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Hypertension New Frontiers

A Textbook of Cardiology

Editors-in-Chief

HK Chopra (India) • Navin C Nanda (USA) • Jagat Narula (USA)
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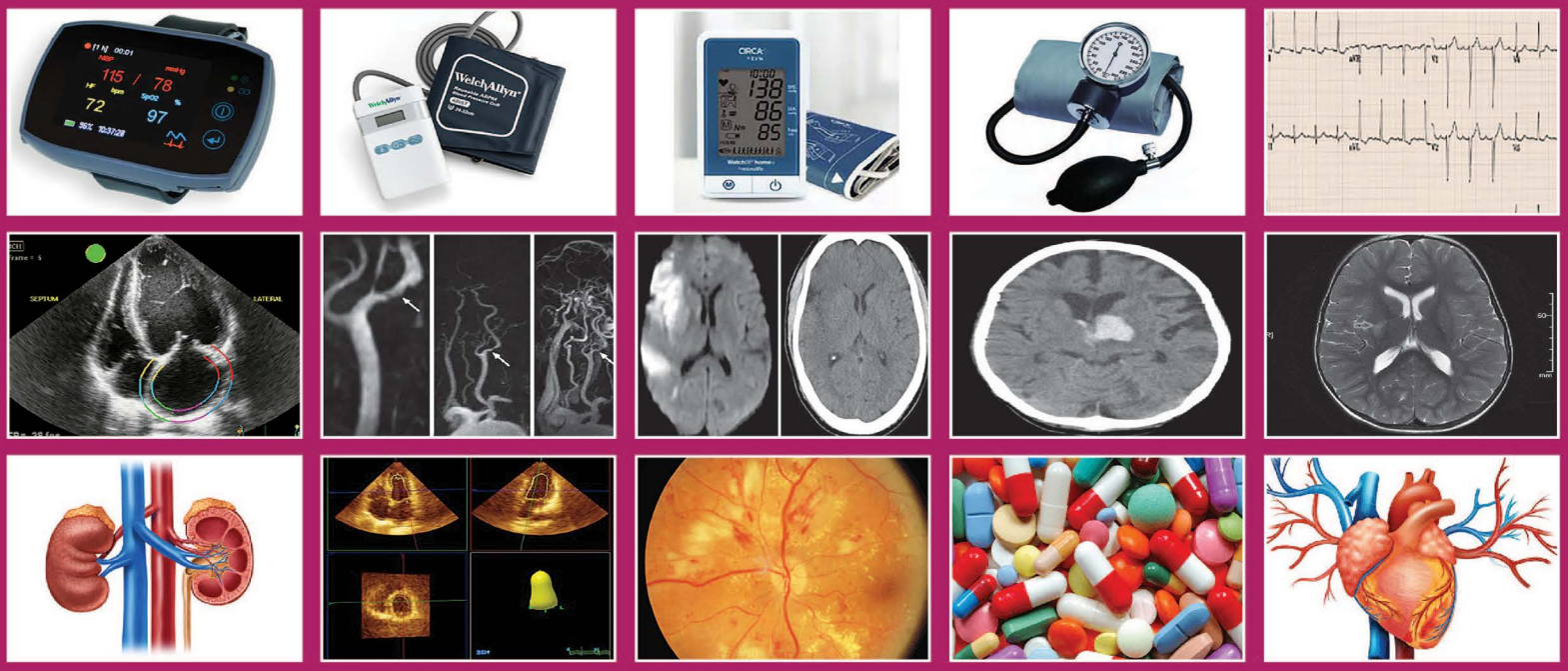

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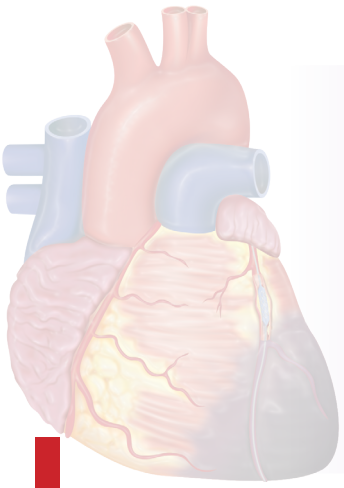

