Fisiologi :

Hepar - Vesika felea – Pankreas - Lien

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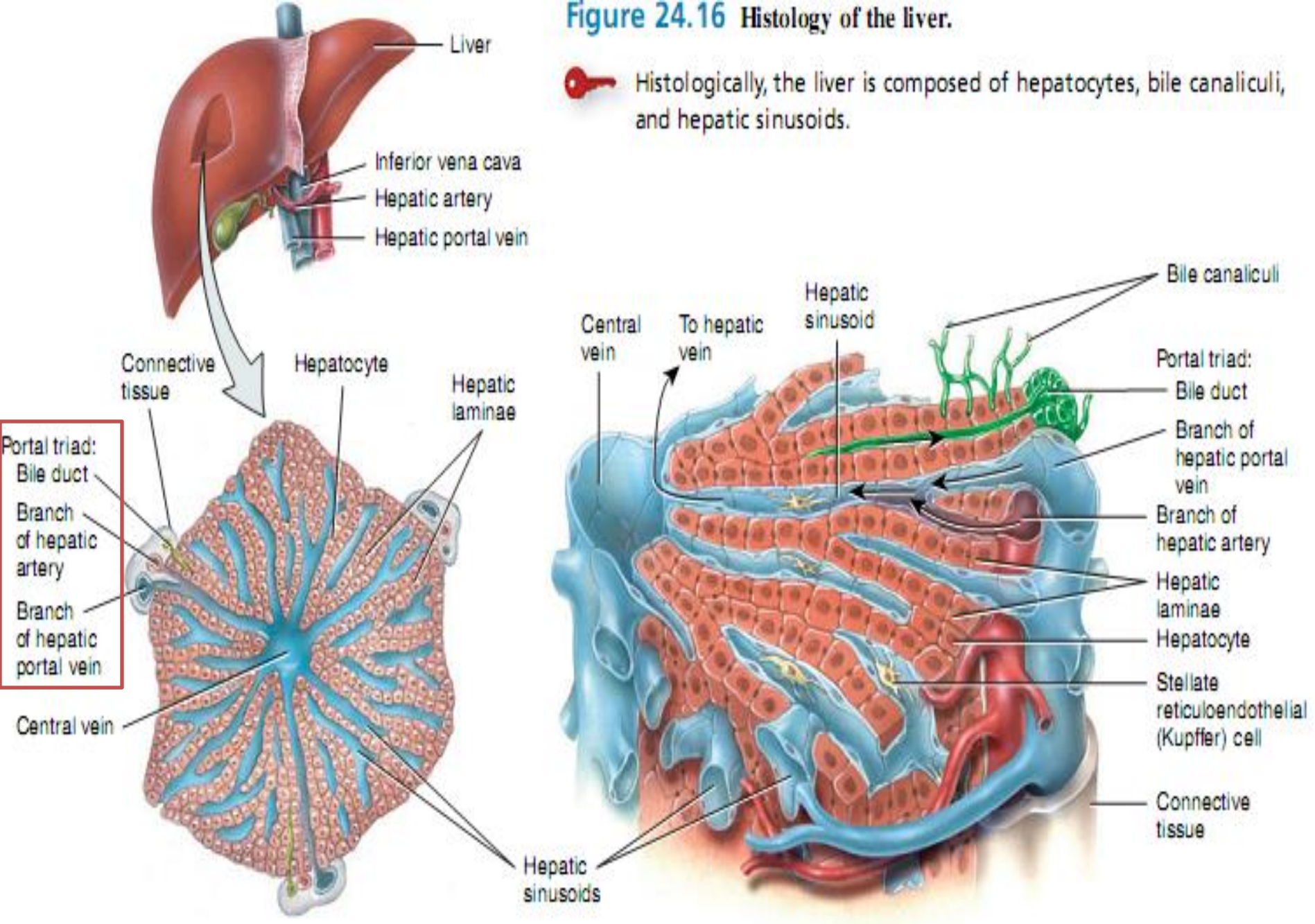
Hepar

- The liver is the largest organ in the body, 2% dari total BB (1.5 kg) orang dewasa.
- Unit fungsional liver adalah lobulus hepar, berbentuk hexagonal.
- The human liver contains 50,000 – 100,000 individual lobules

Figure 24.16 Histology of the liver.

Histologically, the liver is composed of hepatocytes, bile canaliculi, and hepatic sinusoids.

