A Theory that any Organism is a Single Chemical Molecule

Put forward as the key to the problem of the causation of neoplasms

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PREFACE TO 1941 EDITION

The theory outlined in these pages is that any organism is a single chemical molecule, and that the organism developing a neoplasm is this single molecule becoming chemically unstable at some point and breaking down at that point, for reasons that will be given, so that a second, smaller, and different type of molecule results there, which then acts independently. The author is convinced that this theory is the key to the problem of the causation of neoplasms. The theory will be referred to for convenience as the molecular theory.

The molecular theory is presented here *only in general outline*, but if it finds some measure of acceptance it will be presented in the fullest detail.

The present edition duplicates the 1932 edition, except for the more detailed application of the theory to neoplasm-production, and the presence of a valued introduction by Dr. C. P. Stewart.

INTRODUCTION

At school one was taught that molecules were amazingly small; that, for example, if a drop of water were magnified to the size of the earth, the individual molecules would be about the size of golf balls. To anyone who still thinks of molecules in these terms, Surgeon Commander Cleave's conception of any living organism, however complex, as a single molecule will be incredible.

But in recent years chemists' ideas on molecules have undergone profound changes. Groups of atoms in stable combination through their primary valencies are now considered able to combine by means of secondary valencies to form larger particles which are still true molecules, and there is no limit conceived to the size of such molecules. And as a further consideration, it is now held that castings, no matter how large, of thermo-setting plastics, are, through the agency of primary valencies alone, single molecules. For example, a casting of the resin, bakelite, produced by heating phenol and formaldehyde, even if large enough to be forming the fuselage of an aircraft, is held to be a single molecule. In short, to-day there can be no objection on the score of size to this molecular conception of an organism.

And if such a conception of an organism be objected to on the score of the complexity of the molecule involved, it may be pointed out that recent and very remarkable discoveries, such as those of W. M. Stanley of the Rockefeller Institute, New Jersey, have shown that viruses, which respire, grow and reproduce themselves just like more complex living organisms, are single molecules of visible and measurable size. This practical evidence, which was non-existent when the molecular conception of an organism was first published in 1932, stands as a powerful and sustained support for it to-day.

I am not attempting to prove that this molecular conception of an organism, presented here, is a statement of fact. But I am attempting to point out that such a hypothesis cannot be dismissed as incredible or as demonstrably wrong. Bold it undoubtedly is, but so was the original atomic theory, and so was the idea of the atom itself as a complex structure built up of still smaller units. Like other bold hypotheses, that are not impossible but not yet capable of direct proof, the present hypothesis is worthy of attention. And if later it becomes accepted, it will revolutionize biological thought.

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PART I

Reasons for believing that a multicellular organism is, through protoplasmic continuity between its cells, in reality fundamentally unicellular

It is first necessary to give reasons for believing that there is protoplasmic continuity between *all* the cells considered to be fundamentally part of a multicellular organism (this excludes the blood-corpuscles, which are considered to be separate, satellite organisms—see later), for clearly no organism composed of separate cells could ever be a single molecule. Formerly there was much controversy between biologists (notably Adam Sedgwick and Gilbert S. Bourne) on the subject of this protoplasmic continuity, but the subject has now fallen into neglect, and except as stated below, it would be hard to find a recent reference on it. Nevertheless, the subject is of the most crucial importance, as this work will indicate.

1. The first reason is the direct evidence provided by the microscope, as follows:—

Let the protoplasmic continuity between the cells of an embryo multicellular organism be taken first. The following passage is quoted from the writings of Driesch:—"At one time it was thought that . . . the result of cleavage was a mass of isolated cells which became reunited to give rise to the later connections between the tissues, which were known to exist." But later it was found that "in the great majority of eggs the nuclear division of cleavage is not accompanied by a complete division of the ovum into separate cells, but only by a re-arrangement of the protoplasm, which produces, indeed, the so-called cellular arrangement, but an appearance, only, of separate cells. But there still remain . . . those small eggs . . . in which division of the nuclei does appear to be accompanied by a complete division of the surrounding protoplasm into separate unconnected cells—ova of many Annelida, Mollusca, Echinodermata, etc., and of mammalia amongst vertebrates. In the case of these also (G. F. Andrews, *Zool. Bulletin*, 1898, ii) it has been shown that the apparently separate spheres are connected by a number of fine anastomosing threads of a hyaline protoplasm, which are not easy to detect and are readily destroyed by the action of reagents. It is, therefore, probable that the divisions of the nuclei in cleavage are in no case accompanied by complete division of the surrounding protoplasm, and the organism in the cleavage state is a continuous whole, as it is in all the other stages of its existence." In the forty years that have elapsed since this was written, nothing has been discovered to disprove it.* But it has been well forgotten.

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* The latest relevant paper known to the author is Condé's "Sur la continuité de la matière dans l'organism", published in *Comptes rend. Assoc. Anat.*, 1937, xxvii, 158–160. In this paper Condé stresses the continuity of tissue elements in multicellular organisms.

