REVISION

GIT PHYSIOLOGY

(Final Exam, L7-L12)

(Important Notes)

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Lecture 7: Large Intestine:

-Colon consist of: Ascending - Transverse - Descending - Sigmoid - Rectum - Anal canal.

-Functions of the Large Intestine:

1.Reabsorb water and compact material into feces.

2.Absorb vitamins produced by bacteria.

3.Store fecal matter prior to defecation.

-The Large Intestine secretes large amount of Mucus (Goblet cells).

-The mucosa of the large intestine has many crypts of Lieberkühn and Absence of villi.

-The epithelial cells contain almost no enzymes.

-Stimulation of the pelvic nerves from the spinal cord can cause:

1-marked increase in mucus secretion.

2-increase in peristaltic motility of the colon.

*Gastrocolic & duodenocolic reflexes are increase the colon movement by filling the Stomach or duodenum.

ILEOCECAL VALVE	
-it prevents backflow of contents from colon into small intestine. It remains closed and open only when an intestinal peristaltic wave reaches it.	
Relaxed By:	Contracted By:
Gastrin, CCK, B adrenergic	Distension of the cecum, Secretin, Ach, alpha adrenergic

Bacterial Action in the Colon:

-Colon bacilli bacteria are capable of digest small amounts of cellulose.

-Vitamin K, vitamin B12, thiamine, and various gases can be formed by colon bacteria.

-The bacteria-formed vitamin K is especially important because the amount of this vitamin in the daily ingested foods is normally insufficient to maintain adequate blood coagulation.

physiology of different colon regions			
Ascending Colon	Transverse Colon	Descending Colon	recto sigmoid region, anal canal, and pelvic floor musculature
-The ascending colon is specialized for processing chyme delivered from the terminal ileum. -When chyme is instilled (put gradually) into cecum, half of the instilled volume empties from ascending colon in 87 min. -This period is short in comparison with the transverse colon	The transverse colon is specialized for the storage and dehydration of feces. -The labeled material is retained for about 24 hrs. -The transverse colon is the primary site for the removal of water and electrolytes and the storage of feces.	-The descending colon is a conduit between the transverse and sigmoid colon "transportation". -Labeled feces begin to accumulate in the sigmoid colon about 24 hours after the label is instilled in the cecum. -This region has the neural program for power propulsion that is involved in defecation reflex.	-They maintain fecal continence (the ability to voluntarily control urinary and fecal discharge). -The sigmoid and rectum are reservoirs with a capacity of up to 500 mL. -The puborectalis muscle and external anal sphincter comprise a functional unit that maintain continence. -Fibers of puborectalisjoin behind the anorectumand pass around it to form a U-shaped sling (physiological valve)

-**External** and Puborectalis muscles: Contraction of them blocks the passage of feces and maintains continence in **large** amounts.

-**Internal** and Puborectalis muscles: Contraction of them blocks the passage of feces and maintains continence in **low** amounts.

-Most of the **absorption** in the large intestine occurs in the **proximal one half of the colon** giving this portion the name absorbing colon

-The distal colon functions principally for **feces storage** until a propitious time for feces excretion and is therefore called the storage colon.

The transit of small labeled markers through the large intestine occurs in 36-48 hrs.
-The large intestine can absorb a maximum of 5 to 8 liters of fluid and electrolytes each day.
•The mucosa, like that of the small intestine, has a high capability for active absorption of sodium, Cl and water.

-Reabsorption in the large intestine includes:
•Water, Sodium and Chlor.
•Vitamins –K, biotin, and B5
•Organic wastes –Urobilinogens and Sterobilinogens.
•Bile salts
•Toxins
•Ammonia (By Catalyzing Urea by Urease).

-The large intestine secretes bicarbonate ions and Potassium.

-Sensory innervation of large intestine:
1-**Mechanoreceptors** in the rectum detect distention and supply the ENS.
2-The anal canal in the region of the skin is innervated by **somatosensory nerves** that transmit signals to CNS, This region has sensory receptors of pain, temperature and touch .

Movements of the colon		
Mixing movements (Haustrations).	Propulsive movements (Mass Movements).	Antiperistalsis Movement.
-At: Ascending colon + 1st part of transverse colon. -Ring-like contractions (about 2.5 cm) of the circular muscle divide the colon into pockets called haustra. -The contracting segment and receiving segment on either side remain in their respective state for longer periods. In addition, there is uniform repetition of the haustra along the colon. -Net forward propulsion occurs when sequential migration of haustra occurs along the length of the bowel.	-Rest part of transverse colon + Descending colon. -The motor events in the transverse and descending colon. -May be triggered by the increased delivery of ileal chyme into ascending colon following a meal (gastrocolic reflex). Irritants, e.g., castor oil, threatening agents such as parasites and enterotoxins can initiate mass movement. -Start at the middle of transverse colon and is preceded by relaxation of the circular muscle and the downstream disappearance of haustral contractions.	-It starts at the junction of ascending and transverse colon and traveling towards the cecum. It mixes contents and help water absorption.

