CLINICAL INVESTIGATION

Chronic inflammation plays a role in the genesis of disease throughout life

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Introduction

Although intermittent increases in inflammation are necessary for survival during physical injury and infection, recent research has revealed that certain social, environmental, and lifestyle factors can promote Systemic Chronic Inflammation (SCI), which can lead to a variety of diseases, including cardiovascular disease, cancer, diabetes mellitus, chronic kidney disease, and non-alcoholic fatty liver disease. In this Perspective, we discuss the multi-level mechanisms that underpin SCI as well as many risk factors that contribute to this health-damaging phenotype, such as infections, inactivity, poor diet, environmental and industrial toxicants, and psychological stress. We also propose prospective ways for improving the early detection, prevention, and treatment of SCI.

The immune system and inflammatory processes are engaged in a wide range of mental and physical health problems that dominate today's morbidity and mortality globally, according to one of the most important medical discoveries of the last two decades. Indeed, chronic inflammatory diseases have been identified as the leading cause of death in the world today, with inflammation-related diseases such as ischemic heart disease, stroke, cancer, diabetes mellitus, chronic kidney disease, Non-Alcoholic Fatty Liver Disease (NAFLD), and autoimmune and neurodegenerative conditions accounting for more than half of all deaths. Evidence is accumulating suggesting the risk of developing chronic inflammation may be traced back to early development, and that its consequences can last throughout a person's life, affecting adult health and mortality risk. We detail these consequences in this Perspective, as well as several possible routes for future research and intervention.

Inflammation is an evolutionary conserved process that involves the activation of immune and non-immune cells to defend the host from bacteria, viruses, poisons, and diseases by removing pathogens and encouraging tissue repair and recovery. Metabolic and neuroendocrine changes can occur to preserve metabolic energy and provide more nutrients to the active immune system, depending on the degree and intensity of the inflammatory response, including whether it is systemic or local. Specific bio behavioral impacts of inflammation include depression, anhedonia, weariness, decreased libido and food intake, altered sleep and social-behavioral disengagement, as well as increased blood pressure, insulin resistance, and dyslipidemia. In times of physical injury or microbiological threat, these behavioral adjustments can be crucial for survival.

When a threat is present, a typical inflammatory response is defined by a temporally limited elevation of inflammatory activity that develops and then resolves once the threat has passed. However, the presence of certain social, psychological, environmental, and biological factors has been linked to the prevention of acute inflammation resolution and, as a result, the promotion of a low-grade, non-infective (that is, 'sterile') Systemic Chronic Inflammation (SCI) characterized by the activation of immune components that are often distinct from those involved in an acute immune response.

Chronic systemic inflammation and the risk of non-communicable diseases

The acute inflammatory response differs from SCI, despite the fact that they share similar pathways. Most importantly, the acute inflammatory response is often triggered during infection by an interaction between pattern recognition receptors expressed on innate immune cells and Pathogen-Associated Molecular Patterns (PAMPs), which are evolutionarily conserved structures on pathogens. Damage-Associated Molecular Patterns (DAMPs) are generated in response to physical, chemical, or metabolic unpleasant stimuli-that is, 'sterile' agents-during cellular stress or

damage, and can initiate the acute inflammatory response. Following infection, chemicals such as lipoxins, resolvins, maresins, and protectins are produced, which help to resolve inflammation.

SCI, on the other hand, is usually induced by DAMPs in the absence of an acute viral insult or PAMP activation. Studies demonstrate that older people have higher quantities of cytokines, chemokines, and acute phase proteins in their blood, as well as higher expression of genes implicated in inflammation. Furthermore, SCI is low-grade and persistent (as the term implies), and it eventually causes collateral damage to tissues and organs, such as oxidative stress, over time.