratyphoid bacilli may likewise cause cholecystitis and cholelithiasis, but more rarely, and the various dysentery bacilli still more rarely. The following case is of particular interest and brings out points for discussion :—

Case 139

A man, aged fifty-nine, was seized with acute abdominal pain, and upon examination, it was obvious that the gall-bladder was enlarged. Operation was advised but deferred for five days, when it became an emergency, the gall-bladder having perforated. At the operation it was found to be a bag of pus communicating with an abscess behind, and containing stones. A month later the patient developed cystitis and *Bacillus Morgan* was found in the urine. On account of a persistent rise of temperature, the excreta and blood were examined six weeks after the operation. The pathogenic micro-organisms found in the excreta were the *Bacillus para-typhosus* (*B*) (75 per cent.) and the *Bacillus fecalis alkaligenes* (5 per cent.). The patient's serum agglutinated his own and a stock *Bacillus para-typhosus* (*B*) up to 1 in 250, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 2.6 c.c.
Refractive index of the serum	= 1.3472.
Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 45 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and these were giant particles and ringed particles. There were more particles precipitated as giant particles, ringed particles and giant-particled clumps. The precipitated particles were very refractile.

The patient took hexyl-resorcinol internally and received one injection (1.0 c.c.) of the washings made from 5,000 million of the pathogenic micro-

organisms found in the excreta. There was a reaction for one day, after which the temperature dropped for good, and the cystitis cleared up.

The first point for discussion is the appearance of different non-lactose fermenters, in different parts of the body, in the same individual. In most cases of acute and sub-acute intestinal intoxication the micro-organism found in the uro-genital tract is the *Bacillus coli communis*. This is particularly the case when the non-lactose fermenter, in the fæces, causing the activity, is one not particularly virulent, such as the *Bacillus fæcalis alkaligenes*. When the non-lactose fermenter is of a more virulent type, such as the bacillus of epidemic jaundice, the micro-organisms found in the uro-genital tract may be those which ferment lactose but, in virulence, lie midway between the *Bacillus coli communis* and the mild non-lactose fermenters; such micro-organisms are the *Bacillus acidi lactici* and the *Bacillus lactis aerogenes*.

In cases where a virulent non-lactose fermenter prevails in the fæces a virulent non-lactose fermenter may attack the uro-genital tract, as in the case reported. All this suggests that there is a grading of the mutative forms of the *Bacillus coli communis*, and that site has some influence thereupon.

The second point of interest is the fact that a nurse in charge of the case developed a pyrexia, and after she had been operated upon for appendicitis, and the pyrexia still persisted, para-typhoid bacilli were found in her excreta. Two questions immediately arise: did the nurse harbour para-typhoid bacilli before she had the case, or did bacilli pass from the patient to the nurse?

In the author's opinion, the answers to these questions are as follows: para-typhoid bacilli are mutation forms of the *Bacillus coli communis*. The mutation takes place periodically, and is influenced by many factors. It varies, not only from day to day, but also in the individuals in which it takes place. When excreta from different patients are examined every day, year in year out, the observer cannot help being struck by the fact that one type of non-lactose fermenter prevails at one time and another type at another time. The inevitable conclusion has to be drawn that the *Bacillus coli communis* can mutate into any pathogenic form at any time, and within any space of time. The two main factors regulating prevalence are climate and food, but exactly how they act it is not possible as yet to say.

While the epidemic of *Psittacosis* was prevalent in the winter 1929-1930, the prevailing pathogenic micro-organisms found in the stools of all patients seeking advice at the time were the *Bacillus fæcalis alkaligenes* and the *Bacillus Friedländer*. During May, 1930, when the above case was examined, the prevailing micro-organism was the *Bacillus para-typhosus*, and in one day this

bacillus was found in six specimens of excreta from different patients in the metropolis and in the country. During the para-typhoid epidemic traceable to milk supplied by a certain farm in Ireland no para-typhoid bacilli were found in the milk, and para-typhoid bacilli were grown from the excreta of those who had neither drunk the milk nor been in contact with those who had. Once a mutation into a pathogenic form has occurred, and a certain degree of pathogenicity has been acquired, the activity resulting therefrom may be such as to cause the same mutation to occur in others. Experimentation points against the actual conveyance of infection from person to person. It is possible that the ingestion of contaminated foodstuffs may lead to the implantation in the victim of the contaminating micro-organism, but, even when this happens, it is very doubtful if the infection occurs primarily in the intestinal tract. It is more probable that the typhoid or para-typhoid bacilli enter the blood-stream *via* the mouth, the tonsils in particular, and reach the intestines in this way. It would appear to be more common for another morphological form of the pathogenic micro-organism, such as the ultra-microscopic form, to find other hosts and thus spread infection, than for the bacilli themselves to be disseminated. But, in the author's opinion, the most common way of all is for the activity resulting from the sudden increase of pathogenicity to occasion the same mutation to occur in others.

In the case in point the author holds that neither the para-typhoid bacilli, nor another morphological form, travelled from the patient to the nurse, but that the activity resulting from the pathogenicity of the para-typhoid bacilli in the patient occasioned the same mutation to occur in the nurse. Several people looked after the patient, but in only one did the mutative form cause symptoms. This does not imply that a similar mutation did not occur in the others, but it leads to the question: why is one selected and another neglected? The author suggests that it is something other than the direct passage of bacilli which causes such infections as are being discussed. Although it is impossible to give absolute proof of all the statements made below, they are based upon numerous observations made by the author in his laboratories. It would appear that the *Bacillus coli communis* cannot mutate into such pathogenic forms as the *Bacillus para-typhosus* unless a simpler mutation has already been effected. In other words, there are many steps taken, or many intermediate and less pathogenic bacteria formed, in the mutation of the *Bacillus coli communis* to the *Bacillus para-typhosus*. Consequently the person who is most likely to fall a victim will be the one in whose intestinal tract mutation was already well advanced before the activity began to play

its part. This part varies in degree in different sites, and additional explanation is forthcoming for the occurrence of different mutation forms of the same bacillus in the intestinal tract, uro-genital tract and circulatory tract respectively. The activity is the same whether it occasions a disease-producing mutation in one victim as in the nurse in the above case, or death of the mutative form in the original victim, as evidenced by the beneficent effect the washings of the bacilli, used as vaccine, had on the patient. Whether the activity is harmful or beneficial depends upon the dose and strength of the activity travelling at the time, and upon the individuals affected by it. The smaller the dose and the more often repeated, the greater the protective action of the activity, and *vice versâ*. This explains why doctors, nurses, etc., who are in constant touch with patients, more often than not, escape infection. The ones who fall victims are those where the individual, rather than the activity, is at fault, those where the mutation in the intestinal tract has advanced so far as to cause any activity to act as a stimulus to still further mutation, rather than in a lethal manner upon the micro-organisms already mutated.

The whole subject either narrows itself down to a matter of degree, or else, the activity produces what amounts to hydration on the one hand, and dispersion on the other, the former carrying the mutation further, and the latter causing it to retrogress. This discussion shows how epidemics are produced, and it must stimulate the thinker to wonder if the notification of infectious diseases, and the segregation of the victims are wise or desirable. All that is really needed is adequate hygiene, and the sole aim should be to get everybody's intestinal tract into such a condition as to enable the *Bacillus coli communis* to reign supreme.

(e) The Spleen

Little is known about the functions of the spleen, and should full knowledge ever be acquired, it will probably be found that the organ is no more than a large lymphatic gland wherein the various corpuscular elements of the blood are manufactured.

Within the last twenty years the spleen has been brought into prominence by surgeons who have removed the organ for a variety of conditions. It was merely enlargement of the organ which led in the first instance to splenectomy, and because its removal caused no apparent harm, and in some cases was followed by an improvement in the clinical condition, it has been accredited with playing a causative rôle in conditions with which it is really not connected.

The facts that a normal spleen can be removed without harming the individual, and that benefit may follow removal in conditions in which splenomegaly is merely a result and not a cause, go far to support the opening remark.

Splenectomy has found most favour in cases of so-called "splenic anæmia." There is no such clinical condition as splenic anæmia, and if the spleen happens to be enlarged in certain cases of anæmia, the cause of both conditions is the same, and the splenomegaly has nothing to do with the anæmia. In cases of so-called "Banti's disease," which falls into the category of splenic anæmia, the patient may fail to give a blood-picture of anæmia, and the spleen may diminish in size if the cyclical change responsible for the enlargement now occurs, and if an attempt is made to get rid of the cause, as evidenced by the following case :—

Case 140

A woman, aged fifty-nine, complained of attacks of acute prostration, associated with abdominal pain, nausea, vomiting and pyrexia, for five years before the author saw her. A year after the attacks began one was followed by jaundice and, as the liver was found to be enlarged, a laparotomy was performed. The liver was nodular, each lobule was marked out with a dark centre surrounded by pale tissue, and the lymphatic glands in the free edge of the gastro-hepatic omentum were enlarged. A small piece of liver was removed and also the appendix. The section of the liver showed infiltration of the portal canals, and peri-cellular cirrhosis, with degeneration of the liver cells here and there. Two years later the patient was stung by a wasp. She became very ill, and developed poly-articular rheumatism, and rheumatic nodules, in various parts of the body. The following year the spleen was found to be much enlarged and, soon after, the patient developed ascites, and had attacks of epistaxis. The patient's father and paternal grandfather were chronic asthmatics, the mother and one brother each succumbed to an operation performed for the removal of gall-stones, and one sister died of infective endocarditis. The patient used to suffer from hay-fever and asthma, which cleared up when the abdominal trouble began. She had had migraine, and was troubled with insomnia and bad dreams. She also had attacks of dysidrosis, and intense itching of the palms and soles. The climacteric occurred at the age of forty-one. The patient was anæmic, her hair was white, all teeth had been removed, the tongue was dry, furred and fissured, and there were varicose veins. The pulse was 114, and the blood-pressures registered 140 and 90 mm. of Hg. respectively. The left colon was spastic, there was a colonic loop,

and the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligenes* (75 per cent.) and the blood-count and blood-picture were as follows :—

Red blood-corpuscles	= 4,480,000 per cmm.
White blood-corpuscles	= 4,000 „ „
Hæmoglobin	= 90 per cent.
Colour index	= 1
Polymorphonuclear leucocytes.	= 66.25 per cent.
Lymphocytes	= 26.25 „ „
Large mononuclear leucocytes	= 4.00 „ „
Eosinophile leucocytes	= 3.50 „ „
Suspension stability of the red blood-corpuscles	= 1.4 c.c.
Refractive index of the serum	= 1.3510.
Percentage of the blood-sugar	= 0.131 grm.
Percentage of the blood-urea	= 22 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, with some giant particles, ringed particles and giant- particled clumps. Many particles, giant particles and giant-particled clumps precipitated.

The patient was dieted, and taught to give herself treacle enemata, because colonic lavage, owing to the kink, could not be satisfactorily performed. She took internally iodine, ichthyol and thyroid, and received injections of contra-mine, and of the fæcal vaccine. Her condition improved, the epistaxis ceased, the ascites cleared up, and the liver and spleen returned almost to their normal size. But the improvement had set in before the treatment was begun, as shown by the following blood-count which had been made six months before the above.

Red blood-corpuscles	= 4,460,000 per cmm.
White blood-corpuscles	= 2,000 „ „
Hæmoglobin	= 88 per cent.
Colour index	= 1
Polymorphonuclear leucocytes.	= 40.6 per cent.
Lymphocytes	= 45.8 „ „
Large mononuclear leucocytes	= 7.2 „ „
Eosinophile leucocytes	= 6.4 „ „

Banti's disease, or interstitial splenitis, is an overgrowth of mesenchymatous

tissue occurring as a sequence of a long-continued dehydration of the protein particles in the portal system. The dehydration may be of the gelation type, and when this is the case venous thrombosis is almost certain to occur, but veins other than the splenic vein may be the first to be attacked. In the case just described, for example, the hepatic part of the portal circulation was involved before the splenic. When the chemico-physical change of hydration of the protein particles in the portal circulation prevails, and occurs as a cyclical change to dehydration, one of the first effects is a retrogression or degeneration of the already hypertrophied interstitial tissue. As a result the organ diminishes in size and, from the clinical and blood-pictures of the case recorded, this is what had undoubtedly occurred. The chemico-physical changes of dehydration and hydration go hand in hand, although one change prevails at one time, and the other at another time. As the patient had had hay-fever and asthma, hydration was the chemico-physical change to cause the first manifestations of disease. These symptoms vanished when the hydration gave way to dehydration, and the latter caused interstitial hepatitis and splenitis. When hydration prevailed again, the hypertrophied interstitial tissue became atrophic and the signs of Banti's disease began to disappear. Hydration may prevail throughout, in which case the parenchyma of the organ attacked is involved. Should the spleen be attacked a variety of changes occur, according to the degree of the hydration prevailing, and to whether there is a concomitantly occurring dehydration or not. In all cases there is a splenomegaly, the enlargement being roughly of three types, according to whether the hydration is mild, medium or severe.

In the first type the enlargement is caused by an over-development of lymphocytes, in the second type of plasma cells, and in the third type of endothelial cells. In the last case the endothelial cells may undergo a lipid change to produce the clinical condition known as "Gaucher's splenomegaly." This form of splenomegaly is a familial condition, but a somewhat similar condition may be produced in animals by drug intoxication. The endothelial cells may also undergo a malignant change, when a form of splenomegaly is produced akin to the skin condition and lymphatic gland condition, known as "*Mycosis fungoides*" and "Hodgkin's disease" respectively.

The more the hydration is confined to the spleen, the better the result following splenectomy. The benefit derived from the operation is due not to removal of the spleen, but to the removal of the hydrated protein particles, one of the effects of which is to start the cyclical change of dehydration of the hydrated protein particles in other parts of the body. When the hydration

is more general, removal of the spleen is without effect. The same applies to thyroidectomy in cases of exophthalmic goitre. The benefit following removal of a portion of the thyroid gland is not due to checking the output of thyroid secretion into the circulation, as is usually thought, but to the removal of the hydrated protein particles in the thyroid area, and to the cyclical change of dehydration which the hydrated protein particles, particularly those precipitated in the brain and heart, undergo. The reader would do well to call to mind that in the worst cases of exophthalmic goitre the thyroid gland is so disorganised as to be unable to secrete a hormone.

Splenectomy is advised in cases of so-called "essential thrombopenia" and "thrombocytopenic purpura," with the object of restoring the numbers of the blood-platelets. But, if the author's view is correct that blood-platelets are merely agglutinated protein particles, another reason is adduced to show that the operation is unnecessary. There is nothing peculiar in the type of purpura referred to, and although splenectomy may be followed by a cessation of the hæmorrhages, equally good, if not better, results may be obtained by removing the chronic intestinal intoxication, and by correcting the abnormal chemico-physical changes the protein particles undergo to produce the purpura and splenomegaly. As a matter of fact, the spleen is not enlarged in the majority of the cases of purpura, and in most cases the purpuric lesions are widespread. Hæmorrhage from a vessel in such cases is only a sequence to hydration, and when hydration is general splenectomy does more harm than good. Summing up the position, splenectomy would appear to be called for only in cases of trauma, cyst formation and new-growth.

(f) The Pancreas

The chemico-physical changes the protein particles undergo in the portal system to occasion the conditions described as occurring in the liver and spleen may cause similar changes in the pancreas. But the pancreatic condition which comes most to the fore is an acute one, and is usually secondary to a cholecystitis. Acute pancreatitis may also occur *de novo*, and as the condition is far from common, the following case is of interest.

Case 141

A man, aged thirty-seven, after recovering from an attack of *Delirium tremens*, developed an acute pain in the upper part of the abdomen. As the patient presented all the signs and symptoms of an acute abdomen a laparo-

tomy was performed. The operation revealed a normal liver and gall-bladder, an œdematous omentum, a septic pancreas, with commencing fat-necrosis, and three pints of blood-stained fluid free in the abdominal cavity. As there was a continued pyrexia, the fæces and blood were examined three weeks later. The only abnormal bacillus found in the excreta was the *Bacillus acidilactici*, and this was atypical in that it was motile. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 6.1 c.c.
Refractive index of the serum	= 1.3469.
Percentage of the blood-sugar	= 0.143 grm.
Percentage of the blood-urea	= 15 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving. There were some particles, giant particles and giant-particled clumps precipitated <i>en masse</i> .

From the great reduction in the suspension stability of the red blood-corpuscles the author thought it probable that the primary pancreatitis was the result of an acute gelation of the protein particles, occurring as a cyclical change to the hydration responsible for the *Delirium tremens*. Consequently Sum. 468 in 0.001 grm. doses was injected intra-muscularly, daily for ten days, and followed by two injections of Sup. 36. The patient recovered.

As with the liver and kidneys, tests have been devised to estimate the functional capacity of the pancreas, and they are likewise equally valueless. There are tests for detecting deficiency of both the external and internal secretions. The former are useless, because it is impossible to collect, in anything like pure form, the so-called "carbohydrate-splitting," "protein-splitting" and "fat-splitting ferments." In the first place, there are no such bodies as ferments, and the so-called "splitting" process is achieved by substances chemically identical, but physically slightly different from the material analysed. Secondly, it is not known whether the bodies referred to as ferments are three distinct substances, or the same substance in slightly different forms, the difference being regulated by the material analysed at the time. Thirdly, it is necessary to collect the duodenal contents, a procedure to which patients rightly object, particularly when the results throw a false light, if any, upon the clinical condition presented. The third difficulty is overcome by estimating the amount of diastase in the urine; but this examination is no test of pancreatic efficiency, because there is no such substance as diastase, and all that is regarded as diastase does not come from the pancreas.

The result of the examination of the fæces for steatorrhœa may suggest a lesion of the pancreas, but it by no means confirms the diagnosis, because if this is present it may be congenital, and in any case is liable to occur, particularly in children, when hydration is well to the fore.

The test most usually employed to detect deficiency of the internal secretion is that known as "Loewi's test." It is regarded as positive when the pupil dilates with a local application of two drops of a 1 : 1000 solution of adrenalin. When there is a deficiency of internal secretion a state referred to as "hypo-insulinism" is produced, which in turn causes a relative hyper-adrenalism. This hyper-adrenalism is supposed to increase the sensitivity of the sympathetic nervous system, thereby causing the pupil to react to the instillation of adrenalin. The test is of no value; it may be positive whenever acute dehydration of the protein particles is the abnormal chemico-physical change prevailing. There is no relationship whatever either between acute dehydration and hypo-insulinism, or between chronic hydration and hyper-insulinism. It is not necessary to reiterate here what has been already written in these volumes regarding insulin, but it is as well to make a few remarks regarding what is being so commonly referred to in medical literature as "hyper-insulinism" or "idiopathic hypo-glycæmia" and to bring forward a few new points which support the author's view that *Diabetes mellitus* is merely a clinical expression of chronic dehydration. There is no such condition as hyper-insulinism, and the term "idiopathic hypo-glycæmia" is superfluous, because the low percentage of the blood-sugar is only one of several manifestations of protein hydration, and one which plays no part in producing the clinical picture presented. The hydration is caused by a chronic intestinal intoxication, and not by an over-production of insulin. These points are illustrated, and others are brought forward in the cases reported below.

Case 142

A man, aged fifty-nine, had acute attacks of abdominal pain which had been diagnosed as biliary colic. He was on the point of having his gall-bladder removed, but sought other advice first. The patient was a typical example of familial chronic intestinal intoxication, he had suffered from migraine and furunculosis, had generalised arterio-sclerosis, and both fingers and toes were affected by Raynaud's phenomenon. He complained of loss of memory. His appendix had been removed eight months previously. Severe shock followed the operation, and he was more or less unconscious for five days. He lost his only child, a boy, aged sixteen, from congenital heart

disease. The pulse was 84, and the blood-pressures registered 120 and 65 mm. of Hg. respectively. An examination of the abdomen showed that the patient had a sub-acute colitis, and this suggested that the so-called attacks of biliary colic were attacks of acute colitis of the hepatic flexure. The urine gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3448.
Percentage of the blood-sugar	= 0·062 grm.
Percentage of the blood-urea	= 48 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with some giant particles, ringed particles and a few clumps. There were some giant particles, ringed particles and clumps precipitated with a tendency towards the formation of precipitation <i>en masse</i> .

