CYTOLOGY OF LEPROSY*

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TWO GREAT GROUPS of diseases are caused by bacteria which multiply within the endothelial or reticulo-endothelial cells of the host. These are the Rickettsioses and the Mycobacterioses, respectively. Their study is one of the most fascinating problems in cytology because in no other situations in mammals are the relations between living cells and living microorganisms so intimate. It was as an extension of my work on Rickettsia that I became interested in mycobacteria.

The first is caused by tiny gram-negative organisms which are insect transmitted, and are called Rickettsiae after Howard Taylor Ricketts who died from typhus contracted during his investigations. They include, in addition to Rocky Mountain spotted fever, typhus, trench fever, heartwater, Tsutsugamushi disease, and probably many other less well defined conditions.

The second is caused by mycobacteria, that is to say, by large acid-fast fungous bacteria. It includes tuberculosis and leprosy in human beings and quite a large number of diseases in animals. But there are many sorts of mycobacteria which are not intracellular parasites, whereas all Rickettsia appear to be intracellular during at least one phase of their life cycle.

The Rickettsia are injected into the body by the bites of insects, find a home in the endothelial cells limiting the blood stream, provoke often widespread cutaneous lesions, and systemic reaction with fever; as a rule they confer a lasting immunity in those who recover.

The mycobacteria, coming from other individuals or animals, or conceivably in some cases, from the soil, gain entry through the skin or nasal mucous membrane and produce lesions which pass for a long time unnoticed and which often progress but slowly. The mycobacteria are, through long association with the host cells of the particular species, well adapted to them and are but feebly pathogenic, but when the defenses are broken down, as in miliary tuberculosis and in the lepra reaction, the spread is rapid indeed. The organisms may have propagated themselves in this way in generation after generation of human beings for millions of years, and there has probably been adaptation on

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the part of the host cells also. Of the individuals exposed, only a fraction (larger in tuberculosis than in leprosy) contract the disease.

In the Rickettsioses, on the contrary—presumably a more recent association of organisms and hosts—the incidence of infection on exposure is higher, in some cases a hundred per cent, and the reaction is, as we have intimated, more violent.

Tuberculosis and leprosy naturally take the lead among mycobacterioses. Next in importance are bovine tuberculosis, avian tuberculosis, etc., and rat leprosy, water buffalo leprosy, mouse leprosy, and so on. The relationships between these and other diseases caused by acid-fast bacteria, which cannot be labelled either tuberculosis or leprosy, are discussed by Long.

In general, the mycobacteria of the leprosy group differ from those of the tuberculosis group in having a longer incubation period, in causing a more localized tissue response, with little or no induced hypersensitiveness, and in difficulty of cultivation on artificial media. But it is unwise to indulge in generalizations because they require so many qualifications. Impetus has recently been given to research on the mycobacteria by a well-planned symposium on the subject, under the chairmanship of Long.

The study of human leprosy has lagged behind that of tuberculosis. The cases are far removed from research centers, and the urge as well as the opportunity to advance is lacking. Yet leprosy exhibits many interesting features. In no other infectious disease of man is the incubation period so long and in no other are the cells so densely packed with bacilli. It will give conciseness to this discussion if I attempt to present the evidence bearing on certain definite questions which have occurred to all of us.

1. IS THE INCUBATION PERIOD ACTUALLY OF THE LENGTH REPORTED? McCoy estimates the average period of incubation to be from 6 to 8 years but states that he knows of cases in which it lasted for over 15 years. Others give a maximum of about 40 years. Accurate measurement is difficult. Two dates must be established: that when the invasion by mycobacteria takes place and that when the lesions develop to the point of being positively diagnosed as leprous.

The date of invasion is usually not established, but presumed. It is given as the most recent date on which the individual could have become infected from contact with a case of leprosy. If, for example, John Doe has lived to the age of fifteen in a northern community where leprosy has never been reported, visits Central America where there are