Let the protoplasmic continuity between the cells of an adult multicellular organism now be taken. In his standard work on histology Schafer writes of cardiac muscle that "the fibres branch and unite by their branches"; of bone that "protoplasmic processes connect adjacent bone cells with one another and with connective tissue cells and blood-vessels in the canals"; of cartilage that "histologists have described fine communications in the matrix, uniting the cartilage cells with one another"; of nerve endings in tactile discs that "the actual ending of the axis cylinders is intracellular" and "it is not improbable that this will prove true for many other instances of sensory nerve endings: it has long been known to be the case with motor endings"; of the spleen that "the reticular cells of the sponge-work are connected by branches with one another and with the endothelial cells of the vessels"; and so on. For example, he writes frequently of the cell bridges occurring amongst epithelial and endothelial cells, such as amongst the prickle cells of the skin and the endothelial cells of the serous membranes. Incidentally, the basement membrane now becomes intelligible, if conceived as a sheet of protoplasmic continuity between the bases of epithelial cells. Recently (*Lancet*, Dec. 18, 1937) Boeke, Stöhr, and several others have produced evidence against any discontinuity at the synapses of nerve-cells, and assert that the separateness of the nerve-cells is no longer a tenable theory (as forecast five years previously, in the first edition of this work).

It will be noted that in both the above paragraphs only the cells which are considered to be fundamentally part of a multicellular organism have been shown to be in protoplasmic continuity. Such cells as the blood-corpuscles and wandering phagocytes are not considered to be fundamentally part of the organism, but to be separate, satellite organisms, budded off from the main organism and retained by it through evolution because of their usefulness. Their independence is shown by their free mobility, and also by their replaceability by other similar cells (as by a blood transfusion) without *in any way* affecting the main organism, neither of which characteristics could occur in any cells constituting the main organism itself.

2. The second reason is that it is almost inconceivable that the cells of an embryo, if not in continuity, could bud so that the resulting formations always assumed the same relative positions. It is even difficult to see how they could, if not in continuity, *preserve* these positions constantly in the adult—especially in complicated structures, like the liver.

3. The third reason is the singleness of consciousness in multicellular organisms, as pointed out by the author in this work in 1932. Consider the following (note that the argument to be given deals only with the presence of consciousness, not the nature of consciousness, in organisms, thus avoiding metaphysical complications):—

Now cells occurring as unicellular organisms possess a single consciousness each. Thus a single amœba possesses a single consciousness, and a million amœbæ possess a million consciousnesses. But cells occurring as a multicellular organism do not possess a single consciousness each: they possess a single consciousness between them. Thus a dog composed of, for argument's sake, a million cells, does not possess a million consciousnesses: it possesses a single consciousness.

The explanation of this that would probably be advanced at the present day would be that the *nervous system* in multicellular organisms allows of perfect co-operation between the separate cells. There are, however, two objections to this explanation. The first is that the lowest multicellular organisms have no nervous system. The second is that co-operation between separate cells is not at all the same thing as the single consciousness of one cell. For consider the individuals in a large business house: they are all in communication with each other and acting in co-operation, but they are still individuals, possessing a single consciousness each; and this would apply equally to the separate cells of a multicellular organism possessing a nervous system.

Doubtless the objections to the foregoing explanation could, though with difficulty, be removed; perhaps, also, other explanations are possible; but no explanation appears as simple, and therefore as likely to be correct, as the author's, which is that *the cells of a multicellular organism are all protoplasmically continuous*—i.e., that just as a unicellular organism has a single consciousness, so a multicellular organism, being (on account of the protoplasmic continuity between its cells) in reality fundamentally unicellular, also has a single consciousness.

This strong argument must, however, be used with intelligence. Thus though it appears that a single consciousness is accompanied by protoplasmic continuity, it does not follow that protoplasmic continuity is always accompanied by a single consciousness (though the author has not thought of a case where it is not); a subsidiary factor might also be involved, which might lie in the very nature of molecular structure and which might indeed correspond to the nervous system in the higher organisms and to an undifferentiated equivalent of it in the lower organisms. But if this were ever proved to be the case, it would not lessen the force of the argument that the main factor in singleness of consciousness is protoplasmic continuity.

4. There is yet a fourth reason for believing that a multicellular organism is in reality fundamentally unicellular—this is that it allows any organism to be explained in one stroke on a physical basis, by allowing it to be explained as a single chemical molecule, as the following pages will indicate.

PART II

The molecular conception of organisms

A Unicellular Plant Organism.—The molecular theory explains this organism as a single chemical molecule, of the figurative formula, COHN, which represents the main elements (carbon, oxygen, hydrogen, and nitrogen) of which the molecule is composed. Needless to say, the molecule consists in practice of countless atoms, arranged in an infinitely complex manner.

This organism feeds and grows (in preparation for cleavage) mainly on the inorganic substance, carbon dioxide, turning it—especially under the influence of sunlight—into starch. It also feeds on other inorganic substances —e.g., nitrogen, water, etc.—present in its environment, and produces generally much more complicated substances than starch. This is the molecule, COHN, combining with more of the elements, carbon, oxygen, hydrogen, and nitrogen, as they exist in the free state and in inorganic compounds, to form a larger molecule, $\begin{array}{l}\text{COHN}\\ |\\ \text{COHN.}\end{array}$ Needless to say, the link shown consists in practice of countless atoms, but forming a relatively narrow isthmus in the structure of the molecule.

The organism reproduces itself by completing this cleavage. This is the molecule, $\begin{array}{l}\text{COHN}\\ |\\ \text{COHN,}\end{array}$ breaking down into two molecules of the original formula, COHN.

And just as the two new organisms, because they resemble the parent organism, go through the same cycle as it did, so do the two new molecules.

A Multicellular Plant Organism.—The molecular theory explains this organism as a single molecule, of at first the same figurative formula, COHN, that the unicellular plant organism had.

