Raynaud’s Syndrome

- Excessive sympathetic tone in nerves supplying hands and feet. Minor cold, or even thought of cold, causes pronounced vasoconstriction that can be severe enough to cause necrosis of tissues
- Discoloration of the fingers and/or toes when the patient is exposed to changes in temperature (cold or hot) or emotional events
- Abnormal spasm of blood vessels causes diminished blood supply
- Initially, the digit(s) turn white because of diminished blood supply.
- Then turn blue because of prolonged lack of oxygen
- Finally, the blood vessels reopen, causing a local “flushing” phenomenon, which turns the digit(s) red
- Three-phase color sequence (white to blue to red), most often upon exposure to cold temperature
- Treatment if severe: Ca++ blockers

Myasthenia gravis
Autoimmune disease

- 1:10,000 (250,000 USA)
- Antibodies to NMJ nicotinic receptors leads to degradation
- Simplified synaptic folds
- Normal nerve terminal and transmitter
- Widened synaptic junction
- Diagnosis: Edrophonium (Tensilon, short acting) is used for diagnosis and determination of maintenance dose
- Treatment: Neostigmine has direct (stimulates receptor) and indirect actions (inhibition of AchE). No CNS activity.

Renal Stenosis
Primary cause of 2o HT

- Decreased renal blood flow
  - ↓ renal BP
  - ↑ renin release
  - ↑ aldosterone
  - ↑ Na+, water retention
  - ↑ systemic BP
- Treatment: insertion of stent

Pheochromocytoma

- Tumor: ↑ synthesis, ↑ release of NE & EPI into the circulation.
- Result: ↑ BP, ↑ HR → hypertensive crisis
- Treatment: surgical removal for solid tumor
  - α-β-blocker ie, Labetalol
  - α-blocker ie, phenoxybenzamine or phentolamine
  - inhibitor of tyrosine hydroxylase ie. α-methyl-p-tyrosine
  - β-blocker only after α-blockade
- Rule of Ten
  - 10% Pheochromocytomas are:
    - Malignant
    - Bilateral
    - Extra-Adrenal
    - In Children
    - Familial
    - Recur (within 5 to 10 years)
    - Present after stroke

Benign Prostate Hypertrophy (BPH)

- Enlarged prostate leads to difficulty in urination
- Alpha-receptor blocker (ie Prazosin) cause prostate relaxation
- Relaxed prostate improves urination
Glaucoma
Increased intraocular pressure: Untreated → blindness
Glaucoma:
- Open angle (wide, chronic) – treated with beta-blockers and other agents
- Closed-angle (narrow-angle) – dilated iris can occlude outflow
  Pilocarpine or surgical removal of part of iris (iridectomy)

Glaucoma treatment
1. α-Agonist: ↑ Outflow
2. M-Agonists: ↑ Outflow
3. β-Blocker: ↓ Secretion
4. α2-Agonist: ↓ Secretion
5. Prostaglandins: ↑ Outflow
6. Carbonic acid inhibitors: ↓ Secretion

Miosis, Mydriasis & Cycloplegia
Miosis: pin point pupils
Mydriasis: dilated pupils (bella-donna agents)
Cycloplegia: loss of accommodation (focus)

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Drug</th>
<th>Pupillary Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Sympathomimetic</td>
<td>Dilation (mydriasis)</td>
</tr>
<tr>
<td>Normal</td>
<td>Parasympathomimetic</td>
<td>Constriction (miosis)</td>
</tr>
<tr>
<td>Normal</td>
<td>Parasympatholytic</td>
<td>Mydriasis, cycloplegia</td>
</tr>
<tr>
<td>Horner’s syndrome</td>
<td>Cocaine 4-10%</td>
<td>No dilation</td>
</tr>
<tr>
<td>Preganglionic Horner’s</td>
<td>Hydroxymephalamin</td>
<td>Dilation</td>
</tr>
<tr>
<td>Postganglionic Horner’s</td>
<td>Hydroxymephalamin</td>
<td>No dilation</td>
</tr>
<tr>
<td>Adie’s pupil</td>
<td>Pilocarpine 0.05-0.1%</td>
<td>Constriction</td>
</tr>
<tr>
<td>Normal</td>
<td>Opioids (oral or intravenous)</td>
<td>Pinpoint pupils</td>
</tr>
</tbody>
</table>

Eye - Horner’s Syndrome
Destruction of Sympathetic innervation to the iris
- loss of preganglionic fibers
- loss of postganglionic fibers
- parasympathetic innervation left unopposed

Horner’s Syndrome (note sagging left eyelid and miosis)

Botulinum toxin - Action
Inhibits Ach release
Single treatment can last 3-4 months

Before
![Before image]

After
![After image]

Adie’s Pupil & Iritis
Adie’s Pupil
Muscarnic blocker to dilate pupil to prevent attachment to lens. Steroid to treat inflammation.

Iritis

Botulinum toxin - Strabismus
Parkinson's Disease

- General population 1:1000, over 60 1:75
- Tremor, stiffness, or clumsiness, usually involving one side difficulty walking, fatigue, depression
- Progressive destruction of the dopaminergic nigrostriatal pathway
- Elevated cholinergic activity

Treatment:
- MAO inhibitors:
- Dopamine agonists: bromocriptine
- L-Dopa
- Anticholinergics: benztropine
- Decarboxylase inhibitor: carbidopa
- Amantadine: inhibit D-uptake, M-rec, NMDA-block, release dopamine

Tyramine Interaction with MAO Inhibitors
Can cause hypertensive crisis (↑BP, ↑HR)

Aged cheese & red wine are rich in tyramine

MAOI and Tyramine Crisis

↑Blood pressure, ↑Heart rate

Treatment: α-blocker or labetalol (α-, β-blocker)

