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ADDRESS.

THE PROGRESS AND RESULTS OF PATHOLOGIC WORK.

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To trace the history of pathology during the last sixty years would be to follow the science practically from its commencement and to go back to a state of matters which it is almost impossible for us now to realize. Even going back twenty-five years, the changes which have taken place are enormous. At that time the lectures on pathology consisted practically entirely of morbid anatomy—long descriptions, for the most part very accurate and not materially different at the present day, were given of the naked-eye appearances of the diseased parts, but as to how or why these changes were brought about hardly any reference was made. Indeed, very little was known, and when an explanation was attempted it was generally of a mechanical or physical character. At the present time, while of course the changes which take place in disease must be known, the study of pathology is especially directed to the discovery of the mode in which these changes occur and the reasons why they appear. Today it is the etiologic side of pathology which occupies our attention, and deservedly so, for, so far as practical results in the treatment of disease are concerned, the knowledge of the changes produced is of comparatively minor importance as compared with that of the reason why they are set up and how they take place.

The most striking and important advance has been the growth of the great science of bacteriology. Twenty-five years ago bacteriology as a science was non-existent. So far as I remember, bacteria were not even alluded to in our course of pathology, and it was only from Lord Lister that we heard the real facts so far as they were known, or gained any idea of the importance of their study; but even at that time, although his methods of treatment were already yielding brilliant results and saving many lives, and although he had deduced from clinical facts many points in the life-history of bacteria and their relations to the living body, which were only confirmed by experiment subsequently, still the number of actual proved facts was extremely few.

It is difficult for those who have only taken up the subject of bacteriology comparatively recently to realize the absolute blank which it presented even twenty years ago. When I became house surgeon to Lord Lister in 1876, objections of all kinds were urged against the theory on which Listerism was based, some denying the existence of bacteria at all, others main-

taining the theory of spontaneous generation; some asserting that organisms were always present in the healthy tissues, others denying that they had anything to do with disease. These objections led me to take up bacteriology, for it seemed to me of great importance to ascertain whether or not, as the result of antiseptic treatment, organisms were absent from the discharges from the wounds. Although at the present time such an investigation would be one of the simplest, yet when I came to carry it out I was met with the greatest difficulties. Practically nothing of the kind had been done before, and all the means of investigation had to be devised. Methods of staining bacteria had not been introduced, we had no oil immersion lenses, and I very soon found that by looking at discharges from wounds containing leucocytes, granular matter and debris with dry or water immersion lenses, and without substage condensers, no satisfactory result could be arrived at. Hence I came to the conclusion that attempts must be made to see whether organisms grew in suitable fluids inoculated from the discharges. Here again everything had to be devised. A suitable pabulum, methods of sterilization, of inoculation and of incubation had to be worked out. A large amount of time was spent in getting over the preliminary difficulties, and after a satisfactory method had been found, much labor had to be devoted to preliminary questions, such as spontaneous generation, morphologic characters of bacteria, their presence or absence in the living body, conditions of growth, and so on.

A great advance which followed soon afterward was the remarkable research by Lord Lister on the bacterium lactis, in which he devised a method of separating bacteria by fractional cultivation, which resulted in the separation of the bacterium which causes lactic fermentation from other organisms. By this research, apart from the method, a great step was gained in the proof of the specificity of a particular bacterium, both as regards morphologic characters and chemic action.

Then came Koch's work on infective diseases of wounds, and the publication of his methods of staining and examining bacteria and of cultivating them on solid media, and this work is at the foundation of all modern bacteriologic research. From this period the investigations have branched off in two directions: 1, almost all the infective diseases have been investigated for parasitic organisms, and in a large number the causal agents have been identified; 2, researches have been carried on tracing out the life history and functional activity of bacteria, and in ascertaining what occurs in the body when organisms or their products are introduced.

From the latter point of view we come to another great landmark in the study of bacteriology, namely, Metchnikoff's work on phagocytosis, a theory which has proved a most suggestive working hypothesis, leading to many of the researches which have given bacteriology its present position.