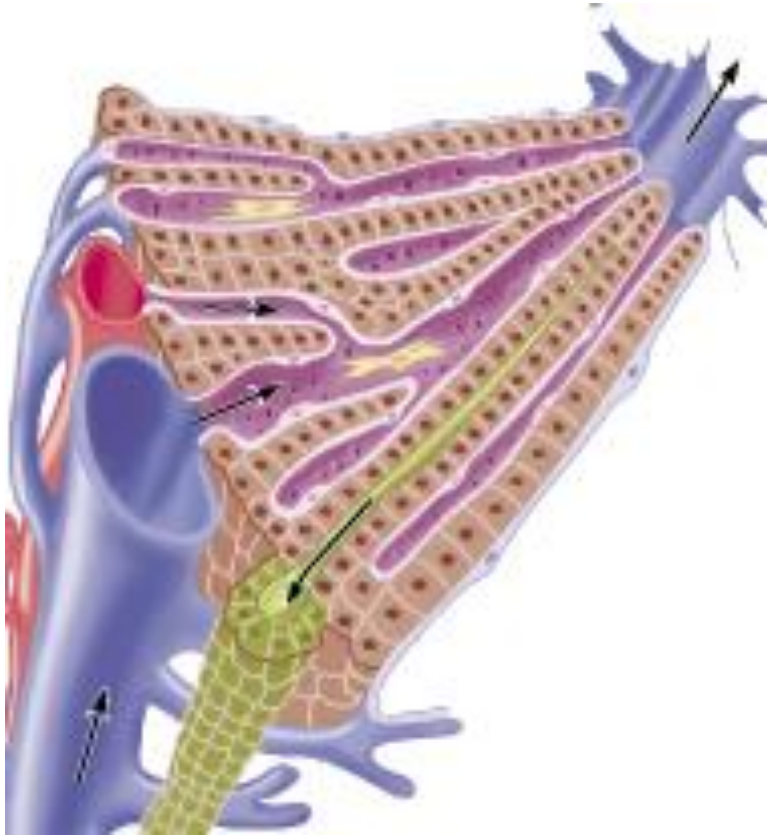


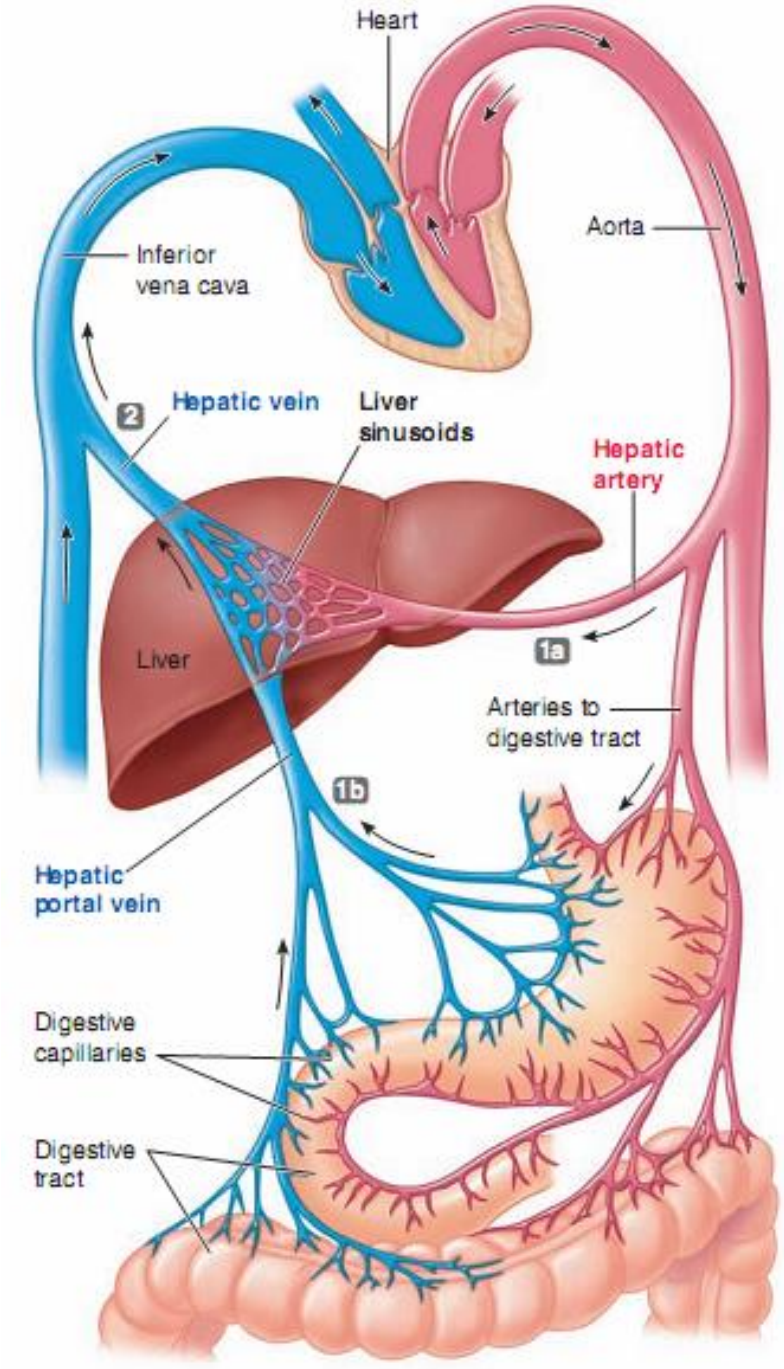
(a) Overview of histological components of liver

(b) Details of histological components of liver

Blood flow in liver

- Hepatic artery branch
  - Oxygenated blood to lobule
- Portal vein branch
  - Deoxygenated blood with substances from intestine
- Blood flows through sinusoids
  - Kupffer cells phagocytize bacteria, foreign material, old RBC's
- Plasma seeps out and bathes hepatocytes





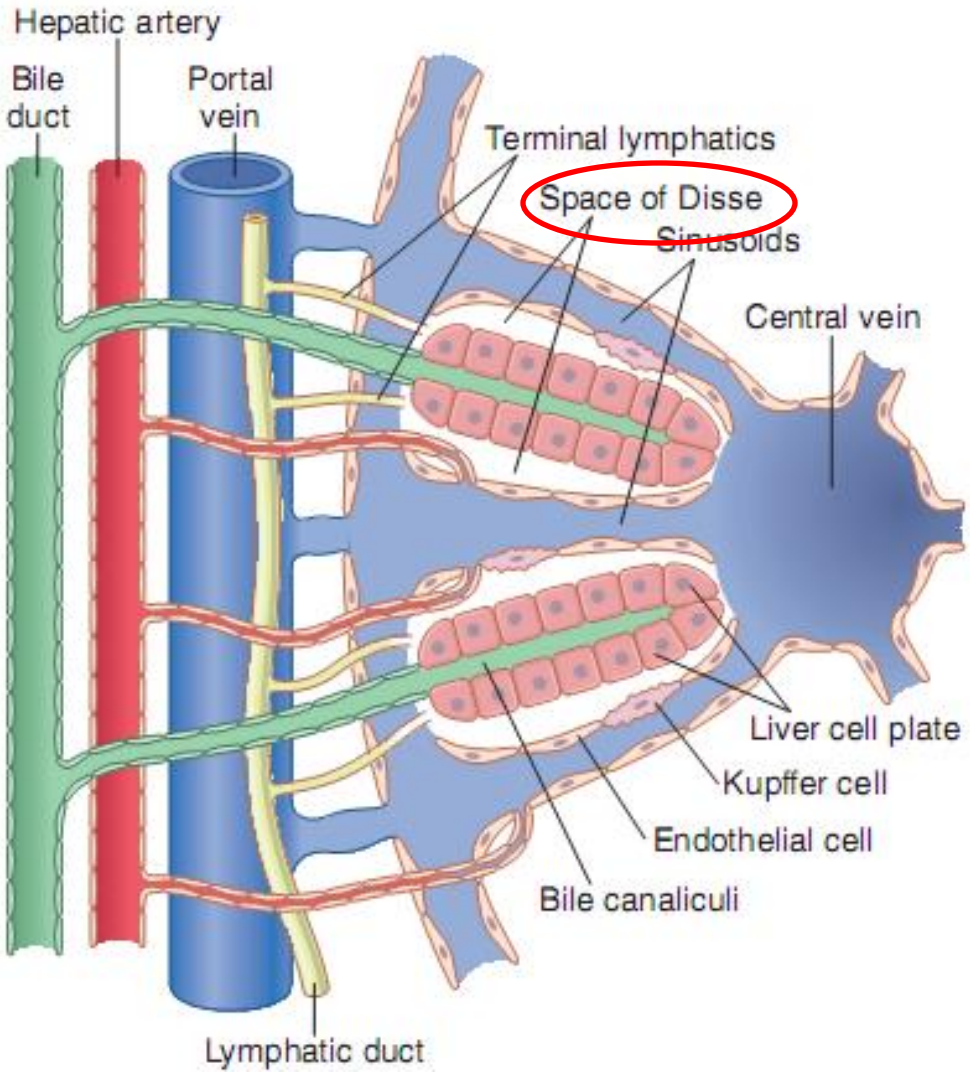
The liver receives blood from two sources:

