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CELLULAR REACTIONS DUE TO INFECTIONS

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G.M. Pontiera

Among the organism's defense mechanisms against bacterial and viral infections, those present in the secretions [liquids] seem to play a preeminent role; but it is nevertheless a good idea to consider here all of those cell reactions which constitute the foundation for the dynamic equilibrium which is established in the relationship between the host organism, on the one hand, and the parasite, on the other hand. This is important not only because of the fact that the so-called humoral immunity factors themselves spring from cell elements but also because recent discoveries have made it possible for us to establish the cellular foundations for inherent and acquired resistance toward some of the pathogenic agents -- foundations which reside primarily in the elements of the RES (reticuloendothelial system). Experimental investigators have for many years suspected that these elements are active here and the results agreed, in other words, these elements were credited with having a rather special property of phagocytary activity which is manifested outwardly through the incorporation [grouping] of all of the particulate substances in the organism. The general significance or value of phagocytosis exercised both by the polymorphonucleates and by the fixed and mobile elements of RES as a valid defense mechanism in both bacterial and viral infections has been discussed at length but there is no agreement on this subject. The differences of opinion here are due to observations to the effect that both the germs and the phagocyted viruses are not always inactivated in the cytoplasm of the phagocyte and that, therefore, phagocytosis then represents a means for spreading the infectant agent around. Although this may turn out to be true in one case or another, there is irrefutable proof as to the real effectiveness of phagocytosis in numerous ineffective processes, in the course of which the pathogenic agent is incorporated and destroyed by the phagocytes which essentially represent an aspecific immunity mechanism that is valid even before the organism responds specifically to the constituents of the pathogenic agent, with the formation of antibodies. Phagocytosis is therefore a valid means for defense above all during the period of infection

following contagion. This observation is supported by experimental data demonstrating how, in selected animal strains, in which we can obtain constancy in susceptibility or resistance toward some pathogenic agents, the latter are manifested through the smaller or larger number, respectively, and the leucocytes and macrophages. Moreover, congenital resistance to a specific viral infection is coupled with the inability of the macrophages to sustain the viral replications: the arbo-virus B [unorganized virus B] does not develop in the cultures of macrophages from mice which genetically resist the infection whereas, on the other hand, it does develop in the cultures of other cells in the same animal. Like the leucocytes, the macrophages are therefore producers of interferon, as was demonstrated recently, so that the action which they exercise should not be considered only as a mechanical process involving the incorporation of the viral particle. Numerous substances with antibacterial and antiviral activities have been isolated from cells endowed with phagocytary activities whereas the metabolic changes, which occur in the process of phagocytosis, including the increase in glycolysis seems to be preeminent, have also been studied very thoroughly.

The elements of various sectors of the RES are endowed with the capacity of changing into other elements and it is widely believed that there is interconvertibility between the cells of the RES, on the one hand, and the plasm cells and the small lymphocytes, on the other hand; this fact is a very important link between the so-called cellular immunity factors and the humoral immunity factors. According to some authors, the first phase of the multiform aspect of the formation of antibodies is represented by the formation of complexes between the antigen molecules and the RNA of the macrophages. In phagocytosis we therefore not only have an incorporation of the bacteria or viruses and their inactivation but we also have a release of determinant antigenic groups; this fact constitutes the initial trigger in the antibody formation mechanism. These recently obtained data cast new light on the significance of the phlogistic reaction in which the phagocytes assume a preeminent position, not only because of the hydrolytic enzymes and the inhibitors which they might possess, but also because of the multipotentiality which at least the youngest forms possess.

Another demonstration of great interest here involves the increase in the phagocytary activity which enters the picture in those animals which underwent prior contact with a microorganism. The opsonins are only partly responsible for this behavior whereas, even "in vitro," the macrophages demonstrate the fact that they have greater inhibitory activity with respect to the pathogenic agent in question here.

For the time being, we know very little about the molecular bases [foundations] which are involved in these modifications; nevertheless, the concept of the "immune phagocyte" is open to consideration on the basis of the explanation of those phenomena which follow prolonged contact between the organism and those germs (microbacteria, brucellae, salmonellae, pathogenic fungi, Listeriae, etc) which are capable of producing -- in the host

-- a state of delayed hypersensitivity; this event seems to be closely tied in with the state of cellular immunity. The cell reactions which play a role in the dynamics of infections involve not only the elements of the RES and the polymorphonucleates but, in some cases, also the cells in other regions. Thus, for example, in influenza, the newly formed epithelial elements, which replace those that have been subject to the cytopathogenic effect of the virus, turn out to be incapable of being infected and of sustaining viral duplication. Other cases of modification of the susceptibility to infection with a specific pathogenic agent involve hormone and vitamin influence. The mechanisms involved in this behavior are partly known and they differ from one case to the next; we either find changes in the structure of the cell surface or we find rather considerable metabolic changes.