The multicellular plant organism grows by its cells, when appearing to divide, really remaining adherent by protoplasmic strands. This is the molecule, COHN, forming a larger molecule by adding to itself more groups of COHN, thus (figuratively):—

$$\begin{array}{l}\text{COHN}\\ |\\ \text{COHN }(a)\\ |\\ \text{COHN }(b)\\ \vdots\\ \text{COHN }(n)\end{array}$$

The letters (*a*) and (*b*) represent slight differences in the groups, and group (*n*) is the last of a vast number of such groups. (The word "group" will be used in the figurative sense throughout.)

The lowest form of multicellular plant organism reproduces itself by budding off a truly independent cell, which resembles the parent organism as it was at the beginning of its life. This is the above larger molecule splitting off a smaller molecule, COHN, which resembles the larger molecule as it was at the beginning of its cycle.

The higher forms of multicellular plant organism have a sexual method of reproduction. For example, the highest forms, such as the date tree and holly tree (and most forms of animal organism, to be described next), have the following variation of this method:—Each organism is either a male, that buds off a male type of cell, called a unit of pollen (spermatozoon); or is a female, that buds off a female type of cell, called an ovule (ovum). These two types of cell have a biological affinity for each other, and when brought into contact fuse to form an embryo, that resembles either the male or the female parent organism as it was at the beginning of its life. This is the above larger molecule being either a variety that splits off one type of smaller molecule, or a variety that splits off another type of smaller molecule. These two types of smaller molecule have a chemical affinity for each other, and when brought into contact combine to form a small molecule that resembles either the one or the other variety of larger molecule as it was at the beginning of its cycle.

In many forms of animal organism (to be described next) the embryo (fœtus) keeps temporarily in close physical association with the female parent, which results in its obtaining nourishment and so passing through the early stages of its life more easily. This is the above small molecule, that resembles the one or the other variety of larger molecule, having temporarily a close physical contact (but probably not chemical continuity) with that molecule, which results in its combining with substances that diffuse into it from the molecule and so passing through the early stages of its cycle more easily.

The multicellular plant organism eventually dies. This is the molecule, through wear and tear in its chemical cycle, becoming eventually so altered in composition as to be no longer chemically reactive with surrounding substances.

A Unicellular Animal Organism and a Multicellular Animal Organism.—These organisms closely resemble the corresponding plant organisms, except that instead of living (as the plant organisms do) upon carbon dioxide and other inorganic substances in their environment, they live on the plant organisms themselves and on other animal organisms. The molecular theory explains these organisms as single molecules closely resembling the molecules which the plant organisms are, combining with the same elements, but not with these elements as they exist in the free state and in inorganic compounds, but as they exist in organic compounds.

It is not of course suggested for a moment that an animal organism eating food is a molecule combining then and there with other substances. Actually, such an organism eating, digesting, and absorbing food is a molecule exhibiting certain reflex physico-chemical reactions (e.g., see later under movement) which result in the arrival of certain (now simpler) substances into spaces honeycombing its structure; and it is then that the molecule combines with these (simpler) substances, at the surfaces of these spaces (a process representing anabolism in the organism).

Needless to say, the "substances" spoken of above, and in future, are also molecules, though relatively of infinite minuteness.

The spaces just mentioned as honeycombing the molecule's structure are of three kinds: (*a*) blood-vessels; (*b*) tissue spaces; (*c*) probably intracellular spaces (for it has been shown that a red cell is structurally like a sponge, and this is probably true of other types of cell). Only by means of these spaces could enough surface area be available for the molecule to be able to interact with the myriads of substances (separate, minute molecules, as just said) which occur in its structure as honey does in a honeycomb.

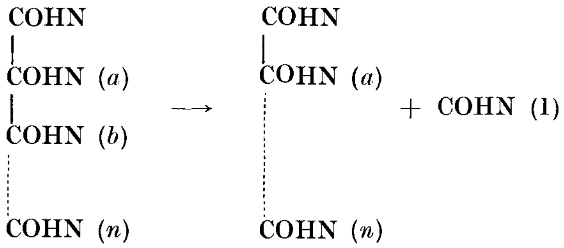
It is important to point out that the molecular theory is not weakened through the *size* of the molecule which it postulates an organism to be. There is no theoretical limit to the size of a molecule in organic chemistry. Thus there can be a gradual increase in the size of a molecule from CO_2, containing three atoms, to one of the polypeptides first built up by Emil Fischer, containing thousands of atoms, to an ultra-microscopic virus, to a bacterium, to a protozoon, and so on up to the largest plant and animal.

Some years after the author's molecular theory was first published, W. M. Stanley, of the Rockefeller Institute, found that the virus of mosaic disease in tobacco plants could be crystallized, and that the crystals could be seen under the electron microscope. For details the papers of Stanley and other workers in this field must be consulted, but it may be stated here that as the result of these discoveries it is now known that viruses are single molecules. The author's molecular theory is thus now capable of considerable experimental verification, and should be still more so in the future.

PART III

The molecular conception of neoplasms

The molecular theory explains an organism developing a neoplasm as a large molecule becoming chemically unstable at some point, and breaking down at that point so that a second, smaller, and different type of molecule results there, as follows (to continue using the figurative formula of a few pages back):—



$$\begin{array}{l} \mathrm{COHN} \\ | \\ \mathrm{COHN}\ (a) \\ | \\ \mathrm{COHN}\ (b) \\ \vdots \\ \mathrm{COHN}\ (n) \end{array} \longrightarrow \begin{array}{l} \mathrm{COHN} \\ | \\ \mathrm{COHN}\ (a) \\ \vdots \\ \vdots \\ \mathrm{COHN}\ (n) \end{array} + \mathrm{COHN}\ (1)$$

The large molecule has broken down at the point COHN (*b*) (it could equally have done so at any other point), so that a second, smaller, and different type of molecule has resulted there, COHN (1).