1a Arterial blood, which provides the liver's O_2 supply and carries blood-borne metabolites for hepatic processing, is delivered by the **hepatic artery**.

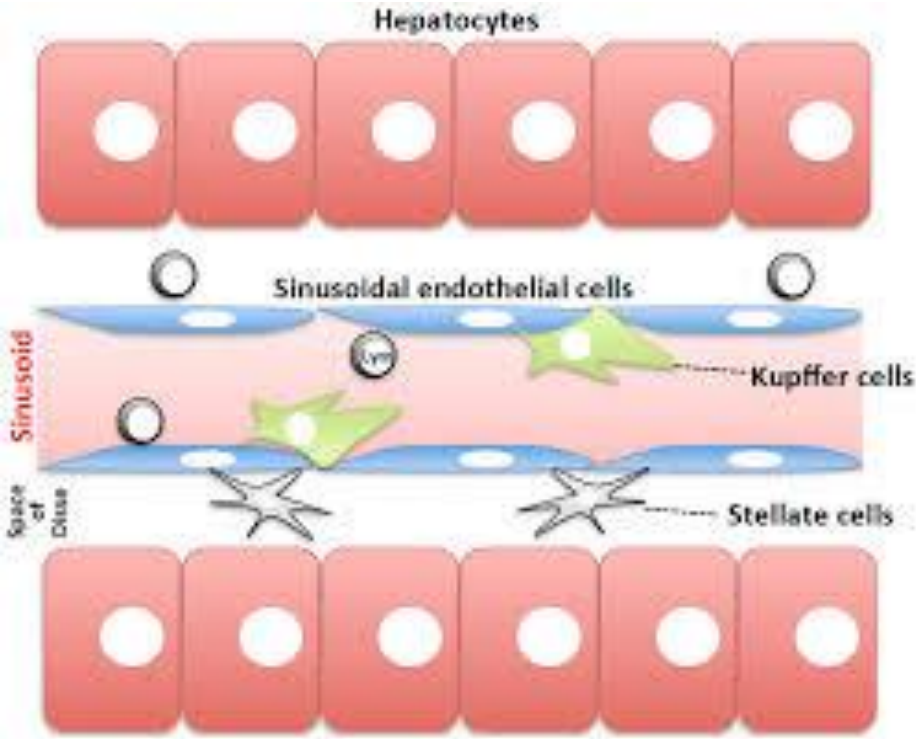
1b Venous blood draining the digestive tract is carried by the **hepatic portal vein** to the liver for processing and storage of newly absorbed nutrients.

2 Blood leaves the liver via the **hepatic vein**.

Space of Disse

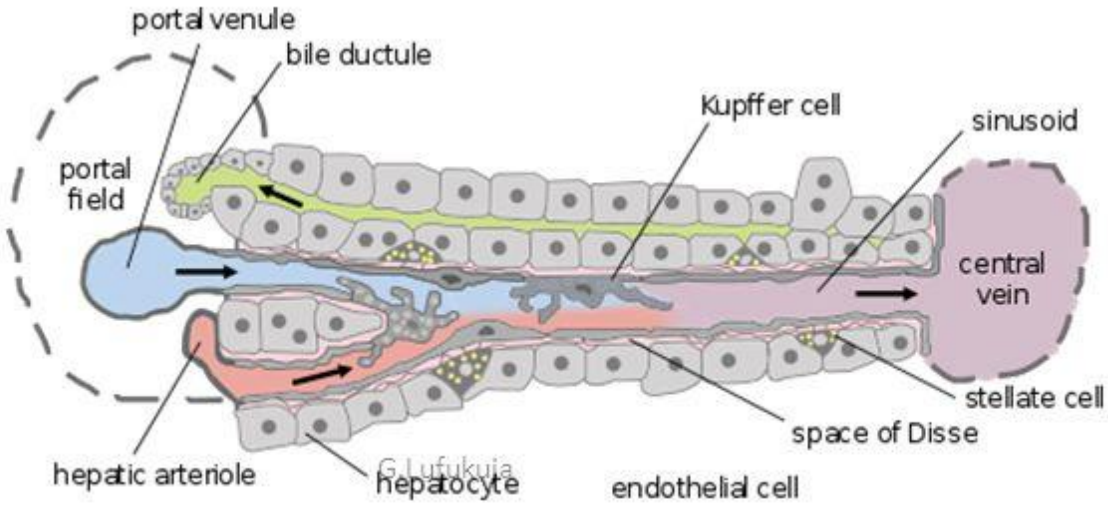


Space of Disse : diantara sel endotel dan sel hepatosit., disebut juga perisinusoidal spaces



Sinusoids & perisinusoidal space (space of Disse)

- Between the hepatocytes and sinusoids there is a space called **perisinusoidal space of Disse**. It is thought that materials that come from sinusoids enter this space before they are taken by the hepatocytes. Also when the hepatocytes secrete, the materials enter this space first before entering the sinusoids.
- The Space of Disse also contains **Ito cells**, also called hepatic stellate cells, **which store fat** or **fat soluble vitamins** (like vitamin A). A variety of insults that cause inflammation can result in Ito cells transforming to myofibroblasts, resulting in collagen production, **fibrosis**, and **cirrhosis**.