Pathophysiology of Hypertension

Hanumanth K Reddy, Ravi Komatireddy, Mohammad Ijaz, Geetha Komatireddy

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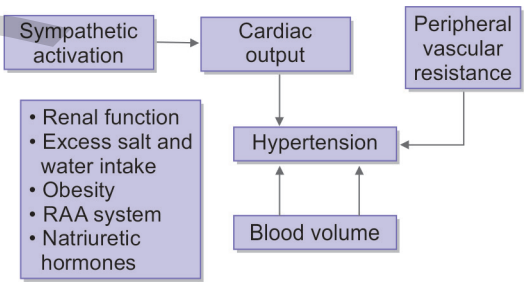
INTRODUCTION

Arterial hypertension is a chronic systemic disorder manifested as high blood pressure with profound health consequences. Hypertension is multifactorial in origin with one or more factors derailing the complex and delicate homeostasis responsible for normal blood pressure. With appropriate work-up, the predominant contributors of hypertension can be identified and therapeutically targeted. Treatment of hypertension should be individualized, because hypertension has multiple origins and targets different organs in different patients. It is not clear why hypertension targets different organs in different individuals. Interestingly, some organ systems such as heart, vascular system, and kidney are both contributors and victims of hypertension. A single or multiple of array of factors play a role in hypertension and these include genetic predisposition, activation of autonomic nervous system, upregulation of sympathetic nervous system (SNS), stimulation of renin–angiotensin–aldosterone system (RAAS) and antidiuretic hormone (ADH), and obesity-deconditioning and dietary excesses involving abuse of salt and water intake **(Flowchart 1)**.

Primary hypertension is the predominant type of hypertension associated with 95% of the patients. About 5% of patients have secondary hypertension with one of the following causes:

- Cushing's disease
- Renal artery stenosis
- Hyperaldosteronism
- Chronic kidney disease

Flowchart 1: Pathophysiology of hypertension.



- *Adrenal diseases:*
  - Cushing's disease
  - Conn's syndrome
  - Pheochromocytoma
- Sleep apnea
- Familial hypertension with hyperkalemia
- Liddle's syndrome where hypertension is associated with low plasma renin and aldosterone levels.

COMPONENTS AND SUBSTRATES OF HYPERTENSION

It is important to understand the three important components of hypertension: (1) blood volume, (2) cardiac output, and (3) peripheral vascular resistance **(Fig. 1)**. One or more factors such as fluid overload, hyperdynamic cardiac function, and increased peripheral resistance feed these components to cause hypertension.

For all practical purposes, all hypertension patients can be categorized into one of four subtypes as depicted in **Figure 2**. This type of pathophysiological understanding guides therapeutic choices in a given patient **(Fig. 3)**.

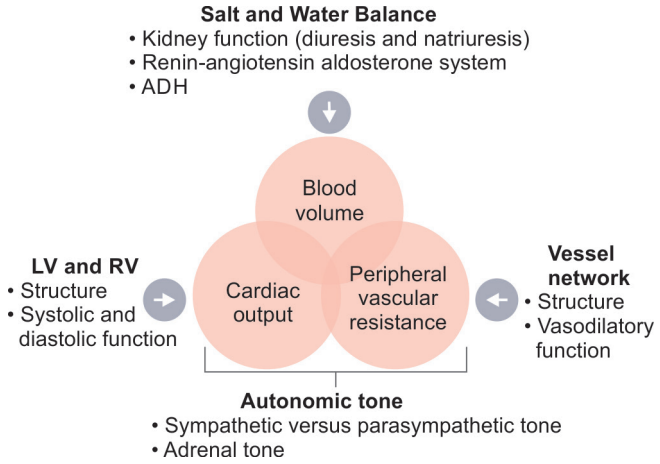


Fig. 1: Components of blood pressure. (ADH: antidiuretic hormone; RV: right ventricular; LV: left ventricular)

