

# Introductory Lecture

ON

## UNFIXED TERMS IN PATHOLOGICAL EQUATIONS.

By WILLIAM RUSSELL, M.D., F.R.C.P.E.,

LECTURER ON PATHOLOGY IN THE SCHOOL OF MEDICINE; PATHOLOGIST TO, AND CLINICAL MEDICINE TUTOR IN, THE ROYAL INFIRMARY; PHYSICIAN TO THE NEW TOWN DISPENSARY, EDINBURGH.

GENTLEMEN,—The work which we have specially to do here is to study the changes which occur in the various organs and tissues of the human body in disease. We have further to trace the evolution of these changes, and to discuss their causes and their consequences. This does not, however, include all disease. There are many conditions you will meet with as practitioners of medicine which have a comparatively uninteresting or an altogether unknown morbid anatomy, and which you will not find described in any work on pathology, but which are nevertheless of the utmost importance.

Disease literally means absence of ease or comfort, so its range is wide; and yet it includes much which is not associated with any consciousness of discomfort. It may in its beginnings be regarded as an alteration or modification of function. What is this modification of function, and what do we know about it? We have many facts stored from long observation and experience, but our knowledge of the intimate changes implied in modified function is practically *nil*. Take as an illustration the introduction of narcotics into the circulation. One paralyses the thinking centres; another paralyses the motor centres; a third arrests respiration; a fourth paralyses the heart; and a fifth in proportional doses may do all four. These effects are attributed to the drugs, and we are accustomed to regard them from this standpoint only; but we may ask the question: Is there not an animal or human term in the equation? Must there not be some law of affinity? If the narcotic directs its influence towards, and spends its power on, a certain group of cells, say in the medulla, must not they on their part present certain enticements (if we may so put it) to it to do so? Must there not be both the aggression by the narcotic and the drawing by the cell? Does the cell wantonly revel to its own destruction, or is it simply a victim falling in the fatal embrace of the narcotic? These are interesting questions, and they have not hitherto been much studied. And then, if there is this law of affinity, what is it dependent upon? Is it some delicately adjusted arrangement of visible particles, or some cunningly devised and elaborate chemical formula? We can only assume that one of these it must be; and if we concede this, we are met with the stupendous fact of, let us say, the variety of the molecular arrangements or the infinity of chemical formulæ represented in the great multitude of cells in the nerve centres alone. Does every little speciality of function imply a like speciality of structure? Have the cells whereby we feel pain a different structure from those which store up pathological facts, and, indeed, knowledge of all kinds?—and if they have, is it a chemical difference, or only a difference in the arrangement of granules? In the one cell do the granules move when in action in the form of a spiral, and in others do they collect themselves and diffuse themselves as the pigment granules do in the cells of the dermal covering of the frog? Function, indeed, in so far as we may judge of a whole by the revelation of a part, implies modification of structure; the cells in the peptic glands swell and burst when in functional activity, and so with the cells of other glandular organs. In many instances the deviation of structure is as palpable as the presence of function, but this is by no means universal. In many conditions the changes in the cells have still eluded us, if, indeed, as much attention has been paid to the subject as it deserves.

There is, next, what we may call instability of function. You all know how easy it is to put certain persons into a rage. The manifestation of temper is but the result of an unstable condition of cerebral nerve cells and their undue explosiveness. A similar explosiveness in motor nerve cells produces a clinical, if not yet a pathological, entity in the

form of epilepsy. This instability shows itself in other persons in the bronchial muscles. Atmospheric conditions which pass unnoted by the average respiratory organs set those of the asthmatic into rigid spasm, and interfere grievously with the respiratory function, and there is again a clinical entity presented to you, while it remains a matter of speculation as to what really is the modification of structure which is expressed by this instability, and yet there must be some modification. Most probably it is a chemical rather than an anatomical one, the chemical equilibrium or health equation being altered by influences inappreciable to the more stable and ordinary equation. The intricacy of the problem you can readily appreciate; and how hopeless is at present the outlook that pathological chemistry should ever solve it; and yet on its solution depends any advance that may be made in our knowledge of what we call constitution on the one hand and temperament on the other.