Many problems remain unsolved. In tuberculosis, why is it that in one part of the body we have a slow growing lupus disease, and in another part, perhaps of the same body, a rapidly developing tuberculosis? None of the explanations usually given, such as differences in the structure or resisting power of the tissues affected or of the individual, differences in the virulence or activity of the organism, etc., seem to furnish sufficient explanation. And the same problem is apparently presented with regard to the bacilli of diphtheria, in that we may have in one case a true diphtheria, in another a membranous rhinitis, while in a third, although the bacilli are present in the throat, the individual may be apparently healthy.

Another very remarkable problem is presented by the results which follow free incisions into tuberculous tissue. An incision is made into the abdominal cavity, masses of tuberculous tissue and tubercle are found scattered over the peritoneum, nothing whatever is done, the wound is stitched up, and yet in many cases the patient, who up to that time has been going steadily down hill, begins to pick up, and the disease may come entirely to a standstill. This phenomenon is not limited to peritoneal tuberculosis. When I was a student, the tuberculous nature of what are now recognized as tuberculous diseases of the bones and joints was then only suspected, and was not generally accepted by the medical profession. At that time Lord Lister, under the impression that these diseases were of a simple inflammatory nature, and having observed the improvement which often followed free incisions into chronically inflamed tissues, began as an ordinary line of practice to make free incisions through the thickened synovial membrane of tuberculous joints with the view of relieving tension, which he looked on as the chief cause of the continuance of the trouble. Nothing else was done, the joint was not even washed out, nothing was taken away, and yet in a considerable number of cases so treated improvement began from the time that the incisions were made; the patients lost their pain, the wounds gradually healed up and the disease subsided. Even in cases in which the results were not so satisfactory it could as a rule be noted that, although the swelling continued in other parts of the joint, and although the disease began again after a few weeks as vigorously as before, yet for a time at least the thickening disappeared in the neighborhood of the scars, showing that there at any rate temporary benefit had occurred. What possible explanation can we give of such a result? The older surgeons used to speak of "setting up a healthy action in the part," and were quite satisfied with that statement. Such a view is too vague for us nowadays, but may there not be here a possible working hypothesis which if followed out might throw light on this matter? May not the occurrence of healing processes at one part influence in some way or other morbid processes in the vicinity?

Again, what is the meaning of a chronic abscess? How is it that the tubercle bacilli at one time produce a quantity of tuberculous tissue, at another a cheesy mass and at another a chronic abscess?

In connection with the pyogenic organisms also we have many problems. How is it, for example, that after an abscess is opened antiseptically suppuration at once ceases? If instead of opening the abscess antiseptically a poultice be applied, suppuration goes on and may be very profuse. But if it be opened at a time when there is free fluctuation and when it is

beginning to point, and if the necessary antiseptic precautions be taken and proper drainage provided, no more pus forms, and yet when the abscess is opened it is found to contain living pyogenic organisms. We can easily understand that the subsidence of the fever and general disturbance is due to diminished absorption of toxic products. But why do not these living pyogenic organisms keep up the suppuration? and why is it that after two or three days one may fail to obtain any cultivations from the serum which escapes from the wound? If the inflamed part be opened up antiseptically, however, at an early period, just when pus is beginning to form, there is not always the same complete absence of suppuration, although it seldom goes on to any considerable extent.

Again, an operation wound becomes septic and one naturally opens it up freely and establishes drainage; but here suppuration does not cease at once in the same typical manner as in the case of an abscess which has existed for some days. The old surgeons used to speak of an abscess being "ripe," and they allowed it to remain unopened for some days until it was pointing. They found that if they opened a deep abscess early suppuration went on and was apt to extend. No doubt a variety of causes led to this dictum; they did not provide proper drainage; they introduced other and more vigorous organisms at the time of operation and afterward, etc.; but do not the facts seem to indicate that, as regards the cessation of suppuration, there is some ground for this idea of ripeness. Is it possible that when the abscess has attained a considerable size and the tension of the pus in it is great the sudden release of the pent-up fluid may lead to such a pouring out of serum containing antitoxic substances as to absolutely destroy the organisms present, while, the case being treated antiseptically, no fresh organisms can come in to take their place? And yet I can hardly think that that is the whole explanation.

