THE CROONIAN LECTURES

ON THE RELATIONSHIP BETWEEN

CHEMICAL STRUCTURE

AND

PHYSIOLOGICAL ACTION.

Delivered before the Royal College of Physicians of London.

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LECTURE I.—(Concluded from page 1279.)

ELEMENTS AND RADICALS.

Atoms and Molecules.—In their chemical relations these substances—acetylene, ethylene, methane, benzene, and furfuran—are practically *elements formed at a low temperature*, and may be fitly compared with the alkaline metals and those of the alkaline earths which, if Lockyer's hypothesis be right, have formed at enormously high temperatures. In describing this hypothesis I spoke of single atoms of elementary matter, or protyle, as Crookes calls it, as having been existent at first, but under the conditions which now prevail single atoms, with one or two exceptions, seem incapable of independent existence, and a molecule is the smallest quantity capable of such existence. Atoms are supposed either to join together with atoms of a like nature to form a molecule of an element, or with atoms of another element to form the molecule of a compound. When the molecule of an element is split up into single atoms, as, for example, the molecule of

Diagram to show relation of differentiation with affinity for
(A) Acid Aniline Dyes, (B) Basic Aniline Dyes.

Diagram to illustrate the formation of ozone.

oxygen, by the electric spark, the single atoms do not remain apart, but immediately coalesce, either with other single atoms to re-form a molecule of oxygen, or with other molecules of oxygen containing two atoms to form a molecule of ozone containing three atoms. Many elements seem to have but very slight chemical affinities for others when the atoms are already united to form a molecule, but when the molecule is split up, as, for example, during the process of chemical combination with other elements, the atoms, just at the moment when they are set free, or, as it is termed, in their nascent condition, have extremely active affinities. Thus nitrogen, which forms the bulk of our atmosphere, is, in its ordinary condition, when all its atoms are united, as we suppose two and two to form molecules, an extremely inactive element. Yet, according to Armstrong,⁵ this

very inactivity probably depends upon the strength of its affinities, which hold the molecules together so strongly that they refuse to separate from each other and combine with other elements; but when the molecule is broken up, and the atoms separate, their powerful affinities impart to gunpowder, dynamite, or roburite their tremendous explosive powers. Nitrogen, in its molecular condition, is the type of stability and inaction. Nitrogen, in its atomic condition, is the type of mobility and activity, and forms along with carbon the basis, not only of our explosive compounds, but of organic life. The properties of carbon and nitrogen depend very greatly on the mode in which they are combined, but if I were asked to describe in a few words the general effect of carbon on the animal organism, I should say it was sedative, while that of nitrogen was exciting.

Radicals and Residues.—When the molecule of an element such as hydrogen or oxygen is broken up, it simply falls apart into two atoms which resemble each other, but when a substance containing more than one element is disintegrated, it may not break up into the elements of which it is composed, but one or more atoms may, as it were, be knocked off, leaving a residual group of two or more atoms. This group behaves in much the same way as a single atom, and is, like it, incapable of independent existence. Such a group used to be called a residue, but the term radical is now given to it.

The Decomposition of Water.—Long ago water was regarded as an element. When chemists began to decompose it, and thus recognise it as a compound, they supposed that it was formed by the union of one atom of oxygen and one of hydrogen, and during decomposition these simply fell apart, and the atoms of each element united together to form the two resulting gases. But now that we regard water as a compound of two atoms of monovalent hydrogen and one of divalent oxygen, we see that the process of decomposition may be much more complicated. Thus when water (H_2O) is broken up, it may not fall apart simply into oxygen or hydrogen, but one atom of hydrogen may be removed, leaving a single atom of hydrogen combined with one of oxygen. But the atom of oxygen being divalent ($-O-$) has only one of its affinities saturated by hydrogen, and the other remains free, so that the whole hydroxyl group ($H-O-$) acts like an atom with one free affinity, and is incapable of independent existence.

