Diseases & Conditions

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 digits 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 digits 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.

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. Labelatol
- α-blocker ie, phenoxycyanzine 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

Renal Stenosis

Decreased renal blood flow
- ↓ renal BP
- ↑ renin release
- ↑ aldosterone
- ↑ Na+, water retention
- ↑ systemic BP

Treatment
- Insertion of stent

Benign Prostate Hypertrophy (BPH)

Enlarged prostate leads to difficulty in urination
Alpha-receptor blocker (ie Prazosin) cause prostrate relaxation
Relaxed prostate improves urination

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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)

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)

Adies Pupil & Iritis

Adies Pupil
Muscarinic blocker to dilate pupil to prevent attachment to lens. Steroid to treat inflammation.

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

Facial wrinkles, FDA Approval: Apr 2002

Botulinum toxin - Strabismus

Before
After

Fig. 10B: Tonic pupil; the left pupil is dilated compared to the right.
This 31 year old woman had been aware of pupillary asymmetry for some time. She presented with left face numbness, the sensation of which was indistinguishable from true facial. Examination showed a right focal tonic pupil. The triceps and ankle jerks were depressed.
**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, ↑secretions, ↓blood pressure
- Epinephrine: bronchodilation, vasoconstriction

**Asthma Prevalence USA 1980-94**

- Rate per 1,000
- NH Survey 1980-94
Anaphylaxis - Mechanism

Type I (Anaphylaxis) Hypersensitivity

(a) First allergen exposure

- Allergen stimulates mast cell to differentiate into a plasma cell
- Plasma cell produces IgE antibodies (monogamy) with the help of T cells
- IgE binds to mast cell receptors and sensitizes the cells

(b) Second allergen exposure

- Allergen attaches to bound IgE causing degranulation of mast cell
- Release of histamine and other physiological mediators that trigger anaphylaxis

Cardiovascular Regulation

- alpha1 vasoconstriction $\uparrow$ TPR $\uparrow$ BP
- beta1 $\uparrow$ HR $\uparrow$ CO $\uparrow$ BP
- beta2 $\ast$ vasodilation $\downarrow$ TPR $\downarrow$ BP
- M2 (vagus) $\downarrow$ HR $\downarrow$ CO $\downarrow$ BP
- M (vascular) $\ast$ vasodilation $\downarrow$ TPR $\downarrow$ BP

* not innervated

New Classification of Hypertension

**JNC VII**

<table>
<thead>
<tr>
<th>Systolic (mmHg)</th>
<th>Diastolic (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>normal</td>
<td>&lt;120 and &lt; 80</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120-139 or 80-89</td>
</tr>
<tr>
<td>stage 1 (mild)</td>
<td>140-159 or 90-99</td>
</tr>
<tr>
<td>stage 2 (moderate)</td>
<td>&gt;160 or &gt;100</td>
</tr>
</tbody>
</table>

*Require three measurements (repeat visits)
BP lowest in the morning $\rightarrow \uparrow$ during the day

BP Daily Fluctuation

Fluctuation Throughout a Day
(Case: Male, 35 years of age)

Hypertension Is Largely Uncontrolled

<table>
<thead>
<tr>
<th></th>
<th>Undiagnosed, unaware</th>
<th>Acknowledged, untreated</th>
<th>Treated, uncontrolled</th>
<th>Treated, controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites (n=32.6 million)</td>
<td>31</td>
<td>17</td>
<td>29</td>
<td>24</td>
</tr>
<tr>
<td>African Americans (n=3.7 million)</td>
<td>27</td>
<td>17</td>
<td>32</td>
<td>24</td>
</tr>
<tr>
<td>Mexican Americans (n=1.3 million)</td>
<td>41</td>
<td>19</td>
<td>25</td>
<td>15</td>
</tr>
</tbody>
</table>

Health Consequences - 1

USA
40-60 million HT

$\downarrow$ Na$^+$ $\rightarrow$ $\downarrow$ 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

BP (mmHg)
95 100 95
95 100 195
105

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!

10,000 cases per year
Muscarine poisoning
5,000 mushroom species
100 “bad”, 10 “deadly”

Deadly Nightshade
"Belladonna"

Approx 5,000 cases per year

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

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
- ↑HR, 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</td>
</tr>
<tr>
<td>Ca++-Blockers</td>
<td>+ + +</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
<td>CHF, Gingival hyperplasia</td>
</tr>
<tr>
<td>ACEI</td>
<td>+ + +</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
<td>Low GFR, renal stenosis, glossitis, heterotopic</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, low K⁺, toxic if hypertensive</td>
</tr>
<tr>
<td>Vasodilators</td>
<td>+ + +</td>
<td>+ +</td>
<td>+ +</td>
<td>+ +</td>
<td>Flushing, dizziness, headache, reflex tachycardia</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, dizziness, headache, reflex tachycardia</td>
</tr>
</tbody>
</table>