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Reasons for considering that toxigenic types of Streptococcus salivarius and Streptococcus mitis are the common denominators of chronic diseases.

The claim of Sir Almroth Wright that infection is responsible for almost all chronic illness, which idea is closely associated with the "focal infection" hypothesis advocated particularly by Billings, Rosenow and their associates, has received considerable substantiation from the laboratory work of Chapman in association with the clinical investigations of Drs. Berens, Combes, Eaton, Fiske, Griffiths, Longstreth, Rawls, Ressa, Roberts, Stiles, Sturtevant, Tilney, Titus and many others which forms the basis for the following conclusions.

The only microorganism that is constantly present in chronic invalids and is directly related in number and proportion to the severity of symptoms, blood sedimentation rate, hematology, urine findings and other laboratory findings is the toxigenic type of Streptococcus salivarius and Streptococcus mitis. Moreover, the number and proportion of these toxigenic bacteria return to normal when the disease is cured. The following relationships have been found.

Except when they are highly toxic, streptococcal cultures are mixtures of both toxic and nontoxic cells, the proportion of toxic cells, determined under precise conditions, being a measure of the toxicity of the culture or of the streptococci in the part of the body from which the culture was obtained. In chronic illness, toxic streptococci multiply on the mucous membranes whereas nontoxic ones do not. Therefore, the total number of streptococci is another expression of their pathologic significance.

The number and proportion of toxigenic streptococci, particularly in the pharynx, tonsils, teeth and feces, is parallel to the severity of the illness, as also are the erythrocyte sedimentation rate, the nonfilament: filament ratio of neutrophilic leukocytes, the total number of filamented leukocytes, the urine titer of bacterial products, thyroid and liver function, etc.

Although the bulk of streptococcal intoxication may be confined to certain circumscribed areas (foci of infection), almost all patients show extensive involvement of the mucous membranes lining the nasal and oral cavities and the gastrointestinal tract. It is this diffuse infection, usually overlooked, which is responsible for failure of usual methods of treating "focal infection".

When the streptococcal intoxication becomes so severe that it markedly lowers the resistance of the mucous membranes and other tissues, nonpathogenic bacteria are then able to invade the tissues. This explains the finding of coliforms in the nose, throat and urine in many such cases and the presence of nonpathogenic bacteria in the blood stream. When streptococcal infection is reduced, these nonpathogenic bacteria disappear.

When there is any degree of gastric acidity, the swallowed streptococcal toxins inhibit proliferation of coliforms in the gastrointestinal tract. The greater the intoxication, the smaller the number of coliforms in the feces. The inhibiting effect on coliforms dininishes on prolonged stay in the intestines or after the stool is passed, giving rise to higher counts. The streptococcal toxins also damage the lactose fermenting enzyme of Escherichia and Aerobacter producing high counts of paracoli.

If the defensive mechanism of the body is effective the toxic streptococcal products are rendered innocuous, but when it is ineffective the unaffected bacterial products are excreted in the urine where they can be determined quantitatively by a simple method devised in this laboratory. With few exceptions, the amount of these bacterial products is proportionate to the severity of the streptococcal intoxication.

The streptococcal toxins may damage any tissue in the body. The commonest effect is on the hematopoietic tissues where it produces "low normal" erythrocyte

counts and particularly low leukocyte counts. Although leukocytosis and polynucleosis are characteristic of infection, the prolonged intoxication of chronic illness causes inhibition rather than stimulation. Not only is the total number of leukocytes reduced far below normal (7,500 to 8,900 per cu mm), but the proportion of mature neutrophiles is reduced also, the maturation being hindered by the streptococcal toxins. Thus, the total number of mature (filamented) leukocytes becomes an excellent index of the severity of intoxication. The normal person has about 3,600 mature leukocytes per cu mm of blood but the average chronic invalid shows only 2,500. Preparations that increase the number of mature leukocytes produce improved resistance to infection.

Summing up, the role of streptococcal intoxication in chronic disease is shown to be a significant one by the following findings. The severity of the illness is proportionate to (1) the number and proportion of toxigenic streptococci in the pharynx, tonsils, teeth and gastrointestinal tract, etc., (2) the erythrocyte sedimentation rate, (3) the nonfilament-filament ratio of netrophilic leukocytes, (4) the number of coliforms in the nose, throat, etc., (5) the inverse number of Escherichia and the direct number of paracoli in the feces, (6) the amount of bacterial products in the urine, and (7) the extent of reduction in the total number of mature leukocytes.