Hydroxyl.—This radical, hydroxyl (HO), is one of the most important in chemistry, and its presence in organic substances influences their physiological action to an enormous extent. If the other atom of hydrogen were removed from hydroxyl, we should have, instead of a radical (OH), the simple atom of oxygen.

Amidogen, etc.—In the same way, other compounds, such as ammonia, may have one or more of their atoms removed. When one atom of hydrogen is removed from ammonium NH_4 , it leaves the remaining group ($-N=H_3$) with one free affinity, and the monovalent radical amidogen NH_2 is formed. If two atoms of hydrogen are removed, they leave the divalent group imidogen ($=N-H$) NH' , and, if three are removed, they leave the trivalent atom of nitrogen N''' . As, according to the theory now usually accepted, no atom, with the exception of that of mercury (perhaps there may be others), is capable of independent existence, it follows that if one atom of carbon is free, it at once tends to unite either with another atom to form a carbon molecule, or else with other elements to form a carbon compound.

RECENT VIEWS OF CHEMICAL ACTION.

The Nature of "Affinity."—The fact that the hypothesis usually held at present regarding the chemical affinities of atoms and molecules is not of universal application, but finds an exception in the case of mercury, and perhaps of one or two other elements, appears to indicate that something more is required. Indeed, the idea of affinities which we now hold is simply to be regarded as a very useful working hypothesis which enables us to class together chemical phenomena already known, and even to predict new facts in the same way as the Ptolemaic theory of the movements of the planets in cycles and epicycles enabled men to predict eclipses. But just as that cumbrous theory has now been completely swept away, so it seems probable that our present cumbrous ideas of chemical affinity may also give way to simpler views. Mendeleeff, who with prophetic insight has not only predicted the existence of new elements but described their properties correctly while they were still practically unknown, in a recent lecture has expressed his view that chemical affinities will shortly be brought under Newton's third law of motion. According to this idea chemical compounds and solar systems are built upon

⁵ Armstrong, *Journal of the Society of Chemical Industry*, July 30th, 1887.

the same plan; and methane, consisting of a carbon and four hydrogens, might be compared to Jupiter and his four moons.

SUBSTITUTION.

Carbon Compounds.—By treatment of the carbon compounds belonging either to the fatty or the aromatic series, it is found that one or more atoms in the molecule may be replaced by others.

Thus, one atom of hydrogen in methane, $\text{H} > \text{C} < \text{H}$, may be removed and replaced by chlorine, iodine, or bromine, forming chloro-methane, $\text{H} > \text{C} < \text{Cl}$, bromo-methane, $\text{H} > \text{C} < \text{Br}$, or iodo-methane, $\text{H} > \text{C} < \text{I}$. These in their turn may be replaced by hydroxyl, forming methylic alcohol, $\text{H} > \text{C} < \text{O}-\text{H}$. In all these

changes the group $\text{H} > \text{C} < \text{H}$, has remained intact, and has played the same part in the compound that an atom of potassium or sodium would have done in similar circumstances. This group, CH_3 , which has thus acted as the basis or root of the compound has therefore been called a radical. Such radicals may belong either to the fatty series, CH_3 , like methyl, $\text{H} > \text{C} < \text{H}$, or to the aromatic

series, like phenyl, $\text{H}-\text{C} < \begin{array}{c} \text{H} \text{ H} \\ | \quad | \\ \text{C}-\text{C} \\ | \quad | \\ \text{H} \text{ H} \end{array} > \text{C}-$. They may unite either

with other radicals of the same series, as methyl with methyl to

form ethane, $\text{H}-\text{C} < \begin{array}{c} \text{H} \text{ H} \\ | \quad | \\ \text{C}-\text{C} \\ | \quad | \\ \text{H} \text{ H} \end{array} < \text{H}$, phenyl with phenyl to form diphenyl,

