

MAYO CLINIC  
PROCEEDINGS

## In the Limelight: May 2022

This month's feature highlights four articles that appear in the current issue of *Mayo Clinic Proceedings*. These articles are also featured on the *Mayo Clinic Proceedings'* YouTube Channel (<https://youtu.be/4EbNJeIxcTw>).

**PSYCHE AND SOMA REDUX: MENTAL STRESS AS A DETERMINANT OF CARDIOVASCULAR DISEASE**

The interplay between the psyche and soma in general, and the extent to which debilitation and disease in one adversely affect the welfare of the other in particular, is of longstanding and mounting interest. In the current issue of *Mayo Clinic Proceedings*, Sara et al discuss this dyad from the perspective of mental stress as a determinant of vascular disease. The authors summarize the salient findings regarding cardiovascular outcomes observed in prospective cohort studies published in the literature from 1990 onwards in which mental stressors were imposed. From this analysis, some studies inferred that a greater sensitivity to or impact from mental stress may be a harbinger for worse cardiovascular outcomes. In assessing these studies, Sara et al appropriately emphasize the distinction between acute and chronic stress as the former may induce acute hemodynamic, inflammatory, and other immediate responses, whereas the latter may lead to the steady accretion of pathologic changes that culminate in cardiovascular disease. How the latter occurs is uncertain, but a critical proximate event appears to be injury to the vasculature for at least two reasons. First, based on a summary of cross-sectional studies that assess peripheral vascular reactivity, it may

be inferred that these responses are affected by mental stress, and that such vascular responses may be abnormal, in particular, in individuals with cardiovascular risk factors or disease. Second, a critical pathogenetic process early in the course of virtually all cardiovascular diseases is endothelial dysfunction; this abnormality impairs vasorelaxant responses and leads to a proinflammatory, proadhesive, and prothrombotic endothelial phenotype. Each of these components of endothelial dysfunction is potentially vasculopathic. What then is the concatenation of processes that link endothelial dysfunction back to mental stress? This efferent arc, as envisioned by the authors, is as follows: mental stress leads to sequential activation of the cerebral cortex, the limbic system and its constituent amygdala, and engagement of and outflow from the hypothalamic-pituitary-adrenal axis; increased production of catecholamines and corticosteroids; activation of the renin-angiotensin-aldosterone axis; derangements in lipid metabolism; increased sympathetic output; and decreased parasympathetic activity. Such effectors along with the attendant systemic inflammation and immune responses all converge onto the vasculature and, through a plethora of pathways, lead to endothelial dysfunction. Repetitive targeting of the endothelium and the vasculature by these processes occasioned by intermittent mental stress, in time and in aggregate, leads to overt disease in the central and peripheral vasculature. The authors conclude by emphasizing the need for studies on mental stress that are cognizant of the pathobiologic differences of acute and chronic stress; and for studies that are applicable and



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generalizable to the “real world” setting of cardiovascular disease, the latter commonly multifactorial in its origins. The authors also conclude by discussing therapeutic strategies that target mental stress (including meditation and cognitive and behavioral treatment) and those that interrupt the occurrence of endothelial dysfunction. This timely review is important for multiple reasons. First, it draws attention to a poorly recognized but likely driver for cardiovascular disease, and one that may be targeted by appropriate strategies. Second, it underscores that there is more to the accounting of cardiovascular disease than the current complement of traditional risk factors; indeed, in this issue of *Mayo Clinic Proceedings*, these authors also extend their previous studies and demonstrate the fascinating and unexpected association of a non-invasive voice biomarker with incident coronary artery disease and its prognosis. And, third, while life stressors are clearly unavoidable, our response to them may be tractable, at least in part; such tractability and our success in consistently allaying the impact of attendant mental stress may influence our cumulative and long-term risk for cardiovascular disease.

Sara JDS, Toya T, Ahmad A, et al. Mental stress and its effects on vascular health. *Mayo Clin Proc.* 2022;97(5):951-990.

Sara JDS, Maor E, Orbelo D, et al. Noninvasive voice biomarker is associated with incident coronary artery disease events at follow-up. *Mayo Clin Proc.* 2022;97(5):835-846.