Blood Flows Through the Liver From the Porta Vein and Hepatic Artery

- **The Liver Has High Blood Flow and Low Vascular Resistance**. P vena porta – ke liver : 9 mmHg, P v.hepatica – ke vena cava : 0 mmHg, Beda hanya 9 mmHg → resistensinya rendah.
- Cirrhosis of the Liver Greatly Increases Resistance to Blood Flow.

Regulation of Liver Mass—Regeneration

- After partial hepatectomy or acute liver injury, as long as the injury is uncomplicated by viral infection or inflammation. Liver can regenerate rapidly, 5 to 7 days in rats.
- Hepatocyte growth factor (HGF) control the regeneration, Other GF(especially epidermal growth factor) and cytokines such as tumor necrosis factor and interleukin 6.

The Hepatic Macrophage System Serves a Blood-Cleansing Function

- Sel Kupffer, yang memfagosit bakteri yang melewati sinusoid.
- darah dari intestinal → vena porta → dibersihkan sel Kupffer → <1% yang berhasil lolos ke sirkulasi.

The Liver Functions as a Blood Reservoir

- Volume termasuk dalam v.hepatica dan asinus hepar = 450 ml (hampir 10% total volume tubuh). Ketika P atrium kanan ↑ → backpressure di hepar → hepar membesar dan bisa terisi 0.5 -1 L tambahan darah
- Pori-pori sinusoid hepar sangat permeabel → menyebabkan cairan limfe banyak terbentuk → ½ dari limfe yang terbentuk di tubuh berasal dari pembentukan di hepar.

Fungsi metabolik Hepar

- Metabolisme Karbohidrat, Lemak, Protein.

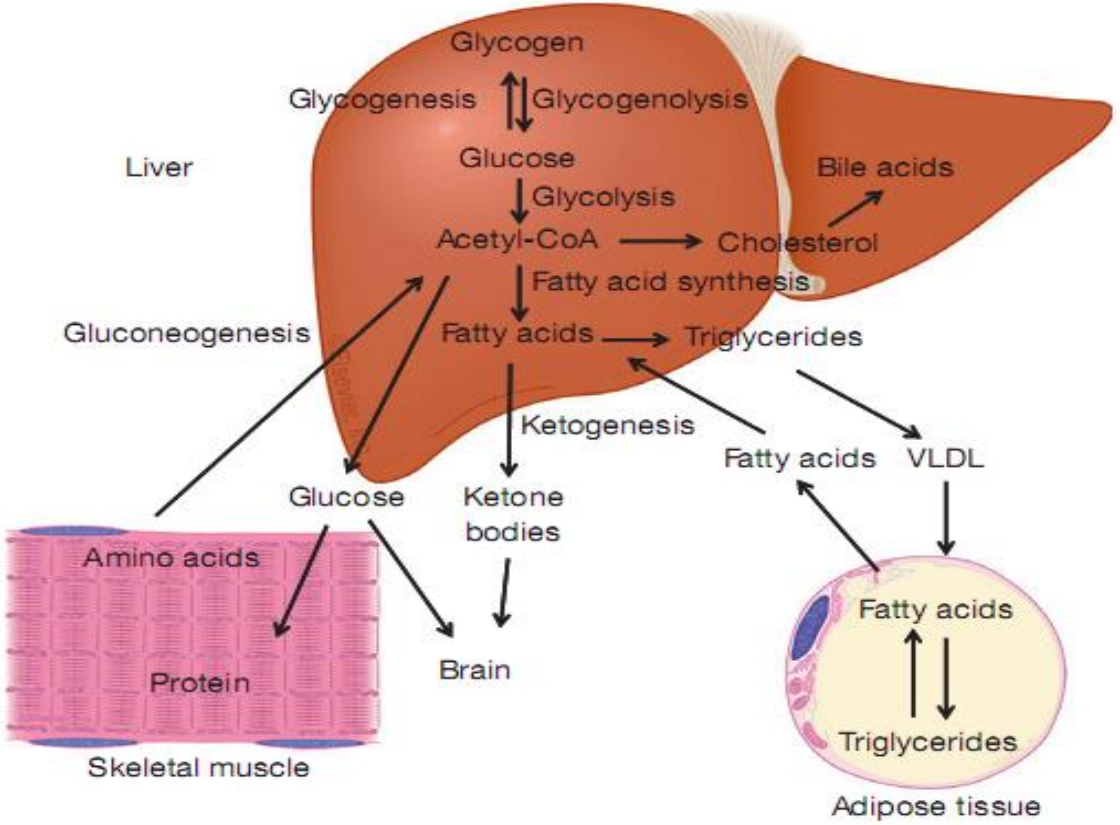
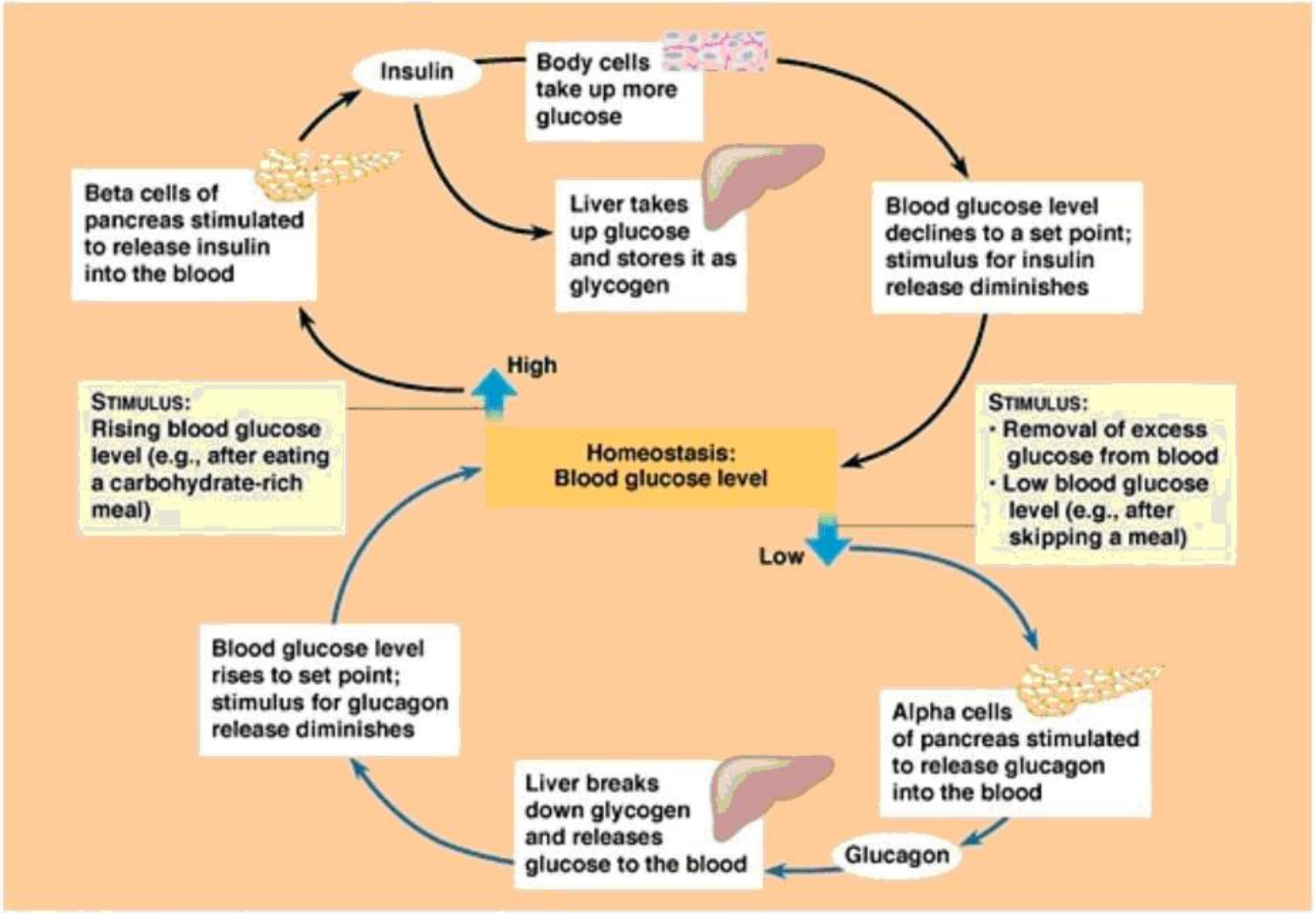


