Coagulation

• It is an amplification pathway (cascade, positive feedback).
• Requires clotting factors such as:
  – Calcium ions.
  – 12 different factors, some synthesized by the liver.
• Many are proenzymes or zymogens (inactive enzymes).
• The synthesis of some of them requires Vit. K (II, VII, IX, X).

I- Fibrinogen
II- Prothrombin
III- Tissue factor
IV- calcium
V- doesn’t exist
VI- doesn’t exist
VII
VIII
IX
X
XI
XII
XIII

Future Physiologists take fun classes 5-13 years.

Extrinsic Pathway

• Begins with the release of tissue factor by damaged endothelial cells or peripheral tissues.
• Fast, but not as much PAS made.
• More damage, even faster.
• 3+4= 7 to activate ten, the extrinsic pathway is fast to begin.

Intrinsic Pathway

• Begins with trauma to the blood itself or exposure of the blood to collagen fibers at the injury site.
• Blower, but much more PAS formed.
• platelet factor called PF-3 (a phospholipid).
• Twelve and platelet factor three, eleven they be, then comes four to put nine on the floor, then comes eight to get ten to initiate.

Formation of Prothrombin Activator substance (the beginning of the Common Pathway)

I. Extrinsic pathway
  tissue trauma → tissue thromboplastin (+VII) → X activation
  Rapid and explosive in nature (15 seconds)

II. Intrinsic pathway
  blood trauma, contact with collagen or activated platelets
  XII → IX (+VIII) → X activation
  slower (2-6 minutes) many components (cascade)

Other Common pathway
  Xa combined with V and platelet phospholipids (PF3) + Ca²⁺

Blood Flow within the Fetal Heart

- Foramen ovale-right to left shunt. Most of the blood goes through here.
- Ductus arteriosus-right to left shunt.

Fetal Circulation

- Foramen ovale-right to left shunt. Most of the blood goes through here.
- Ductus arteriosus-right to left shunt.

Birth

- Prostaglandin levels drop
- Baby breathe-lowers pressure in pulmonary circuit
- Umbilical cord is clamped and cut and increases systemic pressure
- Foramen ovale closes and becomes fossa ovalis
- Ductus arteriosus closes and becomes ligamentum arteriosum (oxygen content is signal for vessel to close)
PDA- patent ductus arteriosus

- Left to right shunt
- Blood flows back to lungs repeatedly - why?
- Net CO decreases so blood vol increases and CO goes back toward normal
- Left and right ventricular hypertrophy
- Characteristic cyanosis of baby

Tetralogy of Fallot

- “Blue Babies”
- Right to left shunt
- Tetralogy of Fallot made up of 4 heart defects but not all four are necessarily present in each baby with TF:
  - Prolapse - valve doesn’t close properly
  - Stenosis - valve has difficulty opening
  - Regurgitation - backflow of blood
  - Auscultation - “listening” to heart sounds — more of them when valves don’t work correctly

Terms

- Prolapse - valve doesn’t close properly
- Stenosis - valve has difficulty opening
- Regurgitation - backflow of blood
- Auscultation - “listening” to heart sounds — more of them when valves don’t work correctly

Dynamics of Streptococcal Damage to Heart Valves

- Streptococcus
- release of M antigen
- Heart valve cell with M antigens attached
- Antibody formed against combination
- Complement damage to heart valves

Dynamics of mitral stenosis

- Stenosis: blood flow from left atrium to left ventricle decreased
- Murmur heard in last part of diastole - why?
- Reduced movement of blood.
- Enlarged left atrium.
- Pulmonary edema.

Mitral valve prolapse

- Blood goes back into left atrium
- Blowing murmur heard throughout systole - high pitch

Dynamics of Aortic valve Stenosis

- Stenosis: Contracting left ventricle fails to empty adequately (ESV?)
- SV decreased
- Left ventricle hypertrophy
- Leads to increased blood volume (due to decreased MAP) — kidneys release erythropoietin.

Aortic Regurgitation

- Murmur heard during diastole
- May have stroke vol. of 300ml with 70ml going to periphery and 230 leaking back

Anatomy of the Baroreceptors

- spray type nerve endings located in the walls of the carotid bifurcation called the carotid sinus in the walls of the aortic arch:
- pressoreceptors that respond to stretch.
- Signals from the carotid sinus are transmitted by the glossopharyngeal nerves.
- Signals from the arch of the aorta are transmitted through the vagus into the NTS.
- Important in short term regulation of arterial pressure.
- Opposes either increases or decreases in arterial pressure thereby reducing daily variations in arterial pressure.
- Important in short term regulation of arterial pressure.
Response of the Baroreceptors to Arterial Pressure

- **Baroreceptors** respond to changes in arterial pressure.
- As pressure increases, the number of impulses from **carotid sinus** increases, which results in:
  1. Inhibition of the vasoconstrictor
  2. Activation of the vagal center

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**Functions of the Baroreceptors**

- Maintain relatively constant pressure despite changes in body posture.