Normally dietary tyramine is metabolized by MAO

With MAO inhibition, octopamine is produced and stored in vesicles with NE

Aged cheese, red wine are rich in tyramine

Asthma

- Albuterol
- Terbutaline, Metaproterenol
- β₂-selective agonists - bronchodilation
  - Inhalation vs oral - less side effects
- Ritodrine - premature labor

Anaphylaxis

- Epinephrine - bronchoconstriction, Tachycardias, ↑Blood pressure
  - Bronchoconstriction
  - Vasoconstriction
**Classification of Hypertension**

<table>
<thead>
<tr>
<th>Classification</th>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>&lt;130</td>
<td>&lt;85</td>
</tr>
<tr>
<td>high normal</td>
<td>130-139</td>
<td>85-89</td>
</tr>
<tr>
<td>stage 1 (mild)</td>
<td>140-159</td>
<td>90-99</td>
</tr>
<tr>
<td>stage 2 (moderate)</td>
<td>160-179</td>
<td>100-109</td>
</tr>
<tr>
<td>stage 3 (severe)</td>
<td>180-209</td>
<td>110-119</td>
</tr>
<tr>
<td>stage 4 (very severe)</td>
<td>&gt;209</td>
<td>&gt;119</td>
</tr>
</tbody>
</table>

*Require three measurements (repeat visits)

BP lowest in the morning → ↑ during the day

**Health Consequences - 1**

USA
40-60 million HT

\(\downarrow \text{Na}^+ \rightarrow \downarrow \text{rise rate}\)

### Postural (Orthostatic) Hypotension

- Venous return falls
- Blood pressure falls

- Sympathetic activity increases
- Constriction of great veins
- Constriction of arteries (↑ TPR)
- Increase in heart rate

reflex

no reflex

reflex

BP (mmHg)

95
100
195

100
105 → 100

100
95
55

**Baroreflex Response**

Opposes direct change in BP

Not HR changes
Not PP changes
Congestive Heart Failure (CHF)

CO inadequate for body demand of oxygen (demand-supply)
2.5 million in USA, 50% mortality @ 5 year
350,000 new cases each year

Compensated heart failure:
- resting cardiac function, OK; stress or exercise, No

Congestive heart failure (CHF, uncompensated):
- resting cardiac function inadequate

CHF Hemodynamic Changes

Blood pressure is well maintained:
- ↑ sympathetic tone (tachycardia)
- ↓ parasympathetic tone
- activation of renin-angiotensin system
- ↑ blood volume
- ↑ vasopressin release

Consequences:
- ↓ force of contraction
- ↓ CO, ↑ TPR, ↓ stroke volume
- ↑ venous pressure
- ↓ tissue perfusion
- cardiac hypertrophy
- Na+ & water retention
- edema

ADHD

The lower portion of the brain contains an area known as the Reticular Activating System. It keeps the higher brain centers alert and ready for input. There is some evidence that this area is not working properly in ADHD, and that the brain is, in effect, “going to sleep”. Hyperactivity is really the brain’s attempt to generate new stimulation to maintain alertness (Kinomura et. al., Science, 1996)

ADHD PET Scan

Brain with ADHD has much less activity (red/white)
ADHD individuals do not have enough activity in their brain to focus on what they are doing or control their thoughts

Treatment aims to give a person with ADHD more “mental energy” so they can control their thoughts and actions

Wild Mushrooms - Amanita

WARNING!
PICKING AND EATING WILD MUSHROOMS CAN KILL YOU!

100 “bad”, 10 “deadly"

Muscarine poisoning

Deadly Nightshade “Belladonna”

Approx 5,000 cases per yr

Mainly atropine
Devil’s apple
Stink weed
Devil’s cherries

Datura

Mainly scopolamine & hyoscyamine
Thorn apple
Jimson weed
Hyperkalemia
- burn & trauma
- usually small ↑K+
- cardiac arrest
- support: dialysis glucose / insulin

Malignant Hyperthermia
- more likely with halothane
- 60% mortality
- ↑Ca++ → ↑ body temp
- tachycardia
dysrhythmia
- THR, muscle rigidity

Treatment:
- Dantrolene
drug of choice
- ↓Ca++ release

Gingival Hyperplasia
- Calcium blockers – especially nifedipine (10%)
- Phenytoin (Dilantin) – for seizures (40%)
- Cyclosporine – immunosuppressant (30%)

ACEI - Glossitis
- Dry mouth
- Glossitis
- Oral ulceration (Stevens-Johnson Syndrome)
- Oral bleeding

Agents used in the treatment of HT, CHF, Arrhythmia and Angina

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Hyper-</th>
<th>CHF</th>
<th>Arrhythmia</th>
<th>Angina</th>
<th>Contraindications/Cautions/Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Blockers</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Caution: CHF (unstable CHF, bronchospasm, significant bradycardia); or in diabetes, asthma (use β1-selective)</td>
</tr>
<tr>
<td>Ca++-Blockers</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Caution: CHF, Gingival hyperplasia</td>
</tr>
<tr>
<td>ACEI</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Low GFR, renal insufficiency, glomerulonephritis</td>
</tr>
<tr>
<td>Diuretics</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Low GFR, hypokalemia; CG; glucose intolerance; diabetes</td>
</tr>
<tr>
<td>Cardiac glycosides</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Many Rx interactions, (CV) important, low K+; qU toxicity</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Flushing, diaphoresis, headache, reflex tachycardynia</td>
</tr>
<tr>
<td>Na+-Channel blockers</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Effects enhanced in depolarized tissue</td>
</tr>
<tr>
<td>Nitrates</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>❌</td>
<td>Tolerance, flushing, diaphoresis, headache, reflex tachycardynia</td>
</tr>
</tbody>
</table>