Immune Response to Mycobacteria

Characterization of Immunocompetent Cells in Tuberculous Lesions of Humans

ANTONIO SCORDAMAGLIA, MARCELLO BAGNASCO, and GIORGIO WALTER CANONICA

1. THE FIRST CONTAGION: THE ALVEOLAR MACROPHAGES REPRESENT THE FIRST-LINE DEFENSE IN DEEP LUNG

Tuberculosis is an extremely severe infectious disease that commits the defense mechanisms of the host profoundly and for a long time. Antibiotic therapy is undoubtedly the most important treatment in such disease for blocking the growth of tubercle bacilli, but complete recovery as well as immunity against reinfections depend on the perfect functioning of the immunocompetent system.

When Mycobacterium tuberculosis penetrates the respiratory apparatus (or another organ of the body), immunologic changes occur in order to defend the host both from the development of the intercurrent infection and from possible future infections by the same agent. Nevertheless, it must be pointed out that the first penetration of M. tuberculosis in the
airways does not necessarily cause the disease. If inhaled tubercle bacteria stop at the trachea or bronchi level without reaching the deep lung, they can be easily removed from the tracheobronchial tree by the mucociliary clearance. If *M. tuberculosis* reaches the alveolar spaces, the possibility of developing the disease is related to two basic aspects: (1) the characters of the mycobacterial agents (bacterial charge and virulence); and (2) the genetic and acquired factors of host resistance or susceptibility to the infection.

The role of genetic factors in the immune response to *M. tuberculosis* has been extensively investigated, especially in animals.\(^1\)\(^–\)\(^3\) The factors that may play an important role in controlling resistance to tuberculosis are multiple, including race, and major histocompatibility complex, but the most important is surely the efficiency of alveolar phagocytic cells in blocking the growth of tubercle bacteria. In fact, even when the characteristics of the infecting agent (virulence, charge) are the same, there is considerable individual variation in the response of macrophages to mycobacteria. In some cases, the mycobacteria are destroyed by macrophages; in others, the macrophages can ingest but not kill the mycobacterium, which can survive without growing within the phagocytic cells; in still other cases, the macrophages are unable either to phagocyte or destroy *M. tuberculosis*, which can grow and cause the disease. Undoubtedly, what determines whether the disease progresses or regresses is the power of the macrophage to inhibit the growth of tubercle bacilli within its cytoplasm.\(^1\)

The killing of tubercle bacilli by macrophages is strictly dependent, at first, on the ingestion of mycobacteria and, afterward, on the fusion of primary lysosomes with the mycobacteria containing phagocytic vacuoles. It follows that one of the most important genetic factors connected to tuberculosis resistance (or susceptibility) can be identified in the congenital power of macrophages. On the other hand, the congenital ability of macrophages to kill tubercle bacilli may also be influenced by the virulence characteristics of the infecting *M. tuberculosis* strain. The virulence might be identified in secretory substances or in cell-wall constituents that can interfere with various phases of the phagocytic process, for example, by preventing the fusion of lysosomes with phagocytic vacuoles or by rendering the mycobacterial cell-wall resistant to lysosomal hydrolytic enzymes. For instance, some mycobacterial strains are resistant to the action of oxygen radicals, because they are protected by a thick lipidic wall and are able to produce a catalase that destroys hydrogen peroxide.

Soon after the first contagion, the cellular defenses are exiguous, scarcely effective, and limited, at least in the early phase, to the resident alveolar macrophages (and some recruited circulating macrophages).