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**Drugs Affecting CO**

- **Atropine**: parasympathetic blocking (blocks muscarinic AchR agent) (+, +)
- **Pilocarpine**: drug that causes acetylcholinergic neurons to release Ach. Since Ach decreases heart rate, it causes (-, -) effect on heart.
- **Propranolol**: reversible, competitive blocker of beta1 receptor. So blocks sympathetic effect of heart (-, -)

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**Drugs Affecting CO (2)**

- **Digoxin (shorter ½ life) or Digitoxin**: come from group of drugs derived from digitalis. Digitalis derived from foxglove plant. It has a (+, +) effect, neg chronotropic and positive inotropic effect; slows heart rate but increases force of contraction. It is only drug with this effect on heart.
- Increases intracellular concentration of Ca.
- Increases force of contraction by inhibiting Na+/K+ pump. So cells start to accumulate Na.
- Disadvantage of using digitalis is that it's extremely toxic. The optimal dose is very close to lethal dose - stops heart.

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**adrenergic or sympathomimetic drugs** act like norepi and epi

- These drugs have an effect which is much more prolonged than that of either norepi or epi:
  - phenylephrine stimulates alpha receptors
  - ephedrine stimulates both beta, and beta2 receptors
  - adrenaline stimulates only beta, receptors
- Some drugs act indirectly by increasing the release of norepi from its storage terminals.
  - ephedrine, amphetamine
Pharmacology of the Sympathetic Nervous System

- drugs that block the effect of norepi and epi
  - alpha blockers
    - phentolamine
  - beta blockers
    - beta1 and 2 - propranolol

Pharmacology of the Parasympathetic Nervous System

- parasympathomimetic drugs
  - pilocarpine
  - atropine
  - physostigmine
  - muscarine
- cholinesterase inhibitors
  - neostigmine
- antimuscarinic drugs
  - atropine

Anemia - Condition where the blood has an abnormally low oxygen-carrying capacity from low Hb concentration

1. Too few circulating erythrocytes (low RBC count, low HCT, low Hb concentration, but normal MCH and MCHC values; normocytic, normochromic)
2. Normal erythrocyte counts, but each RBC contains lower than normal amount of Hb (low Hb concentration, and low MCH and MCHC values; microcytic/hypochromic)

Why are anemic individuals often short of breath, fatigued, and chilly?

Types:
- Hemolytic/Hemorrhagic
- Aplastic and hypoproliferative
- Thalassemia
- Megaloblastic
- Iron-deficiency

Aplastic anemia

- Primary
  - idiopathic
- Secondary
  - Drugs - chemotherapy, antibiotics,
  - Chemicals - benzene
  - Radiation
  - Immune suppression of stem cell
  - Malignancy

Iron Deficiency

- deficiency in dietary Folic acid or Vitamin B12
- Concomitant in synthesis of thymidine, DNA synthesis is halted and therefore mitosis rates are low
- RNA production is elevated, Elevated rates of protein synthesis
- Cells become megaloblastic, irregularly shaped (poikilocytic) and have fragile membranes so they are removed sooner (hemolytic)
- Increased MCV and normal MCH; increased Hb synthesis
**Megaloblastic Anemias-2**

- Folic acid
  - Green veggies
  - Greater demand during pregnancy for neural tube closure.
  - Stored supply- 6-9 months
  - Alcoholism, sprue, and anti-cancer drugs interfere
- Stomach mucosa produces intrinsic factor which is necessary for Vitamin B$_12$ absorption
  - Pernicious
  - Gastrectomy or gastric atrophy- lack of intrinsic factor
  - Stored supply- 3-5 years

**What are the Thalassemias?**

- A group of diseases characterized by defects in synthesis of one or more globin chains (α-, β-
  - Thalassemia)
  - Some severe, others mild
  - Unaffected chain is in excess and accumulates in erythropoietic cell and causes impaired DNA synthesis
  - Hypochromic, microcytic
  - Organ failure
  - Splenomegaly/hepatomegaly

**Thalassemia- 2**

- Thalassa (Greek) = Sea
- β-Thal or Thal. major (Cooley’s anemia)
  - Shortened RBC lifespan, early removal (hemolysis)
  - Expansion of intramedullary spaces (erythropoiesis)
  - Skeletal abnormalities
  - Increased iron absorption, iron overload and its consequences
  - HbF can persist

**Classification of Anemias**

<table>
<thead>
<tr>
<th>Category</th>
<th>MCV (fl)</th>
<th>High Content (MCHC) (g/dl)</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normocytic (80-100)</td>
<td>Normochromic (32-36)</td>
<td>Bone marrow failure, renal failure, hemolytic anemia (acute) Megaloblastic anemia</td>
</tr>
<tr>
<td>2</td>
<td>Macrocytic (&gt;100)</td>
<td>Hypochromic (&lt;32)</td>
<td>Iron deficiency, thalassemia, hemolytic anemia (chronic)</td>
</tr>
</tbody>
</table>

**Inositol Trisphosphate & DAG**

**β adrenergic receptor mechanism**

**Summary**

- DNA transcription (in nucleus)
- mRNA translation (at the ribosome, in cytoplasm)
- Protein (chain of aa, sequence determines structure, structure determines function)