EDITORIAL

Inflammation: The Root of Our Chronic Diseases

It takes time—sometimes decades, sometimes hundreds of years—for our bodies to adapt to a new environment. In the past 60 or so years, we have added tens of thousands of new environmental factors, including chemicals, human-made substances, foods, liquids, and others. The onslaught defies the possibility of adaptation.

For example, the 80 000 chemicals that are used commercially throughout the United States were discovered within the last several decades; they did not exist before. The US Environmental Protection Agency (EPA) estimates that emissions from industrial plants and facilities will easily reach 2.5 billion pounds annually, making it very likely that every person in this country is exposed. The Integrated Information System of the EPA is the where all data are kept regarding toxicities reached by scientific consensus. However, the list is woefully short—only 550 chemicals. One can only wonder why the other 79 450 chemicals are not currently on this list—an indication of the very serious gap in the knowledge necessary for calculation and evaluation of risks associated with exposures to these chemicals. Yet even the few chemicals included by the EPA are mainly occupationally oriented.[1]

Our immune system is responsible for protecting us from this environment, attacking all pathogens and xenobiotics, while ignoring all the cells of our own bodies—all 100 trillion of them. This is done in a highly complex and choreographed manner. However, the incessant daily onslaught of stress, of environmental factors in the air we breathe, in the foods and beverages we consume, and in what is absorbed by the 3 trillion pores on the average human body has brought us to the edge of the immune system's capacity. As a result, we now have to contend with many more chronic diseases than ever before. The root cause of these new scourges of humankind is inflammation: chronic, often silent, but persistent. When inflammation continues in a low-grade state, it is a known factor in numerous age-related chronic conditions and causes a wide range of chronic health problems, including metabolic syndrome (MetS), type 2 diabetes, nonalcoholic fatty liver disease (NAFLD), cancer, cardiovascular disease (CVD), and others.

The immune system is essentially divided into 2 parts: the innate immune system with which we are born, and the adaptive immune system—also known as the antibody mediated immune system—that we develop. Put in a very simple manner, the cells of the innate system are the first to go into action and respond to pathogens, whereas the adaptive immune system confers long-lasting protective immunity. Inflammation is one of the main elements of the innate immune system and is triggered as a local response to cellular injury: It is led by neutrophils. Neutrophils are the most common type of leukocytes and are highly motile, allowing them to quickly congregate at the site of injury or infection. Following this we have the release of chemicals, bradykinin, leukotrienes, prostaglandins, and others, which sensitize pain receptors and attract more neutrophils. The average person produces 100 billion neutrophils per day, with the bone marrow keeping mature neutrophils in reserve in case of an infection. If it occurs, 10 times more neutrophils will be released into the circulation. These neutrophils have 3 methods by which they attack microorganisms and other substances: phagocytosis, degranulation with the release of reactive oxygen species—also known as a respiratory burst—and the production of neutrophil extracellular traps (NETs). Under a microscope, these look like a spider web or a net, trapping pathogens in them. This inflammatory response is well known and is characterized by increased blood flow, capillary dilatation, leukocyte infiltration, and the production of chemical mediators, which initiate the elimination of toxic agents and start the repair process of damaged tissues.[2] The resolution of inflammation is an active process with cytokines and other anti-inflammatory mediators; it is not only a switch that turns off proinflammatory pathways. It involves cytokines and other chemical mediators.[3,4]

Inflammation can be either a friend or a foe: It is an essential part of our innate immune response, or it can be a chronic low-grade inflammatory condition. This latter part is what is at the root cause of type 2 diabetes mellitus, CVDs, MetS, NAFLD, and others.[5,6]

We have known for more than 20 years that inflammation plays an important role in the pathophysiology of CVD. When arteries are damaged, inflammation is triggered and leukocytes infiltrate the area and release inflammatory mediators. Cytokines and chemokines promulgate atherosclerosis by formation of lipid-laden foam cell formation; they initiate the proliferation of smooth muscle cells; they increase the formation of chemokines, which stimulate further leukocyte mobilization; and they stimulate plaque instability and potential rupture.[7]

NAFLD is the most common liver disease in Western countries, and inflammation plays a direct role in its development. The National Health and Nutrition Examination Survey (NHANES) recently showed a 30% prevalence of NAFLD in the United States between 2011 and 2012. NAFLD is associated with insulin resistance, diabetes, obesity, dyslipidemia, and MetS. A study in the *World Journal of Gastroenterology* showed a link between NAFLD and soft drink consumption, mainly due to the artificial sweeteners used in these beverages. This disease ranges from benign steatosis to cirrhosis. In a simplified way, NAFLD starts with increased levels of fatty acids in hepatocytes with triacylglycerol (TAG) synthesis and decreased fatty acid oxidation. This results in a pro-oxidative and proinflammatory condition, which if unabated can result in fibrosis and cirrhosis. Hepatic inflammation is mediated by Kupffer cells, the local leukocytes.[8-10]

At a recent conference titled "The Gut–Brain Relationship Conference" sponsored by InnoVision Professional Media, a number of outstanding speakers discussed the latest findings of how the microbiota plays an essential role in our health, including the intimate and essential connection with our central nervous system (CNS). One aspect of the microbiota is the effect on the immune system and keeping gut permeability intact. Lipopolysaccharides are found on the outer membrane of Gram-negative bacteria and are an important inflammatory stimulant in the gut. However, in the elderly, there are more Gram-negative bacteria in the colon, thereby giving rise to increased gut permeability due to inflammation. Inflammation in the gut leads to a leaky gut, which then affects the CNS. The inflammatory response in our brain includes fever and behavioral and metabolic changes, which include fatigue, depression, problems with cognitive function, and others. The principal players are the microglia, the macrophages of the CNS, which induce interleukin (IL) 1β, tumor necrosis factor α, and PGE_2, all proinflammatory mediators.[11] In a recent prospective clinical study, patients with Alzheimer's disease were followed for 6 months. They were tested for circulating cytokine levels, episodes of microbial infections, and cognitive function. These patients had elevated levels of TNF-α at baseline: Any microbial infection showed a 4-fold decline in cognitive function. Alzheimer's disease patients also demonstrate apathy, agitation, anxiety and depression, along with elevated serum levels of TNF-α and IL-6, but, interesting, not C-reactive protein.[12,13]

Gut microbiota play an important role in autoimmunity, including type 1 diabetes mellitus, celiac disease, rheumatoid arthritis, and others. The incidence of autoimmune disorders has risen dramatically in the last several decades and affects 5% to 10% of the population. When a condition of gut permeability exists, antigens may be produced that mimic normal human proteins and trigger the abnormal production of autoantibodies.[12]

Our bodies were not made for this daily onslaught of toxins, infectious agents, and stress. These kinds of demands require much support to maintain the immune system's resilience. Our rapid, go-go, stressful lifestyle has shown what happens if we do not pay attention to what is in our environment: chronic inflammation leading to chronic diseases. All of us need to pay attention to what we breathe, eat, drink and absorb, and feel. If we do not, and if we do not help our patients do the same, for most of us the factors are skewed toward inflammation.

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