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BONDS OF UNION BETWEEN TROPICAL MEDICNE AND GENERAL MEDICINE

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As a suitable subject for discussion this evening let us consider some of the ways in which tropical medicine and general medicine have influenced each other. It will be profitable to point out some of the instances in which general medicine has profited from the advances made in tropical medicine; likewise we will see wherein advances in general medicine have furnished a direct stimulus to workers in the tropics. We will not attempt to survey the progress of tropical medicine but we will review only those phases which are of direct interest in general medicine.

In my judgment, the most fundamental influence that tropical medicine has exerted in the field of medical sciences is to be found in the discovery of vitamines and the group of diseases sometimes designated as avitaminoses.

You remember when we studied medicine, not so very long ago, beriberi was classed among the specific infectious diseases with the reservation that some unknown toxin might play a more or less decisive role. We now know that neither of those factors plays any part whatever. The clinical and epidemiological evidence seemed at times to offer almost convincing evidence of the infectious nature of this disease.

But the Dutch investigators knew and had known for many years that beriberi was due simply to lack of proper nourishment. This discovery was made by Eijkman in 1890. There is some strange substance in rice, bran, in various grains, and in many other substances which is necessary for normal nutrition; in the absence of this substance polyneuritis develops. There is no flaw in Eijkman's experimental data though his interpretation has subsequently undergone some revision.

A quarter of a century after Eijkman's first publication, the physiologists began an accurate investigation of the requisites of a

balanced diet. The first steps were difficult. It was necessary to give up some old-established comfortable views. Proteins, carbohydrates and fats with a little salt and water had long been regarded as an adequate bread of life. Now it was rather disturbing to have to admit that some utterly unknown substance, even in minute quantity, exerts a powerful influence and is an essential item in our daily diet. Funk used the term vitamine to designate this substance which prevents the development of beriberi. As the interest in this phase of nutrition increased, other vitamines were discovered. Recently one has been described by Evans in California which is concerned not with ordinary nutrition but with the process of reproduction. In the field of medicine investigators naturally sought to explain other diseases on the basis of a dietary deficiency. It had long been known that scurvy is relieved by lime juice. This disease as well as rickets is now considered to be due to the lack of vitamines, and you have with you now the Commission from Yale Medical School for the study of rickets. Work of outstanding importance was accomplished by Goldberger in pellagra. Now in beriberi the problem is relatively simple; in pellagra it is more complicated. Undoubtedly much valuable progress has been achieved in pellagra but it is by no means certain that we have the complete story in hand as yet. It is not clear whether a vitamine is lacking or whether the deficiency lies in some other factor. The process of disproving the theory of a specific infection proved to be a long task even in the simple conditions of beriberi. One frequently hears of pellagrins whose symptoms do not yield to dietary measures. In this type of patient, it is particularly desirable to obtain additional evidence before utterly dismissing the idea of an infectious disease. In brief, we are forced into a somewhat unwelcome situation for it is clear that a dietary disorder can produce symptoms sufficiently like those of a specific infection to cause long-standing confusion.

In the subject of etiology, let me mention first of all, an interesting association between two diseases that, let us say, never meet. One of them, namely sprue, is truly a product of the tropics. The other, progressive pernicious anemia, is a serious mystifying disease of cold climates. So far as we can tell at present, it occurs at least very irregularly and atypically in the tropics. Here in Porto Rico sprue is endemic. You all know of the important work of Dr. Ashford on the role of monilia in this disease. As regards the causation of pernicious anemia, so little is known that one is fancy free to hold almost any view. Any suggestion would be very welcome.

On the face of things it does not seem that any help could come from a very different disease such as sprue. However, on closer examination these two diseases often show certain similarity of symptoms with respect to the development of anemia, achylia gastrica and even changes in the spinal cord. Here we have clearly a clue to be followed up and it is being followed with interest by several investigators in the United States. Considerable work is now in progress on the occurrence of monilia in pernicious anemia. It is much too early yet to say what course this work may take, what it may develop into, or where it may eventually lead us. You see that we are only at the very beginning of our knowledge concerning the cause of pernicious anemia.

But in the treatment of anemia very gratifying progress has recently been accomplished through dietary measures by Minot. Now you all know that the old established treatment of sprue rests solely on dietary measures. This type of therapy, though very new in pernicious anemia, is an old procedure in sprue. It is already time to consider the inter-application of dietary measures in the case of refractory patients afflicted with either of these diseases.

Sometimes an apparently trivial exception is worthy of examination. Scarlet fever is virtually unknown in the tropics but streptococcal infections occur not infrequently. Here we have, in a minor way, something of a paradox. The weight of opinion in the United States at present tends decidedly toward the acceptance of the streptococcus as the cause of scarlet fever. It has always been a puzzling question as to why scarlet fever does not occur in the tropics; if it is caused by a streptococcus this question becomes even more difficult of solution. You are all familiar with the happy results that are being accomplished in the treatment of scarlet fever with serum, this work having been initiated in your affiliated school in New York by Dochez and by the Dicks in Chicago. Clearly there is an opportunity here in Porto Rico which does not exist in New York and Chicago to furnish supplementary evidence regarding the etiology of scarlet fever.

Long ago Schaudinn suggested the cause of yellow fever would prove to be a spirochaete and Stimson demonstrated a spirochaete in the kidney in one patient during a yellow-fever epidemic in New Orleans. The demonstration of leptospira as the causative agent of infectious jaundice added a fresh impetus to the search for spirochaetes in yellow fever. Noguchi worked intensively in this field. His results raise questions of fascinating interest regarding the rela-

tionship between yellow fever and infectious jaundice, *i.e.*, Weil's disease. The subject is an intricate one and it will be reserved for detailed discussion at a later period.

