By the same Author

HIGH BLOOD PRESSURE

ITS VARIATIONS AND CONTROL

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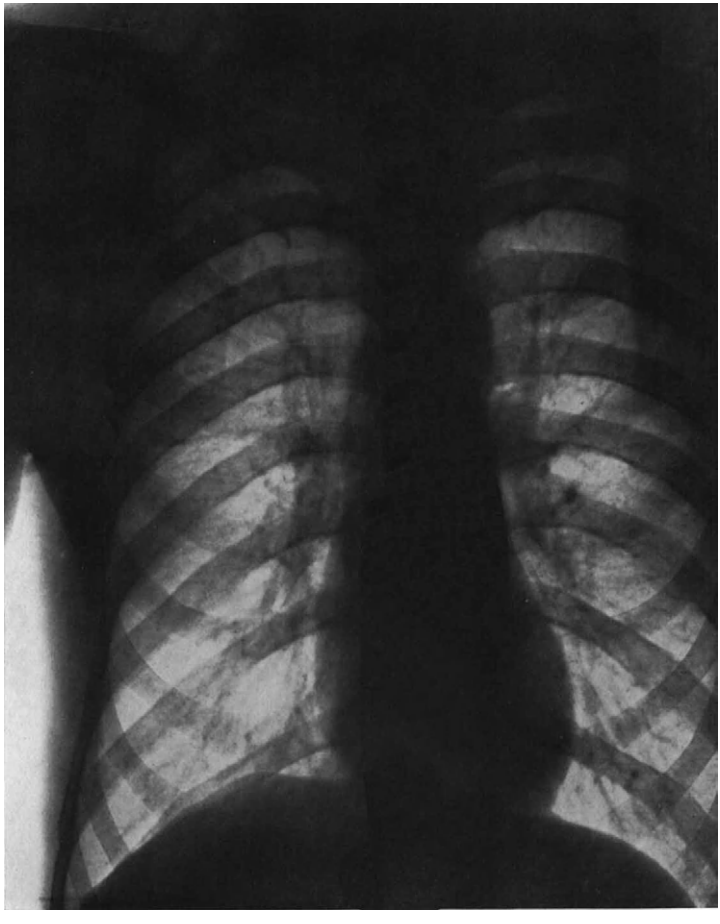

FIG. I.—The Hyposthenic Habitus (*pp.* 47—52).

LOW BLOOD PRESSURE

ITS CAUSES AND SIGNIFICANCE

BY

J. F. HALLS DALLY

M.A., M.D., B.Chir.Cantab., M.R.C.P.Lond.

PHYSICIAN TO MOUNT VERNON HOSPITAL

SENIOR PHYSICIAN TO THE ST. MARYLEBONE GENERAL DISPENSARY AND DIRECTOR OF THE CHILDREN'S SUPERVISORY CENTRE FOR PREVENTION AND CONTROL OF RHEUMATISM AND RHEUMATIC HEART DISEASE

CONSULTING PHYSICIAN AND MEMBER OF THE ADVISORY PATHOLOGICAL BOARD, SHRINERS' HOSPITAL, MONTREAL

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To
MY WIFE

PREFACE

ALTHOUGH the literature of Medicine abounds with references to high blood pressure states, little mention is made of the conditions under which low blood pressures occur, and the little that is known is imperfectly understood. Therefore, it will be realised that innumerable difficulties have been encountered in an endeavour to break new ground.

Especially does this lack of knowledge become evident as one approaches the problems of causation and control. Hence the present volume has been put forward as the first attempt to rationalise the important and interesting subject of low arterial pressure, and to exhibit it from various aspects which hitherto have been overlooked.

Starting from the broad viewpoint of biology, the author has propounded the fundamental law that low arterial pressure is invariably an expression of low individual vitality. Once this ætiological proposition is appreciated, seeming contradictions become capable of reconciliation. On this basis, the occurrence of hypopiesis in apparently healthy subjects, as well as its association with maladies of the most diverse kinds, is readily explicable for the reasons set forth in Chapter III. Moreover, one is enabled to weave scattered and previously unconnected observations into logical and coherent sequence, and so to formulate a guiding and unifying principle of effective control (Chapter XII.).

Additional reasons for the appearance of this volume are first, that numerous practitioners have expressed a desire for further knowledge about low arterial pressure and its associations in dealing with cases which at times are apt to cause considerable perplexity ; secondly, that the presentation in book form of the most recent views on this subject may be deemed opportune ; and thirdly, that the study of blood pressure has interested the author for the past twenty

years, during which time he has had the advantage of investigating an unusually large number of hypopietic states.

In the hope that he has succeeded in placing before his readers a clear picture of the low arterial pressure problem, the author begs to offer the contents of this work for their kind consideration.

For the benefit of those who wish to study hypopiesis more exhaustively, a full bibliography is appended which includes all references of importance up to the present time concerning this subject and its associations.

Grateful thanks are tendered to several friends for helpful suggestions and criticism; in particular to Drs. Sidney Bontor, Henry Ellis and Edgar Obermer. To the latter my acknowledgments are also due for revision of the proof sheets and inclusion of three illustrative metabolic charts.

93, Harley Street,
London, W. 1.
January, 1928.

LIST OF ILLUSTRATIONS

LOW BLOOD PRESSURE
ITS CAUSES AND SIGNIFICANCE

CHAPTER I

Physiological Blood Pressure

General Considerations.—For many centuries Medicine has been content to dwell in watertight compartments. To one dogma another has succeeded, and exponents of the Art have remained under the thrall with little expression of a desire for freedom. Only now and again has a Hippocrates or a Harvey arisen to stir men's pulses and to create a broader vision. So much easier it is to follow the beaten track than to risk the perils of the explorer.

One has only to study the history of Medicine to see how very gradual has been the process of emancipation from rigid doctrines, for, in the light of later knowledge, many discoveries long hailed with enthusiasm are found rather to have hampered than to have enhanced progress.

Especially is this true of the circulatory system, to which field of research since the time of Harvey[1] little of importance has been added until the last half-century. In cardiology, for example, prognosis based upon differentiation of cardiac murmurs now yields priority of place to assessment of the degree of functional capacity of the heart muscle. With recognition of this vital issue, and with important advances also in other directions, the name of the late Sir James Mackenzie must ever be associated.

Similarly, with regard to progress in the domain of arterial pressure, from early gropings in obscurity with instruments capable of measuring only one end of the pressure scale, and even this with no exactitude, the careful observer is now enabled—always provided that he employs

an instrument that is accurate—to gain a clear insight into the meaning of variations from standard limits in both low and high arterial pressures. Touching low arterial pressure, up to the present time our concepts have been vague and indeterminate, yet indications are not lacking that, with the increasing amount of attention now beginning to be devoted to this special and important aspect of the whole arterial pressure problem, such concepts will become more definite and condensed.

Low arterial pressures are wont to occur under the influence of, and in association with, a large variety of conditions which may be physiological or pathological.

Till recently, however, manifestations of subnormal pressure have failed to make such strong appeal to the interest of the clinician as have the incidence and progress of those maladies which are attended by heightened arterial pressure. Hypopiesis, therefore, has remained one of the indefinite problems of medicine.

This fact is, perhaps, less to be wondered at if one reflects that the evolution of maladies associated with pressures of high grade is ordinarily fraught with grave issues, and that the liability of patients afflicted by such diseases to sudden extinction of life by some or other dramatic and perchance totally unexpected fatality is great.

Hence, lay as well as medical attention has been so largely focussed upon the upper portion of the pressure scale that readings of the lower levels have suffered comparative neglect.

Less sensational are the conditions attendant upon low arterial pressures. Nevertheless, it must be conceded that these constitute an integral feature of the syndrome in a large series of disorders and diseases which are of considerable clinical interest and importance.

For these reasons, and also because high and normal arterial pressure states are met with more commonly in daily practice, the bulk of medical literature has been devoted to consideration of these two groups, low arterial pressure being usually dismissed in a few summary words. By certain well-known writers it has even been stated to be of little clinical value in diagnosis, prognosis or treatment.

That this impression is largely a mistaken one, brought about by lack of sufficient opportunities for observation or by lack of interest, the author hopes to show in the following pages, which represent an attempt to place before the reader a synoptical picture of our present knowledge of low arterial pressure states, their classification, development, progress and termination.* Should he desire to probe more deeply into the subject, a full bibliography is appended which includes as far as possible all work of outstanding importance up to the present time.

Further, by collecting within the compass of a single volume all data so far available from widely scattered sources, and after revising and correlating these data to deduce and formulate therefrom a unifying ætiological principle, at once simple and comprehensive, constitutes the ultimate purpose which the author has here endeavoured to accomplish.

Special Considerations.—An additional and special reason for low arterial pressures having been passed over with brief mention may be found in the fact that, until comparatively recent times, the diastolic pressure could not be estimated with any approach to accuracy.[2] By reason of this lack of opportunity of direct measurement, earlier investigators were much handicapped. Hence the omission by them of all reference to abnormally low pressures is not so astonishing as at first sight it might appear.

Amid the wealth of literature concerning blood pressure that has now accumulated, direct references of any real value to conditions under which abnormally low arterial pressures become evident are few and far between, observations thus far made being rather experimental, surgical and pharmacological than clinical, pathological and biochemical.

Yet when one pauses to consider the matter in greater detail it becomes clear that, in the make-up of a large number of pathological processes of diverse origin, from acute infections on the one hand to chronic cachexias on the other, reduction in the levels of arterial pressure constitutes

* By a contrast of these conditions with the series of normal and supernormal pressures dealt with in the author's volume on "High Blood Pressure, its Variations and Control," Second Edition, 1926 (Wm. Heinemann, London), the reader will thereby obtain a concise picture of arterial pressure as a whole.

not only an important link in the chain of events, but in prognosis and management affords indications of no inconsiderable value.

Whilst with Cabot and Janeway we may be disposed to agree that in the past, when compared with high arterial pressure as an aid to diagnosis, the study of low arterial pressure has been of little avail, yet nowadays the *relatively* less frequency of the latter does not, in the judgment of the author, constitute a sufficient reason for either cursory and slighting dismissal of the subject in a few lines, or its total disregard. Few there are who, like the late Sir Clifford Allbutt, have the courage of that humility so characteristic of great minds, and are prepared to join with him in the frank admission that the study of low arterial pressure is hardly yet begun.

Definition of Arterial Pressure as a Whole.—Arterial pressure, reduced to its simplest formula, may be defined as that pressure exerted by the blood at a given instant upon a given point of the arterial wall.

Such pressure may not exceed standard limits ; may take the direction of excess, as in states of high arterial pressure ; or of diminution, as in states of low arterial pressure. With the former of these variations from standard levels, the author has already dealt in another volume ; with the latter the present book is concerned.

The term " blood pressure," though frequently used in everyday language in the limited sense of " arterial pressure," in strict parlance also includes pressures which are not only arterial, but may be intra-ventricular, intra-auricular, venous and capillary.

Circulatory Factors in Arterial Pressure.—The main elements which bring about variations in arterial pressure are two, which are primary and basic, the remaining three being secondary and subsidiary.

The basic elements are (1) the cardiac energy, as measured by the volume of blood pumped by the heart into the arteries in a given time, *i.e.*, the unit output ; and (2) the peripheral resistance, *i.e.*, the amount of hindrance offered during that time to the escape of blood from the arterial system.

The subsidiary elements are (3) the resiliency of the arterial walls, (4) the volume of the circulating blood, and (5) the consistency of the blood.

Let us now consider each of these elements more closely.

1. *The Cardiac Energy.*—The heart being the central organ of the body, variations in the force of its beat affect the whole organism. The larger part of the pumping force of the heart is, nevertheless, expended, not in driving the blood through the vessels, but in distending the walls of the arteries.

2. *The Peripheral Resistance.*—Of the two main causal factors, the peripheral resistance is the more important. In itself this is a combination of several elements, including (*a*) general effects due to variation in calibre of the smaller arterioles, and (*b*) local effects due to external pressure exerted upon the smaller arterioles and capillaries by the perivascular tissues. Changes in peripheral resistance are due to alterations in calibre of the walls of the arterioles, and also, as we now know, of the capillaries. Such changes may be either local—affecting a special vascular area—or general, involving either the whole or the major part of the circulation.

The autonomic system by its continuous activity regulates the vasomotor tone of the peripheral vessels. This automatic control is in some instances developed with difficulty, and equilibrium, even when established, is easily upset, so that the due balance between vasoconstriction and vasodilatation becomes a very subtle and delicate matter.[3]

Dilatation with lessening of resistance to the blood stream may be induced by lessening of the tonic activity of the vasoconstrictor centre, or alternatively, by intervention of vasodilator impulses. In these two types of reflex fall of arterial pressure the greatest dilatation of vascular channels occurs when vasoconstrictor tone is abolished and the dilators are universally stimulated.[4] As the result of vasodilatation there is a decline in the diastolic pressure, which may be manifested clinically by cyanosis of the extremities. Without a certain diastolic pressure, man could not assume and maintain the erect posture. If a rabbit is suspended by the ears, after division of the sympathetic in the neck, it

immediately dies, because all the blood gravitates into the abdomen. Only for the resistance created to the outflow by the vasomotor nerves man would have to go on all fours.

The gradual lowering of blood pressure by diminution of peripheral resistance affords, however, a strong contrast to the sudden lowering of blood pressure by vagus inhibition acting on the heart.

3. *The Resiliency of the Arterial Walls.*—The commonly accepted standard level of systolic arterial pressure, which is about 120 mm. of mercury, constitutes a " head of pressure " which is considerably greater than that which is actually requisite for the propulsion of blood from the arterial into the venous system. But the precise object of the circulation is to maintain a continuous stream of blood along the capillaries, through the walls of which the cells of the body are nourished and their waste products eliminated. Therefore the use of this extra head of pressure becomes apparent as soon as one takes into account the varying local needs of the organs and tissues. Arteriolar and capillary relaxation in a limited region of the body produces a markedly diminished resistance, which would have the effect of draining other areas were they not provided with an adequate blood supply, especially if the demands of these areas be excessive.

In normal individuals the total resting time of the heart is about thirteen hours out of the twenty-four, so that, during successive diastolic periods, provision has to be made for the maintenance of blood pressure at its due level. This requisite is attained (*a*) by the head of pressure originated by the vigorous propulsive thrust of the left ventricle in systole being maintained during diastole by the powerful elastic recoil exerted by the resilient walls of the great aortic reservoir, which functions as a second heart, and (*b*) throughout the cardiac cycle by the resistance to the outflow from the arterioles and capillaries into the veins.

Impairment of the resilient properties of the arterial walls, *e.g.*, by thickening, as in certain forms of arteriosclerosis, or by diminution of their tonicity, producing a relaxed condition of the vessel wall, *e.g.*, in vagotonia, tends, of itself, to bring about reduction of arterial pressure.

4. *The Volume of the Circulating Blood.*—The total volume of the blood is about one-thirteenth of the body weight. Adequately to support the circulation at least two-thirds of this volume are required. The total volume of the blood, however, is of less importance than the above-mentioned factors since considerable quantities can be lost from, or, on the other hand, large amounts of fluid can be added to, the circulation, with only transient and slight influences on the level of arterial pressure. Should hæmorrhage be excessive, and beyond the compensatory power of the body, arterial pressure will fall to low levels.

5. *The Consistency of the Blood.*—As a component of consistency, first we will deal with viscosity.

Viscosity merely means "stickiness," and must not be confused with specific gravity, for a high specific gravity may be present with a low viscosity. Burton-Opitz [5] states that the viscosity of the blood falls distinctly with rise of temperature; it is less after hæmorrhage and during hunger, and is increased by taking food, especially fats and proteins. According to observations made in fine glass tubes, with increased viscosity a greater pressure is required to continue the rate of flow undiminished. This laboratory effect is contrary to that noted by Lovatt Evans and Ogawa,[6] who, working with a heart-lung preparation, have shown that increased viscosity reduces the input of the heart, which in turn diminishes the output, and that the smaller ventricular load of concentrated blood is expelled with less endocardial pressure than when it is larger and less viscous. Hence it would appear that increased viscosity of the circulating blood would have the effect of lowering rather than of raising arterial pressure.

Although in respect of the peripheral circulation viscosity presumably plays some part, yet its importance may easily be exaggerated, since changes alike in blood consistency and viscosity are capable in turn of being readily balanced by the tissues, the chief regulating mechanism being situate in the capillary zones. Here, under conditions of low arterial pressure, it is possible that diametrically opposed conditions of viscosity may obtain, a high viscosity being produced under certain conditions, while in others, which

occur less frequently, the viscosity of the serum may be much reduced. In the present state of our knowledge, under all conditions of arterial pressure, and particularly of low arterial pressure, it is not possible to assess the precise *rôle* of viscosity, since in the capillary zone cellular metabolism presents its highest level of activity.

Another component is the hæmoglobin content of the blood, which is rapidly modified by any alteration in blood pressure, a rise of pressure leading to an increase of hæmoglobin and a fall of pressure leading to a decrease. These results can only be explained by forcing of fluid out of the blood into the tissue spaces as a result of increased blood pressure, and the passage of fluid back again from the tissue spaces to the blood when the pressure is lowered.

On the whole the evidence as to the effect of blood consistency upon blood flow so far tends to show that the results are inconsiderable in comparison with the effect produced by vasomotor variations.

The Measure of Circulatory Efficiency.—The above factors in their several degrees and combinations together constitute *the measure of circulatory efficiency.* By reason of the incidence of many variables a precise estimate of the co-ordinated action of these factors is impossible, but an exceedingly useful, though only partial, index to the degree of efficiency of the circulation is afforded by consideration of the combined records of the systolic and diastolic pressure in their numerical relations, that is to say, the difference between the figures for each, and their several places in the pressure scale. In health for each individual and for each particular condition there is an optimum range, within which, other things being equal, a given differential (pulse) pressure will produce the fullest circulation that at the same time is attended with the greatest circulatory flexibility and reserve power. If above or below this ideal place in the pulse scale, differential pressure, to produce an adequate circulation, must ordinarily increase in magnitude, *i.e.*, take on an overload, such overload indicating more or less diminution in the flexibility of the circulation and the reserve power of the heart.

"If the diastolic pressure fails to fall in correspondence

with a falling systolic pressure, and thereby permits the pulse pressure to become unduly small, clinical signs of circulatory insufficiency may appear. For example, if the systolic pressure falls to 100 and the diastolic to 60, there may be an adequate circulation provided the reserve power

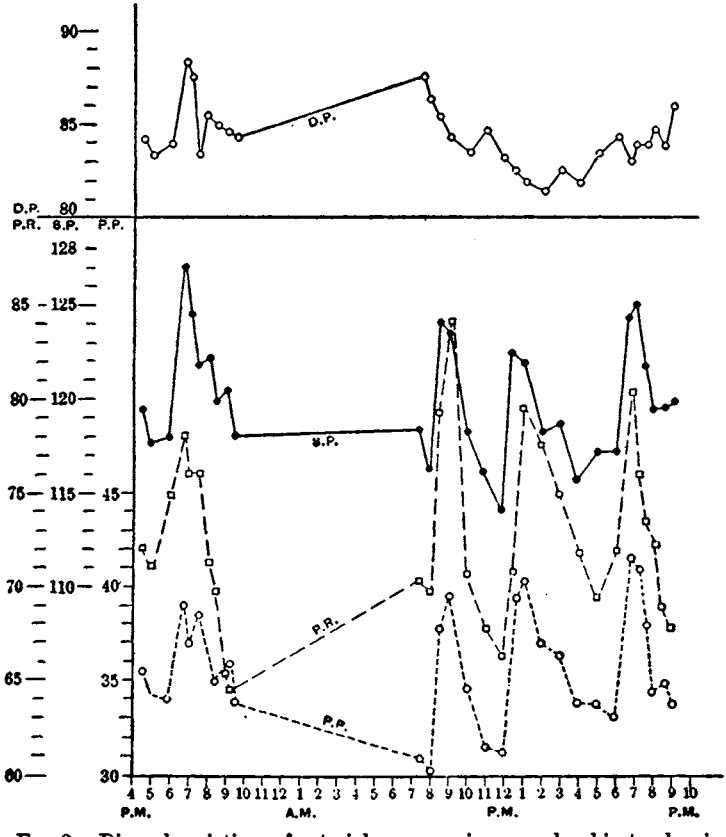


FIG. 2.—Diurnal variations of arterial pressure in normal subjects, showing the rise in pulse rate, systolic, diastolic and differential (pulse) pressures consequent upon the three chief meals of the day. (After Norris.)

of the heart is not too largely drawn upon; but if the diastolic pressure falls to only 80, while the systolic is 100, there may be symptoms of circulatory insufficiency, and if the diastolic pressure falls so low relatively that the pulse pressure takes on a large overload, such symptoms also may appear."

"Movements of the diastolic pressure to any considerable distance from its normal place in either direction, regularly cause the pulse pressure to take on an overload, if the circulatory balance, that is to say, an adequate circulation, is to be preserved. In conditions which considerably raise the diastolic pressure, such as chronic nephritis and arteriosclerosis, the overload may be so great that the pulse pressure exceeds 100; and in conditions of myocardial weakness or irritability or vasomotor dilatation with insufficient filling of the blood vessels, there may be necessitated an abnormally large pulse pressure. In simple overaction of the heart the same thing may happen." [7]

Arterial pressure and pulse rate are subject to frequent fluctuations, and physiologically there are relatively wide variations in individual pressures even under conditions of perfect health, due particularly to the vascular changes which attend digestion, as well as to exercise, sleep, emotion, rest, posture, fasting, body weight and height, etc. Fig. 2 has been plotted by Norris from mean values given by Weysse and Lutz for the pulse rate, systolic and diastolic pressures of students on a normal routine, the three main peaks demonstrating clearly the rise in pulse rate and both pressures consequent upon the three chief meals of the day.

Vasomotor Control of Arterial Pressure.—Arterial pressure is under the control and direction of the vasomotor nervous system in accordance with the needs of the various organs and tissues at a given moment for a greater or less blood supply. There is a vasoconstrictor automatic centre in the medulla, which exercises general control, and is aided by secondary centres in the spinal cord and sympathetic ganglia which govern those areas with which they are specially related. Active vasodilatation is promoted by vasodilator fibres, which ascend as special nerves in the spinal cord at different levels.

"The medulla, which is the seat of life itself, has a paramount need for an adequate supply of blood. Very low arterial pressures, even if transient, are fraught with considerable danger. Hence the arterial pressure can never

for long remain at a much diminished level, otherwise the medulla would be deprived of blood and death would speedily ensue. In grave conditions, *e.g.*, where the pressure, either from extreme feebleness of the heart's action or from excessive diminution of peripheral resistance, or from both causes combined, tends to fall to a very depressed level, the medulla is starved and death speedily ensues, unless in the former case the arterioles by vasoconstriction are able to restore the pressure to an effective level, and so to relieve the labouring heart, or in the latter event the heart can sometimes aid the peripheral circulation by coming to its rescue with increasing vigour of contraction. In terminal events frequently both fail and the pressure drops rapidly to the fatal end." [3]

To summarise—changes in arterial pressure may be brought about by variations in the total volume of the circulating blood, by variations in output from the left ventricle, or by variations in the peripheral resistance. Changes in the latter may be due to (*a*) local influences upon the musculature, or (*b*) to vasomotor intervention.

Sphygmomanometry.—Arterial pressure is measured with instruments, primarily to assess the efficiency or otherwise of the circulatory system in order to gain an estimate of the nature of each problem with which we have to deal, and secondarily to glean other indications which are both psychical and physical.

For these purposes numerous makes of instruments are employed in practice, all of which fall under two main headings: mercurial and aneroid. For accurate results the author finds no instrument so reliable as a correctly made mercurial manometer of modern type, of which the Baumanometer is the best example, though dial aneroids, such as the Vaquez-Laubry or the Tycos, are often preferred by reason of their greater compactness and portability. No matter which type of instrument be used, it is essential to have this calibrated against a standard manometer at least once a year, since opinions based upon the use of an inaccurate instrument can only be misleading. Sometimes one comes across a good man working with a bad instrument, which falsifies his conclusions and tends to promote the

utterance of wrong opinions. Particularly is this the case in respect of the aneroid sphygmomanometers, due either to faults in construction or to weakening of the elasticity of the metal diaphragm, which may undergo permanent distortion.

Methods of Estimation of Arterial Pressure.—The four methods of estimating arterial pressure are :—

1. Tactile.
2. Vibratory.
3. Oscillatory.
4. Auditory.

1. *The Tactile Method.*—By palpation of the radial artery in the forearm, cessation and return of the pulse are observed during the time that the brachial artery is under compression. As usually practised, this method is inexact, and gives readings which are too low. Nevertheless, this method is useful as a check on the auditory reading, which should never be lower than the tactile, though it is frequently higher.

2. *The Vibratory Method.*—This modification of the tactile method serves as a still more effective check, since, by light palpation of the brachial artery below the point at which one listens, the thuds of the third phase of sound are perceived by the finger as vibrations which cease after the last thud, thus denoting with accuracy the diastolic index.

3. *The Oscillatory Method.*—Apart from delicate laboratory instruments, this method is only possible by the use of clinical aneroids in which the oscillations of a long and fine needle measure various pressure heights on a dial. In difficult cases, especially those in which cardiac irregularities are manifest, the oscillatory method affords valuable help.

4. *The Auditory Method.*—This method has now attained universal favour as the quickest, simplest and most accurate yet devised. It can be strongly recommended for general use, with the brachial vibratory method, if necessary, as a check. Should the brachial artery be hard to come at, the radial tactile method gives a fair approxi-

mation by the addition of 5 mm. to the reading as a correction.

A comparison of curves obtained by the use of the above methods is illustrated by Fig. 3.

The Five Points and Phases of Sound.—On placing the bell of a stethoscope over the brachial artery, while the pressure is gradually being lowered within the compressing

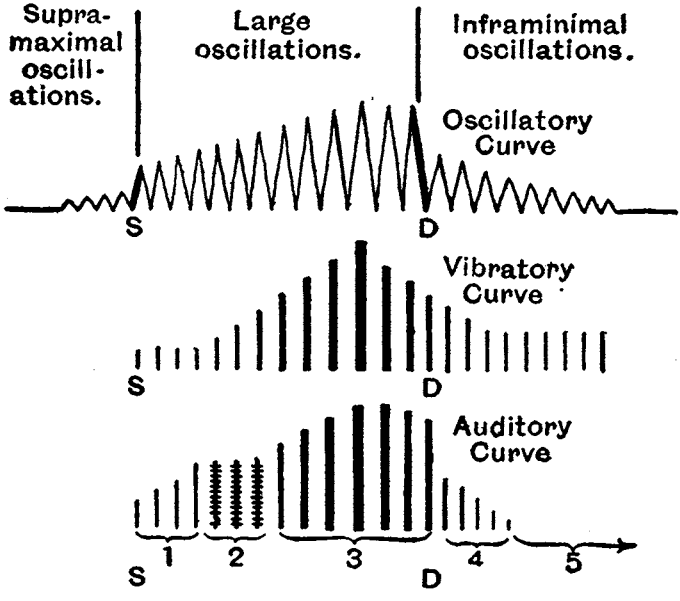


FIG. 3.—Diagrammatic comparison of curves obtained by the use of the oscillatory, palpato-vibratory and auditory methods of estimating arterial pressure. Curves to be read from left to right, showing vertical correspondences between the levels of S, the systolic pressure, and of D, the diastolic pressure. The figures below the auditory curve refer to the five phases of sound: 1 = clicks, 2 = murmurs, 3 = thuds, 4 = dull sounds, 5=no sound.

armlet, a series of sounds becomes audible. These sounds, although presenting similar general characteristics, in individual cases show variations from which useful deductions as to diagnosis can be drawn.[8, 9]

At five points the character of the sounds changes, the duration of successive zones of sound between any two of these points, as measured in millimetres of mercury, being termed phases.

As the pressure within the armlet is lowered, the five phases of sound occur in the following order :—

1. Clicks.
2. Murmurs.
3. Thuds.
4. Dull Sounds.
5. Silence.

1. *The first point, coincident with the first clear sound or click, marks the level of the maximal or systolic arterial pressure.* —The first click is often sharper and clearer in quality than those which succeed it. These together constitute the first phase, which is of short duration, lasting only for a few millimetres.

2. *The second point* denotes the beginning of the second phase, and is recognised by either the addition of a soft blowing murmur to the clear sound or its entire replacement by the murmur. This phase is usually longer than the first one.

3. *The third point* occurs when the murmur disappears and gives place to a zone of sounds somewhat similar to those of the first phase, but louder. They become gradually more accentuated, resembling the throbbing of a drum or the beat of a gong.[10] These sounds constitute the third phase.

4. *The fourth point* is reached at the instant when the thuds of the third phase, after increasing in intensity to a maximum, suddenly lose their special quality and become reduced to a dull tone. These muffled and dull sounds, of variable duration—from 3 mm. even up to 55 mm.—constitute the fourth phase of sound. *The beginning of the fourth phase,* i.e., *the first dull sound following the last loud thud, is the auditory index of the minimal or diastolic pressure.*

5. *The fifth point* registers the disappearance of all sound.

Analysis of the Five Phases of Sound.—*The first phase* is made up of sounds which are light and clear for the reason that it is only the crest of the systolic wave that slightly separates the arterial walls, thus causing only very small vibrations. The first click is often more definite than the

rest because the oncoming blood wave has to push asunder the walls of the obliterated artery, whereas the waves which follow have not to overcome the like degree of inertia.

The second phase, of murmurs, is due to *sounds originating in the blood current.* During its passage through the constricted artery, eddies or whorls are set up as it drops from a raised pressure to one which is lower on entering the uncompressed, and therefore relatively large, portion of the brachial artery below the armlet.

The third phase, of thuds, is probably due to variations in the rate of conduction of sound, and coincides with the period during which the wall of the artery is thrown into vibration, loud thuds being related to normal or heightened arterial tone, whilst an artery with flaccid walls will be associated with sounds of much less intensity. This phase is nearly always the longest of the series, and corresponds with the greatest amplitude of oscillation as recorded by graphic instruments.

The fourth phase indicates the change which takes place when the pressure within the constricting armlet has become so reduced that it no longer causes distortion of the circular form of the artery, even during the time of diastole, nor slows the blood current, *i.e.*, an external pressure equal to the internal diastolic pressure.

The fifth phase, identical with the disappearance of all sound, ensues when normal arterial conditions are again established.

Variations in the Phases of Sound and their Interpretation. In cases of abnormally high arterial pressure the sounds of the first phase are unusually loud. The length of the second phase is probably an index of cardiac efficiency, and when this latter is impaired from various causes, such, for example, as weakening of the heart muscle by toxæmia, etc., or from the effect of valvular disease, the second phase is the first to be affected. Thus a long and strong murmur phase, increased by exercise, denotes a good heart, whereas a murmur vanishing after exercise indicates a feeble left ventricle or a low arterial pressure state. When the blood current is swift the sounds are loud and clear, a condition which is also seen in anæmia, where this paradox is explicable

by the loss of vasomotor tone in association with poor nutrition of the arterial muscular coats. Many authorities consider the third phase as being of the greatest importance clinically.[10], [11] Long, loud and clear thuds indicate cardiac strength while a short, weak and soft third phase affords evidences of cardiac weakness. The fourth phase is commonly lengthened with cardiac weakness and a low diastolic pressure.

Not all the phases can be heard in every case, and the fourth phase is often absent, the transition between the last loud thud and a silence being abrupt. Other gaps also may occur at any part of the series and may involve the whole or a part of any of the phases, or instead of a complete gap only faint sounds may be audible. In general terms it may be stated that modifications affecting the whole of the auditory curve are almost always due to a central cause, cardiac or aortic, while modifications of a portion only of the curve are usually of peripheral origin, arterial in kind.

It may possibly be urged by some that variations in the auditory curve, such as have been described, are but of academic value, and do not come within the range of practical medicine, but if one realises that vibrations set up in the arterial wall are directly brought about by the agency of the sympathetic nervous system, it will become evident that by careful study of arterial pressure, not only of the figures which make up "the complete arterial pressure picture" (p. 19), but also of modifications in the sequence of sounds, one can thus in certain cases obtain valuable information as to the integrity or otherwise of the sympathetic nervous system as well as a further insight into the activities of the endocrine glands.

Technique of the Auditory Estimation of Arterial Pressure.—The auditory method of estimation is by far the most practical in the majority of cases, and is applicable to any modern type of sphygmomanometer. The procedure to be adopted is as follows :—

1. A single layer of thin material round the arm presents no obstacle to effective compression, but in all other circumstances the arm should be bared.

2. The patient should be seated in an easy, comfortable

position *with all the muscles relaxed, and in a condition as far as possible of mental repose,* by the side of a table or consulting-room desk of such convenient height that the patient's arm, when lying outstretched upon it, is at the same level as that of the heart.

3. Carefully wrap the armlet containing the pressure bag around the arm *as high up as possible* so that its upper border touches the axillary fold, the pressure bag being centred over the brachial artery. Wind the soft material round the arm after the fashion of a bandage, taking care that it is equally applied over its whole width, and tucking in the last 2 or 3 inches of the tail so that it is held firmly under the preceding turn.

4. By means of a rubber tube connect the armlet with the instrument and tighten the release screw of the rubber bulb.

5. Warn patients of excitable or nervous temperament that the armlet will tighten upon the arm for a minute or two, but that this pressure is but temporary and need not cause alarm.

6. Find the position of the brachial artery, which runs along the inner side of the biceps muscle, and over it, immediately below the lower edge of the armlet, maintain a *light and even* pressure with the bell of a stethoscope (or auditory tambour), being careful not to exercise undue compression upon the artery with the stethoscope.

7. Next blow up the armlet by successive squeezes of the bulb to a point which is well above the level at which any sounds are audible. Then gradually and evenly release the pressure by turning the screw-valve attached to the bulb.

8. In the mercurial manometer the column of mercury now begins to fall, whilst the needle of the aneroid begins to move counter-clockwise round the dial.

9. According to the type of instrument used, note accurately either the height of the mercury column or the figure reached by the dial needle at which the first sound is audible. **The first click heard on decompression following obliteration of the artery denotes the systolic pressure.**

10. As the pressure continues to fall, the few first clicks give place to a soft murmur of variable duration, which is followed by a longer phase of thuds, which increase in

intensity to a maximum, and then tail off into a few dull and muffled sounds preceding complete silence. **The first dull sound after the last loud thud indicates the diastolic pressure.**

In cases where it is difficult to be sure of the exact level of the systolic and diastolic pressures the tactile method forms a useful check. While the patient's forearm is allowed to lie in a position midway between pronation and supination, the observer lightly grasps the patient's hand and palpates the radial artery with the extended index finger. The systolic reading obtained in this way is, however, about 2 to 10 mm. lower than the true brachial systolic pressure, so that an addition of 5 mm. to the reading should be made as an average correction.

The above methods may be employed with any reliable type of sphygmomanometer and stethoscope (or auditory tambour, which latter is strapped on to the arm by an elastic band, and has the advantage of leaving both hands free). Additional ease and rapidity of compression and decompression is promoted by the introduction of a 10 × 9 cm. pressure bag into the circuit of rubber tubing midway between the rubber bulb and the armlet. By alternate pressure and relaxation of pressure upon this bag by the hand of the observer the mercury column can be more rapidly adjusted, with less disturbance to the patient, than by the use of the release valve and pressure bulb alone. Estimation is best made after taking the patient's personal and family history, and before going on to clinical investigation of the various systems.

Meaning and Value of the Minimal (Diastolic) Pressure.— In the estimation of arterial pressure, on account of the many difficulties and errors inherent in the older types of blood pressure instrument, both as regards mechanical construction and manipulative technique, until recent years it has been a sheer impossibility to measure the minimal pressure with any approach to exactitude, so that observers were forced to content themselves solely with registration of the maximal pressure. Conditions, however, have now entirely changed, and, with lapse of time, much careful and patient work has succeeded in establishing accurate estimation of the minimal pressure on a firm and consistent basis

Regarding the maximal end of the scale, it has been stated with much truth that if our observations are confined to that record alone, their clinical value will be comparatively small, and inferences will be contradicted by other evidence.[7]

During the past seventeen years on many occasions the author [2, 12] has laid considerable emphasis upon the prime importance and necessity of recording the minimal pressure, and has pointed out that, in comparison with the maximal pressure, the minimal pressure is of far greater value in that, being considerably less liable to transitory fluctuations, it is thus a more definite and constant indicator, not only of the propulsive force of the heart, and of the eliminatory capacity of the body, but also of the peripheral resistance, including conditions under which abdominal venous stasis occurs, and of vasomotor nervous tone.[13] For just these reasons the minimal pressure possesses an equally great value in low as well as in high arterial pressure states (p. 84). Since, nevertheless, the relation between the systolic maximum and the diastolic minimum is capable of variation between wide limits, not only in different individuals but in the same individual at different times, it follows that considerable fluctuations in the amplitude of the pulse wave must also occur. Hence, in order to discover the differential or pulse pressure, we must register the pressures at both extremities of the scale.

Meaning and Value of the Maximal (Systolic) Pressure.—The maximal pressure indicates the maximum cardiac energy at a given moment. It is a much more variable factor than the minimal pressure because it is swayed to a far greater extent by physiological influences such as sleep, rest, exercise, food, posture, fatigue, etc., by alcohol and tobacco, and, in particular, by emotional stimuli. Hence, the first reading of the systolic pressure in emotional subjects is considerably higher than that which is recorded on subsequent readings and alters frequently even within the space of a few seconds.

The Complete Arterial Pressure Picture.—If we wish to assess the state of the circulation at a given time, it is not sufficient merely to record the maximal pressure whilst ignoring the minimal, for such procedure resembles an

TABLE II

Theoretical Standard Arterial Pressures in Males of Medium Physique at various Ages * (*Halls Dally*)

Age in Years.	Systolic Pressure in millimetres of Mercury.	Diastolic Pressure in millimetres of Mercury.	Pulse Pressure in millimetres of Mercury.
At birth . .	20—60 (average 40)	?	?
At end of 1st fortnight.	70	?	?
At end of 1st month	80	?	?
Up to 2 . .	81	45	36
,, 5 . .	86	50	36
,, 10 . .	95	55	40
,, 15 . .	110	67	43
,, 20 . .	123	80	43
,, 25 . .	125	81	44
,, 30 . .	126	82	44
,, 35 . .	127	83	44
,, 40 . .	128	84	44
,, 45 . .	129	85	44
,, 50 . .	131	86	45
,, 55 . .	133	87	46
,, 60 . .	135	88	47
,, 65 . .	140	90	50
,, 70 . .	145	92	53
,, 75 . .	150	95	55
,, 80 . .	155	98	57
Over 80 . .	All pressures	tend to fall	

* Pressures determined by auscultatory method with Riva, Rocci or Tycos types of instrument.

attempt to solve a complicated problem of which only one factor is vouchsafed. Rather should we in all cases note : (1) the maximal pressure ; (2) the minimal pressure ; (3) the

differential (pulse) pressure, *i.e.*, the difference between the figures obtained respectively for the maximal (systolic) and minimal (diastolic) pressures; (4) the pulse rate and characteristics; and (5) the product of the pulse pressure multiplied by the pulse rate. The sum-total constitutes the author's "Complete Arterial Pressure Picture," and we thereby obtain a simple and compact formula which can rapidly be entered in the notes of the case (Fig. 4).

The Standard Level of Arterial Pressure

If we desire to know whether a given arterial pressure is high or low, the first essential is to have some approximate idea of what the standard pressure should be for individuals of corresponding age and body weight, "standard" being used in the sense of average "normal," *i.e.*, non-pathological pressures.

Table II (on p. 20) represents theoretical standard arterial pressures at various ages for men of medium physique.

CHAPTER II

Low Arterial Pressure

Definitions.—Hypotonia (Vascular Hypotonus) represents a dynamic and physical state of diminished tonus of the smooth muscle in the *walls of arteries* and veins, as contrasted with low arterial pressure (hypopiesis), which indicates a diminished lateral pressure exerted by the *blood* upon the vessel wall.

Hypopiesis is a term applied to low arterial pressure in general, of which it is the equivalent, and means a diminution of arterial pressure below standard * limits as an expression of lowered vitality arising from any cause whatever, whether temporary or permanent, congenital or acquired, associated or not associated with organic disease.

Hypopiesis is thus a generic term for low arterial pressure. As in high pressure states, however, hyperpiesis the greater includes a congenital form, hyperpiesia the less, so in low pressure states hypopiesis includes the congenital hypopiesia.

Hypopiesia is a clinical series of primary congenital or constitutional origin characterised by persistently lowered arterial pressure occurring as a part of a low vitality state either without *apparent* physical abnormality, or in association with conditions of suboxidation dependent upon physical abnormalities, such as elongation and narrowing of thorax, aorta and heart.

" Hypotension."—By writers of the French and American schools, also regrettably by certain British writers, the ugly term " hypotension " is employed as a synonym for " low arterial pressure," just as to the opposite condition of high arterial pressure the term " hypertension " is applied. Nothing but the plea of brevity can, however, attempt to palliate the use of these truly dreadful hybrids, for, as the late Sir Clifford Allbutt clearly and with justice pointed out,

* Standard = normal, *i.e.*, non-pathological.

"the blood cannot be tense in any but an abstruse mathematical sense." [14] Medical nomenclature is already open to so many charges of loose and incorrect expression that it is wise to abandon the use of words whose derivation is either faulty or leads to confusion of thought.

"Hypotension" is employed by Faught [15] to designate alterations in arterial pressure in which the systolic curve maintains an average level below the established normal minimum. This definition, while covering the greater number of cases that are encountered, nevertheless is rather too limited in scope, since it fails to take into account certain forms of low pressure which in nature are transitory. Just as in the case of normal arterial pressures, the limits of low arterial pressures tend to vary with certain factors which are individual, such, for example, as age, sex, physical development, occupation and temperament. Changes also occur as the result of muscular exercise and during sleep.

Significance of Low Arterial Pressure.—Stated in the simplest terms, low arterial pressure is an arterial pressure the level of which is inferior to the standard level.

"It is difficult to state just how low the systolic pressure may fall and yet be considered normal. In an individual who has been observed over a period of time and in whom one has determined a uniform pressure, any deviation from this standard may with justification be regarded as abnormal if not pathological. But for the rank and file of individuals it must remain a purely arbitrary judgment at what figure to place the lower limit of normal pressure, and the standard thus erected must be regarded as but an individual opinion. Variations in different individuals are so great, both in apparent health and in compensation of circulation necessitated by disease, that one cannot draw rigid lines and say that blood pressure below these lines is abnormally low; only a general statement can be made subject to exceptions." [7]

Low arterial pressure, taking it on the whole, is less definite in its pathological significance than is high arterial pressure. Nevertheless, low arterial pressure is worthy of vastly more attention than has yet been devoted to it,

since its presence may point to some underlying functional or organic malady which needs serious consideration. Furthermore, many patients suffer from symptoms directly attributable to their low pressures, and remedial measures are required for their relief.

Although an arterial pressure which is subnormal may not infrequently indicate a condition of myocardial degeneration with consequent insufficiency, more often than not it denotes vasomotor relaxation or even paralysis induced by toxæmic states or nervous and reflex origins.

The Upper (Systolic) Limit of Low Arterial Pressure.—Attempts to grapple with the somewhat complex problem of low arterial pressures in general are not rendered any the more easy by the fact that as yet there is no unanimity of opinion as to the point on the arterial pressure scale at which a line should be drawn to divide arterial pressures which are low from those which remain within normal limits.

This difficulty is not remarkable, seeing that the methods of estimation adopted at different times by different observers bear to each other no direct relationship. In the endeavour to arrive at a conclusion, palpatory, oscillatory and auditory methods have each been utilised. All the older readings obtained by means of radial palpation, particularly in conjunction with the use of the narrow (5 cm.) armlet, must, however, be discarded as being too high. So, too, must all measurements taken with the older form of Pachon's sphygmo-oscillometer with the 7 cm. narrow wristlet, since for a like reason they are fallacious. Oscillatory readings with the modern type of this instrument in combination with Gallavardin's double armlet, or with other accurate oscillometric instruments, can be accepted, since they are directly comparable with auditory estimations obtained by the employment of the mercury manometer.

Janeway's [16] original view was that for practical purposes the line may be drawn between normal and subnormal systolic pressure in adults at 90 mm. of mercury (12 cm. armlet and palpatory method). After the lapse of eleven years, however, this observer [17] states that he would take 105 to 110 mm. Hg in men, and 100 mm. Hg in women (auditory) as being a definitely low systolic pressure standard,

though attaching less significance to occasional readings slightly below the normal standard.

Emerson [18] indicates the greater difficulty of proving subnormal pressure than of determining an increase of pulse rate or of temperature, and does not regard a patient's arterial pressure as normal from a single systolic reading within the normal limits.

Faught [15] cites 105 mm. as the low limit of normal arterial pressure in young men and 95 mm. in young women (auditory).

Nicholson [19] assigns 100 mm. or below as the figure (auditory).

Bishop [20] groups under the heading of "essential hypotension or constitutional low arterial pressure" many apparently healthy individuals who, during youth and early adult life, normally have a systolic pressure ranging between 100 and 115 mm., and a diastolic pressure between 80 and 60 mm. (auditory).

Norris [21] gives a systolic pressure of 110 mm. as the usually accepted upper limit, generally in association with a diastolic pressure below 80 mm.

Oliver [22] and Goodman [23] give the much higher level of 120 mm. (auditory).

Cornwall [7] is of opinion that variations in different individuals are so great, both in apparent health and in compensation of the circulation necessitated by disease, that one cannot draw rigid lines and say that blood pressure below these lines is abnormally low. This author believes that only a general statement can be made subject to exceptions, *e.g.*, for a young adult a systolic pressure of 100 may be low; for middle age a systolic of 110 may be low; for elderly people a systolic of 120 may be low; for sclerosis or spasm of arteries supplying a vital region a systolic of 140 may be low; for advanced interstitial nephritis a systolic of 180 may be low. Cornwall further states that, from the view-points of circulatory efficiency and pathology, the diastolic pressure is fully as important as the systolic, and that the considerable variations which may take place in low diastolic pressures must always be considered in their numerical relations with the systolic pressure.

Martinet,[24] employing the Pachon sphygmo-oscillometer with narrow wristlet, places the upper limit of low arterial pressure at between 120 and 130 mm. of mercury. The narrow wristlet, however, gives readings which are too high, and had these estimations been made with the modern type of Pachon's instrument with the wide Gallavardin armlet, 110 and 120 mm. respectively would approximately represent the correction required to render these figures comparable with the readings of other observers.

Heitz [25] puts the systolic level at about 120 mm. (palpatory) or 125 mm. (auditory) for men, and for women 5 to 10 mm. lower, whilst for the diastolic level, measured by Pachon's sphygmo-oscillometer or by equivalent methods of auscultation or vibratory palpation, he assigns 70 to 80 mm. Hg.

Potter [26] writes as follows: "Whenever a young adult male presents a systolic pressure of 110 or below (or a point 5 or 10 mm. lower in a female), either in my routine office examination or at the bedside, I search very carefully for some cause for this level, for some accompanying signs or symptoms of weakness in the circulation or nervous system, and have blood pressure estimations repeated one or more times. I am free to confess, however, that many years' experience at the New York City Hospital, where damaged heart, kidneys, and vessels are the rule rather than the exception, may be partly responsible for my selection of 110 as a level below which suspicion should be attracted."

McCrae,[27] Roberts,[28] Uzan,[29] Stevens,[30] Barach,[31] and Fossier,[32] agree in the belief that a systolic (auditory) pressure of 110 mm. or less should be regarded as the dividing line between normal and low arterial pressures.

A most useful series of observations upon the normal limits of systolic and diastolic pressures in a large number of cases has recently been made by Dr. Percy Stocks,[33] who personally examined 1,633 subjects, of ages from five to forty years, using the same Brunton sphygmomanometer throughout with 12 cm. cuff, and the auditory method. The vast majority of observations were made between the hours of 10 a.m. and 1 p.m., the subject being seated with the armlet around the left arm, which was allowed to rest on a table in a

position of relaxation, palm upwards. From his investigations this author concludes that from twenty to forty years of age systolic pressures below 98 mm. should be regarded as almost certainly pathological, and below 109 mm. as open to suspicion.

Between the highest and lowest figures given by the above authorities, when checked and assessed by modern methods of observation, there is thus a difference of over 20 mm.

Since each observer fixes his own empirical level in accordance with his beliefs as to what constitutes in reality a state of low arterial pressure, whose scope varies with his individual classification based on the nature of his own clinical experience, for working purposes it is essential to have in mind some idea as to where to draw the line of demarcation between pressures which are normal and those which are subnormal. Here again, just as in the matters of temperature and pulse rate, the normal for one individual is not identical with the normal for another. The majority of so-called "normal" temperatures are subnormal, and congenital and familial slowness of pulse rate may every now and again be observed. So that the only way in which we can attain any coherent conception as to extent of abnormality in arterial pressure is to apply the knowledge derived from the fruits of experience in the investigation of as large a number of cases as possible, the ideal being to have access to the results of observations ranging over several thousands of subjects. Until large numbers of such observations, made with a standard type of sphygmomanometer, under uniform conditions and with a uniform modern method, upon apparently healthy subjects, shall have become accessible, one finds difficulty in putting forward standard figures for the upper (systolic) and lower (diastolic) limits of low arterial pressure.

If, however, it be clearly understood that any figures assigned respectively as these upper and lower limits are arbitrary and not constant, but necessarily subject to modification by the varying factors of age, sex, physique (including body weight and state of muscular development), occupation and pulse rate, the author's experience disposes him to adopt the figure of **110 mm. of mercury for males, and**

105 mm. for females, estimated under standard conditions of fasting or at least two hours after a meal, as the nearest approximation in the present state of our knowledge to the **upper (systolic) limit of low arterial pressure at adult ages.** For the reasons above stated, however, reservations should be made in the application of these figures to individual cases.

The main reasons for this view are, firstly, that the author regards 110 mm. as a level definitely below that which one would expect the lowest level of standard systolic arterial pressure to be **in health** at adult ages, and, secondly, because, at this level or below it, symptoms indicative of, and associated with, low arterial pressure are likely to occur. It is true that these characteristic symptoms are not constantly encountered at 110 mm., but even a slight drop below this level is usually sufficient for them to become manifest.

As in the case of the arbitrary levels which have been drawn to differentiate arterial pressures which are normal, high, and excessively high, one should avoid too close adherence to standards, and allow a measure of elasticity when dealing with individual instances, so for low pressures one should be guided in similar fashion, paying due regard to the important influences of age and body weight. If one makes a practice of recording arterial pressures in every case that comes under observation, one's clinical ability to assess the value of particular readings thereby becomes considerably enhanced.

Janeway [16] has pointed out that the real dividing line is an individual one, to determine which we should have previous records of the same patient in health. This is seldom possible, and we must take the lowest normal as our standard, just as we do for the leucocyte count.

Systolic pressure values of 95 to 80 mm. are not uncommonly met with, and may persist over long periods of time, to be followed eventually by restitution of standard readings. Apart from terminal low pressures, the lowest reading met with in adult life may be stated as 70 mm. Hg.

Uzan [29] takes the view that the subject of low arterial pressure should be approached from a much wider angle,

and is of opinion that to determine its presence only in cases where the pressure keeps below a conventional level considerably diminishes the field of study. He states that low arterial pressure *can* only be relative, and that it is of frequent interest to compare the arterial pressure of an individual at a given instant, not with the average normal, but with the habitual pressure of that individual. From this evolves the idea of relatively low individual pressure, which may be the index of fresh circulatory phenomena. Further, he regards the dissociation of systolic from diastolic low arterial pressure as important, and points out that a person who presents a pressure lower than his age warrants, is not necessarily in a pathological state, and should be distinguished from the hyposphyxic subject (p. 78) by the absence of any other morbid phenomena, and because the condition is compatible with a normal life.

The Lower (Diastolic) Limit of Low Arterial Pressure.—As regards the diastolic limit of low arterial pressure, little information is to be obtained from the literature, which almost wholly lacks exhaustive studies.

The lower diastolic limit is even more difficult to fix than the systolic, as very frequently the two pressures do not run on parallel lines, and the minimal level may vary within a wide range in different individuals. Such dissociation of pressure may be marked, one patient, for example, manifesting a systolic pressure of 100 mm. and a diastolic pressure of 90 mm., whilst another may exhibit a like systolic pressure of 100 mm. and a diastolic of 55 mm.

A ready but somewhat artificial method of deducing the diastolic pressure in any case, whether of high or low pressure, is by the use of "Lian's [34] law of arterial pressures," viz.,

$$\text{Mn (in mm. Hg)} = \frac{\text{Mx}}{2} \text{ (in mm. Hg)} + 10.$$

Thus, taking the normal limits of variation of the systolic pressure in an adult as between 140 and 110, by the application of this law all systolic pressures below 110 will be regarded as weak and the subject as in a state of "systolic low arterial pressure." When, on the other hand, we dis-

cover the diastolic pressure to be lower than anticipated according to Lian's law, we shall call such condition "diastolic low arterial pressure."

Apart from the co-existence of such special features as those of aortic regurgitation or of a large arterio-venous aneurysm, which are here excluded, the minimal pressure as a rule is reduced by a relatively less extent than the maximal. From this it follows that the differential or so-called "pulse" pressure is usually of small amount in low pressure cases.