The whole question of constitution is of the greatest practical and scientific interest; for it determines in a great measure the pathological history of individuals, families, and races. You will frequently meet in your practical work individuals who present the most striking susceptibility to become attacked by the infective diseases. I have known even medical men who seemed to catch, or, rather, who were caught by, everything; whilst others weather epidemic after epidemic, seeming to bear as charmed an immunity from infection as some great generals appear to have from bullets. But the question of individual constitution is manifested in other ways. Take, for instance, the introduction of extraneous matters into the digestive tract and their absorption from it. One individual takes twenty or thirty grains of iodide of potassium several times daily without the development of any pathological manifestation, while another takes two grains and there follows a morbid increase of function of the nasal mucous membrane. The same is true of arsenic as regards its effect on the intestinal mucous membrane and the conjunctivæ. But the deleterious substances may be produced within the body. In the process of digestion there are various poisonous substances produced and absorbed which are normally transformed by the liver into material fit for the nourishment of the tissues, or are arrested by it and excreted in the bile. If, however, from any cause the liver is unable to cope with all the work thrown upon it, some of the poisonous matters pass into the circulation, while others are not removed from it. The variety of result, as seen in the individual, is of considerable interest. In one there is an attack of gout with acute inflammation of a special joint; in another there is extreme mental depression and physical languor; in a third there is an evanescent urticaria; and in a fourth there may be an intractable eczema or psoriasis. But there is perhaps a still stranger side to this. In some individuals a very small quantity of the juice of the poppy administered by the stomach will bring on sickness and vomiting, while in another a like quantity will produce the most delightful sense of mental exhilaration. It may be said this is mainly a stomach question. I doubt it, for the alkaloids of the poppy introduced hypodermically may act similarly, so that I incline to regard it as a question of constitution in groups of nerve cells; in the one case those of the medulla, in the other those of the higher cerebral regions.

Analogous phenomena are presented by families. Some are not only notoriously liable to take, say, infective diseases, but to develop them in a very malignant form. Every now and again you will find a family in whom scarlet fever is almost certain to be fatal. This is not always a question, as it is usually regarded, of virulence on the part of the specific poison, but rather one of family constitution—family chemical structure in reality. You see how very important and far-reaching is this personal term in pathological problems. It might be followed further into the questions of phthisis, into the problems surrounding premature degeneration of arteries, and into all kinds of minor ailments, such as catarrhs of various systems. It can also be observed in races. Yellow fever is very fatal to the white man, but the negro is proof against its fatal influence. On the other hand, some diseases prevalent amongst long civilised peoples, and by no means to be classed amongst the most deadly, assume an extreme virulence when introduced amongst less civilised peoples. This is true of measles, for example. I want you specially to bear in mind this personal factor, for there is a tendency to lose sight of it in the study of pathology, and

more especially in the study of morbid anatomy, which is but a part of pathology. Unfortunately we are not at present in a position to speak more definitely on the subject; the differences in structure to which the phenomena we have referred to undoubtedly point have only been slightly elucidated by investigations into vital chemistry, and we are not sanguine that they are likely soon to be fully revealed to us.

Let us now look at the individual from the morbid anatomy standpoint, and see if individual tissues present anything analogous to this idiosyncrasy in function; if there is any tendency on the part of certain structures to depart from the normal structure, as we have seen they could depart from the normal function under the influence of obscure, and indeed unknown, causes. The most striking illustrations of this are to be found in the nervous system—the brain and cord, especially the latter, so far at least as our present knowledge goes. In the cord there are various well-defined strands of nerve fibres and well-defined groups of nerve cells. What does morbid anatomy reveal? It shows that changes occur in specialised strands, and that they may be to a considerable extent confined to these. Passing to the groups of nerve cells, we find a degeneration or atrophy of the large cells in the anterior cornua in a well-known disease in children—infantile paralysis. In adults there is a similar degeneration of these cells, which begins insidiously, but advances from cell to cell with almost unerring and fatal certainty—I refer to progressive muscular atrophy. In other cases, if we examine the white substance of brain and cord, we find scattered throughout it islets formed by an abnormal growth of connective tissue, and which materially interfere with the functional vigour of the parts in which they occur. In all these cases we have no clue to the special conditions of the tissues in the various regions which lead to those morbid anatomical changes. In some of them one would almost think they were the result of what our friends on the other side of the Atlantic would call “pure cussedness,” for why the great trophic cells of the anterior cornua should in certain persons begin prematurely to shrivel and decay is a riddle to which pathology cannot even suggest a solution, and one of its most mysterious aspects is that the condition spreads from large cell to large cell with as much certainty as if there were a reproductive infective element at work.

