Diseases & Conditions

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Agents used in HT, CHF, Arrhythmia and Angina

<table>
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<tr>
<th>Drug Class</th>
<th>HT</th>
<th>CHF</th>
<th>Arrhythmia</th>
<th>Angina</th>
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<tbody>
<tr>
<td>Beta-Blockers</td>
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<td>Calcium Channel blockers</td>
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<td>ACEI/ARBs</td>
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<td>Diuretics</td>
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<td>Cardiac glycosides</td>
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<td>Vasoconstrictors</td>
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<td>Norepinephrine</td>
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<tr>
<td>Nitrate</td>
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</table>

Contraindications/Cautions/Notes

- Tolerance, flushing, dizziness, headache, reflex tachycardia
- Nitrates: Many Rx interactions, low TI, [K+], important, low K+ → ↑ toxicity
- Cardiac glycosides: Low GFR, hypokalemia → CG; glucose intolerance → diabetes
- Diuretics: Low GFR, renal stenosis, tetrogenic, cough (ACEI), taste, ↑ renal mechanics, angioedema
- ACEI/ARBs: CHF, Gingival hyperplasia, reflex tachycardia, constipation
- Calcium Channel blockers: CHF (unstable CHF, bronchospasm, significant bradycardia); or in diabetes, asthma (use β1-selective), depression, rebound HT
- Beta-Blockers: Contraindications/Cautions/Notes
- 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 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
  - Wider 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 2+ 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, Labelatol
    - 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 (e.g., Prazosin) cause prostate relaxation
- Relaxed prostate improves urination

Miosis, Mydriasis & Cycloplegia

<table>
<thead>
<tr>
<th>Clinical Setting</th>
<th>Drug</th>
<th>Pupillary Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Sympathomimetic (e.g., phenylephrine)</td>
<td>Dilation (mydriasis)</td>
</tr>
<tr>
<td>Normal</td>
<td>Parasympathomimetic (e.g., pilocarpine)</td>
<td>Constriction (miosis)</td>
</tr>
<tr>
<td>Horner's syndrome</td>
<td>Cocaine 4-15%</td>
<td>No dilation</td>
</tr>
<tr>
<td>Horner's syndrome</td>
<td>Hydroxyamphetamine</td>
<td>Dilation</td>
</tr>
<tr>
<td>Adie's pupil</td>
<td>Pilocarpine 0.05-1%</td>
<td>Constriction</td>
</tr>
<tr>
<td>Normal</td>
<td>Oxydopa (oral or intravenous)</td>
<td>Pinpoint pupils</td>
</tr>
</tbody>
</table>

Miosis: pin point pupils
Mydriasis: dilated pupils (bella-donna agents)
Cycloplegia: loss of accommodation (blurred vision)

Glaucoma

- Increased intraocular pressure: Untreated → blindness
- 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

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)

Adie's Pupil & Iritis

- **Adie's Pupil**
  - Muscarinic blocker to dilate pupil to prevent attachment to lens. Steroid to treat inflammation.

- **Iritis**
  - 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

**Before**

**After**

- Facial wrinkles, FDA Approval: Apr 2002

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Note: The images and diagrams are not transcribed as they are not clearly visible in the text.
Botulinum toxin - Strabismus

Parkinson's Disease
- general population 1:1000, over 60 1:75
- tremor, stiffness, or clumsiness,
- difficulty walking, fatigue, depression
- usually involve one side
- destruction of dopaminergic neurons
- elevated cholinergic activity

Treatment:
- MAO inhibitors:
- Dopamine agonists: bromocriptine, pramipexole
- L-Dopa
- Anticholinergics: benztropine
- Decarboxylase inhibitor: carbidopa
- COMT inhibitor

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

Schizophrenia
- Altered perception or expression of reality
- Affects 1% of the population
- Affects men and women equally
- Strong genetic component
- Dopamine (DA) excess theory:
  - Amphetamine exacerbates symptoms and high doses → paranoia, delusions, auditory hallucination. Effects blocked by DA antagonist chlorpromazine.