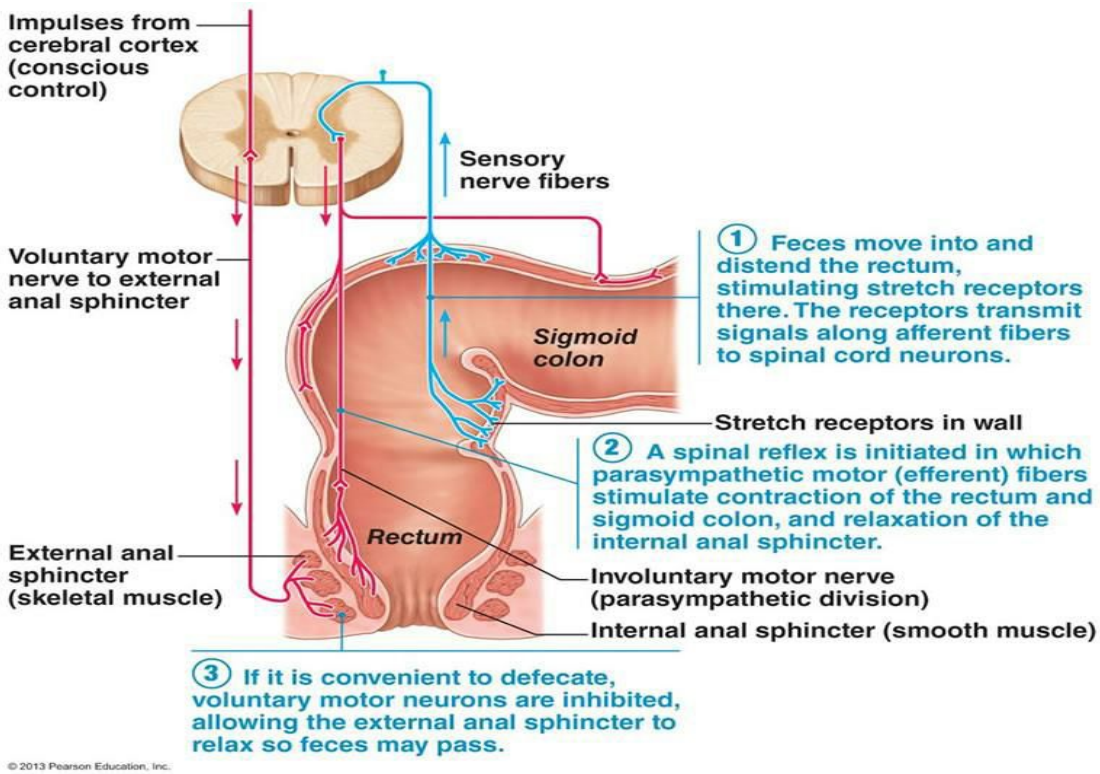
CONTROL OF COLONIC MOTILITY:

The intramural plexuses directly control the contractile behavior of the colon.