$\text{H}-\text{C} < \begin{array}{c} \text{H} \text{ H} \\ | \quad | \\ \text{C}-\text{C} \\ | \quad | \\ \text{H} \text{ H} \end{array} < \text{C} < \begin{array}{c} \text{H} \text{ H} \\ | \quad | \\ \text{C}-\text{C} \\ | \quad | \\ \text{H} \text{ H} \end{array} > \text{C}-\text{H}$ ($\text{C}_{12}\text{H}_{10}$), or with radicals be-

longing to another series, as methyl with phenyl to form methyl-

benzene, $\text{H}-\text{C} < \begin{array}{c} \text{H} \text{ H} \\ | \quad | \\ \text{C}-\text{C} \\ | \quad | \\ \text{H} \text{ H} \end{array} < \text{C} < \begin{array}{c} \text{H} \text{ H} \\ | \quad | \\ \text{C}-\text{C} \\ | \quad | \\ \text{H} \text{ H} \end{array} > \text{C}-\text{H}$, or, as it is usually called, toluene.

But instead of two such radicals becoming directly united, the bond of union may consist either of a carbon atom alone ($> \text{C} <$), or of

a carbon atom with one or two atoms of hydrogen ($-\text{C}-$) attached

to it, or the uniting link may consist of oxygen ($-\text{O}-$), of sulphur ($-\text{S}-$), nitrogen ($-\text{N}-$), phosphorus, arsenic, antimony, boron, silicon, and, indeed, probably of any element the atom of which has at least two affinities, so that it is able to connect two radicals.

Nitrogen Compounds.—Nitrogen seems, like carbon, to have the power of uniting with itself by either one or two bonds, so that it is able to form different compounds according to the mode in which its atoms are connected. Thus, when the two atoms of nitrogen are connected singly ($> \text{N}-\text{N} <$), and the remaining two affinities of one are saturated with hydrogen and those of the other with hydrogen and an organic radical $\text{H} > \text{N} < \text{CH}_3$,

Methyl hydrazine.

or with two organic radicals, we obtain a class of compounds

known as hydrazines; but when the atoms are linked to one another by two affinities they form azo and di-azo compounds.

Nitriles, etc.—Nitrogen is peculiar in another respect, namely, that sometimes it appears to have only three affinities, while at another it has five. When it becomes connected with carbon in its triatomic condition it saturates three affinities of the carbon, leaving one free ($-\text{C} \equiv \text{N}$), and compounds of this description are called nitriles. On the other hand, when nitrogen is pentavalent and becomes united with carbon, the four affinities of the latter element saturate four of nitrogen, leaving one affinity of nitrogen free ($-\text{N} \equiv \text{C}$). In both cases the free affinity may unite with hydrogen or with a radical. It is thus evident that we may have two substances having exactly the same chemical composition (RCN and RNC), but with this difference that R, which may stand for an organic radical, is connected in the one case with an atom of nitrogen ($\text{R}-\text{N} \equiv \text{C}$), and in the other with an atom of carbon ($\text{R}-\text{C} \equiv \text{N}$). It might be considered that this difference is of no importance and that the two bodies would be practically identical, but this is by no means the case. On the contrary, their physiological action is very different. Those bodies (nitriles) in which the nitrogen is trivalent and the radical is united to carbon are very poisonous, whereas those in which it is united to nitrogen are comparatively inactive. This difference in the arrangement of the atoms is usually known as chemical constitution as distinguished from chemical composition, by which we mean the number and kind of atoms of which the substance is composed.

CHEMICAL COMPOSITION, CHEMICAL CONSTITUTION, AND CHEMICAL STRUCTURE.

I had intended at first to call the subject of my lectures "The Relation between Chemical Constitution and Physiological Action," but I found that this title would not include the whole subject which I wished to discuss. For I wished to include the alteration which may be brought about in the physiological action of a substance by the simple multiplication of its parts without altering their arrangement, as, for example, the difference between the action of one of the lower alcohols, ethylic alcohol, and one of the higher, amylic alcohol. These two alcohols are built on exactly the same type, and the relation of the parts is similar, but the number of parts is greater in amylic than ethylic. I therefore resolved to change the title of the lectures to the "Relation between Chemical Structure and Physiological Action," as the word "Structure" I think may be fairly made to include the number of component atoms in the substances as well as their relation to one another.