Martinet [24] gives the ordinary limit of low diastolic pressure as 80 mm. of mercury or less (oscillatory or auditory readings), and states that the lowest adult figure that he has met with was 50 mm. in a case of pernicious anæmia. These readings are, however, too high owing to the use of a narrow armlet, and must be reduced by several millimetres in order to render them comparable with modern measurements.

Drs. William and C. W. Curtis Bain [35] made careful observations on 2,000 general cases by the auditory method (patient seated, with arm resting on desk). Of these, 230 of ages varying from 25 to 70 years, the majority being between 35 to 50, presented a total range of systolic pressures from 85 to 140 mm. of mercury, but by far the greater number lay between 100 and 115. The diastolic pressures varied between 60 and 120, 14 being below 70 mm. These cases were grouped as follows: neurasthenia, numbering 93; nervous, 64; mucous colitis, 48; making a total of 90 per cent. The remaining 25 were associated with some organic affection, several being cases of rheumatoid arthritis.

The figures given by Stocks [33] for the probable limits of normality in auditory diastolic readings are more striking than those stated by him for his systolic readings, to which reference has been made above. From a comparison of age curves, he claims that the final rise of diastolic pressure to the early adult level lags several years behind that of the systolic pressure, and does not reach its maximum at the same time as the systolic pressure does, but usually when the period of adolescence is passed. Stocks thus considers

that pressures below the following figures are either pathologically low or suspect.

Diastolic pressure	below 59 mm.	is pathologically low for	ages 20 to 24
	below 58 mm.		ages 25 to 29
	below 55 mm.		ages 30 to 40
	below 67 mm.	is suspect for	ages 20 to 24
	below 68 mm.		ages 25 to 29
	below 65 mm.		ages 30 to 34

The lower (diastolic) limit of low arterial pressure, corresponding to an upper systolic limit of 110 **for males at adult ages** as estimated by modern auditory, vibratory or oscillatory methods, according to the author's view, **is normally 66 mm. of mercury.** This correspondence yields a standard differential pressure of 44 mm. of mercury, which accords with Lian's figures for cases in which the systolic and diastolic pressures are not dissociated. Where there is dissociation of the diastolic pressure, this latter figure may reach a point 10 mm. lower. **For females** the author would place the diastolic limit at approximately **62 mm.**

The lowest average diastolic pressures are often found in association with disturbances of internal secretion, and the highest in nephritis. In some of the latter the difference between the two pressures is small, as in certain cardiac cases in which the difference is only 10 mm. On rare occasions it is not possible to estimate the diastolic pressure by means of the auditory method, for the sounds are inaudible. Under such circumstances one has to rely upon tactile or oscillatory methods.

Range of Low Arterial Pressures.—In general, it may be said that the range of low arterial pressures is from 90 to 110 mm. for the systolic pressure, and from 60 to 80 mm. for the diastolic pressure.

Low Differential (Pulse) Pressure.—The differential (pulse) pressure, though not a *direct* measure, like the minimal and maximal pressures, represents the difference between these two variables, upon which its attributes depend. Nevertheless, it is of prime importance in that it constitutes a sphygmomanometric expression of the cardiac load.

The normal range of differential (pulse) pressure may be stated as between 34 to 54 mm. of mercury, standard differential pressure being 44 mm. **In hypopiesis, differential pressures of 34 to 31 mm. of mercury should be regarded as suspect, and those of 30 mm. or under as pathological.**

Apart from exceptional cases, such as those of aortic regurgitation or a large arterio-venous aneurysm, the diastolic pressure in hypopiesis becomes lowered to a less extent than the systolic, the resultant differential pressure thus being commonly small.

Hence decrease in the differential pressure is more frequently met with than increase, and occurs under two main conditions: (*a*) circulatory, as in tachycardia, especially paroxysmal; in advanced mitral stenosis, and in failure of the circulation; (*b*) nervous, as in neurasthenia and in certain forms of neurosis.

The subjects of constitutional hypopiesis manifest differential pressures often well below the standard 44 mm., at times descending even to 20 mm., in striking contrast to opposite conditions such as are encountered in cardio-renal and arteriosclerotic patients with hypertrophied hearts of bovine type who may exhibit high differential pressures of 110 or so, up to excessively high ones of 180 mm. or more.

Analysis of the Bains' 2,000 general cases above-mentioned showed that 230 of these presented differential pressures of 30 mm. or under on one or more occasions. In 90 per cent. this was associated with nervous phenomena. Those which showed differential pressures of between 30 and 40 mm. were rejected as doubtful. In very few was the pulse rate over 100 per minute, nor were any cases of heart failure or advanced mitral disease included.

The Differential Pressure as an Index of Functional Efficiency.—"Systolic hypopiesis is a sign of weakness which is prone to result in constititional evidence of subnormal nutrition; diastolic hypopiesis indicates a low head of pressure in the nutrient stream for the heart.

So far as numerical values of blood pressure serve as an index of physiological efficiency, in the absence of gross organic lesions the differential pressure is the one invariable determining factor. Where there are symptoms of circulatory

inefficiency a subnormal differential pressure is usually found, and when the erect posture is assumed, there will be an inordinate decrease in the value of the differential pressure to 25, 20 or even 10 mm. of mercury. In 100 cases in which this pressure was low, 30 mm. or less standing, the dominant cause of a fall in the differential pressure was a fall of the systolic in 10 cases, a rise of the diastolic in 69 cases, and combined fall of the systolic pressure and rise of the diastolic in 21 cases." [36]

Frequency of Incidence of Low Arterial Pressure.—It is of considerable interest to determine with what degree of frequency one may expect to meet with arterial pressures which are low, *i.e.*, where the maximal pressure does not exceed 110 mm. Hg under conditions of health.

A fairly close approximation may be made on the basis of recent statistics, of which the largest series is derived from American sources. Examination by Barach and Marks [37] of 4,142 men of student and military age showed an incidence of systolic low arterial pressure in about 3·5 per cent. Of this 3·5 per cent. the majority of the subjects were found to be below standard weight. Another characteristic of the type was manifested by one sub-group, investigated by the same observers, and included in the above total, with reference to chest expansion, which was 2·9 inches (7·2 cm.) for twenty-four low-pressure subjects out of 1,100 normal male students, while for the normals it was 3·1 inches (7·8 cm.). Fisk [38] has also recorded underweight as the chief feature in 70 per cent. of low pressure subjects picked out of a group of 17,000 insurance cases. Similarly Symonds,[39] reviewing a large group of 150,419 insurance risks, observed that groups of lighter build have lower arterial pressures than are exhibited by the heavier groups. Of 6,000 Californian students studied by Alvarez,[40] low arterial pressure was demonstrated in about 2·2 per cent. Diastolic and systolic figures recorded by the author for seventy-two individuals in apparent health, of ages from twenty to thirty years, yield a percentage of 2·9.

Influence on Low Arterial Pressure

(*a*) **Of Sex.**—Between the two sexes there is but little difference in distribution. On the whole, women are inclined

to low arterial pressure in slightly greater degree than are men, especially as regards the diastolic end of the scale.

(*b*) **Of Emotion.**—Under the influence of emotion low arterial pressures are far more stable than are either normal or high pressures, and do not manifest the sudden and extreme leaps that characterise the latter groups. This is because the low-pressure group manifests invariably either a lowering or an absence of reactive capacity in accord with the kind and degree of low vitality state present.

Classification of Low Arterial Pressure.—Low arterial pressure may be classified in a variety of ways according to the particular standpoint from which it is approached. Thus one may formulate classifications which are (*a*) general, (*b*) anatomical, (*c*) incidental, (*d*) clinical.

(*a*) Low arterial pressure may be classified from the point of view of its association with various experimental or pathological states.

(*b*) An anatomical classification strives to link up the manifestations of low arterial pressure with the organs and tissues which together make up the circulatory system.

(*c*) If we regard low arterial pressure from the incidental aspect, cases will fall under the two main heads of (1) *transitory*, under which may be included incidents, insufficiencies, infections (acute), and intoxications; (2) *continued*, which latter heading embraces conditions which are congenital or constitutional, and chronic.

(*d*) Certain authors have adopted a still more arbitrary grouping on the results of bedside experience, by tabulating a series of cases of disorders and diseases with which they have found low pressures to co-exist. As records of individual experiences, nevertheless, such groupings possess a certain clinical value.

On the whole, one finds in the scanty literature of this subject no universally accepted classification of low arterial pressures which can be taken as a standard. Nor is this to be wondered at, seeing that the only satisfactory classification is one which is ætiological and, therefore, basic. This lack the author has endeavoured to supply in the following chapter. "High or low blood pressure is not a disease in itself, but only a symptom due to a disease somewhere. It

may be compared to fever for which we have always to find a cause. In some cases we may have a patient showing fever and little else, so that we are at a loss to make a diagnosis. The same happens occasionally with variations in pressure, although here the difficulty arises more often with high than with low pressure. In both the explanation often lies with more than one causal factor." [27]

CHAPTER III

Ætiology of Low Arterial Pressure

General Considerations.—In proportion as the primary causes of departure from a state of health become more accurately and widely established, the art of Medicine is thus enabled to base itself on foundations which are less empirical and more scientific. "High or low blood pressure is merely a link in a long sequence, and the mere observation of a sequence, or of a part thereof, is no evidence as to the causes of the sequence" (Sir James Barr).

Variations from standard limits in the direction either of low or of high arterial pressure are peculiar to the individual at the moment of estimation, and even for the same individual are by no means constant, but, in response to stimuli of endogenous or exogenous origin, are marked by slow or rapid movements in an upward or downward direction on the sphygmomanometric scale.

Further, the height of the recorded pressure must necessarily be assessed in relation to psychical and physical factors, of which latter the most important are age, sex, weight and height. Thus, a given pressure which for some subjects would be definitely low or high, for others would fall within the normal range. Hence the absolute height of any arterial pressure for purposes of comparison with other readings in the same or in different subjects can only be regarded as relative, and variations in pressure must be looked upon as physiological or pathological in accordance with this relativity.

The Author's Views on the Ætiology of Low Arterial Pressure.—In the study of hypopiesis many current fallacies result from the fact that the subjects of hypopiesis without apparent physical abnormality have been regarded as healthy, apart from the incidence of a low level of arterial pressure.

Taking, however, the hitherto inexplicable hypopiesia

(primary hypopiesis) as the purest example of a low arterial pressure state, and analysing it carefully, one comes to the conclusion that the subjects of hypopiesia, although they suffer from a condition rather than a disease, contrary to generally accepted opinion, are, from clinical and biochemical aspects alike, by no means normal physiological people. Clinically, they are prone to attacks of depression, and on some days feel wretched and uncertain of themselves, although these bad days alternate with others on which they feel particularly fit and well. Such temperamental changes vary directly with the height of arterial pressure at the time, the sensations of well-being coinciding with the hours during which their systolic and diastolic pressures tend towards the upper limits of their personal range, while the times over which their pressures are depressed correspond with their feelings of wretchedness and incapacity. Moreover, they are extraordinarily liable to fall victims to zymotic maladies. Sluggish circulation and chilblains are also not uncommon.

Biochemically, such subjects not infrequently manifest a disturbance of acid-base equilibrium of the tissues in the direction of alkalinity as evidenced by the urinary ratio of free to combined (ammonia) acidity being greater than the normal 1 : 1·75.

It is only when tissue alkalinity lessens that these subjects recover a fleeting physical and psychical fitness. If, for example, they go for a run or a ride before breakfast they feel fitter, and their metabolic equilibrium may be restored for some hours, since exercise in the fresh air promotes increased oxidation and diminishes tissue-alkalinity. The whole matter resolves itself into cellular, lymphatic, capillary and endocrine balance—a tissue resistance problem which varies with age, with bodily configuration, and with acid-base balance.* In an investigation of over 2,000 cases, so far the author has been unable to determine any direct correlation between the height of arterial pressure and the

* Consumptives who are doing badly and putting up no effective resistance to their infection are apt to manifest increased tissue-alkalinity. Thus the explanation is afforded of the value of sanatorium treatment, which, in essence, depends upon acidifying and oxidising measures, such as sunlight (or ultra-violet rays), abundance of fresh air, regulated exercise, and a diet largely consisting of proteins and vitamins.

acid-alkali urinary ratio. Tissue alkalinity undoubtedly occurs under certain conditions of bacterial invasion, but is probably rather incidental to than causative of arterial pressure variations.

Experiments conducted by the author on indubitable cases of hypopiesia, by frequent sphygmomanometric observations over a series of several months, have shown that, apart from the administration of pressor remedies, arterial pressure will usually rise to a height at which the subject recovers a sense of physical and psychical good health under conditions of moderate physical effort. Within a subsequent period of time, varying with the individual, but always within a few hours, arterial pressure falls to a level at or below which it formerly stood. Daily readings must be taken, since these diurnal variations, which are of the highest importance, cannot be discovered by occasional or spasmodic estimations with the sphygmomanometer, and point definitely to the conclusion that, for this type of hypopietic subject, daily physical exercise within the limits of fatigue is not only salutary, but necessary in improving the tone of the circulation. If, nevertheless, effort be carried beyond the limits of individual tolerance and the scanty reserve energy be encroached upon, the already low arterial pressures will become still further depressed with exacerbation of any existing symptoms.

This " apparently healthy " type of hypopiesia is also very dependent upon a good night's rest. Continued late hours, especially in combination with early rising, play havoc with these unfortunates, who are obliged to keep a careful watch upon their activities if they would not suddenly collapse for two or three days together.

In this picture of hypopiesia the more extreme cases have been delineated, and it should be remembered that the slighter grades approximate more closely to normal standards.

Nevertheless, the author's opinion is that **the subject of hypopiesis, whether congenital or acquired, is never a normal person,** and that even the " apparently healthy " class when observed over a period of months or years is found to exhibit lapses from normal standards greater than one would expect in the case of healthy individuals.

The Author's Biological Law of Low Arterial Pressure.—On the view just stated, **Low Arterial Pressure, whether congenital or acquired, temporary or permanent, is always to be regarded as an expression of low vitality.** In other words, the hypopietic subject exists in an inferior constitutional state which connotes inadequate and low reactive capacity to normal and abnormal stimuli experienced during life. Up to a point within the limits of individual reserve energy, stimulation is beneficial, but, even so, the reactive capacity is diminished as compared with that of subjects who are in perfect health, and, if stimulation be carried to a point just beyond the limits of reserve, flagging and depression of the vital energies rapidly ensue.

Autonomic-Endocrine Influences.—The mechanism by which these effects are brought about is a complex one. Nutritional changes in the body cells and tissues constitute the basic element. Over and above these a large part is undoubtedly played by hormones, such as those of the adrenal medulla and posterior portion of the pituitary gland, which exert so great an influence upon the tonic control of the blood vessels through the mediation of the sympathetic nervous system.

But that the *rôle* of the ductless glands is not confined to the mechanical side is shown by the fact that the rate of metabolism, to which raising or lowering of vitality corresponds, is controlled by a balance between katabolism and anabolism. "The thyroid is to the human body what the draught is to the fire," [41] and as such is the gland of katabolism *par excellence.*

In each individual case studied, however, evidence has to be most carefully sifted as to the relative influence of each gland, and as to the effects on each of environment in the broadest sense, of heredity and of infection. Avitaminosis has been shown to exert an adverse influence upon function both of the thyroid and adrenals, and, as these are the two main accelerator or katabolic glands, it follows that in avitaminosis and other depressant states lowering of vitality and of arterial pressure will ensue.[42] Endocrine dysfunction, whether originating as a part of an endogenous or exogenous

toxæmia or from other causes, probably constitutes the largest group of low arterial pressures.

The assertion has confidently been made on numerous occasions that it is difficult or impossible to raise a low arterial pressure for longer than a brief period of time. The author's results of treatment, based upon an exhaustive preliminary biochemical survey of the patient, do not accord with these conclusions, and, provided that the particular combination of remedial measures be found that causes a steady rise in arterial pressure to a satisfactory level for the individual, and that this level be maintained by graduated application, so as to avoid over-stimulation on the one hand and inadequacy on the other, an arterial pressure that has been continuously low for years, even of constitutional origin, can be kept on a plane which affords to the patient the benefits of a more constant and higher functional efficiency of organs and tissues than has been experienced within the patient's remembrance.

That this view taken by the author is not solely an impression gathered from the results of clinical experience is amply supported by biochemical observations of serial twenty-four-hour specimens of urine and fæces, and of specimens of the blood obtained after fasting for at least twelve hours.[43] If such observations be made before treatment is instituted, and again at intervals during appropriate administration of general and special measures of relief, a gratifying rise in the basal metabolic rate, and its equivalent in terms of functional efficiency, as assessed by the more generally useful method of plotting urinary metabolic curves, will be found to have taken place.[44]

Biochemical Influences.—Biochemistry gives important clues in the solution of this interesting and important problem. It has been said that "life is an acid reaction in an alkaline medium," [45] and it is certainly true in the author's experience that the greater the vitality of an individual, the more nearly such an one approaches the "acid" type of humanity (as measured by the acid-base balance of the tissues), the fullest expression of which is seen in young and vigorous subjects of athletic build. The converse of this proposition is equally true. Physical and psychical

efficiency together depend upon vitality of somatic processes, which in turn pivots upon a state of metabolic equilibrium. Any factor or factors which disturb that state of metabolic equilibrium which we term " health " cause disequilibrium which results in dysfunction.

In the case both of low and of high arterial pressures there is a departure from standard pressure levels brought about by disturbances of nutritional and of autonomic-endocrine control. In this regard low arterial pressure forms a far easier object of study and research than does high arterial pressure. Over lengthy periods of time hypopiesis remains pure and uncomplicated, whereas the symptoms and signs characteristic of hyperpiesis *per se* in adult life tend to become overlaid and masked by those of arterial and renal sclerosis.

Metabolic disequilibrium lies at the root of both these conditions. In hypopiesis errors of assimilation predominate, whilst in hyperpiesis faulty elimination is the preponderant factor. Some degree of overlapping, nevertheless, occurs, and arteriosclerosis is found associated with low arterial pressures even as it is with those that are high.

In the present problem the vital issue turns upon the question as to whether or not the condition of the cardiovascular system, as indicated by the presence of hypopiesis, is adequate for the individual.

For years the author has sought a comprehensive and unifying principle that would explain the striking diversity of association of low arterial pressures, and that would link them with the incidence under opposite conditions of high arterial pressures. This unifying principle has been arrived at by the adoption of broad and inclusive views based on recent advances in medicine, and the well-known dictum of the late Sir James Mackenzie [46] that " response to effort " is the most valuable test of cardiac functional efficiency has been expanded in the present volume to cover the whole field of arterial pressure.

These views have already been stated in the form of a law that low arterial pressure constitutes an expression of a failure of reaction on the part of the body to endogenous and

exogenous stimuli, whereas high arterial pressure represents the contrast of excessive reaction.

Let us now turn to a consideration of the views of other writers :—

Views of other Writers.—Former classifications of low arterial pressure from the presumed standpoint of ætiology have been largely associational. No previous writers have ventured upon any adequate and comprehensive explanation of the known occurrence of hypopiesis as a part of the syndrome of acute and chronic maladies at wide variance from each other in regard to their essential characteristics. Various conjectures, indeed, have tentatively been advanced, but the question of *post hoc* or *propter hoc* has remained in considerable doubt. Nor has any further attempt been made to link together aberrations from standard limits in the direction either of lowered or of raised arterial pressure states by the discovery of an ætiological and, therefore, basic factor common to both.

A recent pronouncement states that " Low blood pressure is in many instances compatible with perfect health. It is, however, very often a manifestation of a diseased bodily state." [47] This sounds hardly convincing, and, as that eminent divine, Dr. Paley, once wrote of a totally different subject, would appear to be " a contest of opposite improbabilities."

A. Negative Views on Ætiology

Certain authors are content to approach the subject from the negative side, and there to leave it with no attempt at explanation. Thus Mosenthal [48] states that hypopiesis, by reason of its unknown ætiology, was described during the Great War as " neurocardioasthenia," and queries whether low pressure is a cause or an effect of the malady. Friedländer [49] expresses the pessimistic view that hypopiesis is a symptom which is not even established. " For many of these hypotension states," he remarks, " we have no adequate explanation." Such views carry us no further, and we pass on to known data in the hope of extracting from these some more positive applications.

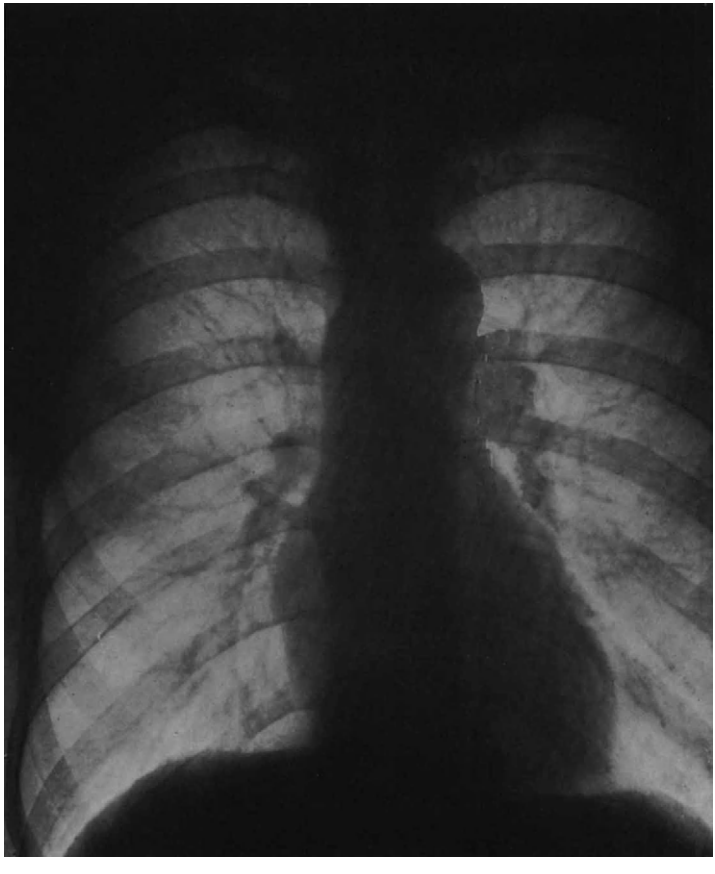


FIG. 5.—The Hypersthenic Habitus.

B. Positive Views on Ætiology

1. The Influence of Respiratory Deficiency and Decreased Oxidation.—May we regard it as not improbable for the reasons already indicated by the author that the true explanation of the ætiology of low arterial pressure may be found along the lines of biochemistry ? In this regard evidence is steadily accumulating which, when correlated, seems to point significantly to the deduction that under certain circumstances *low arterial pressure has direct associations with respiratory deficiency and decreased oxidation.*

(i.) Experimental Evidence.—Considerable support for this suggestion is to be derived from the behaviour of the organism under diminished oxygen supply. Rabbits react to slight variations in atmospheric pressure, and Bartlett [50] found that in them a rarefaction of the air corresponding to 300 metres elevation caused in every case marked difficulty of breathing and in some cases asphyxia. In the aortic system a fall of blood pressure was observed, rapid rarefaction appearing to lower the pressure more than does gradual rarefaction. For the most part, rarefaction diminishes blood pressure suddenly, but sometimes gradually. The pulse frequency shows no clear relation to the rarefaction, but in general decreases with the pressure. The most important of these deductions is the first : that the blood pressure in the aortic system sinks when the pressure of the respired air falls. From these experiments this author concluded that there exists in mountain sickness an increased amount of blood in the pulmonary vessels, due to an increase in their capacity and to a stagnation of blood arising from an equalisation of the atmospheric and intrathoracic pressures. The symptoms are analogous to those seen in dyspnœa and asphyxia, both of which invariably appeared in the experiments.

It is well known that in ascents to high altitudes, as in aviation or in mountain climbing, or at any altitude in a closed chamber or breathing apparatus, a series of circulatory and respiratory adjustments and readjustments take place as a result of the lowered partial pressure of oxygen, different individuals reacting in differing degree to the threatened

anoxæmia. The symptoms of diminished oxygen supply, however produced, are the familiar ones of dizziness, exhaustion, headache, visual disturbances, nausea, vomiting, cyanosis, rapid pulse, air hunger, thoracic oppression, and a transitory rise followed by a fall in arterial pressure. These manifestations are characteristic of altitude sickness, and vary in rapidity of onset according to the physical condition of the subject. They are much intensified in those who have to work in high altitudes, and bear a striking resemblance to the syndrome of hypopiesis.

Along with these symptoms, Greene and Gilbert [51] have demonstrated by electrocardiography that a low oxygen tension induces a depression of cardiac function.

(ii.) **Evidence derived from Aviation Studies.**—In 1914, by experimental investigation of arterial pressure during sixteen flights of variable duration reaching an altitude of 2,850 metres above sea level, Ferry [52] claimed that aeroplane ascents cause in both pilots and passengers (*a*) diminution of the maximum pressure, progressively proportionate to greater velocity of flight, during the ascent and more especially during the descent; (*b*) increase of the minimum pressure under the same conditions; (*c*) diminution of the mean pressure. Records were taken at every 250 metres during ascent and descent by means of Pachon's sphygmo-oscillometer.

Further deductions are that an aeroplane ascent induces lowered arterial pressure, the more notable in degree as ascent, and more especially descent, are more swift. Rapid adaptation of systolic effort in response to constantly changing surroundings brings about speedy cardiovascular fatigue and lassitude. Somnolence, fainting and vertigo may thus connote a certain degree of cerebral anæmia induced by these two factors of cardiovascular fatigue and diminished arterial pressure.

Ferry's conclusions based on limited experience are, however, entirely contrary to the careful and lengthy observations of Schneider and Truesdell, of the American School of Aviation Medicine, to which reference is made in Bauer's [53] more recent book. These observers found that arterial pressure may or may not show a change. With

good circulatory compensation little change in either systolic or diastolic pressure took place until moderately high altitudes were reached, when there followed a rise in systolic and a controlled fall in diastolic pressure giving an increase in differential pressure. In men with high or low systolic pressures no difference in response was elicited. In the so-called rebreather tests, systolic pressure maintained a level or showed a slight terminal rise of 10 to 15 mm. in cases of good compensation. The diastolic pressure stayed on a level until an altitude of 15,000 feet was reached, and then gradually fell by 8 to 10 mm. With poor compensation systolic and diastolic may break and fainting occur. Increased differential pressure in conjunction with increased pulse rate was held to be a form of compensation. Inasmuch as the two were not considered reliable indications of blood flow, increased differential pressure was also considered a sign of distress. Venous pressure was found to be reduced by altitude and capillary pressure to remain unaltered. Further, Schneider and Truesdell,[54] using the Henderson-Pierce rebreathing machine by which the partial pressure of oxygen becomes continually reduced, have shown that in some men the higher or psychic centres become paralysed before the vasomotor, cardiac and respiratory centres—the non-fainting type of reaction. In other aviators the controlling centres for circulation, and sometimes for respiration, manifest inco-ordination before voluntary attention and motor co-ordination are notably affected. Impending circulatory collapse is evidenced either by a rapid fall in the diastolic pressure; by a drop in the systolic pressure, later supplemented by a diastolic fall; or by a slowing of the heart rate—the fainting reaction. Nevertheless, the animal organism has a remarkable power of adaptability to a diminution in the supply of oxygen, even though this gas be reduced to half the amount normally present in the atmosphere. Barach has expressed the accommodation-response by stating that a normal person subjected to diminished oxygen supply, such as occurs at high altitudes, will manifest lowering of arterial pressure. If of the sthenic type, he adjusts himself well; if he has a poor respiratory apparatus, he will experience a

more or less severe attack of mountain sickness. Artificial reduction of oxygen supply produces similar effects.

(iii.) Evidence derived from Acclimatisation to High Altitudes.—Loewy [55] holds that effective acclimatisation to high altitudes depends on changes directed against reduction of oxygen pressure by promotion of increased access of oxygen to the tissues. Increase in frequency of pulse and respiration must be considered as the effect of unaccustomed climatic stimulation. Saturation of the blood with oxygen at a relatively slight altitude of 1,550 metres is almost as extensive as in the valley, and does not explain the initial dyspnœa on muscular effort. Above 3,000 metres the alkalinity of the blood is reduced more notably with muscular work, and abnormal acids appear in greater abundance. Signs of acclimatisation recently demonstrated are increase in the total blood volume, especially in regard to hæmoglobin and number of blood cells, anisocytosis and polychromasia as expressions of an increased delivery into the blood of erythrocytes, and increased gaseous metabolism, as well as increased combination of the oxygen with blood pigment. Other signs are increase of the respiratory volume, of oxygen tension in the alveoli, of the circumference of the thorax, and of the vital capacity.

(iv.) Evidence derived from Pathological Processes.—Barach [56] has demonstrated that in acute infections, notably those involving the respiratory tract, there is usually some tendency to cyanosis, most marked in influenza and pneumonia, and present also in enteric fever. The degree of hypopiesis, cyanosis and increase in the respiratory rate are held by him to indicate the amount of respiratory deficit. Hypopiesis also occurs in other acute infections, such as erysipelas and diphtheria, in which a similar mechanism may be invoked. "Oxygen requirement is high in all fevers, irrespective of the type. Oxygen want may be produced by a high rate of expenditure, a lower than normal oxygen intake, or both, and it is probable that oxygen deficit is the result of diminished vital capacity, a diminution of the respiratory surface, and impermeability of a diseased respiratory mucous membrane. One thing stands out clearly, that in acute infections in which hypotension occurs, we

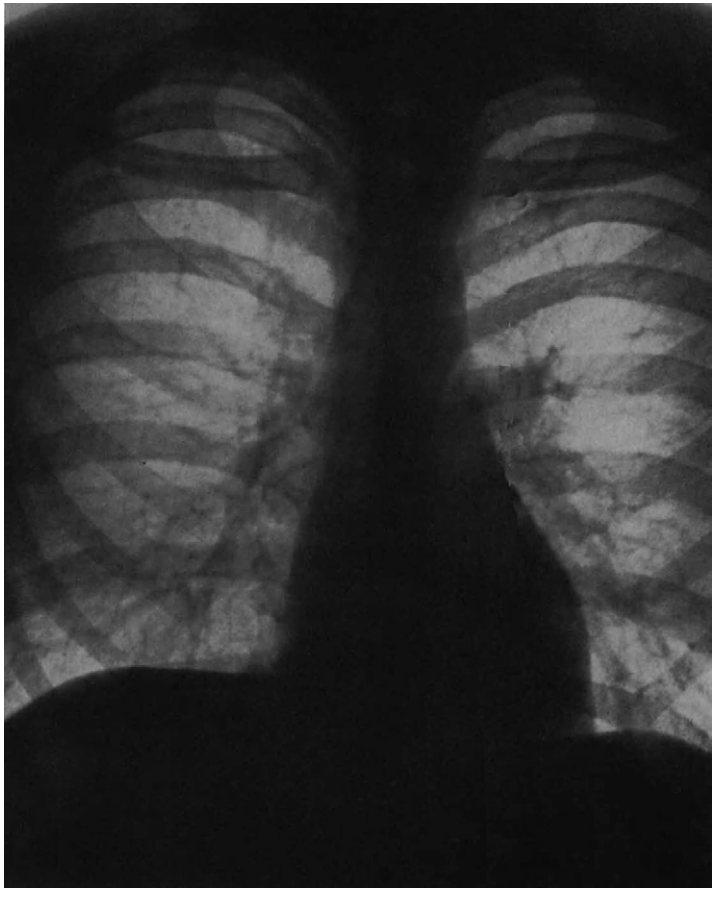


FIG. 6.—The Sthenic Habitus.

find evidences of a respiratory deficit, and, therefore, of oxygen want."

In chronic pulmonary diseases, in certain metabolic disturbances, and in other diseases in which there is an insufficient volume of blood to carry oxygen, as in hæmorrhage and pernicious anæmia, or in which the blood is a poor oxygen carrier, hypopiesis is found as a frequent accompaniment. "All the evidence," says Barach, "points to the deduction that where there is a respiratory deficit and decreased oxidation, there we find low arterial pressures."

The foregoing considerations lead naturally to the further conclusion that the degree of accommodation-response to diminished oxidation, however induced, is in many instances determined by, and varies directly with, particular types of bodily conformation.

2. The Influence of Body Build.—The three main types are the hypersthenic habitus (Fig. 5); the hyposthenic habitus (*Frontispiece*, Fig. 1 and Fig. 8); and the sthenic habitus (Figs. 6 and 7).

The first of these types bears oxygen diminution well, and frequently connotes metabolic excess—the "plus" type. The second, with which the present volume is concerned, bears oxygen diminution ill and frequently connotes metabolic deficiency—the "minus" type; the third varies within fairly wide limits between the two extremes, and represents the "healthy normal" individual with adequately-balanced metabolic processes—the "plus-minus" type.

Although the former two types are not necessarily in a pathological state, yet in most cases their reserve limit is narrower than in those of the third group, which is intermediate.

The physical qualities exemplified by the former two opposite types of humanity affect primarily the mechanism of circulation, and secondarily the mechanism of respiration, and, in turn, are capable of being affected by circulatory and respiratory influences.

In 1908 the author [57] first stated what he has since frequently stressed, that "the clearest idea of the mechanism of respiration is probably gained by regarding man from the

comparative standpoint, and his abdominal and thoracic cavities as together constituting one cœlom ; the diaphragm being considered as a structure subsequently introduced within the body cavity, primarily in order to aid the flow of blood, and secondarily to play its part as a respiratory muscle. On reviewing this aspect we see that the influence of respiration prevails in continuity throughout the body cavity, the whole of the contents being acted upon by the movements of breathing and the regional effects of these being manifested from neck above to perineum below.

" The study of the mechanism of respiration is essentially difficult, inasmuch as fixation of any given portion of the trunk is merely relative. Even the vertebral column, which has been almost universally considered the one portion of the body which is fixed during respiration, although it is more immobile than any other part of the thorax, yet is not a fixed structure, but is subject to variation in position according to the stress of the particular moment. Hence it is not surprising that, throughout many centuries, all kinds of conflicting opinions have been put forward as to the precise movements that occur, and as to the interpretation of their results.

" Further, confusion of thought has resulted from the fact that details of the respiratory mechanism have been considered by themselves without regard to their value in the general economy. Thus it is a matter of experience that, clinically, respiration not infrequently is regarded solely from the thoracic standpoint, whilst the equally important part played by the abdominal muscles is overlooked ; the abdomen being examined merely with reference to the soundness or otherwise of the contained viscera without regard to their movements during the respiratory cycle. . . . Hence the abdominal muscles must be studied equally with those of the thorax, and these, in turn, together with those of the vertebral column. Respiration is not solely a thoracic act ; each time we breathe quietly our abdominal muscles are called into play equally with our thoracic muscles, and in deep respiration this is still more evident." [57]

Let us now apply the foregoing remarks to the three classes to which reference has been made above.

Hypersthenic subjects belong to the athletic class, which manifests general tissue-hypertrophy either of congenital or acquired origin. Such an individual is of large and heavy body build, and presents a short neck, a short and broad chest, with more or less horizontally-directed ribs and wide intercostal spaces; the sternum is broad and short; the epigastric angle is obtuse; the heart is of broad, sessile type, resting on a diaphragm high in position and well arched, thus causing a widening in the transverse diameter of the great vessels at the base of the heart, the aortic hemicircle being observed in radiograms as notably wider than normal; the abdominal wall is slightly concave by reason of good development and tone of the abdominal musculature. In short, the whole picture exhibits preponderance of width over length (Fig. 5).

On biochemical urinary investigation these subjects are in striking contrast to the above-mentioned third class, which comprises healthy individuals with adequately-adjusted metabolic balance—the $\pm$ type (Figs. 6 and 7). In the latter, Dr. Henry Ellis [45] has shown that in the urine the normal ratio of titratable acidity to ammonia-combined acid is between the limits of 1 : 1·5 and 1 : 2. On comparison with these normals the hypersthenic class usually shows a characteristic urinary picture. Hypersthenic subjects, with few exceptions, belong to the " acid " group of Ellis, their acid-alkali ratio being 1 : 1 or less. During youth they are usually healthy, but towards middle life, owing to increasing difficulties in elimination, they tend essentially to diseases such as gout, etc., and to cardio-renal defects, including cerebral hæmorrhage and high arterial pressure. The rise in differential pressure to a figure higher than the healthy standard of 44 mm. is an indication of their need of, and their diminished capacity for, elimination by the kidneys of accumulated waste acid. This class has been fully dealt with in the author's book on " High Blood Pressure," and receives mention here merely for necessary purposes of contrast and comparison.

The Hyposthenic Type of Bodily Configuration.—We are now in a position to review the practical application of the above considerations in reference to the production of one

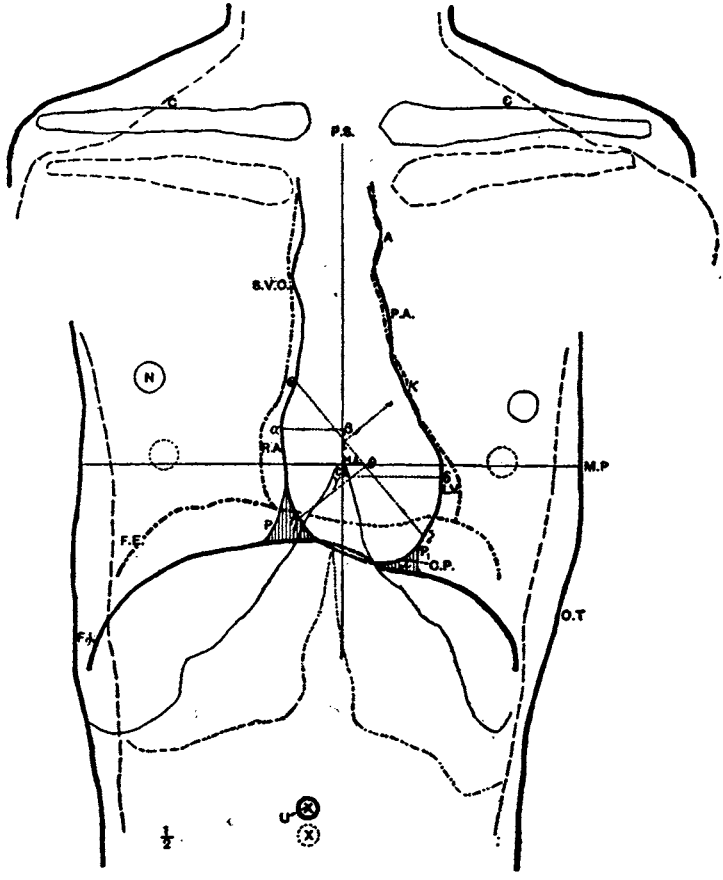


FIG. 7.—Orthodiagram by the author illustrating the Sthenic Habitus. C = mid-clavicular point; P.S. = pre-sternal notch; S.V.C. = superior vena cava; R.A. = right auricle; A = aortic arch and first portion of descending aorta; P.A. = left pulmonary artery; L.V. = left ventricle; P, P_1 = pericardium; $\alpha\beta$ = diameter of right auricle; $\gamma\delta$ = diameter of left ventricle; $\epsilon\zeta$ = longitudinal diameter of heart; $\eta\theta$ and $\iota\kappa$ = diameter of right ventricle; N = nipple; U = umbilicus; F.E. = position of diaphragm in forced expiration; F.I. = same in forced inspiration; M.A. = meso-metasternal articulation; M.P. = meso-metasternal plane; O.T. = outline of trunk; C.A. = infracostal angle; C.P. = cardio-phrenic space.

type of hypopiesia (congenital or constitutional hypopiesis), by contrasting with the hypersthenic and sthenic groups the class of non-athletic subjects of hyposthenic habitus. This represents the outward expression either of a con-

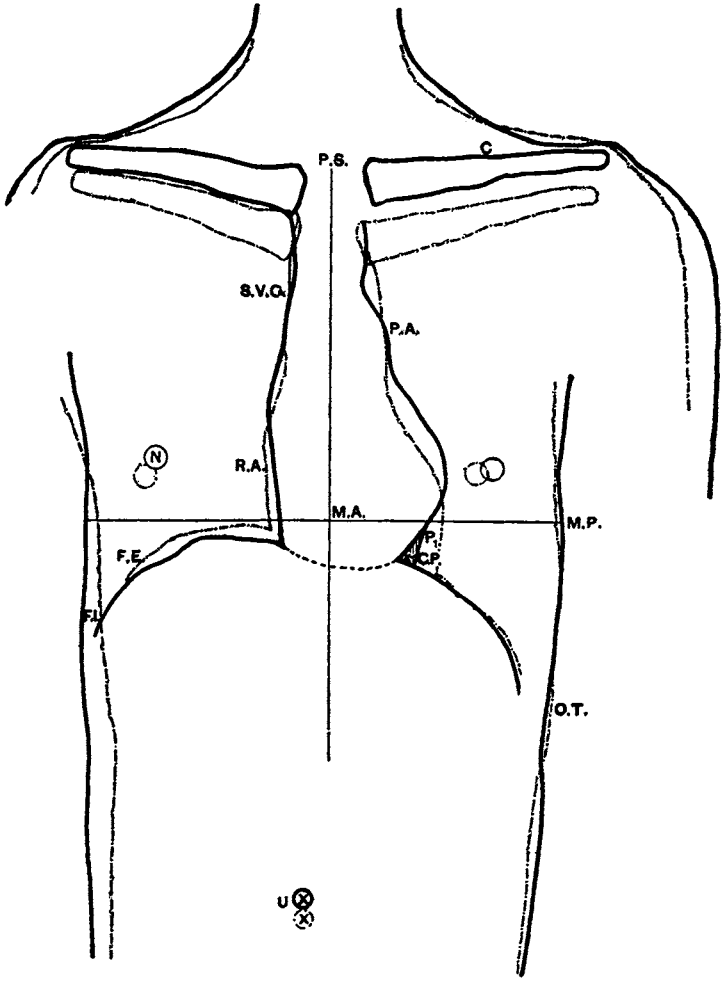


FIG. 8.—Orthodiagram by the author illustrating the Hyposthenic Habitus. C = mid-clavicular point; P.S. = pre-sternal notch; S.V.C. = superior vena cava; R.A. = right auricle; P.A. = left pulmonary artery; P, P_1 = pericardium; N = nipple; U = umbilicus; F.E. = position of diaphragm in forced expiration; F.I. = same in forced inspiration; M.A. = meso-metasternal articulation; M.P. = meso-metasternal plane; O.T. = outline of trunk; C.P. = cardio-phrenic space.

genital lack of development or of a later tissue-atrophy from various degenerative causes. Such a subject is of poor body build, thin and of light weight, presenting narrow nostrils, with frequent nasal obstruction, a long neck, a narrow and elongated chest with sloping ribs and narrow intercostal spaces. The sternum is narrow and long, with an acute and hollow epigastric angle ; the diaphragm is low in position, the heart of narrow " pear-drop " type, the aortic hemicircle thin and narrow, and the ascending aorta narrow and elongated. The lower abdomen protrudes, and is often pendent through laxity of the abdominal musculature ; the thoracolumbar curve is straightened out, or may even become actually convex. In short, the whole picture represents preponderance of length over width (Fig. 8).

To this type of physical configuration corresponds frequently a characteristic biochemical urinary picture. These subjects, as a rule, tend to belong to the " alkaline " group of Ellis, their acid-alkali ratio being 1 : 3 or more, this being associated with errors of assimilation in youth, and with endocrine deficiency in middle and later life. They have tendencies to infection in general, and to pulmonary infections of various types in particular. Their arterial pressures are generally low, the differential pressure being below the standard 44 mm., they have no nocturnal micturition, and fatigue readily.

For an efficient circulatory and respiratory response the whole of the trunk must be supple with good muscular tonus. Decreased chest measurement usually implies decrease in thoracic mobility, which latter is still further lessened by the loss of tone of the abdominal muscles found in the hyposthenic class.

Hence the direct suggestion occurs that one type of hypopiesia results from a mechanical limitation of circulatory and respiratory capacity, congenital or constitutional, resulting from a minus type of bodily configuration, of which the essential features are : (*a*) a small heart, (*b*) a narrowed aortic arch, and (*c*) an elongated and narrowed ascending aorta. Fossier [32] states that the increased resistance to the flow of blood offered by a narrow aortic arch, and to a certain extent by an elongated ascending aorta, will cause a diminu-

tion of 10 to 30 mm. in the systolic pressure. In explanation he invokes the hydraulic principle that the longer the pipe and the smaller the radius of the bend, the smaller will be the final velocity en[illegible]r, in me[illegible]nger the ascending aorta, and the narrower the diameter of the aortic arch, the heart pressure being equal, the lower the systolic pressure. This author, whose observations were made on a group of patients of whom a large proportion were splanchnoptotics, concludes that "essential hypotension is usually found in the asthenics and splanchnoptotics: it is a symptom of splanchnoptosis." Fossier deals, however, only with systolic pressures, which materially limits the value of his observations, and, while it is true that hypopiesia is a fairly constant accompaniment of the gastric type of neurasthenia, more especially when combined with splanchnoptosis, yet in this series, the occurrence of hypopiesia is not invariable, so that it would be wiser to limit its causation to the physical group of hyposthenics above detailed without endeavouring to stretch the association too far by the further inclusion of the splanchnoptotic element. Roberts [28] is of opinion that such individuals are not necessarily neurasthenic, and that, apart from visceroptosis, mild focal infection, hypochlorhydria or secondary anæmia, no active pathological condition can be demonstrated. Out of 350 cases investigated by him, 118 had a systolic reading of 110 mm., or more than 33 per cent.

Information derived from studies of Marathon runners is of particular interest in this regard, and will be found mentioned under the head of "Athletics" on p. 105.

It is by no means true, however, to say that all hypopietics are hyposthenic, for hypopiesia is occasionally met with in those of sthenic habitus, and rarely even in those who are hypersthenic. Thus Larimore's [58] investigation of 417 workers of both sexes showed low arterial pressure to exist in 9·7 per cent. of sthenic and in 68 per cent. of asthenic men, and in 18·8 per cent. of sthenic and 64·5 per cent. of asthenic women. Certain sthenics may be also visceroptotics, but it does not necessarily follow that this latter association is productive of hypopiesia. As for the hypersthenic class, it is distinctly unusual, but nevertheless possible, to find

isolated instances of hypopiesis among its members. So that, whilst one cannot say that essential hypopiesia is limited to any one type of physical configuration, on the basis of clinical experience one may conclude that hypopiesia tends frequently to originate in a physically subnormal group of cases of hyposthenic or asthenic type in association with a lack of respiratory capacity, and that this group derives considerable benefit from properly directed physical and breathing exercises. At the same time, one must repeat that this group by no means constitutes the whole of the series of essential hypopiesia, for a proportion is still left which manifests no physical abnormality.

Riesman [59] claims that essential hypopiesia is found as a permanent feature in persons otherwise in good health, who are subject to colds, have cold hands and feet, a poor circulation, and tend to rapid mental and physical exhaustion. This group has previously been described by Martinet under the label of " hyposphyxia."

Hence, on the above basis, subjects of essential hypopiesia have provisionally been grouped into—

(*a*) Those manifesting no physical abnormality, and capable with benefit of sustained physical and mental exertion.

(*b*) Those with evidence of poor physique and diminished respiratory capacity.

3. Influence of Inefficient Capillary Circulation.—Touching the low systolic and differential pressures found in association with the neuroses, Bain [35] observes that the vasomotor systems of such patients are in an extremely unstable condition. Acidity with flatulence is common, and cold extremities not frequent. " Pressures are liable to fluctuate largely from emotional and other causes. It is, therefore, unlikely that there is any alteration in the total blood volume. The probable explanation is to be found in some deficiency in vascular tone giving rise to inefficient circulation in the capillaries and venous radicles."

How is this lack of vascular tone causing stagnation of blood brought about ? The experiments of McDowall, which Bain adduces in support of the view that most of the above class of patients are vagotonics, show that in the cat in

cases of low venous pressure near the heart following hæmorrhage, or the administration of alcohol, or the injection of histamine, section of the vagus will cause a further reduction in arterial pressure. He considers that under these conditions there is a vago-pressor reflex to prevent excessive lowering of the mean pressure. If in man this reflex occurs in cases where the systolic pressure is low, the result could be obtained by a raising of the diastolic, thus inducing a small differential pressure. Such might particularly apply where vagal influence was already predominant.

An expansion of this view is afforded by the suggestion of Friedländer [49] that inefficient circulation in the capillaries is brought about by their becoming poisoned by autogenous vaso-dilatins. This writer believes that histamins and other vaso-dilatins are constantly produced in the body, and that persistent hypopiesis may be due to poisoning of the capillaries by histamine or histamin-like substances. In support of this assumption, certain evidence has been adduced, but so far it cannot be regarded as conclusive.

McCrae [27] studied 100 consecutive cases of hypopiesis, excluding those due to acute infections, and classified them according to the most marked condition present. He found that nervous disturbances were present in 38 cases, endocrine disturbances in 8, myocarditis in 25, anæmia in 3, whilst 26 were miscellaneous cases of chronic disease, including nephritis, syphilis, aortitis, epilepsy, etc.

The classification adopted, as this writer himself admits, cannot be regarded as other than approximate, and probably a large number of the cases of nervous disturbance should properly belong to the endocrine group.

The lowest average diastolic pressures were found in the endocrine group, the highest in nephritis ; in some of these the difference between the two pressures was small, as for some of the cardiac cases in which the differential pressure was only 10 mm. of mercury. Occasionally the diastolic pressure could not be estimated, since the sounds were inaudible.

As already indicated in the first chapter, the important known physico-mechanical factors which are concerned with variations in blood pressure in general are, first and fore-

most, the peripheral resistance of the smaller blood vessels, next the force and frequency of the heart-beat, and thirdly the quantity and quality of the circulating blood. All of these in turn are capable of being altered by internal and external influences, and decrease in any of these factors tends to produce a lowering of the arterial pressure. Are there any factors more ultimate still, and, if so, what is their nature? Till now the composition of the blood has been thought to be the least important factor of the above three. A broad and sweeping conception has, however, recently been advanced by McDonagh,[60] which, if accepted, would go far towards reducing the problem to its simplest terms.

4. The Influence of Changes in the Composition of the Blood.—McDonagh's conclusions are as follows :—

" 1. The primary cause of both high and low arterial pressures is a change affecting the protein particles in the blood plasma.

" 2. The changes in the vessel walls are secondary thereto.

" 3. The visceral changes are the last to appear."

On this view high and low arterial pressures are interchangeable, and may be either of sudden or of gradual onset, high pressure constituting a dehydrator effect upon the protein particles of the plasma, while low pressure represents either a hydrator or a precipitation effect. Since the two conditions are so readily interchangeable, and since low arterial pressure is stated to be one of the clinical manifestations of the antidotal action of hydrators in dehydrator intoxication, and *vice versâ*, McDonagh believes that the primary cause of the alterations in blood pressure is one affecting the *blood* and not the blood vessels.

The characteristic changes in the blood when the alteration in pressure is of sudden onset, whether induced artificially or not, are divided by him into two classes : (1) when the hypotension is due to hydration, (2) when it is due to precipitation of the protein particles. " In the former there is a fall in the percentages of the blood-sugar, the blood-urea, and the blood-amino nitrogen. The albumin to globulin ratio is raised in favour of the latter. The surface tension is diminished, while the viscosity and the refractive index are raised. The suspension stability of the red blood corpuscles

is unaltered. In the latter there is a marked fall in the constituents of the blood. The coagulation of the blood is retarded. The viscosity and refractive index of the serum collected from the peripheral circulation are remarkably reduced. The protein particles in the plasma do not consist of protein only as is generally thought. They have attached or adsorbed a varying quantity of electricity, salts, carbohydrate, urea, amino acids, etc. . . . The more hydrated the particles become the more stable or resistant they become, although, under certain circumstances, they may become still further hydrated and so be precipitated.

"When high or low arterial pressures have been present for many years the protein particles may undergo changes more characteristic of the state opposite to that represented by the clinical condition.

"In the event of a microbic infection the invader subjects the blood vessels and organs of the host to much the same changes as it does the protein particles in the plasma. The protein particles in the plasma are able to redress most wrongs and to counterbalance the damage wrought. There is a continual effort on their part to strike an equilibrium, a property the cells of the blood vessels and viscera do not possess to the same degree. Consequently, progressive changes may take place in the vessels and viscera while no alteration in the physical state of the protein particles in the plasma can be detected. This seems the most feasible explanation of a severe form of arteriosclerosis with a normal blood pressure. The maximum changes in the blood occur when the alteration of blood pressure is produced suddenly and the minimum when the alteration is of slow and long duration."

This quotation has been made at some length in order fairly to present McDonagh's striking hypothesis. Before such can be accepted, however, as a part of the practical teaching of medicine, confirmation on the part of other workers will be essential.

Martinet [61] claims that in the person whose circulation is normal there exists a close relationship between the differential pressure, an expression of the cardiac load, and the blood viscosity, an expression of the resistance opposed by the blood to the circulation. If this physiological corre-

spondence be not stretched too far, and with certain exceptions depending largely upon body build, weight and height, the author's observations dispose him to agree with these conclusions. Under pathological conditions of the circulation, however, this relation does not obtain. For high and low arterial pressures the author so far has been unable to determine any direct relation between the level of arterial pressure and blood viscosity.

