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A New Look At the Mosaic Theory of Hypertension

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Despite extensive research, the pathogenesis of hypertension is still elusive. Although the origin is known in less than 5% of patients, the majority of patients have primary hypertension when identifiable cause(s) remain unknown. However, what is clear is that the pathophysiology of primary hypertension is multifactorial, multifaceted, and highly complex and includes several interacting physiological systems. This was highlighted more than 70 years ago,¹ when Irving H. Page suggested in his “mosaic theory” that hypertension is a disease of “dysregulation” that involves multiple interacting elements (black elements, Figure 1). This was subsequently conceived as an octagon with regulators on each point, connected by arrows. This paradigm was refined 32 years later² to include genetic, environmental, anatomic, adaptive, neural, endocrine, humoral, and hemodynamic factors as the pivotal components of the octagon (blue elements, Figure 1).

Since then, there has been enormous progress in unravelling molecular, cellular, and organ-system mechanisms that underlie hypertension. Moreover, it has become evident that the development of primary hypertension, from early to established and advanced stages, involves a range of cardiovascular and renal mechanisms ranging from the dysregulation of fetal/neonatal renal programming, the elevation in cardiac output that is characteristic of the elevations in blood pressure in adolescents and young adults, to the increased peripheral resistance that is the hallmark of established and advanced hypertension.

With advancements in hypertension research, it has become necessary to reconsider the comprehensiveness of the hypertension mosaic. This was highlighted in 2013 in a paper

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entitled The Mosaic Theory Revisited.³ In the current issue of the *Canadian Journal of Cardiology*, we further develop the concept with a collection of reviews focusing on some new aspects (red elements, Figure 1) related to genomics;⁴ sex hormones;⁵ the sympathetic nervous system;⁶ the brain aminopeptidase system;⁷ hyperinsulinemia and insulin resistance;⁸ oxidative stress;⁹ inflammation;¹⁰ the angiotensin AT2 receptor;¹¹ and structure, mechanics, and function of the vasculature.¹²

This compendium of reviews, together with the 2 papers on hypertension guidelines,^{13,14} provides state-of-the art knowledge that will keep the reader abreast of the complexities associated with hypertension.

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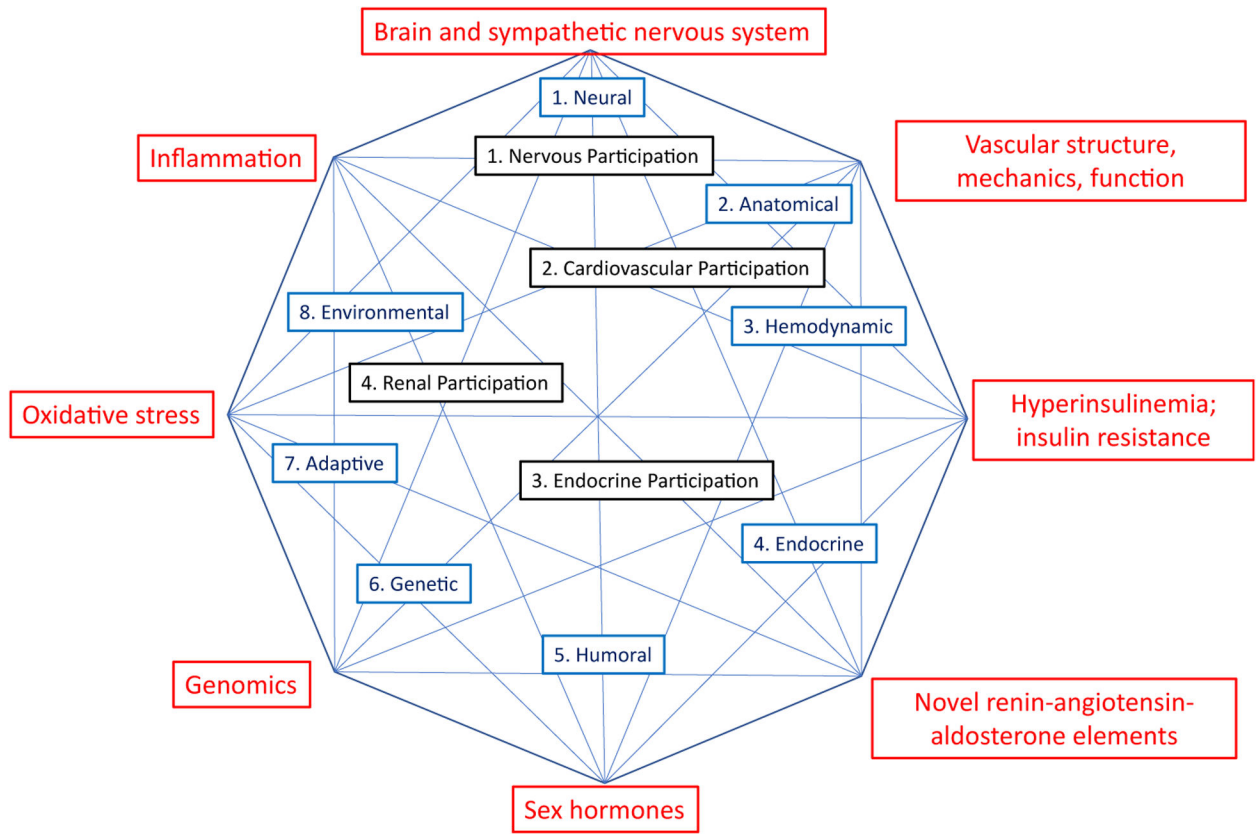


Figure 1. Different aspects of Irving Page’s mosaic theory of hypertension revisited in this compendium. The 4 **black** elements are the principal components mentioned in the original 1949 paper.¹ The 8 **blue** components are enumerated in the subsequent, more extensive revisiting of the theme in 1982.² The 8 **red** components are themes dealt with by review papers in the current issue of the *Canadian Journal of Cardiology*.