#### INCREASING PHYSICAL ACTIVITY AND DECREASING ADIPOSITY: BETTER LATE THAN NEVER

There is a general consensus regarding the salutary effects of adequate amounts of physical activity and limited adiposity. Ahmadi et al used data from the UK Biobank to probe the issue whether a relatively delayed increase in physical activity or decrease in body mass index (BMI) and adiposity still exerts beneficial effects on all-cause mortality and incident cardiovascular disease. Physical activity, BMI, and body fat

were assessed at baseline and after an average follow-up of 7 years. Physical activity was categorized either as inactive, insufficient, or sufficient, the latter two categories based on a cutoff of 150 minutes of moderate- to vigorous-intensity physical activity/week; physical activity was additionally classified as decreased, stable, or increased, as judged from baseline values. BMI and adiposity were categorized as decreased, stable, or increased at follow-up. The essential findings were that individuals who increased their physical activity to the sufficient category at follow-up exhibited all-cause mortality and incident cardiovascular disease that were not only lower as compared with the stable-insufficient group, but, indeed, matched these indices in the category with sufficient physical activity at both time points. These findings were observed across the 3 categories of BMI and adiposity. While the associations between adiposity *per se* and these outcomes were less consistent as exhibited by physical activity, incident cardiovascular disease in obese and overweight individuals who reduced their BMI category was similar to what was observed in the group with an acceptable BMI at both time points. In analyses that combined changes in physical activity and adiposity, the group with decreasing adiposity and increasing physical activity exhibited reduced all-cause mortality and incident cardiovascular disease as compared with the group with stable physical activity and adiposity. These findings indicate that increasing physical activity and decreasing adiposity confer salutary effects when undertaken and successfully incorporated even at a relatively later stage in life. Oscar Wilde famously wrote that “...every saint has a past, and every sinner has a future,” a statement that emphasizes, at least in one interpretation, the ever available opportunity for and the benefits of wise and welcome change. Increasing physical activity and decreasing adiposity are two wise and welcome lifestyle/behavioral changes that are better late than never.

Ahmadi MN, Gill JMR, Stamatkis E. Association of changes in physical activity and

adiposity with mortality and incidence of cardiovascular disease: Longitudinal findings from the UK Biobank. *Mayo Clin Proc.* 2022;97(5):847-861.

#### DEFICIENCY OF PSYCHIATRY SERVICES IN THE ACUTE CARE SETTING IN THE UNITED STATES

The review entitled “Care of the Psychiatric Patient in the Emergency Department,” by the American College of Emergency Physicians in 2014 begins with an overview of such salient issues as: the increasing numbers of patients with psychiatric illnesses; the declining number of dedicated hospital beds for psychiatric patients; the directing of such care to outpatient settings which are limited in their capacity and resources for such care; and, in turn, the growing numbers of patients seeking acute psychiatric care in emergency departments (EDs), the latter challenged in providing such care by their inherent organizational structure, delays, and various regulatory requirements (<https://bit.ly/3ivh3c1>). The present findings of Ellison et al underscore the deficiency of psychiatric services in the ED and the inpatient setting. In their telephone survey of 2394 US hospitals, 54% of hospitals did not provide psychiatrists for consultation in the ED or inpatient services, and for those patients with psychiatric issues

requiring hospital admission, some 60% of hospitals transferred them to another hospital, with approximately half of these patients admitted to a medical inpatient service. The lack of availability of psychiatrists for consultation was higher in rural hospitals (70%), in hospitals with fewer beds, and in for-profit and government-owned hospitals. In their discussion, Ellison et al highlight, among other considerations, reimbursement and administrative issues that may underpin their findings, the adverse effects of such deficiency of psychiatric service, and the extent to which telepsychiatry may mitigate such deficiencies. The present findings of Ellison et al and the broader unsettling landscape of the provision of acute psychiatric care in the United States are, to say the least, quite sobering. Surely, the US health care system can and should do so much more for individuals afflicted with the tragedy of mental illness, with all its attendant tribulations and hardships.

Ellison AG, Jansen LAW, Nguyen F, et al. Specialty psychiatric services in US emergency departments and general hospitals: results from a nationwide survey. *Mayo Clin Proc.* 2022;97(5):862-870.

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