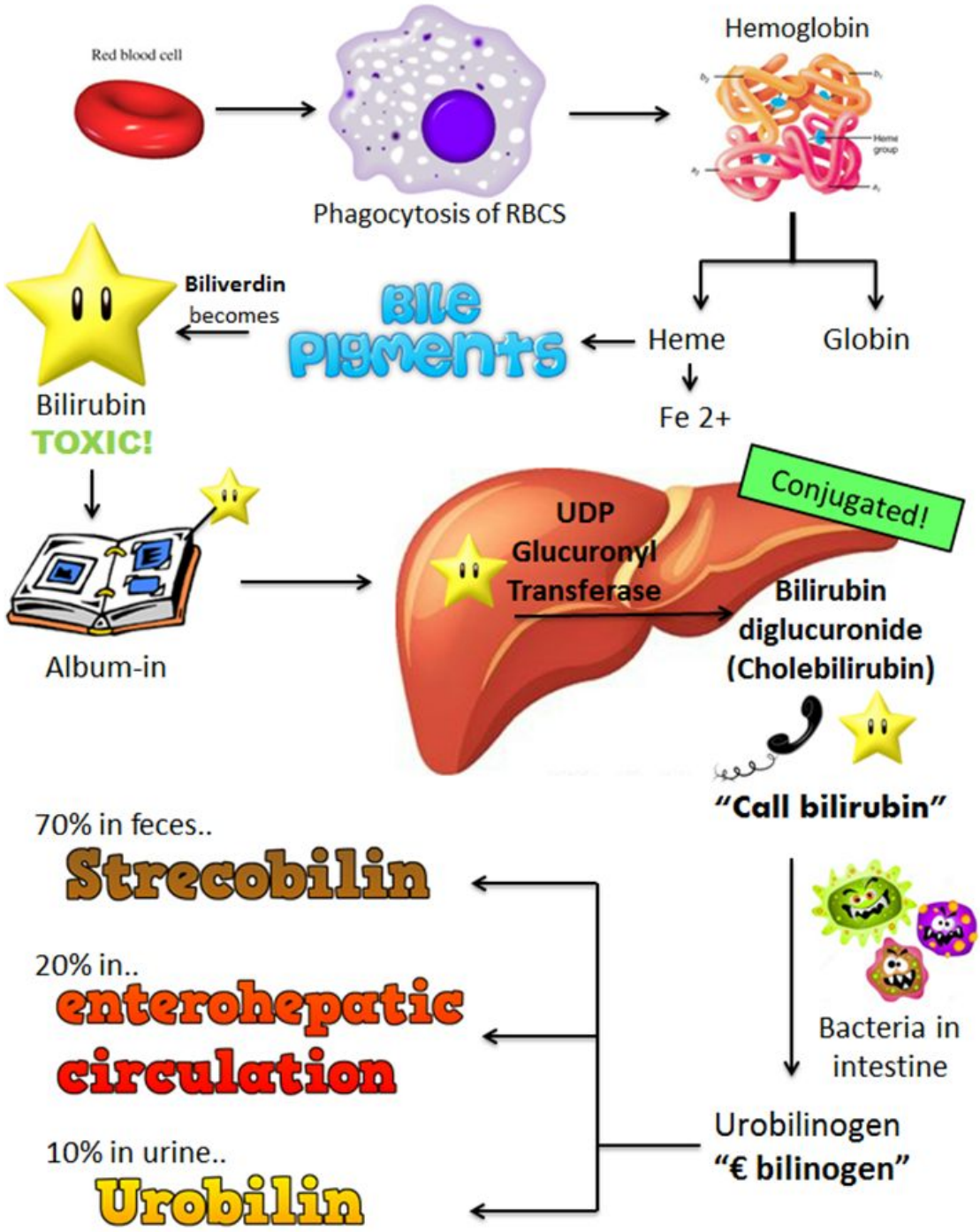
Colon Motility	
Stimulated by:	**Inhibited by:**
acetylcholine & substance P as neurotransmitter.	**VIP & NO onto colonic smooth muscle cells**

Defecation Reflex:

1-Distension of the rectum. 2-Stimulation of the stretch receptors in the rectum.
3-Short reflex: Stimulation of myenteric plexus in sigmoid colon and rectum or Long reflex by stimulation of parasympathetic motor neurons in sacral spinal cord.
4-Increased local peristalsis.
5-Relaxationof internal anal sphincter and contraction of externalanal sphincter.
6-Defecation.



Lecture 8: Bilirubin



Bilirubin	
unconjugated, indirect, free bilirubin, heme bilirubin	**Conjugated, direct, cholebilirubin**
• **Bilirubin bound to albumin:** -Not filtered through renal -glomeruli -Has affinity to brain tissue (can cause kernicterus), toxic.	• **Bilirubin bound to glucuronic acid:** -Water soluble -filtered through renal glomeruli -No affinity to brain tissue

Ranges of bilirubin:

Normal: 0.1-1 mg/dl
Occult hyperbilirubinemia: 1-2 mg/dl
Jaundice: >2 mg/dl

Other substances excreted in bile:

1- Cholesterol & Alkaline phosphatase
- Rise in patients with → jaundice due to intra or extra hepatic **obstruction**
- Much smaller rise → jaundice due to **non obstructive** hepatocellular disease

2- Adrenocortical, other steroid hormones & a number of drugs
- excreted in bile and subsequently reabsorbed (enterohepatic circulation).

Lecture 9: Reticuloendothelial System:

General Functions of RES:

1-Phagocytosis.
2-Immune function (antigen processing and antibody production)
3-Breakdown of aging RBC. 4-Storage and circulation of iron.

