Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

Physical activity for immunity protection: Inoculating populations with healthy living medicine in preparation for the next pandemic

Physical activity (PA) represents one of the primary pillars of health living and is thus a primary component of healthy living medicine[1]; PA is consistently shown to dramatically reduce the risk for developing systemic inflammation, excess body mass and non-communicable diseases known to compromise immune function.[2] In the context of the novel coronavirus outbreak, questions regarding the potential role of PA as an immune function adjuvant to reduce risk of communicable disease (e.g., bacterial and viral infections) have increased appreciably. The general consensus across the exercise immunology literature suggests that the immune system is responsive to exercise, however adaptations to immune system responses to exercise depend on the intensity and duration of effort and type of exercise.[3,4] Following the 2009 H1N1 influenza epidemic, mounting epidemiological evidence has demonstrated a dose-response relationship between PA performed before infection and a reduction in the incidence, duration, or severity of self-reported[5–7] and laboratory or hospital adjudicated[8,9] acute upper respiratory tract infections (URTI). Additional investigations have noted that the lower rate of URTI (weighted mean reduction, ~28%) is associated with regular engagement in moderate-to high-PA levels as compared to lower PA levels.[6,7,10] Significant reductions in mortality risk attributed to respiratory disease, pneumonia, and aspiration pneumonia has also been reported in runners, including those with diabetes.[11] While additional high-quality studies are needed to confirm the robust effectiveness of exercise in altering infection prognosis,[12] more consistent evidence from randomized clinical trials in adults have shown appreciable reductions in the symptom days during an infectious episode.[5,13,14] Appropriately, a growing body of research from experimental studies and animal models have aimed to elucidate the potential mechanism of action underlying the protective effect of moderate-intensity PA against viral respiratory infections. One of the main mechanisms responsible for the immune adaptations to PA appears to be increased immunosurveillance. Briefly, each session of moderate-intensity PA stimulates an increase in the antipathogen activity of immune system macrophages in conjunction with temporary increases in the recirculation of key immune system cells, immunoglobins and anti-inflammatory cytokines in the blood, together resulting in a reduced influx of inflammatory cells into the lungs and decreased pathogen load. Concurrently, subtle elevations in stress hormones released from skeletal muscle, notably interleukin-6 (IL-6), is observed during acute bouts of moderate-intensity exercise; however, the pleiotropic nature of IL-6 appears to provide protection (versus harm) to immunity via directly suppressing potent inflammatory cytokines [e.g., tumor necrosis factor-alpha (TNF-a)] in the lungs, creating an anti-inflammatory milieu for several hours post-exercise. Over time, these transient changes in cell mediated immunity that occur after each bout of moderate-intensity PA are proposed to contribute to enhancing immunosurveillance against infectious pathogens and protect or attenuate symptomatology of infectious diseases.[3,15] Of note, caveats to the exercise-immunity have been proposed as inappropriate exercise regimens consisting of prolonged bouts and/or high-intensity training without adequate rest that may cause immunodepression and increase susceptibility to infectious pathogens and illness.[3]

As history has taught us from the 2009 H1N1 Influenza A Virus pandemic, obesity, old age, and pre-existing chronic morbidity identifies populations who are the most vulnerable to infectious disease.[16,17] Obesity in and of itself is associated with a constant state of low-grade inflammation and immune dysfunction that is presumably due to the increased production and release of pro-inflammatory cytokines from surrounding tissues. Subsequently, there is a large body of cross-sectional evidence that supports an association between PA and lower levels of varying inflammatory biomarkers in overweight or obese individuals. Comparatively, current findings from clinical interventions demonstrating the anti-inflammatory effects of routine exercise training in obese populations are inconsistent, as it is remains unclear whether reductions in chronic inflammation with exercise training are independent of fat or weight loss.[18,19] Other potential explanations for discrepancies across studies include differences in the type and length of exercise training, types of biomarkers studied and prevalence of other chronic diseases, which may otherwise confound the training effect of exercise on inflammation.[18] A better understanding of the mechanisms by which exercise mediates inflammation may lend support for its immune supporting role in obesity. Emerging evidence from mice models indicate that moderate-intensity exercise prior to an infection may improve immune responsiveness to infectious pathogens and minimize infection severity by reversing several impairments in host immunity that occur as a consequence of an obesity-induced inflammatory state.[20] Routine exercise has also been shown to amplify antioxidant defense responses which may in turn augment immunosurveillance. Other mechanistic studies suggest that the immunomodulating effects of exercise are partly mediated by IL-6 which, as stated above, takes on an anti-inflammatory role during exercise[4,18] that helps to stimulate fat oxidation and reduce abdominal visceral fat mass.[21] Moreover, metabolic adaptations associated with routine exercise, including improvements in glucose, insulin and lipid metabolism, and reduced insulin resistance provide further support for obese and diseased populations to engage in regular bouts of moderate-intensity exercise, when not contraindicated, as an adjuvant for immune and metabolic support.