The patient cut out butcher's meat, eggs and milk from his diet, had his bowels opened twice a day, and underwent a course of colonic lavage. The attacks ceased, and the blood-picture two years later was as follows :—

Suspension stability of the red blood-corpuscles	= 0·1 c.c.
Refractive index of the serum	= 1·3461.
Percentage of the blood-sugar	= 0·081 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a fair number of giant particles. There were many giant particles and giant particled-clumps precipitated, with a tendency towards the formation of precipitation <i>en masse</i> .

The attacks were colonic in origin, and in the author's experience, in over ninety out of every hundred cases diagnosed as cholecystitis, biliary colic, etc., the trouble lies in the hepatic flexure of the colon, and not in the gall-bladder.

The patient need not have had his appendix removed, and, judging from the shock which followed the anæsthetic, it is unlikely that he would have survived another operation, an opinion upheld by the blood-picture. This shows marked hydration, consequent upon a long continued dehydration, and before the first operation was performed the hydration was sufficiently

pronounced as to cause almost fatal shock following the anæsthetic. Had it been possible to prescribe treatment by means of injections, etc., to correct the abnormal chemico-physical changes undergone by the protein particles in the plasma, the second blood-picture would have shown a greater degree of dispersion.

Case 143

A woman, aged thirty-two, had complained of hay-fever since the birth of her only child, a girl, aged twelve. The patient had a bad attack while she was being examined, but it passed off before she left, partly through fear, and partly on account of an intra-venous injection of strontium aspartate (0.01 grm.). The patient's mother was a chronic asthmatic, and died, following tracheotomy performed for angio-neurotic œdema of the larynx, aged fifty-two. One sister died of phthisis, aged twenty-seven. The patient used to bite her nails, she had wide-angled and hyper-extended elbows, and her hair was going grey. The pulse was 96, and the blood-pressures registered 120 and 70 mm. of Hg. respectively. The left colon was contracted, and the ascending colon and cæcum were dilated. The pathogenic micro-organisms found in the excreta were the *Bacillus acidi lactici* (5 per cent.), *Bacillus lactis aerogenes* (1 per cent.) and *Bacillus proteus vulgaris* (1 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3468.
Percentage of the blood-sugar	= 0.056 grm.
Percentage of the blood-urea	= 49 mgrm.
Ultra-microscopic picture of the serum	= Not many particles moving, and these were mostly giant particles and ringed particles. There were a fair number of particles and giant particles precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, took lacto-dextrin internally, had a course of colonic lavage, and received injections of strontium aspartate and of the fæcal vaccine. Her condition improved and her hay-fever vanished. As the hay-fever began when her baby was weaned it is obvious that chronic dehydration gave place to hydration. It is clear, also, that both fear and strontium aspartate reversed the chemico-physical change for the time being, but this was in no way connected with any outpouring of adrenalin into the circulation.

If the patient had not had hay-fever, the diagnosis of idiopathic hypo-glycæmia might have been made, but it would not be possible to say that the two conditions are synonymous, although, as the case shows, the hypo-glycæmia and the hay-fever were different manifestations of the same abnormal chemico-physical change (hydration).

There are three new points the author wishes to bring forward to support the view that diabetes is the result of a chronic intestinal intoxication, and a sign of chronic dehydration.

The first point is that under-nutrition is more effective in controlling hyper-glycæmia than is a reduction of the intake of carbohydrate. Under-nutrition checks intestinal intoxication and the mutation of the *Bacillus coli communis*. In fact, starving for one to three days may be the only effective means of stopping the fatal progress of an entero-colitis.

The second point is, that a patient, who suffers intensely from sea-sickness, tends to become immune, even on the roughest sea, on developing diabetes, and returns to his old condition when under the influence of insulin. Sea-sickness is merely a manifestation of portal hydration, which can be overcome with Sup. 36, calcium and strontium aspartate, acetyl-choline, etc. There is no fundamental difference between sea-sickness and the shock following the anæsthetic, and the hay-fever in the last two reported cases.

The third point is that removal of the pancreas in pregnant animals may fail to produce hyper-glycæmia. In pregnancy the protein particles in the plasma tend to undergo first dehydration and then hydration. When a diabetic woman becomes pregnant there is a grave danger of the initial dehydration aggravating the diabetes, but the moment hydration supervenes insulin may be dispensed with. Continuing the use of insulin may provoke eclampsia, a manifestation of hydration, and, on the other hand, the birth of the child or the death of the *fœtus* may cause a sudden rise in the percentage of the blood-sugar from 0.1 grm. to 0.4 grm.

II. The Superior Mesenteric Division

(a) The Small Intestine

Although for the sake of description the small intestine is separated from the large intestine, in disease this is not the case. An enteritis and a colitis may occur as entities, but in most instances, particularly when the condition is acute, it is one of entero-colitis. Speaking generally, the more acute the condition, the more the small intestine is damaged, and the more chronic, the

more the colon is affected. This explains why in shock, the clinical expression of the severest form of hydration, enteritis is more usual than colitis.

Hydration is produced more readily by positively charged than by negatively charged bodies, hence the reason why enteritis is encountered in most cases of metallic intoxication.

Toxic enteritis may occur even when the drug is injected, showing that it is secondary to the chemico-physical changes the protein particles in the plasma undergo. This view is strengthened by the facts, that the earliest changes are to be noted in the area of the gut penetrated by the vessels, and that changes take place in the lymphatic nodes, varying from hypertrophy to necrosis and ulceration, according to the degree of action of the toxic agent. These points are of considerable importance as they throw light upon the *modus operandi* of infective enteritis. The micro-organisms most likely to cause enteritis are those which are most pathogenic. Those less pathogenic cause a colitis, hence it is suggested that pathogenicity is regulated by electric charge. The most pathogenic micro-organisms are those which have mutated longest and furthest from their parent, the *Bacillus coli communis*. From the changes these micro-organisms produce in the intestine, and particularly in the lymphatic nodes or Peyer's patches, changes which are indistinguishable from those found in toxic enteritis, the conclusion seems inevitable that infective enteritis is blood-borne. The difficulty with which an infection can be produced when the intestinal route alone is taken supports this view. Some of these points warrant further discussion. Although an infection stimulates the formation of lymphocytes more readily than does an intoxicant, the latter is not only capable of doing so, but also it aggravates the hypertrophy of the lymphatic glands, the clinical expression of the stimulation occurring in the former. For example, the lymphatic glands become enlarged in syphilis and in gonorrhœa, and this enlargement is increased by arseno-benzene and vaccine respectively when they are first prescribed, because their initial action is one of hydration, which is itself a toxic effect. As mentioned in the previous volumes, the so-called "Herxheimer-Jarish reaction" and negative phase are merely expressions of hydration, or, in other words, mild forms of shock.

The stimulation may stop at the production of lymphocytes, or it may extend further and call for the manufacture of plasma cells. Should the hydration caused by the infection or intoxicant be more marked, there occurs a hypertrophy of endothelial cells which usually fail to manufacture either plasma cells or lymphocytes. Going one step further, complete paralysis of

cellular activity occurs, resulting in necrosis and ulceration, because the hydrated protein particles precipitated locally occasion dehydration and destruction of the protein particles constituting the protoplasm of the manufacturing cells.

The pathogenicity of the mutation forms of the *Bacillus coli communis* increases the further removed the daughter form is from its parent, and the length of time which has elapsed since the removal would appear to have some influence. The micro-organisms far removed from the parent germ are the cholera bacilli, the *Salmonellæ* and the dysenteric bacilli. The author has not done any work with the cholera bacilli, so these are not included in the discussion. The *Salmonellæ* include Eberth's bacillus, the para-typhoid bacilli, Gärtner's bacillus, Morgan's bacillus and *Bacillus Ærtrycke*. The typhoid bacillus has removed further from the *Bacillus coli communis* than the others, and it is possible that its removal occurred at an earlier date. The dysenteric bacilli can be placed in a sub-group, but they should not be sharply differentiated from the *Salmonellæ*, or from the more innocent and recently removed pathogenic mutation forms of the *Bacillus coli communis*. Indeed, it would be better to regard the dysenteric bacilli as a branch of the tree formed in the process of evolution. The further removed the micro-organism is from the parent the more pronounced are the chemico-physical changes to which the protein particles in the plasma are subjected, and it is purely upon these changes that the immunity reactions, and the agglutination tests in particular, rest. The micro-organism first causes dehydration of the protein particles and, later, hydration. When these hydrated particles come in contact with the bacilli in a test tube, they subject the bacilli to dehydration. This is followed by adsorption, and later, when hydration occurs, the bacilli are agglutinated and precipitated. On the other hand, the dehydration to which the bacilli are subjected may be such as to send them into true solution. In the first case the agglutination test is positive, and in the second negative. It thus comes to pass that the agglutination test is negative when immunity is at its lowest and highest. The agglutination test is not specific, as is usually thought; indeed, it not infrequently happens that the serum of a patient agglutinates a bacillus higher in the evolutionary scale of removal, and fails to agglutinate the bacillus causing the infection, or one lower in the scale. The serum of a patient suffering from a Gärtner infection may agglutinate *Bacillus typhosus* and *Bacillus para-typhosus*, and fail to agglutinate *Bacillus Gärtner*. This suggests, so far as the *Salmonellæ* are concerned, that the bacilli included in the group have a common origin. As the serum of a patient

harbouring such micro-organisms as the *Bacillus Asiaticus*, bacillus of epidemic jaundice, *Bacillus Friedländer*, etc., may agglutinate Eberth's bacillus and the *Bacillus para-typhosus* even in the absence of a previous infection or inoculation of these bacilli, the suggestion that all these micro-organisms have a common origin from the *Bacillus coli communis* becomes still more plausible. There is no relationship between agglutination and pathogenicity, as proved by the fact that some of the hydration necessary to give rise to agglutination may be caused by an agent which has nothing whatever to do with the micro-organism in question.

For example, an animal's serum may fail to agglutinate bacilli which have previously been injected intra-venously until the protein particles in the plasma have been hydrated with substances such as insulin, coniine, nicotine, arecoline, etc. The intra-venous injection of pathogenic bacilli into animals may cause the serum to agglutinate the bacilli *in vitro*, both when they cause and fail to produce an infection. When they occasion an infection or septicæmia, judged by a positive blood-culture, the positive agglutination soon becomes negative and the bacilli vanish from the blood-stream, following one or two injections of the washings of the bacilli. But, when no infection or septicæmia occurs, the washings fail to convert a positive agglutination into a negative. Despite this, the animal may succumb quicker to the latter than to the former intra-venous injection of the bacilli. The death in the latter case is due to the bacilli causing hydration, because of their protein nature, and not to the bacilli producing an infection. The death is really of the nature of protein shock, such as may occur after any overdose of a hydration-producing substance. When bacilli injected intra-venously occasion positive agglutination merely because they happen to cause protein hydration, the agglutination does not become negative until the hydrated protein particles are dehydrated or dispersed, preferably by chemical agents.

The expression of the pathogenicity of a micro-organism is a purely surface phenomenon, and is influenced by innumerable factors. The source from which the infecting bacillus springs, the time of year, and the atmospheric conditions existing at the time the mutation occurs, are some of these factors. The conditions under which the micro-organisms are grown are others, and a still more important one is the nature of the soil upon which they are planted, or in which the mutation takes place. The resistance of the victim is paramount in infection, and it has never been realised before that atmospheric conditions occasion marked differences in the blood-picture.

A micro-organism bearing a name which denotes pathogenicity may be

pathogenic at one time and saprophytic at another. The difference is solely one of surface action and depends upon whether the micro-organism abstracts activity from, or gives it up, to the protein particles of the host. If the micro-organism hails from a breed which was able to increase its pathogenicity at its host's expense, it is more likely to put up a stronger and more successful fight when reaching a new host than one hailing from a breed which happened to be saprophytic at the time of its transference. The activity of pathogenic micro-organisms varies from one month to another, and, in the case of the fæcal micro-organisms, it has been the author's experience to find the *Bacillus fæcalis alkaligenes* prevailing in February, March and April, the *Salmonellæ*, proteus group and bacillus of epidemic jaundice in May, June, July and August, the bacillus of epidemic jaundice and Friedländer's bacillus in October and November, and late lactose fermenters, Friedländer's bacillus and the *Bacillus fæcalis alkaligenes*, in December and January. The *Bacillus acidi lactici*, the least harmful of the pathogenic fæcal micro-organisms, is prevalent from May to November. This grouping is naturally subject to variation, because the mensual climatic conditions vary from year to year. Cold, wet and foggy weather increases the activity of Friedländer's bacillus and the *Bacillus fæcalis alkaligenes*, while sultry weather appears to stimulate the activity of the *Salmonella*, proteus and dysentery groups. In winter the blood-picture is one more of hydration than of dehydration, while in summer it is reversed. In cold weather the refractive index of the serum tends to rise and the percentage of both the blood-sugar and the blood-urea to fall, while in hot weather the refractive index of the serum falls below the normal, and there is a rise in the percentage of either the blood-sugar or the blood-urea. When the percentage of the blood-urea is raised that of the blood-sugar is usually lowered. These points help to explain why a vaccine may prove beneficial at one time and useless at another. It is to be hoped that in the future it will be possible to measure the activity of micro-organisms.

There is one particular micro-organism to which attention must be drawn in discussing infective enteritis, and this is the *Bacillus Welchii*. In the author's opinion the *Bacillus Welchii* is not a particularly pathogenic micro-organism. It may be found not infrequently in the various severe anæmias, but it is not the cause of pernicious anæmia, as thought by some. Its activity may hasten death in a patient with ileus, but it is not the cause of the condition. In some cases of both pernicious anæmia and ileus, *Bacillus Welchii* serum may benefit the patient, but this suggests no more than that the micro-organism plays a rôle in these two conditions. The *Bacillus Welchii* lives in an anaerobic milieu,

and as this is the normal state in the small intestine it accounts for the frequency with which this micro-organism is found when abnormal conditions prevail. Ileus is no more than a clinical manifestation of shock, as proved by the fact that, in the absence of obstruction, the condition is readily relieved when the hydrated protein particles precipitated in, and causing paralysis of, the gut are subjected to dehydration or to dispersion. As time is such an important factor it is necessary to employ a drug which breaks up hydrated protein particles with the least delay, and this is undoubtedly acetyl-choline. The author has had five cases where it would appear that acetyl-choline saved the patient's life, and the following is a typical instance.

Case 144

A woman, aged thirty-five, had a normal pregnancy, and all was well until the third day following the birth of her first-born, a girl, when she developed ileus. The patient looked, and was, extremely ill, she had incessant vomiting and constant diarrhœa, and her abdomen was enormously distended. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 5.1 c.c.
Refractive index of the serum	= 1.3483.
Percentage of the blood-sugar	= 0.143 grm.
Percentage of the blood-urea	= 51 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving, and all these were either giant particles or ringed particles. There were about the same number of particles precipitated, consisting mainly of giant particles with a halo around each. There were some large agglutinated masses pre- cipitated, and the Brownian movements of the particles were very sluggish.

The patient took glucose internally, had treacle enemata daily, and received twice daily, for two days, intra-muscular injections each of 0.2 grm. acetyl-choline. After the first injection she passed gas *per rectum*, and by the time the fourth injection had been administered the abdominal distension had completely disappeared.

Instead of using treacle enemata, repeated instillations of human or ox bile can be made into the rectum, as suggested by Brockman.¹⁴ Brockman is under the impression that ileus is the result of the absence of bile in the

intestine. It is more probable that the good effect resulting from the use of bile is due to the effect this natural product has in causing contraction of the muscular coats of the intestine. The natural product, treacle, appears to act in the same way, but the refined product, golden syrup, is valueless. Bile and treacle can be used on the same patient, and form useful adjuncts to the treatment of ileus with acetyl-choline.

In ordinary practice the micro-organisms belonging to the *Salmonella* group cause an entero-colitis, or even a colitis, more frequently than an enteritis, and it is impossible in any individual case to be sure where the inflammation begins or ends. The acute and sub-acute cases of entero-colitis met with in practice are so seldom diagnosed correctly, and even when a correct diagnosis has been made and the causative micro-organism has been found in the excreta, treatment may fail to save the patient's life.

The author has had such trouble with these cases in the past that he thinks it will probably help the reader if he details the method of treatment he employs at present. The patient is starved for one to three days, according to his condition. So long as the abdomen is tender, no aperients are prescribed, and treacle enemata and colonic lavage are withheld. When all abdominal tenderness has vanished the enemata are given, and are followed by colonic lavage when the patient is up and about. Aperients, enemata and lavage are, in an ordinary person, liable to occasion a temporary aggravation of the existing trouble. This aggravation in a patient whose resistance is being seriously weakened, as evidenced by pyrexia, etc., may be sufficient to destroy the resistance altogether, and the author has seen cases where two or three enemata made the patient worse, precipitated a pneumonia, and caused a fatal issue. The death, of course, is ascribed to the pneumonia, which is looked upon as an unfortunate and unpreventable complication of the illness. After the starvation period the patient should drink plenty of fluid and live on fruit. Imperial drink, barley-water, and buttermilk are the most suitable drinks, and the citrus the most suitable fruit. Intestinal antiseptics are of no value whatsoever, and injections of Sup. 36, which are so useful in other forms of pyrexia, are of little use. It is better, on the whole, to avoid giving drugs internally, but there is one drug which, if injected intra-muscularly in half grain doses twice a week, may do good, and this is emetine hydrochloride. Other remedies may be called for, but it is impossible to select them without a blood-picture. No time should be lost in searching for the pathogenic micro-organism in the excreta, and a washing should be made of bacilli from a twenty-four hours culture, and injected as soon as possible. If the patient is going to

recover, the temperature will drop to normal within two days, following a single injection, in which case no more treatment is required until the patient is up and about, and can have the colon thoroughly washed out as far back as the ileo-cæcal valve by the syphon method. Any exacerbation or future recurrence can, as a rule, be combated by making another injection of the washings of the bacilli. It is not necessary to increase the dose; indeed, better results may be achieved by employing even a smaller dose. To diminish the dose, which is equivalent to increasing the potency, it is necessary to adopt the homœopathic method, because any fraction of the contents of an ampoule contains as much activity as the whole. The employment of washings is really a homœopathic manoeuvre; another method is to use the repeated filtrate of the bacillus in question. An emulsion of the pathogenic bacteria is passed through a filter for as many times as is required to enable the filtrate to prevent growths when added to an inoculated culture. Whether a particulate or ultra-microscopic form of the bacillus, known as the "bacteriophage," passes over, or merely its activity, is, and probably always will remain, unknown. But it is a fact that the repeated passage of generations of bacilli ultimately result in preventing the growth of the parent bacilli. The filtrate first able to cause complete inhibition of growth of the parent micro-organisms is injected into the patient. Although the author has not had a sufficiently long clinical trial with both the washings and the filtrate, experimental work shows that the washings cause the greater dispersion of the protein particles in the plasma. Below are reported a case of acute entero-colitis which ended fatally, and one which recovered under the treatment suggested.

Case 145

A man, aged forty-three, had had malaise, diarrhœa and a pyrexia for eleven days. The patient was very ill, his evening temperature ranged between 102 and 104° F., the abdomen was too tender to palpate properly, and he had a patch of erysipelas on the forehead. The pathogenic micro-organism found in the excreta was the *Bacillus Gärtner* (80 per cent.). The patient's serum agglutinated the typhoid and the para-typhoid bacilli, but not his own *Bacillus Gärtner*. He had never been abroad and had never been inoculated against typhoid or para-typhoid. The blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 4·3 c.c.
Refractive index of the serum	= 1·3469.
Percentage of the blood-sugar	= 0·137 grm.

Percentage of the blood-urea	= 53 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and these were mostly giant particles and ringed particles. There were more particles precipitated in the form of giant particles, ringed particles and giant-particled clumps. There were also some big agglutinated masses precipitated.

The patient was living on milk, as he had been since his illness, and, because of the continuous passage of mucus from the rectum and sudden distension of the colon, enemata were employed. A few days later pneumonia attacked the right base, and the patient became unconscious and died.

