

Editorial

Protective or Damaging Immunity in Infection

Within immunology, it is especially important to know the basic mechanisms of innate and adaptive immunity in the defence against infectious agents, the most important physiologic function of the immune system. The development of an infectious disease in a person involves complex interactions between the agents and the host. It starts with the entry of the microorganism, the colonization of the tissues and the invasion, after overcoming the host's defences, and the organic lesion or functional alteration of the tissues. Then some agents start spreading the disease through multiplication, liberation of toxins or events of hypersensitivity [1].

The immune system usually responds specifically against the infectious agents present and fights them with the highest efficiency possible, on the principle of all or nothing. The pathogenic capacity of the agents is linked to their capacity to elude or resist the effectors mechanisms of immunity, which are mainly adaptive, humoral or cellular. However, in many infections the disease can be the consequence of the host's response to the infection rather than the direct effect of the agent itself, through the hypersensitivity phenomena, which involve a more or less significant molecular mimetism. Some strains of *Streptococcus pyogenes* show similarity of capsular epitopes to the host connective tissue, its wall M protein shares epitopes with cardiac myosin; and streptolysin O binds to the erythrocyte membrane cholesterol altering its antigenic configuration. It may also form streptolysin O immunocomplexes and antibodies deposited on tissues, or the anti-streptolysin O may directly injure the cellular membranes [2]. On the contrary, and excluding molecular mimetism, other bacterian agents, such as mycobacteria, may cause granulomatous inflammation and histic destruction [3]. Finally, agents such as *Mycoplasma pneumoniae* may share mechanisms through the modification of the host antigens and direct tissular destruction [4].

Over the past years it has been stated that some diseases deriving from unknown causes, such as atherosclerosis [5], schizophrenia [6], multiple sclerosis [7] and periodontal disease [8], at least in a subgroup of patients, may be caused by sustained chronic infections, together with a genetic component, and perpetuated by the immune system. This hypothesis is based on epidemiologic and biologic evidence proving that these patients were exposed to infection risk factors during the pre- or post-natal period, such as *Toxoplasma gondii*, chlamydias, all the human herpesvirus, parvovirus B19, parotiditis virus or flu viruses. This list of microorganisms has increased with time and it will doubtlessly continue to grow, since there would only be the need to study agents with prevalences that are high enough to be significant risk factors. It is more complex to relate the infection with the clinical process because it first requires epidemiologic studies and then experimental animal studies. Some works have been done in relation to this. The belief is that the infection may distort the synthesis of neurotrophins by immune cells, with significant subsequent repercussions. On other occasions it is believed that maternal antibodies which are directed against infectious agents leave secondary injuries on foetal neuron tissues, which are the part of the anatomy affected by the subsequent lesion in subjects with the disease [9]. In any case, whether the infection is pre- or post-natal, the disease is immune-mediated: it generates an irreversible lesion, of greater or lower level which, with time, leads to the appearance of the disease. The hypothesis that foetal infections during gestation or during the first moments of post-partum may trigger the subsequent appearance of the disease, like an organic sequel, is based on the above. Nevertheless, it is also probable that a possibly unsolved very early chronic infection may exist through an agent able to perpetuate itself (such as DNA viruses, chlamydias or *T. gondii*), which facilitates the appearance or exacerbation of the disease by interacting with other factors. Thus, the subjects may be susceptible to symptomatic treatment of the disease, such as is currently done, but, in addition, in this last case, the subjects may also be susceptible to antimicrobial treatment that may improve their progress. One of the markers to show chronic infection status is the presence of the agent's DNA in leukocytes and an important synthesis of specific IgG and IgA. In principle, herpesviruses are important candidates, since they are cytotropic, they produce latent infection with exacerbations, they may block neuronal function and cause diseases that behave as if they are post-acute.

The main criticism received by these studies centers on the fact that the infection and the antibodies against viruses of the *Herpesviridae* family, *C. pneumoniae* and *T. gondii* families are very frequent in the general population, and that most of the carriers are asymptomatic. Doubtlessly, the field of influence of different infectious agents related to diseases of unknown cause is in the midst of development, and, although conclusive results have still not been found, it is necessary to replicate the studies, start new ones and relate these factors with the different manifestations of the disease. As a result of all the above, it

would be extremely interesting to show or to rule out whether there is a differential replication of the infectious agent, at least in some of the subjects studied. Thus a dynamic would be set in motion to detect a population that could be susceptible to treatment with specific antimicrobial agents, a better definition of the differential phenotype of the disease, and the possibility of prevention.

With the foregoing facts and under the title “Immune-Infectology Principles” we deem it opportune to run a monographic volume of the *Current Immunology Reviews* journal studying the relationship between infectious agents, human immunity mechanisms and disease, from different points of view.

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