Although it is in the department of bacteriology that the most striking advance has been made, great progress has also gone on in pathology generally, in a considerable number of cases no doubt stimulated by the results of bacteriologic research, and more especially by Metchnikoff's work. The subject of inflammation has had much attention paid to it, although I can not say that to my mind it has been made any clearer. The tendency now appears to be to regard inflammation as the natural effort at repair after injury. At one time this was the view held by surgeons, and the doctrine was that inflammation was essential to healing, and in the description of healing by first intention it was stated that a red blush occurred around the wound, not so severe, however, as where suppuration takes place, and that without this red blush the edges did not adhere. When antiseptic treatment was introduced it became evident that no inflammatory blush or other sign of inflammation was necessary for healing by first intention; in fact, it was found that wounds healed best when no visible signs of inflammation was present. I have, therefore, always taught that inflammation and healing are two different and, indeed to some extent, antagonistic processes, and that although in every wound the tissues in resenting the injury show the early stage of inflammation, yet if no organisms be admitted the inflammatory phenomena soon pass off, and where there is destruction of tissue a second process, namely, that of repair, begins. I still look on inflammation as the

mechanism which gets rid of noxious agents or neutralizes their effects, and on the healing process as that which repairs defects, whether they are caused by injury and associated with inflammation or not. In fact, inflammation must be followed by repair if recovery is to take place, but repair need not be preceded by inflammation. The difficulty arises from the close association of the two processes, both of which have to do with the growth of cells, and from the fact that repair follows as soon as the inflammation begins to subside. Hence, under the microscope, except in cases of acute suppurative inflammation, one sees the two processes at work side by side, and it is not a matter of surprise that they should be confounded.

When Cohnheim first published his observations on the emigration of corpuscles, it was thought by many that the leucocyte was everything and did everything, but it was soon evident that other cells of different origin must be taken into consideration. When Metchnikoff's theory of phagocytosis first came out some of those who adopted it assumed that all wandering cells were phagocytes; but here, again, further investigation has shown that cells differ greatly as regards their phagocytic action. I think that a good deal of the confusion of these processes arises from the fact that expressions involving a teleologic argument are becoming very common, more especially with regard to the protective arrangements of the body. On the idea of an acting intelligence on the part of the cells, the two processes would naturally go together; but, looked on as the simple effect of an injury, they should, I believe, be regarded as independent, and the less and the shorter the inflammation the better and quicker the healing process.

A very remarkable thing in connection with these advances, especially in experimental pathology, is the enormous direct practical benefit which has already resulted to the human race; and it is sufficient answer to the antivivisectionists who oppose the use of intelligence and observation and experiment, to point to the saving of human life and the relief of suffering which has taken place in the last few years. Since Pasteur's experiments on spontaneous generation were published remarkable results have been attained in treatment as the result of experimental pathology.

Scientific efforts to arrive at the truth are necessarily slow and must be carried on without any regard to possible ultimate practical results. When the earlier investigators studied the phenomena of electric action they could have had no idea of the revolution which this study of electricity would effect in the history of the world. When Pasteur resolved to test the theory of spontaneous generation, it did not seem likely to lead to any beneficial result; indeed, his friends tried to dissuade him from entering into what was apparently a useless investigation, and yet what numbers of human lives have been saved as the result of that work and what incalculable benefit has accrued. It is greatly the fashion with the opponents of experimental research to demand a single instance in which an experiment has led to the discovery of a means of cure; but in no department of science has a single experiment of itself alone led to the practical result. The final observation which led to the practical result has been built up on numerous and laborious preliminary investigations and observations. And similarly, in regard to the cure or prevention of disease, the

final trials on man have been led up to by numerous preceding observations and experiments. If these deluded people had their way, the result would be that experiments would be limited to man, and everyone to whom a new idea occurred would apply it without any previous investigation—surely an appalling prospect, whether for physician or patient.