Components of RES:

1- Endothelial cells 2-Monocytes 3- Macrophages

Formation of macrophages:

1-Begin by Stem cell in Bone Marrow: monoblast maturing to promonocyte and mature monocytes released into blood.
2-Stay for 10-20 hours in circulation.
3-Then leave blood to tissues transforming into larger cells macrophage.
4-Macrophage life span is longer up to few months in tissues

Transformation from monocytes into macrophages:

1-Cell size. 2-Number and complexity of intracellular organelles Golgi, mitochondria and lysosomes. 3- Intracellular digestive enzymes

Lymphoid organs:

Thymus: has a high rate of growth and activity until puberty, then it begins to shrink and degenerate; its the site of T-cell maturation.

Lymph nodes: are small, encapsulated organs stationed along lymphatic channels and large blood vessels of the thoracic and abdominal cavities.

Spleen: is structurally similar to lymph node, it filters circulating blood to remove exhausted RBCs and pathogens.

Immune function of spleen:

1-Site for Phagocytosis
2-Site of B cell maturation into plasma cells, which synthesize antibodies in its white pulp and initiates humoral response.
3-Removes antibody-coated bacteria along with antibody-coated blood cells.
4-It contains (in its blood reserve) half of the body monocytes within the red pulp, upon moving to injured tissue (such as the heart), turn into dendritic cells and macrophages that promoting tissue healing.
5-it responds faster than other lymph nodes to blood-borne antigens.
6-Destruction and processing of antigens.
7-Reservoir of lymphocytes in white pulp.

General Functions of Spleen:

1-Haematopoiesis (Hemopoiesis): fetal life.

2. Spleen is a main site for destruction of RBCs specially old and abnormal e.g. spherocytosis.

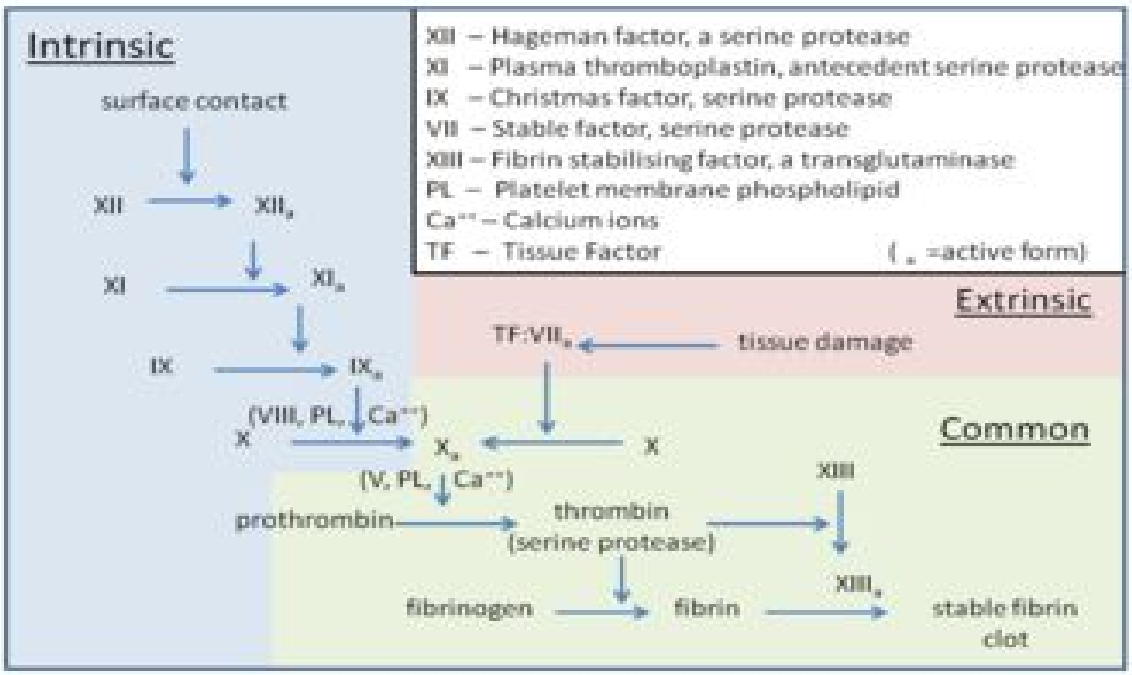
3. Blood is filtered through the spleen.