Chemical Constitution.—To make the subject of chemical constitution clearer, I may perhaps be allowed to make use of a very homely simile. I have here a pocket-knife with a number of blades. At present these blades are all shut, and the knife may be given to a child to play with or carried in the pocket without the least danger. If I open one of the blades, however, the case is very different. The composition of the knife is exactly the same as before, but by altering the relation of the parts to one another I have converted a harmless plaything into a dangerous weapon. In the case that I have just referred to—of the compound of nitrogen and carbon—an alteration in the relation of its parts has a similar effect to the opening of the knife, and converts the comparatively harmless nitrile into the deadly isonitrile or carbylamine.⁶ Again, while I keep the same handle to my knife, I may alter its uses by opening out a boot-hook, a gimlet, or a file, and in a similar way we may alter the functions of an organic radical, which we may compare to the haft of the knife, by attaching to it an atom of amidogen, chlorine, or hydroxyl. If I wish to cut through a piece of cord, or something else out of my reach, with my pocket-knife I may effect my purpose by tying my knife to a piece of stick, and, if that should not be long enough, attaching another and yet another piece until I have got my handle sufficiently long for my purpose. Such a process as this may be compared to adding on carbon atom to carbon atom in a lengthening chain in the higher paraffins, but just as my shank would by and by become too heavy and cumbersome to allow me to handle it and thus become useless for my purpose, so we find that the higher paraffins, although from their high molecular weight they ought to be powerful anaesthetics,

⁶ In using this illustration I have followed the general statements regarding nitriles and carbylamines. Experiments on the action of these substances have given conflicting results, and the whole subject requires investigation. I began some experiments on the subject about thirteen years ago, but they were interrupted by the pulling down of my laboratory in order to rebuild the medical school at St. Bartholomew's, and I have not been able to resume them.

are too sparingly absorbed to have any physiological action at all, and instead of producing either intoxication or anæsthesia like marsh gas, are simply used under the name of vaseline to protect the skin.

Formulae.—In discussing chemical questions we are accustomed to use two sorts of formulae—the graphic, in which we represent diagrammatically the relative position of the atoms in a compound; and the ordinary, in which we write down its nature in symbols. In trying to convey to you an idea of chemical constitution I have used one illustration which might be compared to a graphic formula, and, in order to make the matter clearer, I may, perhaps be allowed to use another which is more analogous to an ordinary formula. In writing down chemical formulae we use certain letters to denote the elements, generally the initial ones of their Latin names, and the number and position of those convey to a chemist in a certain degree an idea of the composition of the substance represented by them. With a comparatively small number of letters of the alphabet we are able to form a great number of words, and to represent a great number of ideas, and with a small number of elements we can form many compounds. Slight alterations in the composition of words, the introduction or abstraction of a single letter, will often completely change their meaning, and slight alterations in chemical substances will change their properties. Thus one often sees in railway carriages the announcement to passengers, “WAIT UNTIL THE TRAIN STOPS,” modified by someone scraping out the T, so that it reads, “WAIT UNTIL THE RAIN STOPS;” and then someone else scrapes the lower half of the letter R, after which it reads “WAIT UNTIL THE PAIN STOPS.” I frequently see an example which is indeed, I think, a common one both in schools and colleges. On a certain door the words CLASS ROOM were originally painted, but certain ingenious students have amused themselves by obliterating first the c and then the l, and turning the original word first into LASS ROOM, then into ASS ROOM. Just as the successive removal of these two letters completely altered the meaning of the original word, so the removal of the letters symbolic of two elements from a chemical formula will completely alter the nature of the substance represented by it.