Figure 1 Major metabolic functions of the liver. During the fed state, glucose is stored in the liver as glycogen. Glucose goes through glycolysis to generate acetyl-CoA, which is used to synthesize fatty acids or cholesterol. Cholesterol is catabolized to bile acids. Fatty acids are esterified to glycerol to form triglycerides, which are assembled to VLDL for secretion and transport to adipocytes for storage and other tissues for energy production. Glucose is up taken by muscle and other tissues for energy production. In the fasted state, triglycerides in adipocytes are hydrolyzed to free fatty acids, which are transported to the liver for synthesis of triglycerides and ketone bodies. Ketone bodies are utilized for energy production in the brain and muscle. Under long-term starvation, muscle proteins are degraded to amino acids, which are transported to the liver for synthesis of glucose by gluconeogenesis.

Metabolisme KH

- Di hepar terjadi **Glikolisis** (glukosa → as. Piruvat → asetil Co.A → produksi energi)
- Glukosa sisa glikolisis, oleh hepar akan disintesis menjadi glikogen (**glikogenesis**). Glikogen hepar → cadangan bila sewaktu-waktu dibutuhkan jaringan.
- Hepar→ organ utama yg bisa membentuk glukosa dari sumber as.amino (alanin di otot), piruvat, dan laktat → disebut **glukoneogenesis**
- Thus, liver plays a key role in maintaining blood glucose levels to prevent hypoglycemia and supplies glucose to the brain and other tissues for energy needs → so called **glucose buffer function**



The principal functions of the liver in lipid metabolism:

- (1) degrade fatty acids into small compounds that can be used for energy
- (2) synthesize triglycerides, mainly from carbohydrates, but to a lesser extent from proteins as well
- (3) synthesize other lipids from fatty acids, especially cholesterol and phospholipids.

Metabolisme Lemak

1. **Oxidation of fatty acids to supply energy for other body functions**

   Lemak → gliserol & as.lemak.

   As. Lemak → Acetyl CoA, melalui **β-oksidasi**.

   Acetyl-CoA → energi, melalui siklus as.sitrat

   β -oxidation bisa terjadi di semua sel, terutama hepatosit

   Hepar tidak menggunakan semua acetyl-CoA yg dibentuk; sisanya, 2 molekul **asetil CoA berkondensasi → acetoacetic acid**, a highly soluble acid yang keluar hepar menuju cairan ekstraseluler → ke seluruh tubuh → diabsorbsi jaringan.

   Di jaringan**, acetoacetic acid** → 2 molekul **acetyl-CoA** → dioksidasi menjadi **energi**.