4. Reservoir of thrombocytes and immature erythrocytes.

5. Recycles of iron. 6. immune function.

Lecture 10: Coagulation Mechanism:

The three pathways that makeup the classical blood coagulation pathway



Most important information about blood clotting factors:

Factor name	Function
Prothrombin (II)	- Plasma protein formed by live (a2 globulin) - Unstable - Vit K dependent + decrease in liver diseases
Fibrinogen (I)	- High MW -Formed by liver
Fibrin stabilizing factor (XIII)	- Release from platelets -Should be activated before it's effects the fibrin fibers -Causing strength of fibrin meshwork
Thrombin	- weak proteolytic capabilities - act on fibrinogen to form fibrin monomer - stimulates platelets to release - ADP & THX A2

Anticoagulant:

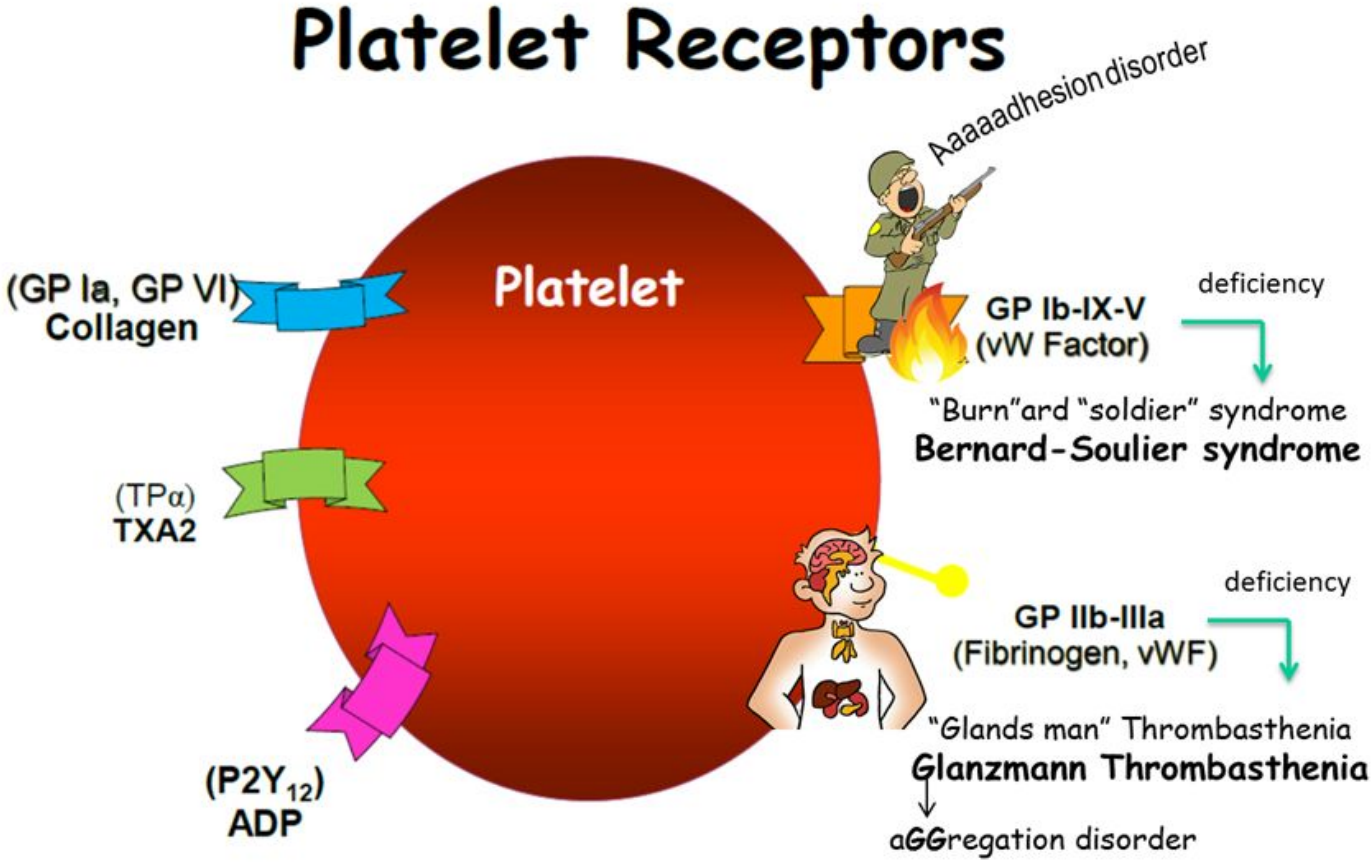
- Endothelial surface factors: Smoothness of the ECS-Glycocalyx layer-Thrombomodulin protein
- Fibrin fibers
- Antithrombin III: combines the remaining thrombin and removes it from blood.
- Heparin, combines with Antithrombin III and quickly removes thrombin from blood
- Protein C: (inhibits Va & VIIIa) , Protein S > cofactor.

