Cardiovascular System & Its Diseases

Lecture #1
Cardiovascular System

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Why do we bother teaching Cardiovascular Pharmacology?
Leading Causes of Death
United States, 2000

- Heart Disease
- Cancer
- Stroke
- Chronic lower respiratory disease
- Unintentional injuries
- Diabetes
- Pneumonia/influenza
- Alzheimer’s disease
- Kidney disease

* Related Disorders
Mainly Thro’ Our Own Habits
Socio-Economic Status Too!
# Overview of Lecture Series

## 1. Cardiovascular System

- **Bits ‘N’ Pieces** Blood, Heart, Blood-Vessels
- **Keeping It Under Control** Heart Rate, Blood Pressure
- **When Things Go Wrong** Hypertension, Ischemia, Heart Failure, Arrhythmias

## 2. Hypertension

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td>Sympathoplegic Drugs, Diuretics, Vasodilators, Angiotensin Antagonists</td>
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</tbody>
</table>

## 3. Myocardial Ischemia

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Diagnosis</th>
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<tbody>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Prophylactic</strong>: Lipid lowering, Anti-coagulant, Anti-platelet drugs</td>
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## 4. Heart Failure & Cardiac Arrhythmias

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Diagnosis</th>
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</thead>
<tbody>
<tr>
<td><strong>Treatment</strong> Heart Failure: Nitrites, Calcium Channel Blockers, Diuretics, Angiotensin Antagonists, β-Blockers, β-Receptor Agonist, Cardiac Glycosides</td>
<td></td>
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<tr>
<td><strong>Arrhythmias</strong>: Channel Blockers (Groups I – IV), Miscellaneous</td>
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</table>
What To Read?

Chapter 8 - 19

Chapters 2 - 3
What Will You Learn Today?

Don’t Put the Cart Before The Horse
*Physiology Then Pharmacology*

1. **Components of the CV System:** Blood, Heart & Blood Vessels

2. **Regulation:** Heart Rate, Blood Pressure (Autonomic NS) & Pharmacology

3. **Playing Doctor:** Mystery Case!!!!!!!!!!!!!!!
There are different types of Circulatory Systems

1. Components of the CV System

**Simple System**
(single-celled organisms use their surface for nutrient and gaseous exchange)

**Open Circulatory System**
(common to molluscs and arthropods; blood bathes tissues with flow being sluggish)
1. Components of the CV System

**Closed Circulatory System**  
(in echinoderms and vertebrates; blood enclosed in specialized vessels)

**Vertebrate Cardiovascular System**  
(multi-chambered heart with complex valves; blood transported in vessels)
A Little Bit of History

**Fish:**
Single (2-chambers) circulatory system (gills to rest of body)

**Amphibians / Reptiles:**
Double (sometimes 3-chambers though)

**Birds / Mammals:**
Complete separation (4-chambers)

**4th Century BC:**
Herophilus distinguished arteries from veins (blood collects in veins at death and empties from arteries; therefore, postulated arteries carried air)

**2nd Century AD:**
Galen assigned different functions to veins and arteries

**1242:**
Ibn Nafis first to describe blood circulation in body

**1628:**
William Harvey described circulatory system in influential book but failed to identify the capillaries
Heart Rate During Embryonic Development

Heart is one of the first organs to appear during development

[Diagram showing heart rate and age relationship]
(i) Blood
Components Of Blood

Some antihypertensives regulate blood volume
Cellular Components Of Blood

Red blood cells
Leucocytes
Platelet

Anticoagulants are used to prevent further blood vessel occlusion

Magnification x10,000
Dynamic Nature Of RBCs

Blood Clotting

Sickle Cell anaemia

Magnification x 5,000
(ii) Heart
**Cardiac Cycle**

- **P Wave**: Atrial Depolarization
- **QRS complex**: Ventricular depolarization
- **T Wave**: Ventricular Repolarization

NB Atrial repolarization is masked by QRS complex

* In hypertension arterial pressure is elevated which compromises the ability of the ventricles to pump effectively *
MidSystolic Murmur

A midsystolic murmur begins shortly after the first sound, peaks in the middle of systole, and does not quite extend to the second sound. It is also known as ejection murmur. The most characteristic feature of this murmur is its cessation before the second sound, thus leaving this latter sound identifiable as a discrete entity. This type of murmur is commonly heard in normal individuals, particularly in the young who usually have increased blood volumes flowing over normal valves.

Continuous Murmur

A pan diastolic murmur begins with the second sound and extends throughout the diastolic period. Patent ductus arteriosus (PDA) is a classical example of this murmur. This condition is usually corrected in childhood. It is heard best at base left and has both a systolic and diastolic component. It is known as a continuous murmur.

Determining Normal Heart Behavior

Normal functioning heart consists of pairs of sounds. Each pair, lub-dub, lub-dub begins with the 1st sound and ends with the 2nd. The major audible components are related to mitral, tricuspid and semi-lunar valve closure.