2. Synthesis of large quantities of cholesterol, phospholipids, and most lipoproteins

   ±80% **kolesterol** disintesis di hepar dirubah → garam empedu; sisanya di transport dalam lipoprotein dan dibawa oleh darah ke jaringan.

   Phospholipids (lechitin, cephalin, sphingomielin) juga disintesis di hepar dan dibawa dalam **lipoprotein**.

   Both cholesterol and phospholipids are used by the cells to form membranes, intracellular structures, and multiple chemical substances that are important to cellular function.

- **3. Synthesis of fat from proteins and carbohydrates**

- Many amino acids can be converted into acetyl-CoA. The acetyl-CoA can then be synthesized into triglycerides. Therefore, when people have more proteins in their diets than their tissues can use as proteins, a large share of the excess is stored as fat.
- Whenever a greater quantity of carbohydrates enters the body than can be used immediately for energy or can be stored in the form of glycogen, the excess is rapidly converted into triglycerides and stored in this form in the adipose tissue. In humans, most triglyceride synthesis occurs in the liver, but minute quantities are also synthesized in the adipose tissue. The triglycerides formed in the liver are transported mainly in VLDLs to the adipose tissue, where they are stored.

Metabolisme Protein

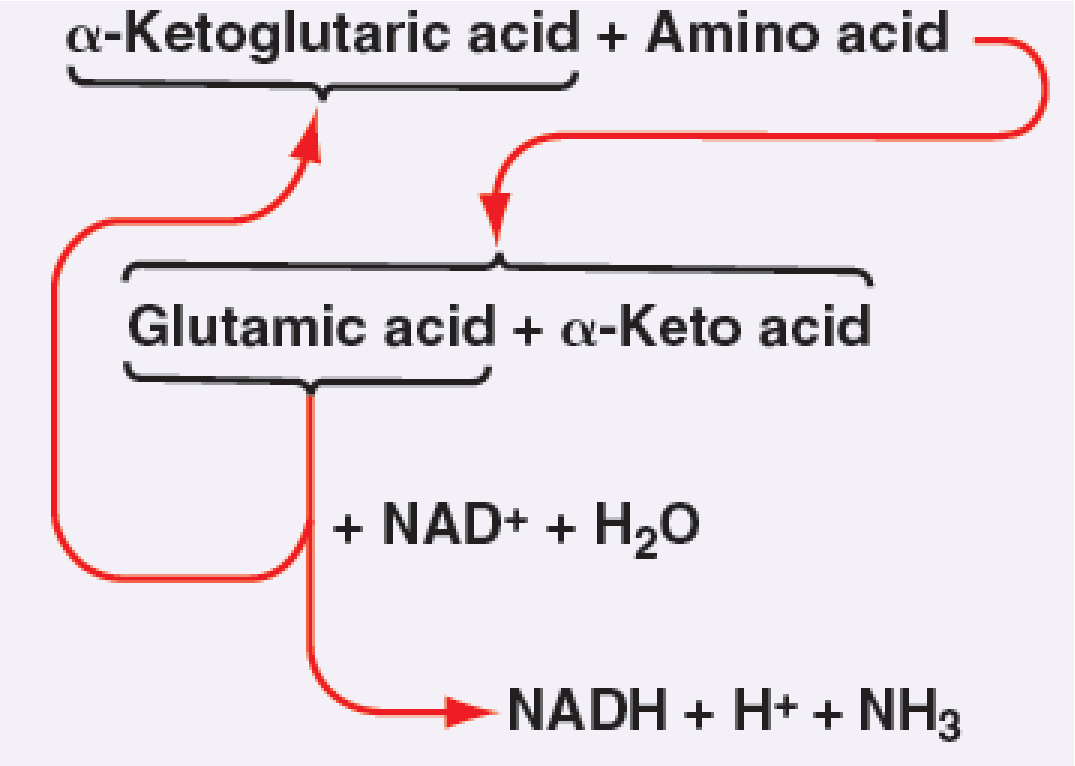
- The most important functions of the liver in protein metabolism:

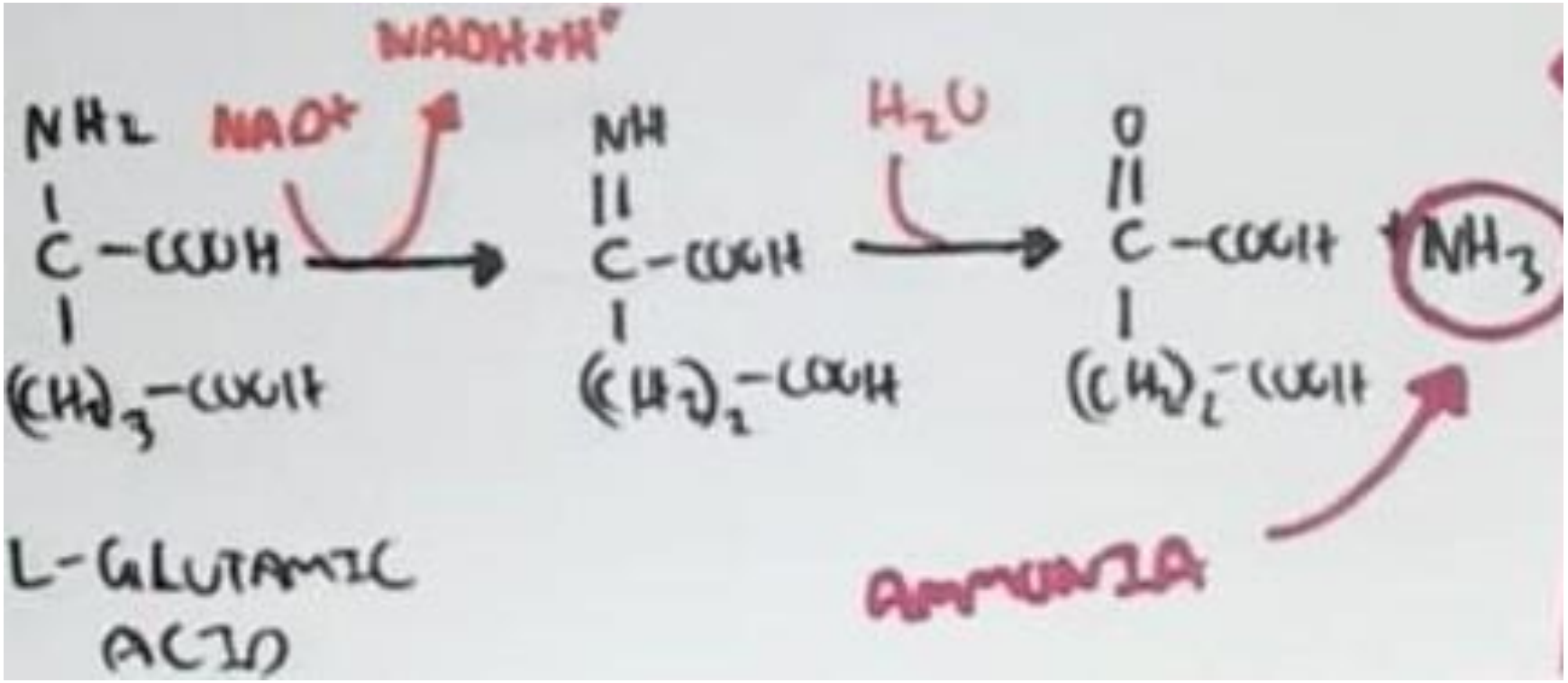
1. **Deamination of amino acids**

Deamination : the Removal of Amino Groups From Amino Acids

Deaminasi bisa terjadi di jaringan lain, tapi paling penting di hepar.

- The amino group from the amino acid is transferred to α-ketoglutaric acid, which then becomes glutamic acid. The glutamic acid can then transfer the amino group to other substances or release it in the form of ammonia (NH3). In the process of losing the amino group, the glutamic acid once again becomes α-ketoglutaric acid, so the cycle can be repeated again and again.



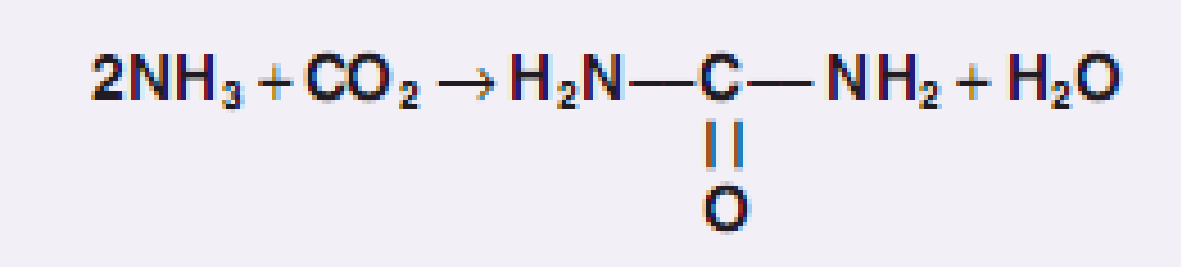


Deamination occurs mainly by t*ransamination*, which means transfer of the amino group to some acceptor substance. This process is the reverse of transamination.

2. **Pembentukan urea untuk membuang ammonia dari tubuh**.

Sejumlah besar ammonia terbentuk dari proses **deaminasi**, dan terus bertambah di GIT oleh bakteri → ammonia diabsorpsi di darah. Jika hepar tidak membentuk urea, ammonia plasma ↑ → kematian.

Ammonia bisa bertambah bila darah yang ke hepar sedikit oleh karena adanya shunt antara vena porta dan v.hepatica.



3. Formation of plasma proteins (albumin, globulin, and fibrinogen)

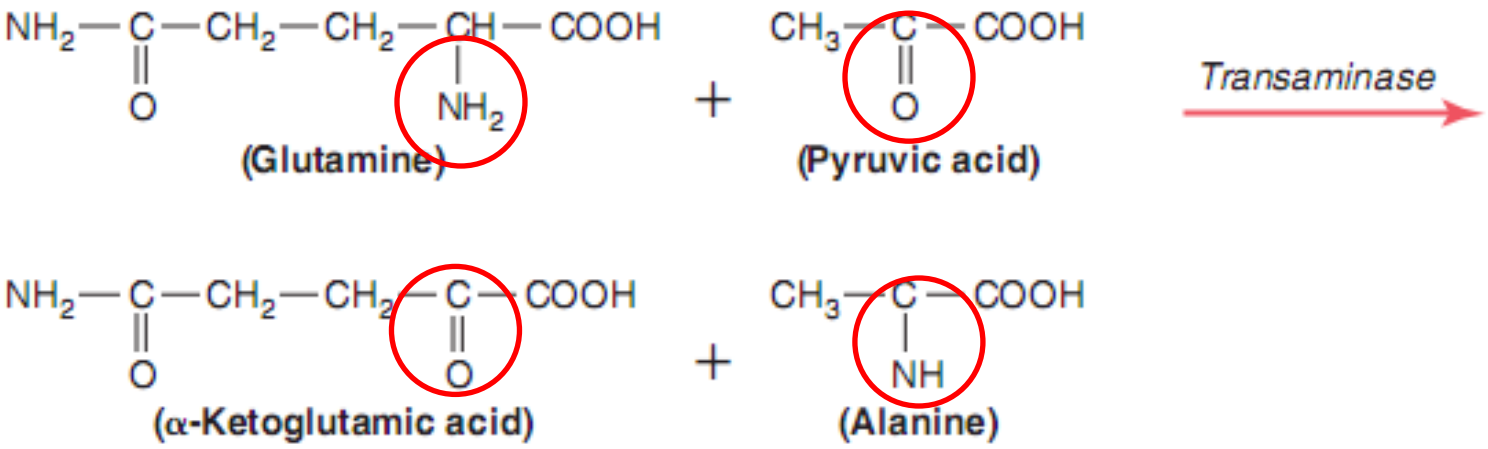
- Di hepar → membentuk 90% protein plasma. Kecuali gamma globulin, dibentuk oleh sel plasma jaringan limfoid
- Kecepatan pembentukan 15 to 50 g/day
- Protein plasma hilang, hepar bisa mengganti kehilangan dalam 1-2 minggu
- Fungsi protein plasma : maintenance osmalility, transporter of many hormone (yaitu lipid soluble/**steroid hormone**)
- *chronic liver disease (e.g., cirrhosis), plasma proteins, such as albumin, may fall to very low levels, causing generalized edema and ascites.*

Ingat! Hormon steroid berasal dari cholesterol, sifatnya larut lemak, dan butuh carrier protein!