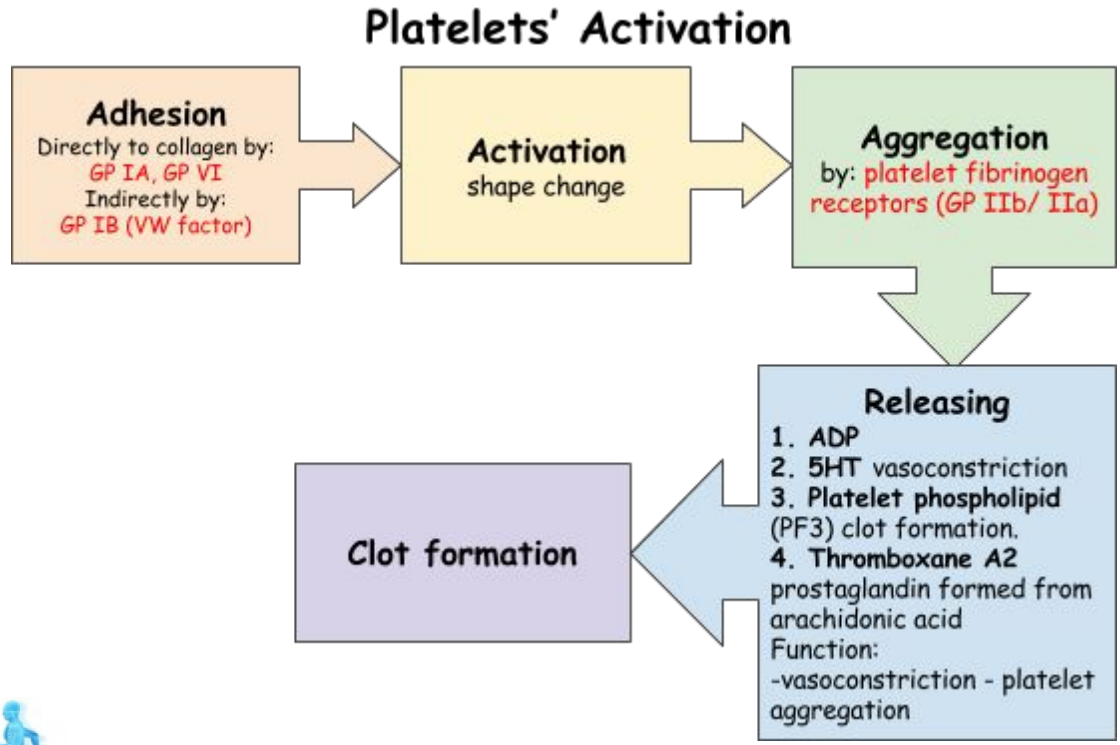
HYPERCOAGULABILITY		Excessive bleeding
Hereditary	**Acquired**	1.Vitamin K Deficiency factors : II / VII / IX /X require it for their synthesis 2.Hemophilia factor VIII > Hemophilia A factor IX > Hemophilia B 3.Thrombocytopenia Very low number of platelets in blood (< 50,000/µl) ***Thrombocytopenic purpura*** ***Idiopathic Thrombocytopenia***
1-Factor V Leiden 2-Deficiencies of AT III, Protein C & S 3-Increased FVIII	1-Increase fibrinogen & FVII 2-Antiphospholipid antibodies (LA & ACAs) 3-Oestrogen therapy -smoking 4-Pregnancy – dehydration Surgery and prolonged immobility - malignancy 5-Major Trauma-varicose vein	

Laboratory tests of hypercoagulability:

Coagulation activation markers	TAT, D-dimer, Prothrombin fraction 1+2
Genotyping	Factor V Leiden, Hyperhomocysteinemia (MTHFR)
Natural anticoagulants	ATIII , protein C, Protein S
Fibrinolysis	PAI-1, D-dimer

Lecture 11: Platelets Structure and function:





Thrombocytopenia (deficiency in platelets number):-

- **Decrease Production:**

Ex.. Leukemia, Lymphoma, anemias, Viruses(chickenpox, parvovirus, AIDS), chemotherapy & radiation, alcohol excess, Medication(diuretics, chloramphenicol).

- **Increased Destruction:**

Ex.. Autoimmune disease, Medication(vancomycin, rifampin,heparin), Surgery, Infection, Pregnancy.