Now the neoplasm either very closely resembles the part of the organism from which it has arisen, in which case during growth its cells keep protoplasmically continuous, as in a growing multicellular organism (the neoplasm then being benign, because its single structure can easily be removed by operation); or it less closely resembles the part, in which case during growth its cells are protoplasmically separate, as in a proliferating unicellular organism (the neoplasm then being malignant because its multiple, often scattered, structure is not easily removed by operation). This is the above new molecule either very closely resembling the part of the large molecule from which it has arisen, in which case during its increase in size (by combining with surrounding substances) it remains a single molecule; or less closely resembling the part, in which case during its increase in size it soon breaks down into two smaller molecules, which then behave in a similar manner. Clearly there can be gradations between the two types of neoplasm and the two types of molecule.

It may be noted that the more malignant the neoplasm, the greater must be the difference in type of the new molecule—i.e., the greater must have been the degree of the breaking-down process.

The **causes** of such a molecule becoming chemically unstable and breaking down in this way (i.e., the causes of an organism developing a neoplasm, which it is the essential object of this work to elucidate) can now be seen without great difficulty, as follows (in order of increasing importance):—

1. An occasional cause would be a blow which, by rupturing the connections of a group with the main structure of the molecule, would result in a new molecule there, occasionally sufficiently altered to react independently. This means, in an organism, that a blow would occasionally be the cause of a neoplasm, and this is known actually to be the case (e.g., a blow causing a sarcoma).

2. A more frequent cause would be wear and tear in the molecule; for the longer the molecule existed, the more unstable it would become. This means, in an organism, that the longer it lived, the greater would be its tendency to develop a neoplasm. And this is known actually to be the case (e.g., the incidence of cancer is roughly proportional to the age).

3. But though not necessarily so frequent a cause as the preceding one, a more important cause (because it could be prevented) would be *abnormal changes in the conditions in which the molecule was by evolution chemically stable.* This means, in an organism, *unnatural changes in its environment,* which comes down to *the arrival of civilized conditions.* Let us see if there is practical evidence that this actually is the case:—

Now to start with, from the molecular theory itself it is clear that, even under the most normal conditions, molecules of the above complexity would, during the age-long evolution of simple molecules into complex ones, frequently become unstable and break down. But at any given level of complexity evolution would be constantly reducing the incidence of such breaking-down, so any small incidence still persisting at this level could appropriately be termed the " evolutionary incidence ". But if the conditions became abnormal, a much greater incidence would rapidly occur. This means, in an organism, that even under the most natural conditions there would be a small, evolutionary incidence of neoplasm-development, but that if the conditions became unnatural (as in the arrival of civilized conditions), a much greater incidence would rapidly occur.

Let us see how this corresponds to the known incidence of neoplasms in organisms:—Now it has long been felt that the incidence of neoplasms in man is related to civilized conditions. But this feeling has been diminished by the fact that there is a definite incidence of neoplasms in relatively uncivilized peoples, and even in wild creatures (living in the wild state). But we can now see, by the molecular theory, that this fact is of no importance whatever, because according to this theory, all that matters is, as shown above, the *relative* incidence of neoplasms in civilized peoples and in uncivilized peoples (or wild creatures). And on this point we have adequate evidence that the incidence in the former is much greater than in the latter. We have no space here to go into this evidence properly, but we can mention the following, not as of any importance in themselves, but merely as typical examples:—

(*a*) Smith and Elmes, quoted in the *British Journal of Surgery* for July, 1937, have shown from a review of the literature and from their own researches extending over eight years, that the old view that cancer in the African native is more or less non-existent is no longer tenable, but that it is very much rarer than in England. (This is in keeping with the general feeling—for which, however, there is little evidence available now—that cancer was much rarer, age for age, in the peoples living in civilized countries in bygone centuries, when of course the civilization was much less developed, than it is in the same peoples to-day.)

(*b*) Similarly, the incidence of cancer in the dog, the most domesticated animal, is known to veterinary surgeons to be much greater than in any other animal. In fact the incidence of neoplasms in wild creatures (living in the wild state) appears to be exceedingly small, if we are to judge by the fact that neoplasms are very rarely encountered in them. Moreover, it is difficult to explain such a small incidence in them by their earlier age of death, for some even in the wild state live to a considerable age: thus, even a herring has been proved to live frequently for more than a dozen years, and of course many wild creatures frequently live much longer than this. It is equally difficult to explain such a small incidence in them by their rapid death when so diseased, for owing to the fact that neoplasms often produce naked-eye masses before noticeably interfering with function, it is inconceivable that such neoplasms, if they frequently occurred, would not also be frequently encountered in the vast numbers of wild animals, birds, and fish constantly being taken for human food.

At this juncture we may point out that abnormal conditions would produce in the molecule a greater breaking-down not only as regards frequency, but also as regards the degree of the breaking-down process. This means, in an organism, that civilized conditions would not only increase the incidence of neoplasms, but also their malignancy. And actually one does feel, after careful consideration, that this is so. But due to little being known about neoplasms in really primitive peoples (e.g., the Esquimaux), and even less in wild creatures, it is not possible at this stage to be dogmatic about the relative malignancy of neoplasms occurring in them and those occurring in civilized man and highly domesticated animals.