The practical results already obtained affect diagnosis, prophylaxis and treatment. The diagnosis of many parasitic diseases has now been rendered certain and easy by searching for the causal organism, and I need only instance such diseases as diphtheria, tuberculosis, malaria, anthrax, gonorrhea, etc. It is not only by the discovery of the parasite that diagnosis is assisted, but also by other effects of the organism, such as the sort of changes set up in the tissue, the reaction to products of the organism, for instance, tuberculin and mallein, etc. If no other practical advance had resulted from bacteriologic work, the possibility of establishing a definite diagnosis in obscure cases is surely a gain of the utmost importance.

The greatest of all the advances, because so wide-reaching, has been in the prophylaxis of the disease, especially in the prevention of septic disease after operations, as brought about by the discoveries of Lord Lister. By these discoveries the occurrence of sepsis in septic wounds are much diminished and numerous lives are saved, not only in this way but also by the fact that the Listerian treatment permits the performance of many life-saving operations which could not otherwise be attempted.

Lastly, I may refer to advances in the cure of disease. In the case of diphtheria there can be no question that the antitoxin is a most potent curative agent and that used in the early stages it is almost certain to cut short the disease. As regards tetanus, the evidence in the case of animals is absolutely convincing, but in patients suffering from the disease the effect is not certain, probably because we have to do with an acute illness, which runs its course before the serum has had time to act. The same may also be the case with the antistreptococcic serum, although I have great doubts of its value as a curative agent. In other instances, such as plague and snakebite, we may apparently look forward to a cure; and researches are being carried on with regard to pneumonia which may lead to valuable results; nor must I forget to mention Pasteur's system of inoculating cattle against anthrax. What are we to say about the new tuberculin? We all know how careful an observer Koch is, and the fact that he looks on it as a valuable remedy is to my mind sufficient to make it necessary to give it a careful and hopeful trial.

But it is not only in the direction of bacteriology that advantage has resulted from pathologic research. Look at the advances in treatment from the use of organic fluids. As the result of observations on man and researches on animals as to the effects of excision of the thyroid gland attempts were made to transplant the healthy thyroid gland into animals and patients in whom it was absent and following these attempts the use of thyroid extract has ultimately come to be a recognized method of treatment. There is, perhaps, nothing more striking in medical treatment than the rapid and remarkable improvement in cases of myxedema from the use of thyroid extract.

I might enumerate many other instances of direct benefit from pathologic research, such as the advances in the treatment of tuberculous diseases of bones and

joints as the result of better knowledge of the nature and distribution of the disease, the treatment of appendicitis and the investigations on peritonitis and diseases of the appendix, the more complete operations for cancer following fuller study of the mode of spread of the disease, and so on.

But while pathologists are thus working out problems which affect the general well-being of mankind and the solution of which can be no personal gain to themselves, is it too much to ask mankind to furnish the means for such research? The English are looked on as a thoroughly practical people, and yet it is a very remarkable thing that England is almost the only country which does not realize the importance of scientific research and the result is that in England, with very few exceptions, men who might otherwise have thrown much light on these matters are compelled to turn their attention to practice in order to make a living. Unless work of this kind is done how can we hope to advance with any rapidity in the treatment and cure of disease? The surgeon or physician must wait till the information of which he is urgently in need has been acquired for him by the pathologist. Such apathy can surely only be the result of ignorance. A rich man affected with an obscure or incurable malady can not understand how it is that he fails to obtain the definite opinion or the relief which he so earnestly desires and for which he is prepared to pay any price. Surely if he understood the meaning and importance of pathologic research and that the practicing physician can only apply and carry out what is taught by the pathologist, he would bestir himself to aid research in order to gather information which might be of much use to him and others.

ORIGINAL ARTICLES.

EXPERIMENTAL BASIS OF THE DIETETIC AND MEDICINAL TREATMENT OF HYPERACIDITY AND GASTRITIS.