Summary

Various ætiological conjectures and hypotheses have been presented in the form of a discussion, since they are capable for the most part of being co-ordinated with a still broader conception.

At the outset it becomes necessary to clear the ground by dismissing those groupings of different writers which are based solely upon clinical or anatomical conditions in association with which hypopiesis is discoverable, but without any successful result in finding basic factors of co-ordination, thus leading to negative ætiological conceptions.

Physical and psychical efficiency depend on vitality of somatic processes, vitality itself depending on a state of metabolic equilbrium. Any factor or factors which disturb that nicely-adjusted metabolic balance which we term health cause either nutritional or endocrine disequilibrium, or both, which results in disturbance of acid-base tissue balance or hormonic dysfunction. The latter, when conjoined with vasomotor disturbance, leads to variations in arterial pressure from standard limits either in the direction of increase (high arterial pressure) or of decrease (low arterial pressure). In this regard low arterial pressure forms an easier study than high arterial pressure, since the former presents itself in simple and uncomplicated guise without, save in rare instances, those secondary accompaniments of arterial and renal sclerosis whose pathological effects so frequently obscure the picture of a pure hyperpiesis.

If one desires to assess the metabolism of a given individual, information of the highest value is yielded by accurate estimation of arterial pressure together with a complete

biochemical examination of blood and fæces with serial specimens of urine over a 24-hour period.

The biochemical aspect of life is that it consists in a series of reactions to stimuli, mechanical, electro-physical and chemical or infective, of varying proportions and degrees. Inability to respond to stimuli in a normal and effective manner causes symptoms of which low arterial pressure constitutes one of the most important.

By escaping from the narrow boundaries which have hitherto circumscribed the conditions under which low arterial pressure exists, and from a standpoint purposely set on as broad a basis as possible, the author believes that, as stated at the beginning of this chapter, he has succeeded in establishing a unifying and co-ordinating principle which explains in accordance with modern tenets founded on recent advances in medicine those aberrations from standard limits which constitute high and low arterial pressures. This unifying principle has been arrived at by the expansion of Mackenzie's well-known dictum, that "response to effort" is the most valuable test of cardiac efficiency, to cover the whole field of arterial pressure.

The comprehensive view put forward by the author is, therefore, that **low arterial pressure, whether congenital or acquired, temporary or permanent, is an expression of low vitality.**

CHAPTER IV

Symptoms and Signs of Low Arterial Pressure

Hypopiesis may be encountered under extremely variable conditions. Hence it is easy to understand that to its incidence have been assigned the most diverse causes. The clinical manifestations of hypopiesis are of widely extended range, ranging as they do, on the one hand, from the slightest functional disorders, such as cyanosis, small and weak pulse, delayed reactions, digestive upsets, mild asthenias, etc., to striking and dramatic events on the other hand of the nature of convulsions, syncope, cold sweats, diarrhœa and profound asthenia.

Perhaps the simplest way of approaching the symptomatology of hypopiesis is first to detail the symptoms and signs of most frequent occurrence which may be regarded as characteristic of this condition, and next to differentiate hypopiesis which is acquired from that which is constitutional.

1. Subjective Symptoms.—*The characteristic subjective symptoms* of low arterial pressure in order of frequency are as follows :—

1. Lassitude } physical or mental, or both com-
2. Ready fatigability } bined.
3. Headache.
4. Defective memory and concentration.
5. Insomnia.
6. Giddiness.
7. Faintness up to convulsions and syncope.
8. Palpitation and anginiform pain on excessive exertion.
9. Gastro-intestinal disturbances.
10. Neuralgic pains.

Let us now deal with these symptoms in greater detail :—

Lassitude and Ready Fatigability.—Easily induced physical and mental fatigue constitutes the dominant symptom of all forms of hypopiesis. It is the one constant symptom of which all low pressure patients complain. To this rule the author up to the present has found no exception.

On the physical side these patients wake in the morning with frequent feelings of lassitude; during the day they prefer to sit or to lie rather than to stand; on slight physical effort or a minimal amount of extra exertion they experience fatigue; they become breathless on going upstairs, or on climbing hills, as well as on rapid movement, while attempts at more strenuous exercise will still further depress their already low vitality and their low arterial pressures, causing them to remain for several hours or even for days in a condition varying from the milder degrees of lassitude to that of utter prostration.

On the mental side there are vague feelings of anxiety or apprehension, and incapacity for more than a slight amount of concentrated thought unless the whole of the will-power can by a special effort be brought into play and steadily exercised. It is with the greatest difficulty that these patients can fix their attention upon their work. Mental functioning is slow, with pauses to collect thoughts. Memory is impaired, and may vary from "patchiness" and frequent lapses up to a point at which the subject becomes mentally defective. Often there is considerable depression, especially in the morning, increased if insomnia be also present.

It is necessary here to repeat that large numbers of these subjects are capable of strenuous efforts, both of body and mind, and that such efforts may be maintained and persisted in owing to strength of will-power even over considerable periods of time. Nevertheless, sooner or later a point, varying with individual capacity, is reached at which a breakdown of the supporting mechanism takes place. As soon as the limits of reserve energy are overstepped, direct warnings in the shape of single or combined symptoms make their appearance, and the subject "flops." Efforts sustained to just within the limits of reserve energy over long periods make such demands upon the already slight vitality of these individuals that they usually break down utterly, especially at the time of middle age or in later life, when the increasing limitations set by Nature are superadded, and are often astonished at finding the bill of costs, presented as a sudden collapse, an acute infection, or an anxiety state

sometimes terminating in a confirmed neurasthenia, far heavier than they expected to pay.

The symptoms above described represent those of a typical well-marked case, and the slighter degrees of hypopiesis in the " apparently healthy," and in those who have reacted satisfactorily to treatment, do not exhibit the same extreme picture of lowered vitality. In the lesser degrees of hypopiesis moderate or even hard mental or physical exertion may be salutary and beneficial within the limits of the individual reserve energy.

Insomnia.—This distressing symptom varies considerably in intensity in different low pressure individuals. The form of insomnia most frequently met with is that which occurs in the early morning, the patient getting off to sleep without much difficulty, but becoming wakeful from about 2 a.m. onwards, with snatches of broken sleep, from which he wakes weary and unrefreshed. This mode of insomnia is more characteristic of the hypopietic states than is the inability to sleep from the beginning of the night.

Headache.—Headache is a symptom common to so many different affections that its diagnostic value thus tends to become impaired. At times, nevertheless, headache assumes such well-defined clinical manifestations as to allow its origin to be traced and a place to be assigned to it as a part of the syndrome of the malady.

Such a type of headache is frequently associated with low-pressure states, the following description being based on Martinet's observations.[61]

Low arterial pressure headaches are often met with in women and possess two subjective features : (*a*) localisation, (*b*) alteration in intensity with change of posture.

(*a*) *Localisation.*—In onset the cephalalgia is usually occipital, and in this situation occurs the dominant sensation of pain which patients compare to continuous pressure as of a leaden weight or a feeling of almost intolerable constriction ; if the headache spreads laterally to the parietal regions, this is only a secondary effect.

(*b*) *Alteration in Intensity.*—The pain is dull and continuous, with definite paroxysmal exacerbations in the recumbent posture. In the vertical position it abates or

disappears. It is often worst in the early morning on waking. In certain patients an exhausting insomnia is induced, which is relieved by the assumption of the recumbent prone position, whilst others can only obtain sleep by sitting up.

"One is necessarily led to believe that one is in the presence of a cephalalgia brought about by venous stasis of meningo-encephalic type at the level of the straight and lateral sinuses and their effluents."

Systematic examination of the cardio-vascular system in the subjects of this type of headache reveals a profound vascular hypotension with a correspondingly diminished cardiac impulse. The cardio-vascular system, as a whole, is feeble, and they exhibit smallness of heart, aorta and other arteries. The maximal pressure is from 115 to 95 mm. Hg, and may even be as low as 85 mm. The minimal pressure varies from 85 to 70 mm. Hg. These figures connote a small and ineffective differential pressure of 30 to 25 mm. Venous stasis, and even œdema of the lower limbs in the vertical position, are not infrequent concomitants.

Apart from this recumbent type of headache due to venous congestion, there is a more usual form induced by change of posture. This occurs on sudden rising from recumbency or on stooping, and may last from a few minutes to some hours. It results from failure of vasomotor adaptation of the circulation, and may be accompained by giddiness which is sometimes severe. A further variety is met with resembling the neuralgic type of migraine, which at times may be of throbbing character. Headache is also associated with certain forms of heart disease, especially when compensation fails, and with weak cardiac action in anæmic states.

Giddiness.—Giddiness is a symptom of low pressure states just as it is in high pressure states, but from opposite causes. In the former the cerebral vessels are too empty, in the latter they are too full. Giddiness, sometimes in conjunction with a feeling of lightness in the head, often accompanies headache, although it may appear independently and, like headache, is particularly common in women. In some persons giddiness is present in association with lassitude as one of the earliest symptoms of a fall in

pressure below the normal level for the individual. The hypochondriac and neurotic types are especially prone to manifest this disturbance, which is also common in anæmic states, convalescence after prolonged illness, and Addison's disease. Under these conditions malnutrition of the central nuclei may be invoked as a cause. A toxic form occurs in chronic intoxications, particularly from alcohol and tobacco.

Faintness, up to Convulsions and Syncope.—These symptoms occur in all degrees either from circulatory or nervous causes, though the former are the more common in association with functional or organic circulatory defects. An encephalic anæmia is thereby produced coincidently with a sharp fall in arterial pressure owing to cutaneous and splanchnic vaso-dilatation. Fainting should, therefore, not be regarded as arising from a primary failure of the heart's action.

Gastro-intestinal Disturbances.—Some hypopietics are prone to sensations of epigastric discomfort, which they describe as a feeling of hollowness or emptiness referred to the pit of the stomach, and to hunger nausea. Both these symptoms are relieved by taking food or by heavy pressure over the epigastrium, as by bending over the back of a chair, but chiefly by lying down. This postural effect can be enhanced by combined heat and pressure in the form of a hot-water bottle applied to the upper abdomen while recumbent.

In other subjects congestion of the liver is not infrequent, at times associated with biliary lithiasis or with varicose veins of the rectum or of the lower limbs as the result of an accompanying venous stasis.

Gastro-intestinal disturbances of other types, such as constipation and diarrhœa, may be combined with depression and insomnia as a part of the picture of a particular type of neurasthenia (p. 135), but do not form part of the ordinary low pressure state.

2. Physical Signs.—*The physical signs* found in frequent association with low arterial pressures are :—

1. Pallor of skin and conjunctivæ, with at times an earthy tint of complexion.
2. Pulse small, soft and frequently dicrotic.

3. Circulatory vasomotor disorders, evidenced by cold and cyanosed extremities with tendencies to chilblains and varices.
4. Delayed return of capillary flow to an area of skin rendered pale by pressure.
5. Diminished ratio of titratable free to combined acid in the urine.
6. Muscular debility and flabbiness.

Hypopiesis is a constant symptom of the "depressor" absorption type of chronic intestinal stasis and resultant toxæmia, and mounts to more standard levels as the result of a course of detoxicating treatment. As regards sensations of general well-being, some few hypopietics say that they feel better when constipated!

The Symptomatology of (*a*) **Acquired Hypopiesis** in conjunction with or consequent upon the various infections, cachexias, toxæmias, endocrine and biochemical disturbances of metabolism, etc., dealt with in the following chapters, presents characteristics so diverse and variable that it is difficult and well-nigh impossible to formulate an inclusive syndrome. It is still open to argument whether such symptoms are dependent upon hypopiesis itself, or whether hypopiesis results from depression of the bodily and mental functions, or whether both are alike due to the operation of some common factor. On the basis of endocrine imbalance one may hazard the supposition that in many instances adrenal depletion constitutes an important cause of acquired hypopiesis and its attendant symptoms, but here again clinical differentiation of symptoms due to dysfunction of one member of the endocrine series from those due to dysfunction or compensatory overaction of other members of the same series is by no means easy. Timmé [62] describes a pluriglandular syndrome characterised by intratemporal headache, ready fatigability, low arterial pressure, low blood sugar content, abnormalities of skeletal growth, and gonadic deficiencies.

(*b*) **Constitutional Hypopiesis (Hypopiesia)** is of two types, the former occurring in the apparently healthy without physical abnormality, the latter in those who are healthy up to a point in association with the physical abnormalities

previously noted. In these latter subjects the balance of metabolism is easily upset and takes time to recover. In childhood they are often lethargic and flabby, with a tendency to put on excess weight; sometimes of stocky build with large bones and muscles, and their limitation of exercise capacity leads to deposits of fat; their movements are slow and deliberate. In adolescence and early adult life they are capable of stationary exercises, and can often lift heavy weights, but are unable to undergo physical exertion which entails rapid or vigorous movement for more than a brief space of time, and for this reason also after middle age not infrequently tend to put on weight. Continuous exertion easily induces weakness and fatigue, and when such is attempted, *e.g.*, playing two sets of lawn tennis consecutively, the arterial pressure becomes further lowered by a few millimetres, thus producing at first discomfort, then lassitude and, if exercise is prolonged, finally general malaise with headache, prostration and sensations of nausea even up to actual vomiting and diarrhœa. Similarly a bad Channel crossing will depress the arterial pressure to uncomfortable levels.

In general there is incapacity for more than the slightest forms of exercise, with tendency to fainting and headache on attempting it. These individuals gravitate towards the armchair or couch and are quite content to do nothing for long periods together. They are difficult to awaken in the morning, and start the day badly. For many hours during the day, however, they are capable of rousing themselves in response to necessary activities, but at night are often glad to seek their bed.

On the mental side they are usually alert and active so long as their pressures maintain the individual standard levels, and are capable of sustained mental effort often of high quality, at times amounting to brilliancy, but as soon as for any reason arterial pressures, particularly the diastolic, sink below the level of comfort, their mental processes become dull, they are unable to concentrate, and when headache becomes persistent, even to think. At these times their utmost mental effort consists in skimming through the lightest of ephemeral literature, *Punch*

or a light novel being acceptable, but the *Spectator* or *Contemporary Review* being banned. The most severe forms are met with where the diastolic pressure becomes considerably lowered, since of the two pressures, as the author has so frequently indicated, the diastolic is by far the more important. Should the depression involve mainly the systolic pressure, the diastolic element undergoing little or no decline, subjective symptoms of discomfort in the lesser degrees may be absent, and in the greater degrees tend in any event to be less pronounced than in the true diastolic form of hypopiesia.

In hypopiesia the line of demarcation on the pressure scale between the zone of no symptoms and of symptoms is a narrow one. As soon as this level is reached, a difference of even two or three millimetres' lowering of pressure is associated with the onset of symptoms.

One case of the " apparently healthy " type of congenital hypopiesis may, perhaps, be quoted here as affording an illustration of the author's Law of Hypopiesis. It is that of a busy man of affairs, possessed of restless energy, who has achieved more during his sixty years of life than the majority of people are able to accomplish, and has been generally most successful in the affairs of life.

As a youth he was neurasthenic and inclined to morbid introspection. At the age of twelve he contracted yellow fever. In adolescence, he discovered for himself that gymnastics and hard physical exercise were absolutely essential to his well-being. For fifteen years he worked at very high pressure, and the higher the pressure at which he worked, the better he felt. At the age of twenty-five he nearly died from a severe attack of enteric fever. As he became more prosperous he found that the slightest slackening in the amount of work caused depression and irritability, and that the lack of sunshine during the English winter brought on feelings of low physical and mental vitality. These he was able successfully to overcome by frequent journeys to warmer climates and sunshine abroad. At the age of forty he had paratyphoid fever. On retiring from the conduct of affairs at the age of fifty he suffered acutely from more than usual depression and boredom. At sixty,

his present age, the complete arterial pressure picture runs as follows :—

$$\frac{115}{70} : 45 : 68.$$

Biochemically, as might be expected, his acid-base balance deviates to the side of alkalinity.

The case is an instructive one in that it demonstrates that the three essentials required to keep this individual in a balanced state of physical and psychical fitness are, (1) hard work, or (2) hard exercise, and (3) sunshine. If he is unable to get two out of these three requisites, he rapidly becomes miserable and weak. Had he been in a less fortunate position as a clerk, for example, confined to business premises for long hours, diving underground for his midday meal, and going to and from his daily work in semi-darkness or fog a considerable portion of the year, working perhaps in artificial light for the greater part of the day and rarely beholding the light of the sun, he would have remained continuously at low levels of arterial pressure, and would probably have succumbed to some infection at an early age.

Moreover, this case is one of many that could be adduced as an illustration of the author's contention that the subject of hypopiesis is never a normal person, and as proving once again the Biological Law of Hypopiesis, which is, that hypopiesis is always to be regarded as an expression of low vitality.

From time to time familial forms of hypopiesia are encountered, the condition being one of lack of cardio-vascular tone involving several members of the same family, often in association with slow pulse rates, and spreading over two or more generations.

CHAPTER V

Autonomic-Endocrine Aspects of Low Arterial Pressure

1. The Influence of the Autonomic (Vegetative) Nervous System on Low Arterial Pressure.—The autonomic or vegetative nervous system consists of two systems, parasympathetic (cranio-sacral) and sympathetic.

The *parasympathetic or extended vagus system* comprises fibres traversing the greater part of the vagus, and also, to a lesser degree, the third, seventh, ninth and eleventh cranial nerves (cranial portion), with other fibres which emerge from the cord in the trunks of the second, third and fourth spinal nervous (sacral portion) and three ganglia in the cervical region, superior, middle and inferior. These, together, form a complex reflex arc, not yet fully worked out, which probably comes into play when reactions of the organism to its external environment take place. Purely vegetative reflexes, however, probably take place by simpler "axon" reflexes through the intermediary of vegetative ganglia situate not in the spinal cord, but in or near the internal viscus concerned.

The sympathetic system consists of a chain of ganglia extending along each side of the vertical column from the first thoracic to the fourth or fifth lumbar vertebra. Certain preganglionic medullated axon fibres (white rami) terminate by synapsis in a ganglion of the sympathetic chain, from which non-medullated axon fibres (grey rami) pass back to the spinal nerve trunk to continue their course to be distributed over the surface of the body. Other preganglionic fibres pass *vid* the sympathetic chain to a synapse in outlying ganglia, whence post-ganglionic fibres pass to the involuntary internal viscera, blood vessels and glands.

Relation of the Autonomic to the Endocrine System.—The

relation of these two great divisions to the endocrine system has been thus summarised by Dr. Langdon Brown [63]:—

"**1. Parasympathetic or Extended Vagus.**—This is anabolic, storing potential energy. It therefore co-operates with the digestive system, which obtains energy for the body from the food, and diminishes the amount of sugar in the blood, storing it in the tissues. The cell-islets of the pancreas and the parathyroids are clearly anabolic in function, and direct vagus control over the former has been proved.

"**2. Sympathetic.**—This is katabolic, producing kinetic energy. It co-operates with the adrenals, thyroid and pituitary. It also raises the amount of sugar in the blood to provide energy for defence against (*a*) the external foe by flight or fight; (*b*) the internal foe of bacterial invasion by pyrexia. . . . Activation for emotional response belongs to the sympathetic group. We find that the gonads chiefly co-operate with this group, as might be expected from the large part sex plays in emotional life."

The action of the sympathetic system is not so distinctly localised as that of the parasympathetic, but allows of diffuse stimulation over large areas. Each system possesses excitatory and inhibitory fibres, which tend to a balanced action for each system of one kind. The vegetative end organs are supplied with excitatory and inhibitory fibres from parasympathetic and sympathetic systems alike, which results in a fine balance of functional control.

Experimental evidence strongly suggests that under normal circumstances a condition of individual and varying tonic equilibrium is maintained as the result of continuous stimuli brought to bear upon both parasympathetic and sympathetic systems. "It is quite possible that in the central nervous system there exists some common centre which controls the antagonistic actions of these two systems. It is clear that a disturbance of the antagonistic control may cause a stronger or weaker irritability, or an increased or decreased tonus in one of the two systems, which may become the basis for the development of a pathological condition."

By reason of its close relationships with the glands of internal secretion, the autonomic nervous system has a

marked influence, not only upon the thyroid gland and pancreas, but also upon the entire metabolic mechanism.

The parasympathetic and sympathetic systems are physiologically antagonistic, and upon a pharmacological basis Eppinger and Hess [64] have described two *clinically* distinct types. These are vagotonia, in which parasympathetic action prevails, and sympatheticotonia, in which the sympathetic system exerts the dominant influence.

Vagotonia is a clinical concept, and may be taken to include "all those constitutional conditions in which, in addition to the manifestations of a functionally increased vagus tone and increased irritability in the anatomical system, there also exist increased sensitiveness to pilocarpin and a relative decrease of reactivity to sympathetic stimuli."

Vagotonia is met with more frequently up to the middle period of life than later, and is evidenced by contracted pupils, which under atropine do not readily dilate, wide palpebral fissure, lachrymation, salivation, slow and powerful heart-beat with irregular pulse, low arterial pressure, eosinophilia, hyperacidity, either sweating and diarrhœa or colic and constipation according to the intensity of the stimulus, increased secretion and motility of the intestine, with tendency to spasm of the œsophagus, pylorus, gall-bladder and bronchi.

Arterial pressure is only secondarily under the influence of vagal impulses, although peripheral vasodilatation as well as slowing and weakening of the heart-beat may cause a reduction in arterial pressure.

Sympatheticotonia forms an opposite clinical picture to vagotonia, and is manifested by large pupils, hypochlorhydria, lessened secretion and motility up to atony of the intestine, augmented heart rate and heightened arterial pressure.

Vagotonic Syncope.—Sir William Gowers [65] described fainting attacks in patients who presented no signs of structural disease, and in whom attacks of faintness were associated with symptoms which he ascribed to overaction of the vagus nerves upon the heart, causing inhibition. Other observations have been published by Sir Thomas Lewis,[66] which implicate the vagus or its centre as a cause

of syncope. Laslett [67] records the case of a female with no apparent structural disease, who manifested frequent standstill of the heart of four to eight seconds' duration, associated with syncope and hypopiesis. The responsibility of the vagus was proved, for atropine prevented recurrence of the attacks.

In certain emotional subjects under slight surgical intervention the pressure falls rapidly at the same time as the pulse becomes slowed, thus inducing a more or less lasting syncope, *e.g.*, in lumbar puncture. Several of these syncopes have been observed by Lewis and Cotton [68] in young soldiers with "irritable heart," and these observers have been able to measure arterial pressure at the moment when the radial pulsations reappeared. Reduction of heart rate and force in these soldiers was almost invariable, together with a fall in systolic pressure at times considerable, often to 60 or 70 mm. of mercury (Riva Rocci), in subjects whose habitual pressure was 120 to 130 mm. Below the lower ranges of 60 mm. or so readings were usually unobtainable, and the pulse rate was weak or imperceptible. Association of lowered rate and force of heart-beat points decisively to disturbance of the inhibitory mechanism. The frequent combination of gastric symptoms, nausea, and more rarely vomiting, along with the cardiac disturbance, accords with this conclusion. Cardiac slowing and reduction of pressure in such cases could only be ascribed to the same nervous action.

2. Influence of the Endocrine System on Low Arterial Pressure.—Although the several endocrine glands occupy positions widely separated in the body without visible connections, they constitute a system, each member of which has one or more functions and contributes to the maintenance of a complex inter-relationship and interaction. Not only is there organic and functional harmony between these glands, but compensatory mechanisms also come into play. If excess or deficiency of hormone products occur as the result of disease or impaired function of any gland, there ensues a lack of balance in internal secretions due not only to abnormality of function in the gland affected, but also to the effects of uncontrolled antagonistic secretion.

Endocrine Insu ciency.—The endocrine system exercises a potent and far-reaching influence upon physical and psychical processes alike. These glands form internal secretions, called hormones, which are active chemical substances manifesting characteristic effects either by katalytic or anabolic action upon cellular metabolism.

Such effects are of two kinds: (1) a direct action upon the cell which may be either (*a*) general, as in the case of the thyroid hormone which activates and regulates the other endocrines, or (*b*) specific, upon certain cell groups, as in the cases of most of the other hormones; (2) through the intervention of the autonomic nervous system.

With the vegetative (autonomic) nervous system as a whole, the endocrine glandular system has wide interactions. The endocrine glands are themselves vegetative organs, with a vegetative nerve supply and with central projection fields. Hence the functions of these glands are largely regulated by the nervous system. In their turn the endocrines influence the excitability of the vegetative nervous system by secretion of hormones which they pour into the circulation.

(i.) *Thyroid Insufficiency.*—It is outside the scope of this volume deeply to enter into the manifold and various interrelationships and antagonisms of the endocrine glands. Suffice it for our purpose to say that of all the endocrines the thyroid has the widest scope, since it elaborates at least one hormone which exerts the most profound katalytic effects upon general metabolism. It is indispensable for normal growth and metabolism; it acts also as a detoxicant, and especially in combination with the adrenal and gonadal hormones exercises a controlling influence. "At puberty an increase of vegetative functions sets in; it is attended with the enormous development of the glands of generation, stronger in woman than in man; often inco-ordinated, giving rise to various disturbances. In especially disposed females the revolutions in the organism at this time lead to an exhaustion which seems to stand in relation with the development of chlorosis. . . . At the climacteric there occurs lability of the vegetative nervous system, especially of the vasomotors, a sort of vasomotor ataxia, which disappears with the complete loss of ovulation." [69] Thyroxin, one of the two known

hormones of the thyroid gland, affects arterial pressure, pulse rate and metabolism, and in hypothyroidic states deficiencies of this hormone produce the well-known characteristic effects.

The bulk of evidence, both experimental and clinical, goes to show that certain types of endocrine insufficiency are closely allied with the production of low arterial pressure. Perhaps the best example of a pluriglandular syndrome is seen in the two diseases in which thyroid insufficiency predominates. The evidences of hypothyroidism are, broadly speaking, cretinism in the young and myxœdema in the adult, both states involving structural degeneration of the thyroid gland. The degree of slowing of all vital processes and diminution of excitability of the vegetative nervous system depends upon the amount of structural degenerative changes in the thyroid glandular tissue. Along with a lowered basal metabolic rate, lowered arterial pressure plays an integral part in association with vasomotor derangement. The pulse is usually small and slow, asthenia and fatigue are the rule, and arteriosclerosis may also be an indication of subthyroid function.

(ii.) *Adrenal Insufficiency.*—In order to appreciate the relationship of low arterial pressure to states of adrenal insufficiency, one must first pass in review the anatomical structure of the adrenal glands, which essentially consist of medullary and cortical portions, and next deal with their function.

Ontogenetically the medulla is developed along with the sympathetic nervous system, which is itself a part of the chromaffin system, and throughout life remains in the closest association with it, the cortex being an epithelial structure developed from the Wolffian body, and forming nine-tenths of the whole gland.

"Preganglionic sympathetic fibres end in the adrenal gland, whose medullary cells *are* the sympathetic ganglion cells, and we have here an interesting example of a nervous structure assuming secretory properties. It is of striking interest to find, as Langley showed, that their secretion, adrenalin, has the same effect on any part as stimulation of the sympathetic nerves to that part." [63]

The chromaffin system includes the adrenal medulla, the carotid and coccygeal glands, and the sympathetic ganglia. It is termed " chromaffin " for the reason that the chrome reaction, as well as other reactions for these tissues, is based on reduction of chromic acid to chromium dioxide by the agency of adrenalin.

The secretion of adrenalin is thus not limited to the adrenal medulla, but is shared by other islets of chromaffin sympathetic tissue scattered throughout the body.[70] This salient fact gives the clue to the discrepancies noted by numerous observers between the extent of pathological changes in the adrenal glands and the clinical manifestations of adrenalin deficiency which has given rise to so much controversy, and for which previously no satisfactory explanation was forthcoming.

Goldzieher [71] notes that healthy human adrenal glands together contain approximately 4 mg. adrenalin, which he found increased to 5·8 mg. in high arterial pressure states, and decreased to an average of 1·5 mg. in septic conditions with low arterial pressure. T. R. Elliott [72] states that the weight of a single normal gland in man is 4 gm., and its adrenalin content 4 mg., and that in many diseases the adrenalin load is diminished, but not often to what might be looked upon as a serious state of depletion. The greatest exhaustion observed by this author to occur rapidly was not in fevers, but in cases of acute cardiac failure associated with great mental distress in which the patient was, so to speak, fighting for his life and struggling to keep up his heart. In these the adrenalin load was less than 0·05 mg. Lucksch [73] finds a normal adrenalin load for each gland of 4 mg., and that this figure is lowered in infections and burns, and increased in nephritis. With inanition the size of the adrenals increases, whilst the adrenalin content falls. The latter phenomenon has also been noted in diabetes and narcosis.

Bru [74] injected adrenal cortical tissue and medullary tissue of the dog intraperitoneally into rabbits. He then injected the serum of these rabbits intravenously into dogs. The effects appeared in four to five minutes, and lasted for over ten minutes. Injection of 10 c.c. anticortex serum

caused a lowering of arterial pressure, whilst the same quantity of antimedullary serum caused a rise.

From the above-mentioned cells of chromaffin sympathetic tissue in the medulla and elsewhere, adrenalin flows continuously into the blood stream and thus exerts an increasing influence upon the adjacent sympathetic system. Probably a similar state occurs in the autonomic system, and it may be that an " autonomin " analagous to adrenalin exists. In fact, recently Santenoise [75] claims to have proved that this autonomin originates in the internal secretory portion of the pancreas.

Diminished secretion on the part of the adrenal glands tends to bring about reduction in arterial pressure. This is seen in Addison's disease, for example, where the glands cannot function to their full capacity by reason of their diseased condition. When the supply of adrenalin becomes exhausted, arterial pressure may sink to very low levels. Apart from Addison's disease, hypo-adrenia may take place in the presence or in the absence of pathological changes in the adrenal glands. In the latter event it is often due to prolonged mental or physical overstrain, the symptoms in the functional form differing from those in the organic form only in degree. Such manifestations are often ascribed to neurasthenia or anæmia when the primary cause has not been sought. Similarly, like changes may occur at the climacteric, when the arterial pressure may be either lowered or raised.

Sajous [76] claims thermogenesis as the fundamental function of the adrenal medulla and cortex.

The medullary portion of the gland is stated by him to act essentially as a respiratory katalyst, its *rôle* being to secrete adrenoxin, a reducing pro-ferment, which, on reaching the pulmonary alveoli, takes up oxygen from the air and so becomes the oxidising enzyme adrenoxidase. As such, and as a component of corpuscular hæmoglobin, it converts the latter into oxyhæmoglobin, and thus takes part in general metabolism.

The adrenal cortex, on this view, sustains tissue respiration by supplying lecithin-phosphorus to all the tissues, whereby the oxygenisation of adrenoxidase is carried out.

Lecithin and cholesterol, like oxygen, are found in all the tissues, and those which are richest in phosphorus, the dominant element in lecithin, are always most active functionally.

The cortex is enormous in the fœtus and in the first months of life. At this time it contains lecithin and no cholesterol. Both these substances are, however, necessary for thermogenesis and growth alike. Thus the giant growth of tadpoles, obtained by feeding with thymus, is explained by the great nuclein (rich in lecithin) content of this gland.

Upon the red corpuscles cholesterol acts antagonistically to lecithin as an antihæmolytic (phospholipoids, including lecithin, render red cells vulnerable to hæmolytic venoms, while cholesterol protects them).

Thermogenesis is then a product of the heat energy liberated by the oxidising action of adrenoxidase on the phosphorus of lecithin, fever being the expression of increased adrenoxidase-lecithin reaction, the purpose of which is to augment the proteolytic activity of the cellular trypsin, to enable it to destroy by hydrolysis bacteria and other toxins, toxic wastes, etc. When this defensive process becomes over-active, even the red cells tend to become digested and undergo hæmolysis. In this case cholesterol moderates the thermogenic activity of lecithin by acting as an anti-hæmolytic and anti-autolytic. Cholesterol is, therefore, a systemic anti-thermic.

Sajous further draws attention to the enormous volume of blood passing through the adrenal glands. Six times the weight in blood of these organs passes through them each minute. Thirteen pounds (6,500 gm.) of blood—the average content of the human body—course through them every two hours. The three products, lecithin, cholesterol and adrenoxidin, synthesised by the adrenals, are appropriated by the circulating red cells, and, after passing through the lungs wherein their adrenoxidin takes up oxygen, proceed to the tissue cells.

The secretion of the thyroid gland is the antagonist of cholesterol in thermogenesis; it increases the lability or sensitiveness of the lecithin-phosphorus to oxidation, thereby enhancing thermogenesis.

From the above it will be apparent how intimate is the relationship between diminution or exhaustion of the internal secretions of the adrenal glands and hypopiesis.

The chromaffin system in a state of adrenalin depletion is a powerful factor in bringing about a temporary or permanent reduction in arterial pressure, and, if one accepts the above-outlined views of Sajous, one will have no difficulty in reconciling these with the opinions of those writers who invoke respiratory deficiency and suboxidation as a part of the ætiological picture. Nor is it difficult to see how diminution of cortical products may share with pituitary or other hormonic deficiencies in causing defective growth, and thus the mechanical factors of small and narrowed thorax, aorta and heart be added.

With reference to the secretion of adrenalin, many workers, especially of the French school, hold that infections depress, or may even abolish, the secretory activities of the chromaffin system, in which the adrenals are included, and in this way may induce a fatal issue.

(iii.) *Pituitary Insufficiency.*—Pituitary insufficiency tends to circulatory sluggishness and venous stasis. Failure of general bodily nutrition and mental and physical deterioration constitute the end-results. The secretions of the body become diminished, together with lessened efficiency of the hæmopoietic system, while gastro-intestinal disturbances form the natural sequence to diminished secretion on the part of the digestive glands. All these conditions are frequently exemplified in pale, asthenic and flabby subjects, who manifest the pituitary type of distribution of excess adipose tissue.

"Hyposphyxia."—For the sake of completeness one is bound to include a circulatory syndrome described by Martinet [77] under the name of "hyposphyxia," as representing the convenient but vague term "poor circulation," characterised by low arterial pressure, a feeble pulse, cyanosis, lividity, proneness to venous congestions, and sensitiveness to cold, in combination with speedy fatigue and constipation.

Martinet regarded his "hyposphyxic syndrome" as consisting essentially of two main elements: (1) low arterial

pressure ; (2) increase in blood viscosity relatively to the level of arterial pressure.

Absolutely or relatively low arterial and differential pressures combined with a relatively high blood viscosity were together taken by this writer to constitute the hypo-sphyxic syndrome " in almost constant association with pluriglandular insufficiency, of which it is a dominant feature, and upon which it depends."

Although Martinet devoted a whole volume to a detailed consideration of this concept, in the light of more recent investigations it cannot be said to possess any real or lasting value. No constant relation has been proved to exist between hypopiesis and increased blood viscosity, and pluriglandular insufficiency of varying kinds and degrees can be invoked in all instances of hypopiesis, so that there is no apparent justification for singling out a certain group. Moreover, this syndrome is of such wide and diverse sympto-matology and association as to include practically all known forms of hypopiesis and circulatory disturbance, and, on careful analysis, one cannot but regard it as having been founded on a basis of erroneous premises. Similar wide groupings of association are found in Lane's chronic intestinal stasis and in Mackenzie's " X-disease," and it is possible that one and the same condition has been independently described under three different names.

CHAPTER VI

Circulatory Factors in Production of Low Blood Pressure

The circulatory factors concerned in the production of low blood pressure are as follows :—

I. The Heart.

1. The Myocardium.
   - (*a*) Lessening of output from the left ventricle at each systolic contraction.
   - (*b*) Insufficiency.
   - (*c*) Bradycardia.
2. The Valves.
   - (*a*) Stenosis.
   - (*b*) Insufficiency.

II. The Arteries.

- (*a*) Hypotonia.
- (*b*) Sclerosis of large vessels.

III. The Arterioles and Capillaries.

Vasodilatation causing diminution in peripheral resistance through—

- (*a*) Local influences upon the vessel walls, *e.g.*, by histamin.
- (*b*) Vasomotor mediation in the direction of—
  - (i.) Inhibition or lessening of tonic activity of the vasoconstrictor centre.
  - (ii.) Intervention of vasodilator impulses.
  - (iii.) A combination of (i.) and (ii.).

IV. The Veins.

1. Dilatation.
2. Heightened venous pressure with stasis.
3. Contraction of the pulmonary vessels.

} Hindering the diastolic input of the heart, and thereby lessening the systolic output.

V. The Blood.

1. Variations in Volume.
   - (*a*) Decrease of the total volume of the circulating blood.
     - (i.) By lessened output from the left ventricle.
     - (ii.) By lowered peripheral resistance, as in III.
2. Variations in Consistency, induced by anæmic states.
   - (*a*) Decrease in viscosity.
   - (*b*) Decrease in hæmoglobin content.
   - (*c*) Hydræmia.

The Circulatory Mechanisms Involved

Failure in the maintenance of an efficient head of pressure within the circulatory system results in the production of an arterial pressure that is unduly low. This condition may be brought about in one of three ways: (*a*) by feebleness of contractile power on the part of the ventricles of the heart; (*β*) by lowered resistance in the systemic periphery; or (*γ*) by feeble heart action in combination with failure of peripheral resistance.

These alternatives may now be considered in greater detail.

(*a*) A falling arterial pressure usually goes hand in hand with weakening of the cardiac sounds. Such fall is variously attributed either to defective activity of the adrenal glands or to myocardial failure. The systolic pressure may fall as low as 60 mm. of mercury, and, when it tends to remain at or about this level, prognosis is particularly serious. Recovery is promoted by arteriolar contraction producing a rise in peripheral resistance, and thus, by redressing the balance, enabling the weakened heart muscle to regain its tone and contractility.

(*β*) If for any reason the peripheral resistance becomes diminished a drop in arterial pressure ensues, and the heart then comes to the rescue of the arterioles by more frequent and more forcible contractions.

(*γ*) Diminished peripheral resistance is " a combination of several elements, including the viscosity of the blood and

the variation in calibre of the smaller arterioles and capillaries under the influence of the vasomotor system and the external pressure exerted on them by the tissues." [78] Depressor reflexes follow a path in the lateral pillars of the cord to reach, in all probability, a distinct vasodilator centre situate in the region of the fourth ventricle.

(δ) When ventricular contraction and peripheral resistance both fail, systolic and diastolic pressures fall rapidly to the lowest levels that can be recorded. Such phenomenon can only be observed in states of notable shock or collapse, or as a terminal event.

"To understand most of the problems in low blood pressure or the factors which may give rise to it, we must keep in mind this central physiological fact. The medulla, the seat of life itself, must be supplied with blood. Starvation of the medulla means death. Hence a really sustained low blood pressure can never occur. Low blood pressures, even when transient, are dangerous in the extreme, and if not recovered from, the medulla being starved, the animal dies." [3] Hence the efforts of the heart on the one hand, and of the peripheral circulation on the other, to supply the bulb with an amount of blood sufficient for its requirements.

Under certain conditions it is reasonable to suppose that persistent low arterial pressure may originate as the result of poisoning of the capillary walls by histamin or histamin-like substances. In support of this view certain evidence has been adduced, although further work still remains to be done before such hypothesis can be finally accepted.

Let us now turn to a more detailed consideration of the circulatory factors involved.

I. The Heart.—1. The Myocardium.—(*a*) *Lessening of Output from the Left Ventricle at each Systolic Contraction.*—In continued low arterial pressure, proportionately to the amount of decline, the heart manifests regressive changes in its musculature—true cardiac atrophy—an opposite picture to that of the hypertrophy which takes place in response to heightening of pressure within the arterial tree.

In permanently low pressure states, however, fluctuations occur within much narrower limits than those which prevail under conditions of high pressure, and variations from an

upper limit of 100 mm. to a lower limit of 70 mm. are the rule. Sphygmomanometric readings at intervals are required in order to pick out early cases of permanent low arterial pressure from those which exhibit simple normal or subnormal variations. The readings themselves must also necessarily be much more exact in determining the limits of variation of maximal and minimal pressure respectively. Hence, one has to look for variations in millimetres rather than in centimetres, and only the larger excursions can be recorded, for the greater the drop in arterial pressure, the more difficult does assessment of the diastolic pressure become.

Although weakness of the myocardium may be a cause of lowered arterial pressure, the problem is not as straightforward or as simple as at first sight it might appear. Myocardial degeneration, even of high grade, as evidenced by the presence of dyspnœa and œdema with consequent ventricular dilatation, may still be associated with a very high pressure up to a brief period before death.[79] Alternatively, with a systolic pressure of 100 or less, the heart muscle is often found capable of meeting all ordinary requirements. Thus a low pressure due solely to myocardial degeneration is not of frequent occurrence. It is not yet sufficiently realised that under ordinary conditions of cardiac disease the arterial pressure is not reduced. On the contrary, it rises to a point at which the heart becomes incapable of further effort, when failure of the cerebral circulation ensues. This is equally true for mitral as for aortic disease. The only really low arterial pressure is met with in conjunction with toxic states in which Dale's [80] histamin effect is present and there is wide capillary stasis and dilatation. Considerable reduction in pressure indicates either loss of vasomotor tone or loss of blood volume rather than a myocardial or valvular lesion, for prolonged low pressure may result in feeble ventricular contractions, as occurs in the course of certain of the acute infections.

Gallavardin,[81] Gravier [82] and Josué [83] have directed attention to a low arterial pressure syndrome of rapid evolution in association with hypertrophic dilatation of the heart (S. 110 to 80), which may happen apart from valvular

defects or demonstrable nephritis; Josué [84] links this syndrome with that of adrenal depletion.

In acute cardiac conditions and pericarditis the vasomotor centre is depressed by the effects of toxæmia in connection with weakness of the heart muscle. Under such circumstances the systolic pressure may vary from 140 to 96 mm.

A fall of arterial pressure of cardiac origin "is often attributed to faulty proportions of extrinsic constituents such as the potash or lime salts; or within of choline-like bodies which lower pressure. When in early convalescence from infectious fevers, or in under-par persons, the heart and nervous energy are weak, on a slight effort both pressure and rate will rise transiently, but after exertion, as pressures are disposed to fall, the pulse rate may often fall too rather than rise." [85]

Following Gallavardin, the circulatory forms of low diastolic pressure may be divided into two main groups—true and false.

(*b*) *True Diastolic Low Pressure.*—This occurs under three conditions: (A) aortic insufficiency; (B) occasionally apart from aortic insufficiency; and (C) rarely in arterio-venous aneurysms.

A. Diastolic Low Pressure in Aortic Insufficiency.—The sole characteristic of this form is the abnormal fall of diastolic pressure in relation to the systolic. All varieties may occur, the figures for the diastolic pressure depending on the height of the concomitant systolic pressure and the amount of the sigmoidean reflux. Thus, reduction of diastolic pressure is not constant, and tends to disappear when the reflux and systolic rise are both small in amount.

"During the early stages (of aortic regurgitation) the systolic is raised and the diastolic remains steady. Subsequently the diastolic becomes lowered, the systolic keeping high, while later still the lowering of the diastolic is out of all proportion to the slight lowering of the systolic. In other words, the support has given way at each end of the blood pressure scale. Thus a very high systolic with a very low diastolic and the largest pulse pressures usually found constitute the clinical picture of blood pressure in fully-developed aortic regurgitation." [86] With a diastolic pres-

sure of below 50 mm., it is always well to bear in mind the possibility of aortic regurgitation being present.

The circulatory modification induced by diastolic low pressure is the only peripheral sign of this disease which is capable of bringing about the abnormal gaping of the sigmoid aperture and the consequent ventricular reflux. Diastolic low pressure may thus be invoked to explain the incessant adaptations brought about by vasomotor reaction. In certain rheumatic hearts it is not uncommon to find absence of all appreciable diastolic lowering of pressure when the signs of simple or double mitral disease predominate, as in a number of slight insufficiencies of arterial origin. Careful auscultation may indeed reveal aortic regurgitation in the absence of all lowering of diastolic pressure.

B. Diastolic Low Pressure without Insufficiency.—This reduction of pressure has been found in cases where at autopsy the aortic valves manifested no visible defect, and is possibly due to increased local peripheral permeability or more probably to modifications in arterial resiliency. With abnormally resistant arterial walls a more profound fall in diastolic pressure naturally occurs.

C. Diastolic Low Pressure in Arterio-venous Aneurysms.—Diastolic hypopiesis in arterio-venous aneurysms is likely to be more marked in proportion as the lesion is situate in large vessels, and as the orifice of communication is large. The maximal effect should be produced in aortic aneurysms opening spontaneously into the vena cava. It can remain localised, or, at least, is not propagated to the brachial artery, in certain distant aneurysms, as, for example, of the popliteal artery and vein.

Makins [87] and Cazamian [88] have independently drawn attention to the onset of cardiac dilatation with symptoms of weakness following arterio-venous aneurysms. These urgent symptoms, however, tend to disappear within a few days as the circulation adjusts itself to the altered conditions.

"In the presence of diastolic low pressure, the heart, in order either to maintain in the arterial tree the same mean pressure or to restore the normal systolic pressure, must propel into the aorta a more abundant blood wave, but as

regards this there is a capital difference between the diastolic low pressure of aortic insufficiency and that of an arterio-venous communication. In the first case the left ventricle, which has received all the blood which has escaped from the arterial system, has immediately to close the aperture ; the ventricle by its plasticity and a moderate degree of hypertrophic dilatation suffices to re-establish a sufficient circulatory equilibrium.

" In arterio-venous aneurysm this same left ventricle does not utilise any reserve blood supply to restore to the arterial tree the quantity of blood of which it has been robbed ; it is necessary that the complement should be realised by the intervention of the right heart and the pulmonary circulation." [89]

(*c*) *False Diastolic Low Pressure due to Slowing of the Heart-beat* (*Bradycardia*).—Here the diastole is prolonged, the time of transmission to the periphery of the blood wave augmented, and the diastolic pressure coincidently lowered. This may best be seen in total heart-block with a slow pulse of about 30 ; it is still very appreciable as the automatic ventricular rhythm oscillates around 40.

The influence of retardation of heart rate upon fall of pressure is still more striking when it can be observed in the same subject at intervals of a few minutes. If the pulse rate be quickened by atropine slight modification occurs in the diastolic fall ; *e.g.*, with a pulse of 78, pressures 120/70 ; with a pulse of 104, a few minutes after injection, 115/75. Thus one realises how necessary it is in order to obtain a balanced judgment of pressure relations always to note alongside the spyhgmomanometric formula the rate of the pulse. (*Vide* " The Complete Arterial Pressure Picture," p. 19.)

Along with the above extremes, there are other cases more limited. With a pulse of 60 to 65, 160/80 would be considered normal, but with a pulse of 120 would constitute a diastolic pressure undoubtedly low.[89]

2. The Valves. — (*a*) *Stenosis* — Habitual hypopiesis, usually of slight degree, is found in certain valvular diseases of the heart. Hypopiesis is thus met with in young people who are the subjects of mitral stenosis, especially when this

is complicated by inanition. Similarly, in some cases of aortic stenosis the like occurs.

"In spite of the undeniable importance of slowing of cardiac rhythm from lowering of diastolic pressure, one should not conclude that there is a mathematical fixed relation between these two factors and thus establish a proportional relation between lengthening of diastole and lowering of the minimal pressure. Variations are always less than they would be in a system of inelastic tubes, for one has to reckon with the production of the double murmur of Duroziez in the femoral artery. The immediate cause of this is found in the lack of agreement of the fall in diastolic pressure at the central and peripheral ends of the compressed femoral, the second murmur being earlier or more intense as this divergence develops more rapidly and becomes more considerable. It is found only in certain cases of diastolic low pressure, and necessitates for its production a certain diastolic fall, which does not always occur." [89]

(*b*) *Insufficiency.*—In rheumatic aortic insufficiency associated with mitral lesions, where the double murmur is most often absent, the systolic pressure is slightly raised and the diastolic fall less abrupt. This double murmur may be produced even apart from any aortic insufficiency provided that the diastolic fall is sufficient, as happens in certain atheromatous high pressure conditions, and is almost absent in diastolic pseudo-hypotension in association with bradycardia.

II. The Arteries.—(*a*) *Hypotonia.*—In the production of hypopiesis, the state of the arterial wall in general has but little influence. To this rule, however, there are certain exceptions. Some effect, albeit a limited one, is exerted upon the vessel wall by the toxæmias of acute infective processes, whereby the muscular tissues become weakened and flaccid with resultant decrease in tone and resiliency.

(*b*) *Sclerosis.*—Similarly, in the senile or decrescent form of atherosclerosis, and in the more localised thickening of peripheral arteries, a lowering of arterial pressure may be observed. The atherosclerosis of large arteries described by Münzer and others is referred to at greater length on p. 88.

There is still a very prevalent idea that arteriosclerosis

usually induces a heightened arterial pressure, so that on the part of many the two conditions are apt to be regarded as synonymous. That this belief is true for some 50 per cent. only of cases of arteriosclerosis has been commented on by the late Sir Clifford Allbutt,[90] who drew attention to the fact that in a very large number of "decrescent" cases, and again in certain chronic diseases, such, for example, as diabetes in children, there was no evidence of high pressure at any stage. Allbutt's decrescent group largely corresponds with the diffuse (senile) type of Warfield,[91] who goes still further by asserting that in this type of case the arterial pressure is invariably low. "The heart in such a case is small, the muscle is flabby, there is brown atrophy of the fibres and some replacement of the muscle cells by connective tissue. The same causes which have produced general arteriosclerosis have also produced sclerosis of the coronary arteries, and probably the lessened blood supply accounts for much of the atrophy of the heart muscle." Furthermore, the symptoms, signs and course of degenerative sclerosis are wholly different from those of the high pressure series to which Allbutt gave the name of "hyperpiesia."

So in chronic aortitis the pressure as a rule is low, the reduction usually affecting the diastolic more than the systolic.

Low arterial pressures in all probability are rarely brought about by degenerative changes in the smaller arteries.

Arteriosclerosis of Large Vessels.—As long ago as 1908 Münzer,[92] of Prague, published an interesting series of cases of low arterial pressure which possessed the common factor of a pulse wave with small impact upon the vessel wall, in virtue of which they were, in his opinion, capable of being distinguished from other forms of low arterial pressure.

In a subsequent article [93] he comments on the scanty and slight attention which the subject had then received, and goes on to say that he proposes provisionally to differentiate certain cases into groups, with the reservation that at the time of writing he was fully conscious of his inability to cover the whole field. Münzer puts forward six main groups. The first comprises arteriosclerosis of the large blood vessels, which he regards as a frequent cause of subnormal pressure,

his explanation being that the blood wave flows through the large hard vessels as it were through a rigid tube, with the result that the percussion stroke reaches the periphery. This results in the peripheral arterioles becoming distended and tortuous with coincident abrupt rise and fall of the pulse wave. The pressure is depressed because of the absence of rhythmic distension of the vessel wall. He found the average pressure of such cases to be 100 mm. S. and 70 mm. D., the lowest systolic pressure being 90 mm. and the lowest diastolic pressure being 50 mm., giddiness up to actual fainting being frequent accompaniments.

Numerous other writers have described low arterial pressure in arteriosclerosis, notably Allbutt [90] and Ferranini,[94] also Devoto, Etienne and Parisot, quoted by Huchard,[95] so that, as we now recognise, it is by no means an uncommon factor in this malady. Goodman [96] quotes an interesting example of an engineer referred to him from an ophthalmic clinic with the diagnosis of retinal hæmorrhages in the left eye. Decided arteriosclerosis and urinary findings, *i.e.*, polyuria, low specific gravity, protein and casts, suggested interstitial nephritis. The arterial pressure, which in this case was a variable quantity, had been as low as 123 to 80 mm. Hg.

Münzer's remaining five groups are arranged under the headings of status thymo-lymphaticus, orthostatic albuminuria, chronic nephritis, paroxysmal tachycardia and cachectic states.

The Pulse in Low Arterial Pressure.—When both maximal and minimal pressures are lowered, the pulse is either (*a*) soft and weak, of small volume and poor quality, exhibiting various grades of dicrotism, difficult to feel and easily obliterated by the palpating finger, a rapid systolic rise being succeeded by a rapid diastolic fall; or (*b*) soft, large and readily compressible.

The dicrotic wave, which under pathological conditions is related with decline in the arterial pressure, particularly when an unusually low diastolic pressure is combined with a moderate or raised diastolic pressure, has been known since the time of Galen,[97] who ascribed it to vibrations set up in the walls of the arteries by the blood current. In modern

times this explanation has received confirmation from the researches of such accurate observers as Bard,[8] Gallavardin, and his pupil Barbier.[98]

A fact which proves that dicrotism is connected with persistently low arterial pressure is found in its frequent absence in atheroma, in which condition arterial pressure is increased, while the elasticity of the vessel wall has almost vanished. Further temporary compression of the aorta or femoral arteries causes disappearance of the dicrotic wave.

In both the above types of pulse the rate tends to be accelerated, a true tachycardia being sometimes present. Coincidently with this the heart manifests weakness of the precordial impulse and of the first sound at the apex, along with diminished intensity of the second sound at the aortic base. Individual differences nevertheless occur.