Let us turn to an example where our information concerning the main features of etiology is complete. It is one in which tropical medicine received a very direct impetus from general medicine. Clinical analogies had long been recognized between yaws and syphilis and even over-emphasized. Following Schaudinn's announcement of the discovery of *Treponema pallidum*, Castellani very promptly supplied convincing evidence establishing a similar treponema as the cause of yaws. The subject of tropical medicine just missed the opportunity of pointing the way to the etiology of syphilis. Yaws and syphilis illustrate well the firm bonds of union between tropical medicine and general medicine. It is impossible to appreciate either of these diseases thoroughly without a comprehensive knowledge of the other.

Thus the development of our knowledge of yaws owes a real debt to the general medical sciences not only as regards its etiology but also in the application of the Wassermann reaction. This debt has been in a large measure repaid in a way that is not frequently appreciated. Chemotherapy of the systemic infections received during its infancy almost its sole impetus from the field of protozoology and the spirochaetal diseases. The development of salvarsan was very closely associated with tropical medicine. As you know, trypanosomes and the disease trypanosomiasis, *i. e.*, sleeping sickness, furnish a practical method for the study of chemotherapy. Erhlich by systematic investigation, tested his long series of compounds on trypanosomes and on various spirochaetes. It so happened that salvarsan proved to be effective for many spirochaetal diseases including syphilis.

Biochemistry has also made its contributions. Some years ago there was a small outbreak of Asiatic cholera in Manila. At that time it fell to my lot to be on duty in the cholera wards. Some of the patients in the stage of reaction showed unmistakable clinical signs of air-hunger, an almost typical Kussmaul's coma. Obviously these cases were not associated with diabetes and the urine, as a rule, was free from acetone. However, the clinical signs of acidosis were characteristic and it seemed advisable to look for some method of recognizing acidosis other than the tests for acetone bodies. Accordingly these patients were injected with sodium bicarbonate. Enormous quantities—90 or 100 grams—were often required to render

the urine alkaline whereas if a healthy person takes a teaspoonful of baking soda the urine changes promptly from an acid to an alkaline reaction. These studies in Asiatic cholera therefore have given us an improvement in its treatment and a demonstration of a type of acidosis that differs markedly in detail from that of diabetes. This acidosis occurs not only in the nephritis of cholera patients but also in the ordinary nephritis of cold climates.

We must at least mention the topic of climatology. In matters pertaining to this subject, I would rather turn to the infectious diseases. Permit me to point out one very interesting organism, namely *B. pestis,* the causative agent of bubonic plague. This disease is transmitted by the rat flea. But at times especially in northern climates, this same bacterium *B. pestis* has given rise to a disease characterized not by buboes but by pneumonia and we have pneumonic plague. Occasionally, cases of bubonic plague also develop pneumonia but epidemics of the pneumonic form occur only in cold climates. Insects play no part whatever in transmission, but droplet infection is the mode of conveyance. The organism *B. pestis* is easily recognized in each of these two types of diseases. Otherwise a strange error might easily have occurred. It would have been only natural to suppose that these two types of infection were totally unrelated diseases, one a pneumonia, always fatal, and epidemic in cold climates, the other a disease of rats and man, carried by fleas and characterized by buboes.

Let us now take up briefly some phases of epidemiology and hygiene. Manson demonstrated in 1878 that certain species of mosquitoes take up filaria from the blood of a patient. Moreover he followed developmental stages of the filariae in the mosquito. The manner in which the mosquito carries the infection back to man was not demonstrated for a period of years. In the meantime it fell to the lot of Theobald Smith to furnish a complete demonstration of the insect transmission of a disease. As you know, he showed clearly that Texas fever which affects southern cattle, is transmitted by the cattle tick. In spite of very clear experimental evidence, this conception proved almost too daring for scientific acceptance by some of the leaders in medicine of that period. In the face of skepticism, the demonstration of the insect transmission of malaria, of yellow fever, and other diseases soon followed. Eventually a long list of infections have been shown to be insect borne. One of the very few absolute triumphs in hygiene in the United States was accomplished by virtue of the demonstration in Cuba concerning the

role of mosquitoes in yellow fever. This disease has now vanished from general medicine of our northern cities probably never to return. A relative triumph in hygiene in our southern states owes its origin to the demonstration by Ashford and his colleagues here in Porto Rico that uncinariasis can be controlled by appropriate field measures. It challenges the imagination to conceive the far-reaching ramifications of this work that had its beginning here only a few years ago. Indeed it furnished the foundation for the International Health Board.

One could easily multiply the instances in which remarkable results have been achieved through public health measures in cold climates for the purpose of driving back to their homes the diseases originating in the tropics.

Recently I had the pleasure of visiting the Department of Health and the privilege of seeing something of the work of your Director of Public Health. The achievements in hygiene in Porto Rico are progressing to such an extent that the workers in this institute will be driven farther and farther from these shores on expeditions for research in its many and varied phases.

It is a matter of importance to the scientific world that the people of Porto Rico have achieved a definite consciousness of their responsibilities in the field of science. The leaders in the development of this Island are not satisfied merely with commercial development. The activities of your investigators here have given Porto Rico a place of leadership in science in tropical America. This is an enviable position which will be challenged by your neighbors in friendly rivalry. But with the foundation of past achievement and with mature plans for the future it is a leadership which Porto Rico is in a position to maintain.