1. Basic concepts, types, pathogenetic factors

Basic concepts and definitions:

Factors determining blood pressure (Fig. 1)

Regulation of peripheral resistance (Fig. 2)

Regulation of circulating volume (Fig. 3)

1. Basic concepts, types, pathogenetic factors
2. Secondary hypertension
3. Essential hypertension
4. Therapy
Types of hypertension:

Resistance hypertension:
In its chronic phase, diastolic pressure is always enhanced, systolic p. as a rule; pressure rise is a consequence of enhanced total peripheral vascular resistance

Output (volume) hypertension:
Only systolic p. rises, owing to enhanced cardiac output

Elastic hypertension
Owing to loss of great vessels elasticity in old age

Recommended values:

<table>
<thead>
<tr>
<th></th>
<th>Age 40</th>
<th>40 - 60</th>
<th>≥ 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic</td>
<td>140 mmHg</td>
<td>150 mmHg</td>
<td>160 mmHg</td>
</tr>
<tr>
<td>Diastolic</td>
<td>90 mmHg</td>
<td>90 mmHg</td>
<td>90 mmHg</td>
</tr>
</tbody>
</table>

Enhanced BP is a sign of underlying condition rather than a disease in itself

“Essential” hypertension can be analyzed utilizing concepts explaining types of secondary hypertension

Types of secondary hypertension range from “volume dependency” to “pressor dependency” (Fig. 5)

Common pathogenic factors of different types of hypertension

Familial load, ↑intracellular Ca²⁺ in SMC
Structural changes of the walls of arteries:
Hypertrophy of media - substantial pathogenetic factor for progression and maintenance of hypertension (esp. essential)

genetic & environm. factors → mild unstable media rise of BP → hyper-trophy → ↑ precapillary resistance

Discrimination between “pathologic” and “normal” BP values is arbitrary (Fig. 4)

Fig. 12-1. The mechanisms of secondary hypertension depending on the degree of volume overload and/or pressor factors.

Damaged endothelium → vasoconstrictory effect of various humoral factors (Fig. 6)
2. Secondary hypertension

Secondary causes of hypertension (Tab. 1)

<table>
<thead>
<tr>
<th>Chronic end-stage renal disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renovascular stenosis</td>
</tr>
<tr>
<td>1st aldosteron</td>
</tr>
<tr>
<td>Adenoma producing adenoma</td>
</tr>
<tr>
<td>Idiopathic adrenal hyperplasia</td>
</tr>
<tr>
<td>Glucocorticoid suppressible hyperplasia</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Hyperaldosteron</td>
</tr>
<tr>
<td>Cushing’s syndrome</td>
</tr>
<tr>
<td>Hypo- and hyper tension</td>
</tr>
<tr>
<td>Alcohol induced</td>
</tr>
<tr>
<td>Renin-producing JG cell tumor of kidney</td>
</tr>
<tr>
<td>Hypertension of pregnancy</td>
</tr>
<tr>
<td>Hypertension associated with drug use</td>
</tr>
<tr>
<td>Oral contraceptives</td>
</tr>
<tr>
<td>Cocaine abuse</td>
</tr>
<tr>
<td>Cytosporin</td>
</tr>
<tr>
<td>Hypertension associated with insulin resistance</td>
</tr>
<tr>
<td>Isolated systolic hypertension in the elderly</td>
</tr>
</tbody>
</table>

Interplay of pressure/volume hypertension (Fig. 7)
Renin-angiotensin system reacts quickly (in minutes) to the renal artery obstruction or to sympathetic activation → via angiotensin II → resistance hypertension (short-term cardiorenal homeostasis)
Volume → renin angiotensin system
RAS depresses itself in a long run, as it activates aldosterone (in hrs or days) → ↑ volume → ↓ RAS
Bilateral renal disease → loss of nephrocytes → ↓ RAS
Diuretics → ↑ RAS!
(Fig. 7)

Pathogenesis of secondary hypertension (Tab. 2)

Overproduction of adrenal hormones
Cushing’s syndrome
Glucocorticoids have specific hypertension producing effect, too, independent on sympathetic & RAS (receptors in CNS ?)