In conclusion, therefore, we may state that there is much evidence that the third cause, above, elucidated by the molecular theory, is true in practice—i.e., that civilized conditions actually are a major cause of neoplasm-development.

As a continuation of the study of this third cause, let us now see if we can, by the molecular theory, discover *which* civilized condition is mainly responsible for neoplasm-development, and then see if there is practical evidence that this is the case:—

Now clearly the abnormal condition most likely to make the molecule chemically unstable and break down would be *abnormality of the substances with which the molecule was combining* (since clearly this would cause the molecule to form abnormal compounds); and the greater the abnormality of the substances, the greater (both in frequency and degree) the breaking down. This means, in an organism, that the civilized condition most likely to cause it to develop a neoplasm would be unnaturalness of those substances which the organism was combining with—*i.e., unnaturalness of its food*; and the greater the unnaturalness (e.g., that produced by milling and refining compared to that produced by simple cooking), the greater (both in incidence and malignancy) the neoplasm-development.

The molecular theory leads, therefore, to the conclusion that **a main cause of neoplasm-development in civilized man is unnatural food.** When it is considered how amazingly complex is the molecule representing civilized man, and how abnormal (unnatural), even allowing for the levelling effect of the process representing digestion, are many of the substances (foods) with which such a molecule is constantly combining, it is easy to see how the molecule must frequently lose its chemical identity and break down (develop a neoplasm). The practical evidence for the above conclusion being correct will, however, be given later.

A suggestion (only), which is independent of the molecular theory, will now be given for believing that the cause of the above neoplasm-development is not unnatural food itself, but unnaturally concentrated types of such food giving rise to certain substances that *are* the cause of the neoplasm-development. At the outset, however, it must be stated that this new conclusion will be perfectly compatible with the conclusion just reached by the molecular theory, and that it will not alter the action (to be described later) rendered desirable by that conclusion; *hence no criticism of it will be able to weaken that conclusion.*

Now for the sake of clarity it was stated above that substances which an organism combines with comprise its food, and this is substantially correct. But it would be still more correct to add that there are a few other substances—e.g., those injected by bees, nettles, etc.—which an organism also combines with, but does so externally. As we should surmise from the molecular theory, such substances, being natural, do not cause neoplasm-development. But in civilized conditions there are a great many *unnatural* substances, ranging from hair-dye to tobacco, which the human organism combines with externally, and the important point is that the only ones among these that cause neoplasm-development are those that act as *irritants* (e.g., tar, soot, etc.). It is therefore logical to suppose that the particular unnatural foods that cause neoplasm-development are, also, those that act as irritants. Are there any unnatural foods that do this? The answer is no, but that unnaturally concentrated types of such food give rise to substances which do act as irritants, as will be shown in the following four steps:—

(i) *Unnatural concentration of foods causes an unnatural increase in their consumption, through preventing the accurate play of the natural instinct of appetite.* As only one example, we may take the case of crystalline sugar. This product shows a most unnatural concentration. It will suffice for our purpose to give the following figures from the *British Medical Journal* of January 29, 1938, showing how this concentration has led to an increase in consumption (the increases in consumption roughly follow the increases in the mechanical efficiency of the concentrating process; to a certain extent they also follow the increases in efficiency of agricultural machinery and shipping, but as the end-result of these is always a larger amount of crystalline sugar, it comes to much the same thing):—In 1844 the sugar consumption in the United Kingdom averaged 18 lb. per person per annum; in 1860 35 lb.;

in 1880 60 lb.; and at the present day, if during peace-time, it is well over 100 lb. For comparison, in Southern Rhodesian natives the sugar consumption at the present time is 13 lb. And there are many other examples of unnatural concentration of foods (notably the refinement of cereals by milling processes) leading to an unnatural increase in their consumption.

(ii) *This unnatural increase in consumption frequently leads to a consumption in excess of bodily requirements.* For there is no reason to believe that this unnatural increase in consumption is at the expense of foods that have not been unnaturally concentrated. In fact the consumption of these latter has nowadays often been raised to the natural maximum by their greater availability (e.g., the greater availability of meat, through modern cold methods of transport). Further, such unnatural increases in consumption as that given in the case of sugar are much too great to be accounted for by the potential bodily requirements of the relatively few people living in this country a hundred years ago. (It may be noted in this connection that any lack of food in England to-day, during peace-time, is mainly a qualitative lack, not a quantitative one.) From all the above, therefore, it follows that the unnatural increase in consumption frequently leads to a consumption in excess of bodily requirements.

(iii) *The excess of food so consumed largely undergoes bacterial putrefaction.* This can be shown by the following consideration:—Let us imagine an individual living quietly in one of the rooms constructed by physiologists for measuring metabolism. If we now cause the individual to eat much more food than he requires for this degree of activity, practically none of the excess food is digested, absorbed, and metabolized. We could prove this fact by measuring the metabolism, but actually we could sense it beforehand, because if such excess food were metabolized, and the individual did not increase his activities, he would either feel hot and perspire considerably to get rid of the extra heat produced, or he would increase his weight commensurately and without arrest. And actually we could sense that he would do neither. Nor on natural grounds should we *expect* the body to digest, absorb, and metabolize more food than it requires. At the same time, the excess food does not appear as such to any appreciable extent in the stools. The deduction is, therefore, that it mostly undergoes putrefaction by the hoards of bacteria in the gut. (It may be added here that through food being eaten after subjection to such mechanical processes as those indicated above, many of the bacterial antibodies present in raw food (e.g., in raw fruit, which is actually alive when eaten) are destroyed, and hence the bacterial attack on the food may be greatly facilitated.)