In cases of intestinal intoxication there is no more toxic article of food than milk, and many are the victims whose death has been brought about by its use, or whose convalescence has been abnormally prolonged. In this case time did not allow of the preparation of the washings of the pathogenic bacillus.

Case 146

A woman, aged thirty-nine, had been running a temperature of about 103° F. for ten days. The patient was very ill, and had herpetic lesions in her mouth and on her lips; there were papules of *Erythema multiforme* on the shins and on the backs of both hands, and the abdomen was very tender. She was passing foul fæces which contained much mucus. The pathogenic micro-organism found in the excreta was the *Bacillus Gärtner* (60 per cent.). The patient's serum agglutinated *Bacillus para-typhosus B*, but no other micro-organism; the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 3·8 c.c.
Refractive index of the serum	= 1·3472.
Percentage of the blood-sugar	= 0·143 grm.
Percentage of the blood-urea	= 38 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving. There were more particles precipitated as giant particles, ringed particles and giant-particled clumps.

The patient starved for twenty-four hours and then had as much Imperial drink, barley-water and fruit as she could take. She received three intramuscular injections of emetine hydrochloride, and one of the washings of 5,000 million of the fæcal micro-organism. The day following the last injection

the patient's temperature dropped to normal, and she made an uneventful recovery. Three months later *Bacillus Gärtner* could not be recovered from the fæces.

In everyday practice the dysenteric bacilli cause entero-colitis even more seldom than the *Salmonellæ*, and it is rare to find them causing more than a sub-acute or chronic colitis. But, as they have not been mentioned in this section, a brief reference is made to them.

In the ordinary routine work five types have been encountered : Shiga's bacillus, *Bacillus alkalescens*, *Bacillus coli anaerogenes*, and the para-dysenteric bacilli of Harris-Wollstein and Park respectively. In the last thousand cases examined Shiga's bacillus was met with once, the *Bacillus alkalescens* twice, the *Bacillus coli anaerogenes* sixteen times, the para-dysenteric bacillus of Harris-Wollstein sixteen times, and the para-dysenteric bacillus of Park twice. The clinical signs and symptoms presented by these patients did not differ from those encountered in other patients harbouring other mutation forms of the *Bacillus coli communis*. From the very large number of cases examined, and this applies to sick animals as well, no relationship could be drawn between the clinical manifestation presented and the pathogenic micro-organism found in the excreta. For example, in cases of rheumatism and skin eruptions, which affect man and animals alike, any mutation form of the *Bacillus coli communis* may be found in the excreta. There is a definite relationship between the type of micro-organism found, the percentage in which it occurs, and the severity of the clinical picture presented, but this is discussed in more detail below. So far as type of micro-organism found and clinical manifestation presented are concerned, all that can be said is that the *Salmonella* and dysenteric groups draw attention to the intestinal tract more than to other parts of the body. Even this broad statement is not entirely correct, because a severe form of entero-colitis may be caused by the *Bacillus fæcalis alkaligenes*, and even by Friedländer's bacillus, which is not a non-lactose fermenter, and is only slightly removed from the *Bacillus coli communis*. On the other hand, what appears to be a simple form of rheumatism may be associated with all the *Salmonellæ* and dysenteric bacilli, in patients where the trouble in the colon is merely dormant. These points are illustrated by the following four cases, in which the four types of dysenteric bacilli were found in the excreta.

Case 147

A boy, aged six, had suffered from asthma since he was six months old. The patient's mother, a Norwegian, had suffered from a similar condition

between the ages of four and ten. A brother and sister were troubled with bronchitis in the winter. He used to have chilblains, and was accustomed to get recurrent attacks of eczema, and *Herpes febrilis* on the left cheek. Four years previously he had had an acute arthritis of the right hip, which lasted for about two months. He had gingivitis, the tongue was furred and fissured, the abdomen was more or less tender all over, and the urine gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organisms found in the excreta were Shiga's bacillus (50 per cent.) and the *Bacillus fæcalis alkaligenes* (50 per cent.).

The boy was dieted, made to sit down after every meal, had a course of treacle enemata, and received two injections of the fæcal vaccine in doses of 100,000 and 250,000, on two days in succession. He improved, but the injections of the vaccine produced an acute attack of asthma which had to be overcome with Sup. 36. Constipation and the ingestion of butcher's meat, eggs, and milk tended to bring on an attack of asthma, eczema or herpes.

Case 148

A woman, aged twenty-five, sought advice for *Acne vulgaris* and furunculosis, from which she had suffered for four years. The patient used to have chilblains, and menstruation did not begin until the age of seventeen. She presented all the usual signs of familial chronic intestinal intoxication. The pulse was 86, and the blood-pressures registered 120 and 70 mm. of Hg. respectively. The left colon was contracted, and there were tender areas in the regions of the flexures and the ileo-cæcal junction. The pathogenic micro-organisms found in the excreta were the *Bacillus fæcalis alkaligenes* (60 per cent.) and the *Bacillus alkalescens* (40 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood corpuscles	= 1·2 c.c.
Refractive index of the serum	= 1·3488.
Percentage of the blood-sugar	= 0·093 grm.
Percentage of the blood-urea	= 22 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with many ringed particles, giant particles and clumps. There were many particles, giant particles, ringed particles and clumps precipitated, with a tendency towards formation of precipitation <i>en masse</i> .

The patient was dieted, had a course of colonic lavage, took strychnine,

iron and arsenic internally, and received injections of Sup. 468, and of the fæcal vaccine. She improved, and the acne and furunculosis cleared up.

Case 149

A woman, aged thirty-eight, had suffered from various forms of rheumatism for seventeen years. The patient's father died as the result of chronic bronchial asthma, and her mother of heart trouble caused by rheumatic fever. The mother had been a martyr to gout. The patient was short, stout and myopic ; she had a chronic nasal catarrh, and was always prone to attacks of tonsilitis. She could not stand with her knees and feet together at the same time, all her teeth had been removed but without benefiting the rheumatism. The pulse was 112, and the blood-pressures registered 140 and 80 mm. of Hg. respectively. The abdomen was too fat to examine satisfactorily. The pathogenic micro-organism found in the excreta was the *Bacillus coli anaerogenes* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·5 c.c.
Refractive index of the serum	= 1·3485.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a fair percentage of giant particles. Fair number of particles precipitated with some giant particles, and a few giant-particled clumps.

The patient was dieted, had colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of contramine, and of the fæcal vaccine. When re-examined a year later, the patient was perfectly well, and had no rheumatism. She had lost a stone and a half in weight.

Case 150

A woman, aged forty-five, was suffering from climacteric dementia. The last period occurred one year previously, and since then the patient had lost weight steadily. She had insomnia, bouts of weeping, and fits of temper, and seemed on occasions to be suicidal. The mouth and tongue were dry, all the teeth had been removed, the elbows were wide angled and hyper-extended, and wherever the skin was touched a bruise appeared. She was troubled with frequency of micturition, and was unable to hold her water ; she felt the cold intensely, even when her temperature was raised. The pulse was 98, and the blood-pressures registered 125 and 90 mm. of Hg.

respectively. The colon was full of faecal material as the patient often had no action of the bowels for several days. The pathogenic micro-organism found in the excreta was the para-dysenteric bacillus of Harris-Wollstein (10 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·5 c.c.
Refractive index of the serum	= 1·3505.
Percentage of the blood-sugar	= 0·093 grm.
Percentage of the blood-urea	= 14 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with an occasional giant particle, both moving and precipitated.

The patient was dieted, had the colon washed out, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the faecal vaccine. She improved, then relapsed, and finally improved again.

Case 151

A man, aged thirty-eight, was in bed, suffering from what was diagnosed as a duodenal ulcer. The patient was on a milk diet and getting steadily worse each day. His mouth was foul and covered with herpes, and there were ulcers on both tonsils. The abdomen was too tender to touch, and the stools contained much mucus and some blood. The patient suffered from chronic nasal catarrh and rheumatism, having had several attacks of lumbago and two of sciatica. He had had scarlet fever once and diphtheria four times. The optic discs were small and mal-developed, the pulse was 62, and the blood-pressures registered 95 and 40 mm. of Hg. respectively. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino benzaldehyde, and contained a trace of protein. The pathogenic micro-organism found in the excreta was the para-dysenteric bacillus of Park (25 per cent.).

The patient substituted fruit for milk, had injections of emetine hydrochloride, and later, treacle enemata and a course of colonic lavage. When the last had been completed he received two injections of the faecal vaccine in doses of 250,000 and 500,000 on two successive days. All the patient's symptoms vanished, and an operation was avoided.

(b) The First Part of the Large Intestine

Under this heading are included the ileo-cæcal area, the ascending colon, and the hepatic flexure of the colon. Structures are considered rather than

bacteria, because this part of the intestinal tract appears to play the chief rôle in familial chronic intestinal intoxication, and because the pathogenic micro-organisms are dealt with again in the next section. In every case of familial chronic intestinal intoxication the ileo-cæcal area is involved. There is always thickening, and also tenderness on pressure, either deep or superficial according to the degree of inflammation present. The thickening is due, in the main, to the changes the mesentery in this area undergoes. The appendix itself is never solely attacked, although in the very acute cases it may be the structure bearing the brunt of the inflammation. In the acute cases it is necessary to remove the appendix, but in the sub-acute or chronic cases no operation is called for because treatment of the chronic intestinal intoxication is more efficacious, being more comprehensive and fundamental. There is probably no operation so frequently performed, and so seldom needed, as appendicectomy, and because the operation is itself successful surgeons are apt to think that the patient is definitely benefited. A few patients are temporarily relieved, but this is the result rather of the rest than of the operation; more are made worse, and in all, the fundamental trouble is left untouched. An operation certainly removes the risk of a very acute condition occurring later, but ridding the patient of his chronic intestinal condition does this more effectually.

The cæcum is almost invariably atonic, and being in this condition it tends to become distended with gas. The atony is probably the result of previous spasm, and occurs when irritation of the nerve endings in the wall gives place to paralysis, a sequence of the local precipitation of hydrated protein particles.

It is held by some of those who do not suggest adhesions as the cause of the persistence of the patient's troubles after appendicectomy, that they are occasioned by a movable cæcum, and instead of re-operating to remove the former, cæcoplexy is performed with equally unsatisfactory results. Failing this, the patient is often advised to have the gall-bladder removed. One of the most common causes of chronic invalidism, in women particularly, is repeated laparotomy.

In most cases of familial chronic intestinal intoxication, when the patient comes up for advice, the ascending colon is found to be atonic, and here again the distension is most probably the result of a foregone spasm. Atony of the ascending colon is the bugbear of chronic intestinal intoxication, first because it makes it difficult to empty the bowel, and secondly because it results in the permeability of its walls to toxic agents being increased. This

last statement requires a little further elaboration. Too little is known about absorption from the intestines, but it is highly probable that it follows the ordinary rules of colloid membranes. The two most important rules of such membranes in the living body are : (1) increased permeability when inflamed ; (2) foreign and toxic bodies can more readily pass through than home and innocuous substances. In the case of the ascending colon the first is not difficult to prove, and this is done by adding substances, capable of detection in the blood-stream, to the water passed through a cæcal tube. It is found that mercury and silver, placed in the ascending colon through a cæcal tube, reach the blood-stream quicker when the ascending colon is damaged than when it is normal.

Stagnation seems to be at its worst in the ascending colon, the gut itself cannot get rid of its contents, and it is not easy to empty it with the cæcal tube owing to obstruction occurring elsewhere, or to gas which is so liable to accumulate in this area. No colonic lavage is perfect until the ascending colon and cæcum have been emptied. The ascending colon is generally regarded as being the only part of the large intestine through which certain products of food metabolism enter the blood-stream, but judging by the aggravation of symptoms which occur so frequently when colonic lavage is first instituted it would appear that, when other parts of the colon are inflamed, toxic bodies can pass through the walls. On the other hand, it must be remembered that some of the water used may pass forward into the ascending colon and carry in solution, or suspension, bodies which otherwise might have lain dormant. Much work still remains to be done upon the permeability of the walls of the intestine.

The hepatic flexure of the colon is, in the author's experience, a site selected for trouble almost more than any other. The tenderness elicited upon examination is phenomenal and at times it is extremely difficult to be sure whether the underlying condition is colitis or cholecystitis. In making the diagnosis of the former in every case the error would not exceed 3 per cent., and this can be reduced to practically nil by going carefully into the history, and by finding similar tender areas in the region of the splenic flexure and in the ileo-cæcal area.

Speaking generally, the characteristic features elicited by a digital examination of the abdomen in cases of familial chronic intestinal intoxication, beginning in the left iliac fossa, are contracted sigmoid, contracted descending colon with tenderness which increases as the splenic flexure is reached, still more tenderness in the hepatic flexure, dilated ascending colon and cæcum, with tenderness and thickening in the ileo-cæcal area.

III. Interior Mesenteric Division

(a) The Remainder of the Large Intestine

In this section a few remarks are made about the intestine itself, further attention is paid to the bacterial flora, and the problem of food-poisoning is discussed.

With the exception of the transverse colon, this portion of the large intestine is, in the majority of cases of chronic intestinal intoxication, found in spasm. In acute cases spasm may give way to atony, and result in a dilatation of the whole of the large intestine, but the dilatation is never so pronounced as when it results from paralysis of the nerve endings, the last stage of the chronic condition. This megalo-colon is fortunately a rare condition, and would be even rarer still if the *Plombières* method of performing colonic lavage were rendered obsolete. The sudden dilatation of the gut with large quantities of fluid is particularly liable to accelerate the degeneration occurring in Auerbach's plexus, and the essence of good colonic lavage is to avoid distension. The syphon method, originally introduced and popularised by Schellberg,^{15, 16} whereby only a few ounces of fluid are let in at a time, and withdrawn before the tube is advanced, is the only satisfactory way of carrying out colonic lavage, but each wash-out takes one to two hours, and there are not many who will devote this time to each case. The method has been modified since its introduction, and Schellberg prefers now to refer to it as "colonic therapy." This is because he pays more attention to placing remedial agents in the cæcum than to removing the old fæcal material from the colon.

There is a congenital form of megalo-colon known as "Hirschsprung's disease," but too little is known about this form of dilatation, which mainly affects the sigmoid, to say whether it is of the same origin as the acquired condition or not. It is also not certain whether an obstruction on the rectal side of the dilatation is necessary or not. In one case the muscular fibres of the dilated portion of the colon may be hypertrophied, and in another case atrophied. The former points to previous spasm and the latter to actual degeneration. It is probable that dilatation may occur as an end stage of spasm, or as the result of a degeneration of Auerbach's plexus before the preceding stimulation of the nerve endings had been sufficiently pronounced to produce spasm and muscular hypertrophy, in which case an obstruction below would not be an absolute necessity. The following is an illustrative case of acquired megalo-colon.

Case 152

A man, aged fifty-four, had suffered from chronic indigestion and constipation more or less all his life, and had been treated with *Plombières* douches in various parts of the world, with the result that he had complete atony of the whole of the large intestine. The patient was an only child, and his mother was still alive. She had been operated upon for appendicitis, cholecystitis and carcinoma of the breast. He had two daughters, both of whom were sensitive to horse dandruff, each had had the appendix removed, one had suffered from cyclical vomiting as a child, and the other was said to have had bilateral apical tuberculosis. The patient had had his tonsils, appendix and gall-bladder removed; he had had several attacks of cystitis, and had suffered from various forms of rheumatism. He was nervy and looked older than his years. He could not stand with his knees and feet together at the same time; he had bilateral *Arcus senilis*, the tongue was furred and fissured, all the teeth had been removed, there was marked central cupping of both optic discs, with venous congestion and arterio-sclerotic changes. The pulse was 74, and the blood-pressures registered 120 and 80 mm. of Hg. respectively. The urine gave a strong reaction with the hydrochloride of di-methyl-*para*-aminobenzaldehyde, and contained some protein. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus*, and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.25 c.c.
Refractive index of the serum	= 1.3485.
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 31 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles and ringed particles. There were a fair number of giant particles, ringed particles and clumps precipitated. The Brownian movements were sluggish, and the precipitation increased with time.

The patient was dieted, had several courses of colonic lavage, took iodine, thiol-amino-methyl-glyoxaline and thyroid internally, and had injections of acetyl-choline and of the fæcal vaccine. In the water used for washing the colon, acid sodium phosphate and potassium permanganate were used.

Sufficient tone was restored to the large intestine to enable the patient to dispense with colonic lavage about eighteen months later.

In other cases, long before the dilatation becomes sufficiently pronounced

to be labelled "megalo-colon," the circular muscle fibres atrophy, the haustration of the intestine is obliterated, the colon increases in length, and the walls are usually thinned. Indeed, almost identically the same process is at work which, occurring in veins, causes them to become varicose. As in varicose veins, the colon becomes redundant and often a loop is formed. There may be muscular hypertrophy on the rectal side of the loop, and even areas of mural thickening in parts of the affected colon, suggesting that muscular hypertrophy accompanying spasm, and atrophy following it are only stages in the same process. The hypertrophy and atrophy need not necessarily affect long portions of the colon, or even a complete circle of the bowel. They may be localised to small areas and result in the formation of diverticula. There may be a single diverticulum or many diverticula which vary in size from a pea to a hen's egg.

Multiple diverticula are most common in the left colon, and seldom give rise to symptoms. A redundant piece of colon or colonic loop renders colonic lavage impossible, and no more can be done than to palliate the patient's signs and symptoms. Removal of the damaged piece of colon is not to be advised. A single diverticulum may catch the tube and prevent satisfactory lavage being carried out, but it is most to be dreaded when it becomes adherent to the bladder and causes recurrent, or even persistent cystitis, and a colovesical fistula. Small diverticula may harbour stagnant faecal material but, as a rule, they are readily emptied by colonic lavage. If colonic lavage is properly carried out and instituted before complete degeneration of the nerve endings has occurred, diverticula may vanish and haustration return.

While changes are taking place in the wall of the gut, similar changes occur in the mesentery. Speaking generally, the first changes are those of inflammation whereby the mesentery becomes thickened. As the inflammation subsides, contraction tends to occur and this adds to the trouble occurring in the bowel by interfering with the blood-supply. The last change is one of atrophy, when the mesentery is lengthened and thinned. This lengthening and thinning of the mesentery is thought to be the main cause of what is known as "coloptosis," and operations have been devised both to shorten the mesentery and to anchor the colon. But coloptosis may occur in the absence of these mesenteric changes, and in the majority of the cases it is merely an expression of general mal-co-ordination, and is caused by the shortening of the whole frame.

Diverticula have been held responsible for cancer of the colon, but this view is incorrect, despite the fact that both show preference for the same part

of the large intestine. Cancer of the colon is more common than is usually thought ; it is not easy to diagnose, and is frequently missed, partly because the subject is generally young, and partly because it may not give rise to signs and symptoms before obstruction calls attention thereto. If blood is present in the fæces it may be apparent or hidden ; when it is discovered ulcerative colitis is thought of rather than carcinoma. This error in diagnosis should not be made, because ulcerative colitis begins in the rectum and spreads upwards, and the initial sign is a marked discharge of mucin. In cases of carcinoma, colonic lavage is, of course, impossible, as the tube cannot be advanced beyond the growth. If the patient is on the point of developing obstruction, colonic lavage seems to hasten its onset, and it undoubtedly increases the cachexia.

The diagnosis of carcinoma should be seriously considered if the percentage of the pathogenic micro-organism found in the excreta is increased at a re-examination made some time after the patient has had one or two injections of the fæcal vaccine. These points are illustrated by the following two cases.

Case 153

A man, aged thirty-eight, had never been really well since he had had a gangrenous appendix removed eighteen years previously. The present trouble began with attacks of abdominal pain eighteen months before, and for the past few months he had been unable to keep down any food. The patient was very emaciated, was too weak to stand, and had not passed any fæces or wind for three days. A large mass was felt in the abdomen, definitely carcinomatous in nature, and too advanced to be removed. He had been much troubled with boils in the past, and had suffered from constipation all his life. The urine gave a marked reaction with the hydrochloride of dimethyl-*para*-amino-benzaldehyde, and contained some protein. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1.5 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.081 grm.
Percentage of the blood-urea	= 54 mgrm.
Ultra-microscopic picture of the serum	= Scarcely a particle moving. There was some precipitation <i>en masse</i> composed in the main of giant particles and giant-particled clumps.