Let us next look at some unfixed terms in the phenomena of the infective diseases. In these there is a poison introduced into the body which has the power of self-multiplication. We have already referred to this when speaking of the part constitution plays in the production of disease. But *all* the effects of morbid influences upon the body require to be recognised and used for the elucidation of pathological problems. Let us look at typhoid fever in the first place. From a morbid anatomy standpoint it is characterised by ulceration of definite structures in the small intestine, and by certain secondary changes in other abdominal organs, as the glands and spleen. We will not stay to consider the question why Peyer's glands should be the structures specially affected by the poison peculiar to typhoid. Nor need we say more about the nature of the specific poison than repeat that it is capable of self-multiplication, and that poisons which behave thus are vital poisons, and that modern research points to micro-organisms as the essential factor in their production. Now, there are diseases produced by micro-organisms—such as ring-worm, for example—in which the local lesion is the alpha and omega of the condition. In typhoid fever there is, however, another element and another term in the equation. It may kill irrespective of the extent of its anatomical lesion, and it does so probably, I might say certainly, by the generation and the reception into the circulation of a poison which produces a true toxæmia. It is not the micro-organism but a product of it, and it kills in the same way as a dose of curara would. The question arises, May this throw any light or suggest any possibilities as to the phenomena of some other diseases—such as scarlet fever, for instance? In this fever there are terms the values of which are not yet fixed. It is characterised by a rose-red rash on the skin and mucous membrane of the palate and by a high temperature. It is, indeed, quite the type of affection in which it would be expected that a micro-organism ought to be found. From the presence of a rash, and the further fact that after the subsidence of the rash the cuticle desquamates, coupled with the popular and almost universal belief that the desquamating cuticle

reproduces the disease when brought into contact with persons who are not proof against it, have led to special efforts to discover in the blood and cuticle the organism which, it is presumed, is the cause of the morbid phenomena.

The observations hitherto made are not conclusive, and without seeking for a moment to prejudice our future position when further investigations have been made, there is a possible view which has in the main been lost sight of. It is this: that the specific micro-organism may be confined to some special locality—perhaps the throat, but perhaps some hitherto undiscovered spot—which forms the spawning ground of the organism, and that from there poisonous matters called ptomaines are absorbed into the system. These ptomaines are the poisons which are produced by the living and dying of micro-organisms, and there is abundant proof that they can kill even when separated entirely from the organism producing them. This is, I should say, almost certainly the way in which diphtheria kills—that is, by the virulence of the ptomaines produced in the throat and thence absorbed into the circulation. But in scarlet fever there is a rash and desquamation, while in diphtheria there is neither, and the question naturally arises, Are these sufficient to indicate the probability that the poison which directly produces the rash by its irritation is a vital poison, as distinguished from a chemical one? Analogy answers in the negative. In certain individuals shell fish or some other special article of diet, or, indeed, a disordered stomach digestion, from whatever cause, produces a skin eruption called urticaria; in other persons what is called a gouty constitution, and which implies the presence of certain substances in the blood, produces skin irritations manifesting themselves as a psoriasis or an eczema. In none of these cases can it be for a moment assumed that the local morbid change is due to the presence of a micro-organism in the blood: the poison is chemical, not vital. There is still further proof of this in the fact that various substances which we use as drugs very readily produce skin eruptions in some persons. I have, for instance, seen a rash produced by the internal administration of belladonna very closely resemble that of scarlet fever. You see, then, that the mere presence of the rash does not necessarily imply that the specific organism is present where it occurs. Chemical poisons, such as the ptomaines, are quite sufficient to produce it. The rash is of course only an inflammatory redness set up by an irritant reaching the skin, and the desquamation which follows depends, in the main, on its intensity. It cannot be assumed that even the desquamating cuticle contains the specific organism. Many proofs might be advanced in support of this, but I shall only mention the latest fact I have observed—namely, a typical case of typhoid fever where there was profuse desquamation during convalescence; not however so profuse as occurred in the same patient a year before, after a very sharp attack of scarlet fever.

I have thus, gentlemen, sought to bring under your notice some factors in disease which, while their exact value is unfixed, are evidently of the utmost importance. I all the more readily do it now, as there is so much of detail in our subject that there is little time for the consideration, much less for the contemplation, of what might be regarded as some of its great underlying principles.

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### THE FACTORS THAT DETERMINE THE HYPERTROPHY OF THE SKULL IN MOL- LITIES OSSIUM, OSTEITIS DEFORMANS, RICKETS, AND HEREDITARY SYPHILIS.

By W. ARBUTHNOT LANE, M.S., F.R.C.S.,

SENIOR DEMONSTRATOR OF ANATOMY, GUYS HOSPITAL; ASSISTANT  
SURGEON TO THE HOSPITAL FOR SICK CHILDREN.

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ONE cannot but be much struck by the habit which exists amongst us of enumerating the pathological conditions which together represent any given disease, without any attempt being made to arrive at the physical causes which determine the development of these several appearances. Instead of carefully defining the laws which govern their production, we rest satisfied by regarding these changes as being the direct result or expression of each disease, the