(iv) *The products of this bacterial putrefaction are frequently highly toxic—i.e., irritant—to the intestine, and, after absorption, to the entire organism.* That foods putrefied by bacteria are frequently highly toxic is shown not only by their more obvious irritant effects after being eaten (diarrhœa, urticaria, etc.), but by their evil odour (and to a lesser extent, taste). (In this connection it is vital to realize that the nose—and to a lesser extent the tongue—is by far the most sensitive detector of naturally-occurring toxins: it is not only the most delicate quantitatively, because it can detect such toxins in immeasurably minute concentrations, but it is also the most delicate qualitatively, since it has been evolved specifically by differentiating between naturally-occurring toxic and beneficial substances.) Even such substances as sugar that are not directly converted into evil-smelling and therefore toxic products, form a pabulum for bacteria attacking other foods that are so converted, and hence greatly increase the production of such toxins.

That the production of irritants from the food, as shown in the above four steps, does occur in practice is shown by the extremely important fact that the stools of civilized man, and of such highly domesticated animals as the dog, do frequently have a revolting odour and do frequently cause such obvious irritant effects as those mentioned. And complementary to this fact is the equally important one that though the stools of all wild creatures have characteristic odours, they do not have offensive ones. As an example of these two facts, farmyard manure is often stacked in the farmyard with no unpleasant results: this would certainly not be true of the stools of civilized man.

Admittedly, intestinal toxin-formation has long been realized to be clinically very important, but not, in the author's opinion, as important as it actually is, owing partly to the non-realization of the value of the nose in detecting naturally-occurring toxins, and partly to the constant confusion of intestinal toxin-formation with intestinal stasis, the curing of which does not cure the toxin-formation. Actually these two conditions are entirely separate, as will be understood from the above conception of intestinal toxin-formation. Thus, if no surplus of food has been eaten, no amount of stasis can result in any toxins. And, *per contra*, if a surplus has been eaten, no ordinary alteration in the stasis can appreciably reduce the toxins, so rapid is the bacterial action at body temperature; in fact, owing to the greater liquidity they produce in the stools, aperients are considered to increase their toxicity. Clearly the only logical way to cure intestinal toxin-formation is to stop the consumption of excess food, by causing the food to be taken in its natural (i.e., unconcentrated) form. The clinical results obtained by this method are often dramatic.

The new conclusion that has been reached, therefore, is that the main cause of neoplasm-development in civilized man is unnaturally concentrated food giving rise to substances that act as irritants to the entire organism. This conclusion is quite compatible with the conclusion reached by the molecular theory (which is that the cause of the neoplasm-development is simply unnatural food), since *it is only a question of whether the molecule is breaking down through combining with one set of abnormal substances, or another set.* Also, this new conclusion will not alter the action (to be described later) rendered desirable by the conclusion reached by the molecular theory, because it happens that the most unnatural food is also the most unnaturally concentrated food (e.g., milled and refined food in each case). It is true that the new conclusion would postulate that the unnaturally concentrated food would not cause the neoplasm-development if not consumed in excess, but as the unnatural concentration is the very cause of the excess consumption (through preventing the accurate play of the natural instinct of appetite), this postulate is of little practical importance. It is clear, therefore, that as this new conclusion does not impair the theory or the practice of the conclusion reached by the molecular theory, **no criticism connected with this new conclusion—e.g., of the intestinal toxin-formation mentioned—can weaken the conclusion reached by the molecular theory.**

The above two conclusions apply to the (usual) general causation of neoplasms (i.e. where there is no obvious local cause—such as smoking, in certain oral and lingual neoplasms). But the second conclusion, if found later not to apply to the general causation, might apply to a local causation, explaining the great frequency of neoplasms of the terminal gut. Also, it is easy to see how a general causation might often be combined with a local causation, for if a tissue is highly active through some unnatural local irritant or other unnatural cause, then the impact of unnatural food materials, or unnatural general irritants, on that tissue might be the deciding factor in its losing its stability.

As practical evidence of the truth of each above conclusion, but especially of the second, may be mentioned the recent research of Frederick Hoffmann into the relationship of neoplasm-production to diet. Hoffmann analysed the dietetic habits of over 2,000 cancer patients and 1,000 controls, and embodied his results in the extensive work published in the United States and in this country,* which was reviewed in the *British Medical Journal* of July 24, 1937. Hoffmann concludes with the following: "I consider my duty discharged in presenting the facts as I have found them, which lead to the conclusion that over-nutrition is common in the case of cancer patients to a remarkable and exceptional degree, and that over-abundant food consumption is unquestionably the underlying cause of cancer in modern life."

In conclusion, it will be noted that it is quite easy to explain by the molecular theory the production of neoplasms by *any* neoplasm-producing substances, including those of laboratory importance (e.g., cell-free filtrates of tumours, many chemicals, etc.). For all of these would merely rank as substances which, after the molecule had combined with them, had a tendency to make it break down, as already explained.

The reason food-substances have been dealt with almost exclusively is merely because it is considered that these are the most likely ones to be the cause of neoplasms in actual practice. For, as stated in a leader of the *British Medical Journal* only this year (February 8, 1941), laboratory workers have discovered large numbers of experimental carcinogens, but, with the exception of œstrone, none of these carcinogens are known to occur in the body under ordinary conditions—i.e., none of them are known to play any appreciable part in the production of neoplasms in actual practice.

