Immunity, Inflammation, and Prehypertension: In What Order?

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The importance of the immunity and inflammation in hypertension has been observed for the past 4 decades.[1] Recently, a proinflammatory cytokine—interleukin (IL) 17, produced by TH_{17} cells—appears to be a consistent characteristic of local tissue inflammation, particularly in the lung, joint space, central nervous system, and intestinal tissue.[1,2] Considering that immune- and inflammatory-mediated responses play a role in cardiovascular diseases, Yao and colleagues[3] investigated the relationship between IL-17 and the prehypertension state. Their cross-sectional study enrolled 394 adults aged 40 to 70 years from Tianjin City, China. Optimal and prehypertension stages were defined according to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure.[4] In addition to providing evidence regarding well-known personal characteristics related to increased blood pressure (BP; ie, age, sex, lifestyle, body anthropometry, blood chemistry, renal function), the analyses revealed higher median levels of IL-17 in patients with prehypertension than in the group with optimal BP (7.0 ng/L vs 5.10 ng/L, respectively; $P<.01$). Additionally, linear regression modeling showed a positive relationship between IL-17 and systolic BP ($P<.01$) after controlling for personal (age and sex) and anthropometric variables (body mass index and waist circumference), lifestyle (smoking and drinking), metabolic diseases (diabetes mellitus and dyslipidemia), and other factors. Collectively, these findings further support that vascular inflammation is associated with the prehypertension stage.

Prehypertension is defined as systolic and diastolic BP values between 120 to 139 mm Hg and 80 to 89 mm Hg, respectively.[4] Clinically, it may be interpreted as a scenario in patients with increased risk of developing more severe sustained hypertension and/or target organ damage (TOD) as compared with persons with optimal BP (<120 mm Hg and <80 mm Hg).[4] Like most "silent" diseases, the early stages of hypertension are difficult to detect and prehypertension may mask hypertension[5] because the clinical horizon of hypertension might be years away from its inception. Following the model of the natural history of this disease, the presymptomatic stage is not clearly separated from the clinically manifested disease since the presence of the majority of—if not all—symptoms of hypertension are not statistically associated with BP levels but rather with TOD.[6]

Recent advances in interventions for controlling BP have taken place within the last decades, but the optimal therapeutic strategy encompassing the immune and inflammatory systems are yet to be derived and it is currently a hot topic for research in cardiology.[7] Prehypertension is a health status in which lifestyle changes are of major importance as compared with drug treatment or other interventions.[4] In addition to major improvements in interventions for treating and rehabilitating patients with hypertension—including immediate drug medication and cardiac rehabilitation—the role of health promotion in preventive medicine has been strengthened over time. As recently proposed, the therapeutic strategy in approaching patients with hypertension should be "the earlier the better to treat who and what are not yet ill."[8] In this sense, the results by Yao and colleagues[3] showing high immune and inflammatory activity marked by IL-17 in patients with prehypertension as compared with persons with optimal BP reinforces that the early recognition of altered immune and inflammatory function is possible. Most importantly, the increase in odds ratios among quartiles of IL-17 shows a clear relationship between this immune biomarker and prehypertension. It is worth noting that prehypertension is no longer an adult-only health problem: its incidence in children and adolescents has increased in the past years.[9] Collectively, these data strengths the need to detect persons with prehypertension who are at high risk for TOD as early as possible, in whom immediate intervention may be of increased benefit.[5]

The study by Yao and colleagues[3] provided interesting evidence on the relationship between IL-17 and prehypertension using cross-sectional data adjusted for confounders for cardiovascular disease. Their data also support the hypothesis by Harrison and colleagues[1] that triggering stimuli that increase BP to prehypertension levels (eg, increased angiotensin II or sodium intake) are followed by immune and inflammatory responses. According to this hypothesis, IL-17 would be released by T cells and through a mechanism in which increased peripheral artery resistance and arterial remodeling generates a more severe hypertension grade. However, as a result of the cross-sectional design of the study by Yao and colleagues it is not possible to infer the cause-effect relationship between IL-17 and prehypertension or in what order those events might have occurred.[10] Unveiling this order comprises a challenge for research and likewise a big step toward the understanding of the natural history of hypertension. Nonetheless, the present evidence reinforces that the immune system should

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be considered in the comprehensive assessment of patients at high risk for developing hypertension.

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