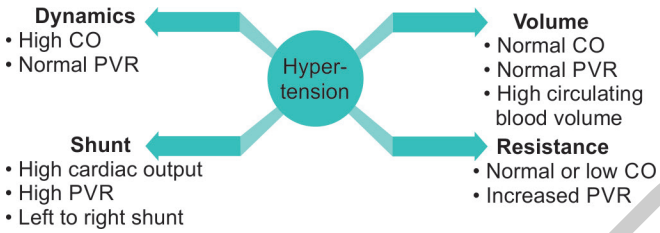


Fig. 2: Substrates of hypertension. (PVR: pulmonary vascular resistance; CO: cardiac output)

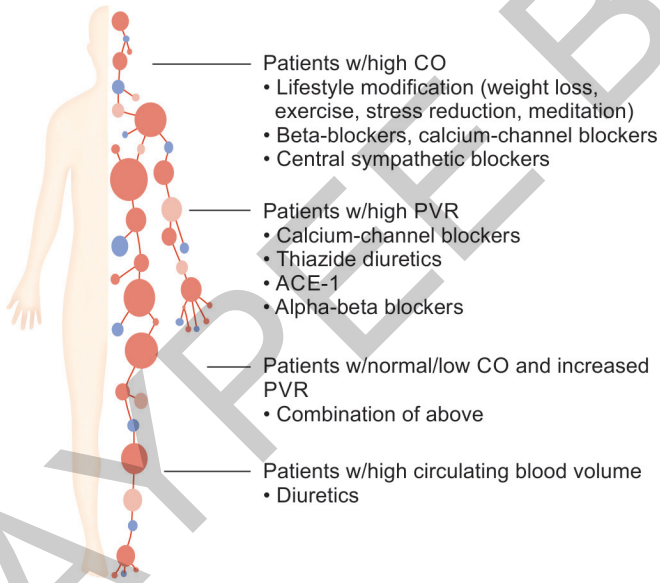


Fig. 3: Therapeutic targets of hypertension. (PVR: pulmonary vascular resistance; CO: cardiac output; ACE-1: angiotensin-converting enzyme 1)

HISTORICAL PERSPECTIVE

Hypertension is one of the oldest known conditions in human history.[1] However, the scientific evaluation began in 1733 when Stephen Hale measured intra-arterial pressure in a horse.[2] More than 150 years later, sphygmomanometer was designed to noninvasively measure blood pressure in humans. Currently used electronic blood pressure measurement devices started appearing in the latter part of 20th century.[3]

GENETIC BASIS OF HYPERTENSION

Hypertension appears to be multigenetic in origin interacting with environmental factors to variable degrees. Genetic data obtained by epidemiological studies of families and twins in South Wales by Miall et al. suggested moderate inheritability of hypertension (30–50%).[4] In a study by Williams and associates, family history was predictive of future hypertension (relative risk = 3.8).[5] Studies of twins have showed greater occurrence of hypertension in monozygotic twin than in dizygotic twins.[6] Furthermore, blood pressure profiles are similar within the same family members.

So far, at least 10 mutated single genes have been described in Mendelian forms of hypertension. However, these types of hypertension are fortunately rare and are often associated with hormonal and electrolyte abnormalities, e.g., Liddle syndrome. Therefore, hypertension in these patients is not considered essential hypertension.

NEUROHORMONAL BASIS OF HYPERTENSION

Autonomic nervous system plays seminal role in regulating heart rate, blood pressure, and cardiovascular function. Sympathetic nervous activation causes transient, labile, and permanent hypertension. In obese patients with hyperinsulinemia, insulin resistance and leptin increase sympathetic activity.[7,8]

In obese patients, both the SNS and the renin–angiotensin system (RAS) are upregulated with mutual positive feedback and enhancement of each other's actions.[9] In animal models, RAS has been shown to activate SNS via AT1R-induced oxidative stress.[10]

Renin–Angiotensin–Aldosterone System

Renin–angiotensin–aldosterone system is a physiological system and working in concert with sympathetic system body controls fluid pressure-volume homeostasis thus regulating blood pressure and fluid balance. Renin primarily originates in the granular cells of juxtaglomerular apparatus (JGA) of kidneys and is released into circulation with the following triggers.