MidSystolic Murmur

Early Systolic Murmur

Early systolic murmurs begin with the first sound and peak in the first third of systole. Early murmurs have the greatest intensity in the early part of the cycle. Common causes are a small ventricular septal defect (VSD), or the innocent murmurs of childhood. This recording is an early systolic murmur from a 20 year-old female with a small muscular VSD.
(iii) Blood Vessels
Circulatory Routes

- Aorta
- Pulmonary trunk
- Superior vena cava
- Right atrium
- Right ventricle
- Inferior vena cava
- Sinusoids of liver
- Hepatic vein
- Right common iliac vein
- Porte vein
- Right internal iliac (hypogastric) vein
- Right external iliac vein
- Capillaries of gastrointestinal tract
- Capillaries of pelvis
- Venules
- Capillaries of lower extremities
- Capillaries of head, neck, and upper extremities
- Left pulmonary artery
- Left pulmonary veins
- Left atrium
- Left ventricle
- Celiac artery
- Left gastric artery
- Splenic artery
- Common hepatic artery
- Capillaries of stomach
- Superior mesenteric artery
- Inferior mesenteric artery
- Left common iliac artery
- Left internal iliac (hypogastric) artery
- Left external iliac artery
- Arterioles
One-Way Valve In A Vein
Skeletal Muscle Aids Returning Blood To The Heart

(a) Toward heart
- Vein
- Valve open
- Contracted skeletal muscles

(b) Away from heart
- Vein
- Valve closed
- Relaxed skeletal muscles
Contractility is regulated by drugs
Atherosclerosis Restricts Blood Flow In Vessels

Can lead to claudication
(leg pain due to poor circulation)
Regulating Heart Rate

2 Things To Remember:

Cardiac Pacemaker Activity & the Autonomic NS
What Is The Autonomic Nervous System?

Autonomic NS (Involuntary)
- Parasympathetic: Cardiac and smooth muscle, gland cells, nerve terminals
- Sympathetic: Sweat glands
- Sympathetic: Cardiac and smooth muscle, gland cells, nerve terminals

Somatic NS (Voluntary)
- Sympathetic: Renal vascular smooth muscle
- Somatic: Skeletal muscle
Sympathetic & Parasympathetic NS Have Opposing Actions On The Heart

<table>
<thead>
<tr>
<th>Transmitter</th>
<th>Receptor Type</th>
<th>G Protein</th>
<th>Location</th>
<th>Effect and Second Messengers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine</td>
<td>Nicotinic</td>
<td>None</td>
<td>Ganglia</td>
<td>Opens Na⁺, K⁺ channel, depolarizes cell</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td><strong>Muscarinic</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td>G₄</td>
<td>Smooth muscle, some glands</td>
<td>Increases second messengers IP₃ and DAG</td>
</tr>
<tr>
<td></td>
<td></td>
<td>G₁</td>
<td>Cardiac muscle</td>
<td>Decreases cAMP, opens K⁺ channels</td>
</tr>
<tr>
<td><strong>Norepinephrine</strong></td>
<td>α₁</td>
<td>G₄</td>
<td>Smooth muscle, some glands</td>
<td>Increases second messengers IP₃ and DAG</td>
</tr>
<tr>
<td></td>
<td>α₂</td>
<td>G₁</td>
<td>Smooth muscle, preganglionic nerve endings, CNS</td>
<td>Decreases second messenger cAMP</td>
</tr>
<tr>
<td></td>
<td>β₁, β₂, β₃</td>
<td>G₅</td>
<td>Smooth and cardiac muscle, juxtaglomerular apparatus, adipocytes</td>
<td>Increases second messenger cAMP</td>
</tr>
</tbody>
</table>
Typical Cholinergic & Noradrenergic Nerve Endings

[Diagram of cholinergic and noradrenergic nerve endings with chemical pathways and blocking agents.]
Marey's Law: Inverse relationship between blood pressure & heart rate

1. Increased arterial pressure
2. Stimulates carotid sinus and aortic pressoreceptors
3. Stimulates cardioinhibitory center
4. More parasympathetic impulses
5. Decrease in heart rate and force of contraction
6. Decrease in cardiac output
7. Decrease in blood pressure
8. Restoration of blood pressure to normal

Inhibits cardioacceleratory center
Fewer sympathetic impulses
Autonomic Nervous System Regulates Heart Rate

Medulla provides autonomic regulation of heart rate

Innervation that contributes to the Carotid Sinus & Aortic Reflex
Regulating Blood Pressure
Controlling Blood Pressure At Multiple Regulatory Sites

- 1. RESISTANCE
  Arterioles

- 2. CAPACITANCE
  Venules

- 3. PUMP OUTPUT
  Heart

- 4. VOLUME
  Kidneys

  - Renin
  - Aldosterone

  - Angiotensin

CNS—Sympathetic nerves
Autonomic Loop is fast (seconds to minutes) whereas the hormonal loop is slower (hours to days)
NAME MY DISEASE
Case Study

The patient is 21 yrs old and has experienced frequent episodes of blurred vision, dizziness, faintness and syncope for as long as she can remember.

She is the only child; her mother has a history of two spontaneous abortions at 12 and 14 weeks of gestation and one stillborn child at 38 weeks. The subject had a normal development during childhood; although she was considered apathetic and she avoided physical exercise.

Is this a disorder of the Sympathetic NS, Parasympathetic NS or Both?
Cardiovascular System & Its Diseases:

Autonomic Nervous System

Case Study

Plasma noradrenaline and adrenaline were undetectable but dopamine was 7 times normal. Upon 60° head-up tilting, noradrenaline and adrenaline did not change (in normal subjects, they increase) but dopamine increased (usually it does not).

What's wrong with this patient?
This patient has a congenital deficiency in dopamine β-hydroxylase;

The enzyme which converts dopamine to noradrenaline.
What’s Next?
Disease States

Lecture #2. Hypertension most common, asymptomatic

Lecture #3. Myocardial Ischemia demand-supply imbalance

Lecture #4. Heart Failure multifactorial Arrhythmias impulse abnormality
What Have We Learned?

1. **Components:** Blood, Heart & Blood Vessels

2. **Regulation:** Heart Rate & Blood Pressure

3. **Diseases:** Hypertension, Angina, Heart Failure & Arrhythmias
Further Reading?

Pages 56 - 64, 99 -115, 121-129

Chapters 11 - 15