In both the instances which I have just given the alterations have been effected in the composition of the words by removal of the constituent letters, but the relation of the remaining ones to one another has not been altered. We are frequently able to make additions to a word which somewhat modify its sense without, however, altering its meaning in any essential particular. The root or radical remains the same, and the omissions only modify it. Thus we may say class-room, dining-room, drawing-room, bed-room, or we may say room, roomy, roomful; but in all these words we have the idea of a room as the essential meaning. By altering the arrangement of the letters, however, we produce a completely different effect, and instead of “room,” we get “moor.” By this slight alteration we convert a word suggestive of comfort, enclosure, warmth, and society into one suggesting expanse, exposure, cold, and desolation, a change which is paralleled by the example I have already mentioned of R C N and R N C. The word “moor” may also be modified in much the same way as the word “room.” Such modifications as I have spoken of usually affect the significance but slightly, yet occasionally a slight addition may alter the sense of the word as completely as a difference in its structure. Thus Moorish, instead of conveying a sense of bleakness and coldness, brings before the mind ideas of oriental grandeur, sunshine, and activity. The reason here of course is that the root “moor” in the two words moorland and Moorish, although alike in appearance and sound, is really quite different in the two cases. But in studying the physiological action of various chemical substances, we find that while usually certain alterations or additions only modify the action of the radical to a slight extent, yet now and again we meet with quite unexpected cases where slight modifications produce an altogether unexpected effect. Thus sodium acetate has a very slight physiological action indeed, but when one atom of hydrogen in the acetic acid is replaced by bromine, the result is mono-bromo-acetate of soda, which has a most remarkable action upon the muscles of the frog, rendering them so rigid that the animal becomes as a piece of wood. Another curious example is afforded by phenol and aniline, both of which are markedly poisonous, but ortho-amido phenol is innocuous.

Another example possesses a special interest from the possible bearing it may have on the causation of uræmic poisoning. This will be discussed later on, but the substance in question is

oxaethylin, which has an action like atropine on the brain, pupil, and vagus, stimulating the brain, dilating the pupil, and paralyzing the inhibitory powers of the vagus. But if one atom of hydrogen in it be replaced by chlorine, the resulting body, chloroxal ethylin, while still retaining its powers over the vagus, no longer dilates the pupil and acts as a soporific to the brain like morphine.

METHODS OF TREATING THE SUBJECT OF THE LECTURES.

The relation between chemical structure and physiological action is a subject which might be treated either from a chemical or from a physiological point of view. Each plan would possess certain advantages and certain disadvantages. A complete treatment of the subject would be easier from the chemical side, and such a method might also be more convenient for reference, but the main object of these lectures is to deal with the subject in relation to the prevention, control, and cure of disease, and the physiological method is, I think, better adapted for this purpose.

I therefore propose to consider the causes of disease and the functions of the organism, and to discuss the manner in which these are affected by alteration in the chemical structure of the remedies we employ.

NATURE OF DISEASES—MICROBES AND POISONS.

We may regard disease as such an alteration in the body as either causes a want of ease in the patient at the time, or will cause it if its action is not arrested. As I have already said in speaking of the progress of pathology, disease was formerly looked upon as something apart from the patient, but now we regard the patient and the disease as living in the same way and influenced by similar conditions.

Ptomaines, etc.—For a good while the microbes were looked upon as directly causing disease by affecting the tissues of the patient, but now, since chemical investigation has been applied to the processes of disease and the products of putrefaction and fermentation, we are beginning to look upon many of the symptoms which occur in consequence of the action of microbes as being due not to their direct action upon the tissues but to their indirect action in forming poisons; to regard, in fact, the symptoms they produce as bearing a similar relation to the microbes as the symptoms of intoxication do to the yeast plant. This plant, when introduced into the body, does not produce intoxication. It is the alcoholic products of its action upon saccharine fluids which make a man drunk.

Panum's Researches.—In 1856 Panum demonstrated that the poison which occurs in putrefying meat is a chemical substance and not a living organism, although it may be formed by organisms, for he was able to boil it for eleven hours, and then to dry it completely at boiling heat without destroying its poisonous properties. He showed that the symptoms produced by the putrid poison were different from those produced by various ammoniacal salts—leucine and tyrosine—which he administered to the animals for the purpose of comparison. He was uncertain whether the poison acted like an alkaloid, such as strychnine, directly upon the nervous system, or whether it acted upon the blood, causing decomposition in it and leading to the production of substances which poison the nerve centres. At all events he felt sure that it did not act like an ordinary ferment, such as pepsin or ptyalin, for it was not destroyed like them by prolonged boiling.