- Sympathetic activation of JGA through beta-1 adrenoreceptors
- Reduced blood perfusion pressure of the kidneys detected by baroreceptors in the afferent arterioles
- Macula densa cells of the distal convoluted tubules detecting decreased sodium delivery

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Renin breaks down angiotensinogen from liver to form angiotensin I which is cleaved by angiotensin-converting enzyme (ACE) from pulmonary endothelium and other tissues to form angiotensin II. A potent vasoconstrictor, angiotensin, causes release of aldosterone from adrenal glands. Aldosterone mediates reabsorption of salt and water by renal epithelial cells leading to excess blood volume and hypertension. Lately, increased screening of hypertensive patients has shown 8–32% prevalence of hyperaldosteronism in hypertensive patients.

Alternate Sources of Angiotensin II and Hypertension

In patients with cardiometabolic syndrome (CMS) increased activity of RAAS and insulin resistance have been associated with hypertension.[11]

Natriuretic Peptide System

Natriuretic peptides (NPs) are a group of neurohormones with important roles in homeostasis of blood pressure and fluid status especially relevant to pathophysiology of hypertension, coronary artery disease, and heart failure. Examples of NPs include atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and c-type natriuretic peptide (CNP).

Atrial natriuretic peptide was the first identified member of NPs and is released from atrial myocytes in response to atrial stretch. BNP is released both from atrial and ventricular myocytes in response to stretch. ANP and BNP work similarly to increase natriuresis, relax myocardium, and to decrease several things including salt water appetite, sympathetic tone, renin and aldosterone in addition to antagonizing effects of antidiuretic hormone, therefore decreasing blood pressure and overall fluid status. CNP is released from vessel walls and plays its role in vasodilation and suppression of neointimal formation, myocardial hypertrophy, fibroblast growth, myocardial scar formation, and cardiac remodeling. RAAS and natriuretic group of peptides are two opposing systems mediating fluid homeostasis via the processes of fluid retention-conservation and diuresis respectively in various pathophysiological states. Blood pressure is therefore directly influenced by the variable balance of these systems especially in fluid states such as congestive heart failure.[12]

Research on NPs is evolving and more therapies targeting natriuretic systems are expected to come into play in future for treatment of hypertension and heart failure.

OXIDANT STRESS, NITRIC OXIDE, AND ENDOTHELIAL DYSFUNCTION

Oxidant stress from various sources has been reported to decrease nitric oxide-mediated vasodilatation and thus contributing to hypertension.[13] ACE inhibitors, AT1 receptor antagonists (ARBs), and aldosterone antagonists have been reported to improve endothelial dysfunction and hypertension.

Endothelin

Endothelin is a product of endothelial cells with potent vasoactive properties. It plays a role in hypertension associated with transplantation, vasculitis, and endothelial tumors.[14]

Renovascular Hypertension

The original hypothesis of renovascular origin (renal microvascular disease) of hypertension has not been conclusively proven. However, it is interesting to speculate that genetically determined activation of SNS and RAAS may lead to increased sodium reabsorption, renal microvascular constriction, renal medullary ischemia, and hypertension.

VESSEL REACTIVITY, STIFFNESS, AND VESSEL REMODELING IN HYPERTENSION

In some hypertensive patients, arteriosclerosis and endothelial dysfunction are responsible for their systolic hypertension. Arteriosclerosis is due to collagen deposition, smooth muscle hypertrophy causing increased vessel wall thickness. Degradation of elastin and nitric oxide deficiency from decreased synthesis and/or release cause arterial stiffness.[15] This together with arteriosclerosis leads to systolic hypertension.

HYPERTENSION DUE TO ABNORMAL BODY SODIUM/POTASSIUM RATIO

Increased intracellular sodium/potassium ratio in vascular smooth muscle due to sodium-rich diet consumption leads to vasoconstriction and hypertension. Studies showed that dietary supplementation of potassium reduces blood pressure.