The patient was given an enema which caused severe vomiting and a large

evacuation of old fæcal material. Although temporarily relieved, he went still more rapidly downhill, and died three days later.

Case 154

A man, aged fifty-eight, had suffered from mucous colitis for some years, and sought advice for an acute attack of lumbago and sciatica. The patient's father died of carcinoma of the rectum, aged seventy-two, his mother of phthisis, aged thirty-five, and two sisters of phthisis. He used to have very bad chilblains, and had had rheumatic fever twice. There had been previous attacks of lumbago and sciatica, and these always coincided with the passage of mucus and blood in the fæces. The pulse was 92, and the blood-pressures registered 120 and 75 mm. of Hg. respectively. The left colon was contracted and tender, but no lump could be felt. The urine gave a reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, but contained neither protein nor sugar. The pathogenic micro-organism found in the excreta was the *Bacillus proteus Valeriei* (30 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.25 c.c.
Refractive index of the serum	= 1.3498.
Percentage of the blood-sugar	= 0.206 grm.
Percentage of the blood-urea	= 37 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving, and all were larger than normal. There were a few giant particles and small giant-particled clumps precipitated.

The patient would not diet, he had a course of colonic lavage, and received injections of contramine, and of the fæcal vaccine in doses of 1 and 2 million respectively. The vaccine produced a marked focal reaction which showed itself by the passage of much mucus and blood from the bowel, and by an acute attack of lumbago. The former lasted for ten days, the latter for one. Three months later the patient looked and felt very much better, and there was no tenderness in the abdomen.

In four months' time, however, the pain and irritation of the colon returned, and a re-examination of the excreta revealed *Bacillus proteus Valeriei* (50 per cent.). As signs of obstruction began to appear three weeks later, a laparotomy was performed, and a carcinoma of the sigmoid was removed.

For the past five years the author has investigated the bacterial flora of

most of his patients, and of many animals, but, as the investigations are far from complete, little more than the views held at present are mentioned in this discussion.

The author's attention was drawn to the bacterial flora, by Bach's¹⁷ work on the rôle played in disease by the non-lactose fermenting micro-organisms. Although most of the non-lactose fermenting micro-organisms appear to be mutation forms of the *Bacillus coli communis*, this is not true of all. Between the *Bacillus coli communis* and the definitely pathogenic mutation forms are to be found micro-organisms which may or may not ferment lactose. These micro-organisms may be pathogenic at one time, and not at another, and this applies also to the more truly pathogenic micro-organisms. The intermediate and pathogenic forms are not denizens of a perfectly normal colon, but unfortunately it is not possible to define what is meant by a normal colon. All that can be said is that these micro-organisms appear to develop in disease at the expense of the *Bacillus coli communis*. They make their appearance if anything upsets the individual, and come to the fore at once if a carnivorous animal is given a vegetarian diet, and *vice versa*. Their appearance is so rapid as to suggest that all may be present and lying dormant, to be awakened into activity at call, but it is more likely that the *Bacillus coli communis* can mutate into any form at almost a moment's notice. Faulty dietary causes mutation, so does the ingestion of toxic bodies, and even injections of poisonous substances have the same effect. Whenever hydration of the protein particles in the plasma occurs, pathogenic forms of the *Bacillus coli communis* are sure to be found in the excreta, consequently, mental anxiety and physical strain may bring about their appearance.

Despite the readiness with which the *Bacillus coli communis* mutates in the body, it is impossible to bring this about in the laboratory, and equally impossible to cause a mutated form to revert to its parent. The differentiation adopted, mainly by means of sugar tests, is purely arbitrary, and, more often than not, the micro-organism found and labelled is atypical. That is, forming acid in a sugar when it should either not do so, or should form both acid and gas, being motile at one time and non-motile at another, having a capsule in one culture and not in another, etc., etc.

As the patient improves in health, particularly if a vaccine has been administered, the pathogenic micro-organisms vanish, or are succeeded by others. If the latter is the case the micro-organisms appearing later are less pathogenic than those found at first.

There seems to be a range of pathogenicity like the rungs in a ladder, and

the rungs already mounted determine to some extent the type of pathogenic micro-organism which appears when the stimulus is applied. The time of year also has an influence upon the micro-organism found, because the intermediate forms such as the *Bacillus acidi lactici* and *Bacillus lactis aerogenes* prevail in the summer months. The prevalence of the intermediate forms in the summer months does not necessarily result in the disappearance of the clinical signs and symptoms ushered in, in the first instance, by the activity of the more pathogenic forms.

It is quite impossible to tell when a micro-organism is or is not pathogenic, and equally impossible to tell beforehand whether a vaccine will help to improve the patient's condition or not. Autogenous fæcal vaccines are of definite value ; the washings seem at present to be the best method of preparation, small doses are required, and frequent repetition is never necessary. A slight reaction following the use of the vaccine is desirable, but a severe one is to be carefully avoided. Should a severe reaction occur it is best overcome with Sup. 36, 0.01 grm. injected two days in succession, followed by half-grain doses of emetine hydrochloride injected twice a week until it has passed. If the reaction causes an acute or sub-acute entero-colitis the patient should take lacto-dextrin, and live *Bacillus acidophilus* culture, internally. In these cases buttermilk, yaghourt or kumyss are indicated. Although positive agglutination tests usually denote pathogenicity, they do not necessarily do so, and they are never a measure of pathogenicity. The reaction is far from being absolutely specific and negative tests do not necessarily infer that the micro-organisms in question are not pathogenic.

Whether all the non-lactose fermenters included in the discussion are derived from the *Bacillus coli communis* is not certain. It is probable that there is a still more common parent form which gives rise to the acid producer *Bacillus coli communis*, and to the alkali producers *Bacillus proteus*, *Bacillus pyocyaneus*, and *Bacillus fæcalis alkaligenes*. As mentioned above, it is possible that the *Bacillus fæcalis alkaligenes* has its origin from a spore-bearer.

The proteus group includes three varieties : the vulgaris, mirabilis and *Valeriei*. So far as this group and the *Bacillus pyocyaneus* are concerned, the author has not come to any definite conclusion regarding the part played by them in forming toxic metabolites from the food. The *Bacillus coli communis* may develop into a still more acid form, the *Bacillus coli communiior*. This micro-organism is not met with frequently ; it ferments lactose, and the author has been unable to form an opinion so far of its pathogenicity. There are four micro-organisms which ferment lactose and which are not far

removed from the *Bacillus coli communis*. These are the *Bacillus acidi lactici*, *Bacillus lactis aerogenes*, *Bacillus Friedländer* and *Bacillus proteus hydrophilus*. All four may be regarded as the intermediate forms, although the *Bacillus Friedländer* is liable to develop marked pathogenic properties. All four may be definitely pathogenic. None are agglutinated by the victim's serum, but vaccines made therefrom are definitely of therapeutic value. After these comes the *Bacillus coli mutabile*, a micro-organism characterised by some of the bacilli in a colony fermenting lactose and some not. The parts of the colony from which the former come stand out as little red spots on the white base of the latter. In the last thousand cases examined this micro-organism was found twice.

The micro-organisms occupying the next two rungs of the ladder are the *Bacillus Asiaticus* and the bacillus of epidemic jaundice. Both may be markedly pathogenic, although the author has not found them to be agglutinated by the patient's serum. When these two micro-organisms are found prevailing in the excreta a vaccine should be prepared and injected.

The higher rungs are occupied by the *Salmonellæ* and dysentery group, which have been discussed above.

One of the most interesting and, probably, important pathogenic micro-organisms found in the excreta is the *Bacillus fœcalis alkaligenes*. The word "probably" is used because, owing to the relationship or connection between the micro-organism and a spore-bearer, it is not always easy to determine when the bacillus in question is pathogenic. This micro-organism may be encountered in the fœces in every manifestation of disease, and the frequency with which it is found, particularly during the late winter months, is very characteristic. The *Bacillus fœcalis alkaligenes* does not cause one manifestation of disease to the exclusion of all others. Indeed, there is no manifestation of disease in which any of the pathogenic micro-organisms may not be found. Although it can be said that no one micro-organism causes any one sign or symptom of disease, the author has the impression that there is some connection between the *Bacillus fœcalis alkaligenes* and mesenchymatous changes. For example, in cases of generalised arterio-sclerosis, hyperpiesis, *Paralysis agitans*, interstitial myocarditis, and nephritis, the pathogenic micro-organism to be found in the excreta is usually the *Bacillus fœcalis alkaligenes*. The *Bacillus fœcalis alkaligenes* may be found in the mildest, as well as in the severest and most acute form of intestinal intoxication. It can cause an enteritis as well as a colitis. On reaching the blood-stream it is apt to develop a coccoid form, and in the most acute cases it is capable of developing an ultra-

microscopic form. In the severe forms of infection occasioned by the *Bacillus fæcalis alkaligenes*, and less often by the other non-lactose fermenters, the serum is apt to give a positive Wassermann reaction in the absence of a syphilitic infection. Any infection may convert a negative Wassermann reaction to a positive in a person suffering from syphilis.

The change into a particulate form small enough to pass through a filter is not peculiar to the *Bacillus fæcalis alkaligenes*, because the author has known the *Bacillus Friedländer* and the *Bacillus Gärtner* do the same. Moreover, it is possible in the laboratory, by repeated passage through a filter, to convert any micro-organism into an ultra-microscopic form, if this is what the so-called "bacteriophage" really is. By passing an emulsion of bacilli through a filter, adding a filtrate to a fresh culture, and repeating these steps many times, the filtrate eventually causes complete inhibition of the growth of the bacilli, and subjects their bodies to dehydration. But it is impossible to say if this lethal action is actually due to an ultra-microscopic virus. Experiments are in hand at present to determine the action of the "live" filtrates injected into animals. Several experiments have been conducted to test the use of the "dead" filtrates as vaccines, but the results have not been satisfactory. In some of the more acute cases ultra-filtration vaccine appears to do good, but it is not so active as the washings. In the chronic cases the ultra-filtration vaccine appears to have no therapeutic action, but many more trials must be made before definite conclusions are drawn.

When the author found that depriving rabbits of green food, or adding powdered egg to their ordinary food, produced not only signs of disease, but also altered the bacterial flora of the fæces, making non-lactose fermenters appear at the expense of the *Bacillus coli communis*: and when the same occurred in cows and horses transferred from the fields to stalls and boxes, and fed on artificial foodstuffs, it struck him that a development of these observations might throw light on the debatable and ill-defined subject of food poisoning.

The term "food poisoning" is obviously a misnomer, because the signs and symptoms produced do not differ from the signs and symptoms of disease which can be associated with the activity of non-lactose fermenting micro-organisms in the intestinal tract. Rabbits deprived of green food may develop an acute or sub-acute entero-colitis, death may occur in a few days and *Bacillus Gärtner* may completely replace the *Bacillus coli communis* in the excreta. Some may develop a more chronic intestinal condition and present lesions akin to those met with in man in so-called "*Pellagra*." One or more of the micro-

organisms mentioned above, and which were not previously present, are found in the fæces. In a case of "*Pellagra*," occurring in a woman who had never been out of London, the pathogenic micro-organism found in the excreta was the *Bacillus proteus Valeriei*.

Feeding herbivorous animals with carnivorous food, and *vice versa*, causes disease, especially rheumatism, and arterial degeneration. Pathogenic micro-organisms develop in the excreta, and micro-organisms, ordinarily saprophytic, such as the streptococcus, tubercle bacillus, etc., develop pathogenic properties. Preventing animals under domestication from living a natural life out of doors, and feeding them with prepared foodstuffs, will also cause pathogenic micro-organisms to appear in the excreta. Their activity lowers an animal's resistance and renders it a ready prey to disease and to infections.

So-called food poisoning in man presents no specific clinical picture, and it may occasion lesions in the intestinal tract, central nervous system, skin or other organs, which do not differ from identical lesions brought about in other ways. There is no difference between the entero-colitis of food poisoning and that caused by known toxic agents, or by bacilli of the *Salmonella* and dysentery groups. The clinical picture presented by botulism is indistinguishable from that encountered in *Encephalitis lethargica*. The causes of urticaria, *Erythema multiforme* and eczema are legion, and so on, and so on. In the enterocolitic form of food poisoning the micro-organisms most commonly held to blame are the *Bacillus Ærtrycke*, the *Bacillus Gärtner (enteritidis)* and the *Bacillus para-typhosus* of the *Salmonella* group, and various bacilli of the dysenteric group. All these pathogenic micro-organisms are to be found in patients presenting signs and symptoms of disease, but who have no food poisoning. In the author's last thousand cases of familial chronic intestinal intoxication, in which the excreta of all was examined, the *Bacillus Ærtrycke* was found twice, the *Bacillus Gärtner* twenty-seven times, and the *Bacillus para-typhosus* nine times. In not one single instance could it be discovered that the patient had been a source of infection to another.

It is certain that in cases of food poisoning there occurs no passage of micro-organisms from the food to the victim, and when mention is made of the passage of preformed toxins it is on very slender grounds, because toxins are, for the most part, unknown and undemonstrable substances. It would be better in this connection to use the term "activity," because the same micro-organism may emit activity at one time and fail to do so at another. This explains why patients harbouring the *Bacillus Ærtrycke*, *Bacillus Gärtner*, etc., may or may not be carriers. In the enterocolitic form of food poisoning

it is most probable that neither bacillus nor toxine passes, but some activity held by the article of food which, on reaching the intestinal tract of the victim, either stirs to activity the micro-organism lying dormant, or stimulates the *Bacillus coli communis* to mutate into the same.

Two of the most interesting and, at the same time, most important points this work brings out are that a micro-organism may be active at one time and inactive, although present in the same percentage, at another time ; and also that the activity may immunise one person and infect another. These are explanations of the periodicity of epidemics, and of why one person escapes and another falls a victim. From the few observations the author has been able to make it would appear that, in cases of the same food poisoning, the same micro-organism is not found universally, nor does it make its appearance at the same time. This suggests that the mutation, set in motion by the activity, occurs in steps. The *Bacilli Ærtrycke, Gärtner*, and *para-typhosus* may be found in different victims of the same food poisoning, and in some of the victims the *Bacillus acidi lactici* replaces the *Bacillus coli communis* before the really pathogenic form appears to take its place. The same sequence of events may be made to occur in animals, but more epidemics of food poisoning must be studied before these points can be definitely established.

Perhaps medical officers of health who read these lines will favour the author with material.

In botulism it is known that no microbe passes from food to victim, and it is impossible to get away from the fact that the signs and symptoms produced are akin to epidemic encephalitis, to the encephalitis following measles, small-pox, influenza, vaccination, etc., to the form occurring as an epidemic in rabbits, and to the form which so often terminates an intoxication with non-metallic chemical agents. Many of the infective forms of encephalitis occur as a terminal stage of a severe infection, and it is impossible to say at present whether the ultra-microscopic virus is derived from the host's own protein particles, which have been subjected to such severe dehydration by the infective agent, or is a particulate form of the infective agent itself. In the most severe infections the infecting micro-organism is prone to develop a form whereby it is able to pass through a filter. Although this ultra-microscopic form does not lose all the features peculiar to its parent form, it nevertheless acquires characteristics peculiar to ultra-microscopic viruses in general. These two points need further elaboration.

When a micro-organism develops into an ultra-microscopic form it does so in stages. If caught in the early stages it can be transformed again into the

parent form, but not so in the final stages. The connection then may be so far lost as to enable the ultra-microscopic form to become a more or less specific organism, and to call forth a more or less specific response, in the form of immunity reactions, in its host or victim. It is possible that the ultra-microscopic viruses responsible for epidemic encephalitis, anterior polio-myelitis, small-pox, chicken-pox, etc., are the ultra-microscopic forms of known micro-organisms which have advanced too far to permit of their journey being traced. All ultra-microscopic viruses have a very powerful reducing action ; or, in other words, carry a powerful negative charge, a property which enables them to cause a rapid and marked degeneration of the cells of the host they attack. The cells most readily attacked are the nerve cells, partly because they are the most vulnerable, and partly because the ultra-microscopic viruses have no difficulty in passing through the choroid plexuses.

The signs and symptoms encountered in botulism resemble the encephalitic form of entero-colitis, and the latter appears to be brought about by the non-lactose fermenter, causing the entero-colitis, developing an ultra-microscopic form. A similar sequence of events may occur in a condition to which the name of "*Psittacosis*" has been given. Therefore, carrying the argument further, botulism is probably that form of food poisoning where the activity carried by the contaminated article causes the existing pathogenic micro-organism in the intestinal tract to develop into an ultra-microscopic form. Another possibility, of course, is the direct conveyance of an ultra-microscopic virus from the faulty foodstuff to the victim.

It is interesting to note that in babies and old people atypical *Bacillus coli communis*, and the intermediate forms, are to be found more frequently than the pathogenic forms. This applies particularly to old people who seldom present non-lactose fermenters in their excreta despite the fact that they have active signs and symptoms of disease. Although the activity of non-lactose fermenting micro-organisms in the intestinal tract seems to increase the pathogenicity of the *Streptococcus faecalis* and the enterococcus, these micro-organisms may generally be regarded as innocuous. In only ten cases (five of each) out of the one thousand cases examined was the growth of these micro-organisms sufficiently pronounced to warrant their inclusion in the vaccine prepared from the pathogenic bacilli. When a rabbit dies from being fed or injected with either the live or the dead bodies of the non-lactose fermenters, only enterococci can be obtained from the heart's blood *post-mortem*.

These and other points about the bacterial flora of the intestinal tract will be dealt with more fully in the next part of this work ; indeed, the volume will

open with a report on the light further research has thrown on the problems raised in this short discussion. The author deems it safe to sum up here, that there is a close connection between the manifestations of disease and the activity of the pathogenic micro-organisms in the intestinal tract, and that so-called "food poisoning" is merely one of the manifestations.

(b) The Rectum and Anus

In this section it is proposed to make a few remarks about ulcerative colitis, ischio-rectal abscess, and piles. Ulcerative colitis begins in the rectum and spreads up into the colon; it is not infrequently associated with an ischio-rectal abscess and, in the author's opinion, is neither of tubercular nor of syphilitic origin. The actual ulceration does not appear to be precipitated by any of the non-lactose fermenting micro-organisms, and is most probably due to a secondary infection. Borgen¹⁸, working at the Mayo Clinic, claims to have grown an enterococcus, which does not ferment mannite, in 71 per cent. of the cases. Moreover, when this micro-organism was injected intra-venously into 459 rabbits, 268 showed evidence of disease, 131 developing lesions of the colon, and 137 having severe diarrhoea. In dogs, massive ulcers were produced in the colon. When treated with vaccines made from this enterococcus, 70 per cent. of the 250 patients were restored to a normal or relatively useful condition of life.

The author has not had sufficient cases of ulcerative colitis through his hands to confirm or refute Borgen's statements, but in the last case examined, which is reported below, the enterococcus could not be found.

Case 155

A man, aged forty-seven, had had ulcerative colitis for two years. As the patient had had syphilis, although he had been thoroughly treated for it fifteen years previously, the ulcerative condition was assumed to be syphilitic in nature, but despite most active anti-syphilitic treatment it continued to spread. For years prior to the advent of the ulceration the patient was very constipated. At the time of its onset he had urgent desire to defæcate, and passed large quantities of mucin and, later, mucus and blood. Eighteen months afterwards an ischio-rectal abscess appeared. The patient was thin and looked ill; he could not stand with his knees and feet together at the same time; all the molars were stopped; the tongue was furred and had patches denuded of papillæ; the elbows were hyper-extended, and there was acro-asphyxia. The pulse was 92 and the blood-pressures registered 100 and 70 mm. of Hg. respec-

tively. The whole abdomen was tender, there were many external piles, an ischio-rectal abscess, a stricture of the rectum due to earlier operative interference, and also ulceration which spread up into the colon. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde, and contained some protein. The pathogenic micro-organism found in the excreta was the *Bacillus proteus Valeriei* (30 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 4·7 c.c.
Refractive index of the serum	= 1·3530.
Percentage of the blood-sugar	= 0·086 grm.
Percentage of the blood-urea	= 32 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, but most were giant particles. There were some giant particles and giant-particled clumps precipitated.
Wassermann reaction	= Negative.