Diminution of the first sound of the heart is an index of weak cardiac contraction; diminution of the second sound at the aortic base is an index of weakness of the arterial pressure. With a rise of pressure in the lesser circulation the pulmonary second sound manifests accentuation. Further, there may be distinct tendencies to venous stasis and congestion of the extremities. Under conditions in which reduction of the diastolic pressure alone is found, although slowing of the heart-beat due to lengthening of the diastolic phase frequently coincides with lowering of arterial pressure, no directly proportional relationship can be established between them by reason of the incessant adaptation brought about through vasomotor influences. If one rarely sees a very slow pulse apart from profound depression of diastolic pressure, on the other hand, a diastolic decline combined with a pulse acceleration of about 120 is often encountered, notably in tachycardia of nervous or thyroidic origin. On the other hand, a neurogenic form of bradycardial hypotonia is found in association with certain cases of exophthalmic goitre.

"A slow pulse gives time for a lower diastolic fall of pressure; conversely, excess rate means shorter diastole, less filling of ventricles, less output, and so, with a constant periphery, a disposition to falling pressure. In paroxysmal tachycardia the fall of arterial pressure is due less to heart

failure than to diminution of output by shortening of the diastolic phase; so that as seen after a while in dilated right chambers, in swollen jugulars, or even in a distended liver and œdema, the venous pressures rise. The best outputs in unit time and the best blood pressures are at ordinary pulse rates. On the other hand, if there be sufficient peripheral tone and the output adequate and equal, a higher pulse rate will, or may, raise systolic arterial pressure. The fall of pressure with accelerated pulse in most of the febrile infections is due in the first instance less to the heart than to dilatation of the peripheral vessels, presumably busy in meeting the excessive tissue and immunity operations." [99]

The Pulse of Aortic Regurgitation.—If we review the interesting problem of aortic regurgitation we find the presence of a hypertrophied left ventricle with reflux through the sigmoid valves in conjunction with reflexly dilated and flaccid arteries. Under such conditions the widely relaxed arterial walls undergo an amount of tensile strain, both longitudinal and transverse, which is probably unequalled in any other known disease. In this way is produced a constantly high differential pressure, which may be due "either to a considerable fall in the minimal pressure (as, for example, maximal pressure 120, minimal 50), as is most common in the endocarditic group, or to a considerable rise in the maximal pressure with relatively little change in the minimal (170 and 90 respectively), such as is usual in the arteriosclerotic form." [100]

The typical Corrigan or "water-hammer" pulse, best seen in the former group, is the direct expression of the sudden shock transmitted to the arterial walls during the initial phases of the sudden and heaving systolic thrust over the greater portion of which phase the pressure is dropping, to fall still more during diastole when the pulse becomes small, soft and collapsing.

This pulse of unfilled arteries is of wide excursion, and in the fully developed disease the sudden impact of the blood upon lax arterial walls is transmitted to the capillary bed, thus producing the visible capillary pulsation. Widespread and excessive dilatation of arteries, arterioles and capillaries may ultimately lead to a general loss of arterial elasticity

with stretching and permanent widening of the arterial circulation, so that vasoconstrictor impulses are no longer able to reduce it to effective proportions. Thus slowing of the whole circulation and a notable and finally grave fall in arterial pressure eventuates, since the total quantity of blood in the body is inadequate to fill the arteries when these are dilated to their extreme limits, and incomplete filling with stagnation of the remainder of the circulation follows.

A like condition takes place in late stages of arteriosclerosis. In this way is explained the faulty circulation in cases of aortic regurgitation where there is no concomitant weakening of the contractile power of the left ventricle.[101]

III. The Arterioles and Capillaries.—From 1919 onwards Krogh [102] has adduced a mass of valuable evidence, which has been independently verified, that the arterial and capillary systems are regulated by their own special mechanisms, and thus react and function independently. He has proved that not only do the capillaries contract and dilate apart from the influence of the arterioles, but that their calibre, when the tissue they supply is at rest, is considerably less than when the tissue is active, showing that the capillaries exist in a state of constrictor tone.

Since the main fall of pressure from heart to periphery takes place between the arterioles and capillaries, this painstaking work of Krogh suggests that in the arteriolo-capillary area really lies the origin of many cases of aberration from standard limits in the direction either of high or of low arterial pressures.

Bernheim's [103] studies of patients suffering from a variety of circulatory disorders of the extremities suggest that far from exhibiting a rise, many of them reveal low pressures, in certain instances extraordinarily low, while most of them exhibit normal pressures. This author is of opinion that in findings derived from arterial pressure we may possibly arrive at the explanation of certain obscure features connected with the production of threatened and real gangrenes.

IV. The Veins.—The veins are implicated when they function as reservoirs containing a large proportion of the total blood content of the body, and thus diminishing the amount of material upon which the heart and arteries depend for

the maintenance of an efficient circulation. In this connection it should be remembered that the adequate filling of the heart is also influenced by the pressure on the venous side of the circulation.

V. The Blood.—1. Variations in the volume of the circulating blood are discussed on p. 81. Decrease of the total volume is caused either by lessened output from the left ventricle, as occurs in certain forms of cardiac valvular disease, notably mitral stenosis (p. 86), or by lowering of the peripheral resistance (p. 81).

2. Variations in the consistency of the circulating blood are induced by—

(*a*) *Changes in Viscosity of the Blood.*—A lowered viscosity is most often accompanied by a diminution in one or more of the following constitutents: (α) blood corpuscles, mainly the erythrocytes, (β) blood protein content, (γ) hæmoglobin. "Blood density curves closely agree with those for percentage of hæmoglobin and number of erythrocytes. Hence one would expect to find correspondingly increased viscosity in such a condition as polycythæmia. Here, however, the blood pressure is not invariably high, nor is the left ventricle usually hypertrophied. Variations in density, which are so readily balanced by increase or decrease of water-content absorbed from the tissues, do not largely affect arterial pressure. Hence we may conclude that, although density has its share in the maintenance of blood pressure, yet changes in consistence and viscosity can readily be balanced by the tissues. The studies of Lyon suggest that the chief regulating mechanism lies not in the arterioles, but in the capillary areas." [78] In the anæmias where the total number of erythrocytes is reduced, viscosity tends to become correspondingly lowered. In certain metabolic disturbances, associated frequently with derangement of hepatic function, the blood protein content is increased with corresponding increase in viscosity.

(*b*) *Decrease in Hæmoglobin Content.*—Decrease in hæmoglobin content of the blood connotes lowered viscosity, and *vice versâ*, increase in hæmoglobin content connotes increased viscosity. This is true of a 20 per cent. change in hæmoglobin content in either direction.

(*c*) *Hydræmia.*—In conditions of hydræmia, for example after a severe hæmorrhage, when fluid is drawn into the blood at a more rapid rate than the bone-marrow can regenerate blood corpuscles, the blood becomes diluted by reason of its higher percentage of water-content, which decreases both the blood viscosity and the cardiac load.

The *rôle* of the endocrine glands which control the water balance of the tissues should also not be forgotten. Thyroid deficiency invariably induces hydræmia of greater or less amount corresponding to the degree of deficiency. So too, on administration of insulin or the internal secretion of the pancreas, particular regard should be paid to the percentage of water, since an increase in hydræmia is always brought about, often to the extent of causing waterlogging of the tissues and resultant œdema, sometimes of the lungs.

On the other hand, posterior pituitary deficiency with diabetes insipidus causes a decrease in the blood water-content, an exhæmia. Raising of the blood water-content ensues when the polyuria is controlled by injections of pituitary (posterior lobe) solution.

CHAPTER VII

Low Arterial Pressure in the Absence of Organic Disease

A. Psychical Low Arterial Pressure

Variations in arterial pressure due to excitement, emotion, worry, and nervous overstrain are usually in the direction of a rise, particularly at the systolic end of the scale, rather than of a fall. Nevertheless, the pressures at either or both ends of the scale may be lowered by sudden deep and intense emotion of depressing nature, or more commonly by long-continued debilitating and gloomy influences acting through the intervention of the endocrine-sympathetic system. "Just as there are individuals who react to excitement by a physiological tachycardia, so also there are others who react in reverse fashion; that is by a neurogenic bradycardia." [104] This condition is frequently associated with diminished blood pressure, and is easily differentiated from cardiac insufficiency of organic origin, which is accompanied by tachycardia and cyanosis.

B. Physical Low Arterial Pressure

1. Hypotonia (Primary or Essential Arterial Hypotonus).— Persistently lowered arterial pressures do not necessarily connote anatomically altered arteries, though presumably the muscle elements manifest some decrease in number and size. Arterial hypotonus, however, is wont to occur as a result of prolonged vasodilatation, as in various paralyses. Under such conditions the arterial walls develop a measure of flaccidity, the amount of which depends upon the degree of lessening of vasoconstrictor stimuli. In hypotonia, as in hypertonia, both qualitative and quantitative alterations in softness occur. Lowered tonus is thus not infrequently allied with persistently lowered pressure.

2. Hypopiesia (Primary or Essential, Congenital and Constitutional Hypopiesis).—An arterial pressure lower than the standard pressure for age and body weight is readily distinguishable from the condition associated with organic disease by the absence of morbid phenomena, and because such type of subnormal pressure is compatible with a physiological state of existence within the limits of a narrowed reserve of energy.

(*a*) **Apart from Apparent Physical Abnormalities.**—Certain writers who have not realised that all subjects of hypopiesis are in an inferior constitutional state of low vitality express the older views that hypopiesis is compatible with perfect health. They believe that arterial pressure should not be regarded as abnormal in any particular case merely because it is relatively below the standard level for healthy individuals of similar age and physique, and find, what is perfectly true, that such subjects, even when middle-aged, in apparently good general health, enjoy their work and recreation, are not breathless on ordinary exertion, and within limits can exhibit remarkable response to effort. Other writers go even further than this. Thus Gallavardin is in agreement with Oliver's [105] conclusion that "when other indications are favourable, the lower ranges of pressure are not only more salutary, but are very often compatible with the highest health. . . . It would, therefore, seem that a subnormal pulse pressure, like a slow pulse rate or a subnormal temperature, may be consistent with good health and the enjoyment of an active life, and is not in itself significant of disease." Oliver gives systolic readings of 135 in a man of 100 years of age, and of 185 to 190 in a woman of 96 years. In children Leonard Hill [106] has found the systolic pressure as low as 80 mm. Hg, to be 80 to 110 in young adults, and to be no higher in several active men, eminent in their walk of life and carrying some 60 years. Janeway [107] has noted systolic pressures which would ordinarily be considered as subnormal—below 110 in men and 95 to 100 in women—existing over long periods of "absolutely perfect health and physical activity."

In this respect Edgecombe's [108] observations on the systolic pressure of a male subject, aged 40, "normal in every way"

apart from a persistently low arterial pressure, are of considerable interest. His records of 200 consecutive daily readings are as follows :—

—	mm. Hg.	Pulse Rate per minute.
Average morning pressure (systolic).	94·1	66·1
„ evening pressure (systolic) .	104·9	74·9
„ day rise . . .	10·8	8·8
„ evening fall . . .	9·5	6·0

Occasionally one comes across instances of this type in adults of both sexes who enjoy apparently good health, and in whom no abnormality save such as is connected with a subnormal pressure can be detected. These people are free from cardiovascular and pulmonary disease, and are capable of taking an active and sustained interest in their life pursuits.

This view receives additional confirmation from Potter, who states that a systolic pressure below 110 is quite compatible with the existence of health and even of a strikingly rugged and vigorous constitution. "I have known," says Potter,[26] "a few exceptionally strong adults, leading very energetic and strenuous lives under great stress and constant strain, whose systolic pressure was never observed to rise above 110, and was frequently between 90 and 100. Although in my own experience such individuals are rare exceptions, unless accompanied by other symptoms or signs of weakness or debility, a systolic blood pressure below 110 in itself is by no means a constant indication of physical deficiency or disease." Experience derived from a study of life assurance statistics goes to show that middle-aged subjects who exhibit low pressures have a greater expectation of life than the average.

Analysis of the opinions above quoted, however, shows that they are all based *upon consideration solely of the systolic pressure*, and are thereby vitiated. As the author has frequently observed, estimations of systolic pressures alone are not only of little value, but are often misleading in that

attempts are thus made to solve a complicated problem of which only one factor is vouchsafed. Careful serial observations will often show that the subject of alleged " absolutely perfect health " is not really in such a happy state, but manifests an undue liability to infective processes, and often by reason of tissue-alkalinity suffers from a narrowed limit of reserve energy. Further, although the systolic pressure may remain at or near standard level for the hypopietic individual, diastolic low arterial pressure is frequently present, and the above observations take no account of this relative form, which is easily overlooked.

The subjects of congenital or constitutional physiologically low arterial pressure are more usually than not of spare habit of body, and admittedly possess adequate muscular and mental aptitude for all *ordinary* demands which may be made upon them. Biochemically, they are usually found to belong to the " alkaline " type of constitution.

From the manifestations common to the essential low arterial pressure group as a whole, it would appear that **this low vitality condition often occurs in association with an inherent diminution of peripheral tonus consequent upon a constitutionally lessened autonomic-endocrine vasomotor control.** Such persons respond well to demands for physical or nervous effort, with corresponding improvement in circulatory tone, provided always that such effort is within their limit of reserve.

A comparatively small sub-group is made up of those who are the subjects of latent or early infections, such, for example, as tuberculosis or of severe anæmia, Addison's disease, cachexia, hypothyroidism or cardiovascular diseases. Differentiation of this latter series is facilitated by the recognition of a still greater limitation of response to effort, whether physical or mental, in frequent association with lassitude, readily induced fatigue and gastrointestinal disturbances. The heart and aorta are usualy of small size in such individuals, who possess correspondingly slight power of resistance to infection.

Hereditary Form.—The influence of heredity is seen in certain families who manifest habitual ranges of pressure which may be in some instances supernormal, and in other

instances subnormal. These are again of "physiological" type.

In addition to the above, there is a second and larger group, which possesses physical abnormalities of various kinds.

(*b*) **With Physical Abnormalities.**—It is not easy to correlate cause and effect where a large number of variations in physique are concerned. Nevertheless, there is considerable evidence in favour of the deduction that where there is a respiratory deficit together with suboxidation, arterial hypopiesia coexists. The picture that Barach [52] has presented of this essential low arterial pressure type is worthy of mention. Taken as a group, the subjects are distinctly undersized. They are non-athletic. They have narrow nostrils and, frequently, nasal obstruction along with narrow chests and slender bodies. In other words, they belong to the hyposthenic and asthenic types. They have a smaller than normal chest capacity, with marked tendencies to muscular relaxation. Often they have drooping shoulders and are shallow breathers. At times respiratory irregularity is noted. This irregular breathing is similar to the periodic type of breathing seen in newcomers to a high altitude, which is plainly due to oxygen want and is promptly relieved by oxygen inhalation. In view of the above, Barach places "respiratory effort and oxygenation" before cardiac energy, arterial resistance and blood characteristics, as the primary causative factor of arterial pressure.

It is interesting to contrast the above clinical picture of essential low pressure with the effects produced by proper acclimatisation to high altitudes. These effects are due to changes in the organism which are essentially directed against altitudinal reduction of oxygen pressure, and have for their purpose increased access of oxygen to the tissues. Thus in the blood occur increase in the total volume, particularly in respect of hæmoglobin and number of cells, as well as a further combination of oxygen with the blood pigment. The respiratory volume and the oxygen tension in the alveoli are increased, the circumference of the thorax is enlarged, and the vital capacity is augmented.

A few observers doubt whether such a state as that of

constitutional low arterial pressure exists. Janeway,[107] for example, remarks that "low pressure, in the cases to which the term 'constitutional low blood pressure' has been applied, is merely one symptom of lowered tone of the central nervous system—though possibly an important one to recognise."

This attitude of mind is readily explicable on the view held by the author that Bishop and certain other workers have under a single heading included not only the true "physiological" state of essential low pressure, but also one or even more pathological groups as well, which fall within the limits of Martinet's "hyposphyxic syndrome." If one carefully analyses Bishop's [109] description of what he calls "constitutional or essential hypotension," one finds, in addition to true cases such as those above described, a group of patients who are stated by him to be "constitutionally feeble," and whilst "not suffering from any definite disease, realise that they are not just like other people. They have probably been told that they are suffering from a variety of diseases according as the phenomena were traced to one or other organ. Such patients are fortunate if they are continually under the care of a practitioner, who finally comes to appreciate the condition and brings judicious management to bear on it. . . . The condition is one of long duration, often congenital, and frequently lasting throughout life. Some gradually acquire a normal tension, and in many the condition becomes less marked toward middle life." "These patients," says Bishop, "frequently have a gouty ancestry, and strangely enough are found in the same families who seem to have had more than their share of cases of high arterial tension." The arterial walls are unusually soft, yielding and compressible, and the pulse may be of a very feeble character over long periods of time. In fact, it is somewhat astonishing to find how slight a degree of tension may exist in the radial wall without coincident symptoms of circulatory disease. This subnormal arterial pressure in an otherwise apparently healthy subject is in all probability due to an inordinate relaxation of the tonus of the peripheral circulation, which makes only slight demands for a head of pressure to be maintained by the heart and

arteries, and thus enables them to function with little effort. "While some of these patients are constitutionally feeble, many of them respond splendidly to demands for physical or nervous effort, and when aroused show a decided improvement in the tone of the circulation. To one who sees a patient of this character for the first time when ill with some other disease, the poor quality of the pulse naturally gives rise to anxiety, but when patients have been known for years to get along perfectly well with this feeble pulse, it becomes recognised as characteristic of the physiology of the individual."

"The condition is much more common than I had at first supposed, and I am sure that there are but few physicians who cannot recall examples of it. It must not be confounded with the low arterial tension that is the result of lack of power on the part of the heart to produce pressure, or which is the result of exhaustion of the circulation from an unusual demand for pressure, as in Bright's disease."

The author believes that he has quoted sufficiently from Bishop's description to show that such grouping is in reality of dual origin, and is capable of subdivision into (1) a true constitutional or congenital group, the symptoms of which are due to a depressed tonus of the peripheral system, able to respond, with benefit, to extra demands, provided that these do not overstep the limit of reserve energy, and (2) a class with hypoadrenia or other endocrine defect as basic factors, to which the symptoms correspond. This latter series must carefully be differentiated from the first group of constitutional low pressure individuals, who are free from other symptoms or physical signs, who manifest an apparently good state of health, and for the most part are as capable of enjoying life as any others.

3. Temporarily Induced as a Result of : (*a*) Normal Sleep.—Blume [110] gives the results of his examination of 20 men, 20 women and 10 children suffering from various affections. In 8 men with a systolic day pressure of under 120, the difference awake and asleep averaged 15 mm. of mercury. In 13 women with a systolic day pressure of under 116, the difference averaged 21 mm., the average day pressure being reduced to 89 mm. during sleep. In the remaining cases

with high day pressures, the difference averaged 31 in the 12 men, and 39 in the 7 women. In one child of 14 years with pneumonia, the systolic day pressure varied between 116 and 132, whilst two hours after the onset of slumber the systolic fell to 87, then 112 and later 79.

These records confirm those of Müller,[111] who found the systolic pressure of normal individuals during sleep, after a small dose of veronal, to be reduced to 94 mm. of mercury in men and 88 mm. in women.

MacWilliam [112] observes that "the slowing of the pulse rate (noted by Galen) and the respiration during sleep has long been known to be accompanied by a lowering of bodily temperature, a great reduction in metabolic activity and heat production, depression of reflexes, diminished secretion, etc. There is general agreement as to a definite lowering of the systolic pressure, varying in different conditions and as recorded by different observers, but often amounting to 15 to 30 mm. Hg at the end of two hours' sleep; the pressure gradually rises in the later portion of the night's sleep. Greater reductions have been noted in persons with high pressures in the daytime." MacWilliam is, however, careful to point out that lowering of arterial pressure, heart and respiratory rates, etc., take place only under conditions of undisturbed or sound sleep, and that precisely opposite effects are apt to be induced by disturbed sleep attended with reflex excitations, dreams, or nightmares.

(*b*) **Posture.**—The experiments of Erlanger and Hooker [113] with the sphygmomanometer on the relation between arterial pressure, differential pressure and the velocity of the blood flow in man show that, upon changing from the recumbent to the standing posture, the diastolic pressure is increased and the differential pressure is diminished. Upon assuming the sitting posture, these pressures return to approximately the same values as when recumbent. Further experiments with the v. Kries tachygraph demonstrate that, in agreement with the changes in differential pressure, the acceleration of blood flow per heart-beat is greatest when recumbent, and smallest when standing. There is an inverse relation between the pulse rate on the one hand, and the differential pressure and velocity of flow

on the other. Under normal conditions, the product of the differential pressure by the pulse rate, therefore, tends to remain constant, as does the product of the acceleration by the pulse rate. In any two postures, the differential pressures are to one another as the acceleration per pulse wave. This is in accordance with the law governing the flow of fluids through large elastic bodies. These experiments, therefore, indicate that the explanation of the changes that accompany alterations in posture is to be found chiefly in changed hydrostatic conditions.

(*c*) **Fatigue.**—In the subjects of hypopiesis, sudden and violent exertion heightens for a brief period both systolic and diastolic pressures just as it does in other subjects who are not habituated to more than a slight amount of exercise, and who lead sedentary lives. Should exertion be continued in either case to the point of fatigue, both pressures subside, the systolic pressure manifesting a greater drop than the diastolic during extreme effort, inducing over-exhaustion, the heart becomes poisoned by unoxidised products such as lactic acid, and thus the compressive action of the diaphragm, which functions as a second heart, is held in check.[114] The systolic pressure becomes depressed to a low level, at which it may remain even for two to three days, accompanied by physical sensations of profound lassitude and disinclination, amounting often to incapacity for more than the minimum of physical or mental endeavour.

" In the fatigue of healthy men, the first change of pressures, unless the fatigue be abrupt, is not in the direction of fall, but of rise. Fatigue-products do not enhance pressure ; rather the contrary ; the rise is probably another instance of the vigilance of the vasomotor centres in keeping up the pressure-head. A fall of pressures by way of the vasomotor system is not asystolic but syncopic." [115]

(*d*) **Moist Heat.**—Transitory hypopiesis may be noted after a warm bath, or after exposure of the body surface to moist warmth, as in a Turkish or vapour bath.

(*e*) **The Menstrual Cycle.**—It is worthy of note that, even in normal women, the rate of metabolism during the menstrual cycle varies to a slight degree. The lowest point in the cycle occurs about the middle of the intermenstrual

interval, at which time arterial pressure is liable to descend several millimetres below the figures determined before onset of the flow. This phenomenon is dependent upon the well-known variation in activity of thyroid function during the cycle. Even in minor degrees of endocrine imbalance these cyclical variations may become considerably accentuated, resulting in a much bigger swing of arterial pressure. Hence it is important not to lose sight of this endocrine factor.

(*f*) **Pregnancy and Labour.—Pregnancy.**—In pregnancy high arterial pressure occurs as a frequent symptom, probably as a result of the effect of circulating toxins in impairing the elasticity of the arterial walls and thus necessitating increased cardiac activity. Normal pressures are also seen, but low pressures are rare. Upshur [116] has recorded such a case in the third pregnancy of a woman of 27 years of age, of good physique who had led an active life. Mild fainting attacks had taken place in each previous pregnancy, with uneventful labour and puerperium. There was no evidence of cardiac lesion, and repeated examination of the urine was negative. After the fourth month she had repeated attacks of unconsciousness, up to two in a day, coming on suddenly, with face pale and lips colourless. The pulse was thready, and the arterial pressure so feeble that it could not be recorded. The day after confinement the systolic pressure was 110 and the diastolic 90, with a normal pulse. Convalescence was uneventful, and on the 17th day the systolic pressure had risen to 130 and the diastolic to 100. This writer tentatively suggests that perhaps the causal mechanism lay in the effect upon the heart of some upset in balance of the internal secretions.

Labour.—After normal delivery, little fall in arterial pressure or shock is induced by the anæsthetic, by operative procedures, including rapid emptying of the uterus, or by physiological hæmorrhage. In the presence of toxæmia, perhaps as a result of cumulation of toxic substances in the blood, these factors nevertheless will frequently bring about a notable drop in pressure, even of 100 mm., and, unless effective stimulation be at once adopted, shock will inevitably ensue. At the time of labour, patients whose

pressures are already depressed not infrequently manifest a considerable degree of collapse.

4. Permanently Acquired.—(*a*) *Athletics.*—It is now generally recognised that in athletes as a rule the habitual pressure ranges low. Dr. Michell [117] examined with the aid of a modified Riva Rocci apparatus and the palpatory method 1,200 Cambridge rowing men, 410 football players and a few running men, and found their maximum arterial pressure to be as follows :—When just awakened and lying in bed, 95 to 100 mm. Hg ; after rising, and while moving about the room, 100 to 115 ; while standing still, 105 to 110 ; in the middle of the day, 115 to 120 ; two hours after hard exercise, and immediately on lying down, 125 to 130 ; from this highest point the fall became rapid, so that after lying down for ten minutes it was very often 106 to 110. " In older and more experienced athletes the subjects of over-stress of the heart, the arterial pressure, on standing, falls rapidly to 100 to 90 mm. Hg, or even less, and the pulse is easily felt to be dicrotic. These patients are liable to recurrent faints not always prevented by the horizontal position."

Oliver,[118] too, has remarked that " those in training for games and athletic exercises demanding the expenditure of spurts of energy, have frequently somewhat low arterial pressures during quiescence—the ventricle possessing the potential energy for sustaining the higher arterial pressure required during the stress of vigorous muscular action."

In 29 men taking part in a ski race of 50 kilometres, Filip [119] found no signs of dyspnœa, and further observed that in all cases there was a fall in the systolic pressure, whilst in the majority the diastolic pressure became lowered, the ratio between the pressures being decreased.

In 1910 Barach and Marks [35] discovered three cases of low arterial pressure among fifty-five Marathon runners. While all the runners trained for months beforehand, of the three low pressure cases, " one dropped out within the first few miles of the race ; another ran 10 miles, and the third ran 13 miles and then dropped out, thus manifesting their physical incapacity for sustained effort. Two of these three were under normal weight. All the losers had smaller chest capacities than the winner. In rating the physical efficiency

of the fifty-five contestants, the low pressure subjects were awarded forty-third, fiftieth and fifty-first place."

Gordon, Levine and Willmaers [120] have also investigated another group of Marathon runners with comparable results.

(*b*) *Exercise and Muscular Work.*—Sir Clifford Allbutt [115] has stated that " observations upon men given to arduous muscular work, but recorded at intervals of complete or comparative rest, seemed to indicate a rule that in them the arterial pressures range habitually under the average. . . . Muscular exercise tends in the long run not to raise, but even to reduce, the mean arterial pressure of the twenty-four hours. . . . It seems probable that during exercise the mean arterial pressure must exceed that of rest, but not enormously sustained, nor without compensation ; and the heart, after exertions which have drawn upon its reserve, then enters into the phase of low rates and low pressures."

Hence it may be stated as a general rule that regular physical exercise tends, by diminishing peripheral resistance, to keep the diastolic pressure at a lower level, and thus promotes greater efficiency on the part of the heart, whereas a sedentary mode of life tends to raise it, the systolic pressure being similarly affected, but to a less extent. Continuance of regular exercise after adolescence probably delays the rise of diastolic pressure to the adult level, which usually occurs when a more sedentary mode of life is commenced.

(*c*) *Temperament and Occupation.*—Individuals of placid and gentle temperament, and those who are engaged in routine occupations, particularly of a physical sort, are thereby inclined to exhibit the lower ranges of arterial pressure. Excitement often induces in hypotonics a physiological bradycardia of neurogenic origin without cyanosis. This condition may thus be readily distinguished from cardiac insufficiency of organic origin which is evidenced by the presence of tachycardia and cyanosis.

(*d*) *Age.*—In old age arterial pressures are found to fluctuate within such wide limits as to be of little value for prognosis or treatment. Thompson and Todd [121] have noted readings varying from 190 to 100 S. and 95 to 45 D. in active Chelsea veterans, with symptoms of neither excessive nor

diminished pressure. This is largely due to the fact that in old age the heart and arteries present no constant factor as they do up to age 40 in the absence of infective or sclerotic changes. The influences of wear and tear upon heart and arteries increase as age advances, and evidences of progressive deterioration of the cardiovascular system in the majority of cases become manifest. Nevertheless, there is a residue of well-preserved elderly people in whom the quality of the " vital rubber " of the arteries has been initially good, and who have not damaged this by excesses. In such persons the arterial pressure is often lower than the standard level for middle age.

Cornwall [7] records that several elderly people with myocardial degeneration, but no apparent arteriosclerosis or nephritis, exhibited pressures of 100 to 120 mm. systolic and 50 to 70 mm. diastolic, but were fairly free from circulatory disturbances while they led quiet lives. Some probably owed the low pressure to causes other than myocardial, chronic intestinal toxæmia being one of the most noteworthy.

Wildt [122] observed reduction of arterial pressure in the aged only in association with tuberculosis and pneumonia, in six cases of granular kidney, and in those with weak hearts. He found a regular tendency to increase in the differential pressure, the diastolic being frequently lower than in early life. In four subjects above 90 years of age the pressure was considerably lower than at preceding age periods.

(*e*) *Climate.*—(i.) **Warmth.**—(*a*) *Temperate.*—In temperate climates a continued spell of warm weather frequently results in reducing the maximal pressure by 10 to 20 mm., the contrary effect being produced by cold.

(*b*) *Tropical.*—In tropical climates the results obtained by different observers show no unanimity. Further investigations are still required to elucidate the reasons for these discrepancies.

In Queensland, Australia, Young and his colleagues [123] discovered that humid heat produced a rise in arterial pressure, and in the Dutch East Indies de Jonge [124] found that the maximal pressure of Europeans does not diminish as the result of prolonged tropical residence.

On the other hand, McCay [125] has recorded in Calcutta the average of a large number of observations on the maximal pressure of Europeans as being only a little above 100 mm., the limits of variation being between 83 and 118 mm. Hg (subjects seated with arm on a level with heart). In the standing posture this observer found the maximal pressure to be no lower, and in some cases even higher, than in the horizontal posture, without more than five to ten extra heart-beats per minute. In exhaustion the frequency may be 30 to 40 beats more in the standing posture, and yet the maximal pressure be lower than when horizontal.

From an examination of 992 American soldiers in the Philippines, Chamberlain [126] has also reached the conclusion that the average maximal pressures in the tropics are lower than the normal averages for temperate climates, and that the pressure is lower during the first three months of tropical residence than subsequently, being on the average about 3 to 5 mm. lower during the hottest season of the year. This author has, however, been unable to find any notable parallelism between maximal systolic pressure and the height and weight of the individual. He finds that the mean pressure of Philippinos for corresponding age-periods did not differ from that of Americans.

The recent inquiries of Roddis and Cooper,[127] of the United States Naval Medical Service, not only indicate that there is a reduction both of systolic and diastolic pressure in white men resident in West Indian latitudes, but show that there is apparently a diminished arterial pressure in natives, an observation already recorded by Arias [128] in the case of Panamans. The American authors consider that a hot climate is in itself hurtful; that, in the tropics, the whole organism is keyed to a lower note; and that, unless the mode of living be adapted to this change, harm will result.

Cadbury [129] notes that the maximal pressure of the Cantonese and other southern Chinese youths averages from 20 to 30 mm. less than the normal for Europe and North America. The minimal pressure is also lower than standard levels, but only from 10 to 20 mm. The average differential pressure exhibits little variation, and is thus relatively high. From the ages of 7 to 22 years the values for the maximal

and minimal pressures show a regular arithmetical increase, with less regularity of increase for the differential pressure.

The deductions are that small stature, light body weight, diet and climate have an influence in reduction of arterial pressure.

From the foregoing it would appear that our knowledge of circulatory changes is still defective. On the whole the balance of opinion favours the conclusion that, as a rule, in tropical climates arterial pressure tends to become reduced. In the case of newly-arrived Europeans the true explanation is probably to be sought in a greater or less degree of failure of adaptation to the altered environment, a hot climate being itself injurious to an organism which has not yet learned to adapt itself to a lower plane of existence.

Touching this question of acclimatisation, Dr. Andrew Balfour [130] remarks that " we lack data which might enable us to distinguish between the effects of the moist as contrasted with the dry tropics, and still less are we in a position to estimate how altitude may modify the malign influence of tropical light and heat and thereby possibly permit fertile and vigorous generations of Caucasians to people highlands within the torrid zone."

(ii.) **Altitude.**—The effects of altitude on arterial pressures, already dealt with on pp. 43–46, are amplified in the following observations.

From experience gained in several expeditions to Colorado Springs, altitude 6,000 feet, and on Pike's Peak, altitude 14,109 feet, and from laboratory data accumulated during six years, Schneider and Sisco [131] conclude that for many men, and probably for the majority, residence at very high altitudes does not influence arterial pressures. In a yet undetermined percentage it will cause a demonstrable fall in the systolic and differential pressures, and in very exceptional cases will bring about a rise. At an altitude of 6,000 feet the systolic pressure is under 120 mm. in about 80 per cent. of college youths.

Further researches on the part of Schneider and Hedblom [132] indicate that :—

1. Considerable elevation in altitude tends to lower arterial pressure and to increase the rate of the heart.

2. The fall in arterial pressure is greatest during the early period of residence at high altitudes, the average fall being 1 to 22 mm.

3. Change in altitude does not affect each individual to the same extent. Slight elevation does not affect arterial pressure, and psychic influences may modify the reading.

Thus most observers are in agreement that notable altitudinal elevations produce in nearly all cases reduction of arterial pressure. To those who are the subjects of low arterial pressure, especially when occurring as a part of some debilitating condition, high altitudes may become a cause of real and considerable peril owing to the tendency for the already existing low arterial pressure to sink further to a dangerously low level.

CHAPTER VIII

Low Arterial Pressure Consequent upon Trauma, Infection and other Agencies

I. Temporary

A. In Association with Acute Conditions

1. Acute Collapse and Shock

Although for many years the origin and nature of shock have engaged the attention of a large number of experimentalists and clinicians, by reason of the marked discrepancies between their several conclusions, until recently it has been far easier to state what shock is not than what it really is. Largely as a result, however, of the increased interest aroused in this important and difficult problem by the World War, shock appears no longer as an "individual entity," but as a condition originating from a variety of causes, certain of which assume a greater practical significance than others.

To attain a clear conception it becomes at the outset necessary to eliminate such loose usage of the term as would render it synonymous with injury. Hence it is wise to exclude all forms of uncertain derivation as "hæmorrhagic," "nervous," "toxic," and the like unless these can definitely be proved as causes of objective signs.

Meltzer [133] has defined shock as "a state of general apathy, reduced sensibility, extreme motor weakness, great pallor, very rapid small pulse, thready soft arteries, irregular gasping respiration and subnormal temperature," and adds that the presence of circulatory phenomena is not absolutely essential for diagnosis. This opinion has been pushed to further extremes by some observers, who conclude that a marked fall of blood pressure forms no part of the experimental picture. Thus Wiggers [134] affirms that a drop in arterial pressure is characteristic of shock caused by

intestinal exposure, but does not regard it as an integral part of shock to the central nervous system produced by sensory excitation. To him "central nervous system shock" is merely a state of apathy and depressed sensibility which does not constitute veritable shock, and which can happen independently of any considerable drop in arterial pressure.

Mcleod [135] regards shock as "a condition in which there is a more or less paralysis of the sensory and motor portions of the reflex arc, with profound disturbances in the circulatory system, subnormal temperature, and frequent and shallow respiration." Certain of the symptoms may be regarded as primary, and others as secondary. To the former belong the grave fall in arterial pressure due to oligæmia, which latter increases coincidently with weakening of the cardiac muscle through failing coronary blood supply, and clinical manifestations "not unlike those of cholera"; to the latter belong the raised threshold of sensory stimulation and muscular inefficiency, both an effect of the low arterial pressure, together with the fall in body temperature which results from muscular weakness. The most recent definition of traumatic (wound) shock is that of Cowell,[136] who states that "shock is that clinical condition which follows an injury, producing depressed vitality associated with lowered blood pressure, deficient circulating fluid, diminished intracellular oxygenation and reduced body temperature, and resulting from one or more of the following factors, acting either singly or in combination: (1) pain; (2) hæmorrhage; (3) cold; (4) toxæmia, either of bacterial, tissue (protein) or other origin."

The mass of modern evidence amply confirms the findings of early investigators that one of the most noteworthy symptoms in shock is a pronounced fall in arterial pressure, although, for the reason given later, it is not apparent in the early stages. This fall is attributable to one of two causes: either diminution in the peripheral resistance, or lessened output of blood from the heart. Subsequently to Goltz [137] (1872), Crile,[138] Lockhart-Mummery,[139] and Roger [140] have held the former to be the cause, postulating the existence of a general arteriolar dilatation brought about by deficiency in tone of the vasomotor centre. Crile explains

the difference between collapse and shock by the degree of involvement of this centre, which, though suffering temporary inertia, nevertheless is said to preserve its capacity for excitation. True shock, on the other hand, is regarded by this observer as being essentially gradual and progressive proportionately to the exhaustion of the centre and its inability to respond to peripheral stimuli.

Meltzer,[133] however, found that "even in experiments where all the clinical signs of shock were present, the blood pressure very low, the temperature subnormal, the heart-beat weak and often irregular, and the irritability of the nervous system apparently much reduced, stimulation of the cardiac depressor nerve lowered the blood pressure by forty-five per cent." Cyon and Ludwig [141] have shown that section of the splanchnic nerves, by provoking a pronounced dilatation of the intestines, reduced the pressure by 50 to 60 mm. The same effect follows stimulation of the central end of the depressor nerve of Cyon, whilst a further reduction of arterial pressure attends destruction of the medullary vasomotor centres.

More recently Rich [142] found that a pressor response could always be elicited by stimulation of sensory nerves during shock, and that adrenalectomised animals, subjected to uniform intestinal manipulation before arterial pressure has begun to decline, fall into shock exactly as do normal controls. Hence, one may conclude that disordered adrenal function is not a factor in the production of shock. From the viewpoint of comparative medicine it is of interest to note that syncope and traumatic shock are rare in coloured races and in wild animals.

The experimental work of the American school, including W. T. Porter,[143] Morrison and Hooker,[144] Seelig and Joseph,[145] Lyon,[146] and Mann,[147] has clearly demonstrated that in shock the tone of the vasoconstrictor centre is practically unaltered, and that the arterioles are maintained not in a state of dilatation but in one of constriction. Pike, Stewart and Guthrie [148] have lent valuable support to these conclusions by the results of their experiments, which show that the vasomotor centre can become totally deprived of blood without losing either tone or reflex activity.

A fall in arterial pressure under these circumstances can, therefore, only be induced by an inadequate output of blood from the heart. The really important and constant factor in shock is a deficiency of the volume of blood in circulation.[149] In a recent discussion at the Royal Society of Medicine, it was pointed out that one of the early effects of such deficiency is an increased rate of heart-beat to make up for the diminished volume of blood reaching the heart. The more or less fixed ratio between the pulse rate and the systolic pressure tends to be upset, and a rising pulse rate is found with an almost stationary arterial pressure. If there be a rising pulse rate unaccompanied by a proportional pressure rise, one may assume that shock is present, and that the volume of blood in circulation is deficient. Hence a low arterial pressure need not be the first, nor indeed the truest indication of the *beginnings* of shock owing to the ability of the blood vessels to compensate for the loss of a large volume of their contained fluid by a powerful vaso-constriction. When, however, this loss has reached approximately a quarter of the total blood volume, arterial pressure tends to fall.[150]

Yandell Henderson [151] has further proved that in early stages of shock there is a distinct diminution in the volume of blood expelled by the ventricles, thus indicating that there must be a compensatory constriction of the arterioles before any considerable fall of arterial pressure takes place.

In shock this diminished output from the heart could be brought about by modification of its action (apart from the inflow of blood), or by inadequate diastolic filling of the ventricles.[152] The former cause cannot, however, be invoked in conditions of shock, for, if arterial pressure be artificially raised by administration of epinephrine or by aortic or cerebral compression, the heart responds to this rise of pressure by slow and powerful beats. Nor is the force of the ventricular contraction lessened, for the exposed heart can be seen beating vigorously. Thus diminished output of blood from the left ventricle must result from imperfect filling during diastole. The oligæmia thereby produced is probably of dual origin ; a stagnation of blood in the splanchnic capillaries and venules, combined with a

loss through concentration of blood in the capillaries of the tissues external to the abdomen, with increase in the blood viscosity.

For this large accumulation of blood in the liver and in the splanchnic pool, commonly met with under conditions of gravity and surgical shock, capillary poisons have been held responsible, and experimental evidence supported by the fruits of clinical experience has been adduced that surgical shock, at any rate, is essentially due to intoxication as the result of the absorption of histamine-like substances derived from severely damaged tissues. The work of Erlanger and Gasser [153] goes to prove that the blood becomes concentrated prior to the development of grave symptoms of shock, so causing a diminution in the volume of the circulating blood not only by reason of loss of plasma, but also as a result of jamming of the corpuscles within the capillaries, thus inducing progressive tissue malnutrition and so favouring the elaboration of further toxic material.

Collapse and shock (apart from its initial stage) are thus attended by hypopiesis, which in collapse is fleeting, but in the case of shock is more pronounced. Hypopiesis is a characteristic of both conditions in that it measures the degree of most of the above-mentioned secondary phenomena, which are thereby explained. The suggestion has further been put forward by Heitz [25] that hypopiesis may be looked upon as a possible cause of the escape of plasma from the capillaries.

From the biochemical point of view, diminution of the alkaline reserve of the blood in shock constitutes an additional factor in reducing the rate of the circulation, so leading to inadequate tissue oxygenation which favours the production of lactic acid. "An excess of lactic acid in the blood has been noted in the later stages of many cases of shock, but this is a secondary effect, and it is doubtful whether it is the only cause for the depressed CO_2 carrying power of the blood." [135]

Experimentally and clinically hypopiesis as a result of shock may manifest itself in various degrees as a sequence of (*a*) gravity, (*b*) trauma, (*c*) hæmorrhage, (*d*) considerable loss of tissue fluids, (*e*) surgical operations and anæsthesia,

(*f*) anaphylaxis, (*g*) toxic agencies, (*h*) depressing influences of physical origin, such as cold or fatigue, or of psychical origin, such as emotion or nervous exhaustion, (*i*) any of the above causes in combination.

(*a*) **Shock consequent upon Gravity.**—Experimental suspension by the ears of a rabbit with large pendulous abdomen induces stagnation of blood in the splanchnic vessels owing to failure of the compensatory mechanism which normally secures an adequate blood supply to the dependent parts. Hence imperfect filling of the heart in diastole ensues, and the animal dies from ingravescent shock. Previous application of an abdominal binder, however, prevents these effects.[154] The effective layers of abdominal musculature, developed as a result of the long-continued assumption of the erect posture, in man, act in a similar wise as a protection against gravity shock unless considerable impairment of the circulatory mechanism is already present.

(*b*) **Shock consequent upon Trauma.**—(i.) *Primary.*—In this section may be included experimental traumatic shock consequent upon section of the spinal cord (spinal shock). This differs from other forms of shock in that it temporarily paralyses the whole of the reflex mechanisms situate in that portion of the cord below the level of the section, rendering the affected part of the body flaccid with absent reflexes, some or all of which gradually recover according to the grade in development of the animal.

Primary traumatic shock is rare. It may occur as the result of serious injuries with or without hæmorrhage, from pain, cold or toxæmia, or during the course of lengthy operations, especially upon sensitive areas. Generally speaking, injuries of the abdomen, genitals and lower limbs are more prone to induce shock than those of the thorax. In the case of penetrating wounds of the abdomen the systolic pressure has been noted to fall rapidly even to as low as 50 mm., and the diastolic pressure to 20 mm.,[155] but shock with extreme lowering of pressure may follow wounds of the soft parts, involving neither nerve trunk nor important artery.[156] For this effect the depressing factors of preceding hæmorrhage and nerve association must be invoked. In certain instances it is the differential pressure which under-

goes rapid decrease, and may even descend to zero, when a fatal termination becomes inevitable.

The symptoms are notable hypopiesis, with icy coldness of the limbs and trunk, cold sweats, feeble or imperceptible pulse, blurred vision and often unconsciousness. The pathology of traumatic shock has now been fairly well worked out. Measurements of the fluid circulating in the vascular system show that the total quantity is diminished and that there is concentration of the blood in the capillaries, with increased viscosity.

This anhydræmia is due to lessened intake of fluids due to army service conditions, extra loss in sweating, etc., and hæmorrhage. In addition, as a result of toxæmia, there is an increased permeability of the capillary walls. Also as a result of the low capillary pressure and stasis the osmotic pressure in the tissues rises, further abstracting fluid from the blood and increasing its concentration. This deficient circulation causes diminished intra-cellular oxygenation, the vital organs suffer, and when the pressure falls approximately below 80 mm. Hg the heart and brain fail unless the condition is speedily relieved.[136]

(ii.) *Secondary.*—Secondary traumatic shock supervenes only after the lapse of some hours, sometimes even a day or two after the injury, and in the absence of hæmorrhage. The early view that secondary shock from trauma is largely preventable has been fully justified by subsequent experience. It is due to resorption of albuminous toxins from the damaged tissues, especially from large masses of muscle.[156, 157, 158] The degree of fall in arterial pressure is related with the time that has elapsed since the occurrence of visceral wounds, as well as with their number and gravity. It is determined and maintained by multiple factors, such as abdominal trauma, secondary trauma due to faulty transport, etc., and absorption of toxic substances.[158] This latter factor probably causes those constant degenerative changes found in the parenchyma of the adrenal glands, especially of the medullary cells, similar to those changes which have been found in fatal cases of diphtheria with preceding hypopiesis not attributable to myocardial causes. Experimental confirmation of these clinical findings has been given

by Delbet,[156] who has reproduced the pictures of shock and hæmorrhage by injecting aseptic autolysates of an animal of the same species. Similarly Cannon and Bayliss,[159] having crushed the hind limb of an animal, have observed the arterial pressure to fall 20 minutes later.

(*c*) **Shock consequent upon Hæmorrhage.**—With moderate loss of blood the arterial pressure shows but little change, and is not lowered by small hæmorrhages of 150 to 200 gm. Small repeated hæmorrhages, however, have the effect of reducing arterial pressure in slight degree.

To diminution of the blood mass the organism opposes a vigorous vasoconstriction which tends to maintain arterial pressure at its primitive value, whilst an active and very rapid blood dilution restores the volume to its original state.[160, 161] That this dilution is real has been proved experimentally.[162]

Acute low arterial pressure is brought about by a pronounced diminution in the content of the circulatory system. Consequent upon a hæmorrhage of 600 gm. or more, transitory lowering of arterial pressure takes place, the original value being more or less rapidly restored after bleeding has ceased, and the vasomotor centre has recovered its normal tone. The more copious the hæmorrhage the greater is the fall in arterial pressure. Ambard's [172] animal experiments show that in order that lowering of pressure may be noteworthy and lasting the bleeding must exceed 20 to 30 per cent. of the blood mass. For this effect to be produced, the loss of blood must take place within a sufficiently brief period of time. In the human subject this reduction corresponds to a loss of 1,200 to 1,500 gm. of blood. Beyond 40 per cent. loss the pulse becomes so feeble as hardly to be perceptible. "When hæmorrhage is accidental, events do not occur quite in the same fashion, for less abundant hæmorrhage may be accompanied by diminution of pressure because to the loss of blood is added a new factor, namely traumatic shock. Moreover, traumatic hæmorrhage may sometimes amount to a litre or more, and such reductions of the blood mass can of themselves be the cause of diminished pressure."

Uncontrolled bleeding from wounds either in war or in

civil life presents similar characteristics to those which are induced by traumatism. In hæmorrhage, however, the symptoms of restlessness, obscured vision, singing in the ears and convulsions are particularly prominent, and in severe cases this state may persist up to 40 hours. Arterial pressure falls to such low levels that registration becomes difficult or impossible by means of the auditory method, whilst oscillometric variations are very slight in amplitude and show inequality from one beat to the next.

Bosquette and Moulonguet [162] state that under war conditions hæmorrhage may be the chief factor in immediate shock, where the brachial systolic pressure, measured with the Vaquez sphygmomanometer, rarely exceeds 50 mm.; the radial pulse, counted with difficulty and beating at 110 to 120, on the slightest movement disappears. If it is possible to note the reappearance of radial pulsations in the course of Riva Rocci readings, figures of 60 to 80 mm. (Sencert), and of 50 to 55 mm. (Bosquette and Moulonguet) are found. In cases of favourable issue the arterial pressure rises suddenly, often without apparent cause, 34 to 48 hours after the onset of the accidents; the pulse is slow and sustained, the systolic pressure mounts to 100 mm., and urine reappears. Ducastaing [163] states that wounded men can recover after remaining pulseless for upwards of 12 hours.

Some minutes after a severe axillary hæmorrhage, Clovis Vincent [164] has noted a systolic of 50 mm., with a diastolic of 20 mm. Death supervened two hours later without modification of the pressure. In a case of ruptured mesentery the pressure was 65 mm.; death supervened five hours later. In another case of hæmorrhagic shock, which recovered, the pressure attained 70 mm.

In extreme cases Jeanneney [165] insists on the value of oscillometric observations; if oscillations persist and tend to increase, there is hope of a change for the better. This event generally happens in unexpected fashion and without appreciable cause, the pulse suddenly rising to 90 or 100 mm. with increasing relief to the patient. Rapidity of the respiratory rhythm, however, and convulsions are precursors of death.

(*d*) **Consequent upon Considerable Loss of Tissue Fluid.**—Diseases attended with much loss of fluid from the tissues manifest arterial pressures which are low in correspondence with the degree of fluid drain. Such are cholera, dysentery and diarrhœa. Low arterial pressure is also consequent upon profuse vomiting from any cause, as in gastric carcinoma, intestinal obstruction and peritonitis. The loss of fluid diminishes the volume of the circulating blood and thus cases the pressure to fall. Hence records are of great value in estimating the extent of the condition and in determining the nature of the treatment to be adopted with efficacy. A marked drop points to impending collapse.

(*e*) **Shock consequent upon Surgical Operations and Anæsthesia.**—(i.) *From Operations under General Anæsthesia.*—Whilst ordinary operations under general anæsthesia have little effect upon arterial pressure, this latter may be previously heightened by psychic causes, such as excitement, anxiety or fear. Surgical intervention, nevertheless, is a complex act, which is capable of reducing arterial pressure by any one of its components. These are (α) Trauma, (β) Anæsthesia, (γ) Hæmorrhage.

In determining the factors of safety during operation and the condition of the patient directly afterwards, Blood-good,[166] McGlannan [167] and König,[168] as the result of practical experience, agree in believing that a knowledge of the arterial pressure variations of the patient, as afforded by careful sphygmomanometric readings, afford information of the greatest value to the surgeon, by enabling him to decide upon the safety of continuing his manipulations or the necessity of limiting them. When in an adult a low pressure of under 100 systolic exists, the circulatory margin of safety is small, and serious operations, unless extra precautions are taken, must end disastrously. A large number of this group of patients would not die if blood pressure were regularly taken.[169] Similar pathogenesis in typhoid and other grave infections is accompanied by degenerative changes in the brain, the supposed result of so-called "noci impulses," which are psychic in nature and in large measure preventable.[170] Hence follows the importance of surrounding the patient before operation with an environment conducive to

mental tranquillity and of all the preliminaries being hidden from view.

(*a*) **Operative Shock from Trauma.**—Continuous control of arterial pressure during operation by repeated sphygmomanometric observations with a reliable instrument allows instructive oversight of the patient's condition, since every serious mishap is preceded by a rapid fall of pressure, which serves as a definite warning. In fact, there is a constant relation between falling arterial pressure and the condition of traumatic shock which supervenes during the shock of lengthy operation in which the patient has lost little blood, but which has involved regions rich in nerve plexuses, thus causing considerable nervous irritation (brain, abdominal and major operations), or which has necessitated prolonged handling of the intestines. Manipulations in the upper quadrant of the abdomen even under deep general anæsthesia cause a more frequent fall in pressure, owing to the proximity of the solar plexus, than those in the lower portion of the abdomen, which is less sensitive.

(*β*) **Operative Shock from Anæsthesia.**—Arterial pressure is liable to more or less sudden increase or decrease in response to the numerous factors which develop during the course of an operation.

The part played by anæsthesia varies according to the anæsthetic employed and the method of administration. During induction of general anæsthesia there is usually a rise of arterial pressure. This is followed by a fall, which is on the whole proportionate to the depth of the anæsthesia, but which varies considerably in degree with the particular anæsthetic. The effects of all anæsthetics partake of the nature of a more or less acute intoxication, which provokes progressive changes in arterial pressure, and if inhalation be prolonged, depresses the systolic to 80 or even to 60 mm. A fatal issue is almost inevitable if the pressure remains at this level for more than twenty minutes. Especially is this true of chloroform, which exerts an almost constant depressor effect on arterial pressure, which falls rapidly and remains low, the only exception being in the case of pregnant women in labour. This fall is almost always definite but rarely reaches very low figures, cases of sudden

death being in all probability more often due to auricular fibrillation than to reduced pressure. Chloroform causes the earliest and most abrupt fall, which begins in about fifteen minutes; ether has a similar but later action in about twenty minutes. König [168] recorded arterial pressures before, during and after operation, and found in several hundred cases that with both chloroform and ether the pressure diminished proportionately to the depth of the general anæsthesia. According to McGlannan, in 40 simple hernia operations ether seldom caused a rise, which even then was never sustained, and about as often caused a fall. Guy, Goodall and Reid,[171] however, maintain that unless inordinate amounts are given, ether tends to raise the arterial pressure, and in subjects with low arterial pressure is the anæsthetic of choice. In most cases ethyl chloride does not appear to lower the pressure. In a hospital study of arterial blood pressure with different anæsthetics recorded in *Rev. Españ de Cir.*, 1922, p. 344, the authors state that their experience with chloroform confirmed the opinion that this drug causes a fall in arterial pressure; with local anæsthetics they found a very slight variation or a rise, and spinal anæsthesia and incision of the peritoneum were accompanied by a fall in both systolic and diastolic pressures.

