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This month's feature highlights three 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/NF5I–eAQs4).

THE LONG SHADOW OF CHRONIC DISEASE CAST BY HYPERTENSIVE DISEASES IN PREGNANCY

Normal pregnancy requires a range of adaptive responses in diverse systems, including, in particular, the cardiovascular system. These cardiovascular responses encompass increased cardiac output, systemic and regional vasodilation, systemic and regional hyperperfusion, and an expansion of the blood volume and extracellular fluid; this vasorelaxed state of normal pregnancy is attended by a reduction in systemic blood pressure. These adaptive cardiovascular responses are geared to the optimization of delivery of oxygen and nutrients to the uteroplacental unit and the growth and development of the fetus. Hypertensive diseases in pregnancy (HDP) of which there are 4 main types — chronic hypertension, gestational hypertension, pre-eclampsia/eclampsia, and chronic hypertension with superimposed pre-eclampsia — compromise these adaptive vascular responses needed for a normal pregnancy, and, not unexpectedly, may predispose to maternal and fetal morbidity and mortality. However, the adverse effects of HDP on the mother are not limited to the pregnancy state as there is clear evidence that women with HDP are predisposed to cardiovascular and cerebrovascular disease in later life. But what about the risks of chronic kidney disease (CKD) in later life, the healthy kidney being an organ *par excellence* that evinces pronounced adaptive vascular responses in normal pregnancy? This question is addressed by the study by Oshunbade et al in the current issue of *Mayo Clinic Proceedings*. Their study utilized the Genetic Epidemiology Network of Arteriopathy (GENOA) of the National, Heart, Lung, and Blood Institute Family Blood Pressure Program. The objective of the GENOA study was to explore the genetics and target organ effects of systemic hypertension. This study recruited sibships with hypertension in at least 2 siblings manifested before the age of 60 years, and included as well the study of normotensive members of the sibship. The study included non-Hispanic Whites from Rochester, Minnesota, and African-Americans from Jackson, Mississippi. A history of HDP, pre-eclampsia, and proteinuria during pregnancy was obtained by a validated standard questionnaire. Glomerular filtration rate was determined by the urinary clearance of iothalamate, and such mGFR measurements were undertaken in 725 women, with history of normotensive pregnancies, hypertensive pregnancies, and pre-eclampsia present in 544, 102, and 17 women respectively. CKD was defined as a GFR that was less than 60 ml/min per 1.73 m^2 or a urine albumin-creatinine ratio that was greater than or equal to 30 mg/g. Women with hypertensive pregnancies, as compared with women with normotensive pregnancies, had a lower mGFR, a higher odds of having an mGFR of less than 60 ml/min per 1.73 m^2, and a higher odds for CKD following adjustments for various factors that included age, race, body mass index, diabetes, hypertension, smoking, and education.

The basis for this occurrence of CKD long after HDP is unclear, but the following speculation is offered. Hypertensive diseases

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in pregnancy incur, as for hypertension in general, the occurrence of endothelial dysfunction, the latter characterized by impaired endothelium-dependent relaxation and a propensity towards a proinflammatory, procoagulant, "activated" endothelial phenotype. Such endothelial abnormalities may be further exacerbated by the hemodynamic stress imposed by the systemic and regional hyperperfusion occurring in a hypertensive pregnancy; this is in contrast with the innocuousness of hyperperfusion occurring in a nonhypertensive normal pregnancy with a healthy endothelium. The adverse consequences of endothelial dysfunction in conjunction with systemic hypertension may be manifested, in particular, in organs that are highly vascularized and endothelium-enriched such as the kidney. Pathogenetic pathways, instigated and imprinted during HDP, and targeting and hemodynamically stressing the abundant endothelium in the renal vasculature and glomerular and tubulointerstitial compartments, are thereby entrained, and will continue to smolder in these major renal compartments long after pregnancy; CKD is thus variably manifested in ensuing years after pregnancy.

The strengths of this study by Oshunbade et al are multiple and include the following: its use of the GENOA database; the relatively large sample size; the determination of GFR by urinary iothalamate clearance; and a cohort that included both African Americans and White patients. This timely study adds important new evidence that HDP casts a long shadow of disease which extends way beyond the pregnancy itself and may culminate, specifically, in CKD.

Oshunbade AA, Linette ST, Windham BG, et al. Hypertensive diseases in pregnancy and kidney function later in life: the genetic epidemiology network of arteriopathy (GENOA) study. *Mayo Clin Proc*. 2022;97(1):78-87. doi.org/10.1016/j.mayocp.2021.07.081.