Special considerations regarding exercise and immune health must be addressed for older adults who represent the fastest growing population, both in the US and globally, and incidentally are the most sensitive to developing infectious disease, including the most recent coronavirus outbreak.[22] In fact, influenza and pneumonia are rated among the top ten leading causes of death among older adults aged

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65 years or older,[23] emphasizing the importance of maintaining immune function and competency during aging. Immunosenescence described robustly as the phenomenon responsible for the inextricable deterioration of immune competency that occurs with increasing age, is believed to be the primary factor explaining the lowered immune vigilance, poorer responses to vaccinations and the greater risk, and morbidity, associated with infectious diseases.[24] Given the known beneficial effects of habitual exercise on aspects of immunity in younger populations, PA is suggested to be a logical therapeutic strategy to moderate the effects of aging on the immune system and counteract the detrimental effects of immunosenescence. This contention is well supported by a growing body of evidence from epidemiological and experimental and studies in older adults indicating that regular participation in moderate-intensity exercise attenuates age-related oxidative stress and reduces the frequency of various immune biomarkers that are associated with compromised immunity, thereby suggesting that exercise may delay the onset of immunosenescence and attenuate the risk of infection.[24–26] Building on this hypothesis, older adults aged 66–84 years who regularly engaged in PA were observed to have a lower incidence of URTI and a reduced duration of infectious days at one year follow up. Not surprising, however, dose-response associations between PA and infection risk were noted, with the lowest risk of infection reported in adults reporting the highest level of PA and the highest risk among those in the lower PA category.[27] Reductions in infection symptomatology have also been evidenced in a structured moderate-intensity PA program delivered to older adults over 10 months.[28] Finally, regular exercise has also been shown to improve responses to vaccinations.[29] While the paucity of sufficient clinical and longitudinal studies limit our understanding of whether exercise can effectively restore immune function during aging, preliminary evidence to date reliably demonstrates that regular PA can enhance aspects of the immunity (e.g., immune competency) and limit immune cellular changes that contribute to immunosenescence.

In conclusion, PA is well-established as an essential component of healthy living medicine for the prevention and treatment of chronic diseases and for the overall maintenance of physical and mental health and wellbeing.[2] Literature in the field of exercise immunology has additionally supported the role of PA as a potent stimulus of immune function. In the face of this novel coronavirus pandemic, the World Health Organization,[30] the Centers for Disease Control and Prevention[31] other public health advisory organizations[32,33] are encouraging individuals to initiate or continue regular engagement in PA to maintain physical and mental health and wellbeing when not contraindicated and while abiding to public health and community safety. The major key points described in this commentary expand on the benefits of PA with well supported evidence demonstrating the potency of regular PA in enhancing immune function and reducing the risk, duration or severity of viral infections. The most consistent evidence suggests routine participation (~150 min per week) of moderate-intensity physical is necessary to achieve optimal immune support. However, even acute bouts of PA have shown to provide protection from viral infections, therefore supporting the notion that just moving more in the form of structured activity each day may be an important strategy for optimizing the functional integrity of the immune system to prevent or attenuate severity of infection, especially among vulnerable populations with immune-compromised conditions.

Statement of conflict of interest

None of the authors have any conflicts of interests with regard to this publication.

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