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## How Obesity Sparks the Immune System and Lessons from the COVID-19 Pandemic

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Abstract: Purpose of Presentation: Obesity and overweight are among the biggest health challenges of the 21st century, according to the WHO. Obviously, obese individuals suffer different courses of disease - from infections and allergies to cancerand even respond differently to some treatment options. Of note, obesity often seems to predispose and triggers several secondary diseases such as diabetes, arteriosclerosis, or heart attacks. Since decades it seems that immunological signals gear inflammatory processes among obese individuals with the aforementioned conditions. This review aims to shed light how obesity sparks or rewire the immune system and predisposes to such unpleasant health outcomes. Moreover, lessons from the Covid-19 pandemic ascertain that people living with pre-existing conditions such as obesity can develop severe acute respiratory syndrome (SARS), which needs to be elucidated how obesity and its adjuvant inflammatory process distortion contribute to enhancing severe COVID-19 consequences. Recent Findings: In recent clinical studies, obesity was linked to alter and sparks the immune system in different ways. Adipose tissue (AT) is considered as a secondary immune organ, which is a reservoir of tissue-resident of different immune cells with mediator release, making it a secondary immune organ. Adipocytes per se secrete several pro-inflammatory cytokines (IL-6, IL-4, MCP-1, and  $TNF-\alpha$ ) involved in activation of macrophages resulting in chronic low-grade inflammation. The correlation between obesity and T cells dysregulation is pivotal in rewiring the immune system. Of note, autophagy occurrence in adipose tissues further rewire the immune system due to flush and outburst of leptin and adiponectin, which are cytokines and influencing pro-inflammatory immune functions. These immune alterations among obese individuals are collectively incriminated in triggering several metabolic disorders and playing role in increasing cancers incidence and susceptibility to different infections. During COVID-19 pandemic, it was verified that patients with pre-existing obesity being at greater risk of suffering severe and fatal clinical outcomes. Beside obese people suffer from increased airway resistance and reduced lung volume, ACE2 expression in adipose tissue seems to be high and even higher than that in lungs, which spike infection incidence. In essence, obesity with pre-existence of pro-inflammatory cytokines such as LI-6 is a risk factor for cytokine storm and coagulopathy among COVID-19 patients. Summary: It is well documented that obesity is associated with chronic systemic low-grade inflammation, which sparks and alter different pillars of the immune system and triggers different metabolic disorders, and increases susceptibility of infections and cancer incidence. The preexisting chronic inflammation in obese patients with the augmented inflammatory response against the viral infection seems to increase the susceptibility of these patients to developing severe COVID-19. Although the new weight loss drugs and bariatric surgery are considered as breakthrough news for obesity treatment, but preventing is easier than treating it once it has taken hold. However, obesity and immune system link new insights dispute the role of immunotherapy and regulating immune cells treating diet-induced obesity.

**Keywords:** immunity, metabolic disorders, cancer, COVID-19

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