Angiotensin II is produced in various regions including brain, heart, adrenal glands, and blood vessels. In spite of its regulation by ACE and non-ACE enzymes such as the serine protease chymase, this angiotensin II plays an important role in hypertension, left ventricular hypertrophy (LVH), congestive heart failure (CHF), atherosclerosis, myocardial infarction (MI), stroke arterial aneurysms, and end-stage kidney disease.

CONCLUSION

Hypertension is a common systemic disorder of cardiovascular system with multiple pathophysiological

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substrates and different targets in different individuals. Therefore, management of hypertension should not only be based upon etiological factors but also the target organs, the blood pressure has affected.

Hypertension is the end result of altered baseline homeostasis at one or more of different levels as shown in **Flowchart 1**.

Substrates of Hypertension

Different components play varying degrees of roles in hypertension. The predominant contributors and comorbid conditions should be considered in planning the treatment. The following factors play a role in hypertension.

- Cardiac output
- Peripheral vascular resistance
- Blood volume
- Renal function
- Renin–angiotensin–aldosterone system
- Sympathetic output

Therapeutic Targets of Hypertension

Figure 3 illustrates appropriate medical therapy based on the predominant contributors to the generation of hypertension.

REFERENCES

1. Nei Jin by Huand Ti, 2600 BC.
2. Hales S. Statistical essays, containing haemastatistics. London: W Innys, R Manby, and Woodward; 1733.
3. Booth J. A short history of blood pressure measurement. Proc R Sic Med. 1977;70:793-9.
4. Miall WE, Oldham PD. The hereditary factor in arterial blood-pressure. Br Med J. 1963;1:75-80.
5. Williams RR, Hunt SC, Hopkins PN, Wu LL, Hasstedt SJ, Berry TD, et al. Genetic basis of familial dyslipidemia and hypertension: 15-year results from Utah. Am J Hypertens. 1993;6:319S-27S.
6. Feinlieb M, Garrison RJ, Fabsitz R, Christian JC, Hrubec Z, Borhani NO, et al. The NHLBI twin study of cardiovascular disease risk factors: methodology and summary of results. Am J Epidemiol. 1977;106:284-5.
7. Landsberg L. Insulin-mediated sympathetic stimulation: role in the pathogenesis of obesity-related hypertension. J Hypertens; 2001. pp. 523-8.
8. Haynes WG, Morgan DA, Walsh SA, Mark AL, Sivitz WI, et al. Receptor-mediated regional sympathetic nerve activation by leptin. J Clin Invest. 1997;100:270-8.
9. Matsukawa T, Gotoh E, Minamisawa K. Effects of intravenous infusions of angiotensin II on muscle sympathetic activity in humans. Am J Physiol. 1991;261:R690-6.
10. Zimmerman MC, Lazartigues E, Sharma RV, Davisson RL. Hypertension caused by angiotensin II infusion involves increased superoxide production in the central nervous system. Circ Res. 2004;95(2):210-6.
11. Segura J, Ruilope LM. Obesity, essential hypertension and renin-angiotensin system. Public Health Nutrition. 2007; 10(10A):1151-5.
12. Brands MW, Freeman RH. Aldosterone and renin inhibition by physiological levels of atrial natriuretic factor. Am J Physiol Regul Integr Comp Physiol. 1988;254(6 Pt 2): R1011-6.
13. Kelm M, Preik M, Hafner D, Strauer BE. Evidence for a multifactorial process involved in the impaired flow response to nitric oxide in hypertensive patients with endothelial dysfunction. Hypertension. 1996;27(3 Pt 1): 346-53.
14. Ergul S, Parish DC, Puett D, Ergul A. Racial differences in plasma endothelin-1 concentrations in individuals with essential hypertension. Hypertension. 1996;28:652-5.
15. Mulvany MJ, Baumbach GI, Aalkjaer C, Heagetty AM, Korsgaard N, Schffrin EI, et al. Vascular remodeling (letter). Hypertension. 1996;28(3):505-6.

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Hypertension: New Frontiers

A Textbook of Cardiology

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Printed in India

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ISBN 978-93-5152-109-9

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