Antipsychotic Pharmacotherapy:
Typical: chlorpromazine, haloperidol
Atypical: risperidone, olanzapine, sertindole

Chronic Obstructive Pulmonary Disease (COPD)
Features:
- Damage to lungs
- Develops slowly
- No cure
- 4th US Cause of death
- Smoking common cause

Treatment (inhaled):
- Beta2-agonists
- M-receptor blockers
- Glucocorticosteroids
- Oxygen
Asthma

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

Anaphylaxis

- Mechanism
  - Type I (Anaphylaxis) Hypersensitivity

Hypertension (JNC VII – 2003)

- BP Classification
  - SBP mmHg
  - DBP mmHg
  - Normal
  - Pre-hypertension
  - Stage 1 Hypertension
  - Stage 2 Hypertension

*Requires three measurements (repeat visits)

BP lowest in the morning → ↑ during the day

β-Blockers
  - Frontline agents
α-Blockers
  - Hypertensive crisis, special circumstances
D₁a-Agonist
  - Hypertensive crisis iv. ie. Fenoldopam
α₂-Agonists
  - Useful, not frontline ie. Clonidine
Reserpine
  - Resistant hypertension, significant side effects, rarely used
Guanethidine
  - Resistant hypertension, significant side effects, rarely used

CV – USA Prevalence of Hypertension (>= 140/90 mmHg)

Hypertension Is Largely Uncontrolled

- Undiagnosed, unaware
- Acknowledged, untreated
- Treated, controlled
CV - Antihypertensive Agents

1. Diuretics (1st of equals) eg. hydrochlorothiazide
2. Renin / AgII (ACEI, ARBs) eg. captopril, losartan
3. Beta-antagonists eg. propranolol
4. Calcium-antagonists eg. nifedipine, verapamil
5. Alpha-antagonists eg. prazosin
6. Potassium sparing eg. spironolactone
7. Vasodilators eg. hydralazine, nitroprusside
8. Central acting alpha2-agonists: eg. clonidine, α-methyl dopa
9. Inhibit/reduce NE release eg. guanethidine, reserpine
10. Ganglionic blockers eg. mecamylamine

BP Daily Fluctuation

Postural (Orthostatic) Hypotension

- Venous return falls
- Blood pressure falls

reflex mediated

BP (mmHg)

no reflex reflex

95 100 95 55 95 100 195 105

CV - Baroreceptor Reflex Arc

- oppose direct change in BP
- bidirectional, responds to ↑ or ↓ in BP
- not concerned with HR
- not concerned with pulse pressure

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
CV - Angina Pectoris
- Chronic disease (3 million in USA)
- Intermittent attacks of chest pain, left shoulder and arm

Need to improve ratio
Coronary blood flow / cardiac work
or Cardiac O2 supply / O2 demand

A. Typical (Stable, Effort) angina:
- ↑ O₂ demand - fixed supply
B. Variant (Prinzmetal's) angina:
- ↓ O₂ supply - unchanged demand
- i.e. at rest, coronary spasm (PGs?)
C. Unstable angina:
- ↓ O₂ supply, fat buildup or clot
D. Microvascular angina (Syndrome X):
- atherosclerosis in small coronary a.

Deadly Nightshade
“Belladonna”
Approx 5,000 cases per yr
- Mainly atropine
- Devil’s apple
- Stink weed
- Devil’s cherries

Hyperkalemia
Hyperkalemia
- burn & trauma
- usually small ↑K+
- 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 – Angioedema; Glossitis

- Angioedema (<1%)
- Dry mouth
- Glossitis (<5%)
- Oral ulceration
- Oral bleeding

Angioedema
Often occurs in the deep layers of the skin, usually near the eyes and mouth.

SNS - Exam Stress

<table>
<thead>
<tr>
<th>Time</th>
<th>BP</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>120 / 80 mmHg</td>
<td>72 bpm</td>
</tr>
<tr>
<td>Before exam</td>
<td>140 / 99 mmHg</td>
<td>97 bpm</td>
</tr>
<tr>
<td>During exam</td>
<td>179 / 149 mmHg</td>
<td>110 bpm</td>
</tr>
<tr>
<td>End of exam</td>
<td>111 / 74 mmHg</td>
<td>76 bpm</td>
</tr>
</tbody>
</table>

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.

Antimuscarinic Toxicity

Belladonna (beautiful lady)

- mad as a hatter: - CNS, delirium
- red as a beet: - direct vasodilation
- blind as a bat: - cycloplegia
- hot as hell (a hare): - ↓sweat, thermoregulation
- dry as a bone: - decreased secretions