The patient was dieted, had colonic lavage, took at different times yatren, lacto-dextrin and *Bacillus acidophilus* internally, and received injections of emetine hydrochloride and of the fæcal vaccine. A bacteriophage was prepared from the *Bacillus proteus Valeriei* and was taken internally and implanted in the colon and cæcum, but all to no purpose, and the patient did not improve at all.

If the enterococcus plays a part in producing a secondary infection, as Bergen's work suggests, it is not improbable that this micro-organism has something to do with the formation of an ischio-rectal abscess. Although attention is usually drawn to an ischio-rectal abscess by an external opening, it is practically certain that the internal opening in the rectum appears first. Provided the case is seen sufficiently early, diet, colonic lavage, etc., will cause the trouble to abort, or will heal a stubborn post-operative case and prevent the condition developing into one of ulcerative colitis as illustrated by the following case :—

Case 156

A man, aged thirty-nine, had been operated upon twice for an ischio-rectal abscess, and the lesion had failed to mend after the second operation. The patient looked and was very ill, he was anæmic, thin and nearly bald. He had been troubled with chilblains and bronchitis as a child, and had had chronic nasal catarrh ever since. He suffered from *Acne vulgaris* and had had rheumatism from time to time. There was bilateral *Arcus senilis*, all the teeth had

been removed, the elbows were hyper-extended and wide-angled, and there was acro-asphyxia. There was central cupping of both optic discs and venous congestion. The pulse was 94, the blood-pressures registered 110 and 65 mm. of Hg. respectively and the heart was elongated, dropped, and narrowed. The colon was tender throughout its length, but particularly in both iliac fossæ and both hypochondria. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus proteus hydrophilus* (15 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 3·5 c.c.
Refractive index of the serum	= 1·3479.
Percentage of the blood-sugar	= 0·075 grm.
Percentage of the blood-urea	= 35 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving with an occasional giant particle and clump. Many more particles, giant particles, ringed particles and clumps precipi- tated <i>en masse</i> .

The patient was dieted, had a course of colonic lavage, and received injections of Sum. 468 and of the fæcal vaccine. When re-examined seven months later he was much improved, he had put on over a stone-and-a-half in weight and the abscess had completely healed.

Piles are a frequent source of worry to victims of familial chronic intestinal intoxication ; they are merely varicose veins, and the injection treatment aimed at sclerosing them is much to be preferred to removal by operation. One of the most suitable sclerosing fluids is alcohol (96 per cent.). Colonic lavage renders the injection treatment in most cases superfluous, but the patient should be warned that the hæmorrhoids will be considerably aggravated at first. A symptom of piles too frequently neglected and wrongly diagnosed is persistent pain in the back. In women this symptom is usually thought to point to uterine trouble, and in men the diagnosis either of fibrositis or of prostatic-vesiculitis is usually made. The following case illustrates these points :—

Case 157

A man, aged forty-eight, had had almost constant pain in his back for four years and had had various kinds of treatment. The patient's father suffered from hay-fever and asthma, and was crippled with rheumatism when he died ; one brother and one sister had succumbed to diabetes, and one sister

living had severe rheumatism. The patient had an attack of rheumatic fever when aged twenty-eight, which was followed by pleurisy and pneumonia. Nine years previously he had had an attack of gonorrhœa with epididymitis. All the teeth had been removed, the tongue was furred, the pulse was 72 and the blood-pressures registered 90 and 55 mm. of Hg. respectively. The left colon was contracted, there was tenderness in the region of the flexures, the ascending colon and cæcum were dilated, and the ileo-cæcal area was very tender although the appendix had been removed five years previously. The patient had very bad internal piles and had been losing blood daily for some considerable time. The urine gave a strong reaction with the hydrochloride of dimethyl-*para*-amino-benzaldehyde and contained some protein. The pathogenic micro-organism found in the excreta was the *Bacillus fœcalis alkaligenes* (1 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3478.
Percentage of the blood-sugar	= 0.068 grm.
Percentage of the blood-urea	= 38 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles, ringed particles and giant-particled clumps. There were many particles, giant particles and giant-particled clumps precipitated, with a tendency towards the formation of precipitation <i>en masse</i> . The Brownian movements of the particles were sluggish.

The patient was dieted, had a course of colonic lavage, took lacto-dextrin internally, and received injections of emetine hydrochloride and of the fæcal vaccine. The piles were considerably aggravated by the first six wash-outs, but, on the completion of the course of twelve, they ceased to bleed and were not visible. In addition, the pain in the back vanished, and the patient was able to continue his work, which he had been forced to give up.

Colonic Lavage

To give the reader an idea of colonic lavage by the written or spoken word is impossible, and the method must be seen and practised before its proper use can be appreciated and the various pitfalls avoided. The best method is that known as the "syphon method" introduced by Schellberg.^{15 16}

The aim of colonic lavage is to rid the colon of old fæcal material, mucus and *débris*, as far back as the ileo-cæcal valve, without causing any distension

or adding to the inflammation present. The patient should be instructed to have the bowels well opened before lavage, to avoid waste of time in washing out the rectum on each occasion. Although the tube can be advanced into the cæcum by a skilled person so long as no obstruction prevents its passage, this should never be attempted until the rest of the colon is clean. The tube should be advanced a few inches at a time whenever the returning water is quite clean. Not more than 6 ounces of fluid at a time should be allowed to run in, and this should be syphoned off before more fluid is admitted. If the tube is advanced too quickly fæcal material is pushed in front and an impassable impaction caused. Experience shows that a fæcal impaction made by the operator is a common form of obstruction. Moreover, it forms a nidus from which toxic material emanates, and passes through into the circulation. This explains why some patients are worse after lavage than before. Too much fluid dilates the gut, permanent atony or paralysis may follow, and the permeability of the intestinal wall be increased. But too speedy advancement is even more harmful, for a central passage is made by the tube which, as it advances, pushes fæces ahead of it and leaves old fæcal material moulded to the walls of the intestine. It is almost certain that injudicious lavage and hasty advancement of the tube may cause a diverticulum.

Therefore, anything in the nature of *Plombières* douching must be avoided. Each lavage, when properly performed, takes one to two hours. The treatments should be given first on two days in succession, and then once or twice a week, according to the conditions existing. The first few may be expected to cause an aggravation of the patient's signs and symptoms, and it is here where experience is so necessary.

In very acute febrile conditions complicating colitis, colonic lavage should not be used. When large quantities of mucus are passed by the patient or brought away by the lavage, the greatest care needs to be exercised, and a fortnight or more may have to elapse before the procedure is repeated. Too frequent lavage may itself produce mucus and cause colitis.

When the manifestations of disease presented by the patient are aggravated by colonic lavage, they may fail to respond to the remedies which previously kept them in check; therefore, medicines internally should be carefully prescribed, and injections used with caution. For example, contramine, so useful in rheumatism, may be valueless when this is being aggravated by a wash-out. It is for this reason, and for the fact that injections of the fæcal vaccine so often themselves produce a reaction, that only drugs exhibiting a conductor effect are advised while the patient is being washed out. Drugs used to palliate the

symptoms are, therefore, given beforehand, and the injections of the vaccine are kept until the lavage has been completed. For reaction caused either by lavage or by the injections of vaccine, it is best to prescribe lacto-dextrin internally in 1 ounce doses twice a day, and to make intra-muscular injections of emetine hydrochloride in $\frac{1}{2}$ grain doses twice a week until the reaction has entirely vanished. Reaction following colonic lavage can sometimes be avoided by the use in the lavage solution of such drugs as sodium bicarbonate, acid sodium phosphate, potassium permanganate, and colloid silver in extremely weak dilutions. When the fæces are very acid, sodium bicarbonate is called for, and when very alkaline acid sodium phosphate. Potassium permanganate and colloid silver are used when a conductor action is required.

When the colon is quite clean and the tube can be passed with ease into the ascending colon and cæcum, direct medication can be practised by this route.

Owing to the ease with which drugs reach the blood-stream through the right colon, care must be exercised, and only those drugs should be used which are designed to render the blood-picture normal. It may not be possible to clean the whole colon with eight to twelve wash-outs, in which case it is best to give the patient three or four months' rest, when a few wash-outs may do all that is desired.

For colonic lavage the apparatus found most suitable consists of a glass receptacle, supported on a stand about 6 ft. from the ground to contain the lavage solution. From this container the fluid is passed through about three yards of rubber tubing to a T-shaped glass connection, one limb of which is connected to a rubber "colon" tube, the other to a piece of soft wide-bored rubber tubing which serves as a waste pipe returning the fluid from the patient into a bucket. The introduction of fluid is regulated by a stop-cock on the tubing from the glass container, and the return by a stop-cock on the waste pipe. The colon tubes found most suitable are those obtainable from L. Gaillard, 9, Rue Danton, Paris, and The Schellberg Manufacturing Corporation, 172, Chambers Street, New York City, U.S.A. They are made of rubber, the French about 28 inches long and the American 54 inches long. At the end that is introduced into the patient there are two eyelets—one on each side of the tube. In choosing a tube it is necessary to make sure that the eyelets are as large as possible, otherwise these so easily get blocked and may cause the patient unnecessary discomfort.

It should be understood from the start that there is no necessity to cause the patient any pain; if anything more than slight discomfort is complained of the treatment is being administered badly.

The glass jar is filled with the solution at a temperature of 100° to 105° F. The end of the tube is first greased for about 6 inches with white vaseline, the solution is allowed to run from the container through the colon tube while the stop-cock on the waste pipe is closed ; the temperature of the solution as it leaves the colon tube should be felt with the hand before introducing the tube into the rectum, and in this way all air in the tube is expelled. With the patient lying on his left side, the tube is introduced with the right hand while the left raises the upper buttock to enable the operator to see the anus. Having passed the tube so that it is securely gripped by the anus, solution is introduced by opening the stopcock from the container and closing the stopcock on the waste pipe. Care should be taken to avoid introducing any air that happens to be in the tube ; this is best achieved by closing the waste pipe only after the solution has been allowed to flow through it. If the limb of the T-connection bearing the waste pipe be elevated, all air will rise and be expelled by the flow of fluid into the pail. It should be borne in mind throughout the treatment, that air rises, and an endeavour should always be made to keep the proximal end of the waste pipe at a higher level than the colon tube, otherwise air bubbles will find their way up the latter into the patient.

The Kidneys

In this section a few remarks are made about renal neuralgia, peri-nephritic abscess, pyelitis, "leaking kidney," nephritis and uræmia.

Renal neuralgia is not an uncommon condition, although it is one which, above all others, lends itself to multiple diagnosis. At the beginning of the present century the diagnosis of movable kidney was general until nephropexy fell into disrepute.

Renal calculus is a common diagnosis, kinking of the ureter another, and if the trouble is on the right side either the appendix or the liver and gall-bladder are taken to task. If attention is finally drawn to the kidneys, X-ray photographs are taken, various tests are performed, and a twenty-four hour specimen of urine is examined, all to no purpose.

In every case of renal neuralgia there is colitis, and the former is brought into being when any factor causes an exacerbation of the latter. It is not possible to describe the process which renders the affected kidney tender on pressure, but, judging from events in particularly severe attacks, it would appear that the kidney becomes engorged with blood. On these occasions large quantities of blood may be passed in the urine, and at operation a varicose condition of the vessels in the cortex of the kidney has been observed. In

the author's experience the left kidney is attacked more frequently than the right. The following case is typical of the condition :—

Case 158

A man, aged forty-seven, had had attacks of acute left renal pain, which at times were as severe as colic, for twenty-three years. They began when the patient ceased to suffer from hay-fever, the precipitation of the hydrated protein particles being transferred from the respiratory to the uro-genital tract. The attacks occurred at irregular intervals, and wrong food, over-drinking, and over-smoking would readily precipitate one, as would physical and mental strain. During an attack the patient felt ill, vomited frequently and had acute pain in the loin over the kidney region. The motions were black and foul, and large quantities of pale coloured urine were passed. When the attack was particularly severe angio-neurotic œdema affected the face, penis and scrotum, and hæmaturia occurred. The patient used to have chilblains, and since the attacks began he had suffered from rheumatism, piles and *Pruritus ani*. He had had his tonsils and all his teeth removed, but with no benefit, and after X-rays and all tests had proved negative an anterior and posterior exploratory operation were made. The laparotomy revealed nothing, but the posterior operation showed that the kidney was fixed to the diaphragm and, on cutting through the kidney substance, that the vessels were varicosed. The patient could not stand with his knees and feet together at the same time, the pupils were small, and reacted sluggishly to light, the optic discs were cupped, and there was venous congestion. The tongue was furred, all the reflexes were sluggish, the elbows were wide-angled and hyper-extended, and there was acro-asphyxia. The pulse was 82 and the blood-pressures registered 95 and 60 mm. of Hg. respectively. The patient was subject to severe fits of depression and had repeated attacks of *Herpes preputialis*. The left colon was contracted and tender, particularly in the region of the splenic flexure. There was tenderness also in the region of the hepatic flexure, and over the ileo-cæcal area, the ascending colon and cæcum were dilated. The pathogenic micro-organism found in the excreta was the bacillus of para-dysentery (Harris-Wollstein) (25 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·05 c.c.
Refractive index of the serum	= 1·3480.
Percentage of the blood-sugar	= 0·125 grm.
Percentage of the blood-urea	= 27 mgrm.

Ultra-microscopic picture of the serum = Very few particles moving, and these were either very refractile giant particles or ringed particles. There were some very refractile giant particles, ringed particles, giant-particled clumps and agglutinations precipitated. The Brownian movements were very sluggish and the precipitation increased with time.

The patient was dieted, gave up smoking, had colonic lavage, took lacto-dextrin internally, and received injections of strontium aspartate and of the fæcal vaccine.

The patient improved enormously. From being a thin, miserable creature weighing 9 stone 10 pounds, he increased to 13 stone 7 pounds, and never had an attack so long as he did not partake of poisonous food.

A peri-nephritic abscess is not an uncommon condition, but it is one where an early diagnosis is not often made. The author has in mind the case of a man, aged twenty-two, who had a daily pyrexia for thirteen months before the cause was found to be a peri-nephritic abscess. In this case the patient had no pain, and the wall of the abscess was over an inch thick. A peri-nephritic abscess is usually tender on pressure, and certain movements may bring on and aggravate the pain. It almost invariably causes a pyrexia and, like most deep abscesses, is present long before it gives rise to symptoms; hence the reason why the suspension stability of the red blood-corpuscles is always very much reduced. A peri-nephritic abscess is hardly ever the primary lesion; that is to say, it occurs after the patient has shown evidence of boils and carbuncles elsewhere. Abscesses in the deep intra-muscular tissue of the limbs are particularly apt to be forerunners of a peri-nephritic abscess, while ordinary boils and carbuncles affecting the face and neck more often precede an abscess in the lungs. A pulmonary abscess of this kind is seldom diagnosed correctly, and therefore a case of each kind is described below.

Case 159

A man, aged forty, had complained of pain underneath the posterior ribs on the left side for over a month, and for the past few days he had been unable to straighten the left leg on account of pain. Two months previously a deep boil had had to be opened on the left thigh, and before this he had had boils on the neck. Since the pain in the back had begun, the temperature had risen every night to 102° F. The patient had suffered from *Seborrhœa corporis et capitis*, which had caused him to go bald when twenty years of age. The appendix was removed in 1912, and enteritis occurred in Gallipoli in 1914, and

persisted till 1917, when the patient was sent to France, where he immediately contracted trench fever. He had had measles twice and scarlet fever once. The pulse was 100 and the blood-pressures registered 90 and 50 mm. of Hg. respectively. The whole of the right side of the abdomen was extremely tender, and the patient was undoubtedly suffering from entero-colitis, much mucus being passed in the stools. There was definite tenderness over the apex of the left kidney behind, and an abscess was found on operating a few days later. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus para-typhosus* B (10 per cent.). The patient's serum agglutinated *Bacillus para-typhosus* A and B, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 5·4 c.c.
Refractive index of the serum	= 1·3485.
Percentage of the blood-sugar	= 0·131 grm.
Percentage of the blood-urea	= 28 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving, and these were mostly giant particles and ringed particles. There were many more particles precipitated <i>en masse</i> .

The patient was operated upon, and after he had convalesced he developed an abscess in the meso-rectum which had given rise to continuous sciatica. Although this abscess was opened from below it was not diagnosed until a laparotomy had been performed.

This case has several points of interest. The enteritis in Gallipoli from which so many suffered was not contracted on the Peninsula, but was merely an acute exacerbation of a familial chronic intestinal intoxication brought about by the wrong food. The acute exacerbation of the intestinal trouble caused hydration of the protein particles in the plasma, and this became further accentuated when the wrong food was partaken of again in France. The extra hydration caused œdema and proteinuria, which went by the name of "trench nephritis," but the kidneys did not become inflamed unless the trouble persisted. The initial proteinuria was caused by the passage of hydrated protein particles from the plasma through glomerular membranes, the permeability of which had been increased by the local arrest of the altered protein particles.*

* There would be no epidemics amongst the soldiers in war-time if they were properly fed. The main faults committed in the last war were the consumption of tinned foods and the absence of fresh vegetables and fruit.

In the last five cases of peri-nephritic abscess, the author has had the opportunity of examining, the abscess was on the left side and the pathogenic micro-organism found in the excreta was the *Bacillus para-typhosus*.

Case 160

A man, aged twenty-six, had a sudden hæmoptysis one Christmas, and the diagnosis of pneumothorax was made. A week later he was said to have developed pneumonia, and six months after this a pleurisy with effusion occurred. On several occasions a diagnosis of tuberculosis was made, but this was negatived by an X-ray photograph which showed an outline of what had obviously been an abscess between the lobes of the right lung. Six years previously he had been troubled with boils and carbuncles on the neck. He used to suffer from chilblains and hay-fever, and had two brothers who were chronic asthmatics and one who had had furunculosis. These two brothers, together with two more, the father and the patient himself had been operated upon for appendicitis. He was grossly mal-co-ordinated, suffered from chronic nasal catarrh, and had had attacks of lumbago and sciatica. The tonsils, adenoids and all the teeth had been removed. The pulse was 90 and arrhythmic, and the blood-pressures registered 115 and 70 mm. of Hg. respectively. The urine gave a strong reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The whole colon was tender, the ascending colon and cæcum were dilated. The pathogenic micro-organisms found in the excreta were the *Bacillus para-typhosus* A (90 per cent.) and the *Streptococcus fæcalis* (25 per cent.). The serum did not agglutinate the *Bacillus para-typhosus* A and B. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3491.
Percentage of the blood-sugar	= 0.112 grm.
Percentage of the blood-urea	= 33 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with many giant particles and some giant-particled clumps. There were some giant particles and agglutinations precipitated. All the particles were very refractile.

The patient was dieted, had a course of colonic lavage, took a tonic internally, and received injections of Sup. 468 and of the fæcal vaccine.

The patient improved enormously. The blood-picture is little changed because it was taken a long time after the pulmonary abscess had burst.

