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Inflammation: the sparkplug for chronic diseases

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The results of an important clinical study show that canakinumab, a new anti-inflammatory medication, diminishes the risks of heart attacks and of lung cancer, confirming the essential role of inflammation in the development of these diseases.

A SMOLDERING FIRE

Inflammation is a defensive reaction orchestrated by our immune system to eliminate pathogenic agents by using molecules which are very reactive and irritating. This type of acute inflammation is easily recognizable by the sensations of heat and pain, reddening and even swelling. This inflammation should be of short duration, however, because if it becomes chronic then the continued presence of the inflammatory molecules becomes extremely irritating for the affected tissues and can provoke intense pain at the site of inflammation, as is seen in cases of rheumatoid arthritis, Crohn's disease and other inflammatory diseases.

Chronic inflammation can also be much more insidious and can develop with no apparent sign, nevertheless creating a climate which perturbs the functioning of cells found within the inflamed location. This type of chronic inflammation plays a particularly important role in the development of two principal diseases which affect the Canadian population, i.e. cardiovascular diseases and cancer, and reduction of this type of inflammation could consequently represent a crucial aspect in the prevention of these diseases.

INFLAMMATION AND CARDIOVASCULAR DISEASES

The standard approach for preventing cardiovascular events such as heart attacks and strokes consists of reducing blood levels of LDL cholesterol (bad cholesterol) with the aid of medications such as statins. However, several clinical studies have shown that this diminution does not succeed in completely eliminating the risk of cardiovascular diseases. For example, patients who have experienced a heart attack and who are subsequently treated with a statin remain at high risk of recurrence, with about 30% of them dying within two years following the beginning of treatment, and this even despite an important reduction in their levels of LDL cholesterol.

The results of the clinical study CANTOS (Canakinumab ANtiinflammatory Thrombosis Outcome Study) suggest that chronic inflammation can largely contribute to this elevated residual risk. In this large, double-blinded study, the effect of an antibody directed against the inflammatory protein interleukin-1 was tested over 48 months with 10,061 patients who had experienced a heart attack and who exhibited elevated blood levels of reactive protein C, which is well established as a marker for inflammation. Along with the standard treatment with statins, one group of patients received no additional treatment (placebo) whereas the other groups received specified doses of canakinumab,

the anti-interleukin antibody developed by the firm Novartis. The results of the study are interesting: the antibody drastically reduced the blood levels of inflammation markers and this diminution was accompanied by a significant reduction (about 15%) in the relative risk of certain parameters measured during the study ("primary endpoints"), being non-fatal heart attacks, non-fatal stroke and cardiovascular mortality[1]. This protection was independent of the levels of cholesterol, which confirms that the reduction of inflammation represents a new avenue for preventing recurrence in high-risk cardiac patients.

INFLAMMATION AND CANCER

In another article published simultaneously in the British journal *Lancet* by the same group, they reported that the antibody could also prevent the development of cancer[2]. By comparing the incidences of cancer between different groups, the researchers found a diminution of 14% amongst those who were treated with 50 mg of the antibody, of 22% amongst those who received 100 mg and of 51% amongst those who received 300 mg of the antibody. Nearly all of this diminution was due to a reduction in lung cancer, which was diminished by 77% in patients who received 300 mg of the antibody. According to the researchers, it is likely that the cancerous cells were present in a latent state which was undetectable at the beginning of the study and that their progression was braked by the anti-inflammatory effect of the antibody.

ANTI-INFLAMMATORY LIFESTYLE

The results of this study are important because they represent one of the first clinical proofs that a reduction in inflammation diminishes the development of cardiovascular diseases and of cancers, the two principal causes of death in our society. It is not, however, necessary to await the arrival of these medications on the market to take advantage of the benefits associated with a reduction in inflammation: stopping smoking, exercising, remaining as thin as possible and adopting a diet rich in plants (e.g. the Mediterranean diet) are all concrete ways of reversing chronic inflammation and thus reducing the risk of cardiovascular diseases, cancer and chronic diseases in general.

(1) Ridker PM et al. Anti-inflammatory therapy with canakinumab for atherosclerotic disease. N. Engl. J. Med, published online August 27 2017.

(2) Ridker PM et al. Effect of interleukin-1 inhibition with canakinumab on incident lung cancer in patients with atherosclerosis: exploratory results from a randomized, double-blind, placebo-controlled trial. Lancet, published online August 27 2017.

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