Finally, the author does not consider it possible at present to state whether cause (2) or (3) (i.e., old age or civilized conditions) is relatively the more frequent in neoplasm-production in mankind to-day, but presumably it is cause (2) (i.e., old age) which is the more frequent.

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* *Cancer and Diet: with Facts and Observations on Related Subjects*, by Frederick L. Hoffman, M.D. 1937. Baltimore: The Williams & Wilkins Co. London: Baillière, Tindall & Cox.

The action rendered desirable by these conclusions, to reduce the neoplasm-development in civilized communities to-day, is clearly not only to continue to prevent, as far as practicable, access to the human organism of external irritants, such as tar, soot, petrol fumes, etc., but also to stop the consumption of those unnatural foods, such as milled and refined foods, which not only are dangerous of themselves, as shown by the molecular theory, but which probably give rise to internal irritants and so constitute a danger of more obvious type. Simple cooking is probably the safe limit to which foods can be altered from their natural state, because man is probably partly evolved by now to cope with this alteration, though even this limit cannot be entirely safe.

Such action over the more unnatural foods would also heavily reduce other unnatural diseases, by its effect on intestinal toxin-formation; by its effect on the tremendous growth (on the excess food) of saprophytic bacteria of slight pathogenicity (e.g., the *Bacillus coli*); by its effect on the production of acids from food around the teeth; by its effect on vitamin deficiencies; and by its effect on other unnatural processes far too numerous to list here. But the author would go much further than this. He would postulate that if such action were pushed to the extent of giving food raw (an experimental measure, necessary for very few diseases; and as a permanent measure, necessary for probably none), it would eliminate virtually all diseases other than congenital malformations, occasional neoplasms, and diseases caused by *specific* pathogenic organisms. For these latter alone are the natural diseases, occurring in wild creatures; whereas all the rest are unnatural diseases, not occurring in wild creatures, and could therefore be prevented by the restitution of natural conditions (which would usually mean a natural diet). But into this fascinating diversion we have no space to go here.*

It is, of course, clear that the action just recommended, to reduce the incidence of neoplasms (and other diseases) in civilized man to-day, might not be very practicable and therefore not very desirable. Not very practicable, because if milling and refining were much reduced, it might not be economically possible to distribute food adequately to the large populations in the world to-day. And therefore not very desirable, as it might be necessary to let the human race become evolved to many of the new conditions imposed upon it by civilization. Nevertheless, recommending the above action may not be waste of time. For if the recommendation is theoretically correct, it will be worth knowing on that score alone; and further, the recommendation may be at least partly practicable, as shown by the Italian Government's decree, some years before the present war, prohibiting the refining of flour; and lastly, any recommendation, although it may be rejected for the race, may be hastily accepted by the individual for himself.

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* This matter has been treated by the author in a paper entitled: *Plea for a Raw Diet Test in Diseases of Unknown Primary Causation*, 1936. Bristol: John Wright & Sons.

PART IV

Explanation of other activities in an organism by the molecular theory

Although the main value of the molecular theory lies in its power of explaining neoplasm-development, the theory can also explain the other activities of an organism, as the following examples, limited to five by considerations of space, will indicate; but it is essential that the attention should not be diverted from the main function of the molecular theory (which is to explain the causation of neoplasms) by such digressions as these five examples, which, though they may be interesting, are relatively of little practical importance:—

1. **Embryonic Development.**—The molecular theory explains an embryo choosing apparently so miraculously those paths of development that lead it to the adult form as a certain substance (molecule) which, placed amongst certain other substances (molecules), always combines with these to form the same compound (more complex molecule).

2. **Animal Heat.**—The molecular theory explains an organism possessing animal heat as a molecule slowly combusting, due to the presence of combustible radicles. The organism maintains its heat by its food. This is the molecule, as it combusts, combining with substances which contain more combustible radicles, which results in the combustion becoming continuous.

3. **Movement.**—Movement in an organism is fundamentally that irritability which is characteristic of all living protoplasm. In the higher forms of organism the irritability occurs locally as muscle contraction. The molecular theory explains this irritability (including muscle contraction) as contraction of certain membranes forming part of the structure of a molecule—the contraction being a physico-chemical (surface tension) phenomenon resulting from certain stimuli.

4. **Pleasure and Pain.**—The molecular theory explains these as follows:—

Desires in an organism are tendencies in a molecule—tendencies to enter into certain chemical reactions. Pleasures in an organism (the fulfilments of its desires) are the fulfilments of tendencies in a molecule—i.e., actual entry into those chemical reactions it tends to enter into. Conversely for the opposite of desires and pleasures in an organism, i.e., desires not to participate in certain procedures, and instances of pain:—desires in an organism not to participate in certain procedures are tendencies in a molecule not to enter into certain chemical reactions; and instances of pain in an organism (which are its desires not to participate in certain procedures being overpowered, it being forced actually to participate in these procedures) are tendencies in a molecule not to enter into certain chemical reactions being overpowered, it being forced actually to enter into these reactions.

It may be noted here that all chemical and physical reactions that tend to occur are accompanied by a dilution of energy (or degradation of energy, as it is sometimes called); and similarly all chemical and physical reactions that tend not to occur are accompanied by a concentration of energy. The same is therefore true of all the reactions of a molecule representing an organism.