McGlannan [173] studied the changes occurring in arterial pressure during 394 abdominal operations and found that in 60 per cent. of cases under general anæsthesia, manipulation was accompanied by a fall in pressure, especially when ether was given. In 35 out of 50 cases of acute appendicitis opening the peritoneal cavity caused some fall in arterial pressure, which became pronounced after manipulation. When complicated by peritonitis, sensitiveness to anæsthetics as well as to peritoneal manipulation was increased by 50 per cent. Gall-bladder operations and hysterectomy gave similar results. In gastric operations a rapid fall of pressure occurred on opening the peritoneal cavity. Manipulation in the upper quadrant of the abdomen caused a more frequent fall of blood pressure than those in the lower portion of the abdomen. In 40 simple hernias nitrous oxide and oxygen caused a rise of from 10 to 30 mm., continuing during operation. In half the other cases there was either no primary

change, or if this took place it was not sustained. Nitrous oxide and oxygen can be given for two hours, in the absence of shock, without causing any material change in either diastolic or systolic pressure, but after two hours a late and progressive fall occurs which differs from that produced by ether, because the fall stops as soon as the anæsthetic is discontinued and within a few minutes the arterial pressure rises nearly to normal.[174]

Rapid induction of anæsthesia, an excessive quantity of anæsthetic, especially during a lengthy operation, rough manipulation of viscera, sudden changes of posture as from the lithotomy to the Trendelenburg position, and hæmorrhage during operation, all make for a fall in arterial pressure, which will often pass unobserved if no attempt is made to record it.

(γ) **Operative Shock from Hæmorrhage.**—The remarks made in the preceding paragraph under hæmorrhage are applicable to this condition.

(ii.) *From Operations under Regional Anæsthesia.*—In regional as in general anæsthesia the arterial pressure as a rule is but little altered. Wiemann [175] ascribes to difficulty of absorption of the anæsthetic the slight influence on arterial pressure during operations for hernia under a local anæsthetic. In the case of operations for goitre under local anæsthesia the conditions are distinctly dissimilar, and both arterial pressure and pulse rate show extreme variations. In the majority of cases a drop of 41 to 80 mm. was recorded, and in some instances it reached 100 to 120 mm.[176]

In spinal anæsthesia no absolute relation between intrathecal and arterial pressures has been determined. Coincidently with the lumbar puncture there is usually a brief rise of arterial pressure, which undergoes different modifications according to the medullary level concerned. König and Wiemann [168] have observed a fall during intraspinal anæsthesia, and this fall is even greater when paravertebral anæsthesia is induced in the cervical or thoracic regions of the spinal cord. Such intense disturbance of the circulation explains many mishaps and shows the necessity of waiting for the circulation to regain its balance before proceeding with the operation.

A sudden drop in arterial pressure during *aspiration of the pleural cavity* is regarded by Capps and Lewis [177] as indicative of reflex inhibition of the vasomotor centre or heart.

(*f*) **Shock consequent upon Anaphylaxis.** — (i.) *Specific Anaphylaxis.*—It is now generally recognised that no ill effect is likely to follow intravenous or subcutaneous injections, or entrance through the intestinal or respiratory mucous membrane, of ordinary doses of a heterogeneous albuminoid substance, *i.e.*, a protein foreign to the body tissues, but that a second administration, even of quite a small amount, following after a few days an initial dose sufficient to promote the onset of intoxication, will induce a series of blood changes with later symptoms together known as anaphylaxis.

Anaphylactic shock, known also as "protein," "peptone," or "antigen" shock, is characterised chiefly by low arterial pressure, which in severe cases may descend to as low a level as 50 or even 40 mm., the other symptoms being dyspnœa, collapse, gastro-intestinal disturbances, and finally convulsions.

Garrelon and Santenoise [178] from their observations conclude that the vagus is a factor of great importance in determining the susceptibility to protein shock, particularly by its excito-secretory action upon the thyroid apparatus. The vagus is considered to regulate the flow of thyroid secretion into the circulation, and even, perhaps, the production by this gland of the substance whose presence in the blood augments the susceptibility of the organism to protein shock.

(ii.) *Non-specific Anaphylaxis.*—In contrast to the specific form, non-specific anaphylaxis needs no preliminary sensitisation. Its phenomena are similar, but much milder in degree, and originate in association with a host of different conditions.

The proof that so many diverse clinical manifestations are traceable to the phenomena of shock is afforded by the *hæmoclasic crisis*, which is evidenced by hypopiesis, variations in blood coagulation time, leucopenia, inversion of the differential leucocyte count, and diminution of blood

platelets. To these signs Widal[179] and his collaborators have added another two, which they deem quantitive. These are : the rutilant aspect of venous blood, and sudden changes in refractive index of the serum.

The hæmoclasic crisis begins immediately the " trigger stimulus " is applied by the provocative agent, and in man precedes the clinical phenomena sometimes by a considerable period of time, during which the patient feels quite well. By the time that the symptoms appear, the blood may nevertheless have recovered its normal character. Widal[180] has been at some pains to emphasise how vast a field in pathology the phenomena of colloidal shock present, the hæmoclasic crisis representing merely the first stage of a far wider crisis which is not confined to the blood stream. To involvement of the whole organism the term " colloidoclasic shock " has been applied, manifested by the typical symptoms of the particular process, *e.g.*, urticaria, asthma, paroxysmal hæmoglobinuria, etc. The same mechanism produces clinical manifestations so diverse as the various accidents due to anaphylaxis, the accidents supervening on parenteral injections, not only of colloids but even of crystalloids, the infective syndromes, such as certain attacks of hyperpyrexia, and the humoral maladies—all these are linked up with the same causal colloidoclasis.

Nitritoid crises may be produced by non-toxic intravenous injection of arsenobenzols used in the treatment of syphilis, probably as a result of a phenolic shock physical in origin and analogous to the fall of arterial pressure registered after intravenous injection of simple phenolic compounds which precipitate the albumins, as do the arsenobenzols. Intensity of shock and degree of decline in arterial pressure are more considerable in proportion as the solutions of phenolic compounds are more acid, and therefore have a greater precipitating effect on the albumins.[181]

In the light of these and other observations the most recent theory of shock propounded by Waud[182] is of considerable interest and significance. In an experimental study of shock from anaphylaxis as well as from injection of toxic agents, this investigator has noted a reduction in blood viscosity. Waud holds that a fall in viscosity induces a fall

in arterial pressure because the less viscid blood passes more readily through small arterioles, and thus the pressure and blood volume in the capillaries show a sudden increase. If reduction in viscosity affects also the endothelial cells of the capillaries, it may conceivably become a contributory factor in the production of œdema in shock. Waud's experiments show that lowering of viscosity of the cell surface results in a more rapid diffusion of substances through the cell, and it is thus possible that an initial lowering of blood viscosity in shock may be associated with a lowering of viscosity of the surface layer of the endothelial cells of capillaries, so allowing more rapid passage of the fluid contents of the blood into the tissues, and thereby increasing the amount of fluid in them.

(*g*) **Shock consequent upon Toxic Agencies.**—Though shock may originate from toxic agencies, nevertheless the phenomena of shock differ from those of intoxication *per se*. Whereas intoxication acts by a chemical process which alters the molecules even to the extent of destroying them, shock is connected with a process which attacks elements far higher in the developmental scale.

Cannon and his co-workers,[155] by crushing the muscles of the hind limbs without external hæmorrhage, discovered that an immediate fall in arterial pressure ensued. This was followed by a more gradual decline to the shock level, with decrease in the CO_2 combining power and notable concentration of the blood. These effects could not have been ascribed to irritation of afferent nerves, since they persisted in animals in whom all nerves of the limbs had been severed, nor were the effects due to local loss of circulating fluid, but were dependent upon the discharge into the circulation of some toxic material, for no shock appeared when the vessels of the damaged limb were clamped, only to reappear as soon as the clamp was subsequently removed. Whipple and Hooper[183] found that absorption of a proteose from the constricted loops is responsible for the true protein shock that occurs in cases of intestinal obstruction, and the former observer, on continuing his investigations, discovered that in this condition the non-protein nitrogen of the blood becomes greatly increased by reason of excessive breakdown

of tissue protein caused by absorption into the blood of this proteose. These and other observations strongly support the view that shock can arise from absorption of autogenous toxalbumins, toxic substances of histamine-like nature from tissues, in particular muscles and viscera, such as for example the liver, which have undergone severe damage. Post-partum shock has been ascribed to the same cause.

(*h*) **Shock consequent upon Depressing Physical or Psychical Influences.**—"In human pathology there is one condition, *i.e.*, paroxysmal hæmoglobinuria, in which one can observe shock quite indistinguishable from anaphylactic or protein shock, *without any foreign substance—whether heterogeneous or autogenous, colloid or crystalloid—being introduced into the organism*. The shock in this case is produced entirely by the intermediary of a physical agent, cold." Widal, Abrami and Brissaud [180] studied four cases carefully over a long period, and found that all the phenomena of a typical hæmoclasic crisis preceded the symptoms, which were akin to those of serum shock. The authors indicate the extreme importance of this observation, since the influence of cold underlies such an enormous variety of minor pathological conditions which affect humanity. If it can be proved that cold always modifies the humoral equilibrium in the same way as they have found to be the case in hæmoglobinurics, it is thus a factor of considerable importance.

Clovis Vincent [164] noted that hypopiesis was almost a constant factor in infantrymen who were in the fighting line, and that cold, fatigue and anguish lower arterial pressure considerably. Bosquette and Moulonguet [162] confirmed these findings, and attach great importance to fatigue preceding wounds as an important cause of shock.

(*i*) **Shock consequent upon two or more of the above Factors in Combination.**—Under such circumstances the degree of shock is often greater than in the case of a single factor.

2. Acute Intoxications

If, for any cause, the peripheral resistance becomes diminished, a drop in arterial pressure will ensue, as stated

in Chapter II. Thus, beginning with the vaso-constrictor centre itself, any condition which brings about paralysis of this centre will inevitably induce a notable and serious fall in arterial pressure. In this regard intoxications, either endogenous, such for example as that which occurs during the course of intractable vomiting in pregnancy as a result of infection or of metabolic error, or exogenous, as the result of poisoning by drugs, constitute a potent factor. In both events, should intoxication become sufficiently severe, circulatory collapse will follow. Lesser grades of intoxication produced correspondingly less vasomotor effects.

The following agents are capable of inducing an acute and progressive depression of arterial pressure :—

(*a*) **By Causing Vascular Dilatation through their Action on the Vasomotor Centre.**—(i.) *Through circulatory depression :*—General anæsthetics, especially chloroform, opium and morphia ; chloral hydrate ; snake venins ; the digitalis and belladonna groups in toxic dosage ; cannabis indica ; alcohol ; lupulus.

Delayed Chloroform Poisoning.—An acute and grave intoxication occasionally ensues after narcosis by chloroform, and more rarely by ether, producing clinical and pathological changes closely resembling those of acute yellow atrophy of the liver and phosphorus poisoning.[184] This action is apparently brought about by the liberation of hydrochloric acid from chloroform within the cells of the liver.[185]

(ii.) *Through profuse depletion from the intestines by cathartic drugs, equivalent to venesection :*—Croton oil, elaterium, colocynth, jalap, scammony, podophyllin, calomel.

(*b*) **By Impairment of Respiratory Capacity and Lowering of Oxidative Processes :**—Irritant and asphyxiating gases, such as chlorine, etc. ; cyanogen.

The effects of poisonous gases are dual : by acute irritation leading to acute inflammation of the lung tissue with consequent toxic effects, and by a greater or less degree of asphyxiation. In poisoning by cyanogen, which acts by impairing oxidation, the alterations in protein metabolism are akin to those of poisoning by phosphorus. Lusk[186] found no lack of general oxidation in phosphorus poisoning,

but this does not mean that local alterations do not depend upon local impairment of oxidation.

(*c*) **By local dilatation of peripheral vessels, when administered perorally or by inhalation :** The nitrite group.

(*d*) **By Food Poisoning.**—(i.) *From meat and fish, due to the products of bacillary action (toxins), or of putrefaction (ptomaines).*—An acute gastro-enteritis with acute hypopiesis is thereby frequently set up, whilst a rare form, botulism, due to sausage poisoning, results in nervous symptoms and general muscular weakness. Shell-fish eaten by susceptible individuals produce symptoms varying with the particular poison. Mussel poisoning, for example, causes symptoms of rapid and acute collapse, often with urticaria, due to mytilotoxin, a bacterial ptomaine. Oysters and crabs may also cause a gastro-enteritis.

(ii.) *From Edible Fungi.*—Mushrooms cause manifestations in sensitised subjects similar to those produced by muscarin.

In all these cases the arterial pressure becomes low.

Diffuse Toxic Necrosis (Acute Yellow Atrophy) of the Liver.—Acute hypopiesis occurs in this condition, whose ætiology is in all probability non-specific, for numerous intoxications, notably septicæmia (particularly the streptococcal forms), acute syphilis, puerperal eclampsia, phosphorus, arsenic, the nitrophenols, and mushrooms, induce autolytic changes in the liver closely resembling those of diffuse toxic necrosis.

" In typical cases of ' acute yellow atrophy ' of the liver, the poisonous agent possibly comes from the intestinal canal, as indicated by a preliminary period of gastro-intestinal disturbance, and secondly by the fact that the liver seems to receive the chief effect of the poison. Whether these hypothetical poisons are produced by abnormal fermentation and putrefaction in the intestinal tract, or by a specific organism elaborating its poisons in this location, is quite unknown. Bacteriological studies of this disease have so far given inconstant and non-instructive results. The atrophy is due entirely to autolysis of necrotic liver cells by their own enzymes, continued until there is so much loss of liver function that systemic poisoning results from the hepatic insufficiency and from the resulting accumulation

of poisonous products of incomplete metabolism."[187] In certain cases of acute hepatic necrosis the blood yields the highest amino-nitrogen figures recorded for any disease. The amino-acids which appear in the urine are probably derived partly from liver autolysis, partly from amino acids produced both in the intestine and within the body during tissue metabolism, which the liver cannot transform into urea as it usually does.

3. Acute Circulatory Disorder

(*a*) **Premature Contractions.** — (i.) *Single.* — Acute low arterial pressure originates either as a result of the long pause during the cardiac cycle following a premature contraction or from actual weakness of ventricular systole. Such fall of pressure is proportional to the greater or less gravity of the original condition.

A definite drop in arterial pressure has been found to happen simultaneously with *isolated premature contractions.* In such instances the duration of low pressure is too brief for it to be associated with nervous symptoms, although sensitive subjects may become conscious of transitory sensations of fluttering in the chest or of giddiness. Busquet's[188] experiments on dogs show that systolic hypopiesis induced by an isolated premature contraction can reach 30 mm. of mercury.

(ii.) *Serial.*—More serious troubles become manifest when *a series of premature contractions occurs,* in which case faintness or actual syncope may coincide. Merklen[189] has noted this in the subjects of mitral disease. Similar observations have also been published by Ortner and by James.

In two patients with painful paroxysmal attacks Gallavardin was able to obtain electrocardiograms at the moment when radial pulsation could no longer be detected by the finger. Tracings showed successive extrasystoles at brief intervals, these, however, being insufficient to maintain the arterial pressure at a level requisite to ensure an adequate blood flow through the cerebral centres.

(*b*) **Adams-Stokes' Syndrome (Heart Block).**—A still

further development may be seen in the excessive slowing or prolonged ventricular asystole which occurs in association with Adams-Stokes' syndrome during the period in which complete heart block is in course of evolution. During transitory blocks of a second or so sudden anæmia of nerve centres is attended by fleeting confusion analogous to that which occasionally appears in cases of aortic regurgitation. Should the block last more than five seconds, more or less syncope and even epileptiform seizures may ensue.

Busquet [188] has demonstrated that, by experimental compression in dogs of the aorta at its source, similar attacks may easily be induced, whilst from 1842 onwards Erichsen,[190] Panum,[191] and von Basch with his pupils, by ligature of the coronary arteries or their branches, have proved the sequence of a drop in systolic pressure, with pulse irregularity and a rise in pressure in the left auricle and lungs, with resultant œdema and death. On tying one of the larger coronary branches, systemic pressure and cardiac output both manifest an immediate fall, the venous pressure begins to rise, and dropped beats to appear. The later researches of Porter [192] accord with these early observations.

(*c*) **Acute Carditis.**—In acute carditis of infective origin the heart becomes weakened through lessened vasomotor tonicity. Ventricular contractility is thereby greatly diminished, with resultant production of feeble and rapid heart sounds, canter rhythm and pulsus alternans. In the great majority of these patients a low systolic pressure is found, this being still further reduced in severe cases proportionately to the gravity of the infection. In a small proportion of cases of cardiac rheumatism the arterial pressure is persistently raised.[193]

In tuberculous pericarditis with effusion arterial pressures are usually low, and fall progressively to low levels, such for example as 64 mm. systolic and 38 mm. diastolic, during the continuance for several weeks of remittent or intermittent fever, rising again gradually with amelioration of the tuberculous process to more normal levels.

(*d*) **Acute Cardiac Insufficiency.**—In acute cardiac insufficiency arising from rapid degeneration with consequent

dilatation of the myocardium, apart from intercurrent nephritis or arteriosclerosis, which tend to maintain a rise in systolic and diastolic pressures, both systolic and diastolic pressures fall. Under ordinary circumstances, in response to increase in circulatory demand, the systolic pressure rises disproportionately to the diastolic, with a corresponding increase in the differential pressure in order to cope with the augmented cardiac load. Failure of the systolic and differential pressures to rise serves as an index of the degree of myocardial degeneration. When the cardiac reserve, already depleted by myocardial insufficiency, is no longer adequate to support the overload, the systolic pressure falls usually to a greater extent than the diastolic and thus marks the onset of cardiac failure.

(*e*) **Acute Vasodilator Crises.**—Transitory acute crises of hypopiesis can arise as the result of local vasodilatation, particularly in the splanchnic area, whereby the whole of the intra-abdominal contents may become affected. Such crises may be connected with a speedy fall of intra-abdominal pressure induced by injudicious tapping for ascites, removal of a large mass from the abdomen or evacuation of an intestine loaded with fæcal matter. Compression of the portal or caval veins may also bring about a vasodilator crisis, which also may accompany the abdominal crisis of tabes and the acute solar syndrome which arises from paralysis of the abdominal constrictors.

(*f*) **Angina Pectoris.**—Despite the fact that angina pectoris is often accompanied by hyperpiesis as an expression of sympathetic irritation arising from a segmentary neurosis (Langley), yet numerous instances have been observed in which seizures have occurred during periods when arterial pressures registered low normal standards.

At times during crises arterial pressures fall, regaining standard levels after cessation of the attack.

As a rule, however, during the anginal spasm, a slight initial rise in arterial pressure takes place for a few minutes, after which arterial and venous pressure stand at lower levels than those which obtain during interparoxysmal periods. "As in the prodromal stage of vomiting, the bulk of the blood stream is withdrawn from the peripheral system of

vessels, and lodged in dilated arterioles, capillaries, and venous lacunæ of the splanchnic system of vessels." [194]

As soon as general recognition is accorded to the fact that the stimulus to pain production in angina pectoris is of varied origin, whether arising in the coronary arteries, the myocardium itself,[195] or rarely in the supra-sigmoid aorta,[196] it will then become easier to assign to each type of manifestation its corresponding form of arterial pressure.

Probably the referred pain of angina is of visceral and not of parietal origin, as certain observers claim, but the imminence of the anginal spasm during digestion has not yet been satisfactorily explained.

4. Acute Respiratory Disorders

Acute Rhinitis, Tracheitis, Bronchitis.—In the acute stage of infectious diseases involving the respiratory tract, transitory low arterial pressure is the rule. This is the case in acute rhinitis and in bronchitis, where symptoms of chilliness, cold extremities and shivering are complained of, in conjunction with a temperature either normal or subnormal.

Respiratory symptoms are of frequent occurrence in several of the fevers. In 500 cases of enteric fever Barach [197] found symptoms and physical signs of bronchitis in 20 per cent. and of pneumonia in 5 per cent. Hypostatic congestion of the lungs is frequent.

B. In Association with Subacute Conditions

What has already been said concerning acute conditions applies also, but in less degree, to those that are subacute. Hence it has not been deemed requisite to deal with these latter in detail.

II. Congenital and Persistent

C. In Association with Chronic Conditions

1. Congenital or Constitutional Psychasthenia.—Psychopathic heredity constitutes the essential and constant factor in the class of congenital or constitutional psychasthenias, which may be regarded as states of neurasthenia with added

obsessions. This class is in reality small, for, in the majority of cases, by diligent search the original trauma (mental shock) inducing the condition can be raised by appropriate psychotherapy to the level of consciousness. At times neurasthenic symptoms are dominant, in others obsessions are well to the fore.

Psychasthenia should not, however, be classified under the heading of neurasthenia, for neurasthenic symptoms, even if dominant, are secondary to the causes which induce the obsessions.

2. Congenital or Constitutional Neurasthenia.—Neurasthenia of congenital origin causes undue leakage of nervous energy, evidenced by symptoms of insomnia with profound mental and physical fatigue, in combination also with heightened sensitiveness to minimal stimuli and weakening of the conscious will.

In both these classes low arterial pressures are the rule, the systolic ranging between 75 and 115 mm. in a large series investigated by the author, with a parallel diminution in the level of the diastolic pressure. Occasionally a systolic pressure may be found as high as 120 mm., but such cases are exceptional.

3. Congenital Syphilis.—In congenital syphilis an inherited cardiovascular hypoplasia frequently forms an integral part of a general state of maldevelopment, evidenced by defects in the teeth, palate, abdomen, etc., which induces nutritional disturbances. Such subjects are prone to exhibit a weak and flabby musculature, along with deficient oxidative capacity and tendencies to early degeneration of arteries (sclerosis and atheromatous plaques) and of veins (varices and varicose ulceration).

III. Acquired and Persistent

1. In Association with Acquired Neurasthenia.—The symptom-complex of *status neurasthenicus* may be looked upon as the expression of nerve-exhaustion. It is of gradual onset, alike for childhood and adolescence as for adult age, in subjects who frequently manifest no evidence of organic disease. The vasomotor centre is thrown out of gear,

hence the border line between marked neurasthenia and the slighter degrees of collapse and shock is not always easy to define.

The chief symptoms are those of low arterial pressure, insomnia, lack of interest and concentration, defective memory; despondency sometimes amounting to hypochondriasis; headaches and feelings of pressure referred to the vertex of the skull, or of constriction round the forehead; increased sensitiveness, especially of the eyes, with sensations of flashes of light, backaches, and vague pains in other parts of the body and limbs.

This condition is frequently coincident with loss of weight, muscular atony and diminished reflexes. A special and obstinate form is found in subjects prone to disturbance of glandular secretion, in which the gastro-intestinal tract is mainly implicated with resultant distension of stomach and colon, often with resultant tachycardia and still lower arterial pressures. The cause is probably either a primary toxæmia of intestinal origin, or exhaustion of the vagus centres allied with endocrine-autonomic lack of balance, whether of congenital origin or arising from some acute infection. Such individuals suffer from metabolic errors of assimilation, and biochemically show deviation of the acid-alkali urinary ratio to the alkaline side.

Low arterial pressure is the rule in acquired pure neurasthenia, the systolic pressure being habitually not more than from 80 to 120 mm., with corresponding reduction in the diastolic pressure. When mental depression supervenes, the pressure is usually very low. Should arterial pressure, however, be found normal or raised, one should search for some organic complication, which will usually be discovered either in the arterial system or the kidneys.

These groups should be carefully differentiated from the large mass of the anxiety neuroses and from hysteria. In the latter condition there is no constancy in the arterial pressure, which may be high, medium or low. "Generally speaking, we may say that the vasomotor disturbances of neurasthenia are those of dilatation and hypotension, while those of an anxiety neurosis are of constriction and hypertension." [198]

A frequent example of the low pressure type of nerve exhaustion is seen in " captains of industry " who have been striving with might and main to put through some large business deal in which important interests are involved, and in stockbrokers harassed by rapidly fluctuating markets. In reality, such individuals belong to the relatively low pressure type, since in earlier periods their condition is one of nervous excitability and irritation—an anxiety state—which later culminates in a condition of absolute nervous exhaustion.

Acquired hypopiesis frequently results from a combination of circumstances. Devitalising chronic or acute maladies of organic nature in combination with nervous strain serve to upset the balance. Thus a doctor, the subject of chronic appendicitis of some years' standing, underwent a stage of gradual exhaustion through insufficient and poor food supply, together with induced adrenal depletion, as the result of dangerous and distressing experiences whilst tending the victims of war and famine in Poland, finally manifesting definite and persistent signs of hypopiesis.

Other notable instances of nervous exhaustion leading to acquired hypopiesis were seen during and after the Great War in men who took part in strenuous fighting, and in those who for long periods were left unrelieved in front line trenches. Continuous exposure to danger and noise by night as well as by day, the depressing influences of cold and damp, of emotion and poor food, all played a greater or less part according to individual circumstances in lowering the psychical resistance and arterial pressure, the systolic being in most cases lowered disproportionately to the diastolic, with consequent reduction of the differential pressure.

In the Air Service similar effects were noted, the systolic pressures of observers and pilots being found during several days up to a month continuously below 100 mm. In fatigued aviators, as well as in soldiers overdone by prolonged trench warfare, Josué observed the existence of " the white line." [199]

2. In Association with Insanity.—Different forms of insanity are associated with different levels of arterial pressure, which is thus regarded by Sir Maurice Craig

and others as affording information of much diagnostic value.

Arterial pressure is chiefly influenced by the emotional as opposed to the ideational forms of mental disorder. In states of mental depression and simple melancholia arterial pressure is often heightened, whereas in states of excitement attended by motor restlessness and in acute mania the pressure is usually low, returning to normal after the excitement has become allayed.

As the day advances the melancholic improves, whilst the excited patient becomes more excited. The feeling of pressure on the top of the head, so common in melancholia, is vascular in origin, and is lessened or disappears when arterial pressure is lowered by erythrol tetranitrate or other means.[200]

In delirium tremens the pulse is rapid and of low tension, and in fatal cases it is usually the heart that gives out.[201]

At the onset of dementia præcox the pulse is frequent, and at times irregular. The arterial pressure is usually low; in depressed cases it is raised. Dr. John Turner, of Brentwood Asylum, found arterial pressure raised in 30 per cent., lowered in 30 per cent., and normal in 40 per cent.[202]

In all states of mental exhaustion, whether combined with excitement or with depression, and in cases of stupor the arterial pressure is low. Similarly, hypopiesis is the rule in the excited state of general paralysis of the insane, and in the later stages of all types of this malady.

CHAPTER IX

Low Arterial Pressure in the Presence of Acute Organic Disease

In Association with Acute Specific Infectious Diseases

The main reasons why low arterial pressure is so frequent an accompaniment of acute infectious processes have thus far been insufficiently appreciated. To these acute infections much careful thought and study have been devoted, but writers for the most part, having given to a particular incidence of symptoms its special label, and having arranged it in its fitting place as a member of a causal sequence, have been satisfied there to leave the matter.

It will be noted that in a subsequent section, which deals with the association of low arterial pressures with tuberculosis, the author from his numerous investigations in this disease has been enabled to state that the readings of arterial pressure recorded by many previous observers are entirely fallacious. So far the author has not had the opportunity of directly recording such a large mass of figures for the acute infective maladies, and has, therefore, been obliged to include in the following pages the results of other observers. The reader, however, who has become imbued with the author's opinions, which have been crystallised in the form of his Biological Law of Arterial Pressures, will probably call these opinions and figures of other writers in question. It is more than likely that the same Law applies to all infective processes. An acute and active reaction to an acute infection, when successful, at this early stage is invariably accompanied by **a rise in arterial pressure of short duration, and very liable to be overlooked** unless pressure tests are made at regular intervals under standard conditions of observation, in correlation with the temperature chart and with clinical and biochemical findings, which does not appear to be the case in any of the figures of the various

observers that have been passed in review. Haphazard observations are thus not only a waste of time, but serve to mislead. Unsuccessful reaction to an acute infection, as well as the stage of depression during convalescence, are accompanied by a fall in arterial pressure, which usually lasts for a much longer time than the duration of the rise.

The chief exceptions to the initial rise above mentioned, to which the author has not succeeded in finding any reference but his own, are found in true influenza and diphtheria, where, by reason of the potency of the depressant toxin, the shorter incubation period, and the rapidity of onset, the pressures fall, sometimes to extraordinarily low levels.

At the onset of most of the other acute infections arterial pressure tends to rise, but when the augmented deviation in the direction of acidity produced by acute reaction to the infection begins to decrease—which often happens on the second day of the disease—then frequently the arterial pressure is found to drop coincidently.

The chief causes of hypopiesis in association with acute infective processes are as follows :—

1. Because hypopiesis in general has received scanty notice, far too little attention has been directed to the effect of the acute infections upon the glands of internal secretion. This effect may not only be transitory, but in many cases becomes permanent.

2. Another cause of hypopiesis is the slowing of the rate of blood flow in the arteriolo-capillary system which takes place during the febrile period.

3. A third cause is found in the weakening of splanchnic tone by reason of toxæmia.

4. Should infection be sufficiently acute or prolonged, toxic effects of the nature of cloudy swelling or brown atrophy become manifest in the myocardium. In the parenchymatous form the heart muscle becomes pale and soft, with granular degeneration of its fibres ; in the interstitial form small round cellular infiltration occurs between the muscle fibres, which themselves undergo degeneration. Should the infection be long continued, these acute manifestations may progress into chronic interstitial myocarditis.

Herein lies the keynote of the problem, since it is only by a realisation of the endocrine disturbances induced by depletion of certain hormones, especially those of the adrenal and thyroid glands, during acute or continued febrile attacks, together with simultaneous upset in the balance of endocrine katabolism and anabolism, that one can form an adequate conception of the causation of hypopiesis and other symptoms of depression under such conditions.

In point of fact, the acute infections form a notable example and illustration of the author's law that hypopiesis constitutes an expression of low vitality.

In the following pages the acute specific and non-specific infectious diseases will be found grouped under their ætiological headings, the diseases themselves being arranged as far as possible in descending order of importance in their relation to low arterial pressure.

(*a*) Microbic Infections

(i.) **Cholera Asiatica.**—Cholera Asiatica is one of the acute specific infections which manifests a considerable drop in arterial pressure. During the algid stage the pressure is notably depressed as a result of the loss of plasma from the circulation, whereby the total blood volume is diminished. In fact the death rate in this disease has been found to be directly proportionate to the amount of fluid lost. The actual severity of a given case may best be estimated by the degree of concentration of the blood according to the glycerine and water specific gravity tests of Lloyd-Jones. Sir Leonard Rogers,[203] by centrifugalising defibrinated blood in a hæmocrite, was thus enabled to measure the relative percentages of corpuscles and serum. In a typical, very severe case, instead of the normal figures for Indians of 45 per cent. of corpuscles and 55 per cent. serum, 71 per cent. of corpuscles and only 29 per cent. serum were found, indicating a loss of two-thirds of the fluid portion of the blood. Mild cases showed an average loss of 35 per cent. serum, collapsed cases a loss of 52 per cent., with recovery after hypertonic saline intravenously, whilst the most severe class showed a loss of 64 per cent., and all these terminated fatally. This writer made a series of observations with the Brunton

sphygmomanometer, noting pulse obliteration at the wrist, and found that in patients with cholera the systolic pressure was invariably below 70 mm. on admission to hospital, and commonly as low as 50 to 60 mm. In extreme collapse it is too low to be measured at the wrist, and such cases formed over one-third of the admissions to Calcutta Hospital. Observations were mainly made on native patients, whose normal blood pressure is only from 100 to 120 mm.

If the systolic pressure remained below 100 in adult males for two or three days after the collapse stage was over, uræmic symptoms almost invariably developed and proved fatal unless the pressure could be raised to over 105 mm.

(ii.) **Enteric Fever.**—Next to typhus fever and cholera, in which the pressure may be lowered to such an extreme degree that it becomes impossible to estimate, of all acute infections enteric fever is the one which causes most frequently the greatest reduction in arterial pressure. Huchard [204] (1889) was the first to note the tendency of enteric fever to cause lowering of blood pressure, and pointed out that this drop could be recognised not only by the dicrotism and compressibility of the pulse, but also by a feeble first sound of the heart, diminution of the second aortic sound and fœtal heart rhythm. Vasomotor and to a less extent cardiac factors are probably both responsible for the reduction.

Alezais and François [205] investigated 150 cases with Verdin's instrument and confirmed the views that Huchard had expressed. Potain [206] observed that enteric fever causes a greater reduction in arterial pressure than does any other acute disease, and that the arterial pressure does not appear to bear any relation to severity of the malady. Teissier,[207] working with Potain's instrument, concluded that in twelve cases a normal or raised pressure was of bad omen as indicating a prior pathological factor. Apart from this, nevertheless, raised pressure may be present (*a*) in association with active delirium, high temperature, abdominal distension and flushed face in sthenic cases, which constitute a small minority; (*b*) at the onset of a relapse, when a slight and transitory rise is not infrequent; or (*c*) accompanying inflammatory complications, such as cholecystitis and pleurisy. Durand-Viel [208] examined ten children, aged seven to fourteen

years, with Potain's instrument and found distinctly low pressures even at the earliest stage. The older the child the lower the pressure. So often do very low pressures occur in enteric fever that one comes to look upon a low arterial pressure from 90 to 100 mm. systolic, and from 60 to 80 diastolic, with a differential pressure of 20 to 40, as an almost constant accompaniment. It is present in approximately 94 per cent. of all cases, appearing at the onset of infection or during the first week, and decreasing still further with the duration and gravity of the malady. Frequently it attains its lowest level during the fourth week of the disease. Seldom is it low enough to cause anxiety, and may even be regarded as beneficial. In the stage of convalescence it begins to rise a little, but J. D. Rolleston's [209] study of fifty-eight hospital cases showed that no less than twenty-two of these, or 45·8 per cent., discharged between the fifth and twenty-third weeks of disease, never regained the standard level of arterial pressure for their age while in hospital. Towards the termination of the illness a systolic pressure of 80 mm. is not infrequent, while it may even fall as low as 65 mm. Such readings imply grave disturbance of the vasomotor centre in the medulla. When associated with insufficiency of the heart muscle, in the absence of cardiac failure the pulse pressure is usually large, and the systolic may be raised to 120 or 130, possibly by reason of myocardial irritability.

The progressive character of the fall in systolic pressure is well seen in the following sets of figures, given respectively by Janeway [210] and Barach [197] (81 cases, 4 readings daily).

TABLE III

Showing Progressive Fall in Systolic Pressure during the Course of Enteric Fever

—	Janeway.	Barach (1907).
	mm. Hg.	mm. Hg.
Systolic pressure in 1st week . .	115	93
,, ,, 2nd ,, . .	106	92
,, ,, 3rd ,, . .	102	83
,, ,, 4th ,, . .	98	83
,, ,, 5th ,, . .	96	85
,, ,, 6th ,, . .	90	—

Reduction involves both the maximal and minimal pressures, more especially the latter. This sign is so constant that its determination has in certain cases a diagnostic value. During the typhoid state exaggerated reduction of pressure, especially of the maximal, usually heralds some complication and may cause one to suspect the incidence either of myocardial failure or of intestinal hæmorrhage.

On arterial pressure anti-typhoid inoculation exercises also a depressant effect. In perforation, in the absence of association of the vasomotor centre, the irritated peritoneum is stated to cause reflex vaso-constriction with abrupt rise in arterial pressure,[212] which later gives place to a pressure which is definitely subnormal. In striking contrast to this general opinion, Knyvett Gordon [213] writes: "I have never observed the rise in pressure that is said to occur at the onset of perforation, though I looked out for it for the reason that I always submitted cases in which perforation had occurred to laparotomy at the earliest possible moment, and therefore availed myself of any sign that might be of assistance in diagnosis."

When defervescence is established a rise often initiates a relapse of fever.

A definite drop in the arterial pressure is also a part of the evolution of paratyphoid fevers, in which extremely low readings have been recorded for patients who, nevertheless, made good recovery.[214]

In treatment, the study of arterial pressure will be found of much use as pointing out the need for stimulation.

J. D. Rolleston [209] has reviewed the literature of enteric fever and has added thereto the results of his personal investigation of fifty-eight cases, thirty-nine males and nineteen females, all of whom, except fourteen below the age of fifteen, were adolescents or adults. The clinical diagnosis in each case was confirmed by Widal's reaction and the systolic pressure alone was estimated by the Riva Rocci method. Rolleston's conclusions are as follows:—

1. The systolic pressure was subnormal in 93·8 per cent. of cases, the extent and degrees of the depression being in direct relation to the severity of attack.

2. The systolic pressure of females showed a decided

tendency to keep at a lower level than that of the males. (Contrary to diphtheria and scarlet fever.)

3. 45·8 per cent. of those discharged from hospital from the fifth to the twenty-third week of disease, whilst in hospital never regained the normal systolic pressure for their age.

4. In the majority the systolic pressure fell below 100 at some period of the disease and was higher in convalescence than in the acute stage.

5. In 93·1 per cent. of convalescents readings in the recumbent or erect position were the same, and the recumbent was higher than the vertical record till convalescence was firmly established.

6. Intestinal hæmorrhage and myocarditis caused a considerable fall; cholecystitis and pleurisy were accompanied by a transient rise.

Rolleston concludes that, though not essential for successful management, sphygmomanometry furnishes interesting illustrations of the profound effect on the cardiovascular system by the toxins of typhoid fever.

Not infrequently the author has noted that arterial pressure is lowered for a considerable time, even up to several months, after the subsidence of pyrexia. Hypotonia is often present, as well as hypopiesis. This observation accords with the experience of several clinicians who have found evidence of myocardial degeneration to persist during the "post-typhoid state," and with greater frequency and intensity for much longer time than is perhaps generally realised.

(iii.) **Diphtheria.**—The systolic arterial pressure in diphtheria, particularly in children, has been studied by several investigators. Since Friedemann [215] in 1893 the investigations of Durand-Viel [208] on fifty-five children, and of Denis [216] on 400 children, confirmed by the clinical observations of Knyvett Gordon [213] during 1901–9 at the Manchester City Fever Hospital, indicate that in every variety of diphtheria, whether mild or severe, a fall of pressure took place, which persists well into convalescence, the fall being relatively more definite in elder children and in severe forms of the disease, especially when attended by myocardial complications or early general paralyses, Knyvett Gordon

states that diphtheria patients ready for discharge have almost always a lower systolic pressure than those who have suffered from scarlet fever. Other observers, including Taddei [217] and Weigert,[218] have found that in mild and uncomplicated cases the pressure was almost unaffected; in cases of moderate severity the depression was slight and brief; while in toxic and fatal cases very low pressures were registered.

J. D. Rolleston [219] investigated with the Martin sphygmomanometer the systolic pressure of 179 patients in the Grove Fever Hospital, all but fifteen being children, the ages of the remainder varying from fifteen to forty-seven years. Ninety were males, eighty-nine were females. The arterial pressure was lowered in sixty-three (35·1 per cent.) of these, the extent and duration of the depression having as a rule a direct relation to the severity of the faucial attack. The highest readings were usually found in the first and the lowest in the second week of the disease, the pressure reverting to the normal by the seventh week. In laryngeal cases disproportionately high readings for the age were obtained, especially when the dyspnœa was apparent enough to require operation. Relief by tracheotomy was followed by an immediate and steep fall of pressure (20 to 40 mm.). Albuminuria was accompanied either by a fall or by no change in the arterial pressure, except in a case of uræmia in which the pressure was high. In early paralysis arterial pressure tended to fall, but in late paralysis was for the most part not affected.

The reason for this progressive fall in arterial pressure is not yet conclusively determined. In many cases it appears to depend upon paralysis of vessels in combination with increasing cardiac failure, the effect of the diphtheria toxin being manifest chiefly upon the cardio-inhibitory centres. These cases are characterised by uncontrollable vomiting, rapid pulse and collapse, and in such the systolic pressure drops to an alarming extent, in a few instances a distinct drop taking place before the onset of vomiting. Otherwise in diphtheria the arterial pressure depends largely upon the state of the heart. In cases characterised by dilatation of the left ventricle—presumably due to defective functioning of

the nerves supplying the cardiac muscle—the pressure remains low. A further effect of the diphtheria toxin is apparent in the diminution of the pressor content of the adrenal glands.

Considerable light has been thrown upon these various factors as a result of recent experimental work upon the temperature and arterial pressure during acute and sub-acute experimental diphtheria. A useful survey of these investigations may be found in the report on Diphtheria of the Medical Research Council Bacteriological Committee, London (1923).

(iv.) **Influenza.**—Of the acute infectious diseases of the northern temperate zone, influenza is the one in which the lowest levels of arterial pressure may in certain epidemics be reached. One great characteristic of true influenza is to be noted in the pulse, which is small, soft and, so long as the patient is at rest, only quickened in moderate degree. Inequality of the beats with dicrotism may be manifest. This instability is continued into convalescence, the pulse rate being liable to rapid quickening under the influence of a minimal amount of exertion or even of movement, especially in sudden change of posture from horizontal to vertical. In other instances, especially in the low arterial pressure accompanying post-influenzal depression, bradycardia with slow pulse becomes a notable feature. Influenza lowers arterial pressure by disposing to cardiac hyposystole or even to asystole.

In grave forms of influenza during the epidemic of 1918, Tixier [220] has observed a drop in systolic pressure to 100 or even to 90 mm., and of the diastolic to 70 or even 50 mm., along with vomiting and the production of the "white line." During the same epidemic Levinson [221] made daily observations upon fifty-five cases which showed a declining pressure to the fourth day of the disease, whilst Barach [31] studied the arterial pressure in a series of fifty hospital cases. For his entire group, the average systolic pressure was 89 mm., and the diastolic pressure 53 mm. of mercury. The lowest systolic pressure was 72 mm., and the diastolic pressure 48 mm. of mercury. In uncomplicated cases the pressure continued to fall during the first, second and third

days of the disease, and began to rise on the fourth day. Typical curves are shown in the accompanying table.

TABLE IV

Typical Systolic Pressure Curves in Influenza. (Barach.)

First Day.	Second Day.	Third Day.	Fourth Day.
115	92	85	112
70	60	60	70
72	60	72	72

This same observer has also noted the tendency to cyanosis displayed in most acute infections; chiefly in influenza, to a less extent but constantly in pneumonia, and also present in enteric fever, diphtheria and erysipelas. Cyanosis and increased respiratory rate mark the degree of respiratory deficit.

(v.) **Pneumonia.**—In lobar pneumonia, lowering of arterial pressure is probably due to the effect of toxæmia upon the vasomotor centres, and, as a rule, takes place only to a moderate extent, notable reduction occurring with less consistency than in the majority of the other acute infective processes. By the correlation of pulse rate with arterial pressure Gibson [222] believed that he had lighted upon a most valuable guide in the prognosis of this disease, and upon this basis formulated what has been termed "Gibson's Law," which affirms that, so long as the systolic pressure in millimetres exceeds the number of pulse beats per minute, the prognosis should be regarded as favourable and *vice versâ*. More recent observers, including Kempmann,[223] Newburgh and Minot,[224] have shown that in the majority of cases Gibson's Law does not hold good, and that deductions drawn from it are likely to be erroneous. Arterial pressure may be raised above normal by various complications, *e.g.*, nephritis occurring during the course of the pneumonic attack.

Howland and Hoobler,[225] using the Faught sphygmomanometer, found that a rise in arterial pressure was always

caused in children of eighteen months to ten years by placing them in cold fresh air during the active stage of pneumonia. This rise did not become manifest until the end of half an hour or more, and attained its maximum two hours after the children had been put out of doors. The effect lasted for thirty hours, with no fall in pressure until the patients were moved back again into a warm, well-ventilated room. The pressure fell in fifteen to twenty minutes, reaching its minimum in one hour. The cause is attributed to reflex stimulation of the vasomotor centre by the action of cold air upon the skin of the face and the nasal mucosa.

(vi.) **Cerebrospinal Fever.**—At the onset of infection mild and moderate cases manifest little change in arterial pressure; in acute types, especially when a purpuric rash is present, the arterial pressure is usually much diminished, not infrequently being too low to record. Of twenty-six patients examined on the first and second day by Fairley and Stewart,[226] nineteen exhibited a systolic pressure below 120 mm. of mercury; in the remaining seven the pressure was above this level. Of the former, seventeen died; of the latter, only one. Low arterial pressure during the first two days is of grave import.

In all types of cerebrospinal fever, serial arterial pressure records of the systolic pressure show an average level below 120 mm. of mercury. Cases with a continued systolic pressure above 120 mm. are uniformly more fatal than those in which the average pressure is below this level. Rapid variations may occur even within twenty-four hours.[227] In children up to the age of puberty, with the onset of severe meningitis, the arterial pressure frequently reaches a considerable height, which with subsidence of symptoms returns to a moderate level.[228]

All severe infections produce a general fall in arterial pressure, the low degree of which is a clinical indication of the severity of the process. This and the fact that the fulminating type of cerebrospinal fever represents a severe blood infection by the meningococcus would amply account for the diminishing arterial pressure and muscular flaccidity which is almost invariably present towards the end in all cases which terminate fatally. During the coma that

precedes death the curve of arterial pressure falls rapidly. Since, however, hæmorrhagic adrenalitis is by no means always present at autopsy in fulminating cases, it is probable that generalised toxæmia constitutes a more important fact in arterial pressure reduction.

(vii.) **Malta Fever.**—Malta fever is an acute specific infection of septicæmic type due to *M. melitensis*, conveyed by goat's milk, and endemic along the Mediterranean littoral, with sporadic instances in the tropics and in goat-rearing districts. Infection is characterised by irregular undulations of temperature lasting from one to three weeks, with apyrexial intervals over a total period of six months or longer, even up to two years. Other noteworthy clinical features are profuse sweating, neuralgic pains, joint affections, constipation, enlargement of the spleen, headache and dyspepsia. As the disease advances, progressive and often prolonged lassitude and anæmia ensue in association with considerable and progressive lowering of both systolic and diastolic arterial pressures.

(viii.) **Septicæmia.**—Septicæmia is characterised by the presence and multiplication of micro-organisms in the blood and tissues, apart from demonstrable metastatic foci of suppuration. The causal pathogenic organisms are varied: streptococci are the most common, whilst staphylococci, pneumococci, coli-typhoid and other bacilli are of less frequent incidence. Rigors and sweating, with high daily irregular fever, a total leucocytosis (except in grave cases), with a relative increase in polynuclear cells, great prostration and rapid wasting are prominent signs. Coincidently there is progressive reduction in both arterial pressures, which sink to very low levels in the acute typhoid type of this infection.

(ix.) **Erysipelas.**—Erysipelas consists in a sharp-bordered spreading inflammation of the deeper layers of the skin and mucous membranes, with local and constitutional symptoms.

In ordinary cases the drop in arterial pressure is slight, but in severe cases may be considerable, and is then probably connected with damage to the adrenal glands as a result of the streptococcal infection, as shown by the concomitant symptoms and *post-mortem* evidence. Low arterial pressure is an early and sure sign of a grave attack.

(x.) **Infective Endocarditis.**—Infective endocarditis for all practical purposes may be regarded as a septicæmia. In a majority of cases it is a local process originating as an accident in various of the acute infections. Its evolution, even when slow, is accompanied by more and more reduction of arterial pressure, figures lower than 100 mm. systolic being not infrequent within the first few weeks.

(xi.) **Acute Toxæmia.**—In contradistinction to septicæmia, toxæmia, acute or chronic, is an expression of the constitutional effects produced by absorption of poisonous products from a site of local infection in which the pathogenic organisms multiply, and from which their toxins enter the circulation. Of acute toxæmia, diphtheria, pneumonia and erysipelas form excellent examples.

Low arterial pressure is usually found as an early and constant symptom of acute toxæmia. It is also present in all cases when such is profound, and towards the end in cases which terminate fatally.

(*b*) Infections of Doubtful Ætiology

(i.) **Typhus Fever.**—In this disease extremely low arterial pressures are usually observed from the first week onwards. In 1917 Daniélopolu and Simici [229] found that typhus fever, especially in its grave forms, was accompanied by notable reduction of arterial pressure, due partly to the vasodilatation so pronounced in many of the patients and partly also to lesions of the adrenal capsules, particularly affecting the medullary substance. These observations were confirmed by Jonescu clinically, whilst the histological researches of Daniel and Scribau [230] brought forward new arguments in support of their contention. The original research was completed by recording at regular intervals the arterial pressures in eighty-four typhus patients during the whole of the febrile period and convalescence. (The Riva-Rocci method was employed in estimation of the maximal pressure and Pachon's oscillometric method for the minimal pressure, taking the last large oscillation during progressive decompression.) These observers found the maximal pressure to be distinctly reduced in typhus fever. The lowest figure

found in the same patient during the whole malady in the majority of cases is about 90 mm. Hg. It rarely exceeds 100 mm., but is often much lower, down to 80 or even 70 mm., these latter figures implying a gloomy prognosis.

The minimal pressure is also usually lowered, but relatively to a less extent than the maximal. It varies around the figure 60, rarely 70 ; in grave cases it may descend

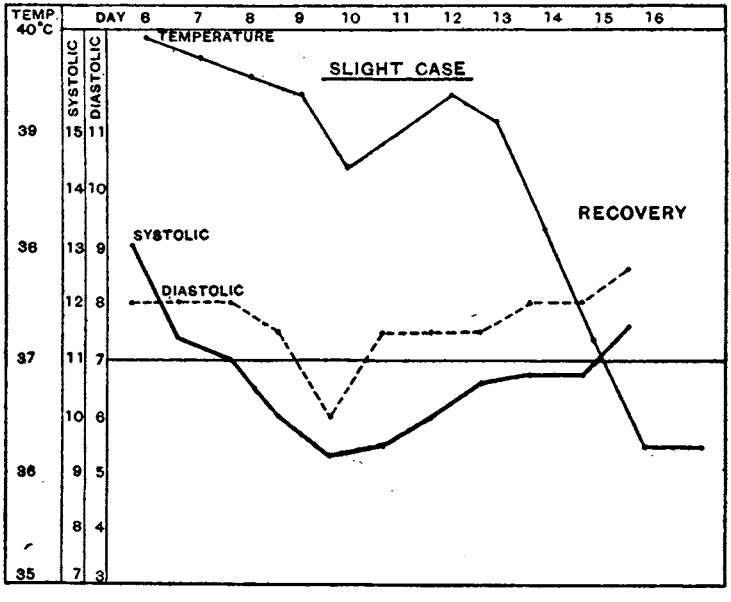


FIG. 9.—Systolic, diastolic and temperature curves in a slight case of typhus fever. (Daniélopolu.)

to 50 or even 40 mm. Hg. The relation between the two pressures is not, however, constant.

During the time of fever low pressures are accentuated ; during convalescence they rise little by little. The evolution varies in different cases. In slight forms (Fig. 9) the reduction of arterial pressure begins towards the end of the first or second week, but sometimes from the first few days after infection. This reduction is hastened during the second week ; the pressure rises after defervescence, but does not regain a normal level for several days.

In more toxic forms the arterial pressure becomes still

further lowered during the febrile period, especially in the second week; it remains low during the apyrexial period when intense toxic phenomena are observed. If the patient recovers the pressure again rises, but it takes a very long time to recover normal figures; convalescents retain for many weeks, and sometimes months, a state of pronounced asthenia. If the patient does not recover, during the

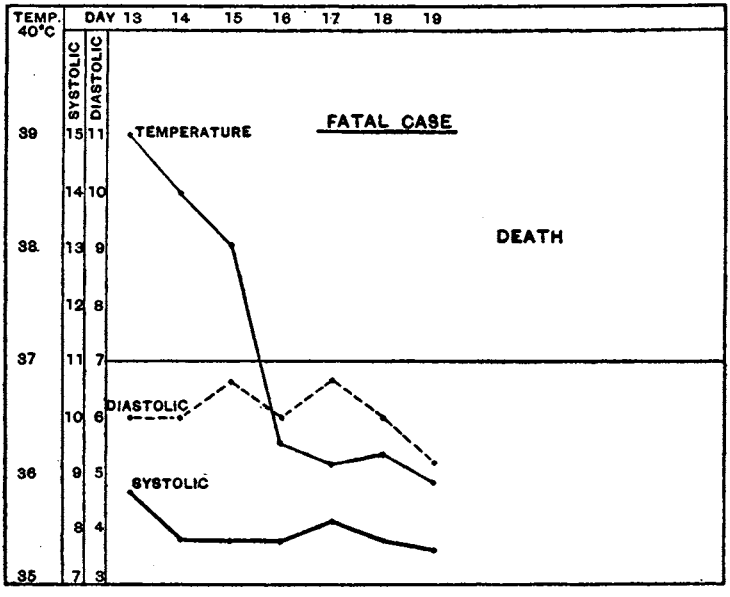


FIG. 10.—Systolic, diastolic and temperature curves in a fatal case of typhus fever. (Daniélopolu.)

apyrexial period the pressure drops continuously to still lower levels until death ensues (Fig. 10).