Selmi's Researches.—In 1870, Selmi brought prominently forward the chemical nature of the poisonous products which resulted from the decomposition of albuminous matters by microbes. He concluded that their actions might resemble those of the vegetable alkaloids, but he did not separate or identify any individual substance, although he gave the whole class the name of ptomaines.

Cholera and Muscarin Poisoning.—In 1873 I read a paper before the British Association at Bradford, in which I pointed out the striking resemblance which exists between the symptoms of cholera and those of poisoning by muscarin; and I suggested atropine as a possible remedy in cases of cholera, on account of its remarkable power to antagonise muscarin. I came to no conclusion regarding the exact nature of the cholera poison, nor did I distinguish between microbes or actual alkaloids which might be present in it.

Bacteriology and Chemistry.—Since that time the researches of Koch and the methods he has introduced have given an enormous

impetus to the study of bacteriology; and the isolation by Nencke of a definite ptomaine, and the discovery of many more by Brieger, has put the chemistry of putrefaction on an entirely new basis.

The Relation of Microbes to Disease.—In discussing the relation of microbes to disease, we may consider, first, the microbes themselves outside the body, and the poisons they may produce; secondly, the microbes themselves, and the poisons they may form in the intestinal canal; and, thirdly, the action of microbes or their products when actually circulating in the blood or present in the tissues. It is, of course, a question not only of great theoretical interest, but one likely to be of great practical importance. Do the microbes break up the albuminous substances or hydrocarbons which they attack, by means of their actual protoplasmic structure, or do they, like the higher animals, secrete organic ferments or enzymes, by means of which the disintegration is actually carried on?

Mode in which Microbes attack Protoplasm.—It is evident that if the decomposition of albumen, starch, or fat, for example, is due to the actual protoplasm of the living microbes, it will at once cease if these microbes be killed, but if it is dependent on a ferment which is secreted by the microbes, it may continue to a certain, though limited, extent after they have been destroyed, just as the pepsin which is secreted by the stomach of a pig may carry on digestion after the pig itself has been killed. This question was investigated by Kühne in 1877. He came to the conclusion that the fermentative action of bacteria was not the same as that of the pancreas, and he did not succeed in isolating any ferment by extracting bacteria with water or glycerine, as he would have done on treating a pancreas.

Microbes and Ferments.—The probability that microbes formed ferments seemed so great, however, that I thought it worth while to take up the question again. The difficulty of such a research, and the time required to make the necessary experiments, completely prevented me from attempting to do it alone, but I have been so fortunate as to secure the co-operation of Dr. Alan Macfadyen, whose skill in experimenting has enabled us to get some positive and interesting results.

The object of the inquiry was to ascertain whether (1) microbes act upon the soil upon which they grow by means of a ferment, and (2) whether such a ferment can be isolated and its action shown apart from the microbes which produce it in the same way that the ferments of the stomach and pancreas can be separated from the cells by which they are originally secreted. The results of the inquiry show that bacteria liquefy gelatine by means of an enzyme which can be isolated, and which will continue to act after the microbes have been destroyed. Like the ferments of the pancreas, this enzyme acts most readily in alkaline solutions. Bacteria seem to have the power of adapting themselves to the soil on which they grow, and of manufacturing a ferment suitable to their needs; for the same bacilli, when grown in starch paste instead of on gelatine or in beef-tea, produced a different ferment, which would convert starch into sugar, but would not act upon gelatine.