- **Abnormal Destruction**
- **Splenomegaly.**
- **Pseudothrombocytopenia:**
- **Partial clotting of specimen**, EDTA-platelet clumping, Platelet satellitism around WBCs, Cold agglutinins and Giant platelets.

Lecture 12: Bile salts & Enterohepatic Circulation

The The Bile		
Characteristics	**Functions**	**Secretion**
• Golden yellow/ Greenish fluid • *Isotonic* / slightly alkaline. • $NaHCO_3$ is responsible for alkaline.	*Fat digestion and absorption. *Excretion of waste products from blood. i.e.: Bilirubin	Hepatocytes → Bile canaliculi → Hepatic duct → Common Hepatic duct: Either • Common bile duct → Duodenum • Cystic duct → Gall bladder

Gall Bladder Bile VS Hepatic Bile

- Gall bladder **Stores & Concentrate** bile that comes from liver by:

✓ Active absorption of Na, Cl and HCO_3.

✓ Passive water movement out of lumen.

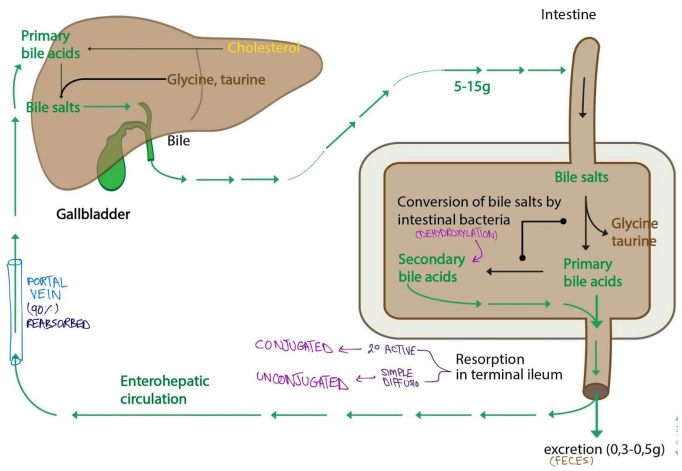
Thus pH and conc. of solutes will be ***LESS*** *in gallbladder bile than of hepatic bile.*

Control of Biliary System:

Choleretics Substances that stimulate *hepatic secretion* of bile	**Cholagogues** Substances that stimulate *evacuation* of bile by gall bladder
• Bile acid *dependent* component: -Integrity of enterohepatic circulation. -Bile acids (Reabsorbed & Newly synthesized).	• **Nervous Component: -Vagal stimulation-** ✓ Contraction of gallbladder ✓ Relaxation of sphincter of Oddi ✓ Increase bile formation
• Bile acid *independent* component: -Hormones i.e.: *Secretin*, Glucagon, CCK and Gastrin. -Vagal stimulation -indirect-	• **Hormonal Component:** ✓ CCK

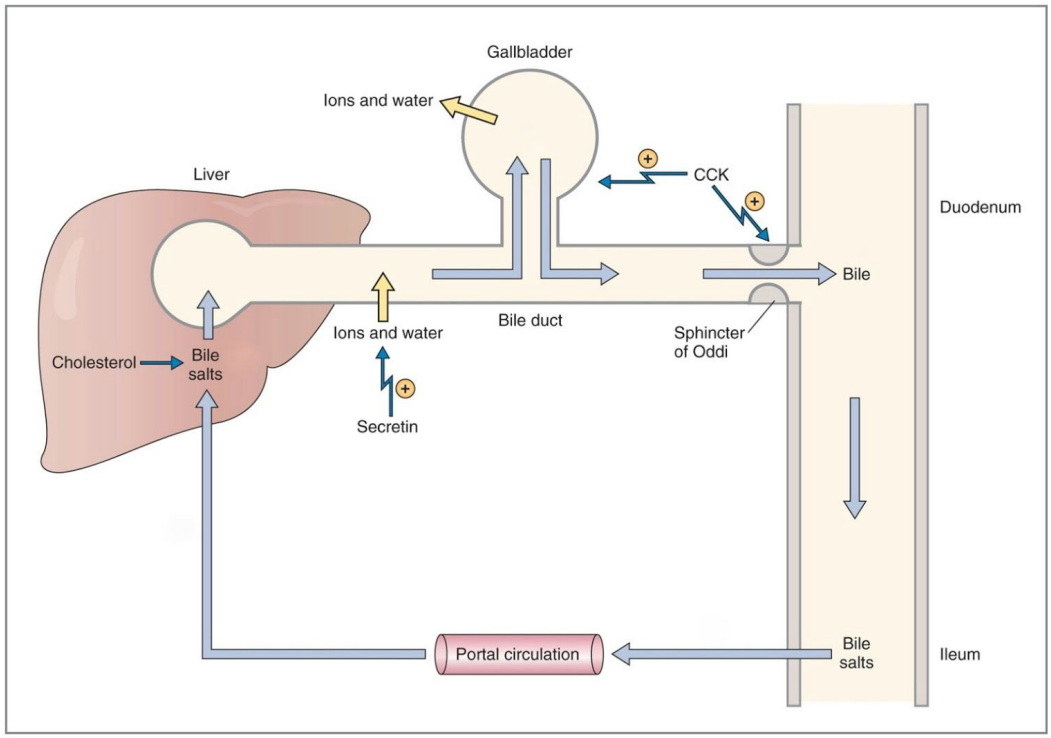
- ↑ **Portal blood flow** = ↑ **bile secretion.**
- **Liver Congested** (↑ intrahepatic vascular pressure) = ↓**bile secretion.**