The pathogeny of the condition is as follows: the radial pulse is small and thready, and one is inclined to attribute this to myocardial weakness. It is true that this smallness of pulse is often accompanied by a notable acceleration, but the two phenomena are not related, for, if almost all exanthematics have low pressures, there are numbers of cases where the maximal pressure is lowered to 90 or even to 70 mm. without the rhythm exhibiting acceleration. Low pressures are found also to occur prior to myocardial

insufficiency, and are wont to disappear more slowly than the latter. Finally, at times myocardial weakness is seen to yield to cardiotonic drugs, the rhythm again becoming normal, whilst the arterial pressure nevertheless maintains a low level, and does not rise until much later during convalescence. This particularly follows injections of strophanthine when used in small, frequently repeated doses, when the sphygmomanometer shows that this drug does not raise the arterial pressure. Daniélopolu and Simici found that the curve of arterial pressure in those patients treated with strophanthine does not differ from that of subjects not so treated. When rhythm slows and the force of cardiac contraction is augmented, the radial pulse yields to the finger the impression of a more satisfactory pressure, but one does not obtain any notable augmentation of the sphygmomanometric figures so long as the peripheral resistance is unaffected.

Gottlieb and Magnus [231] have shown that toxic doses of digitalis and strophanthine provoke an increase of pressure by general peripheral vasoconstriction, small doses not raising the pressure, and the vasoconstriction limiting itself to the vascular intestinal territory and being accompanied by a renal and peripheral vasodilatation.

(ii.) **Tsutsugamuchi Disease** (Japanese flood fever) belongs to the typhus group of fevers, multiple forms of both maladies being now recognised.

Tsutsugamuchi disease has been carefully studied by numerous observers, the consensus of opinion being that it conforms with the clinical type of a *Rickettsia* disease transmitted by means of the larval stage of a *Trombidium* (*T. akamushi Brumpt*), a small rodent (*Microtus Montebelloi*) acting as a reservoir of the virus, and harbouring mites which drop off and bite human beings, thus communicating the disease, which begins as a sore, followed by febrile exanthema and generalised adenopathy.

(iii.) **Scarlet Fever.**—The most recent review of the literature appertaining to arterial pressure in scarlet fever has been made in 1923 by Doria,[232] who has included the results of preceding observations, such as those of Nobécourt and Tixier (1908), and of J. D. Rolleston (1912). Doria's

own conclusions are based on the study of sixty-seven patients of ages varying from sixteen months to thirty-two years, of which thirty-two were males and thirty-eight females. Both systolic and diastolic pressures were recorded with Riva Rocci's instrument and the auscultatory method, the measurements being taken at the same hour, usually in the early afternoon. No differences were observed as regards either pressure between males and females of the same age.

This observer gives the following summary :

1. Like almost all the acute infectious diseases, scarlet fever causes a fall in arterial pressure.

2. This fall takes place more or less early, and may appear in the pre-eruptive, eruptive or desquamative stage. It is more or less persistent, lasting usually at least a week. Its intensity varies, being most pronounced in severe cases (fourteen in this series), while in others it is slight or barely perceptible.

3. The fall is connected with a general vasodilatation, and more especially with weakening of the left ventricle. It is not necessarily due, even when pronounced, to severe organic lesions of the suprarenals.

4. The peripheral circulation is comparatively satisfactory, since the diastolic pressure is not only not depressed, but shows a tendency to increase throughout the disease. Sometimes in convalescence there is a diastolic fall for a short period, which should serve as a warning of a sudden attack of cardiac insufficiency.

5. Accidental rises of systolic pressure have no special prognostic value, and are often due to painful complications. Rises of systolic pressure to the normal level in association with albuminuria should make one fear the onset of nephritis, whereas albuminuria without a rise of arterial pressure, or with low pressure, is usually not followed by nephritis.

6. Injections of anti-streptococcic serum cause a more or less considerable fall of arterial pressure. Apart from these and similar incidents, a sudden fall, especially if associated with a diminution of diastolic pressure, indicates the onset of a complication, particularly one affecting the heart.

7. The low pressure of scarlet fever cannot be atttributed to diet, for it is found in patients who are taking adequate

nourishment, and sometimes appears at a very early stage, nor can it be explained by rest in bed, as it often persists after the patients have got up again.

The above quotations from Doria's paper represent the substance of the conclusions at which he has arrived, but in view of his statement in the last paragraph that the low pressure of scarlet fever is apt to appear early in the disease, it seems probable that this reduction in pressure is more likely, as in the case of the other acute infections, to be due to the effect of toxæmia upon the adrenal glands,[233, 234] for although severe pathological changes in them may not be apparent, precisely as in the case of typhus fever, the reduction in pressure due to cardiac enfeeblement occurs at a much later date.

In cases of toxic or " malignant " type, particularly when combined with pharyngeal ulceration, both systolic and diastolic pressures drop to distinctly low levels. From the outset prostration is a marked feature and is accompanied by general cyanosis. In such cases streptococci are commonly found in the blood. In the various complications due to sepsis, *e.g.*, cervical adenitis, otitis or suppuration elsewhere, the systolic pressure undergoes but little alteration.

(iv.) **Rheumatic Fever.**—One of the prominent symptoms of rheumatic fever is anæmia. During the initial ten to fourteen days of the malady there is a rapid decrease in the numbers of the red cells, with a corresponding or greater diminution in their hæmoglobin content. Profuse sweating is common, but disturbance of kidney function is not one of the noteworthy features. Hence, under ordinary conditions, one does not expect to find more than a small drop in arterial pressure. In grave types of articular affection, however, both systolic and diastolic pressures are frequently depressed.

(*c*) Protozoan Infections

(i.) **Malaria.**—During an attack of malarial fever, especially of the pernicious type, the diastolic pressure manifests a definite and constant reduction, whilst the systolic pressure may also be lowered but to a less extent, or may even show slight increase.

"Loss of vascular tone is constant. Even during the 'hot' stage of an acute attack the minimum blood pressure (which represents the true arterial tension) is much below normal, although the maximum pressure may be somewhat increased. The diminution of the blood pressure is greatest shortly after the febrile attack, but persists until the apyrexial intervals between the relapses, even when these intervals are of several weeks' duration. Average pressure readings for a strong, healthy man should show a maximum of about 120 mm. Hg, and a minimum of about 80 mm. Hg, but, according to Plehn,[235] in any soldiers who contracted malaria in Macedonia during the war the maximum pressure reading was usually not more than 80 or 90, and the minimum between 40 and 50 or even less."

The causation of this is still open to discussion, but probably loss of vascular tone with consequent reduction of arterial pressure results from a direct and specific action of the malarial parasites upon the tissue cells of the blood-vessels and an indirect effect upon the vasomotor nervous system. Another probable causative factor results from alteration in the capillary blood stream consequent upon plugging of the capillary vessels by the plasmodium during certain stages of its development.

Even apart from grave forms of the malady, Paisseau and Lemaire,[236] from observations during the war epidemic in Macedonia, found the arterial pressure in malaria much lowered, in conjunction with abdominal pains, vomiting and evidences of adrenal insufficiency; in three cases profound lesions of the adrenal bodies were found at autopsy. Dudgeon and Clarke,[237] however, who in thirty-five cases combined systematic examinations of the adrenals with examination of the heart muscle and cerebral and other tissues, question whether the syndrome can rightly be attributed to adrenal insufficiency alone. In intense malignant tertian infection the same observers noted reduction of the fatty lipoids of the cortical layers as the most constant lesion in the adrenal glands, the chromaffin content in the cells of the medulla being diminished. In five cases the parasites were found massed in the capillaries of the brain, and this in all likeli-

hood formed the pathological basis of the symptoms, at least as regards those referable to the nervous system.

Lacapère, in Morocco, has also verified the decline in arterial pressure in malaria, whilst Monier-Vinard and Caillé [238] discovered the minimal pressure especially low in algid forms, down to 30 or even 20 mm. in the initial stages, whilst the maximal pressure on the contrary tends slightly to rise.

Carmalt Jones,[239] from war experience in Egypt, reported that malaria is likely to produce greater evidence of myocardial change than most of the other contributory causes of disordered action of the heart. This observation is not in accordance with the opinion of most investigators, who find that myocarditis and other characteristic changes in the hearts of patients dying from malaria are nearly always absent at autopsy, whilst in many cases the fall of arterial pressure precedes cardiac symptoms. Hence it would appear that in the majority of cases one is unable to invoke weakness of cardiac contraction as a factor in pathogenesis.

Notwithstanding lack of agreement on the part of various observers, the one salient point emerges, that the action of toxins produced by the parasite of malaria exerts an action in greater or less intensity upon the vasomotor centres. Whether this action is exercised directly on the centres or whether through the intermediary of inflammatory processes in the adrenal glands noted in most autopsies must still remain a matter for conjecture.

(ii.) **Leishmaniasis.**—Under the generic heading of Leishmaniasis is included a group of diseases which owe their common origin to parasitic protozoa of the *Herpetomonad* class, and of which several clinical types exist. A large group is constituted by dermal Leishmaniasis, where the parasite is transmitted by sand-flies. With this form we are not concerned. The visceral form (*Kala Azar*), of yet unknown mode of transmission, comprises both adult and infantile types, in which the spleen is invariably enlarged and the liver usually so. A progressive anæmia is present, which is more marked in the infantile type, and associated with this and with the advancing cachexia, a gradual and finally considerable reduction in arterial pressure becomes manifest.

(*d*) Metazoan Infections

(i.) **Trichiniasis.**—Cheney,[240] of San Francisco, reports the interesting case of a man, aged twenty-five, who was admitted to hospital complaining of general weakness of two weeks' duration. He appeared poorly nourished, apathetic and ill. The lungs and heart showed no abnormality; the arterial pressure was 82 S. and 46 D. Stiffness and tenderness of the neck, abdomen and limbs were present. On the second day the arterial pressure fell to 44 S. and 18 D., checked by three observers with different sphygmomanometers. There were, nevertheless, no other signs of circulatory failure and the urine output was normal. One cubic centimetre of epinephrine was given subcutaneously, and the pressure rose to 110 S., and 48 D., after six hours falling gradually to a constant level of 70 S. and 42 D. It gradually rose during the remainder of the four weeks' stay in hospital, reaching 102 S. and 64 D. at discharge. *Trichina spiralis* infection was diagnosed on the third day by examination after biopsy of a piece of the left pectoral muscle.

(ii.) **Ascariasis.**—Though most frequently found in children, *Ascaris lumbricoides*, the round worm, and *Oxyuris vermicularis*, the thread-worm, occur at all ages. As habitat the former prefers the small intestine, while the latter seeks the rectum and colon. By reason of intestinal disturbances, produced by these parasites, the general health becomes impaired, and low arterial pressure often results.

(*e*) Spirochætal Infections

(i.) **Epidemic Jaundice** (*Spirochætosis Ictohæmorrhagica*). —The pulse is at first big, soft and atonic, but finally small, weak and rapid. Dicrotism is not uncommon, the systolic pressure being less than 90 mm. and cardiac weakness very pronounced.[241]

(ii.) **Syphilis.**—Upon the circulatory system in general acquired syphilis exercises a destructive effect, and as the processes of degeneration become increasingly manifest, so a gradual fall in arterial pressure takes place. Such destruction, however, takes place very unequally both in the same and in different subjects, so that it is possible for the arterial

pressure to remain within normal limits, or even to be raised over long periods, the actual level being dependent upon the condition of the circulation and upon the incidence of degeneration in particular organs and tissues at the time of observation.

Friedlander [49] advanced the view that hypopiesis at times found in the secondary stage of syphilis was associated with the frequently resulting aortitis. This suggestion is negatived by Warthin,[242] who found that the cardiac wall is itself involved, the essential lesion in the early stages being an interstitial myocarditis, characterised by infiltration with lymphocytes and plasma cells along the vessels between the muscle fibres. The entire heart wall, including the papillary muscles, may be involved in the infiltration. Eventually there is a progressive fibrosis of the cardiac muscle.

Thus hypopiesis appearing early in cardiovascular syphilis probably results from myocardial degeneration.

Syphilis, hereditary as well as acquired, plays a definite part in the pathogenesis of certain pluriglandular syndromes, and various types of polyglandular disequilibrium of syphilitic origin have been recorded, chiefly in women, the chief signs being headache, vertigo, fleeting pains, slight œdema and asthenia. Rarely is the latter the only outstanding phenomenon, orthostatic albuminuria, in association with dizziness and dyspeptic troubles, being often coincident. Hence Merklen [243] and his school believe that many cases of asthenia should be regarded as a polyglandular disturbance resting on a luetic basis. These authors and others have of late directed considerable attention to syphilis of the adrenal bodies, which induces an almost invariably constant and marked hypopiesis. Addison's disease of demonstrable syphilitic origin is, nevertheless, rare.

Touching parenchymatous syphilis of the nervous system, low arterial pressure is found in tabes dorsalis, as well as in the earlier stages of exaltation and excitement, and in the later stages of all forms of general paralysis of the insane. With the onset of depression the arterial pressure rises. Schmiergeld [244] has estimated the arterial pressures of 40 subjects of general paralysis. Among 13 below the age of 40 years, 9 had low pressures, 1 had normal pressure, and 3

were above normal; among 21 of ages from 40 to 50 years 9 had low pressures, 6 were normal and 6 were high; among 6 older than 50 years, 4 had low pressures, whilst the remaining 2 had high pressures. From these observations this writer concludes that arterial pressure in general paralysis of the insane is very variable, but in the majority of cases is lower than in normal individuals. No relation was discoverable between the moods of paretic subjects and arterial pressure, since it was possible for high pressures to exist in the elated and low pressures in the depressed.

CHAPTER X

Low Arterial Pressure in the Presence of Chronic Organic Disease Acquired and Persistent

A. In Association with Chronic Conditions usually attended by Wasting

The Cachexias.—Low arterial pressure is an accompaniment, albeit not an invariable one, of chronic conditions associated with impairment of general nutrition. In the later stages of the cachexias hypopiesis is the rule and may become extreme. Under these circumstances brown atrophy of the heart muscle is frequently present along with asthenia and emaciation.

Investigation by Müller-Dehan [245] of seven cases of acquired persistent and pathological hypopiesis in association with chronic nephrosclerosis, Addison's disease, gastric carcinoma, and duodenal ulcer showed great disturbance in water elimination, as well as in the concentrating power of the kidneys. Mason's observations suggest that the diastolic pressure is the most important factor in maintaining a constant arterial pressure to the functioning glomerulus.

1. Adrenal Insufficiency.—Addison's Disease.—In slowly progressive adrenal insufficiency chronic and persistent hypopiesis is frequently met with, and forms a part of the syndrome. In the greater number of cases the systolic pressure rarely exceeds 90 mm., and may be much lower. The triad of hypopiesis, asthenia, and the "white line" of Sergent [277] has been regarded by many clinicians, particularly of the French school, as being pathognomonic of adrenal insufficiency, although the "white line" produced by stroking the skin with a known even pressure of a blunt instrument or roller is no longer held to assume the diagnostic importance that Sergent originally claimed for it. It is

probable that most instances of hypopiesis arising in the course of or subsequent to acute infections and accompanying cachectic states are either wholly or partly due to adrenal insufficiency.

Addison's disease constitutes the fullest expression of adrenal insufficiency.

Although low arterial pressures are particularly common in this malady, and are frequently met with in slowly progressive adrenal deficiency arising from various causes, it is, nevertheless, erroneous to accept the current impression that hypopiesis is an invariable accompaniment of Addison's disease.

In many cases it is true that a progressively greater diminution in the systolic pressure and a lesser diminution in the diastolic pressure go hand in hand with advance of the malady. Nevertheless, such is not always the case. Hence one arrives at the conclusion, borne out by *post-mortem* evidence, that the existence of hypopiesis in this disease cannot in all cases be directly associated with lesions in the medulla of the renal gland.

Thus Janeway[17] has reported two cases in which Addison's disease was associated with a systolic pressure well above the standard level, whilst out of seven cases of the same disease investigated by Porak,[246] low arterial pressure was discovered only in one, that of a patient suffering from a coincident and diffuse pulmonary tuberculosis manifesting rapid advance. Further evidences alleged by this observer in support of his contention that adrenal deficiency *per se* is insufficient to explain lowering of arterial pressure are (1) that there is no relation between arterial pressure levels and the glandular content of adrenalin, and (2) that the administration of adrenal extract in cases of Addison's disease attended by hypopiesis caused no rise in systolic pressure, the curve tending continuously to fall just as if the patient had remained untreated, whilst the effect of adrenalin either in massive doses or long-continued was to produce constriction in the peripheral circulation favouring grave complications, such as that of acute œdema of the lung.

The solution of this and of other apparent paradoxes is

afforded by the recognition, as already mentioned in dealing with adrenal insufficiency in general, that the adrenal glands form only a part of the chromaffin system. Thus, if other members of the series be damaged by bacterial or chemical toxins, a state of adrenal inadequacy may be induced, notwithstanding the fact that no injury, macroscopical nor histological, of the medullary cells can be detected at autopsy.

It is possible, therefore, to have "any amount of destruction of the adrenals without Addison's disease if there is sufficient compensation by the other chromaffin structures, or, conversely, Addison's disease may occur when the adrenals seem morphologically little altered, which occurs in about 10 per cent. of all cases. In typical cases, however, the adrenals have been found entirely devoid of epinephrine, and usually the structural alterations are conspicuous.

"That there is a deficiency in the formation of epinephrine is attested by the low blood pressure and general low tone of the unstriated muscle tissue. Whether the adrenals exert a detoxicating effect, and the symptoms of the disease are partly the result of an autointoxication of some sort, is at present unknown, although this idea has often been advanced. The general metabolism shows no characteristic or striking changes over and above those associated with the emaciation. Because of the low blood pressure renal function may be much depressed, but there usually are no striking changes in the blood chemistry, and little change in the blood volume, red cells and hæmoglobin. Basal metabolism is little altered." [247]

2. Malignant Disease.—Contrary to generally accepted opinion, the author's experience leads him to believe that the primary stages of malignant disease are characterised by very high systolic and diastolic pressures—a reactionary response due to irritation of the tissues by the growth itself and the entrance of proliferative malignant cells into the lymph and blood streams. The value and importance of routine estimations of arterial pressure is thus indicated, since in such instances the presence of a malignant mass is liable to be completely overlooked, unless the undue height of the arterial pressure causes some suspicion of the real facts. During this period, unless the mass is superficial

enough to be apparent, in the absence of sphygmomanometric observation it will probably remain undiagnosed until a late and often inoperative stage, with the likelihood of disastrous results for the unhappy victim. With further progress of the malady both pressures gradually fall, and by the time the patient first comes under observation, particularly if the growth be deep-seated, the pressures may be already low. Rapidity of growth of the malignant mass has a greater influence in promoting lowering of arterial pressure than has actual position, although interference with important visceral functions, such for example as occurs in the case of carcinoma of the stomach, may also provide additional factors in bringing about pressure reduction. Failing arrest of infiltration of any of the more rapid forms, the pressures continue steadily to fall, until finally a very low level is reached.

In the later stages of most forms of malignant disease the patient becomes sallow and emaciated as the result of a resorption of toxic products, minute metastases into the lymphatic and blood circulation, pressure on important structures, and pain. In these cases hypopiesis is the rule.

The author is of opinion that, apart from primary soft malignant growths that very rapidly cause destruction of vital organs, and thus mechanically lead to a fatal issue, the type of growth commonly met with, somewhat like a pure tuberculous invasion, causes death by slow degrees, and that it is a secondary infection by micro-organisms, together with absorption of the products of cellular disintegration, superadded to the primary manifestation in each case, that is responsible for the marked toxæmia which constitutes so large a part of the clinical picture, and so materially hastens the patient's end.

3. Tuberculosis.—(i.) *Pulmonary.*—During the past thirty-five years an almost universal, but erroneous, impression has gained credence that in chronic pulmonary tuberculosis low arterial pressures are the rule. Led by Marfan,[248] numerous French writers, including Potain,[249] Regnault,[250] Teissier,[251] Sergent,[277] Vannieuwenhuyse,[252] Besançon,[253] etc., and in other countries Strandgaard[254] and Haven Emerson,[255]

have successively proclaimed this view. They unite in stating that from the outset, in the majority of cases, permanent hypopiesis is present, and that the pressure becomes still further reduced as the disease advances.

Whilst it is perfectly true that low pressures *may* occur under certain conditions and in certain grades, they are by no means specifically characteristic of the disease as a whole. The mistake has arisen from the recorded experiences of early workers, who necessarily laboured under serious disadvantages in that they were handicapped for two main reasons, firstly, because their primitive instruments were capable solely of registering systolic pressures, and secondly, owing to the fact that in their day diagnosis was not reached until a late stage of the disease at which hypopiesis tends to prevail.

Observations made over a long time and at frequent intervals show that the arterial pressures of tuberculous patients are subject to considerable fluctuations, the diastolic being less affected than the systolic. The author maintains that " the level of arterial pressure gives no direct indication as to extent of invasion of the lung by the tuberculous process. Where the disease is latent or where there is very slight activity, the diagnosis being perhaps still in suspense and the general condition good, low pressures may be entirely absent, whilst normal or even high pressures may be found at the onset of many cases of ' open ' tuberculosis, as well as in those which are advanced in respect solely of chronicity and extensive changes in the lung tissues. Thus from the point of view of extent of disease but not of intensity, in both slight and severe cases daily estimations of arterial pressure may demonstrate sometimes a rise and at other times a fall.

" The essence of the whole matter is intimately bound up with the problems of specific immunity and allergy (specific hypersensitiveness). Both vary directly with activity of disease, which in turn largely depends on the virulence of the infecting tubercle bacilli. The level of blood pressure closely accords with this variation, or, otherwise expressed, **the degree of decline of arterial pressure in pulmonary tuberculosis is directly dependent upon the amount of absorp-**

tion into the system of tuberculous toxins. As toxæmia waxes, so arterial pressure wanes.

"Once this basic fact is appreciated, the variations between blood pressure records in cases which present similar clinical characteristics as regards the extent of lung affected will be readily understood. As the author has insisted for many years, classification of pulmonary tuberculosis into stages corresponding with the extent of involvement of each lobe is of little value either for prognosis or treatment, the reason being that **extent of tissue involved is of far less practical importance than intensity of infection.** Hence it is not surprising that much confusion has existed as to the meaning of blood pressure determinations in tuberculosis of the lungs, for slight forms of still 'closed' tuberculosis, but with toxic absorption into the blood or lymph streams from the tubercles present, may exhibit lowered pressures as well as the gravest 'open' cases, though not to the same extent."[256]

It is true that persistent hypopiesis may be discovered in apparently unaffected members of families with tuberculous taint, thus pointing to an inherited disposition to infection. Indeed, a continuously reduced arterial pressure without demonstrable cause is an indication in some subjects of existing tuberculosis, even in the absence of the usual physical signs. Investigations should be carried out with the utmost care, and, if reliable tests reveal no definite evidences of disease, the subjects should, nevertheless, be kept under supervision, for later on manifestations of activity may become apparent.

In active and uncomplicated pulmonary tuberculosis which has not been treated, the systolic pressure tends to fall, whilst the diastolic may rise, remain stationary, or undergo some reduction. On the other hand, in individuals with latent disease, or presenting only slight tuberculous activity, of good general physique and vigorous powers of resistance and recuperation, low arterial pressure is usually entirely absent. Janeway's[17] conclusions that there were no great differences in arterial pressure between a series of non-tuberculous and incipient tuberculous patients have been confirmed by Shalet,[257] who investigated 1,000 cases. In such subjects arterial pressure may even be maintained

at a comparatively high level. This latter is found to coincide with an optimum environment comprising good hygiene and effective treatment. The 140 cases of pulmonary tuberculosis recorded by Grant [258] showed in all stages a higher systolic level than that found by Pottenger,[259] yet exhibited the characteristic decline in pressure as the disease progressed. The diastolic pressure was also lowered, though usually to a less extent than the systolic. In some cases, however, the fall was considerable, even down to 60 mm. of mercury.

A rise in systolic pressure persisting over some length of time is evidence of improvement, whilst an appreciable fall indicates regression, rapidity of fall corresponding with activity of disease. Fluctuations are evident, but in the absence of arterio- or nephro-sclerosis, and of diabetes in fat subjects, the general tendency in progressive disease is downward, respiratory deficiency going hand-in-hand with pressure reduction. When the disease is already advanced, emaciation of itself still further tends to depress arterial pressures, the levels of which vary directly with body weight.

Upon the vasomotor centre in the medulla, and upon the endocrine sympathetic system in general, tuberculous toxins exert a potent depressor effect, chiefly by stimulation of the depressor fibres in sensory nerves, thus inducing rapid cardiac action and disturbance of vasomotor equilibrium. These effects are combined with over-excitation and consequent depletion of the adrenal glands. As a result of these factors, along with lessened diaphragmatic action, especially during inspiratory descent, and the frequent presence of adhesions and diminished elasticity of lung tissue, grave impairment of function ultimately eventuates with the production of hypopiesis, relatively empty arteries and full veins, insufficient arteriolo-capillary pressure, impaired oxidation and assimilation, digestive troubles, subnormal temperature, muscular asthenia and fatigue, leading finally to atrophy of the essential somatic organs—a functional Addison's disease. Degeneration or destruction of chromaffin tissue, whether situate in the adrenal medulla or elsewhere in the chromaffin system, acts also in tuberculosis as an additional factor productive of low arterial pressure. In

the production of low arterial pressure and of tachycardia it is not improbable that lessened vagus inhibition also plays its part. Rapid heart action is a usual and necessary sequel to low arterial pressure and, if extreme, will aggravate the latter by the very act of its shortened diastole.

Some writers attribute the hypopiesis of advancing tuberculosis, with scanty powers of resistance overborne by a virulent infection, to a further cause which they postulate in the action of tuberculotoxin upon the muscle of the arterial walls and heart, producing laxity of vessel wall and inefficiency of myocardium. Such toxic action, however, has not been demonstrated, and although the degenerated heart muscle in advanced cases might exercise an additional influence in promoting hypopiesis, in any event it is a factor of minor importance for the reasons already given (pp. 83, 195, 200).

The lowest arterial pressures are found in patients with low resisting power who manifest clinical evidences of rapid tuberculous invasion in the earlier stages by multiple foci with considerable toxæmia, or in the later stages by emaciation, destruction of lung tissue with cavity formation, or laryngeal, bronchial or intestinal complications.

Not infrequently, before or during hæmoptysis, a patient whose usual condition is one of hypopiesis, but with congestive tendencies, may become hyperpietic, the outlook then being more serious than it is in the case of hæmoptysis arising on a low pressure basis. In dry tuberculous pleurisy arterial pressure is usually little altered. In pleurisy with effusion, lowering of pressure corresponds with extent of effusion. Intestinal ulceration, with diarrhœa and laryngitis, are complications which cause still further lowering of pressure.

Induction of artificial pneumothorax usually has little influence on arterial pressure, though symptoms of shock, or even sudden death, have been known to ensue.

(ii.) *Glandular and Osseous.*—The degree of hypopiesis in these conditions, as in other forms of tuberculosis, depends directly upon the amount of circulating tuberculo-toxin.

(iii.) *Renal.*—In tuberculous affections of the kidney the arterial pressure declines only when the malady has attained a moderately advanced stage or when amyloid degeneration

supervenes. In renal tuberculosis Reitter [260] found hypopiesis to be present in contrast with non-tuberculous forms of pyelitis and pyelonephritis where the pressure was normal or definitely increased.

4. Diabetes Mellitus.—In this chronic disorder of carbohydrate metabolism the height of the arterial pressure in uncomplicated cases varies according to whether the main symptoms are on the one hand due to difficulties in assimilation, or on the other hand to difficulties in elimination, and tallies with the metabolic picture of the moment.

The acute (thin diabetic) type, most often seen in young people, is associated with errors in assimilation. The appetite is usually voracious, but notwithstanding the enormous intake of food, rapid and progressive emaciation with asthenia ensue. Up to the age of thirty-five arterial pressure is usually somewhat below standard levels, and diminishes proportionally with the degree of asthenia.

The chronic (fat diabetic) type, which is usually discovered at or after the age of thirty-five, is frequently associated with errors of elimination. The patient is stout and florid, with a moderate appetite, and manifests an arterial pressure either (*a*) normal for age, where the kidneys are still uninvolved, or (*b*) heightened, in conjunction with kidney strain, as evidenced by the complications of cardiac hypertrophy, arteriosclerosis, aortitis, or nephritis. Neither hyperglycæmia nor acidosis appear to reduce arterial pressure, but have commonly the opposite effect.

As to clinical incidence of hypopiesis in diabetes, Barach's [31] records during eighteen months showed that of 118 cases, 44 had a systolic pressure of 110 mm. of mercury, 46 had a systolic pressure of from 110 to 150 mm., and 28 had a pressure higher than 150 mm. In an analysis of 500 cases of diabetes since 1919 Joslin [262] found definite hypopiesis in only 35 (7 per cent.), the suggestion being that the number of cases of hypopiesis had increased since under-nutrition was introduced prior to insulin therapy.

Whilst uncomplicated diabetes in young people shows a normal or diminished arterial pressure, in elderly diabetics hyperpiesis, falling during sleep, is the general rule. This rise in pressure is, however, mainly due to complications.

Hence one may say that diabetes, of itself, exerts no marked influence upon the level of arterial pressure.

Recent experiences of the author dispose him to believe that the variations of arterial pressure which occur in diabetes correspond with the grade of the malady, and particularly with its complications. In other words, that true diabetes, as we see it, represents the end-result of a chain of metabolic errors of particular type, which, insidious in onset as a form of perverted metabolism due to endocrine disturbances, either apart from or consequent upon toxæmia, in which the glycogenic functions of the pancreas and liver are upset, terminate in the production of sugar in the tissues, by which the blood becomes loaded, and which the kidney endeavours to the best of its ability, and with greater or less success, to eliminate.

From this one striking fact emerges, that if one is able successfully to combat any existing toxæmia, and by diet in combination with insulin or by other means to co-ordinate hormonic function, such attempts are followed by considerable reduction in the sugar content of the blood and urine *pari passu* with amelioration of symptoms. Known diabetics, emaciated and asthenic, of the type in which insulin is not likely to be serviceable, or in which this remedy has already failed, on a detoxicating *régime* will at times be found to regain energy and capacity for the affairs of life, with simultaneous reduction in autogenous manufacture of sugar, and can gradually be brought to tolerate an increase in the carbohydrate constituents of their daily food.

5. Deficiency Diseases.—In May, 1927, at the Royal Society of Medicine, with reference to the experimental effects of a deficiency in diet of vitamin B, an important discussion was held, in the course of which the author [263] pointed out that one group of low arterial pressures in association with small hearts and diminished tone in the peripheral circulation was associated with malnutrition, caused (1) by a diet insufficient either in quantity or quality, or both, particularly in regard to the content of particular vitamins, or (2) by an inherent defect in the capacity for assimilation, even if the diet be sufficient in quantity and quality.

Such conditions are evidenced by trophic changes akin to those found in the polyneuritis of beri-beri, along with intestinal muscular atrophy, stasis and toxæmia, all of which can be abolished by appropriate feeding with detoxicated wheat embryo or whole-meal containing the requisite amount of vitamin B.

The contractile power of the heart muscle becomes lessened by fatty infiltration, the muscular fibres being separated by deposits of fat, lymphocytic exudates also occurring in certain cases in the neighbourhood of the blood vessels in the cardiac musculature.

Malnutrition, caused by a diet which is either insufficient in quantity, or in a particular vitamin content or by a defect in capacity for assimilation, forms an important factor in the evolution of many disease processes with which low arterial pressures are frequently associated.

6. Atrophic Cirrhosis of the Liver leads to permanent reduction of arterial pressure. In the presence of ascites the pressure is notably lowered. It is probable that toxins apart from alcohol arising in the portal blood can cause degeneration of liver cells, but the classical form described by Laennec [264] is commonly met with in habitual consumers of spirits, gin being the most potent. In other states of hepatic insufficiency hypopiesis may not infrequently be observed.

7. Tropical Diseases of Doubtful Ætiology.—(*a*) **Sprue (Psilosis).**—Sprue is an insidious and chronic affection of indefinite ætiology which may yet be found to include different diseases of varied causation or one morbid condition due to several causes acting in union.

The disease prevails in India, China, Java and the West Indies. Originally it was thought to be resticted to tropical regions, but later investigators have shown a similar syndrome to occur in much wider areas. Thus it has been observed in persons who have never been out of Europe, or even out of Great Britain.

It is characterised by glazing of the tongue, hypersensitiveness of the mucous membranes of the tongue and mouth, with ulceration, intestinal atony with resulting frequent passage of copious pale, frothy and fermenting stools. Certain

Monilia, connected with abnormal fermentation of the intestinal contents and present as a terminal feature in the vast majority of fatal cases, are no longer looked upon as causative but as secondary invaders.

Sprue is attended by great wasting, sallowness and profound anæmia, the hæmoglobin falling even to below 20 per cent., both arterial pressures being notably reduced, especially during the cachectic stage.

(*b*) **Tropical "Low Fever," Debility, Cachexia and Anæmia.**—Under this somewhat vague classification are included manifestations which arise in Europeans after prolonged residence in the tropics, and for which it is at times difficult to find adequate explanation. In differential diagnosis arterial pressure estimations are of value, since in most cases low pressures are the rule, a definite rise being appreciable as improvement of the general condition takes place. The important observations of de Langen and Schut [265] upon the sugar content of the blood has not only helped to explain the effect of heat upon the economy, but has indicated that the "low fever" of the tropics may have a climatic, not a parasitic origin.

(*c*) **Pellagra.**—The ætiology of this malady is obscure, no explanation of the peculiar symptoms being yet forthcoming. What is known is that the characteristic roughness and redness of the skin appears chiefly in situations where the surface of the body is exposed to sunlight.

Frequent accompaniments are mental symptoms, usually of melancholic type, and the disease may go on to the production of considerable asthenia, emaciation and hypopiesis, often terminating in death.

B. In Association with Chronic Conditions not usually attended by Wasting

1. Constitutional Affections. (*a*) **Status Lymphaticus.**—Status lymphaticus is characterised by hyperplasia of the glandular tissue of the thymus, and of the lymphoid tissues in other parts of the body, including the tonsils, pharyngeal ring, lymph glands, and intestinal follicles. Other notable features are splenic enlargement, defective genital develop-

ment, and considerable hypoplasia of the circulatory system. The heart sounds are muffled and faint, the pulse is slow, and arterial pressure is lowered.

This constitutional dyscrasia is of obscure origin and occurs mainly in children, rarely also in young adults, with tendencies to sudden death. Its clinical type varies according as to whether met with in the stage of evolution, during which the thymus is hyperplastic, or in the stage of recession, during which progressive atrophy of the thymus and other lymphoid tissues takes place.

Symmers [266] has shown that the frequency of incidence is greater than has formerly been supposed. In the Bellevue Hospital, out of 5,652 autopsies he found 457 cases (8 per cent.) of status lymphaticus. In 222 cases (88 per cent.) of these some form of acute infective lesion was demonstrated, the commonest being endocarditis, pneumonia and meningitis. The first 249 cases were carefully analysed by Symmers : in 118 of these, all in the evolutionary stage, the thymus was hyperplastic ; in seventy out of eighty-nine cases in the stage of recession the thymus was not visible macroscopically. Of the 249 cases, fifty-one showed hypoplasia of the heart, and 40·5 per cent. of these same cases showed hypoplasia of the aorta.

Hypoplasia of the chromaffin system has been noted in association with status lymphaticus by Wiesel,[267] and later by Hedinger,[268] who finds an analogy between these cases and those described by Münzer,[92] of hypopiesia with lessened vascular tonus and diminished percussion stroke of the pulse wave.

The form of hypopiesia, which is a constant accompaniment of status lymphaticus, is again an expression of lowered vitality originating on the one hand from the presence of a congenital and constitutional cardiovascular hypoplasia, with resultant lessening of the propulsive force of the heart, and on the other hand from hypoplasia of the chromaffin system, which together constitute this particular diathesis.

(*b*) **Myasthenia Gravis.**—This disease is characterised by rapid exhaustion of voluntary muscles, particularly those innervated by the bulb and cranial nerves on repeated movements or faradism, with recovery after rest. The

lesion is of muscular and not of nervous origin, small round-celled infiltration and serous exudates occurring between the muscle fibres and in the tissues.

Persistence of the thymus with proliferation may occur, but is not constant. In several cases there has been association with Graves' disease and with adrenal insufficiency. Irradiation of the enlarged, or persistent, thymus, with resulting involution of the gland, has been followed by marked improvement in the myasthenic symptoms, including hypopiesis.

In 50 per cent. of cases coming to autopsy and reported since 1901, hyperplasia or tumour of the thymus gland was noted to be present.

2. The Anæmias.—The main clinical symptoms common to all the anæmias are hypopiesis, hæmic murmurs, pallor, dyspnœa and asthenia.

(*a*) **Primary.**—(i.) **Pernicious Anæmia.**—The views as to the constitution and causation of pernicious anæmia are still conflicting, and probably conditions of various origin, when the primary cause is still indeterminate, are grouped wrongly under this heading.

According to the most recent and promising line of investigation, **true** pernicious anæmia is regarded as a definite malady of congenital origin affecting primarily the liver during fœtal existence, and secondarily the bone marrow. On this view the enormous polymorphic cells, with dividing nuclei and megaloblasts, invariably found in the blood of such cases, are considered to be histologically identical with the most primitive forms of erythroblast, which occupy an intravascular position on the wall of the embryonic yolk sac. Similar cells are subsequently visible in the portal capillaries of the fœtal liver, disappearing before birth in normal subjects, but persisting throughout life and found at autopsy in the livers of those who may develop actual from potential pernicious anæmia as the result of intercurrent favouring circumstances.[269] This hypothesis accords with the congenital achlorhydria and familial incidence of pernicious anæmia.

By reason, nevertheless, of the similarity of the symptoms of profound asthenia without wasting, gastro-intestinal

upsets, absence of hydrochloric acid from the gastric juice, and remissions of the disease, all of which are constant phenomena, along with frequent lemon tinting of skin and soreness of tongue, true pernicious anæmia is often confused clinically with other conditions in which the blood changes are due to syphilis, hæmorrhage or hæmolytic toxæmia of septic origin.

In the early stages there is little alteration in the arterial pressure levels. These do not fall because of loss of weight, since the patient is usually well nourished throughout. With increase in the anæmia, however, there is a coincident reduction in both arterial pressures, and hæmic murmurs become readily audible.

(ii.) **Leukæmia.**—The author has failed to find any recorded observations of arterial pressure either in the lymphatic or spleno-medullary forms. So far as his personal experiences extend, the arterial pressures are both found persistently lowered in each form of the disease, more especially when advance is rapid. In the lymphatic form, after treatment of the affected glands or spleen with radium, the pressures tend to show a gradual rise parallel with improvement in the patient's general and local conditions. With relapses, the pressures again fall.

(iii.) **Chlorosis.**—Reduction of arterial pressure appears as a constant factor in chlorosis. Hæmic murmurs are frequent, and constipation almost invariable.

(*b*) **Secondary.**—(i.) **Post-hæmorrhagic anæmia,** either acute, subsequently to large hæmorrhages, with symptoms of pallor, cold sweats, irregular, small pulse, weak heart sounds and palpitation, or subacute, subsequently to small repeated hæmorrhages, is always associated with persistent hypopiesis, which often takes a long time, months and even years, to recover its original level. The red cells and hæmoglobin are diminished, the blood coagulability is increased, and there is a transitory polymorphonuclear leucocytosis.

(ii.) **Simple anæmia** consequent upon severe sepsis, cholæmia and malaria, or due to toxic conditions, such as acute infection, sepsis, syphilis and malignant disease causing disturbance of balance between production and

destruction of erythrocytes; or poor food and bad hygiene; or exhaustions, *e.g.*, chronic gastro-intestinal catarrh, lactorrhœa and other debilitating states, is attended by lowering of arterial pressure sometimes to a considerable extent, varying largely, however, with the degree of cardiac enfeeblement.

3. Chronic Infections.—(*a*) **General.**—Certain of the general chronic infections lower arterial pressure, though this result does not obtain in all, the actual height of the pressure depending upon the nature of the infective process and the resisting power of the patient.

(*b*) **Focal.**—Focal sepsis originating in sites, such as, for example, the teeth, dental sockets, tonsils, nasal sinuses, antra and gall-bladder, a smouldering appendix, or chronic pelvic sources, such as the seminal vesicles, prostate, Fallopian tube or uterus, may deplete the vitality and resistance of the patient to such an extent that hypopiesis is thereby induced. Occult tuberculosis has also a potent, but often unrecognised, influence in the same direction.

Under these circumstances stimulation of vaso-dilator nerves or paralysis of the vaso-constrictors or of the muscular fibres of the arterioles is usually brought about by chemical products of bacterial growth or of tissue disintegration acting either directly or through hormonic intervention. Vaso-dilator effects are produced by those amino acids which have an action akin to that of histamine. Thus acetyl-choline acts through relaxation of arterial tone, while the dilator effect of histamine and adrenalin is localised in another part of the circulatory system, probably in the capillaries.[270]

4. Chronic Intoxications. — (*a*) **From Gastro-intestinal Sources.**—Metchnikoff's wide biological researches led him to assert that a slow and insidious absorption of poisons from the large intestine chiefly promoted those processes of disease which result in thickening and degeneration of vital organs and tissues. These beliefs are supported by the clinical studies of Sir Arbuthnot Lane,[271] whose views have been summarised as follows: "By chronic intestinal stasis the passage of the contents of the intestinal canal is delayed sufficiently long to result in the production, in the small intestine especially, of an excess of toxic material, and

in the absorption into the circulation of a greater quantity of poisonous products than the organs which convert and excrete them are able to deal with. In consequence there exist in the circulation materials which produce degenerative changes in every single tissue of the body and lower its resistance to invasion by deleterious organisms. These disturbances are primarily due to delay of fæcal material in the large bowel, which loading tends to downward displacement and dragging on other intra-abdominal organs. Delayed passage of the contents of the small intestine ensues, as also of the duodenum and stomach, with resultant infection of these organs and accumulation of deleterious bodies from the stagnating material."

The possible sources of gastro-intestinal intoxication are many. They may be formed as a result of disintegration of food-stuffs within the gastro-intestinal tract either by digestive ferments or by bacterial activity. Exotoxins are also formed by the bacteria of the intestinal contents, which act upon the secretions and excretions of the body entering the alimentary canal.

Although the number of these toxic substances is great, positive data concerning intestinal intoxication are few. Experimental evidence, when applied to human pathology, is so far largely inconclusive. Many of these poisonous products are probably not yet isolated, while those that are may eventually be shown not to exert the most toxic influence.

The products of normal protein digestion include proteoses, peptones and amino-acids. Polypeptids and amino-acids have been stated by Wolf [272] to cause no fall in arterial pressure. Intravenous injections in large doses of the albumoses may, however, cause a fall, while the abiuret products of tryptic digestion are far more actively depressor than the albumoses.

As regards the products of fermentation and putrefaction within the intestinal tract, the majority of fæcal poisons are believed to act as circulatory depressants, the best known of these being histamine and cadaverine.

Histamine, a derivative of histidine, acts as a poison by dilating the walls of the capillaries and thus causing oligæmia by reason of the increased permeability to plasma, and

retarded peripheral blood-flow through loss of capillary tonus.[211] Minute doses injected into man produce dizziness, rapid heart-beat and a considerable drop in arterial pressure. Intravenous injections into anæsthetised cats caused a sudden and sometimes fatal fall in both arterial and venous pressures. Direct observation of the capillaries demonstrates that, coincidently with these changes in blood pressure, there is a corresponding dilatation of capillaries and venules. Hence a condition is induced resembling traumatic shock, which has led to the suggestion that in traumatic shock histamine, or some body possessing similar properties, is liberated in the damaged tissues.[247]

Histamine is constantly present in the intestinal mucosa, being presumably formed therein by bacterial activity, and, according to Abel,[273] histamine, or some substance with similar effects, is widely distributed in all animal tissues, organic extracts, and Witte's peptone. In putrefaction of proteins within the intestine, histamine is formed from histidine by the action of colon bacilli.

Thus, from the above and from additional evidence, there are grounds for assuming that histamine, or a similar body, as yet unidentified, possessing similar properties, acts as a cause of hypopiesis, under conditions of intestinal stasis and resultant toxæmia, by poisoning and so dilating the walls of the capillaries.

A further effect of chronic intestinal toxæmia is the induction of thyroid atrophy, which connotes suboxidation. Hence a further link is forged which connects intestinal toxæmia with the production of low arterial pressure.

(*b*) **From Alcohol.**—Alcohol temporarily raises arterial pressure through reflex vasoconstriction in the splanchnic area, but as soon as the alcohol reaches the blood stream dilatation ensues and the pressure falls. Taken in moderation with the chief meal of the day, the writer has found its use beneficial in the case of patients with low arterial pressure who are mentally or physically exhausted, and who approach food with no appetite, or even with actual distaste. Such instances are frequent in the gastric form of neurasthenia, and in this class of patient a glass of port or a tankard of stout is at times a valuable aid.

(*c*) **From Tobacco.**—In general the occasional or moderate use of tobacco at first causes a rise in both pressures, the systolic being heightened to a greater extent than the diastolic, along with increased rapidity of pulse rate. Smoking in excess diminishes the systolic pressure by reason of the toxins contained in tobacco, which consist of pyridine bases and nicotine, the latter being the chief toxic element. When arterial pressure is already depressed, it is advisable to prohibit tobacco entirely, since smoking even in slight amount is of itself sufficient to keep arterial pressure continuously at a low level.

5. Chronic Arthritis and Fibrositis.—Chronic arthritis and fibrositis arise either from infective or from metabolic causes. As to the former, the commonest organisms are streptococci, notably of the viridans type, of low virulence but great chronicity. The metabolic causes are of dual origin, either from elimination errors or from assimilation errors. The members of the excess metabolic group belong to the acid type of constitution, which commonly goes with high arterial pressure manifestations and difficulties in elimination; the members of the assimilation error group suffer either from inability to obtain sufficient food, or from lack of knowledge to select a balanced dietary suited to their constitution, or from inability to digest, absorb and assimilate adequately, even if the food be suitable in quantity and kind. This group is the one with which hypopiesis is frequently associated by reason of the alkaline trend of the acid-base equilibrium. Such subjects, often young, and especially women, tend to suffer from rheumatoid arthritis. Low arterial pressures are the rule in these as well as in other subjects who are liable to recurrent attacks of fibrositis, especially in the shape of lumbago, or of sciatica and other forms of neuritis. Nervous instability and depression, with at times copious urinary phosphatic deposits, are a part of the clinical picture.

6. Tinnitus Aurium.—Mr. Mortimer Wharry [274] finds that cases of severe tinnitus aurium, with abnormal arterial pressure, form a large and important group, in which much distress can be relieved. He has published a series of cases which show that severe tinnitus aurium may be due to a high

pressure alone or to a low pressure alone, in which case it is usually found to be bilateral. If the tinnitus is due to an aural lesion combined with a low arterial pressure, the tinnitus is on the side of the lesion, and may be improved or cured either by removing the aural lesion or by bringing arterial pressure to approximately normal, or by doing both. In a group of four cases of severe tinnitus associated with low arterial pressure, two women, aged respectively seventy-nine and forty-one, exhibited each a systolic pressure of 105 mm., whilst one woman, aged sixty, and one man, aged fifty-four, exhibited each a systolic pressure of 115 mm.

It may be objected that because a low arterial pressure co-exists with the tinnitus and aural conditions it is not necessarily a causative factor. Mr. Wharry, however, regards it as such because of its frequency, and especially because of an instructive case which he adduces of a woman, aged twenty, who complained of deafness, tinnitus, and paracusis. Otosclerosis was present with a marked catarrhal element, which latter disappeared on treatment. The systolic pressure was 125 mm. Trinitrin, gr. $\frac{1}{100}$, was given twice daily for a week as an experiment. The tinnitus became infinitely worse, and the systolic pressure fell to 105 mm. On leaving off the trinitrin the tinnitus returned to its usual condition and the arterial pressure again became normal.

"This case," adds the writer, "shows how lowering of blood pressure adds to the severity of the tinnitus in a patient with a normal pressure suffering from tinnitus from another cause; and taken with the previous cases proves the causative effect of a low blood pressure."

C. The Lowest Limits of Arterial Pressure compatible with Life

Neu has seen recovery after a transient drop in systolic arterial pressure to 50 mm., and mentions a case associated with unconsciousness and subnormal temperature in which there was a temporary fall to as low as 45 mm. Systolic

pressures of 40 mm. have been observed by Janeway as fleeting phenomena during the course of operations.

Rolleston has recorded the striking case of a man with a lingual carcinoma, who lingered on for several weeks with systolic and diastolic pressures respectively of 70 and 35 mm.

In protracted maladies the vital processes can, however, be carried on for several days with a systolic pressure amounting only to 60 mm., which represents the lowest figure at which medullary and coronary circulation sufficient for life can be sustained.

D. As a Terminal Event

With the approach of death from any cause, the arterial pressure falls more or less abruptly towards zero. The rapidity with which this constant fall occurs, and its relation to the actual cause of death, are determined by so many factors about which little is known that it is difficult to say much that is definite, save that a fall in pressure of this nature to a level which is strikingly below the normal limits can only take place when a lack of resistance in the systemic periphery is conjoined with weakness of ventricular contraction.

Under such circumstances the excessively low pressure is of some value as a sign of impending dissolution. More usually a terminal fall of arterial pressure is a matter of only a few hours or minutes. Low pressure is a frequent terminal event in patients with previously-existing high pressure who succumb to uræmia, and, just as in the case of apoplexy, is of grave prognostic significance.

As evidence of circulatory failure it has been found by Krehl [275] and others that in the last stages of arteriosclerosis, widespread dilatation of the splanchnic area, together with failure of the heart to cope with the demands made upon it, results in a falling pressure upon which therapeutic measures have little or no effect.

In the case of sudden death from aortic disease, the fall in arterial pressure is both severe and rapid.

The accompanying chart (Fig. 11) illustrates the grave fall

from a previously constant but slight hyperpiesis which occurred within thirty-six hours before death as the result of

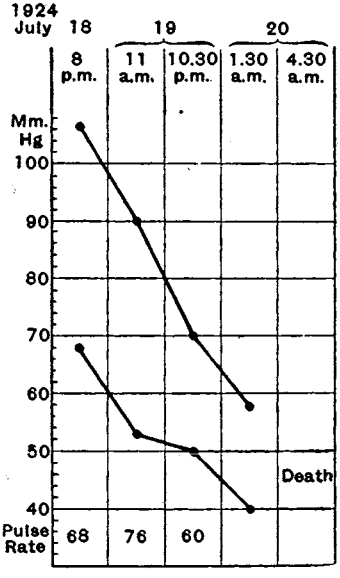


FIG. 11.—Chart illustrating terminal fall of arterial pressure as a result of circulatory failure.

Abstract of Case.—Prostatectomy nineteen days before death; took anæsthetic (C.E.) badly on this occasion, also seven years previously. (Father and one brother died of heart failure.) Hæmorrhage a week after operation for four days. Collapse after aperients on 17th July.

cardiac failure in a gentleman aged sixty-eight seen in consultation at a nursing home with a surgeon who had performed an operation for prostatectomy.

CHAPTER XI

Diagnosis and Prognosis of Low Arterial Pressure

Procedure in Diagnosis

The level of 110 mm. of mercury on the sphygmomanometer scale is generally adopted as the upper limit of states of low arterial pressure, any systolic pressure below this level being taken to indicate the presence of hypopiesis. Diagnosis of low arterial pressure, therefore, in the majority of cases presents no difficulty to a practitioner accustomed as a matter of routine to methods of precise estimation with an accurate arterial pressure instrument, and depends directly upon the levels of the recorded diastolic and systolic pressures.

Although in order to define what is meant by low arterial pressure, some upper limit such as that of 110 mm. becomes necessary, this does not in reality constitute the main objectives, which are (1) to differentiate the kind of case which is capable of reacting to stimuli from that which is incapable of so doing, and (2) to determine in the latter class the amount of reactive capacity.

On these lines the following diagnostic procedure will be found simple and rapid in application. First obtain the complete arterial pressure picture (p. 19); next inject subcutaneously 1 c.c. of 1 in 1,000 adrenalin solution; then take the pressures again at the end of each five minutes for four consecutive readings. By a series of observations it will be seen that whilst in some subjects the pressure levels remain practically unaltered, in others subsequently to injection there is a rise.

Utility of Biochemical Investigation

In the differentiation of cases and selection of lines of treatment appropriate for various types and degrees of hypopiesis, as well as in the elucidation of perplexing cases in general, the author has also derived considerable assistance

from an exhaustive biochemical examination of blood, urine, and fæces. This constitutes one of the most rational methods at our disposal of obtaining a physico-chemical picture of individual constitution and, when combined with the results of careful clinical examination, including tests of arterial pressure, gives valuable indications as to functional efficiency at the time of investigation.