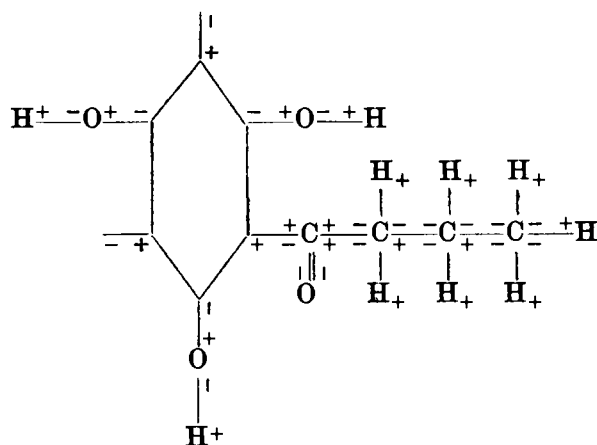
Pulmonary abscesses may be rapidly fatal, and they are almost invariably wrongly diagnosed, which should not be the case if a previous history of furunculosis is forthcoming. Pneumonia is the most common diagnosis made, and then tuberculosis. The diagnosis of the latter is particularly apt to be made if recurrent hæmorrhages occur, and they are not uncommon if the cause, the chronic intestinal intoxication, is left untouched. The patient whose case has just been reported had three small hæmorrhages at intervals of some months after the initial hæmoptysis. There is little doubt that the tubercle bacillus is ordinarily a saprophyte which may develop pathogenic properties when a chronic intestinal intoxication lowers the patient's resistance sufficiently, and many are the patients sent to sanatoria who would be treated better and at less cost at home. Catarrh of the pulmonary apices occurs before the tubercle bacillus becomes implanted, and the latter would never gain a foothold if the cause of the former was removed. There are many pulmonary conditions labelled tubercular which are not due to the activity of the tubercle bacillus, but further discussion on this subject must be deferred till the chapter on "Disease and the Lungs" is published in the next part.

Pyelitis is a condition which the author has learnt to dread because it tends to relapse despite treatment, and because it seems to be on the increase. In the author's opinion, pyelitis is seldom, if ever, cured; it often progresses without the patient's or physician's knowledge, and a recurrence occurs whenever the patient's resistance is lowered. Pyelitis is more common in women than men because pregnancy is often the precipitating factor. Although signs and symptoms may point to the affection of only one kidney, the other is never spared. The primary cause is a chronic intestinal intoxication which, by lowering the patient's resistance, enables the *Bacillus coli communis* to reach, settle and multiply in the pelves of the kidneys. The micro-organisms reach the kidneys *via* the lymphatic vessels, and any spread is downwards along the ureters into the bladder. If the intestinal intoxication is severe, pathogenic mutation forms of the *Bacillus coli communis* may replace the parent form in the uro-genital tract. Long continued activity of the fæcal micro-organisms may damage and cause inflammation of the pelves of the kidneys, ureters and bladder, but severe inflammatory changes do not as a rule occur till a superadded coccogenic infection gains a foothold. When this occurs, miliary abscesses form throughout the whole of the kidney substance, and the ureters become thickened and dilated. In really bad cases the kidneys and ureters may become completely disorganised, and what is most astonishing is the fact that the severity of the trouble is generally only

recognised *post-mortem*. In early cases the urine, although thick, tends to be colourless ; but when a coccogenic infection replaces the fæcal micro-organisms, the urine may regain both its colour and clarity. In the very worst cases the patient may be going about her work a few days before her death, all renal deficiency tests may be negative, and a microscopic examination of the kidneys removed *post-mortem* may yield not a field of healthy renal tissue.

A woman who develops a pyelitis during pregnancy should never be allowed to become pregnant again, because each succeeding pregnancy aggravates the condition even if it has seemed to be at a standstill meanwhile. Treatment to be effective must be aimed at ridding the patient of her chronic intestinal intoxication. Sup. 36 is of the greatest value during an acute attack, and hexyl-resorcinol should be prescribed internally. Sup. 36 should be used at the beginning of every acute attack, as it may frequently abort it. Hexyl-resorcinol does not act as a urinary antiseptic, as generally thought, but merely as a conductor, and its place may be taken by other conductors such as phlor-butyro-phenone, a drug advised for helminthiasis. The fact that hexyl-resorcinol and phlor-butyro-phenone are of equal value as urinary antiseptics and vermifuges, goes far to substantiate the author's view that chemotherapeutic preparations function merely by increasing the patient's resistance.

The author made an error regarding the electronic formula of phlor-butyro-phenone in the previous volume, and wishes to state that the signs should be reversed as follows :—



A few cases of pyelitis are reported below.

Case 161

A woman, aged thirty-six, had had her second miscarriage seven months previously, and had evidenced signs of pyelitis two months before then. The patient had not been well since the miscarriage. She had suffered from chronic indigestion and constipation all her life, and had had several attacks of cystitis. She had been troubled for many years with leucorrhœa, and had been operated upon for appendicitis, piles and an anal fistula. The patient was pale, all her teeth had been removed, and she had wide-angled and hyper-extended elbows. The pulse was 77, and the blood-pressures registered 105 and 80 mm. of Hg. respectively. The left colon was contracted and tender, the ascending colon and cæcum were dilated, and there was marked tenderness in the ileo-cæcal area. A catheter specimen of urine was very pale, and contained pus and large quantities of *Bacillus coli communis*. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (15 per cent.), and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3490.
Percentage of the blood-sugar	= 0·093 grm.
Percentage of the blood-urea	= 21 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving, many giant particles and ringed particles. There were a few giant particles and ringed particles precipitated with one or two giant-particled clumps.

The patient was dieted, had colonic lavage, took hexyl-resorcinol and lacto-dextrin internally, and received injections of Sup. 36, Sup. 468 and of the fæcal vaccine.

In spite of living most carefully the *Bacillus coli communis* never vanished from the urine, fully two years elapsed before the patient felt really well, and on the slightest indiscretion the pyelitis would return but would clear up at once if two injections of Sup. 36 each of 0·01 grm. were made on two days in succession.

Case 162

A woman, aged twenty-seven, developed pyelitis, without ever having had cystitis, when seven months pregnant with her first child, a boy. The patient's father died of a stroke, aged sixty-five, and her mother of toxic nephritis of pregnancy at the birth of her sixth child, a girl, aged forty-two. The patient suffered from hay-fever and asthma and was sensitive to horse dandruff. She had suffered from furunculosis, had had her appendix removed, and was sup-

posed to have had typhoid fever when a year old. She could not stand with her knees and feet together, all her molars had been stopped, the tongue was furred, the elbows were wide-angled and hyper-extended and she had acro-asphyxia and leuconychia. The pulse was 94 and the blood-pressures registered 130 and 90 mm. of Hg. respectively. The optic fundi showed arterio-sclerotic changes, and there was evidence of aortitis. A catheter specimen of urine contained pus, and large quantities of *Bacillus coli communis*. The pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici* (100 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·4 c.c.
Refractive index of the serum	= 1·3500.
Percentage of the blood-sugar	= 0·156 grm.
Percentage of the blood-urea	= 29 mgrm.
Ultra-microscopic picture of the serum	= Many particles moving with a high percentage of giant particles. Many particles, giant particles and giant-particled clumps precipitated. All the particles were very refractile.

The patient was dieted, had colonic lavage, took caprokol internally, and received injections of Sup. 36, Sup. 468 and of the fæcal vaccine.

She improved but, against advice, became pregnant eleven months later. The pregnancy had to be terminated because the pyelitis became active again in both kidneys. Even one year after this the patient was far from well and was always liable to recurrent attacks of pyrexia which were caused by the activity of the *Bacillus coli communis* in the pelves of the kidneys.

Case 163

A man, aged thirty-six, had an attack of cystitis and pyelitis, which began with hæmaturia when he was fifteen years of age. The condition had recurred in exactly the same way six weeks before the author's advice was sought. The patient used to have bronchitis as a child and had dysentery, scarlet fever and jaundice together while serving in Gallipoli. One year later he was inoculated against typhoid fever, and had a " pyrexia of unknown origin " for the eight months following. He had been operated upon five times for cervical adenitis in boyhood, had had tonsils, adenoids and appendix removed, and also had several operations for nasal catarrh, all of which left the condition a little worse than before. The patient presented all the cardinal signs of familial chronic intestinal intoxication, and his only boy was an achondroplastic. The pulse was 88 and the blood-pressures registered 85 and 50 mm. of Hg. respec-

tively. The left colon was contracted, the transverse colon had dropped, and the ascending colon and cæcum were dilated. A catheter specimen of urine revealed pus cells, and the *Bacillus acidi lactici* in large quantities. The pathogenic micro-organism found in the excreta was the bacillus of epidemic jaundice (20 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·15 c.c.
Refractive index of the serum	= 1·3482
Percentage of the blood-sugar	= 0·106 grm.
Percentage of the blood urea	= 22 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving. There were a fair number of giant particles and small clumps precipitated and the precipitation increased with time.

The patient was dieted, had colonic lavage, took hexyl-resorcinol internally, and received injections of Sup. 36, Sup. 468, and of the fæcal vaccine.

He improved considerably, but whenever his resistance was lowered the cystitis and pyelitis returned. Fortunately both could be kept in check with Sup. 36.

In many cases of pyelitis there is a definite history of cystitis occurring previously, but this is by no means always the case. Most women with a familial chronic intestinal intoxication have an attack of cystitis some time or other but, fortunately, only a minority develop pyelitis. In no case is the pyelitis due to a direct extension of the *Bacillus coli communis* along the ureters to the pelves of the kidneys. In the author's experience washing out the pelves of the kidneys *viâ* ureteric catheterisation does the patient more harm than good.

In this connection a word should be said about congenital cystic kidney, because the renal organs when in this condition are particularly prone to develop pyelitis, and the appearance of the latter may be the means whereby the presence of the former is ascertained, as illustrated in the following case.

Case 164

A woman, aged thirty-nine, suddenly developed pyelitis which rapidly responded to Sup. 36. A lump was felt after the attack had subsided and, hydronephrosis being feared, an exploratory operation was made and a cystic kidney discovered. The mother died of congenital cystic kidneys, aged fifty-eight, and the patient was her only child. Hay-fever developed when the patient was twenty-one years of age and had continued since, becoming more

severe with each succeeding season. Menstruation began at the age of thirteen, but as she suffered so much from menorrhagia and metrorrhagia an artificial climacteric was produced. It was just after this that the first attack of pyelitis occurred. The patient looked old for her years and began to go grey at the age of twenty-two, all her teeth had been removed and the tongue was furred and fissured. The pulse was 114 and the blood-pressures registered 200 and 130 mm. of Hg. respectively. The whole colon was tender, and mucus was invariably passed with the fæces. A catheter specimen of the urine contained pus and the *Bacillus proteus hydrophilus*. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (20 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.5 c.c.
Refractive index of the serum	= 1.3496.
Percentage of the blood-sugar	= 0.156 grm.
Percentage of the blood-urea	= 42 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a fair number of giant particles and ringed particles. There were a fair number of particles, giant particles, ringed particles and giant-particled clumps precipitated.

The patient dieted, had colonic lavage, took hexyl-resorcinol internally and received injections of Sup. 36 and of the fæcal vaccine.

Sup. 36 kept the pyelitis and hay-fever in check, but the patient went steadily downhill and died. For some time before her death her hands used to be œdematous, first thing in the morning, and enormous bruises appeared spontaneously in various parts of the body. The mother exhibited the same phenomena before she died. The urine never contained more than a trace of protein.

The term "leaking kidney" is applied to the condition where a constituent of the blood finds its way into the urine without its percentage in the blood being necessarily raised. Like most terms in medicine it is a misnomer, and in this case the term is a bad one because the fault is centred on the kidney when it as often rests with the blood, and in many cases lies with both. When the protein particles in the plasma are hydrated the liquid part of the plasma becomes more and more like pure water. The less colloid the liquid portion of the plasma becomes, the less it is able to hold any planet liberated suddenly from a hydrated protein particle undergoing the cyclical change of dehydration.

The liberated planet readily passes through the kidneys into the urine without its percentage in the blood being raised. The passage is accelerated if the permeability of the glomeruli is increased, and this it tends to be when the protein particles in the plasma are hydrated. When the hydration is most acute, and in disease this is usually a sequence of acute dehydration, the permeability of the glomeruli is raised to its maximum, and red blood-corpuscles and protein are liable to pass through into the urine. But, the occurrence of this phenomenon does not warrant the diagnosis of nephritis. It is true that should the abnormal chemico-physical changes to which the protein particles in the plasma have been subjected persist, inflammatory changes result. But, nevertheless, for a long time before the designation nephritis is permissible there is no more than an increased permeability of the glomeruli. As regards the blood, and particularly where it concerns the passage of protein, the state in which the protein particles happen to be is of paramount importance. Hydrated protein particles pass through the glomerular membranes more readily than normal protein particles, despite the fact that they are generally larger. This is because hydration interferes with their surface electricity and makes them behave as foreign bodies. Therefore, in many cases of proteinuria, although there may be an increased permeability of the glomeruli, there is at first no inflammation of the kidneys, and the protein is passed mainly because it has collected in the kidneys and is behaving as a foreign substance.

The so-called "leaking kidney" is more a blood than a renal phenomenon. The continuance of the dehydration causes, in the end, glomerulitis and mesenchymatous or interstitial nephritis, while persistence of the hydration causes parenchymatous or tubular nephritis. If the cases are seen sufficiently early and the primary and secondary causes of gelato-hydration are removed, nephritis does not result. When the condition is acute, and dehydration prevails over hydration, red blood-corpuscles pass into the urine, but when hydration prevails over dehydration, protein passes into the urine. The passage of both blood and protein may be encountered in children as well as in adults. Renal hæmorrhage in children is most common when streptococci are active somewhere in the body, while in adults it is usually a sign of generalised arteriosclerosis. Proteinuria in children may be congenital, in which case the protein passed is mainly globulin, but both in children and adults it is always secondary to a familial chronic intestinal intoxication, and in the latter it is usually precipitated by any factor which augments the hydration already in existence. This explains why physical and mental strain, bad food and toxic agents may cause a proteinuria which can vanish as quickly as it can appear. It is surprising

how frequently, in cases of familial chronic intestinal intoxication, the addition to urine of two or three drops of a saturated solution of salicyl-sulphonic acid reveals a trace of protein. Not only may lipoid-globulin, globulin, and albumin appear in the urine, but also products lower in the scale than the last, such as peptones, polypeptides, amino-acids, etc. Two of the most convenient urine tests for these last-mentioned substances are the pink colour given with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and the olive green colour given with nitric acid. These tests are often negative when protein is present, and the former of the two is seldom positive in the urine of women, the reason for which the author has so far been unable to discover. The following cases illustrate the points raised.

Case 165

A man, aged forty-one, was found to have glycosuria when examined for life insurance. The patient's father succumbed to diabetes after being short-circuited for a duodenal ulcer, aged sixty, and his mother to *Morbus cordis* following rheumatic fever, aged fifty-four. The patient had suffered from indigestion and constipation all his life, he had had chilblains, rheumatic fever, migraine, and three attacks of jaundice. He had passed sugar in the urine continuously for over two years at least, he looked ill, and presented all the cardinal signs of familial chronic intestinal intoxication. The pulse was 92 and there were extra-systoles; the blood-pressures registered 105 and 75 mm. of Hg. respectively. There was marked tenderness in both iliac fossæ and in both hypochondria, the sugar tolerance test was positive, the pathogenic micro-organism found in the excreta was the *Bacillus fecalis alkaligenes* (100 per cent.) and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3482.
Percentage of the blood-sugar	= 0.107 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving, many of which were giant particles. There were some giant particles and giant-particled clumps precipitated.

When the patient was examined he had glycosuria, although he had been dieted as a diabetic for some months. After the examination he was placed on ordinary diet with the exception of butcher's meat, eggs and milk. The colon

was washed out, iodine, ichthyol and thyroid internally were prescribed, and injections of contramine and of the fæcal vaccine were made.

The patient improved and for the past two years has passed no sugar in the urine.

Case 166

A man, aged fifty, had suffered from rheumatism and neurasthenia for many years. The patient's mother used to have hay-fever, and she died of scarlet fever, aged thirty. His only sister suffered from hay-fever, and was operated upon for cancer of the colon when aged forty-six. His daughter, aged ten, suffered from both hay-fever and neurasthenia. The patient had had his tonsils, teeth and appendix removed, without benefit to the rheumatism. He was tall, thin, and presented the usual signs of familial chronic intestinal intoxication. Like many such patients, there was no superficial area of cardiac dullness, owing to the heart being elongated and narrowed. His tongue was furred, fissured, and raw in places, and all reflexes were sluggish. An ophthalmoscopic examination revealed arterio-sclerotic changes, and there was marked central cupping of both discs. The pulse was 64, the blood-pressures registered 110 and 75 mm. of Hg. respectively, the urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and the abdomen was tender in the usual three areas (splenic, hepatic and ileo-cæcal). The pathogenic micro-organism found in the excreta was the *Bacillus proteus Valeriei* (50 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·2 c.c.
Refractive index of the serum	= 1·3480.
Percentage of the blood-sugar	= 0·118 grm.
Percentage of the blood-urea	= 24 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles, ringed particles and a few small giant-particled clumps. There were a few giant particles and giant-particled clumps precipitated. The Brownian movements were sluggish.

The patient was dieted, had a course of colonic lavage and received injections of contramine and of the fæcal vaccine. His condition improved except for the neurasthenia, which persisted. In an attempt to combat the latter, a second injection of the vaccine was made (dose one millic) three months after the first dose of 0·5 million. Two weeks later the patient had pyrexia, headache, abdominal pain, pain in the region of the kidneys, profuse

sweating, spontaneous bruises, and hæmaturia. This was obviously a reaction produced by the second injection of the vaccine, although it appeared much later than usual. The patient recovered from the reaction, but never lost his neurasthenia.

Case 167

A man, aged fifty-five, had had periodic attacks of hæmaturia for seven years. They usually continued for three days but the last persisted for over three weeks. The patient's father died of diabetes, aged fifty-seven, the mother with obesity, aged sixty-seven, one sister from Bright's disease, aged sixteen, another from colitis, aged forty, and the third from exophthalmic goitre, aged fifty. He suffered from rheumatism, migraine and colitis, he was grossly mal-co-ordinated, and was going deaf (arterio-sclerosis). He had marked *Arcus senilis*, the pupils were small, all the reflexes were sluggish, and there was generalised arterio-sclerosis. The nails were dry, ridged and hyperkeratotic, the pulse was 80 and the blood-pressures registered 120 and 80 mm. of Hg. respectively. The whole colon was tender, the pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici* (50 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3480.
Percentage of the blood-sugar	= 0.068 grm.
Percentage of the blood-urea	= 26 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving and these were either giant particles or giant-particled clumps. There were similar particles precipitated and the Brownian movements were sluggish.

The patient was dieted, had colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the fæcal vaccine.

The patient improved and has had no further hæmorrhage to date.

Case 168

A man, aged thirty-two, sought advice because he had been refused life insurance on account of proteinuria. He lost his father from cancer of the stomach, aged sixty-five, and his mother from pneumonia, aged fifty-five. He suffered from chronic nasal catarrh, had been much troubled with furunculosis, and had had a mastoid operation performed. He had protruding ears,

could not stand with his knees and feet together at the same time or straighten his elbows, the tongue was furred, and the optic discs were mal-developed. The pulse was 104, and the blood-pressures registered 145 and 75 mm. of Hg. respectively. The urine gave a heavy precipitate with salicyl-sulphonic acid. The left colon was contracted, the ascending colon and cæcum were dilated, and there was tenderness in the usual areas. The pathogenic micro-organism found in the excreta was the *Bacillus Gärtner* (25 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.1 c.c.
Refractive index of the serum	= 1.3495.
Percentage of the blood-sugar	= 0.143 grm.
Percentage of the blood-urea	= 41 mgrm.
Ultra-microscopic picture of the serum	= Very few particles moving and these were all giant particles. There were about the same number of particles precipitated. The Brownian movements of the particles were very sluggish and precipitation increased with time.

The patient was dieted, had colonic lavage, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the fæcal vaccine.

He improved enormously and when examined six months later the urine was free from protein.

In this case it is impossible to say how long the proteinuria had been present, but, judging from other cases where treatment has succeeded, but failed in checking the proteinuria, the author would suggest at least two years and not more than five years. Where treatment fails to influence the proteinuria the case should be regarded as one of nephritis. The presence or absence of blood cells and casts is not a sure criterion of either leaking kidney or nephritis, the urea concentration test is not of great service and the result of treatment is the only reliable guide. In actual fact leaking kidney runs into nephritis, consequently there is no dividing line, but from his experience, the author would suggest that the insurance companies are wrong in refusing to take applicants merely because their urine contains sugar, protein, etc. Even with a mild form of nephritis, so long as the patient gets rid of his familial chronic intestinal intoxication, and prevents its recurrence, the normal expectancy of life can be anticipated. The following is an excellent example of proteinuria occasioned by alcohol, because the patient was known to be protein-free before he drank to excess.