Enterohepatic Circulation: Circulation of bile salts between small intestine and liver.



Total amount of bile acid in body = *Total bile acid pool* = 2-4g

- **Absorption of bile acids in intestinal lumen:**
  - ✓ 2ry active transport (Conjugated)
  - ✓ Simple diffusion (Unconjugated)
  - ✓ Bound to proteins
- **Absorbed bile acids in portal vein are bound to albumin.**
- **Uptake of bile acids from sinusoidal blood:**
  - ✓ 2ry active transport
  - ✓ Facilitated diffusion
  - ✓ Passive diffusion
  - ✓ Bile acid-HCO3/OH exchange



Importance of Enterohepatic Circulation:

- Stimulation and maintenance of bile secretion by hepatocytes.
- The *greater* the bile in enterohepatic circulation the *greater* the bile secretion.
- Cycling several times during a meal → Promotes lipid absorption.
- If enterohepatic circulation is interrupted:

✓ Obstruction, surgical removal or inflammation of terminal ileum:
- bile flow reduced
- Bile salts lost in feces
- Malabsorption of fats = *Steatorrhea*

✓ Excess amount of bile enters colon = *Diarrhea*

Functions of Bile Acids:

- Digestion of fats (emulsifications)
- Absorption of fats (Formation of micelles)
- Absorption of fat soluble vitamins (A D E K)
- Stimulation of colon motility

- Stimulation of bile secretion and flow in liver.
- -ve feedback in release of CCK
- Anti-putrefaction

***Recall:**

Hormone, Enzyme, Neurotransmitter	Effect on stomach	Effect on Small intestine	Effect on pancreas	Effect on Large intestine
Secretin (S cell)	1. ↓ stomach emptying by constricting the antrum. 2. ↑ constriction of pyloric sphincter 3. ↑ pepsinogen secretion 4. ↓ gastric H secretion & gastrin release	1. ↓ intestinal motility 2. ↑ intestinal secretion (Brunner's secretion & intestinal juice)	1. ↑ secretion of HCO3 & H2O (on pancreatic duct cells) 2. ↑ hepatic bile flow & HCO3 secret	**Contract** ileocecal sphincter
CCK (I cell)	1. ↑ constriction of pyloric sphincter (increase tone) So, it decreases stomach emptying 2. ↑ pepsinogen secretion & gastric motility. 3. ↓ the pyloric pump. so, it decreases stomach emptying 4.Act as inhibitor to block increase in stomach motility caused by gastrin	↑ intestinal juice secretion	1. ↑ enzyme secretion (on pancreatic acinar cells) 2. Trophic effect 3. **Contracts** gall bladder. 4. **Relaxes** sphincter of oddi	**Relax** ileocecal sphincter
Gastrin (G cell)	1. ↑ H,HCL secretion 2. ↑ pepsinogen secretion 3. ↑ antrum & pyloric contraction. so, it increases stomach emptying 4. ↑ growth of gastric mucosa	↑ intestinal motility & intestinal juice secretion	_____	**Relax** ileocecal sphincter
Glucagon	_____	1. ↓ intestinal motility 2. ↑ intestinal juice secretion	_____	**Contract** ileocecal sphincter
Motilin	_____	↑ intestinal motility & regulates MMC	_____	_____
Insulin & serotonin	_____	↑ intestinal motility	_____	_____
Somatostatin , GIP & PG	↓ HCl Secretion ↓ Gastric Emptying	_____	_____	_____