Presented to the Section on Materia Medica, Pharmacy and Therapeutics, at the Forty-eighth Annual Meeting of the American Medical Association, held at Philadelphia, Pa., June 1-4, 1897.

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Boas, who first used the finding of fragments of mucosa in the vomited matter and gastric wash water for diagnostic purposes, attributed great importance to this way of finding out the real state of the mucosa. He held that, in certain conditions of suppressed secretion, the differential diagnosis between a possible neurosis and a genuine gastritis with a glandular atrophy was only possible by examination of such pieces of mucosa. Rosenheim, Boas and Julius Friedenwald, *Med. News*, June 22, 1895, emphasize the value of qualitative and quantitative testing of rennet zymogen to differentiate between chronic gastritis with glandular atrophy and carcinoma on the one hand, and nervous dyspepsia and secondary gastritis on the other. However, Ewald and also Einhorn have asserted that absolute deficiency of rennet zymogen is not pathognostic for atrophy, therefore it would indeed seem as if a certain diagnosis could only be made by a small piece of mucosa.

Is there any clue which can be derived from these

pieces regarding the state of the mucosa in the secretory disorders? This I will try to answer in the following. Hayem, to whom we are indebted for the best histologic investigations of the gastric mucosa, emphasizes that the individual elements of the mucosa, gland ducts, superficial epithelium and interstitial tissue can become diseased in a variety of ways; the various portions of the stomach fundus, pylorus and cardia may exhibit different affections; and finally the mucosa may at different parts show different phases of disease. He distinguishes a parenchymatous and an interstitial gastritis. First the parenchymatous:

1. *Gastrite parenchymateuse hyperpeptique chloro-organique*.—Under this he has two subclasses: *a*, *d'emblée*—dyspepsia coming on at once, in the first stage of digestion; *b*, *tardive*—coming on in later stages, in one and one-half to two hours. Under this hyperpeptic parenchymatous gastritis Hayem means, clinically, a hyperpepsia with hyperacidity, and anatomically, degeneration of the principal central or chief cells with proliferation of the parietal border or oxyntic cells.

2. *Gastrite parenchymateuse muqueuse*—"gastritis mucipara," by which he means a mucous degeneration, a process taking place principally in the vestibules to the gland ducts (which are lined with columnar epithelium), and corresponds to the Schleim Katarrh of most German writers. This is associated with hyperpepsia and subacidity.

3. *Gastrite parenchymateuse atrophique*, which signifies anatomically the total atrophy of the glands without interstitial processes, and clinically, anacidity or achylia. The interstitial forms he separates into two classes: those in which the round cell infiltration, and those in which the sclerosis, *i. e.*, connective tissue proliferation, predominates. These processes are described as occurring purely as such, or mixed with forms of parenchymatous gastritis, and as leading to sub- or anacidity. In order to bring my results in critical consideration with those of Einhorn, I have adopted his classification of the anatomic conditions found in these fragments. There is, however, one objection that can be urged against it, and that is the apparent fact that he has based his system on conditions of the gland tubes and interglandular tissues exclusively, and mentions the state of the cells only once in six types described. I will therefore supplement his categories by adding the state and condition of the vestibular or alveolar columnar cells (*Vorraum Zellen*), and the condition and numeric relations of the chief, central or ferment cells (*Hauptzellen*) and the parietal, border or oxyntic cells (*Belegzellen*).

1. Normal. Gland ducts and interglandular tissues exist in normal proportions. Columnar epithelium of the surface and that of vestibule normal, with scarce cells showing at their free ends slight mucoid metamorphosis. The average number of parietal or oxyntic cells in six ducts which were sectioned very nearly down the center was twenty-two to forty.

2. Connective tissue excess. Proliferation of connective tissue around the glands, glands and epithelial cells as in normal condition.

3. Proliferation of glands. Under this class I have in nineteen cases been impressed with the probability that there must be three types of this condition:

Type *a*.—In this subtype there is a proliferation of gland tubules. Under the same field of microscope there will be more than under normal conditions, since they are much closer to each other, but the number