A biochemical examination conducted in this manner yields information as to the water content and acid-alkali balance of the tissues, the functional activity of the chief abdominal organs, especially stomach, pancreas, liver and kidneys, and also aids in determining the balance or otherwise of the autonomic-endocrine system.

Twenty-four-hour urinary curves reflect the rate of metabolism as measured by the output of free and combined acid and products of katabolism.

Technical Details.—The acidity is titrated by the Ellis modification of the Malfatti-Ronchèse method. Each specimen of urine passed over the 24-hour period is analysed separately. The horizontal line in the graph represents a 24-hour period.

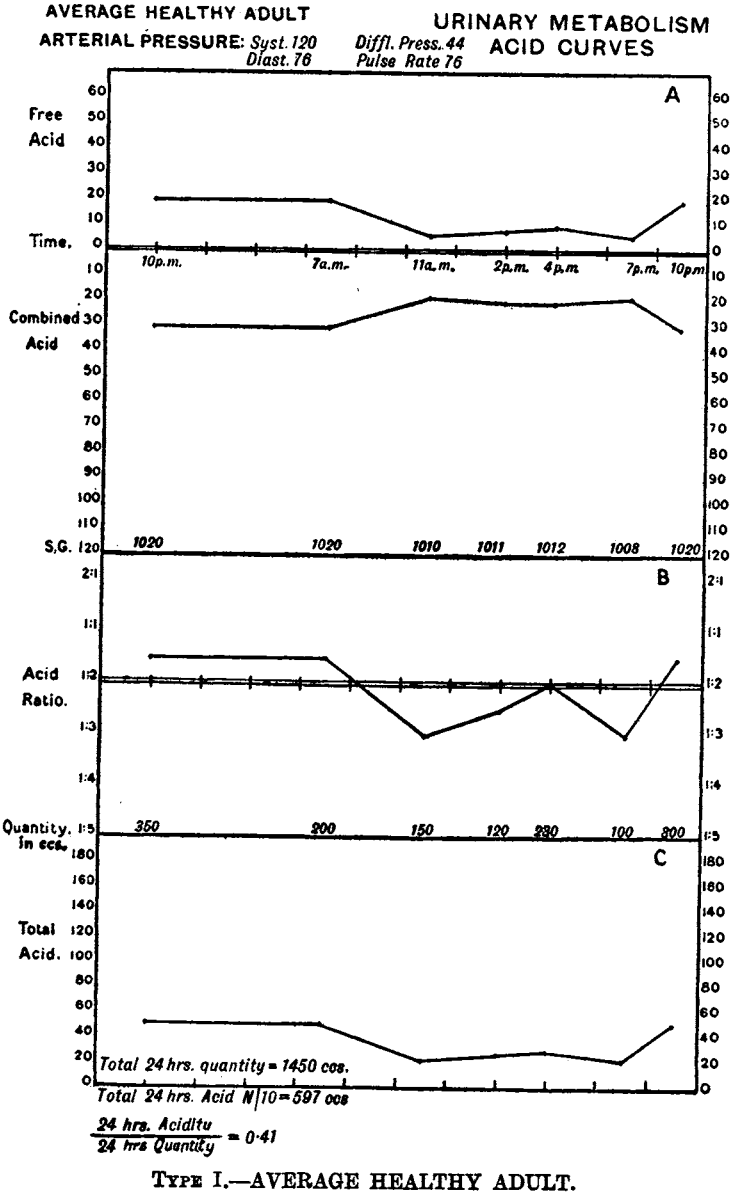
In section A, the free titratable acid, expressed as N/10 caustic soda used for neutralisation per 100 c.c. urine, is plotted out above the base line and the ammonia-amino-combined acid fraction plotted out below the base line.

In section B, the line represents the ratio of the free to the combined acid fraction.

In section C, the line represents the free and combined acid fraction added together.

The dip in the curves which occurs at 11 a.m. is the so-called alkaline tide. This is the result of hydrochloric acid secretion during digestion, and is a normal phenomenon. In a healthy person the distance between the two lines in section A should be roughly the same both night and morning, and the ratio in B should be on or above the base line at these times.

The accompanying graphs (Figs. 12, 13, and 14), for the preparation of which I am indebted to Dr. Edgar Obermer, illustrate three types of metabolism as revealed by their corresponding arterial pressure and urinary pictures



TYPE I.—AVERAGE HEALTHY ADULT.

FIG. 12.

taken in combination. The first represents the standard arterial pressures and 24-hour urinary findings, both within normal limits, of **I. An Average Healthy Adult, Type I.** (Fig. 12).

The next two represent different types of low vitality (Figs. 13 and 14).

II. Cellular and Endocrine (Katabolic) Deficiency Type (Fig. 13).—A low vitality type usually accompanied by polyglandular deficiency. The endocrine group which is most often actually or relatively deficient in these cases is the katabolic group, *e.g.*, thyroid, adrenal medulla, posterior pituitary, and gonads. The rate of metabolism

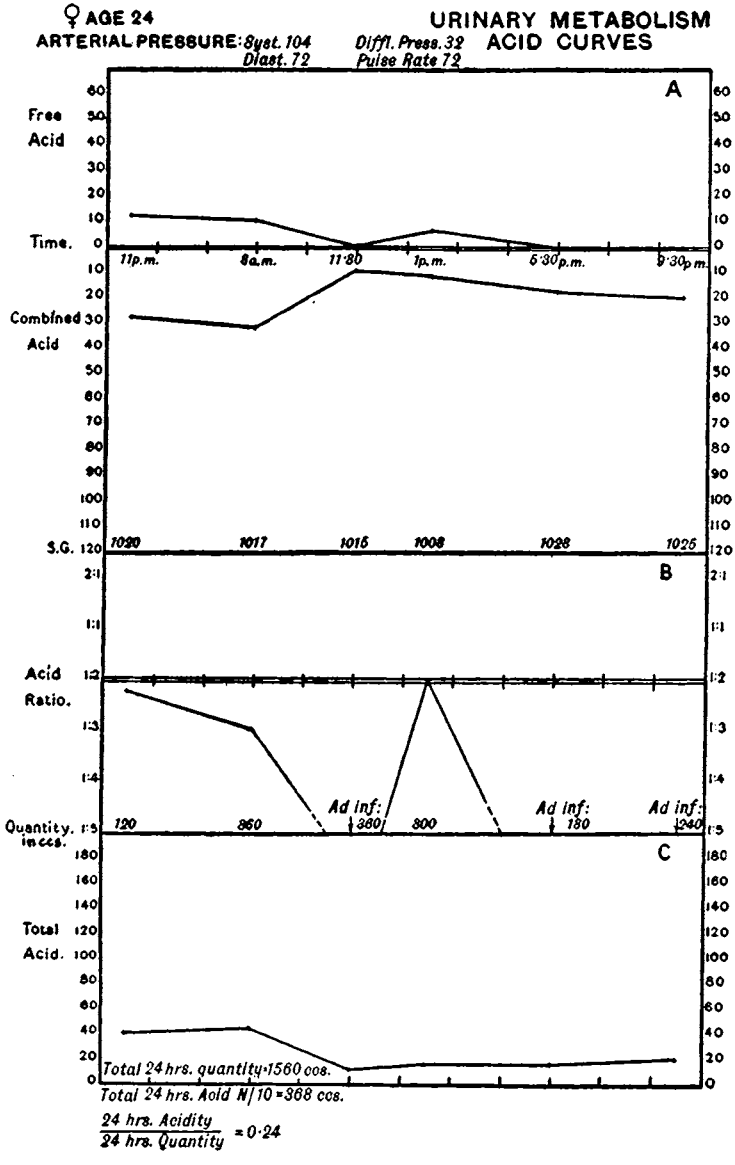
TABLE V

Contrasting Normal Metabolism with that of Low Vitality States

Arterial Pressure.	Type I. Average Healthy Adult.	Type II. Low Vitality—Retarded Metabolism.	Type III. Suboxidation with hepatic dysfunction.
Systolic	120	104	108
Diastolic	76	72	78
Differential	44	32	30
Pulse rate	76	68	76
24-Hour Urinary Output			
Acid	6–700 c.c. N/10	318 c.c. N/10	1,120 c.c. N/10
P_2O_5	2 gm.	2·41 gm.	4·71 gm.
SO_3	2 „	1·32 „	4·58 „
Calcium	Up to 0·3 „	0·213 „	0·515 „
Chlorine	„ 5–10 „	2·17 „	8·21 „
Urea	„ 20–30 „	16·9 „	32·2 „
Uric acid	„ 0·6 „	0·61 „	1·41 „
Creatinine	„ 1·5 „	1·03 „	2·76 „

generally is slowed down. As a result the katabolic products excreted in the urine tend to be low in quantity (see column 2 of accompanying table). In these cases there is no evidence of suboxidation, the oxygen intake being sufficient for the metabolic requirements of the individual. These requirements are usually low, and they have very little energy and tend to be languid and uninspired.

III. Suboxidation-Hepatic Type (Fig. 14).—Suboxidation is the predominant factor in these subjects. It is met with in



TYPE II.—CELLULAR AND ENDOCRINE (KATABOLIC) DEFICIENCY TYPE.

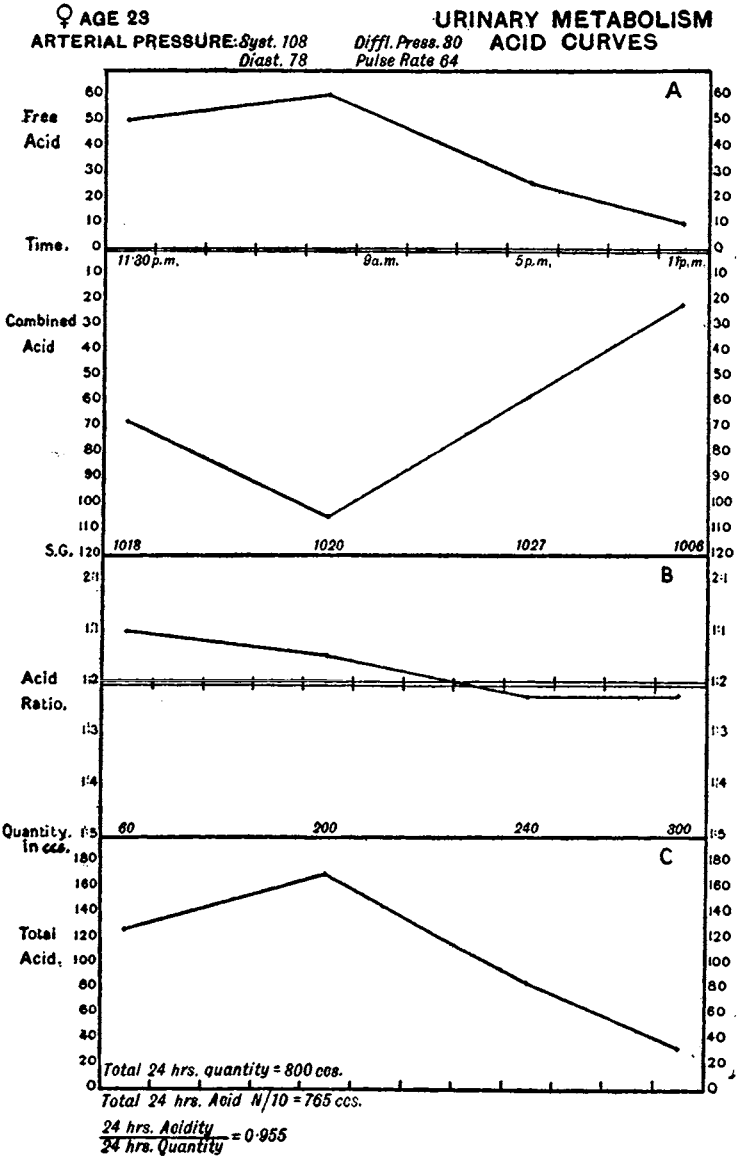
FIG. 13.

all types of physical habitus. The endocrine factor is a minor one, although adrenal medullary deficiency is very frequent. The blood usually shows a low hæmoglobin figure and leucopenia, with a relative lymphocytosis. These individuals tend to be " vagotonic " and frequently suffer from muscular and joint " rheumatism." Evidences are present of hepatic dysfunction with a poor bile flow, and inefficiency of the proteopexic and thiopexic mechanisms. The suboxidation present results in an accumulation of incompletely broken down katabolites, as shown by the example given in column 3 of the Table V on page 186.

Occasional Difficulties in Diagnosis

Every now and again estimation may not be quite so simple from causes arising on the part of the patient or the observer. On the part of the patient one reason is discoverable in an enfeebled circulation through weak cardiac action, whereby the sounds proceeding from the artery below the zone of constriction become faint and muffled, or in extreme cases inaudible. Recourse must then be had to palpatory or oscillatory methods. Another reason is afforded by the presence of gaps at varying levels in the series of sounds, thus causing a possible error in appreciation of the true levels for diastolic and systolic pressures. Still a third reason depends partly upon great laxity of arterial wall (hypotonia) in combination with a fault which is common on the part of the observer, who, while watching intently the shifting levels of pressure upon the scale, tends to press too hard with the bell of a stethoscope upon the yielding walls of a lax brachial artery, which thereby may suffer complete obliteration. Increase of muscular tension in the hand of the observer which compresses the inflating rubber bulb is often quite unconsciously transmitted to the other hand holding the stethoscope. Hence the brachial artery is thought to be difficult to find because undue pressure is exerted upon the overlying tissues, and the reading becomes vitiated.

Rarely estimation of the correct diastolic level may be difficult or even impossible because the sounds gradually tail off into silence, with little or no appreciable distinction



TYPE III.—SUBOXIDATION-HEPATIC TYPE.

FIG. 14.

between the end of the third and the beginning of the fourth auditory phase.

As in high pressure states, so in conditions of low arterial pressure, the systolic level may fluctuate rapidly even from second to second, in emotional, sensitive and nervous patients, so that the results of several successive estimations may be discrepant, although the variations of necessity cannot attain such a wide range of excursion as in high pressure states by reason of the curtailment of the upper end of the pressure level at 110 mm. Under these circumstances, the pressure at the fourth reading may be even higher than those of the former three variables, and, in order to obtain the true residual pressure, it may be requisite to divert the patient's attention and allay apprehensiveness for a short while before proceeding to further estimations.

If the sphygmomanometer be employed as a routine measure in clinical examination, instances of hypopiesis will be discovered with greater frequency than is generally supposed to be the case, the actual proportion varying considerably, however, with the particular type of practice.

To many practitioners fixation of the exact level of the diastolic pressure still leads to so great confusion that it cannot be too clearly stated that the first dull sound following the last loud thud, *i.e.*, **the beginning of the fourth phase of sound, marks the level of diastolic pressure.**

In arterial pressure tests generally, estimation of the level of diastolic pressure is at all times of the highest importance alike for diagnosis, prognosis and management of a case. It is never sufficient to be satisfied with assessing the level of systolic pressure alone, since in the absence of exact figures for each end of the pressure scale one is unable to deduce the figure for the differential pressure, which constitutes a measure of the cardiac load.

Diagnosis of conditions associated at the time with an evident low arterial pressure is made by reviewing the patient's symptoms in conjunction with the physical signs revealed on examination, and again usually presents few difficulties. When, however, one proceeds a step further in the endeavour to arrive at a true ætiological diagnosis,

the problem may then become infinitely more complex. A train of circulatory symptoms, fainting and anginiform pain, for example, may incorrectly be attributed to causes entirely cardiac in origin, and it is only when the exhibition of digitalis or other cardiac remedies are found to have produced no beneficial result, but even possibly to have markedly increased the patient's discomfort, that the true nature of the condition becomes evident, and the practitioner comes to realise that he is in reality dealing with a hypopietic state in which the reserve limit of safety has been exceeded.

Diagnosis in Autonomic-Endocrine Conditions.—The influence and importance of the nervous system may in turn be similarly underestimated, and in cases of sympathetic vasomotor disturbance due regard may not be paid to that metabolic disequilibrium brought about by excess or defect in hormonic proportion which constitutes the vital issue. Dysfunction of one or more members of the series of ductless glands cannot take place without corresponding disequilibrium of the endocrine system as a whole, katabolism being no longer balanced by anabolism, but by patient investigation along the lines of therapeutic tests based on previous careful biochemical investigation, it is often possible to determine where lies the particular fault which leads to imbalance, and to correct it.

In the later developments of pluriglandular insufficiency hypopiesis may be said to occur as an almost constant accompaniment, and this is true not only of the endocrine group of glands, but also of those gastro-intestinal disturbances consequent upon inadequacy of the several digestive glands, including the stomach, intestines, liver and pancreas, as well as of the asthenias, in which category fall the psychasthenias and neurasthenias. Hence result such familiar associations with low arterial pressure as the characteristic type of headache, together with migraine, asthma, dysmenorrhœa, alopecia, defective nutrition of the skin and cutaneous structures such as the finger and toe nails, and the flabby type of obesity with its loss of cutaneous elasticity and of muscular tone. These, with other examples too numerous to detail, at once spring to recollection on reviewing the histories of cases that have come under observation.

The "White Line" of Sergent

In 1903 Emile Sergent [276] described a phenomenon which he termed "la ligne blanche surrénale." The mechanism of production of this "white line" is as follows: If the skin of the abdominal wall be gently and evenly stroked with a smooth round object such as a small india-rubber wheel, a finger-tip or a stylograph, allowed to impinge with no pressure greater than that of its own weight, at the end of a latent period of some twenty to thirty seconds a white line appears in the skin tissues, and, gradually increasing to a maximum in half a minute or more and spreading beyond the original line of contact, after the lapse of a minute or so slowly fades. If, however, too great a pressure be exerted, a red line speedily develops, possibly with white margins which increase in breadth.

In 1921 Sergent [277] claimed that this white line was constantly associated with (*a*) low arterial pressure, though seldom manifest when the systolic pressure was higher than normal, in which event the diastolic was low, and the differential pressure necessarily amplified; (*b*) all types of adrenal insufficiency, whether due to typical Addison's disease or not, in which symptoms of asthenia and low arterial pressure were evident, but inconstant in the presence of melanodermia, which he regarded as being mainly of pluriglandular origin. For the above reasons he regarded this phenomenon as being of great diagnostic and prognostic value.

These views are still upheld by many writers of the French school, who allege that the white line is never visible in normal subjects, but is apparent in most cases associated with a moderate reduction in arterial pressure, and invariably with a notable diminution, particularly in infectious maladies, disappearing spontaneously with improvement, or under the influence of adrenalin (Heitz, Renon, Josué, Tixier).

Sergent believed that the mechanical stimulus induced by light stroking brought about constriction of previously dilated arterioles with resultant bleaching of the skin. This opinion is opposed by many competent critics, notably Massalongo,[278] Leon Bernard,[279] Masary,[280] Müller [281] and

Samson Wright,[282] who adduce strong evidence in favour of their individual contentions that the phenomenon is essentially a capillary one and is neither a sign of hypopiesis nor of adrenal deficiency. It is highly probable that theirs is the correct interpretation, which receives added support from the observations of Cotton, Slade and Lewis,[283] who found that, by placing the arm in the horizontal position, and rapidly increasing the pressure within an armlet to 70 to 80 mm. above the arterial pressure of the subject, the white line can still be obtained, and that its time-reactions remain unchanged even ten minutes after application of the armlet, *i.e.*, after the usual latent period. The effect of compression is to induce stagnation of the circulation in the vessels below the block. In such a system, the vessels which by their content of blood are responsible for the colour of the skin must have contracted or dilated. These vessels must be the capillaries and venules,[284] and blanching of the skin must, therefore, be due to contraction of the capillary wall, which actively drives the blood out into the neighbouring veins.

Flushing of the skin due to a pinprick or other painful stimulus can readily be proved to be an arteriolar phenomenon. If over such area a line of light pressure be drawn, a white line appears, replacing the erythema over an area strictly limited to the zone stimulated. This constitutes the characteristic line of capillary constriction superimposed upon an irregular hyperæmia due to dilatation of the arterioles.

The normal vascular responses of the skin may be thus summarised :—

With all grades of stimuli the arterial response of the skin is vasodilatation (flushing). The capillaries, however, respond differently to weak and strong stimuli, a weak stimulus producing vasoconstriction (white line), a strong one producing vasodilatation (red line). Further, these responses may be entirely absent.

As the result of an investigation of 100 healthy young medical students, Wright found that :—

1. The white line occurs in a large proportion of normal subjects, and is without pathological significance.

2. It is not related to adrenal insufficiency nor to abnormally low systolic and diastolic pressures.

3. It is produced by local emptying of the capillaries due to the active contraction of some elements in their walls, and is quite independent of the condition of the arterioles.

4. A nervous mechanism of the nature of an axon reflex may be involved.

"The white line of Bäumler, Vulpian and Sergent, the dermographia alba of Müller, and the white tâche of Lewis appear to be the same phenomenon which has no diagnostic significance."

These opinions of Wright are in agreement with the findings of Tracy [285] as well as of Kay and Brock,[286] who discovered the white line to be of frequent occurrence in normal individuals and to bear no relation to adrenal activity or to arterial pressure. It can be caused to appear in face of a subcutaneous injection of adrenalin.

Hence, in the light of the above consensus of experimental evidence, the diagnostic phenomenon of the white line should be regarded as denoting a state of heightened sensitiveness of the sympathetic nervous system (sympathetic-cotonia), but not as having any necessary links with hypopiesis nor as possessing any real pathological significance.

Influence of Posture.—(*a*) *On Heart Rate.*—The effects produced on heart rate and on arterial pressure by alterations in posture are of assistance in establishing a diagnosis of hypopiesis when a pressure instrument is not available, or in confirming an opinion already arrived at by sphygmomanometric observations.

Standard heart and pulse rates in the horizontal position are slower than those in the vertical position by 8 to 10 beats per minute. Thus undue lability of heart rate, as evidenced by acceleration of 20 to 40 beats per minute, on sudden change from the horizontal to the vertical position, is an indication of sympatheticotonia. The greater the divergence between the recumbent and standing rates the more marked is the vasotonic deficiency and the drop in arterial pressure. Following excessive peripheral dilatation, the heart increases the number and force of its contractions, with resultant tachycardia. In the absence

of causes due to the heart, deficient arteriolar and capillary tonus should always be suspected.

(*b*) *On Arterial Pressure.*—Here also detection of functional cardio-vascular insufficiency is aided by observations on arterial pressure in changing from the horizontal to the vertical posture, hypopiesis being accompanied by a drop of some 15 to 20 mm. in arterial pressure, which continues to fall as the patient remains standing, until in well-marked cases after the lapse of a quarter of an hour or more, sensations of faintness or of lassitude may be complained of. In some instances the systolic pressure may show no decline, but the diastolic pressure rises, thus causing a definite reduction in the differential pressure, pointing to a lack of vitality and lowered physical efficiency.

Cardiological Aspects of Diagnosis and Prognosis

From the cardiological aspect one question presents itself at the outset, as to whether or not hypopiesis is the expression of inadequate response on the part of the heart itself. In regard to this, the main source of propulsive energy, the dictum of Mackenzie that the integrity or otherwise of the cardiac muscle can be assessed by its response to effort stands supreme. Thus, by a careful review of the patient's history with reference to previous capacity for physical exertion in conjunction with tests of effort response at the time of examination, we have a ready means of gauging the functional efficiency of this vital organ.

Hypopiesis, nevertheless, does not invariably depend upon weakening of myocardial energy, but is often due to some extrinsic cause, such as insufficiency of the chromaffin system. " Some writers, starting from the premise that the differential pressure expresses the ventricular energy, maintain that its diminution enables us to foresee heart failure ; but this premise, while correct when the volume of blood is measured at the mouth of the aorta, is inaccurate for man in whom the pressure is estimated at the periphery. Moreover, it gives very different results according to the form of heart failure, for the differential pressure is incapable of giving information of the energy of the right heart, and

is often normal in most advanced mitral disease. Of failure of the left heart its indications are limited. When the left heart fails suddenly, the systolic pressure usually falls. The diastolic changes very little, and the differential pressure diminishes; but these changes never precede heart failure, and are therefore of no premonitory diagnostic value. They have more prognostic significance; when, following failure, the differential pressure does not increase, the condition is serious, no matter what the other symptoms may be." [287]

The next procedure in clinical investigation is to determine whether the state of the cardio-vascular system as a whole, as indicated by the existing low arterial pressure, is sufficient or not for the daily metabolic needs of the individual. If the pressure figures be the same, or vary but slightly on several readings, we may infer that the peripheral resistance is in satisfactory equilibrium. Rapid fluctuation of level during the time of estimation, or from reading to reading, may point to vasomotor instability.

In mitral insufficiency the arterial pressure presents no special features, since in this condition the cardiac symptoms are due mainly to changes in the pulmonary circulation, whilst arterial pressure changes depend only upon the systemic circulation. The figures obtained should, therefore, rather be regarded as the algebraic sum of various circulatory factors than as absolute measures of cardiac energy. A weakened pulse, with low arterial and differential pressures, may thus either indicate the results of the valvular damage unaltered by compensatory influences, or failure of the left ventricle to maintain circulatory efficiency.

In mitral stenosis of adults the arterial pressure is little altered, owing to compensatory changes in the arterial bed.

Since the time of Marey and Chauveau numerous animal experiments have confirmed the original findings of these observers that the production of aortic insufficiency is immediately succeeded by a large fall in diastolic pressure due in part to regurgitation into the ventricle.[288, 289] This enormous drop in pressure during diastole, best observed in the endocarditic group, is the most noteworthy characteristic of aortic insufficiency, and this leakage is responsible for the low diastolic pressure although the actual quantity of

regurgitant blood is usually not more than one-tenth of the total systolic output. The greater the amount of leakage, the wider becomes the differential pressure.

In cardiac dilatation, attended or otherwise by valvular implication, arterial pressure is at times low, and a return to normal or raised levels affords a valuable indication of progress towards recovery. Out of 500 cases investigated by Roberts,[28] 347 showed no cardiac abnormality, evidences of cardiac disease being found in 153. Hypopiesis was present in 47 per cent. of the former group and in 26 per cent. of the latter. That myocardial degeneration or disease plays a relatively minor part in the production of hypopiesis is explicable on Starling's [79] Law of the Heart; and Dock has further pointed out that myocardial disease with hypopiesis does not usually manifest corresponding depression of the diastolic pressure, which is often elevated. If really low pressures do occur these may point to a previously existing and relatively high pressure in a state of decompensation, and thus be of grave prognostic significance. Failure of the left ventricle may be diagnosed clinically by a distinct loss of muscular tone in the first cardiac sound, which, instead of exhibiting the normal booming quality, becomes short, sharp and weak, thus approximating in tone to the second sound. With a rapid heart rate the long pause becomes shortened to the same interval of time as that of the short pause between the first and second sounds, when sounds resembling the ticking of a watch follow one another with uniform regularity. This " tic-tac " rhythm is similar to that which is normally heard over the fœtal heart, and has thus been termed embryocardia. Middle-aged or elderly subjects, who manifest signs of low arterial pressure, a tic-tac rhythm, and a 1 : 1 ratio with the differential stethoscope, are specially liable to ventricular fibrillation and take anæsthetics badly.[291] Fatalities from the administration of chloroform frequently occur in such subjects.

In acute carditis arterial pressure is usually low, and progressively diminishes in proportion to the severity of the attack. " A rapid fall in pressure is a bad sign, proving as it does the existence of a gross inefficiency on the part of the left ventricle. . . . In acute rheumatic carditis with

auricular failure, a certain amount may be learnt as to prognosis, and as to reaction to digitalis treatment, by noting the proportion of beats with a low maximal pressure to the total number of heart-beats. As the condition improves, these low pressure ineffective beats decrease in frequency."[193]

In angina pectoris after an attack the arterial pressure frequently returns to its former level. Verdon [194] has shown that in certain types of this malady low arterial pressures are met with, and in such cases prognosis is far more grave than in those associated with high arterial pressures. In the latter a sudden drop in systolic pressure is of the utmost gravity, and usually implies a fatal prognosis, especially when a big drop follows a seizure. The systolic pressure may show a notable fall in the crisis of angina pectoris, the diastolic pressure remaining relatively high. The differential pressure thereby becomes considerably reduced, indicating an unfavourable prognosis. In severe forms terminating fatally after a drop, for example, from 250 to 90 mm., very rapid pulse, feeble and unequal heart-beats, and sensations of suffocation replacing those of pain have been noted.

Diagnosis and Prognosis (*a*) In Shock, Hæmorrhage and Operation

In shock, prognosis becomes more grave in proportion as the differential pressure sinks lower.

In hæmorrhage or loss of tissue fluid, diminution in absolute volume of the blood constitutes the crucial and determining factor in the production of hypopiesis. Hæmorrhage, however produced, makes for a fall in arterial pressure, which will frequently be overlooked if pressure tests, whether in medical or surgical practice, are not made as a matter of routine. Acute low pressure is brought about by a pronounced diminution in the contents of the circulatory system, *i.e.*, a sudden and profuse bleeding. In the detection of internal hæmorrhage the discovery of a falling arterial pressure and pulse rate are of importance. Small repeated hæmorrhages reduce arterial pressure only to a slight extent, since the blood mass becomes rapidly restored by dilution.

In extrauterine pregnancy an abrupt fall of pressure may indicate rupture. Similarly, in enteric fever, a sudden fall in pressure indicates hæmorrhage rather than intestinal perforation. In thoraco-abdominal wounds, progressive hypopiesis points to continuance of the bleeding. Thus, in the above and in other numerous conditions post-hæmorrhagic hypopiesis can assume a diagnostic importance.

In operation and shock hypopiesis also serves as a diagnostic and prognostic indicator. Till now arterial pressure has been almost universally regarded as lying within the province of the physician, and the vast majority of surgeons have been content to ignore the information to be derived from accurate estimations, or even to scoff at their utility. Yet the work of Crile and others has shown that when in an adult arterial pressure ranges low, the margin of circulatory safety is small, and unless more than ordinary precautions be taken, the results of a serious operation may be disastrous to patient and surgeon alike. No matter how good be the operative technique of a surgeon, if the patient dies at or soon after an operation of causes which are preventable by the exercise of a little foresight. Estimations of arterial pressure in combination with the simple capillary method, devised by Ellis, of taking the hydrogen-ion concentration and alkali reserve of the blood, adopted as a routine measure both before and during operations, are not only likely to enchance the reputation of the surgeon, but to give timely warning of impending danger and to yield data of considerable prognostic value.

(*b*) In Acute Specific Infectious Diseases

In all the acute infective maladies, whether of bacterial or of uncertain origin, there is usually a progressive acceleration of the rate of the heart-beat together with a gradual fall of arterial pressure. The heart rate quickens to about 100 beats per minute, or, with a severe infection in a patient of high resisting power, may reach 140, the regularity of the rhythm being as a rule unaltered. Coincidently the systolic pressure, which during the first few days has kept its normal level, undergoes slow reduction to 100 mm. Hg or less, even

down to 80 mm. As a general rule in acute infections the maximal pressure will be found not to exceed 100 mm., falling gradually during the acute stage of the malady and again gradually tending to rise during the period of convalescence. The minimal pressure may undergo depression to 60 mm., or in extreme cases may even reach a point which is difficult or impossible to estimate. A fall to below 40 mm. indicates a grave prognosis. Other things being equal, the more prolonged and intense the febrile attack, the more reduced does the arterial pressure become. To this generalisation, however, there is one notable exception, namely acute meningitis. In the course of this disease, by reason of the increased intracranial pressure arising from the presence of a thick exudate, hyperæmia of the cerebral tissues, and distension of the ventricles, the arterial pressure necessarily becomes heightened.

In the remainder of the acute infections of specific type, lowering of arterial pressure, in certain instances even to an extreme degree, is caused primarily as a result of toxæmia, which induces vasomotor paresis or paralysis, and secondarily, from the same cause but in lesser degree, by progressive enfeeblement of the cardiac muscle with consequent structural damage.

Symptoms due to cardiac insufficiency are so often preceded by lowering of arterial pressure, which continues until the period of defervescence, becoming even more pronounced under conditions of toxic pyrexia which too often reach a fatal termination, that lack of cardiac tonus can hardly be invoked as other than a secondary factor in the causation of hypopiesia. "It is only towards the end, even in the last few hours, that there appear, in association with increasing dyspnœa, signs of congestion of the pulmonary bases, and, on the side of the main circulation, cyanosis and chilliness of the extremities, which together hasten the fatal issue. At other times there is abrupt collapse." [292]

From a mass of evidence which has now accumulated, it is reasonable to suppose that the functions of the adrenal glands become more or less profoundly impaired in accordance with the extent and virulence of circulating toxins. The more acute the infection, the greater the degree of toxæmia,

and consequently the higher the degree of impairment of the adrenal hormone.

The height of the arterial pressure may thus be regarded as a valuable index by which one can gauge not only the greater or less power of resistance of the organism to the particular infecting agent or toxin, but also by which one can infer the presence of a condition characterised by deficient oxygenation.

(i.) **In Enteric Fever.**—In enteric fever usually the lowered pressure does not run parallel with pulse acceleration. It drops from a normal level after the patient has taken to bed and stays down till convalescence is established, when it again returns towards normal limits. The arterial pressure is governed by factors of its own, and bears no constant relation either to pulse rate or to temperature. There is no disease in which sphygmomanometric readings are of greater prognostic value. In the diagnosis of complications it is also of great importance. Preceding intestinal hæmorrhage there is often an initial slight elevation in systolic pressure, which is succeeded by a sudden and profound depression which may be due to diminution in the volume of the blood and may also be indicative of cardiac failure, in severe instances of either condition the fall being due to lessened volume of circulating blood. Certain observers deny that an initial rise in pressure takes place and state that the onset of intestinal hæmorrhage is accompanied by a definite fall. Perforation of the bowel is also stated to be usually accompanied by a rise in systolic pressure, but a lowered pressure is not invariably a safe indication that perforation has not taken place. Knyvett Gordon [213] has never observed a rise in pressure at the onset of perforation, although he watched for it constantly, since he always submitted cases in which perforation had occurred to laparotomy at the earliest possible moment, and therefore availed himself of any sign that might be of assistance in diagnosis.

(ii.) **In Influenza.**—In true influenza a drop in arterial pressure follows soon after the onset of the disease, and the pressure may remain low for many months after recovery. In post-influenzal asthenia a low arterial pressure is present

as a rule, and persists until asthenia has passed away. This is also true of convalescence from other grave and acute maladies, such as enteric fever, all adynamic states, chlorosis, exophthalmic goitre and certain forms of neurasthenia.

To medical referees and others who are interested in assessing the working capacity of patients convalescent from infectious and other illnesses, this point is of considerable prognostic import, since it would be obviously undesirable to pronounce a patient fit to return to work involving physical strain so long as a persistent hypopiesis is present. Conversely, although a patient may still complain of inability to pursue his previous occupation, an arterial pressure found to be within standard limits, in the absence of other disabling causes, would suggest that return to work was not only possible but desirable.

Bain [35] indicates the diagnostic advantage of a low differential pressure in that it occurs at times where the opposite might be expected, and may be the means of revealing the presence of an otherwise obscure neurosis which the patient may be reluctant to disclose, as well as a useful index of the response to treatment.

(iii.) **In Lobar Pneumonia.**—Cotoni, Truche and Raphael [293] state that "in pneumonia Potain called attention to the parallel fall of temperature and of arterial pressure during the crisis. Pongier, confirming the conclusions arrived at by Gilbert and Castaigne, François and Reynaud, emphasises the unfavourable character of the prognosis where the arterial pressure was low. Laubry estimated arterial pressure in pneumonia, with the Riva-Rocci apparatus, chiefly from the point of view of the crisis, and while he found that the figures varied with different individuals there appeared to be one fairly common type in which there was arterial hypopiesis at the height of the disease, a transitory hyperpiesis during the precritical phase, hypopiesis during the crisis, and a return to normal during convalescence. In several cases, notably in a young man aged nineteen, this association of hypopiesis with the crisis was observed. All estimations were made with Pachon's oscillometer at the same time of day. A comparison of the temperature with the arterial pressure is instructive in this connection. In

another patient who died after a pseudo-crisis the same lowering of blood pressure was noted after the eighth day, when the expected crisis appeared to occur; the temperature and respiration-rate fell, and there was sweating with a sensation of ease and well-being. It was on the tenth day, when the crisis was at its height, that the pressure was at its lowest (125 and 75), rising again to 155 before death. Thus at the height of the pneumonic crisis there was a temporary lowering of the arterial pressure, the pulse simultaneously becoming full and ample. From a study of sphygmographic charts published by Hamelin it would appear that lowering of arterial pressure was associated rather with the precritical exacerbation than with the crisis itself; but in those cases in our own series in which this relative and transient hypotension was noted it occurred more often on the day on which the temperature began to fall. In any case, whatever may be the exact moment at which the pressure begins to fall, *it falls during the crisis.* This fact, correlated with a diminution in the number of leucocytes, is of great significance in the explanation of the mechanism of the crisis."

Kempmann [294] found that in the majority of cases of pneumonia arterial pressure underwent little or no variation, whilst in certain instances a definitely lowered pressure persisted. The author's view is, however, that in pneumonia reduction of arterial pressure is not invariably of unfavourable significance and, except in conditions of cardio-vascular failure, arterial pressure observations are too variable to afford any very important clues as to prognosis or management.

In Pernicious Anæmia.—Pernicious anæmia is characterised clinically by profound asthenia, which occurs apart from wasting, and hypopiesis; by a lemon tint of the skin, chronic gastro-intestinal disturbances, including dyspepsia and intermittent diarrhœa; frequently soreness of the tongue, and occasional remissions of the malady. Microscopical examination of the blood reveals the presence of a low erythrocyte count, a high hæmoglobin index invariably above 1, and an almost constant diminution in the total leucocyte count together with a relative predominance of lymphocytes.

Prognosis as to Life, and in Operative Procedures

The practitioner is often in difficulty when asked to decide upon the fitness or not for major operation of a patient who is the subject of congenital hypopiesia or of acquired hypopiesis with persistently low pressures. Provided that the general health has been good, and that no arterio-sclerosis or other grave defect is detectable apart from that for which operative intervention has been advised, the author's experience is that such subjects stand operation well, and that low pressures, *e.g.*, 90 to 65, ranging over months or even years, should be regarded as habitual to the patient, and in no way indicative of serious prognosis either immediate or remote. In other words, these persistently low pressures, unless forming part of a grave constitutional malady, do not tend to shorten the prospect of life, but rather to enhance it. Nor do they add to operative risk. Shock and operation appear to exert but little influence upon their levels, since the total range of cardio-vascular and autonomic-endocrine response is but slight. Hence in most low pressure subjects operation can be performed with no greater degree of risk than that which attends similar procedure in patients with standard arterial pressures.

Of quite a different character is the persistently **progressive** low arterial pressure which occurs in severe acute infections, in wasting diseases, in failing hearts and in anæmic states. Such persistent and progressive fall is of the worst possible omen, and invariably presages a speedy dissolution. Similarly in cases of relative hypopiesis, in which the pressures have formerly been maintained at high levels.

CHAPTER XII

Control of Low Arterial Pressure

Starting from the basic proposition laid down in Chapter III, that hypopiesis is always an expression of low individual capacity for reaction to environment based on inherent or acquired defects in nutrition of the cells and tissues of the body, one will not be tempted, through insufficient appreciation of the principles involved, to agree with the assumption that "every case of low arterial pressure revealed only by the sphygmomanometer can be ignored." Touching this and similar statements, it is first requisite to know the pressure limits that the writer of the above quotation had in mind. If the upper limit of low pressure were taken at 120 mm., then many instances of pressures revealed only by the sphygmomanometer, and ranging between 120 and 110, are met with which require no treatment, since the subjects thereof are not conscious of any symptoms. When the upper limit, however, is taken at 110 mm., as being the most useful division in the author's belief between pressures above this point, which are normal for many persons, and pressures at and below this point, which are less than they should be for a state of good health, the latter pressure, as indicating a state of low vitality, should always be raised if such procedure be at all possible.

A method of gleaning advance information as to the probability of success or failure from therapeutic measures designed to raise an existing low arterial pressure is afforded by the subcutaneous injection of 1 c.c. of a 1 in 1,000 solution of adrenalin, mentioned on p. 183. Thereby differentiation becomes practicable between two groups of hypopietics: the one, which manifests no capacity for reaction whatever, and the other, which manifests a greater or less reactive capacity, as indicated by the extent to which the arterial pressure rises after injection. The

first group, a comparatively small one, in which all the vital processes of the body are at a very low ebb, either through inherent debility, or through acquired exhaustion as the result of the depleting influences of infections, infestations, impairments, injuries, stresses or strains, represents a minus quantity, wherein the character of the negative sign cannot be changed to a positive by any efforts, however well directed. Of this group congenital neurasthenia forms a good example. Here exists no vital force greater than that which barely suffices to prevent the onset of psychical dissociation or of physical disintegration, consequently no reserve energy is available upon which to work. For this class, as a rule, one can do nothing. The second group presents a striking contrast in that, although the actual levels of arterial pressure may be absolutely identical with those of the former group, the opposite condition of capacity for reaction to stimuli, which one may represent by a plus sign, prevails. Prior to injection of adrenalin, both groups are minus as regards their respective pressure levels, but subsequently the former group remains continuously minus, whilst the original minus quantity of the latter becomes changed into plus. In other words, the first group represents a condition of hypopiesis that is static, the second represents a capability of conversion into one that is dynamic.

From the previous general remarks (anent differentiation of low pressure cases (Chapter XI)) it will be evident that if one approaches the important matter of treatment from a broad biological point of view, one is likely to be saved from the " hit-or-miss " lack of therapeutic principle, and to run less risk of " putting into bodies of which we know little drugs of which we know still less." Medicine will of necessity always be an art and never an exact science, but applied biochemistry has within recent times placed in our hands a valuable means of obtaining additional exact information, qualitative and quantitative, which it would be unwise to ignore. By its use one can gain a closer idea of the degrees of aberration from average metabolic function in a more comprehensive and exact manner than has previously been afforded by estimation of the basal metabolic rate, which is capable only of limited application.

Like other applied aids to clinical medicine, the biochemical method is a good servant but a bad master, and should be used only as a means to an end. Inferences derived from its findings necessarily vary in correctness with the skill of the interpreter, and should invariably be correlated in their due perspective with information derived from clinical examination, which should always include as exact a history of the patient as possible.

Till now it has been universally stated, almost *ad nauseam*, that it is far more difficult to raise a low arterial pressure than to reduce a high one. Apart from the non-reactive group just mentioned, this view is only correct if one looks for a considerable rise on the sphygmomanometric scale, since at the outset of treatment it is essential to recognise that an increase of even only a very few millimetres will make all the difference between restored capacity and comfort on the one hand, and a state of inertia and discomfort on the other.

From the point of view of control, therefore, the whole matter must be reviewed from the broad biological aspect. Regarded from this standpoint, the low vitality and low reserve energy of the hypopietic is due to a low general standard of cell and tissue nutrition, congenital or acquired, which connotes a low level of metabolic processes. However produced, hormonic deficiency or exhaustion attributed to one or more glands of internal secretion with overaction of the antagonists forms but a part of the whole picture. Thus we shall not expect the symptomatic application of substitution therapy invariably to be efficacious, but must look beyond this to a wider horizon for an adequate explanation of the rationale of control. Where defective nutritional causes are dominant, there general measures of stimulation and support are indicated; alternatively, where endocrine dyscrasia plays the major part in causation, there the exhibition of hormonic products in various proportions and degrees is likely to render the more valuable aid.

It is true that, even for long periods of time, the congenital subject of the lesser grades of hypopiesis can adequately carry on the affairs of life, but that sooner or later the limits of reserve energy are overpassed is proved by the heightened

liability to zymotic diseases and the frequency and suddenness of attack even when these subjects are thought to be in perfect health.

Having regard to the importance of metabolic balance, it is unwise to endeavour too rapidly to raise a temporarily or persistently low arterial pressure, for by so doing one defeats one's own object. Further, if the pressure be raised to a level which is above the standard for the individual, sensations of throbbing in the head, followed some hours later by intense irritability, may be experienced. What happens is as follows : just as in the case of neurasthenic depression, so in the profound depression of arterial pressure, when either becomes relieved too quickly, excessive response to minimal stimuli in the shape of irritability supervenes. Hence there is no cause for concern if within a few hours one is unable to raise a pressure of 100 or less to 120 mm., for a difference in level of only one millimetre in a low pressure subject is proportionate to about 5 mm. in a high pressure case. Rather be content gradually to raise the pressure to a level which appears to be the optimum for the individual, at which he or she feels most comfortable, checking the results of treatment by sphygmomanometric observations at regular and frequent intervals.

Seldom is it necessary, or even possible, to augment a low arterial pressure by any large amount. Small rises of only a few millimetres are amply sufficient to produce large differences in the clinical picture. Supposing 96 to 106 mm. to represent the limits of systolic pressure in an untreated case of hypopiesis, apart from the effects of exercise or of mental concentration or emotion. Within this range the subject is more often than not apathetic, miserable and depressed, with bad days on which concentration is difficult and physical inertia great until some stimulus or other happens to send up the pressure by a slight amount. Even so small a rise as from 106 to 110 mm. in the systolic pressure will cause immediate relief of symptoms, while a further rise, say to 116 mm., will effect marked benefit in the feelings and state of the victim.

Having completed the investigation of the patient, as detailed in Chapter XI, we are now in a position to determine

whether the case is in origin congenital or acquired, and in the latter event, whether hypopiesis be slight or severe, relative or absolute, and associated or not with accessory morbid phenomena.

The reactive form of congenital hypopiesis can be directly controlled, whereas for acquired hypopiesis special measures are indicated in accordance with the varying conditions of association.

In respect of therapy the congenital and acquired groups of hypopiesis may be taken together, the measures required for special conditions of association being dealt with later.

I. General Measures of Co-ordinated Control

1. Mode of Life.—The hypopietic subject should be taught consciously to regulate his daily mode of life so as to secure in fullest measure co-ordination of control. He should be helped by advice and precept so that he can attain for himself a well-regulated psychical and physical balance, and should be shown how to conserve his store of energy so that he may avoid the necessity of having to draw upon his scanty reserves. Moderation in all things should be insisted upon as the key to restoration of well-being.

2. Diet.—(*a*) *Solids.*—Patients always ask whether any particular form of diet is to be followed. The hypopietic subject should be told that diet in general should be nourishing, ample, easily digestible and properly balanced ; proteins, fats and carbohydrates being taken in due proportions having regard to the nature of the case. Particular care should be directed to ensure that a sufficiency of vitamins be incorporated in the diet, these being best taken in the form of **fresh** vegetables, butter, milk, cream, etc. Bottled vitamins so widely advertised should be eschewed in favour of natural foods, and only utilised should an adequate supply of fresh foods not be obtainable. Bearing in mind that deficiency diseases, including avitaminosis, play a large part in the production of low vitality conditions with which low arterial pressure is coincident, this point should be made very clear to the patient. Deficiency or lack of certain foodstuffs or of accessory food factors will largely negative any attempts to raise an existing low pressure to more normal

levels. Excess of protein, fat or carbohydrate constituents of the diet is harmful, since it leads to the manifestation of dyspeptic symptoms, by which the pressure not infrequently is still further lowered.

Provided that careful directions are given by the patient's medical adviser as to a suitable diet based on the above general indications so as to avoid any possibility of under-nutrition, and any existing dietetic errors receive correction, no special diet tables are called for, unless necessitated by the particular demands of some individual condition that may be present in association.

(*b*) *Fluids.* — (i.) *Water.* — Most hypopietics, especially women, do not drink enough water. A useful working rule is a pint of water for each five stone of body weight, taken in quantities of half a pint at a time on rising, at bed-time, and at conveniently spaced intervals between meals during the rest of the day. Water can be taken plain, hot or cold as preferred, or in the form of Salutaris, Malvern, Springwell or other pure waters. The main object is to promote adequate elimination by way of the kidneys, and to lessen tendencies to constipation. In toxæmic states this procedure is especially to be prescribed.

(ii.) *Alcohol.*—Alcohol, as a general rule, is best avoided, except in cases of gastric neurasthenia, or anorexia due to mental or physical fatigue, under which circumstances a tankard of stout, a whisky and soda, or a glass of port, taken at the time of the meal, by acting as temporary stimulants, often restore the vital balance.

3. Rest.—In severe cases, physical and psychical exhaustion are best combated by recumbent rest in bed at the outset for as long a period of time as the circumstances require. The lassitude of cases which are less severe is alleviated by rest during stated hours after the chief meals, and by keeping early hours of going to bed. Rest in bed or with the feet up on a couch, in conjunction with other remedial measures, restores the balance of cell nutrition, circulatory activity, and autonomic equilibrium. Subsequently, massage and hydrotherapy in combination with static electricity or ultra-violet radiation, still further promote a return to higher pressures and increased vitality.

4. Exercise.—Exercise should always be within the patient's power of reserve. Physical exercises of stretching and bending, combined with deep breathing, performed on rising, and followed later in the day by walking at a medium and regular pace, at first on the level and then on gradually increasing slopes, favour oxidation and counteract respiratory deficiency. The daily walks should be increased proportionately to the patient's ability and freedom from discomfort, care being taken throughout never to overstep the limits of reserve energy.

With the above proviso, horse-riding and games should be encouraged in those who are physically fitted, but vigorous games such as lawn tennis should never be persisted in till breathlessness, palpitation or other symptoms of discomfort supervene.

5. Change of Air.—Holidays are always beneficial to the hypopietic manual or mental worker, when these are taken judiciously, but their effects are little more than transient when sites are chosen at or little above sea level. Real and more lasting benefit is attained by change of air to high altitudes of 5,000 feet and upwards, which have a stimulating and powerful influence in augmenting metabolic rate and general vitality through the abundant supply of pure air, rich in oxygen, and the greatly increased number of hours of sunshine. Considerably more exercise with less fatigue can be undertaken at high altitudes, except by the victims of active pulmonary and uncompensated cardiac disease.

6. Sunshine.—Sunshine is a potent factor for good in the treatment of most hypopietics who live in cold, damp and changeable climates. These subjects exhibit a craving for sunshine in some cases greater than that for food. On sunny days they are bright and happy; on dull days they are gloomy and discontented. Many of them know if the weather is wet before they get out of bed, and, like rheumatic subjects, are very sensitive to climatic changes. Nevertheless, of itself sunshine will not have a large effect in altering the level of arterial pressures, its effects on metabolism being psychical and indirect rather than physical and direct. It must be understood that the above remarks refer only to limited amounts of sunshine on fine days and on holiday

travels, and do not apply to prolonged residence in tropical climates, the effects of which have already received consideration.

II. Special Measures of Co-ordinated Control

1. Relaxation Exercises and Passive Movements.—Conservation of energy is a fundamental natural law. In the inanimate world this principle is constant; in the animate world it is variable, since over-activity of bodily or mental processes does not permit that perfect repose which should be aimed at in intervals of exertion. Such excess energy is injurious in that energy is frittered away to no purpose. To achieve any undertaking a stock of energy not only adequate to the immediate demand, but also a reserve store or complement, are requisite. Either or both of these may be lacking in hypopietic subjects, and relaxation of mind and body forms a valuable aid in their restoration.

Muscular relaxation is a state of complete muscular rest, the muscles at the time, nevertheless, retaining their inherent property of tonicity. Complete relaxation is attained by causing the patient to recline at length in a position which is naturally the most comfortable. Mental repose is at the same time induced by thinking of pleasant things and breathing automatically. In suggestible patients the eyes close of their own accord, or, if they are still open, the patient is directed to shut them.

Passive movements of the limbs can then be undertaken, beginning with the fingers, which are alternately flexed and extended passively, then following with wrist, elbow and shoulder joints in the order named, the patient being instructed to allow the limbs to remain lax. Certain patients find great difficulty in relaxing, and at the first attempts may fail completely, the limbs being held in positions of great rigidity. By persuasion and re-education, this difficulty in permitting the upper limbs to be moved passively is overcome, after which the lower limbs are similarly moved, and next the neck and trunk, so that eventually patients acquire a habit of muscular and mental relaxation which can daily be practised for themselves at will. Conservation of energy is thus attained with a minimum

expenditure of effort, and beneficial results speedily appear.

2. **Deep Breathing Exercises.**—Following on the above exercises of relaxation and of passive movement, deep regular breathing in and out in a measured way can be practised by the patient, at first under supervision (Fig. 15). Initially the patient may be able to take only short and inefficient breaths, owing to respiratory inefficiency as a result of contracted thorax or natural faulty method of breathing, but with practice these difficulties are largely

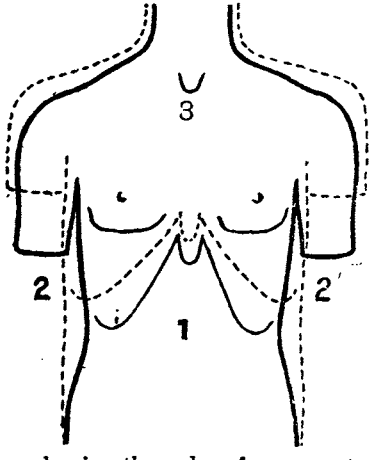


FIG. 15.—Diagram showing the order of movements of abdomen and thorax in the author's "complete cycle of full inspiration."
1 = abdominal, 2 = lower costal, 3 = upper costal inspiration. In full expiration these movements take place in the reverse order.

overcome, and increased thoracic mobility together with augmented volume of inspiration and expiration ensue. The system is thus harmonised, and biochemical changes promoted which have the effect of increasing oxidation and removing waste products.