OSTEOPOROSIS IS GENERALLY ATTENDED BY WORSE OUTCOMES IN MEN AS COMPARED WITH WOMEN

Osteoporosis, the most common metabolic bone disease, and one considerably more prevalent in women as compared with men, is attended by an increased risk for fractures, frailty, and an impaired quality of life. As pointed out by Rodriguez-Gomez et al in their study of osteoporosis in the current issue of *Mayo Clinic Proceedings*, most studies that have examined the association of osteoporosis with morbidity and mortality have largely involved women rather than men, especially older, postmenopausal women. To examine the sex-specific associations of osteoporosis with morbidity and mortality, Rodriguez-Gomez et al utilized the UK Biobank Prospective Cohort Study. The UK Biobank study seeks to elucidate the development of disease as it relates to lifestyle, the environment, and genetic determinants, by the long-term follow-up of approximately half million participants from the general population in England, Scotland, and Wales. Participants were recruited between 2007 and 2010, with ages ranging from 37 to 73 years old. Using this repository of data, Rodriguez-Gomez et al demonstrate, not unexpectedly, osteoporosis was more likely to occur in individuals who were older, underweight, prescribed corticosteroid, or have a number of comorbidities. The occurrence of osteoporosis in men was associated with increased risk for mortality from all causes, cardiovascular disease, and respiratory disease (including chronic obstructive pulmonary disease), even after adjusting for age, BMI, and comorbidities. The occurrence of osteoporosis in women was attended by an increased mortality risk from respiratory diseases and breast cancer, and an increased risk of cardiovascular and respiratory disease. In distilling the salient findings of their analysis, Rodriguez-Gomez et al emphasize that osteoporosis occurring in men, as compared with women, is attended by a greater range of adverse outcomes, with more statistically robust associations. As men are generally less likely as compared with women to develop osteoporosis, this finding by Rodriguez-Gomez et al suggests that a more inimical disease occurs in men once those factors/mechanisms that confer relative resistance to osteoporosis in men are abrogated for whatever reason. Osteoporosis, so often a silent disease that lurks unnoticed, often

manifests itself when fractures occur. As made clear by this study by Rodriguez-Gomez et al such silence masks a disease with risks that go way beyond fractures to include diverse morbidities and increased mortality, outcomes that may be worse in men.

Rodriguez-Gomez I, Gray SR, Ho FK, et al. Osteoporosis and its association with cardiovascular disease, respiratory disease, and cancer: findings from the UK Biobank Prospective Cohort Study. *Mayo Clin Proc*. 2022;97(1):110-121. doi.org/10.1016/j.mayocp.2021.17.019.

COMMUNICATING WITH CLINICIANS IN TIMES OF A PANDEMIC AND BURNOUT

The COVID-19 pandemic imposes added and particular stresses on caregivers and clinicians, the latter as a group already challenged by a preexisting and prominent public health crisis - clinician burnout. In the present issue of *Mayo Clinic Proceedings*, Palamara and Sinsky address how best to support clinicians during the current phase of the COVID-19 pandemic, and one which has left in its wake rising concerns about increasing clinician burnout. This perspective of these authors draws upon experiences that accrued during Massachusetts General Hospital's Department of Medicine listening sessions for clinicians held between May 2020 and March 2021, and their analysis of data of the AMA COVID Caring for Caregivers initiative. This perspective is addressed to health care leaders and offers for them a semi-structured strategy based on 4 salient questions that ask clinicians how they have been affected by the pandemic, what makes them feel valued, what are the impediments in achieving pride and joy in their professional activity, and what can be done to remedy this. For each of these 4 questions, Palamara and Sinsky provide a number of illustrative responses that illumine the range and adverse impact of the specific issue. These reflections and suggestions of Palamara and Sinsky are important and timely because they may enable effective communication with clinicians; reaffirm their value and contributions to health care; identify how their professional and personal lives have been adversely affected; outline ways that make them feel appreciated; delineate constraints and challenges that diminish their sense of satisfaction and professional fulfilment; reaffirm their trust and belief that health care leadership is committed to them in tangible and meaningful ways; and, most importantly, identify specific issues that need to be addressed and specific resources provided such that their professional work and contributions recover and enkindle a sense of personal accomplishment, pride, and joy.

Palamara K, Sinsky C. Four key questions leaders can ask to support clinicians during the COVID-19 pandemic recovery phase. *Mayo Clin Proc*. 2022;97(1):22-25.

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