Case 169

A man, aged forty-nine, but looking fifty-nine, had drunk to excess for over two years, having been much troubled with vasomotor rhinorrhœa and bronchorrhœa. The patient was a typical example of familial chronic intestinal intoxication, and had suffered from chilblains and furunculosis. He had widespread arterio-sclerosis, the pulse was 92 and the blood-pressures registered 140 and 80 mm. of Hg. respectively. The urine gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde and contained large quantities of protein. The abdomen was too stout to permit of a proper examination. The pathogenic micro-organisms found in the excreta were the *Bacillus acidilactici* (33 per cent.) and the *Bacillus proteus Valeriei* (1 per cent.). The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.3 c.c.
Refractive index of the serum	= 1.3488.
Percentage of the blood-sugar	= 0.093 grm.
Percentage of the blood-urea	= 20 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving and most of them were giant particles. There were a fair number of particles, giant particles, ringed particles and small giant-particled clumps precipitated. The Brownian movements of the particles were sluggish.

Before the treatment advised was begun the patient had an extra bout and nearly developed *Delirium tremens*, but this was checked by injecting 100.0 c.c. colloid iodine intra-venously, and 0.125 grm. contramine intra-muscularly. This treatment was suggested by the author many years ago, and has proved successful in a large number of cases. If the patient actually has *Delirium tremens* the treatment should be augmented by lumbar puncture.

When the patient recovered he cut out butcher's meat, eggs and milk from his diet, had colonic lavage, took iodine, ichthyol and thyroid internally, and had further injections of contramine and of the fæcal vaccine. At the beginning of this treatment the proteinuria increased, and œdema of the ankles, with an erythema of the shins appeared, but, before its completion, all the symptoms had cleared up.

Nephritis, considered to be one of the most devious paths in medicine, is in reality one of the straightest. There are two fundamental types and a mixed one. The former are, glomerulitis, the result of dehydration, and tubulitis, the result of hydration. The latter is a mixture of the two. True glomerulitis,

mesenchymatous or interstitial nephritis is rare, it is merely an accompaniment of generalised fibrosis; the patient invariably has high blood-pressures, and he passes large quantities of clear light-coloured urine which contains no protein and little or no foreign substance.

Case 170

A man, aged sixty-two, complained of insomnia, loss of memory, and giddiness. His mother died of cerebral hæmorrhage, aged thirty-one, and a brother and sister of the same condition, aged fifty-six and fifty-eight respectively. There were two sisters and one brother living and all had hyperpiesia. The patient had attacks of temporary aphasia and amaurosis, he was old for his years, tall and very thin. The pupils were miotic, and reacted neither to light nor to accommodation; an ophthalmoscopic examination revealed marked arterio-sclerotic changes. All the reflexes were sluggish, the nails were dry, ridged and hyperkeratotic. Some of the finger nails presented lesions such as are found in psoriasis. The pulse was 86, the blood-pressures registered 220 and 120 mm. of Hg. respectively, and there was evidence of aortitis. The arteries were hard and there was no pulsation in the posterior tibial arteries or in the dorsal arteries of the feet. The patient had to pass water every two hours day and night, and he complained of sudden choking and sneezing fits, which occurred whenever he was eating. The colon was generally spastic, there were no pathogenic micro-organisms found in the excreta, and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.4 c.c.
Refractive index of the serum	= 1.3500.
Percentage of the blood-sugar	= 0.106 grm.
Percentage of the blood-urea	= 34 mgrm.
Ultra-microscopic picture of the serum	= Myriads of particles moving with an amicronic haze.

The patient was dieted, had first treacle enemata and then colonic lavage, took iodine and ichthyol internally, and received injections of insulin.

The patient improved and is alive to date, three years later. Whenever insulin depressed him, an injection of Sup. 36 was made. Glomerular nephritis is frequently referred to as "azotæmic nephritis" on the ground that nitrogenous waste products collect in the blood because they cannot be excreted into the urine. It was upon this hypothesis that MacLean¹⁹ introduced the urea-concentration test. In this type of nephritis, water and substances soluble therein have no difficulty in passing through the glomeruli; indeed, in the

beginning their passage is accelerated. There is no special tendency for nitrogenous substances to accumulate in the blood-stream and the term "azotæmic" is not justified. In the many cases examined there has been no rise in the percentage of the blood-urea, and in cases which die with a hyperuræmia the clinical and pathological features are different.

In true glomerular nephritis the protein particles are extremely dispersed in which state the various planets remain adsorbed, and it is unusual to find a rise either in the percentage of the blood-sugar or of the blood-urea. It is true that a sudden addition to the dehydration may cause a rise in the percentage, first of the blood-sugar and then of the blood-urea, but this phenomenon practically only occurs when there is some hydration, and in kidney cases where there is some tubular nephritis. The urea-concentration test is of no real value because a thorough examination of the blood, and the specific gravity and refractive index of the urine, throw more light upon the case and suggest a line of treatment.

In cases of true glomerular nephritis the specific gravity and refractive index of the urine are low because the blood is in a perfect homogeneous colloid state and not because the kidneys fail to let this or that substance pass. Insulin is the correct treatment because it functions as a hydrator, makes the protein particles larger and the plasma less of a homogeneous colloid or gel. The hydration results also in vascular dilatation, but if the large capillary network, which was thrown out of action through becoming fibrosed, and which caused the blood-pressures to become raised, is damaged beyond repair, the blood-pressures will not fall, although insulin occasions hydration of the protein particles in the plasma. Dehydration or glomerular nephritis would be better referred to as "gel nephritis" than as "azotæmic nephritis," because the various phenomena observed are influenced more by the colloid state in which the protein particles happen to be than by what the kidneys allow or disallow to pass through them.

True tubular or parenchymatous nephritis is likewise rare. It is merely an expression of excessive protein hydration although it is frequently referred to as "hydræmic nephritis" or "nephrosis." In the initial stage the patient may be perfectly well despite the fact that the urine may become solid on boiling. Later, œdema sets in, the quantity of urine passed in the twenty-four hours becomes less and less, and the specific gravity and refractive index rise higher and higher. The term "nephrosis" is meaningless, the term "hydræmia" is good because, owing to the extreme hydration the protein particles in the plasma undergo, the liquid part becomes more and more like water. The fault

made in this type of nephritis is to assume that the kidneys are unable to permit of the passage of chlorides, and on this false assumption a chlorine or salt-free diet is advised. The condition is primarily one of the blood and not of the kidneys, and chlorine is not retained.*

When protein particles undergo hydration the planets are more firmly adsorbed, and become less readily detected in the liquid part of the plasma which no longer contained the various constituents of the protein particle in solution. There grows an ever greater disparity between the particle hydrated and the liquid part of the plasma, and this creates a no man's land between them which is recognised by a halo around the particles, and a capsule around micro-organisms. The hydrated protein particles become too large to circulate, they become precipitated, and later, act as a dam to the passage of water. The following is a typical case of hydration nephritis.

Case 171

A woman, aged thirty-five, became suddenly very ill during her third pregnancy. She had had trouble with her two previous pregnancies and was known to have had nephritis. The present illness began with headaches, and pain in the small of the back, and it was noticed that there was much protein in the urine. A routine examination of the blood was made and because the Wassermann reaction was positive, although there had been no suggestion or evidence of syphilis, anti-syphilitic treatment was prescribed. After the first injection of nov-arseno-benzene into the arm, and of mercury into the buttock, the patient developed incessant vomiting, became very oedematous and had almost complete anuria. The blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 3·5 c.c.
Refractive index of the serum	= 1·3550.
Percentage of the blood-sugar	= 0·068 grm.
Percentage of the blood-urea	= 8 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving and these were mostly very refractile giant particles each with a halo around. There were some particles precipitated in the form of giant particles and giant-particled clumps.

The patient received 1000·0 c.c. of a 10 per cent. solution of glucose intravenously and sub-cutaneous injections of oxygen, each of 200·0 c.c. every two hours. In addition, lumbar puncture was performed, but the patient did not

* It is interesting to note that *Natrium muriaticum*, a great stand-by of the homœopath, causes hydration when first administered, so much so that in animals the first dose of histamine produces fatal shock—sensitisation by a previous dose of histamine being unnecessary.

recover. More recent experience leads the author to think that, if the patient had been bled and then transfused with blood, her life might have been saved. In really bad cases of shock, such as this, it is not wise to inject dehydrators, particularly in a large bulk of fluid, because the plasma becomes more like water than ever and the protein particles are not split up. In shock the liquid part of the plasma acquiring the properties of water may be more serious than the protein particles undergoing hydration.

The above was a typical case of excessive hydration—a type of case which, even in the absence of a syphilitic infection, is very liable to give a positive Wassermann reaction. A drug like arseno-benzene with its positively charged amino groups causes a marked initial hydration, and the author has seen eight non-syphilitic cases, within the past five years, succumb to arseno-benzene prescribed merely because the Wassermann reaction was positive. The death in all cases was due to the augmentation of the hydration produced by this drug.

In most cases of nephritis it may be assumed that the mixed type exists, and at one time dehydration may prevail over hydration, while at another the position is reversed. Rarely the two changes may run concurrently. Whenever signs and symptoms of disease are being produced they can usually be regarded as resulting from the activity of hydration. With the blood-picture at hand it is possible to decipher the actual sequence of events. The further advantage of the blood-picture is that it centres attention on the blood, the principal actor in the drama, and not on the kidneys. Nephritis *per se* is really of little moment, because so long as even a small area of functioning kidney substance is left, life can be maintained. This is evident from the study of congenital cystic kidney where, with the minimum of functioning kidney substance, life may be maintained for over fifty years. It is never the nephritis which kills, but the abnormal chemico-physical changes present in the blood-stream, by producing one or more breaks in the vasculature. Either the pump breaks down, or the tube gives at one or more points. It is either cardiac failure, consequent upon a degeneration of the myocardium, or a rupture of one of the cerebral vessels, which terminates a case of nephritis. The nephritis is never more than a subsidiary condition, hence there is never a call for renal function tests, even if one could be devised to record the workings of the kidneys. The most constant feature of mixed nephritis is proteinuria. When proteinuria is associated with high blood-pressures, glomerulitis is probably more marked than tubulitis. When proteinuria is associated with low blood-pressures and œdema, the position is reversed. But in this differentiation there are certain pitfalls. Dehydration causing glomerulitis may have had

the ascendancy sufficiently long to prevent any subsequent change having an influence upon the blood-pressures. Consequently, when the cyclical change of hydration occurs with its ensuing tubulitis and proteinuria, despite its severity the hyperpiesis may persist. Similarly, a long continued hydration, causing tubulitis, may have been accompanied by a less marked dehydration sufficient to cause a progressive arterio-sclerosis, or may undergo the cyclical change of dehydration which, however pronounced it becomes, cannot, because of the degeneration existing and resulting from the hydration, cause hyperpiesis. The actual treatment required at the time must be regulated by the blood-picture. The study of many blood-pictures shows that the storage of nitrogenous waste-products and chlorides in the blood-stream plays no part whatever in disease and is based upon entirely false premisses. Therefore, cutting down the protein intake in the one case, and prescribing a salt-free diet in the other, are never necessary. In every case treatment must aim at removing the cause, and at correcting the abnormal chemico-physical changes to which the protein particles in the plasma have been subjected. The former rests in ridding the patient of his chronic intestinal intoxication ; the latter can be decided only by the blood-picture. When dehydration prevails, hydrators are called for, and *vice versa*. Although there is not much difficulty in selecting the antidote indicated, experience is needed in using it, because an overdose only augments the chemico-physical change it is desired to correct. When dehydration is well to the fore, and a hydrator is strongly indicated, insulin is the drug of choice. When hydration is well to the fore, and dehydrators are called for, glucose should be injected intra-venously, and oxygen sub-cutaneously. But, should it be more necessary to render the fluid part of the plasma more colloid, the patient should be bled and afterwards transfused with whole non-citrated blood. When the case is urgent, and it would seem that both changes have been going on concurrently, and that hydration has at last come to the top, acetyl-choline is the best drug and cardiazol the next best. When the condition is more or less chronic, it is always safe to prescribe iodine, ichthyol, thiol-amino-methyl-glyoxaline and thyroid internally, and to make intra-muscular injections of contramine. The following cases illustrate these various points.

Case 172

A man, aged forty-three, complained of headaches and vomiting, following an attack of hemiplegia, which had occurred about two months previously. The patient had had scarlet fever as a child, two attacks of pneumonia, and

three attacks of jaundice. He had been nervy all his life, and had suffered from chronic nasal catarrh and *Acne urticata*. The patient looked very ill, was pale, and nearly bald, all the teeth had been removed, and the tongue was furred. An ophthalmoscopic examination showed advanced arterio-sclerotic changes, and retinitis. The pulse was 92 and the blood-pressures registered 230 and 170 mm. of Hg. respectively. The patient had mucous colitis and the abdomen was tender all over. The urine contained much protein, a little blood, and two per cent. urea; over 60 ounces were being passed *per diem*. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (20 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1·2 c.c.
Refractive index of the serum	= 1·3498.
Percentage of the blood-sugar	= 0·118 grm.
Percentage of the blood-urea	= 32 mgrm.
Ultra-microscopic picture of the serum	= Very many particles moving with a few giant particles and ringed particles. There were a few giant particles and giant-particled clumps precipitated.

The patient was dieted, took lacto-dextrin internally, and received injections of insulin and emetine hydrochloride. The colitis was too acute for treacle enemata or lavage. When the fæcal vaccine was ready, one injection was made (one million), and four days later the patient felt much better, the headaches and vomiting vanished and the blood-pressures came down to 170 and 120 mm. of Hg. respectively. A few weeks later the injection of the fæcal vaccine was repeated. A week later there was a set-back in the clinical condition, the blood-pressures rose to 220 and 145 mm. of Hg. respectively, and three weeks later the patient died.

Insulin was prescribed because dehydration was to the fore, and it was hoped, with the emetine hydrochloride, to check the colitis, which it did not do. An error was doubtless made in prescribing the second dose of vaccine, but the patient was so desirous of having it, as the first had given definite relief. In any case it is doubtful if life could have been prolonged much further.

Case 173

A boy, aged thirteen, son of the above, was discovered to have proteinuria. The boy was mal-co-ordinated; he had chilblains, and all his molars had been stopped; the tongue was furred and the nails were ridged. The pulse was 74,

and the blood-pressures registered 100 and 65 mm. of Hg. respectively. There was evidence of chronic colitis, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0·8 c.c.
Refractive index of the serum	= 1·3483.
Percentage of the blood-sugar	= 0·093 grm.
Percentage of the blood-urea	= 45 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with a fair number of giant particles with a halo around each. There were a fair number of giant particles, ringed particles and giant-particled clumps precipitated. The Brownian movements were sluggish and the precipitation increased with time.

The boy was cut off meat, eggs and milk, was instructed to have his bowels moved twice a day, and had the colon washed out, with the result that the proteinuria completely disappeared. It is practically certain the boy would have followed in his father's footsteps, would have contracted every infection possible at school and been treated for each sign and symptom as it arose with no thought ever being given to the fundamental trouble. Preventive medicine instituted at the right time would have saved the father an untimely demise, and the two cases show that curative medicine does not exist. The two cases likewise illustrate the relationship between leaking kidney and nephritis.

Case 174

A man, aged forty-three, but looking ten years older, and very stout, sought advice for asthenia. The patient had severe fits of depression, and suffered from migraine and rheumatism. The pupils were small and reacted sluggishly to light, the tongue was furred, and all the teeth had been removed. The pulse was 80, the blood-pressures registered 90 and 70 mm. of Hg. respectively, and there was generalised arterio-sclerosis. The urine passed in the twenty-four hours did not exceed 25 ozs., it contained much protein, and gave an intense reaction with the hydrochloride of di-methyl-*para*-amino-benzaldehyde. The pathogenic micro-organism found in the excreta was the *Bacillus faecalis alkaligenes* (20 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood corpuscles	= 0·3 c.c.
Refractive index of the serum	= 1·3504.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 44 mgrm.

Ultra-microscopic picture of the serum = Fair number of particles moving with some giant particles and ringed particles. There were a few giant particles precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, and gave up tobacco and alcohol, the colon was washed out, iodine, ichthyol and thyroid were taken internally, and injections were made of contramine and of the fæcal vaccine.

The patient improved, more urine was passed, it contained less protein, and the blood-pressures rose to 120 and 85 mm. of Hg. respectively. But, whenever the patient ate beef, the proteinuria returned, and an attack of gout usually occurred.

Hyperpiesis is the most common clinical accompaniment of glomerulitis, and rheumatism of tubulitis. Hyperpiesis and gout may occur together, or one at one time and the other at another, in the same case, as evidenced in the following report. This case illustrates another not uncommon clinical manifestation, namely, spontaneous bruising.

Case 175

A woman, aged forty, sought advice for headaches, giddiness and irascibility. For the past ten years she had suffered from recurrent attacks of gout, and bruises appeared, for the most part on the thighs, for no apparent reason. The patient was a typical case of familial chronic intestinal intoxication; she had one boy, aged nine, who suffered from nocturnal enuresis. The pulse was 104 and the blood-pressures registered 180 and 120 mm. of Hg. respectively. The urine contained much protein and 0.8 per cent. urea. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (25 per cent.) and the blood-picture was as follows:—

Suspension stability of the red blood-corpuscles	= 0.2 c.c.
Refractive index of the serum	= 1.3518
Percentage of the blood-sugar	= 0.125 grm.
Percentage of the blood-urea	= 49 mgrm.
Ultra-microscopic picture of the serum	= Few particles moving and these were mostly giant particles. There were some giant particles and giant-particled clumps precipitated. The Brownian movements of the particles were sluggish.

The patient was dieted, took iodine, ichthyol and thyroid internally, and received injections of contramine and of the fæcal vaccine.

The patient improved although she was subject to attacks of gout, and developed spontaneous bruises, from time to time. All went well till two years later when she developed an attack of acute colitis, and passed mucus and blood. While this lasted, bruises appeared all over the body, bleeding of the gums was pronounced, headaches were troublesome, and œdema of the ankles occurred. The blood-pressures registered 165 and 95 mm. of Hg. respectively, the urine contained much protein, and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 1·0 c.c.
Refractive index of the serum	= 1·3499.
Percentage of the blood-sugar	= 0·100 grm.
Percentage of the blood-urea	= 51 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some giant particles and a fair number of small clumps. A fair number of particles, giant particles, ringed particles and giant-particled clumps precipitated.

The patient took lacto-dextrin internally, and was given intra-muscular injections of emetine hydrochloride. When the colon would permit of lavage, this was undertaken, and on its completion two more injections of the vaccine were made. The following year the patient had one attack of gout, and likewise the year after, in the summer-time, when gout is liable to relapse.

On the last occasion bruises occurred as well, the blood-pressures rose to 170 and 110 mm. of Hg. respectively, and more protein appeared in the urine.