The three movements necessary for correct breathing (Fig. 15), are :

1. A slight forward movement of the abdomen corresponding to active contraction of the diaphragm in descent (abdominal).

2. Full lateral and backward movement of the lower set of ribs, seventh to eleventh, caused by lifting and slight

eversion of these by further vigorous diaphragmatic contraction (lower costal).

3. Full upward and forward movement of the upper set of ribs, first to fifth (upper costal). The sixth rib is intermediate between the two sets.

The first movement should glide evenly into the second, and the second into the third, so that the whole process properly performed constitutes the author's "complete cycle of full inspiration." During the whole of the latter two movements there is a continuous straightening of the curve of the thoracic spine.

In full expiration the above movements take place in the reverse order.

3. Massage and Resistance Exercises.—A course of graduated and skilful massage, combined with gently increased resistance exercises of the Schott type, not only benefit muscular tone in general and that of the heart and great vessels in particular, but also by helping to empty the network of blood vessels which is contained within the muscles improve arterial flow and venous return alike, the heart being thus enabled to respond with enhanced vigour of contraction. Thus for cardiovascular types of hypopiesis these methods are specially applicable.

4. Ultra-Violet Radiation.—What has been said of sunlight applies also to artificial sunlight, but with this important difference, that whereas in sunlight only a small proportion of ultra-violet energy filters through the atmosphere from its far distant source even at the optimum times of early morning and late evening on cloudless days, by the employment of suitable lamps one can administer not only a much greater proportion of ultra-violet rays at short range, but also can accurately determine the quality and kind of rays suitable for particular purposes.

Ultra-violet radiation does not activate all kinds of metabolism in like degree. It has a special influence upon protein metabolism, assessable by the urinary nitrogenous metabolism, which is increased, and upon mineral metabolism.[295] Biochemically it is probable that ultra-violet radiation swings the acid-base equilibrium of the tissues towards acidity. If this observation of the author's be

substantiated it will easily be understood that individuals of acid constitution, of which gouty and plethoric types of excess metabolism suffering from difficulties in elimination are examples, stand the application of ultra-violet rays badly, and speedily reach their limit of tolerance. For such subjects treatment on these lines is not only unnecessary but harmful, because, being already in a state of inability to deal with acid waste products, they fare ill if their difficulties in this respect are increased. With subjects having a normal ratio of 1 in 1·75 titratable acidity to the ammonia fraction in the first specimen of urine passed after the night's rest one is safe, and still more so with those who possess a ratio of 1 in 3 or more, and are thus definitely "alkaline." In other words, benefit from ultra-violet radiation is proportional to decrease in tissue alkalinity. Oxidation is promoted, and low arterial pressures are raised.

To these ends the author finds that the best systemic results are obtained from biological irradiation with the quadruple carbon arc lamp, having solid cores of boron, calcium, magnesium and aluminium in descending order, which gives uniform, rapid and satisfactory results. The average initial dose is five minutes respectively to the front and back, gradually increasing to a quarter of an hour or upwards, exposures throughout being gauged by the sensitiveness of the patient's skin and by the height of the arterial pressure. Rapid induction of erythema points to enhanced sensitiveness, so that patients who burn stand far less exposure to the rays than those who tan. Better effects biologically are produced by weekly or bi-weekly applications of gradually lengthening time and intensity than by short exposures at frequent intervals.

When one finds patients under treatment with the quartz mercury vapour or carbon arc lamp begin to complain of easily induced symptoms of lassitude, headache, depression and insomnia, etc., these untoward effects are usually found to be associated with low arterial pressure readings. In such cases by subminimal dosage, exposing only small portions of the face, body and limbs at a time, with several days' interval between successive irradiations, these patients will often respond well, showing increasing energy, appetite,

and *bien-être*. There is a very definite "critical point" in the dosage of such cases, and this must not be passed.[296]

5. Static Electricity.—Static electricity, particularly in the form of the static breeze, constitutes one of the most valuable measures at our disposal for raising arterial pressures that are low.

From a Wimshurst machine, capable of registering 750,000 volts, a unidirectional current of high potential is applied by means of a brush electrode over the bared back of the patient at the level of the adrenal glands (anatomically, over the twelfth rib) at a distance of about 6 inches. This electrical current is rich in ultra-violet, violet and blue-violet rays, causing dust particles in the atmosphere to glow with a violet luminosity, and making a crackling noise with liberation of ozone. Restoration of a normal circulation and a return of arterial pressure to within standard limits are materially aided by fine vibrations thereby set up in the deeper tissues of the body. Arteriolar and capillary tonus are also stimulated.

Other forms of electricity, more especially galvanism, have been recommended by various workers for the relief of symptoms such as headache, but for general utility cannot be compared with the static breeze employed in the above fashion recommended by Dr. Howard Humphris.[297]

6. Oxygen.—In the nutritional changes which take place within the cells and tissues of the body oxygen plays a primordial part. Not only is it made use of by the organism for breaking down and building up organic substances in the tissues, but it also aids in getting rid of the products of cellular disintegration and of toxins. At rest the oxygen requirements of the organism are great, while in the physiological conditions of feeding and exercise as well as in pathological states these requirements are enhanced.

In hypopiesis due to suboxidation in general, or respiratory deficiency in particular, oxygen demand is increased. This demand can be met through an increased oxygen supply (*a*) by inhalation, (*b*) by intravenous injection, (*c*) by subcutaneous injection. Of these three alternatives the last is to be preferred, since the first is wasteful and expensive, and the second necessitates skilled personal application. By

the subcutaneous route one can supply by means of a needle and tube connected with an oxygen cylinder fitted with a pressure gauge a measured quantity of oxygen, usually from 500 up to 2,000 c.c., directly into the subcutaneous tissues, from which it readily becomes absorbed into the capillary plexus. Rapidity of absorption can be increased by covering the area of injection with a hot fomentation. The injected oxygen, being under a higher pressure than the blood gases, in part becomes absorbed until the pressures are equalised, while the other part acts as a reserve which during the next few hours is slowly taken up by the tissues.

7. **Hydrotherapy.**—Few hydrotherapeutic measures have other than a temporary influence upon hypopiesis. The best and most lasting effects result from application of the Vichy douche, followed by the Russian needle spray, or from the aerated Nauheim bath.

8. **Organotherapy.**—In the treatment of low arterial pressure states organotherapy often proves of considerable assistance. Especially is this the case in that form of hypopiesia associated with endocrine dysfunction.

Hypopiesia in general is a low vitality state dependent upon inherent defect in nutritional exchanges of the body cells and tissues, whereby a condition of suboxidation is induced. Alterations in endocrine glandular secretion frequently follow, so that endocrine dyscrasia in varying sort and degree may be held to constitute a valuable indication of this primordial nutritive deficiency. Such indication, nevertheless, is not invariable by reason of the fact that the glands of internal secretion possess considerable powers of adaptation directed towards the maintenance of metabolic equilibrium. In this purpose for long periods of time they may achieve success, until some malady occurs to upset or wreck their co-ordinated efforts by disturbing the balance between katabolism and anabolism.

Hence, as a result of experience, one is led to believe that the effects of a low quality and rate of cell and tissue nutritional exchange may either exist independently, or may exert a secondary influence upon the glands of internal secretion. Cases of the former group, though in the minority, are the most obstinate with which one has to deal. In these

substitution therapy is of no avail, and one is obliged to fall back upon the general measures outlined above. Cases of the latter group can successfully be managed by appropriate substitution therapy designed to redress hormonic balance. The numerous failures along these lines which have been reported have largely been due to over-stimulation of a single gland, or to the employment of products that are to all intents and purposes inert. Some have been administered perorally when adequate effects can only be obtained by injection; in other instances the preparations employed have not been sufficiently active. In the case of certain glands, notably the parathyroid, there is still room for considerable improvement in content of active substance, and to obtain satisfactory results it is always necessary to make sure that any endocrine substance used in practice really possesses the value and composition alleged.

(*a*) *Thyroid Therapy.*—In the words of McCarrison "the thyroid is to the human body what the draught is to the fire." The thyroid is the master gland of metabolism. Hence, in hypopiesis occurring along with pallor and deposition of flabby fat, apart from the well-recognised localisation of adipose tissue due to pituitary defect, as well as in cases which exhibit stigmata of thyroid deficiency in the lesser degrees, as exemplified by scantiness or loss of the outer half of the eyebrow or dryness and harshness of skin and hair, the administration of thyroid substance is called for. Abnormally low arterial pressure may accompany any form of hypothyroidism. It is not reasonable to suppose, however, that the height of arterial pressure depends upon the thyroid gland alone, or upon the amount of its secretion of thyroxin, for we know that there is no constant parallelism between basal metabolic rate and levels of arterial pressure. Therefore, in the frequent cases in which thyroid medication is indicated, this gland should always be combined with various others in accordance with biochemical findings as to the nature of the particular fault in metabolism.

The author believes that thyroid is commonly given in dosage which is too great. If one over-stimulates the powerful thyroid, the delicate balance of internal secretion is tipped adversely in the direction of excess katabolism, so

that, in place of the stable endocrine equilibrium which is desired, a further instability due to upset of other members of the chain may be superadded.

Success often attends administration of daily small doses. Rarely a dose as small as that of $\frac{1}{50}$ grain produces a definite beneficial effect, but in the majority of cases it is necessary to give $\frac{1}{8}$ to $\frac{1}{2}$ grain or more of the desiccated gland.

(*b*) *Pituitary Therapy.*—The gland of katabolism next in importance to the thyroid is the pituitary. Of all the endocrine substances employed in raising low arterial pressures to more satisfactory levels none have been so generally useful in the author's practice as various preparations of the pituitary gland.

In grave cases of hypopiesis, intramuscular or subcutaneous injections of 0·5 c.c. pituitary (posterior lobe) extract daily, or on alternate days, gradually increased by 0·5 c.c. until the typical intestinal reaction* and headache appear, have the most speedy and potent effect. Caution is, however, necessary in the use of this remedy, as it is neither desirable to continue with it too long nor to send up the arterial pressure by too rapid bounds.

More usually whole gland pituitary substance is administered by mouth in doses of two grains two or three times a day, according to the appearance and body weight of the patient, until slight throbbing in the head, palpitation or precordial pain, with general discomfort, point to the limit of individual tolerance having been reached. Immediately on the onset of any of these symptoms the dose should be reduced by two-thirds or a half, and this lesser dose should be continued for several weeks or months, increasing or diminishing in accordance with indications afforded by (1) the levels of arterial pressure recorded at successive regular intervals, and (2) a maintenance of sensations of well-being on the part of the patient. Usually one is satisfied if an initial systolic pressure, say of 106 mm., becomes constant after a course of treatment at a level of about 116 mm. or a little more. If such a pressure be pushed up to above 120 mm. the low pressure is likely to become converted into a relatively

* After a varying number of weeks a saturation point, evidenced by the above symptoms, may be reached, at which the patient becomes intolerant, and the dosage should then gradually be reduced by 0·5 c.c. at a time to the final point of toleration.

high pressure for that individual, who soon begins to exhibit symptoms of intolerance.

In that form of pluriglandular syndrome evidenced by intratemporal headache, considerable lassitude, low arterial pressure, low blood sugar, and abnormalities of skeletal development, frequently combined with gonadal deficiencies, the exhibition of pituitary gland causes notable amelioration.

For internal medication the use of adrenalin, or even of desiccated whole gland adrenal substance, is giving way in the treatment of hypopiesis to that of whole gland pituitary substance, which is less toxic and more lasting in its effects.

(c) *Adrenal Therapy.*—The immediately preceding remarks, nevertheless, do not apply to cases in which the adrenals can definitely be invoked as the incriminating cause of disease conditions. In such, adrenal therapy will always hold the chief place.

The adrenal glands appear to possess two main functions, vasoconstrictor (medullary portion), and antitoxic (cortical portion). Failure of either function leads to different states of adrenal inadequacy.

(i.) The secretion of *the medulla* (adrenalin) sensitises the sympathetic nerve-endings. Under conditions of medullary inadequacy, adrenal therapy by means of medullary or whole gland substance given by mouth should be employed, and when there are evidences of organic change in the medulla itself no other organotherapeutic measures can be used as substitutes.

In emergencies, 1 c.c. of a solution of adrenalin chloride, 1 in 1,000 of normal saline solution, with 0·5 chloretone added, should at once be given hypodermically. By mouth it has little or no effect. A less rapid and intense method is to give supramedulla tablets of $\frac{1}{1000}$ or $\frac{1}{400}$ grain, up to $\frac{1}{64}$ grain if necessary. These tablets contain the active principle in crystalline form, and are administered by mouth or allowed to dissolve under the tongue. By such procedures the action of the adrenal medulla receives temporary stimulation. After the urgency has abated, the medulla or whole gland may be exhibited by mouth as above in

combination with thyroid, pituitary or gonads, according to the merits of the individual case.

(ii.) There is still much controversy as to the functions of *the cortex* and its relations to the adrenal medulla. It is known that the cortex plays some part in regulating the metabolism of cholesterol, in virtue of which it presumably exerts an antitoxic function. Cholesterol being hæmolytic, this antitoxic function becomes of special importance under circumstances of infection by hæmolytic organisms. However, as it is not yet determined whether adrenal cortex is absorbed or has any action if given perorally, it is yet premature to hazard any statement as to its effects on arterial pressure. Recently the author has been investigating the results in suggested cortical inadequacy of hypodermic administration of ½ to 1 c.c. of a 20 per cent. sterile solution of adrenal cortex, and finds that sensations of devitalisation abate, and energy becomes restored, but a sufficient number of suitable cases of hypopiesis have not been thus treated for any definite conclusion to be reached as to its utility or otherwise in this condition.

(*d*) *Gonadal Therapy.*—The gonads, together with the thyroid, pituitary and adrenal glands, are the katalysers of the body, and have close interactions with the sympathetic nervous system. As mentioned above, pluriglandular syndromes, of which hypopiesis is at times an expression, not infrequently originate in gonadal disorders. The profound effects on secondary sex characters of ligature of the spermatic cord goes far to suggest that the testis possesses an internal secretion. "The hormone supplied by a testicular graft may tide a patient over a critical period until compensatory changes in other endocrine glands have succeeded in restoring the endocrine balance."[298] With testicular and ovarian extracts given by mouth for hypopiesis, the results have been more uncertain. Beneficial results have been reported from the administration of products said to contain the interstitial or Leydig cells, though it is even then doubtful if these cells are the source of the testicular hormone.

The ovarian hormone is formed from the Graafian follicles, and extract of corpus luteum is found in climacteric

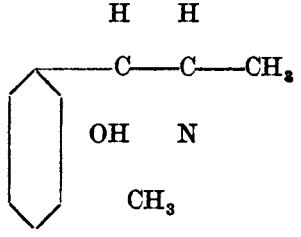
aberrations sometimes to be of more service than ovarian extract, though neither in the author's experience have altogether fulfilled their promise.

Over-activity or depletion of any single endocrine gland cannot take place without disturbing the other members of the series, so that uniglandular administration in the author's view is usually of no avail in the treatment of low arterial pressure conditions. Each glandular product has, nevertheless, its own several application, particular indications for due combination of these glands being afforded by a complete biochemical examination of blood, urine and fæces. By proceeding on these lines one arrives at far greater precision in the adjustment of hormonic balance than up to the present time is possible of attainment in any other manner.

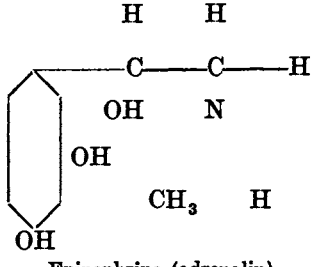
Finally, in working with whole gland preparations, it is wise to prescribe only those that are definitely standardised by a firm of repute in terms of a known content of dried gland.

9. Drug Therapy.—(*a*) *Ephedrine.*—Ephedrine is the active principle of *Ephedra vulgaris, var. Helvetica.* Under the name of Ma Huang, it has been extensively employed as a medicine for upwards of 5,000 years in China, where its reputation appears to rest on a sound basis. The investigations of Read, Chen and Schmidt,[299] of the Peking Union Medical College, and of Rudolf and Graham, [300] have rescued Ma Huang from the realms of empiricism by the discovery that this drug provides the source of an alkaloid, ephedrine, which is capable of chemical standardisation so as to secure uniformity of therapeutic results.

Ephedrine and epinephrine (adrenalin) have certain similarities in chemical composition as the following comparison shows :—



Ephedrine.



Epinephrine (adrenalin).

Adrenalin has two hydroxyl groups connected to the benzene nucleus that are lacking in ephedrine. These two hydroxyl groups in the adrenalin molecule make it so susceptible to oxidation that the drug is not stable when exposed to air. On the other hand, the ephedrine molecule is stable in air to the extent that no change took place in a 5 per cent. solution of ephedrine hydrochloride after it had stood for six months. The melting point of the alkaloid, ephedrine, is from 39 to 40° C., while that of ephedrine hydrochloride is 216 to 220 C. The hydrochloride is soluble in water and alcohol, but insoluble in ether.

The physiological effects of ephedrine and its salts, of which the hydrochloride is most generally employed, resemble those of adrenalin and tyramine in nature and action, but over these possess two distinct advantages. Thus ephedrine hydrochloride is effective when given by mouth, as well as by injection, whilst its results by either route are far more lasting. Ephedrine raises both systolic and diastolic arterial pressures, stimulates cardiac action by slowing and strengthening the heart-beat over a period of several hours, and in many cases increases both urinary output and basal metabolism. It is readily absorbed from the intestinal tract, and possesses low toxicity. Its mode of action is probably by peripheral stimulation of the sympathetic nervous system.

The therapeutic effects of ephedrine hydrochloride resemble those of pituitrin more closely than those of adrenalin, in that the rise of low arterial pressure is more continuous, and under favourable conditions may be permanent. Tablets are made of the strength of half a grain. These are effective when administered perorally. A more rapid effect can be attained by dissolving a tablet in 1 c.c. of sterilised saline solution or water, in which the hydrochloride is readily soluble, and dosage can be continued at intervals which should be decided by the height of the arterial pressure until this has become restored to standard limits. The drug is not harmful unless administered in excessive amount, when symptoms due to cardiac overaction and arterial constriction will become manifest.

The author is able to speak most favourably of the use

of this remedy, which is of much service in all forms of hypopiesis, and is one of the best at our disposal for treatment of that form of hypopiesia already mentioned which depends upon primitive defects in nutrition of body cells and tissues. It is of immediate benefit in emergencies arising from shock and hæmorrhage, and in myocardial failure, Addison's disease, and the low pressure form of asthma, in which the author has found symptoms to disappear in cases otherwise intractable.

During the past two years the drug has been imported into this country from China, and there is no difficulty in obtaining a supply. Recently a synthetic ephedrine has been prepared, whose chemical composition is not identical with that of the natural drug but isomeric. Time is yet too short to permit of definite indications as to its efficacy.

(*b*) *Caffeine Sodium Benzoate.*—Caffeine itself and caffeine citrate in ordinary doses have little effect on arterial pressure, any rise that may occur being slight and transient. The combined salt, caffeine sodium benzoate, is however a good drug in the treatment of hypopiesis, especially in emergencies, such as shock following trauma, operation and anæsthesia, and in poisoning by depressants such as morphine and fungi, after getting rid as far as possible of the source of the intoxication. Here caffeine sodium benzoate has appropriate and valuable uses as a most reliable temporary stimulant to the circulation in desperate cases.

(*c*) *Cardiazol.*—This is one of the newer analeptics or restoratives which, in contrast with camphor and its substitutes, is readily soluble in water. So rapid absorption thus results that a subcutaneous injection at once causes as high a concentration in the blood and as rapid an effect as can be attained by intravenous injection. Cardiazol is stated to be a pentamethylenetetrazol of constant composition, containing, like camphor, a bi-cyclical system. It is a white crystalline powder, dissolving easily in water and most organic solvents without decomposition, the solution having a neutral reaction.

The therapeutic effects are fundamentally the same as those of camphor and the camphor substitutes. Its additional advantages are (1) high and active concentration

in the blood by reason of its complete solubility in water, (2) its stimulant action upon the heart, brain cortex and vegetative nerve centres. Thus its action is more rapid and potent than that of camphor, the best results being obtained in acute circulatory disturbance due to functional failure, especially in collapse and respiratory troubles consequent upon anæsthesia, but also in cardiac insufficiency and infective diseases.

Administered by mouth or by rectum, the effects are less prompt than by injection, the dose for which is 0·1 gm. (1½ grains) every two or three hours. In less severe cases, up to six tablets can be given *per os* with a little water in the twenty-four hours.

(*d*) *Camphor.*— While the author has obtained satisfactory results with cardiazol in hypopiesis associated with circulatory and nervous disturbances, acute and chronic, his experience with camphor and its substitutes has been disappointing. Injections make a hypodermic syringe oily, and some patients find them irritating. From the point of view of efficacy there is extreme doubt as to whether camphor has any considerable influence as a cardiac stimulant. On the Continent, especially in Italy, it is utilised considerably more by injection than at home, and good results have been reported during the course of chronic myocarditis with simple cardiac insufficiency, alterations in rhythm, and auricular fibrillation, in sustaining the activity of the heart and steadying the pulse.

Camphor slows the pulse and produces a temporary rise in arterial pressure, but to produce definite effects on the circulation doses of not less than 0·2 gm. (3 grains) must be injected. With large doses there is always the likelihood of toxic manifestations.

(*e*) *Digitalis.*—Records of the height of arterial pressure following administration of digitalis made by various observers have been collected by Eggleston.[301] Out of 181 cases the systolic pressure rose in 66 (about 36 per cent.), fell in 57 (31 per cent.), and remained unaltered in 58 (32 per cent.). In 116 cases the diastolic pressure rose in 24 (15 per cent.) and fell in 76 (65 per cent.). Thus digitalis lowers the diastolic pressure more than the systolic, thereby

increasing the differential pressure. The drop in diastolic pressure is neither due to lessened cardiac output nor to arterial dilatation, but the blood stream leaves the arterial circulation at a higher rate than under ordinary conditions. Digitalis also usually promotes diuresis, though not to such an extent as does scillaren, the active principle of squill. Hence one concludes that in therapeutic dosage digitalis has little effect on the systolic pressure in normal cases, whilst it lowers the diastolic pressure. In hypopiesis, where an uncompensated heart is failing against an overload due to cardio-vascular defects, digitalis tends to balance the arterial pressure. It should be reserved, however, for this particular class of case, for in states of vasomotor depression it is useless or even harmful.

(*f*) *Strychnine.*—Strychnine has no direct stimulant effect upon the heart or rest of the circulatory system, so that beneficial results in hypopiesis reported from its employment are probably due to an indirect action through the higher centres. The brain and spinal cord are stimulated, and thus its exhibition becomes of use in tiding over states of circulatory depression resulting from inefficiency of the vasomotor centre, to which its sphere of utility is confined. For other conditions, including shock, it is of no appreciable value.

(*g*) *Ergot.*—The effects of ergot are uncertain, owing to variations in its content of active principles, the chief of which, tyramine, is similar in action to adrenalin, but weaker, slower, more continuous and less toxic. In animals, tyramine given hypodermically in doses of $\frac{1}{2}$ grain, repeated if necessary, causes a considerable rise in arterial pressure, with corresponding increase in the vigour of cardiac contraction. Opposite effects appear to be produced in man by hypodermic injection of a solution of crystallised ergotamine tartrate (1 c.c. of a 0·05 per cent. solution), reduction of arterial pressure taking place as the result of cutting out the pressor mechanism of the sympathetic. It is the antagonist to adrenalin, and brings about a fall of arterial pressure in sympathicotonic subjects. Ergotoxin gives results in some ways comparable with those produced by adrenalin, and is more potent than tyramine in causing a sudden rise in arterial pressure due to peripheral vasoconstriction. The

usual dose is from $\frac{1}{100}$ to $\frac{1}{60}$ grain. On the whole, ergot is best avoided in low arterial pressure states.

(*h*) *Ammonium.*—Ammonium, in the form of aromatic spirits of ammonia, is well known for its restorative effects, although these are evanescent. Constriction of the peripheral arterioles and capillaries ensues as a result of stimulation of the vasomotor centre, with consequent rise of arterial pressure. It is useful in cases of fainting due to transient vasomotor paresis, and also acts as a diffusible stomachic in conditions attended with gaseous distension.

10. Treatment of Symptoms.—The most constant symptom of which hypopietics complain is that of easily induced fatigue, in some instances amounting to utter prostration and exhaustion. If, on biochemical investigation, indications are present that some member or members of the chromaffin system are at fault, particularly the adrenal gland, pure crystalline adrenal extract should be given by mouth.

℞. Tab. supramedulla crystal. gr. $\frac{1}{1000}$.
Mitte L.
Sig.—One tablet swallowed with a little water at bedtime.

For many patients this dosage suffices, and a sense of well-being and increased vitality ensues. Where grave deficiency exists, it may be necessary to increase the dosage to gr. $\frac{1}{400}$ on rising, and again later in the day upon the reappearance of fatigue symptoms. Other cases receive more benefit from hypodermic injections every two or three days of posterior pituitary extract, and for this product the parenteral route should always be adopted, since the extract does not appear to act satisfactorily when given by mouth. If several other remedies are already being administered by mouth, Hoechst's liquid extract of post-pituitary (hypophysin) may be exhibited by the intranasal route, which forms a convenient way of giving certain endocrines, such as pituitrin and adrenalin. A small quantity is placed in a pocket nebuliser, and the patient is directed to use the solution in the form of a spray, squeezing the rubber bulb about eight times on rising and retiring.

For morning depression and headache, associated with a pulse of low tension, caffeine citrate, either plain or effer-

vescent, in doses of 3 to 5 grains of the former, or of 1 to 2 drachms of the latter, perorally according to body weight, may be prescribed.

Here a useful warning may be acceptable that aceto-salicylic acid (aspirin) and salicylates hardly ever suit low pressure patients, since they aggravate any existing depression and still further lower vitality. Acetanilide (antifebrin) is to be preferred in small doses of 2 to 3 grains by mouth, repeated if necessary, since it is entirely eliminated within the course of twenty-four hours. In many of the acute infections, notably in influenza, typhoid and pneumonia, this forms a useful remedy to combat headache and pyrexia. Acetanilide also acts as a hypnotic sedative and nervine tonic. By checking the chills and fever of acute processes, it soothes the nervous system and promotes rest.

Defective memory and concentration arise as a part of the general fatigue syndrome, and are ameliorated by psychotherapy and by toning up the nervous system by polyglandular preparations such as hormotone, two tablets of which may be given by mouth twice or thrice daily according to individual indications.

Insomnia likewise results in frequent instances from over-fatigue, mental or physical, and from general exhaustion. The simpler nerve sedatives should first be tried in the form of small doses of ammonium bromide in combination with liquid extract of cinchona. Should the insomnia persist, allonal may be prescribed in tablets of $2\frac{3}{4}$ grains, one to three at bedtime. A distressing form of insomnia often met with in low pressure states is that in which the patient sleeps for the earlier part of the night, but in the early morning becomes wide awake, and afterwards may either not be able to get to sleep at all, or sleep comes only lightly and in fitful snatches, so that the patient rises to begin the day's activities unrefreshed and already tired out. For this type of insomnia no remedy is so useful as sulphonal by reason of its delayed hypnotic effect. Administration of 10 to 20 grains of this drug, either in the form of cachets or suspended in mucilage, in half a pint of hot water at 9 p.m., to which, if desired, a little brandy or whisky can be added, produces its beneficial results in inducing sleep in the early

morning hours when it is most needed. It should not, however, be prescribed consecutively over long periods of time, nor should it be given to persons suffering from intestinal stasis, since its rate of excretion is slow, and it is liable to produce renal irritation and hæmatoporphyrinuria if given for long without a break. For cardiac cases trional is the best all-round hypnotic, in 10- to 20-grain cachets with a large cup of hot milk or water. For low pressure cases in general, veronal is toxic and is best avoided.

For giddiness, quinine hydrobromide in doses of 1 to 5 grains or more, but not exceeding 10 grains, is often efficacious. The most effective general dosage is $2\frac{1}{2}$ grains thrice daily, the hydrobromic acid, by its action as a nerve tonic, calming nervous excitability and lessening exhaustion, and the quinine acting by its effects on the sympathetic system. For the relief of this symptom supramedulla crystals, aromatic spirits of ammonia, and strychnine are also of service.

Fainting, convulsions and syncope are dealt with in the section which is concerned with shock and collapse. Adrenalin and caffeine are here alike of service.

Palpitation and anginiform pain on exertion, if of cardiac origin, should be met by the exhibition of appropriate remedies suited to the individual condition, each case being dealt with on its merits. Amyl nitrite, erythrol tetranitrate, and inhalations of chloroform are contraindicated in low pressure states. If these symptoms are of dyspeptic or nervous origin, tincture of sumbul with aromatics in an acid gentian mixture will often relieve them. Some forms of palpitation are cut short by atropine, small doses of which in a large volume of water on an empty stomach lessen gastric secretion.

Gastro-intestinal disturbances should receive treatment in accordance with the special condition present. For symptoms pointing to hyperacidity of the gastric juice, belladonna, as the liquid extract in doses of $\frac{1}{4}$ to 1 minim, or as the tincture in doses of 5 to 20 minims or more, or in the form of bellafolin, by hypodermic injection of 1 c.c. ampoules containing $\frac{1}{130}$ grain of the total alkaloids of belladonna leaves, or tablets containing $\frac{1}{65}$ grain of the total alkaloids, one to two as required, allays gastro-intestinal

spasm, and by its inhibitory action on the gastric glands diminishes the secretion of acid.

In many low pressures combined with exhaustion, and in one group of neurasthenics, acids on the other hand are needed, but caution is required at the outset lest acid sensitiveness prevent the exhibition of the drug, some people being susceptible even to small doses of a dilute acid such as hydrochloric. Pepsin is useful in certain of these cases, combined with dilute hydrochloric acid, minims 3 to 10, with liq. pepsini et caffeinæ, 2 to 4 drachms, p.c., to aid its action and to convert the pepsinogen of the gastric tubules into pepsin. Pancreatin is often more efficacious than pepsin, and is given either with food or two hours later in doses of 2 to 20 grains or as liquor pancreatis, B.P., 1 to 2 drachms. In many cases of hyperacidity, the pain which occurs upon the opening of the pylorus, when the acid contents of the stomach are shot into a hypersensitive duodenum, is assuaged by the immediate exhibition of 15 to 30 grains of sodium bicarbonate, but since it is primarily the lack of acid that predominates in this gastric neurasthenic class which tends towards general tissue alkalinity, this lack can be met by the following prescription :—

R. Tincturæ cardamomi co. . . ℥i
Bismuthi subnitratis . . aa. ℥ij
Aquam ad . . . . ℥ss.
Tritura ad pastam mollem et adde
Acidi nitrici diluti . . . ℥ij
Spiritus chloroformi . . . ℥ss.
Aquam ad . . . . ℥viij
Ft. mistura.
Sig.—One tablespoonful in an equal quantity of water thrice daily ½ to 1 hour after meals.

For this class of case the carminative acid bismuth mixture affords greater relief than can usually be obtained by any other remedial measure, and is often invaluable.

11. Treatment of Emergencies in States of Depressed Vitality.—(*a*) *Shock.*—The general treatment of traumatic shock is by means of warmth, day and night, even during

the summer, by means of blankets, hot water bottles, hot affusions, and other means.

After arrest of hæmorrhage, if any, states of traumatic or surgical shock are best combated by the method advocated by Fisher and Snell,[302] which consists in the gradual intravenous introduction of 1,000 c.c. of a 10 per cent. solution of glucose, in normal saline with 15 units of insulin given hypodermically five minutes after the glucose injection has been begun. This solution is a further modification of one recommended by the late Sir William Bayliss [149] in 1917, whereby 6 to 7 per cent. of gum acacia in 1,000 c.c. distilled water is administered intravenously. A solution of 5 per cent. or over permanently restores low arterial pressure due to hæmorrhage. Both these methods are excellent save in those cases of severe secondary shock which are unable to anabolise, in which event blood transfusion from a donor of Group IV, or other suitable group, may be practised. In less severe cases of shock, with or without loss of blood, ephedrine hydrochloride, adrenalin intravenously in doses of 1 c.c. of a 1 in 50,000 solution every hour, or supramedulla (crystalline) may be given.

In operative shock, should the arterial pressure drop to below 100 mm., intravenous infusions should be given as above and the operation stopped. More rapid cessation of symptoms is stated to have followed the method of Fisher and Snell than has been obtained by other means. Patients begin to react within an hour, and a few hours later are free from any evidence of shock.

General anæsthesia in shock is safe if gas and oxygen alone are used.

Cannon, Fraser and Cowell [155] state that an alkaline injection of 4 per cent. sodium bicarbonate at body temperature at the beginning of anæsthesia prevents the dangerous depressant effect which anæsthetics such as ether and the operative procedure have in cases of shock with acidosis. Operation ends with the acidosis overcome instead of augmented, and with an alkaline reserve provided. Arterial pressure, instead of being perilously lowered, is actually raised during the critical period. Later

it may decline, but the improved state of the patient during operation is unmistakable, and the subsequent course of shock cases in which operation has been performed with these precautions has been highly gratifying.

(*b*) *Chloroform Poisoning.*—When the heart stops beating from failure consequent upon an overdose of chloroform, there is a general consensus of opinion that the most serviceable remedy is to be found in adrenalin. To be effective, however, adrenalin-saline solution must be brought into contact with the lining of the arteries by perfusion through an artery in the direction of the heart, combined with rhythmic pressure upon the thorax over the precordial area.

Martindale [303] affirms that "no known drug is comparable with adrenalin in efficacy to start an arrested heart or to antagonise the action of chloroform. The power of adrenalin, which is equivalent to stimulation of the sympathetic nerve of the heart to antagonise a *muscular* paralysis, has not been sufficiently realised." In cardiac arrest, following hard upon artificial respiration, a 1 in 50,000 solution of adrenalin may be injected in two or more parts intravenously. Intracardiac injection into the right ventricle of 0·5 to 1·0 c.c. adrenalin solution 1 in 1,000 has also favoured rapid resuscitation.

(*c*) *Anaphylactic Shock.*—In anaphylactic shock ephedrine or pituitrin are of great value.

(*d*) *Acute Circulatory Disorders.*—In premature contractions look to any causal factor, such as errors of diet or excess of tobacco. If the patient is of nervous temperament tincture of sumbul in combination with bromides often affords relief. In such conditions digitalis is contra-indicated. During the evolution of heart block no special treatment is requisite. Digitalis may be of service generally, although it is likely to increase the degree of block.

Acute carditis demands rest in bed continued for as long as is necessary, often from three to six months. In the rheumatic form no known treatment has any effect in preventing the onset. Local indications are met by the use of blisters, 1 inch in diameter over the precordial area, or the application of an icebag to the same region in cases of acute endocarditis. The treatment of the infective form

is yet unsatisfactory, and only palliatives can be adopted. Recently success has been claimed from the employment of immunogens.

Acute cardiac insufficiency is met by the use of digitalis in sufficient dosage combined with rest in bed.

(*e*) *Acute Specific Infections.*—Acute specific infections should be treated so as to prevent as far as possible the onset of hypopiesis due to exhaustion. This is attained by measures designed to promote free elimination and to support the circulatory system. Hydrotherapy and early administration of digitalis before symptoms become grave are thus of much importance.

Exhaustion consequent upon the hormonic depletion that occurs during the time that hyperpyrexia is burning up the body tissues, or consequent upon fever of lesser degree prolonged for weeks or even months, is best combated not by mere stimulation but by supporting the depleted glands along lines of appropriate organotherapy. In acute infections, particularly influenza, pneumonia and enteric fever, administration of oxygen by subcutaneous injection is often of great benefit, and atropine or belladonna should be given freely on the appearance of sudden collapse due to splanchnic vaso-dilatation. Excessive perspiration is thus checked, and restoration of vasomotor tone promoted.

In cholera high specific gravity of the blood, accompanied by greatly diminished urinary secretion, is an indication for dilution of the circulating fluid, even though the systolic pressure may still be above normal.

In scarlet fever symptoms of acute adrenal insufficiency, such as extreme asthenia, low arterial pressure, fall of temperature with profuse sweating, meteorism, nausea, vomiting, abdominal pain, headache, somnolence, tachycardia and tendencies to syncope have been reported by various observers in which recovery followed administration of adrenalin.[232, 233] Contrariwise, other observers who have found adrenalin of great value in diphtheria have seen no benefit from its use in scarlet fever.[304]

In malaria a swift drop in arterial pressure usually follows intravenous injection of quinine in concentrated solution (10 grains to 20 c.c.); in dilute solution (10 grains to 200 c.c.)

a less rapid and severe drop may ensue, but this is not constant, and the slower the rate of injection the less likelihood is there of a fall in arterial pressure.[305] Should this take place, it may persist for twelve hours or so after injection, and may be minimised by 0·2 c.c. of a 1 in 1,000 adrenalin solution combined with the quinine in intravenous injection. A similar fall which occurs during the algid stage should be counteracted by hypodermics of atropine, adrenalin or brandy, with normal saline for the post-febrile collapse.

In acute pneumonia and broncho-pneumonia, besides good nursing throughout, and appropriate therapy directed against emergencies as they arise, a vital point is to give digitalis *early* in sufficient doses to hold the heart in check. Since this remedy takes up to forty-eight hours before its effects become definitely manifested, a method of treatment advocated by Dr. H. W. Nott [306] has met with considerable success. This consists in the administration of rectal injections of varying amounts of a standard solution of pure potassium permanganate made as follows. A one grain-tablet of permanganate is crushed to powder in an earthenware basin with a teaspoon ; cold water is poured on to it, and hot water added to make 1½ pints. The injection is given slowly by means of a funnel and tube with the patient lying on the left side after the bowels have acted. Should the bowels not have acted sufficiently, the first injection will usually act as a wash-out and speedily be returned. In this event a second injection should then be administered with the object of its being retained. From three ounces to half a pint of the standard solution are used on each occasion, according to the age of the patient.

If treatment be begun early in the course of the disease, intervals of three or four hours between each injection can be allowed ; if on the fourth or fifth day, especially when symptoms are severe, the intervals may be reduced to two hours, short intervals being necessary if the fluid be quickly returned. When the temperature reaches normal, injections are reduced to two a day for three days, and once a day for three more days. In young children, however, injections should be continued twice daily for ten days after the

temperature has returned to normal, as there is a tendency to recurrence if they are given up too early.

It is possible that the benefits which undoubtedly accrue from this treatment are due to absorption of manganese by the rectal veins, from which the drug enters the general circulation, and after bathing the tissues is excreted by the intestinal mucosa at which it arrives still in possession of its germicidal properties.

(*f*) *Vagotonia and Vagotonic Syncopal Attacks.*—Upon vagotonic symptoms in general, and particularly on those referable to the gastro-intestinal tract, in association with hypopiesis, atropine and epinephrine exert a favourable influence, whilst pilocarpine definitely aggravates them. In vagotonic syncopal attacks, as in bradycardia of extra-cardiac origin, atropine promptly restores the circulation to efficiency. The effect of atropine is to paralyse the nerve-endings of the vagus in the heart, so that its pulsations cannot be slowed by circulation of any portion of the nerve. Two cases of vagotonia occurring in big, strong and energetic men are recorded by Heimann.[307] One patient, aged sixty-seven, had for eighteen months complained of attacks of giddiness, preceded by sweating, and followed by nausea, headache, and occasional unconsciousness suggestive of heart block. Epilepsy and the Adams-Stokes syndrome were excluded by the absence of nervous symptoms during the seizures. Electrocardiographic examination disclosed no abnormality, but during coughing and on deep inspiration the pulse became slowed. Under graduated gentle exercise, avoidance of tobacco, removal of septic teeth, and dieting to prevent gastric distension, together with five minims of tincture of belladonna thrice daily, the attacks ceased. The second, aged fifty-two, complained of breathlessness and inability to lie down. His lips were blue, but there was no jugular distension, nor sign of cardiac, pulmonary or hepatic abnormality on physical or X-ray examination. It was concluded that the vagus was hypertonic, thus accounting for the bronchial spasm, breathlessness, and arterial pressure, low for his age, of 120 systolic and 65 diastolic. As this patient had spent most of a strenuous life in the blazing sun near Nairobi, it was thought that the condition was secondary to

suprarenal exhaustion due to a combination of hard work and excessive exposure to sunlight. Improvement followed residence at a lower altitude, dental treatment, dieting and medicine, as in the first case, with the addition perorally of suprarenal gland cryst. gr. i, and ext. thyroid. sicc. gr. ½.

12. Treatment of Conditions of Association.—(*a*) *Neurasthenia.*—If the term "neurasthenia" be used in its proper limited application, one may regard it as the expression of nervous exhaustion, and its origin as either congenital or acquired.

Certain of the congenital cases do not react to any form of treatment, save at times temporarily, with subsequent relapse, and in these little or no change in arterial pressure occurs. When uncomplicated by organic disease such as chronic nephrosclerosis or arteriosclerosis, the arterial pressure as a rule is subnormal. When mental depression supervenes, the pressure is usually very low. If a cause can be found for the neurasthenia the condition then becomes more hopeful. Thus Léopold Lévi [308] gives a detailed description of ten patients, eight women and two men, who suffered from profound neurasthenia, in some cases amounting to melancholia with suicidal impulses. Several of these had been ill from three to seventeen years. Rapid improvement in all of them was noted after administration of adrenal gland, 0·25 c.gm. to 1 gm. of the powdered substance daily. Some of the patients, of whom two were sisters, appeared to be the subjects of congenital adrenal deficiency; others showed evidences of latent tuberculosis. Certain of the women had combined adrenal and ovarian deficiency, which speedily yielded to administration of extracts of these glands.

The acquired form of neurasthenia often results from toxæmia of various kinds: either primary, of which the intestine constitutes the chief source, or arising from focal sepsis; or secondary, consequent upon acute infections or endocrine deficiency. Chronic and profound prostration leads to depletion of pressor substances, and thyroid and adrenal inadequacy are found in cases in which somasthenia and extreme exhaustion form a notable part of the syndrome.

In the low arterial pressures which co-exist with gastro-

intestinal atony, which is usually followed by absorption of toxic products, the splanchnic area is involved. Such patients derive considerable relief from the application of a properly fitting abdominal belt which gives the desired support, and from the administration of cachets of $\frac{1}{8}$ grain potassium permanganate combined with $\frac{1}{2}$ to 1 grain thyroid extract. "In from five to eight days many miserable and depressed individuals of middle age find themselves remarkably improved, and after two weeks' treatment they look and feel rejuvenated with an intellect and body so invigorated as to be reflected in occupation, business and sport; and this improvement has been accompanied in some cases by a slight rise in arterial pressure." [308]

(*b*) *Focal Sepsis.*—Focal sepsis, wherever arising, should immediately upon discovery be treated by appropriate measures. Dental sepsis and pyorrhœa should receive attention at the hands of a competent dental surgeon together with subsequent vaccine therapy, if sufficient indications are present therefor. Dr. Knyvett Gordon [309] stresses the point, with which the author agrees, that vaccines prepared from cultures of mouth organisms alone produce little if any beneficial effect upon the oral condition or upon a systemic infection resulting therefrom, since oral streptococci exert their pathogenic effects and cause systemic infection when growing, as they almost invariably do, in the intestine. Hence a vaccine prepared from the fæces of the patient should be administered.

Focal sepsis arising from tonsils, sinuses, gall-bladder and pelvic organs should be dealt with on surgical lines, when relief of hypopiesis and other attendant vasomotor nervous symptoms may be expected.

(*c*) *Gastro-intestinal Toxæmia.*—Generally speaking, a chronic intestinal infection lowers arterial pressure by reason of the toxic effect produced by absorption of depressor amino-acids and their action upon the vast area of the capillary network. Treatment should be initiated by restricting activity and by prescribing a non-putrefactive diet rich in vitamins and of lacto-vegetarian type, with the addition of wholemeal bread and the avoidance of all kinds of meat, which will frequently result in expanding the differential

pressure by 10 to 20 mm. within a fortnight or so with corresponding improvement of the symptoms.

To increase the tone of the abdominal muscles, if these are capable of stimulation, exercises should be prescribed. The most useful are those of body-bending and stretching, together with leg-raising, parting, and circling. Failing the induction of adequate abdominal tonus, a Curtis belt, or adequate abdominal support, with taxol (one to two tablets with each meal), and sufficient liquid paraffin and phenolphthalein ($\frac{1}{2}$ to $\frac{3}{4}$ grain to the ounce) to overcome stasis in the large intestine. Belladonna is useful to relieve sphincteric spasm due to the intestinal catarrh, and may be prescribed in 5 minim doses of the tincture thrice daily. Colloidal kaolin is of additional service in counteracting processes of decomposition within the intestinal canal. If the lower ileum is loaded with septic material, this can be cleansed by means of saline aperients. If fæcal examination reveals the presence of serum-resisting streptococci or serum-resisting *B. coli*, an autogenous vacine should be administered. Rectal injections of potassium permanganate solution (p. 234) daily for three weeks followed by oral administration of cachets of potassium permanganate gr. $\frac{1}{8}$ to $\frac{1}{4}$, combined with desiccated thyroid gr. $\frac{1}{4}$ to $\frac{1}{2}$, are frequently efficacious in gastro-intestinal stasis and in chronic mucous colitis in promoting restoration to normal conditions and thus in raising arterial pressure. As treatment proceeds, regular daily walking or riding exercise should be enjoined, with natural or artificial sunlight, and general regulation of faulty habits of hygiene and environment.

In addition to the low pressure group of cases associated with intestinal toxæmia, it should be remembered that there is also a high pressure group resulting from absorption of pressor substances from the gastro-intestinal tract. **Functional cardio-vascular insufficiency** can readily be diagnosed by the notable fall in arterial pressure which ensues on change from the recumbent to a standing posture; leg-raising and body-bending exercises should be prescribed in order to restore the tone of the abdominal muscles. The diaphragm is thus raised, and intra-abdominal tension increased. Should the muscles prove too flabby for such

procedure to be of avail, considerable comfort to the patient accrues from the wearing of a properly fitting Curtis or other abdominal belt. The symptoms of headache and weariness are thereby relieved, and treatment may turn out to have been so successful that after a few weeks the belt may be dispensed with for considerable periods. In the **thin neurasthenic** class, by aiding digestion and assimilation, there is often an increase of fatty tissue in the abdominal walls which also helps to achieve the above objects; if in bed, hydrotherapy and massage with gentle passive movements, lying flat, and later regulated exercises; if internal glandular disturbance, adrenalin 5 drops of 1 in 1000 soln. t.d.s. up to 10 drops daily, or combined extracts in small doses. McCrae [27] recommends ergot, which in some cases has a marked effect in alleviating headache, which is so common.

If up and about, revise the mode of life, promote peace of mind by alleviating causes of disturbance and worry as far as possible, and prescribe regulated rest with gentle passive movements whilst recumbent, and later regulated and gradually increasing exercise. Static electricity is often of great service in these cases.

(*d*) *Pulmonary Tuberculosis.*—All tuberculous implantations are accompanied by low arterial pressure provided that the vitality of the subject is low and resistance against the infection is impaired. Proportionately to decrease in the amount of circulating toxin, arterial pressure again rises.

In cases where embarrassment of the pulmonary circulation presents a notable feature, evidenced by the presence of cyanosis and dyspnœa, Burnand,[310] of Leysin, during the past twelve years has extensively employed digitalis in small repeated doses, 0·10 gm. of the powder for three days out of every ten, or a quarter of a milligramme of digitalin per week. This observer claims to have thus obtained amelioration of the general condition and of the low pressure symptoms. For cases with marked asthenia total adrenal extract has been recommended by Sergent in doses of 0·03 to 0·60 gm. daily, which he stops at the appearance of the least speck of blood in the sputum.

General treatment should be carried out on sanatorium

lines, which tend to promote a lessening of tissue-alkalinity and so to combat the infective process.

(*e*) *Syphilis.*—In the course of this disease low arterial pressure may be an early phenomenon, and is then probably due to interstitial myocarditis, which leads to progressive fibrosis of the cardiac muscle.[242] In such cases strophanthus, added to the usual antiluetic treatment, may be of service.

The general effect of intravenous injections of neosalvarsan, administered during the secondary stage of the malady, is rather to lower, certainly not to increase, the arterial blood pressure.[311]

Considerable attention has recently been paid to syphilitic lesions of the adrenals. In syphilitic subjects, who manifest asthenia and pigmentation, Covisa and Bejarano [312] find hypopiesis to be present as a constant symptom. They regard these manifestations as evidence of adrenal involvement, and advise administration of adrenalin together with regular therapy.

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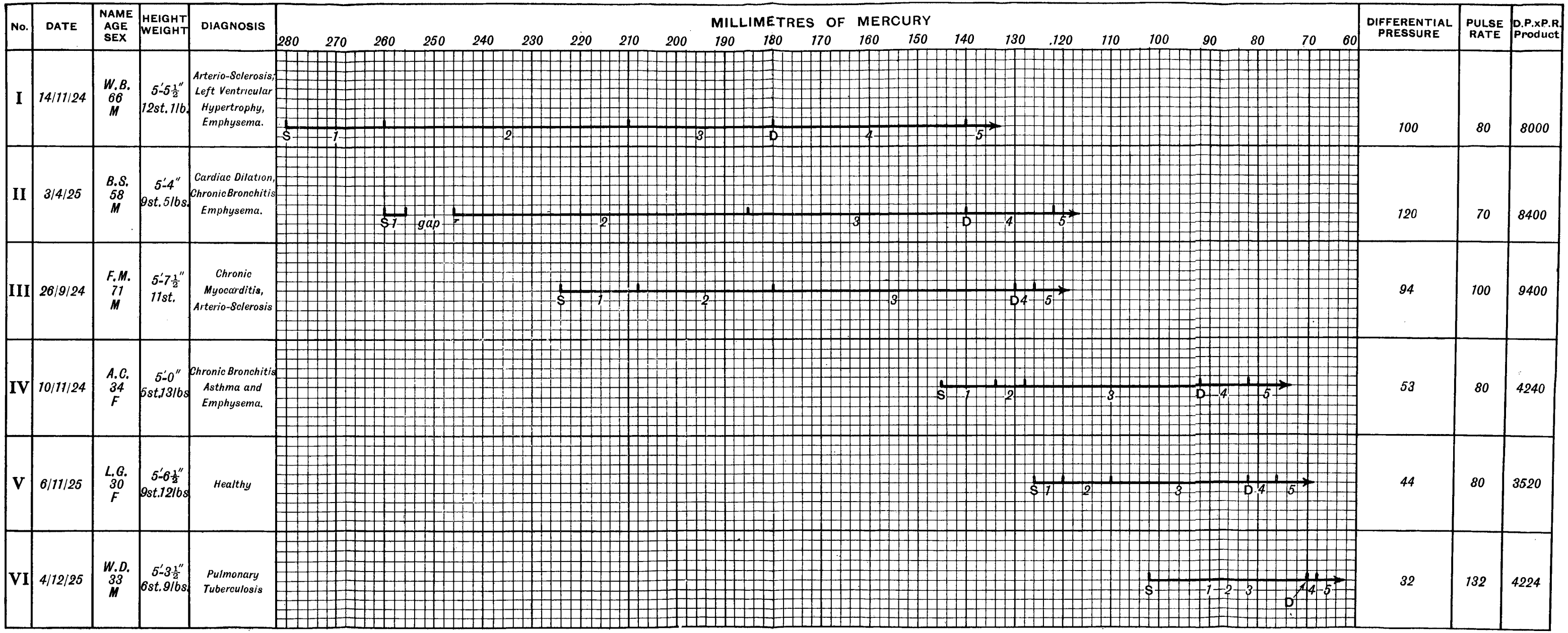

No.	DATE	NAME AGE SEX	HEIGHT WEIGHT	DIAGNOSIS	DIFFERENTIAL PRESSURE	PULSE RATE	D.P.xP.R. Product
I	14/11/24	W.B. 66 M	5′-5½″ 12st. 1lb.	Arterio-Sclerosis; Left Ventricular Hypertrophy, Emphysema.	100	80	8000
II	3/4/25	B.S. 58 M	5′-4″ 9st. 5lbs.	Cardiac Dilation, Chronic Bronchitis Emphysema.	120	70	8400
III	26/9/24	F.M. 71 M	5′-7½″ 11st.	Chronic Myocarditis, Arterio-Sclerosis	94	100	9400
IV	10/11/24	A.C. 34 F	5′-0″ 6st. 13lbs	Chronic Bronchitis Asthma and Emphysema.	53	80	4240
V	6/11/25	L.G. 30 F	5′-6½″ 9st. 12lbs	Healthy	44	80	3520
VI	4/12/25	W.D. 33 M	5′-3½″ 6st. 9lbs.	Pulmonary Tuberculosis	32	132	4224

FIG. 4.—The Author's Complete Arterial Pressure Picture. [*From* "High Blood Pressure," 2nd ed., 1926, Heinemann.]

Specimen cases are here recorded from actual observations to illustrate the author's graphic method of representation on squared paper of arterial pressures of various grades :—

I. Excessively high ; II. Very high ; III. High ; IV. Suspiciously high, if before age forty ; V. Normal : VI. Low.

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