1. The Pathophysiology of Hypertension

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2. The Pathophysiology of Hypertension

The Pathophysiology of Hypertension

- Blood pressure is generated by cardiac contraction against the vascular resistance, according to Ohm’s Law:
  - \( V = IR \)
  - \( MAP = CO \times SVR \)
  - \( MAP = DBP + (SBP - DBP)/3 \)
  - \( CO = \) cardiac output
  - \( SVR = \) systemic vascular resistance

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3. Cardiac Output

Cardiac Output

- Cardiac output can be broken down as:
  - CO = SV x HR
  - SV = stroke volume
  - HR = heart rate
- Stroke volume is affected by pre-load, after-load, and contractility
- The primary determinant of cardiac output in normal individuals is volume status (sodium content)
- An increase in CO is rarely the cause of hypertension

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4. Systemic Vascular Resistance

Systemic Vascular Resistance

- SVR is affected by humoral and local factors.
- Humoral factors
  - Balance of vasoconstrictors and vasodilators
  - Angiotensin II and norepinephrine are two of the more important
- Local factors
  - Some arterioles are able to auto-regulate flow to their capillary beds, constricting at times of high blood pressure and dilating at times of low blood pressure
  - This is common in the brain and the kidney, and mediated by EDRF (NO)

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5. Essential Hypertension

Essential Hypertension

- No identifiable etiology
- Accounts for 90% of hypertension
- Onset typically in 40’s to 50’s
- Genetic pre-disposition
  - 70 - 80% of patients have a family history
  - Racial patterns

6. Secondary Hypertension

Secondary Hypertension

- Identifiable etiology
- Many of the factors that influence CO, SVR, and BP can be primarily disrupted by disease processes
  - Volume status - kidney disease and poor Na+ handling
  - Angiotensin II – renal artery stenosis and perception by the kidney of hypo-perfusion despite conditions of hypervolemia
  - Aldosterone – primary hyperaldosteronism resulting in unregulated aldosterone production and sodium retention
  - Adrenergic tone – pheochromocytoma will result in excessive catecholamine production
7. Kidney Failure

Kidney Failure

- With the loss of kidney function, virtually 100% of patients become hypertensive
- Chronic kidney disease is the most common form of secondary hypertension
- Hypertension can be cured with hemodialysis and ultrafiltration

8. Impaired Sodium Excretion

Impaired Sodium Excretion

- Blood volume correlates with SBP in patients with chronic kidney disease
- Blood pressure is very responsive to manipulations of volume status
- Seems to be mediated by abnormal vasoregulation and an increased SVR
9. Impaired Pressure Natriuresis

Impaired Pressure Natriuresis

- Chronic kidney disease results in a loss of the ability to alter sodium handling based on small changes in BP
- Impaired ability to handle sodium load

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10. The Role of Pressure Natriuresis on Blood Pressure

The Role of Pressure Natriuresis on Blood Pressure

The hypertensive response to Ang II and aldosterone is diminished when the increased pressure is transmitted to the kidney

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11. Contributions to Hypertension by the Kidney

Contributions to Hypertension by the Kidney

The kidney plays an essential role in modulating systemic blood pressure by adjusting the sodium excretion rate. Sustained systemic hypertension is believed to necessitate a disturbance of this phenomenon, resulting in impaired sodium excretion. Modulation of sodium intake and sodium excretion (diuretics) effectively reduce blood pressure in the majority of patients.

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12. Renin & Angiotensin System

Renin – Angiotensin System

- Angiotensin II infusion causes hypertension
- Hypertensive patients drop BP much more significantly than euvoletic normotensive patients when angiotensin II is blocked

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13. Effects of Angiotensin II

- Direct vasoconstriction and increased SVR
- Enhanced sodium reabsorption by the proximal tubule
- Stimulates aldosterone release with sodium reabsorption by the collecting tubule

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14. Goldblatt Model I

- A clip is applied to 1 renal artery in an animal with 2 functioning kidneys
- Model of unilateral renal artery stenosis
- Hypertension due to unilateral RAS is associated with both an increased SVR and impaired natriuresis in the contra-lateral kidney

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15. Goldblatt Model II

Goldblatt Model II

- A clip is applied to 1 renal artery in an animal with 1 functioning kidney
- Model of bilateral renal artery stenosis
- Total renal mass is hypo-perfused
  - Impaired clearance
  - Intolerance of ACE inhibitors
  - No off-setting pressure natriuresis

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16. Renal Artery Stenosis

Renal Artery Stenosis

- Clinical Presentations
  - Severe and difficult to control hypertension
  - Kidney failure
  - Flash pulmonary edema
- Two disease processes
  - Atherosclerotic renal artery stenosis
  - Fibromuscular dysplasia
- Therapy
  - Medical – anti-hypertensives +/- ACE inhibitors
  - Interventional – renal artery angioplasty +/- stenting
  - Surgical – renal artery bypass

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17. **Aldosterone**

- Excess aldosterone leads to hypertension
- Aldosterone results in sodium retention and hypervolemia
- Excess potassium excretion leads to hypokalemia
- Volume expansion may be clinically absent due to “aldo-escape”

18. **Sympathetic Nervous System**

- Increased adrenergic tone leads to hypertension
- Blockade of the sympathetic nervous system reduces blood pressure
- Adrenergic tone increases
  - vascular tone
  - sodium retention
  - cardiac inotropy
Summary

- Blood pressure is a result of cardiac output and systemic vascular resistance.
- Essential hypertension is the most common cause of elevated blood pressure.
- Disease processes that affect the determinants of blood pressure can result in secondary hypertension.
- These processes often affect sodium handling by the kidney, angiotensin II, aldosterone, and the sympathetic nervous system.

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