1. Primary hyperaldosteronism
Adenoma/hyperplasia (zona glomerulosa) → retention of Na & H₂O → ↑ volume → paradigmatic volume hypertension
Later, however, autoregulation → ↑ TPVR → resistance hypertension
2. Pheochromocytoma

Tumor of adrenal medulla → ↑ mixture of catecholamines → paradigmatic resistance hypertension
Pressure natriuresis & tonization of veins → ↓ volume → orthostatic problems

Hypertension caused by drugs

Contraceptives

Manifest hypertension in 5% of women, esp. when other risk factors of hypertension are present (incl. age). Estrogen and progesterone component. RAS?
Indomethacine → vasodilatory prostaglandines

3. Renovascular hypertension (unilateral)

Stage 1 - Resistance hypertension
Constriction of art. renalis → ↑ renin → ↑ AG II → vasoconstriction → ↑ BP

Stage 2
↑ AG II → ↑ aldosterone → Na & H2O retention → ↑ volume → ↓ RAS Later.
↑ volume → autoregulation → ↑ TPVR → resistance hypert.

Stage 3
↑ TPVR → vascular & parenchymal damage of contralateral kidney → state similar to renal-parenchymal hypertension

(Tab. 2)

4. Chronic end-stage renal disease (renal-parenchymal hypertension, bilateral renovascular hypertension)

Loss of nephrons → ↓ GFR → Na & H2O retention → ↑ circul. volume → ↑ venous return → ↑ CO → autoregulation → ↑ TPVR → circul. volume → ↓ RAS
Loss of nephrons → disruption of BP/Na excretion relation
Autoregulation: ↑ CO & ? → ↑ TPVR
In some patients or with volume suppressed by diuretics → ↑ RAS (normal absolutely, but enhanced relatively to Na & BP)

Evidence of RAS participation: bilateral nephrectomy → normalization of pressure (excretion being ensured)

3. Essential hypertension

Definition: No recognizable organ pathology as a cause. Dg per exclusionem

Development of EH (Fig. 9)

TPVR normal: ↑ CO = TPVR → ↑ MAP
↑ TPVR later (due to secondary changes in vasculature):
CO = ↑ TPVR → ↑ MAP (Fig. 10)
Etiology of EH is heterogenous
There are several important factors promoting manifestation of EH, none of them is dominant, however (Fig. 9 and 11)
More important, interplay of BP regulating factors is disrupted
Factors may be important differently in individual patients

Genetic and environmental factors
Genetic factors → about 30% of BP variance
Racial differences
  Some envirom. factors → ↑sympathoadr. activation
    - stress (noise, flying personnel)
    - psychosocial factors
Na consumption
  15 g → 6 g NaCl daily → BP ↓ by 9 mmHg.
  This is due to salt sensitive individuals (genetically determined).
  Animals: CI- important, too!

Hypothesis:
↑ permeability for Na → ↑ Na intra-cellar. → ↑Ca²⁺ intra-cellar. → ↑ tonus of vaso. muscular.
Hypothetical natriuretic hormone blocking Na-K-ATPase

Atrial natriuretic peptide (ANP): no effect on Na/K-ATPase, no role in pathophysiology of hypertension
**Overweight → hypertension**

**Sympatoadrenal system**

- mechanism: hyperinsulinemia → Na retention
- norepinephrine: ↑ in plasma (mildly), ↑ sensitivity to it

**Plasma volume, RAS**

Normals:

```
<table>
<thead>
<tr>
<th>Renin</th>
<th>AG</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>↑</td>
<td>↓</td>
</tr>
</tbody>
</table>
```

Ess.hypertonics:

```
<table>
<thead>
<tr>
<th>Renin</th>
<th>AG</th>
<th>BP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>↑</td>
</tr>
</tbody>
</table>
```

Plasma renin activity is not enhanced absolutely in majority of ess. hypertonics, but relatively to BP

ACE inhibitors therefore → ↓ BP

**4. Therapy**

May be used to exclude some of the primary causes when unsuccessful.

Two strategies for exclusion of secondary hypertension

Single reading insufficient ("white-coat hypertension", a.o.)

With mild hypertension, observation may be prolonged for months under recommended change in life-style

Changed way of living = first choice therapy

- obesity
- diet (↓ Na, ↑ K, ↓ alcohol; caffeine does not produce hypert. itself)
- smoking → equivocal effect on BP
- relaxaton therapy

**Pharmacology**

- diuretics
- sympaticolytics, peripheral vasodilators (e.g., Ca^{2+} channel blockers)
- ACE inhibitors
- AG II receptor antagonists

Therapy should be combined and individualized