After we had been occupied with this research for several months we learned that similar results had been obtained by Bitter, who has found that Koch's cholera bacillus produces in meat peptone a peptonising ferment which is quite distinct from the bacillus itself, and continues active after the bacillus itself is destroyed, and similar results have also been obtained by Sternberg. This ferment resembled pancreatin rather than pepsin by acting more vigorously in alkaline than in acid solutions. We have not seen the original work of Bitter and Sternberg, and know it only from a brief abstract.⁷ The difficulty of such investigation is so great that, however carefully the experiments may have been made, there is always a natural hesitation to accept the results of any observers till they have been confirmed by others. At the same time, I believe that the results are substantially correct; and one point that comes out in the experiments is that the microbes themselves may be destroyed by a temperature which does not destroy the activity of the ferment which they have formed.

Relation of the Ferments formed by Microbes to Poisoning by Meat.—The practical application of these results in regard to the prevention of disease is that they seem to show that meat which has become tainted by the presence of putrefactive microbes may possibly be cooked sufficiently to destroy the microbes themselves, while the ferments they have formed continue to decompose the

meat, and give rise to poisonous substances. We can thus see how a cold beefsteak pie, or other cold meat, may become poisonous and produce serious symptoms, although the same food may have been eaten with impunity immediately after being cooked; for during the process of slowly cooling poisons may have been formed in the meat, although there may have been none in it immediately after it had been removed from the oven, and any microbes present were likely to have been killed by the cooking. The frequency with which meat, very slightly tainted, must be eaten in summer, and the common rule of not eating game at all until it is somewhat "high," as it is termed, makes one rather wonder why poisoning by ptomaines formed in such meat and game does not occur more frequently, although I believe that it occurs, in a slight degree, more frequently than people are generally willing to allow.

ABSTRACT OF THREE LECTURES

ON

THE MORBID ANATOMY, PATHOLOGY, AND TREATMENT OF HERNIA.

Delivered at the Royal College of Surgeons of England.

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LECTURE I.

IN the following lectures it is proposed to give the result of an attempt which has been made to ascertain how far the peritoneum and suspensory apparatus of the abdominal viscera are concerned in the pathology of hernia. Afterwards, some questions with regard to the morbid anatomy and pathology of hernial sacs will be discussed.

The last branch of the subject has been most exhaustively studied, as is witnessed by the works of Scarpa, Cooper, Cloquet, Lawrence, and of others too numerous to mention; but the contrary is the case as regards the relation which the peritoneum and suspensory apparatus bear to the morbid anatomy and pathology of hernia. Our information about this is incomplete, and in need of further elucidation. One school of pathologists believes that in hernia the fault is in the abdominal walls, the other that it is in the attaching membranes of the intestines, the abdominal walls playing a secondary part. The questions at issue, therefore, are quite simple, and a moment's consideration shows the importance of a correct solution of them. It may be inferred that surgeons who deal with the hernial sac and the abdominal wall in cases of non-strangulated and strangulated hernia do so because they agree with Mr. John Wood that the fault lies in the abdominal wall, whilst those who refrain do so because they think the prime fault is not in the abdominal wall, but in the peritoneum and mesentery. This uncertainty has hitherto deterred me from operating for the cure of hernia except in special cases, and what follows has been undertaken with the object of doing away with this uncertainty.

The writings of Kingdon, Treves, Birkett, and many others were quoted by the lecturer in support of the proposition that hernia was due to an elongation of the mesentery. The statistics of operations for the cure of hernia were also discussed, with the view of ascertaining whether the results threw any light upon the problem.

Taken altogether, the tables show that the operation for the permanent cure of hernia is upon an unsatisfactory basis. Their results are such that they support either the "mechanical" or the "pathological" schools. Those which are successful merely show that the fault in the abdominal wall is capable of remedy; the unsuccessful, that the remedy is inadequate, or that the fault is elsewhere. Authors were quoted to show that there was great doubt as to whether the small intestines could be extruded from the abdomen, and also to show that the height of the attachment of the mesentery was in need of elucidation. Thus three main questions require to be dealt with, namely, the length of the mesentery, the attachment of the mesentery, and the range of movement which the mesentery permits to the intestines.

⁷ *Ptomaines and Leucomaines.* By Victor C. Vaughan and Frederick G. Novy. Philadelphia Lea Bros. and Co. 1888. P. 96.