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Editorial

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In response to an infectious insult (e.g., bacterial or fungal infection), the body has to mount an immune response which will deal with the foreign invader and restore normality. However, for an immune response to occur, it is essential that tissue inflammation occurs. The hallmarks of inflammation are the extravasation of plasma proteins and leukocytes, which are necessary for the early antigen processing and presentation and the later effector functions of the immune response, i.e., antibody production and cell-mediated immunity. Thus, a proper and controlled inflammatory response is absolutely essential for the ability of a host to deal with infectious agents.

On the other hand, tissue inflammation does not only occur when there is microbial infection and the list of human diseases now associated with inappropriate or uncontrolled tissue inflammation in response to known or unknown stimuli is increasing. To cite just a few examples, the infiltration of leukocytes, especially neutrophils, in the joints of patients with rheumatoid arthritis appears to be largely responsible for the destruction of cartilage and bone which may lead to deformities. In chronic smokers, inflammation of the airways in response to smoke and repeated airway infections also appear to play a determinant role in the development of chronic obstructive pulmonary disease. Thus, in the examples above and in many other inflammatory diseases, tissue inflammation is clearly deleterious and inhibition of inflammation may be of therapeutic benefit.

Can the beneficial effects of inflammation be separated from the deleterious effects? Will we be able to identify novel drug therapies which are capable of preventing unwanted disease while maintaining the ability of the host to mount protective immune responses? This is certainly not a simple task and can be illustrated by models of septic shock in animals. In these models, neutrophils are clearly associated with lethality and strategies which inhibit neutrophil accumulation and/or activation in tissues may decrease neutrophil-mediated tissue injury and early mortality. Nevertheless, inhibition of neutrophils is often associated with uncontrolled bacterial growth and subsequent bacteremia, which may then lead to increased lethality. In order to move forward and answer the questions above, much research will be needed to identify and evaluate the functional role of mediators and/or processes responsible for leukocyte-mediated injury and to compare them with those responsible for leukocyte-dependent protection against infection.

Do we need novel anti-inflammatory drugs? To answer this question, one must remember the agents with anti-inflammatory activity which are commonly used in clinical practice: glucocorticosteroids, inhibitors of cyclooxygenase (COX-1 and COX-2) and, possibly, the immunosuppressant drugs (e.g., cyclosporine, methotrexate) that inhibit tissue inflammation by primarily inhibiting lymphocyte function and/or proliferation. Steroids are very effective anti-inflammatory drugs, but in addition to important metabolic effects, they are very strong immunosuppressors, especially when given in high doses and prolonged treatment. COX inhibitors possess weak anti-inflammatory activity and gain most of their clinical use from their very important analgesic effects. Clearly novel and better drugs are needed. What would be an ideal drug? Possibly, a drug which possesses the effectiveness of steroids at inhibiting tissue inflammation but lacks the immunosuppressive and other side effects. As mentioned above, it is uncertain whether the development of such drug will be achieved.

The present series of reviews in the Brazilian Journal of Medical and Biological Research marks the launch of the Brazilian Society of Inflammation and will focus on essential basic mechanisms which are the backbone for the development of novel anti-inflammatory therapies. Papers will discuss novel mediators involved in leukocyte recruitment and activation, cell adhesion molecules and their role in leukocyte recruitment, the mechanisms underlying leukocyte differentiation and release from the bone marrow, signal transduction mechanisms and their potential for drug development and, finally, the possible use of apoptosis as a strategy to resolve inflammation. No series on aspects of the inflammatory response would be complete if we did not include a chapter on inflammatory hyperalgesia.