In the following paragraphs "a molecule breaking down into simpler molecules" is meant to convey that it is entering into a chemical reaction which it tends to enter into (one involving a dilution of energy), and "a molecule being forced to build itself up into a more complex molecule" is meant to convey the exact opposite. Such breaking-down as that to be described is clearly far greater than that mentioned in connection with neoplasm-development, and the resulting molecules bear no resemblance to any group in the main molecule, but are of a much simpler character (CO_2, etc.).

We will now give one or two actual examples of pleasure and pain in an organism, with their explanations by these means:—

As an example of an organism experiencing pleasure, take a man greatly excited (as evidenced by a flushed face and an increased power of the heart-beat and respiration) at hearing that he has won a fortune by a speculation (which is really a man having a rapid katabolism occur in certain parts of his body, consequent on a certain stimulus from the exterior). Explained by the above means, this is a molecule breaking down rapidly in certain parts of its structure, consequent on a certain stimulus from the exterior. And the molecule breaking down in this way is similar to any other substance entering into a chemical reaction that it tends to enter into—e.g., alcohol burning away to lower substances.

Now, as an example of an organism experiencing pain, take the same man greatly shocked (as evidenced by a pallor of the face and a decreased power of the heart-beat and respiration) at hearing that he has lost this fortune again by a further speculation (which is the man undergoing the exact reversal of the above process, in his body). Explained by the above means, this is the molecule also undergoing the exact reversal of the above process—i.e., being forced to build itself up again. And the molecule being forced to build itself up again in this way is similar to any other substance being forced to enter into a chemical reaction that it tends not to enter into—e.g., the lower substances into which the alcohol burnt being forced to build themselves up again into alcohol.

Some pain processes in an organism are actual reversals of pleasure processes, like this one, but usually pain and pleasure processes are not reversible in practice. This is because they are chemical reactions in a molecule that are not reversible under existing conditions. However, pain in an organism that is not actual reversal of pleasure is explained in exactly the same way as pain that is. For example, an organism being hurt in some part of its body by a knife-cut is a molecule being forced in some way, through cleavage of its surface, to build itself up in part of its structure into a higher compound.

Now if katabolism in an organism is a molecule breaking down into simpler molecules, which means the organism experiences pleasure during the act, it might be thought that anabolism, being apparently the reverse of katabolism, would be the molecule being forced to build itself up again into a more complex molecule, which means the organism would experience pain during the act. Yet actually anabolism is never painful—an organism never experiences pain when restoring its energies from its food. In order to explain this by the molecular theory, it will be necessary first to show that anabolism is not in reality the reverse of katabolism. Thus, since katabolism is an organism breaking down in certain parts of its structure, which parts the organism had previously formed by combining with its food, it follows that anabolism, if the reverse of katabolism, would essentially be the organism being forced to build itself up again in these parts of its structure from the end-products into which it had broken down. Clearly the organism never is forced to build itself up from such end-products, but combines instead with new food. Hence anabolism is in no sense the reverse of katabolism. It is now easy to see why an organism restoring its energies from its food experiences no pain during the act, for such an organism is a molecule combining—probably catalytically—with a set of fresh substances, a process not accompanied by any concentration of energy.

Different *types* of pleasure and pain in an organism are essentially different types of chemical reaction in a molecule. Different *degrees* of pleasure and pain in an organism are different degrees of chemical reaction in a molecule, which the molecule either tends to enter into or tends not to enter into. Sleep in an organism, which is practically absence of consciousness and due to katabolism in most parts of the organism being almost at a standstill, is practically absence of chemical reaction in a molecule, due to so many parts of the molecule having disappeared during chemical reactions.

5. Mind.—Although this subject cannot be adequately treated here, the following may be pointed out:—

Now mind is basically a modification of an organism's desires by its memory. For example, a rat eats cheese on a trap and gets caught. Supposing it escapes, then the next time the rat sees cheese on a trap, its instinctive desire to eat the cheese will be modified by its memory of the previous painful event and it will no longer eat the cheese. But without its memory the rat could get caught and escape an indefinite number of times, and yet would still be caught just the same on the next occasion. This is mind brought down to its simplest basis, and however much this is elaborated, mind is always basically a modification of an organism's desires by its memory.

The molecular theory now explains mind as follows:—The memory in an organism is a retentive property in a molecule. It is no more difficult to accept the existence of this retentive property in a molecule than to accept the existence of memory in an organism. Such a retentive property is presumably due to an impression left on the structure of a molecule by a chemical reaction. Whether all molecules have such a retentive property or whether only those of stupendous size and complexity, forming living organisms, have the property, it is impossible to say, but since memory (and therefore mind) only decreases gradually in organisms as they become lower in the scale (witness even the flies soon avoiding the fly paper), so that even in the lowest organisms it must, though infinitesimal, still be present, so also in the simplest molecules (inorganic, of course, and not forming living organisms) the retentive property, though even more infinitesimal, must still presumably be present in traces (which suggests an interesting metaphysical line of thought). Mind, which was stated above to be basically a modification of an organism's desires by its memory, is now explained by the molecular theory as *essentially a modification of a molecule's tendencies by a retentive property.* Further than this it would be most undesirable to go, here.

Conclusion

In conclusion, it may be pointed out that the strength of the molecular theory lies in its simplicity. Whether or not related to the fact that the Universe is an expression, in many different combinations, of only one ultimate reality (a view held at varying periods since the earliest times, and proved to-day by the knowledge of the electron), the usual correctness of simple explanations is, as Emerson largely pointed out, one of the great empirical and valuable facts discovered by man during the last few thousand years.

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