Uræmia is a subject which has always excited interest despite the fact that each fresh investigation has added to, rather than cleared, the mystery attached to it. So long as the clinical condition was associated with a hyper-uræmia, the fits, convulsions and coma could be ascribed to the rise in the percentage of the blood-urea. But, when identically the same clinical picture was presented with no rise in the percentage of the blood-urea, another name and cause had to be found. The name, "pseudo-uræmia" was applied to the condition, and it was considered to be caused by an excess of phenol and its derivatives circulating in the blood-stream, although no tests have ever been devised for detecting these substances. When, in addition to all this, fits, convulsions and coma do not necessarily occur even if there is a hyper-uræmia, the reader can see that the subject is merely another of the innumerable *cul-de-sacs* met with in medicine. In the first place there is no such condition as uræmia, and in the second place there is no causal relationship between the clinical condition called

“uræmia” and “hyper-uræmia.” Urea is not a toxic compound, and its chemico-physical action upon the protein particles in the plasma is one of dehydration and not hydration. The fits, convulsions and coma occurring in so-called “uræmia” are occasioned by the precipitation of hydrated protein particles in the peri-capillary lymphatic vessels and capillaries of the brain and by the fluid part of the plasma becoming too aqueous. The sequence of events is the same as that occurring in cerebral shock, spasmophilia, eclampsia, diabetic coma, insulin hypo-glycæmia, etc. All these conditions are the result of the protein particles in the plasma being subjected to hydration. The hydration may occur *de novo*, or be secondary to dehydration, and in the latter case, some of the hydrated protein particles may undergo the cyclical change of dehydration. When the hydration occurs *de novo* there is no rise in the percentage of the blood-urea. When it is secondary to dehydration, there may be a hyper-uræmia. This is most likely to occur in diabetics. Diabetic hyper-uræmia is characterised by a sudden disappearance of sugar and acetone from the urine, and a fall in the percentage of the blood-sugar. If insulin is prescribed without glucose death will result, the fatal issue being caused by the insulin merely augmenting the cyclical change of hydration. When hydrated protein particles undergo the cyclical change of dehydration, an enormous rise in the percentage of the blood-urea may be encountered. The cyclical change is most likely to occur as recovery ensues; in fact, the two run parallel, and the paradox is produced of the clinical condition known as “uræmia” ushered in when there is only a small, if any, rise in the percentage of blood-urea, and ending in recovery with an enormous rise in the percentage of the blood-urea. It is perfectly clear then that a hyper-uræmia plays no part whatever in the causation of fits, convulsions and coma which are diagnosed, sometimes as uræmia and at other times as diabetic coma, etc. People may walk about apparently in the best of health when the percentage of the blood-urea is over 100 mgrm., and, in many cases of fatal shock, and of a fatally terminating fever, a hyper-uræmia may be encountered in the absence of fits and convulsions. “Uræmia” is another of the many terms which should be deleted from the medical vocabulary.

The following cases illustrate these points, and to avoid repetition the reader should study cases 87, 113, 115, 120, 129, 144 and 145 reported in the previous volume.

Case 176

A woman, aged sixty-one, sought advice for increasing deafness, which proved to be arterio-sclerotic in nature. The patient's mother was a martyr

to rheumatism, two sisters were crippled by rheumatism, and another suffered from sciatica and psoriasis. The patient used to have chilblains, she had had bronchitis for the past few winters, and had suffered, earlier in life, from cervical adenitis and furunculosis. Menstruation began at the age of nineteen and ceased at forty-four; there were no children. Arterio-sclerotic changes were well marked, the pulse was 104 and the blood-pressures registered 160 and 90 mm. of Hg. respectively. The pathogenic micro-organism found in the excreta was the *Bacillus fæcalis alkaligenes* (10 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 0.45 c.c.
Refractive index of the serum	= 1.3492
Percentage of the blood-sugar	= 0.100 grm.
Percentage of the blood-urea	= 141 mgrm.
Ultra-microscopic picture of the serum	= Fair number of particles moving with some refractile giant particles and ringed particles. There were a fair number of particles, giant particles and ringed particles precipitated. The Brownian movements were sluggish and the precipitation increased with time.

The patient was dieted, had colonic lavage, took iodine, thiol-aminomethyl-glyoxaline and thyroid internally, and received injections of contramine and of the fæcal vaccine. Three months later the percentage of the blood-urea was 22 mgrm.

In this case the dehydration was penetrating deeply some of the protein particles in the plasma, and the hyper-uræmia caused did not apparently trouble the patient in any way. This type of dehydration seldom leads to the cyclical change of hydration which, in turn, causes the clinical condition known as "uræmia." The rise in the percentage of the blood-urea did not take place because the kidneys refused its passage into the urine. The amount of urea in the urine exceeded 3 per cent., and the treatment early reduced the blood-urea figure to normal.

Case 177

A man, aged thirty-one, had a bad headache one day in April and became unconscious later in the day. He was unconscious for two days, and remained confused for a fortnight. Three months later the so-called "uræmic convulsions" re-appeared. At this time the urine contained a large quantity of protein, many casts, and 0.7 per cent. urea. The quantity of urine passed

per diem varied between 70 and 150 ounces. The percentage of the urea in the blood was 50 mgrm., but when venesection was performed and the patient showed signs of recovering, the percentage rose to 306 mgrm. The patient was an only child ; he suffered from chilblains in the winter, and hay-fever in the summer. He had chronic nasal catarrh, had had attacks of lumbago and sciatica, and was subject to recurrent *Herpes febrilis* on the left cheek. When examined about a year later, the ophthalmoscope revealed central cupping of both optic discs, arterio-sclerotic changes, and albuminuric retinitis. All the molars had been stopped, the tongue was scarred from being bitten, the pulse was 90, and the blood-pressures registered 210 and 150 mm. of Hg. respectively. The heart was elongated, dropped and narrowed, there were tender areas in both hypochondria and in both iliac fossæ. The urine contained much protein, many casts and 0·8 per cent. urea. The pathogenic micro-organism found in the excreta was the *Bacillus acidi lactici* (75 per cent.) and the blood-picture was as follows :—

Suspension stability of the red blood-corpuscles	= 2·5 c.c.
Refractive index of the serum	= 1·3470.
Percentage of the blood-sugar	= 0·112 grm.
Percentage of the blood-urea	= 92 mgrm.
Ultra-microscopic picture of the serum	= Normal number of particles moving with many giant particles. There were some particles, giant particles and giant-particled clumps precipitated, as well as some precipitation <i>en masse</i> .

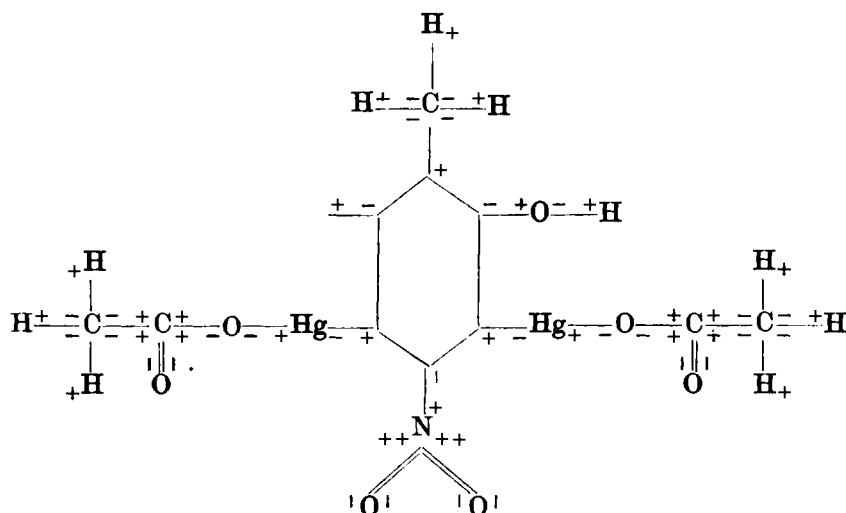
The patient was dieted, had first treacle enemata and then colonic lavage followed by one injection of the washings of 10,000 million of the *Bacillus acidi lactici*. The arm swelled, became red and painful at the site of injection, and the reaction reached its zenith on the sixth day. It then subsided and the general condition of the patient improved.

The great interest of this case lies in the fact that the hyper-uræmia was at its highest following the venesection, which brought the patient out of his comatose state. Venesection causes the protein particles in the plasma to undergo a cyclical change ; that is to say, hydration occurs when dehydration was the prevailing chemico-physical change previously, and *vice versa*. The effect of venesection upon the blood-picture will be illustrated in the next part.

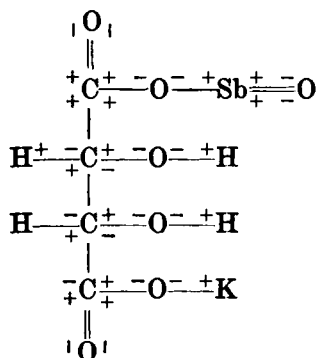
Although the subject of *Bilharziasis* does not belong to this section, the author desires to say a few words regarding this and kindred infections because no opportunity is afforded of doing so in the next volume, and because he has something new to add to the action of antimony. The author introduced

the use of tartar emetic in *Bilharziasis* in 1915²² and suggested later that the antimony acts as a conductor and stimulates the host's resistance to destroy the parasite. Further work has shown that antimony does not attack the parasites directly, and that there is nothing specific in its action. Antimony merely subjects to dispersion the protein particles in the plasma which have undergone a certain type of hydration. This type of hydration is met with in the chronic stage of certain infections, such as *Bilharziasis*, *Leishmaniasis*, *Ulcus molle serpiginosum*, syphilis, etc. This type of hydration is corrected neither by pure conductors nor by pure dehydrators, but by agents which exhibit both actions. A combination of conduction with dehydration is most readily exhibited by polyvalent metals in organic form. If the organic compound is aliphatic the metal may have all its valencies positively charged, because aliphatic compounds, provided their nucleus is not too big, have a dehydrator action. If the organic compound is aromatic and the metal is directly attached to the ring, one of its valencies must be negatively charged.

Provided these conditions are fulfilled, it is found that mercury directly attached to a benzene ring with one of its valencies negatively charged has the same action as antimony in an aliphatic compound with all its three valencies positively charged. For example, di-acetyl-oxy-mercuri-nitro-cresol, known as "metaphen," has an action akin to that exhibited by tartar emetic. The following formulæ depict the electronic characters of these two preparations :—



Di-acetyl-oxy-mercuri-nitro-cresol.



Antimony potassium tartrate.

Summary

Buccal, pharyngeal, nasal and aural sepsis are most frequently secondary to a chronic intestinal intoxication. Nasal catarrh is, perhaps, the most common manifestation of inherited disease, and the common cold is nothing more or less than an acute exacerbation of this condition. The common cold has no cause, in the ordinary sense of the word, and it is not conveyed from person to person, as is generally thought. Hay-fever and vaso-motor rhinorrhœa are other clinical manifestations of nasal catarrh. Tonsils become septic when the patient's resistance, already below par, as the result of inherited disease, becomes still further reduced by faulty living, wrong food and insufficient elimination of the waste products of food. When the tonsils are septic, micro-organisms ordinarily saprophytic tend to become pathogenic, enter the blood-stream and cause manifestations of disease. But, these micro-organisms and the septic tonsils are precipitants, and not causes, of disease, and this explains why removal of the tonsils and measures employed to vanquish streptococci so often fail. Rheumatic and scarlet fever are not specific infections, but merely manifestations of disease occasioned by streptococci becoming pathogenic. When micro-organisms develop pathogenic properties they may undergo morphological changes into smaller and even ultra-microscopic forms.

It is possible that measles, and the encephalitis following it, are infections precipitated by a streptococcus, some different form in the one case and the ultra-microscopic form in another.

Cervical adenitis, once so common in children but now less so, is an attempt, on the part of the body, to combat the invader, as is enlargement of the tonsils when it first occurs. An effort is made by manufacturing lymphocytes to aid the host's resistance. In the breakdown of this effort the lymphatic

glands may become septic, and later on the saprophytic tubercle bacillus may settle there and become active. The enlargement is never primarily tubercular and tubercle bacilli would never cause trouble if the familial chronic intestinal intoxication was removed. Although a chronic intestinal intoxication is congenital, manifestations of disease seldom arise until brought into being by protein particles in the plasma, hydrated by abnormal metabolites of food, reaching the blood-stream from the intestines. The hydrated protein particles become precipitated in any organ or structure, and the area chosen is usually the *locus minoris resistentiæ* of the particular individual. The first effect of the precipitated particles is to stimulate the cells around them, later signs of inflammation may appear, and finally the cells are paralysed. The abnormal metabolites result from the faulty breaking down of food-stuffs, by mutation forms of the *Bacillus coli communis*. The food-stuffs from which these abnormal metabolites are most readily formed are butcher's meat, eggs and milk. Beef is the most harmful butcher's meat, particularly if it has been frozen or chilled. Imported eggs are a great source of danger, and milk is probably the most deleterious article of food a sick or convalescent person can have. The *Bacillus coli communis* is a normal inhabitant of the large intestine, and even when it reaches the uro-genital tract *vid* the blood-vessels and lymphatics it cannot be regarded as a pathogenic micro-organism. The bacillus multiplies in the uro-genital tract because the patient's resistance is lowered by the activity of one or more of its mutation forms. The *Bacillus coli communis* seldom causes a true pyelitis, ureteritis or cystitis and when inflammatory changes occur in the uro-genital tract they are generally caused by a secondary infection with coccogenic micro-organisms. The mutation forms of the *Bacillus coli communis* are commonly referred to as "non-lactose fermenting micro-organisms," but a few of the more innocent varieties ferment this sugar. The mutation or pathogenic forms of the *Bacillus coli communis* may be active at one time, and inactive, or dormant, at another. The activity may be acute or chronic. When it is acute, fevers occur which go by various names, such as "influenza," "glandular fever," "Psittacosis," "P.U.O.," etc. When the activity is chronic almost any manifestation of disease may be produced. The activity is influenced by many factors, such as climate (the most important), wrong food, environment, mental and physical strain, pre-existing bowel trouble, etc. Mutation appears to occur in steps like rungs of a ladder, and as it advances, the pathogenicity of the micro-organism increases.

Activity and pathogenicity do not necessarily go hand in hand, because the activity of a more or less innocent micro-organism, such as the *Bacillus Fried-*

länder, may give rise to a more fatal infection than that of a highly pathogenic micro-organism, such as the *Bacillus typhosus*. The activity of a micro-organism may result in its entering the blood-stream, changing into another form, or giving rise to ultra-microscopic particles. These ultra-microscopic particles are particularly liable to attack the central nervous system, and cause an encephalitis. *Psittacosis* is a good example of an infection brought about by the activity of a mutation form of the *Bacillus coli communis* so great as to result in the particular micro-organism forming ultra-microscopic and extremely virulent particles. Infection from person to person is probably conveyed by what is best termed "activity" and not by the passage of the micro-organisms themselves. The greatest proof in support of this view is, that washings of the micro-organisms containing only activity, given as vaccines, are the best means of combating the activity. If micro-organisms function in virtue of this activity then there is no difference between an intestinal infection and food-poisoning. There is certainly no difference between an enteritis caused by bacteria and one caused by toxic chemical substances. It is this fact which makes it tolerably certain that, when micro-organisms cause an enteritis, they reach the small intestine *viâ* the blood-vessels and lymphatics, and not by way of the stomach.

Achalasia, hypertrophic stenosis of the pylorus, ileo-cæcal spasm, atony of the colon, etc., may be caused either by precipitation of hydrated protein particles in the vagus centre or in Auerbach's plexus.

Ulceration of the stomach and duodenum results from altered chemico-physical changes undergone by the protein particles arrested in the affected area. The collection of hydrated protein particles in the gastric area produces first hyper-chlorhydria, and later hypo-chlorhydria. The hypo-chlorhydria itself gives rise to no manifestation of disease and there is no connection between it and pernicious anæmia. The tests devised to estimate liver, pancreas and kidney efficiency do not do so, and the results are valueless.

The main cause of splenomegaly is the precipitation of hydrated protein particles in the spleen. If the precipitation was limited to this organ there might be an excuse for splenectomy, but as it is usually more or less general the operation is not called for, because there are other and better ways of causing the desired dispersion. The benefit resulting from removal of part of the thyroid gland in exophthalmic goitre is due to taking away the hydrated protein particles precipitated in the organ, and not to diminishing the amount of thyroid secretion entering the blood-stream. The same applies to the spleen.

Whatever passes through the kidneys, from the blood to the urine, is deter-

mined far more by the chemico-physical state in which the protein particles in the plasma happen to be than by the renal organs. It is therefore an error to speak of the renal threshold for sugar, urea, etc. Urea is an innocuous substance and its presence in the blood, even in unheard-of quantities, could never give rise to the signs and symptoms usually associated with uræmia. In actual fact there is no such clinical condition as uræmia. The most satisfactory way to render a chronic intestinal intoxication inactive in an individual, is to cut out butcher's meat, eggs and large quantities of milk from the diet, to open the bowels at least twice a day, to wash out the whole of the large intestine by the syphon method, to correct the abnormal chemico-physical changes met with in the blood, and to set up an immunity against the pathogenic micro-organism found in the excreta.

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EPILOGUE

THE author proposes to continue the discussion on Chronic Intestinal Intoxication in the next part, when he hopes to throw more light upon the rôle played by the pathogenic micro-organisms in the excreta. Then are to follow chapters upon Infections, Disease and the Lungs, Disease and the Skin, Disease and Women, Rheumatism, and Certain Affections of the Blood and Blood-Vessels. The chapter on Infections will deal with infections from without, such as syphilis, gonorrhœa, etc., and infections from within, caused by micro-organisms ordinarily saprophytic becoming pathogenic in an individual whose resistance has been lowered by a familial chronic intestinal intoxication.

Recent work has shown the author that the routine treatment of infections is bad practice, because the course run by all infections is influenced to a marked degree by the state in which the patient's resistance happens to be. In many cases the infection should be neglected and attention paid solely to the intestinal intoxication. There is no such thing as the specific treatment of an infection.

The chapter on Disease and the Lungs will deal with such subjects as hay-fever, asthma, tuberculosis, etc. Hay-fever and asthma are merely forms of shock occasioned by the precipitation of hydrated protein particles in the lymphatic vessels and capillaries of the respiratory tract. Tuberculosis is less an infection from without than from within, and it would vanish, if there was no such condition as familial chronic intestinal intoxication. Many of the cases of apical catarrh are not tubercular in origin, and probably none are to begin with.

The chapter on Disease and the Skin will show that most of the cutaneous affections are the result of changes which the corium and epidermis undergo at the hands of the altered protein particles in the plasma.

Skin diseases as such do not exist, and there is no justification for the names which have been given to them, and no need for the local treatment in vogue at present.

The chapter on Disease and Women will deal with the factors regulating sex, and it will show that the anomalies of menstruation, and the toxæmias of pregnancy, are due to the changes undergone by the protein particles in the plasma.

The chapter on Rheumatism will show that although it may be infective in

origin, whether this is so or not, the actual clinical condition is caused by the arrest of damaged protein particles in the tissues affected. In other words, gonorrhœal rheumatism may be caused, either by the gonococcus reaching the parts affected, or by the protein particles it has altered from its seat of invasion, and there is no difference, either between these two forms or between so-called "gonorrhœal rheumatism" and rheumatism of other origin.

The chapter on Certain Affections of the Blood and Blood-vessels will contain some new work which is in the process of completion, and the discussion will be extended to shock, and to hyper- and hypo-piesia. It is in this chapter that the effect of venesection on the blood-picture will be illustrated. If further evidence can be adduced to show that cancer is merely an end stage of disease and, therefore, one for which there is no specific cause, a chapter will be given up to it.

The final section of the third part of "The Nature of Disease" will deal solely with Chemotherapy. The chapter will be a long one, because it will consider the action of most of the drugs in common use on man and animals. Light will be thrown upon the action of herbal and homœopathic remedies. The author will attempt to place homœopathy on a scientific basis, and to fill up the gulf, at present existing, between so-called "homœopathy" and "allopathy." The work suggests already that Hahnemann deserves to be placed in the first rank of men who have advanced the science of medicine, and to take precedence of many whose names are more familiar.

ADDENDUM

OWING to the increasing number of requests made by medical practitioners to the author for information regarding "The Nature of Disease," and the difficulties editors of medical journals experience in publishing his articles, he has decided to issue his further work in journal form. The time is singularly ripe to do this as owing to the formation of the "Nature of Disease" (N.O.D.) Institute the Journal can function as its mouthpiece and issue reports upon the results of research work conducted there.

Each number will contain a new chapter on the "Nature of Disease," a review of current medical literature and a report upon any notable piece of research work. A point will be made of correcting errors in the already published parts so as to keep the work up to date. The first number will contain a chapter upon Disease and Infections, wherein an attempt will be made to elucidate the problems of the common cold and influenza.

It is hoped in course of time to bridge the gulfs existing between orthodox medicine, homœopathy and osteopathy, and to connect these with the kindred sciences. The author is prepared to accept any article which helps to do this and aids in making medicine a united science instead of being separated into watertight compartments as is the case at present.

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