Introduction to:

The role of infection in chronic eye diseases.

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In this lecture I shall not deal with bacteria that can be isolated from infections of the eye but with the mechanism by which bacteria in other parts of the body affect the eye. Many attempts have been made to establish the "focal infection" hypothesis as an explanation of the cause of many chronic illnesses but this idea still has as many severe critics as it has fanatical supporters. It is well known that extraction of a tooth or other obviously infected tissue sometimes results in dramatic improvement in the disease symptoms but it must also be admitted that similar treatment in other patients with the same disease produces no effect. There has never been an adequate explanation of this discrepancy except to claim that the failures were caused by "hidden foci". Attempts to immunize against the supposed focal bacteria likewise have failed.

During the past 26 years I have developed laboratory methods which are believed to throw considerable light on this controversial subject and this lecture will be concerned with a discussion of the present status of the work. Some of the technical developments have been published, many are unpublished and others are still under investigation.

The usual concept of focal infection is that a particular, circumscribed, infected focus, the so-called "primary focus", contains a reservoir of bacteria which are transported by the blood stream to other parts of the body where they set up secondary foci. However, immunologists now realize that other mechanisms, such as the Arthus and Shwartzman phenomena and the direct action of bacterial toxins can produce inflammatory reactions without the presence

of living bacteria in the affected part. This explains the disputed role of bacterial invasion, for example, in inflamed gall bladder tissue and the failure to isolate viable bacteria from eyes that have been enucleated because of symptoms of severe inflammation. Therefore, the focal infection hypothesis should be revised to take this into consideration. My experiments indicate that the major incitant of chronic illness is a bacterial toxin. Streptococcal toxin can be demonstrated in every case but in some it may be accompanied by toxins produced by other bacteria. The beneficial effect sometimes observed after treatment of a focus of infection can be explained largely on the basis that the tissues are no longer being bombarded with toxins formerly produced in the focus. Symptoms that persist even after supposed eradication of infected foci do so because infection rarely is confined to these circumscribed areas but is diffusely distributed throughout most of the entire membranes lining the upper respiratory and gastrointestinal tracts. These extensive residual areas often harbor so much infection that they remain as major sources of intoxication.

Another difficulty of the focal infection hypothesis is caused by the fact that chronic infection frequently does not produce demonstrable local tissue damage or local symptoms and consequently is usually ignored. Still another difficulty lies in the fact that the organisms claimed to be the cause of focal infection cannot be differentiated from commensal saprophytes by usual methods. Because of these diagnostic difficulties it has been impossible until now to establish the role of such obscure infection in chronic illness. Consequently, hematological and biochemical standards are excessively broad because a person must be assumed to be normal unless the infected foci are easily demonstrable and the symptoms severe enough to be obvious. Therefore, present methods offer little scientific experimental evidence to support the focal infection hypothesis. However, I hope to demonstrate this morning that by the intelligent use of improved methods it is possible to obtain a clear understanding of the role of infection in chronic illness, including eye diseases, and to point the way to more effective

treatment. These new methods show a surprisingly high relationship to each other in contrast to the lack of correlation shown by previous methods.

If the circulation of bacterial toxic principles, rather than of bacterial bodies, is the principal basis for "focal infection" then it would be better to call the underlying mechanism "chronic bacterial intoxication". The French refer to such conditions as "toxi-infections". The focal reactions that sometimes occur with minute amounts of bacterial antigen probably are caused by sensitization of tissues to the bacterial products.

A clear understanding of chronic bacterial intoxication demands better understanding of the natural history of chronic infection. Toxigenic bacteria can only invade the body through the nasal and oral orifices. This probably takes place in early life and then remains there to be permanently implanted in the adjacent tissues as a result of avitaminosis, excesses (tobacco, alcohol, sex, fatigue, etc.), a severe illness or as a result of an insidious and almost imperceptible daily absorption of the bacterial products over a period of many years. The severity of the symptoms depends on the nature of the toxigenic bacteria, their location, relative toxigenicity, relative number and the power of the body to prevent their entrance or to neutralize their products. These are all variable and it is for this reason that a high degree of correlation among different methods cannot be expected. Even a large number of toxigenic bacteria in the gastrointestinal tract may produce little systemic effect if they pass rapidly through it. These conditions make it unwise to confine the laboratory examination to only one or two foci or methods. It should embrace a complete study in every patient, regardless of the clinical findings.

I have found a high degree of correlation when laboratory investigations are done with meticulous care and the bacteria used for comparison with the other methods are Streptococcus mitis and Streptococcus salivarius. No such correlation exists with other bacteria. In individual cases other bacteria may be responsible for some outstanding symptoms but they are not constantly present in chronic ill

health. On the contrary the two species of streptococci just mentioned are present in toxigenic form in all chronic invalids, the number and proportion of toxigenic variants being directly related to the severity of the illness. They are always present in the pharynx and in "pre-colon" semisolid specimens of feces except in persons with schlorhydria where the heavy growth of coliforms makes it difficult to find them. When they are present in other parts of the body there is also good correlation between the number and proportion of toxigenic dissociants and the severity of the local inflammatory process. In fact, other findings, such as the number of Escherichia and paracoli in the feces can be shown to be directly related to streptococcal intoxication. Technical considerations play a major role in such investigations.

These toxins can affect any tissue in the body, including all types of nerve tissue. The toxins can either increase or decrease the normal function of a cell and result in hypofunction or hyperfunction of the organ. Thus, any type of disease condition can be produced by this type of bacterial intoxication, the symptoms and pathology depending on what cells are affected.. For example, the commonest subjective symptoms are postnasal drip and tiredness. The commonest objective symptoms are a reduction in the number and proportion of mature leukocytes and an increase in the amount of bacterial products in the urine. Thyroid hypofunction is present in almost all chronic invalids. Another frequent finding is a subnormal or low normal number of erythrocytes, which results in a high color index.

Let us consider how the laboratory can demonstrate these changes. First let me interject a word of warning. It is not merely a question of telling the technician how to do the test and having him do it. There are so many minute details that require precise execution. Most of the patients that come to this laboratory have been studied in excellent institutions and nothing has been found to explain the disease condition. Why then do I find so many abnormalities using what are ostensibly the same methods, viz., blood counts, urinalysis, sedimentation

rate and bacteriological examinations. The answer is to be found in minute attention to technical details. When these are changed, even slightly, as is usually done at the whim of the investigator or because he finds it more convenient, then there is a decrease in the reliability of the findings. In culture media, selection of ingredients was not made haphazardly but each separate ingredient was studied both quantitatively and qualitatively. Therefore, a specification of "tryptone" must not be changed to "peptone" and K_2HPO_4 must not be changed to Na_2HPO_4. I shall now elucidate on the different factors that contribute to the reliability of the laboratory examinations.