Symposium

Symposium on Microbial Infection and Host Response*

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Introductory Remarks

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The infection, inflammation and the immune response are each other independent concepts, but they are related to one biological item designated as the cellular body defense, in which cellular elements such as macrophages, granulocytes and lymphocytes play an essential role. Among these cells the macrophage is phylogenetically the oldest, the prototype of which could be found in the nutritional behavior of Protozoa characterized by the amoeboid movement, discrimination, uptake and the intracellular lysosomal digestion of foreign materials. As seen in Mesozoa, multicellular organism originates from colony-formation of Protozoa-type phagocytes, which differentiate through phagocytella to various types of body cells. In some species of Protospongia, colony-forming cells are differentiating to superficial flagellar cells and internal amoeboid cells. Analogous differentiation can be found in choanocytes and in archaeocytes of Porifera. Archaeocytes are of nutritional functions and also participate in body defense through phagocytosis and plasmodium-formation. In much more highly organized Metazoa, phagocytic cells resident mainly in the mesoglia coelomic space. In Annelida there are two types of free cells, coelomocytes and chloragogen cells, in the coelomic space. Among them coelomocytes are

phagocytic, and they have also the memory capacity in allogenic and xenogenic second set graft reactions.

The true immunological defense mechanism is established first in vertebrates. It originates in Cyclostomata and develops from class to class, so that in mammals a highly organized body-defense mechanism with lymphocytic immunological surveillance and with the immunoglobulin production is realized. Main event of this mechanism is interaction between lymphocytes and macrophages, which is structurally organized as the lymphomyeloid complex including the bone marrow, thymus, spleen, lymph nodes and the lymphatic apparatus of the mucous membrane. Granulocytes, in which destructive functions of the activated oxygen are utilized for killing of bacteria, appear also in vertebrates.

In mammals invasions of foreign materials, especially of microorganisms, are operated at first in the defensive environment including bacterial flora and secreted chemical agents of the skin and the mucous membrane. Then the epithelium and endothelium of the outer and inner body surface act as barriers. The subcutaneous and submucous loose connective tissue are main fields, where foreign materials broken through the above mentioned two fronts are

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disposed by the cooperation of macrophages, granulocytes and of lymphocytes. Humoral agents such as secreting antibodies are also of significance. These connective tissue areas are homologous to the mesoglia of invertebrates, so that they could be designated as the mesoglia zone.

Foreign materials escaped from the mesoglia disposal are caught by the lymph nodes or by the lymphatic apparatus via lymphatic vessels and also by the spleen if the materials spread through blood vessels. Immune phagocytosis is the essential mechanism in these peripheral lymphoid organs and at the same time they are main source of specific antibodies. If we understand under the

concept of the inflammation a focal mobilization of phagocytes and lymphocytes with vascular reactions, the processes of the disposal of foreign materials in the mesoglia zone and in the peripheral lymphoid organ are not other than inflammation, although they takes place physiologically. The inflammation is, however, pathological on the other side, and the conversion or progress of the physiological inflammation to the pathological phase of the inflammation is a critical point of the cellular body defense. Attentions must be paid to this critical point, where various factors of hormonal and nervous regulation concern.

(1) Activation and Antibacterial Mechanisms of Alveolar Macrophages

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Alveolar macrophages (AM) are the main means of cellular defense for the lung against microbial invasion and they are highly active in clearing organic and inorganic particulate materials. As AM reside upon the alveolar surface and function in the alveolar lining materials which contain phospholipids, immunoglobulin G (IgG) and many other materials, their morphology and functions are affected by some of these materials. In the present report, we studied on the activation and antibacterial mechanisms of AM in the presence and the absence of the lung lavage fluids obtained from normal or BCG-infected granulomatous lungs in rabbits.

Lung lavage fluids from normal rabbits were freed of cells and added to the monolayers of homologous AM. When AM incubated with the lung lavage fluids, many more cells adhered to glass, spread out and showed enhanced nitroblue tetrazolium (NBT) reduction. The AM activated by the lung lavage fluids showed a higher capacity to inhibit the growth of intracellular BCG, and that capacity was correlated with the intensity of NBT reduction by the AM. The superoxide

production of BCG-infected and non-infected AM was measured by superoxide dismutase-inhibitable NBT reduction. Superoxide, one of bactericidal agents, is a potent reducing agent of NBT. When control AM were infected by BCG, superoxide production was decreased markedly, probably due to bacterial cytotoxic factors. In contrast, the production of superoxide in AM exposed to lung lavage fluids was increased and not appreciably influenced by BCG infection. Superoxide production by AM was dependent on time and on the protein concentration in the lung lavage fluids. In control, it was inversely proportional to the infection dose of BCG. Superoxide which produced in the test tubes with xanthine oxidase-purine system killed BCG extracellularly, especially in the presence of catalase at acid pH.

Gel filtration of the lung lavage fluids through Sepharose 4 B yielded five fractions. The factor that activated the AM functions was in fraction 4. When the IgG in the fraction was removed by an immunoadsorbent column, AM activity was abolished. The effect of the IgG was dose de-