4. Interconversions of the various amino acids and synthesis of other compounds from amino acids

Hepar mampu mensintesis a.a tertentu dan komponen kimia lain dari asam amino. Terutama melalui transaminasi

Misalnya, a.a non essential bisa disintesis di hepar



Other Metabolic Functions of the Liver

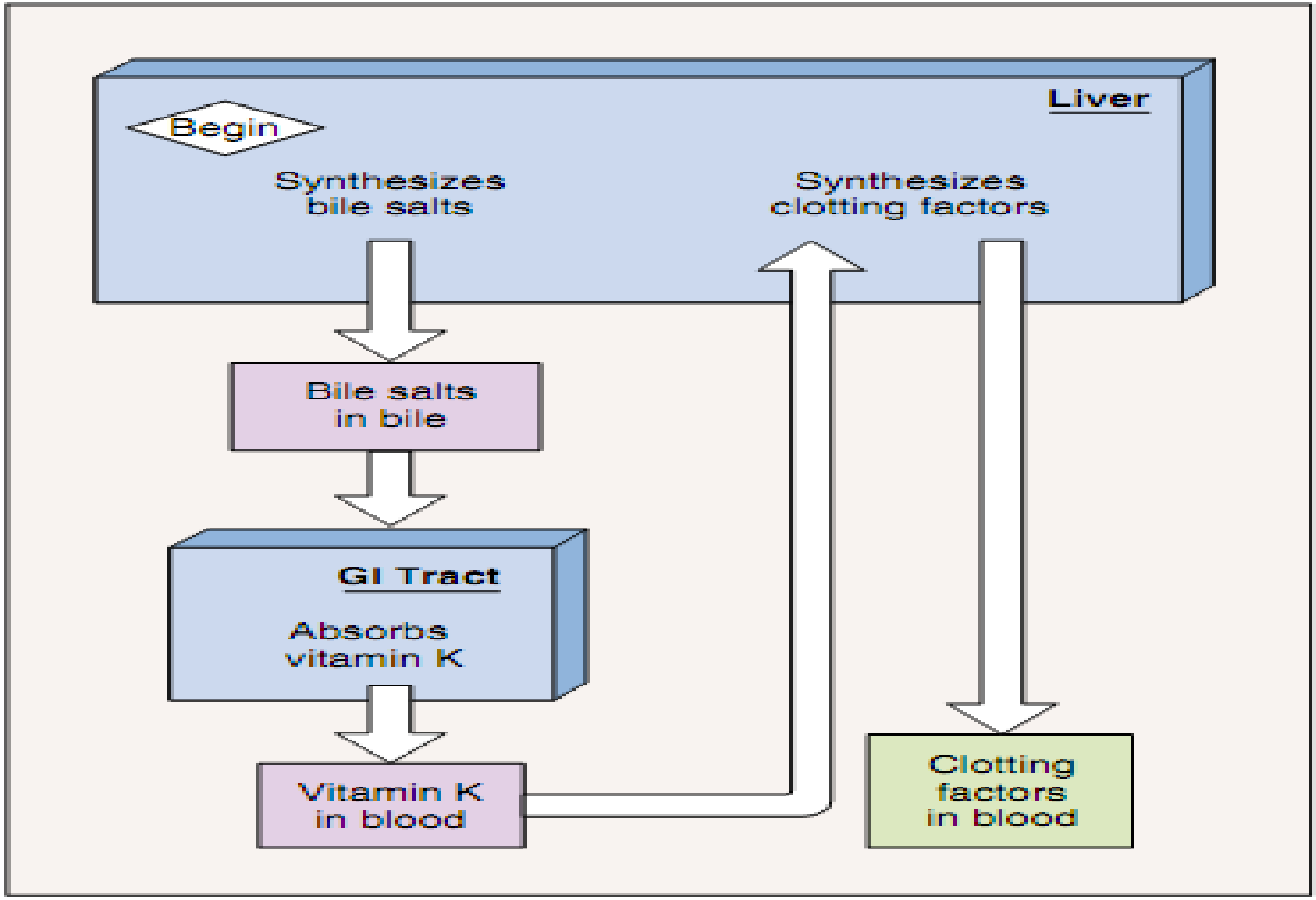
- **The Liver Is a Storage Site for Vitamins.**
  - ❖ Vit A bisa disimpan di hepar selama 10 bulan untuk mencegah defisiensi vit.A
  - ❖ Vit D disimpan dalam 3-4 bulan cukup untuk cegah defisiensi
  - ❖ Vit B12 yang cukup dapat disimpan minimal 1 tahun – beberapa tahun
- **The Liver Stores Iron as Ferritin**
  - ❖ Hepatosit mengandung apoferritin, yg mampu berikatan dg Fe scr reversibel.
  - ❖ Apoferritin-ferritin system → blood iron buffer

- **The Liver Forms Blood Substances Used in Coagulation.**
  - ❖Substansi yg dibentuk : fibrinogen, prothrombin, accelerator globulin, factor VII, and several other important factors.
  - ❖Vitamin K diperlukan oleh hepar untuk membentuk substansi tersebut, terutama prothrombin dan factors VII, IX, and X.

Role of Vit K in coagulation substance production in Liver

- Vit K disintesis di GIT oleh bakteri. Vit K diabsorbsi bersamaan dengan lemak.
- Defisiensi vit K biasanya terjadi karena malabsorbsi lemak.
- Penyakit hepar → tidak mampu sekresi empedu → lemak tidak dicerna dan tidak terabsorbsi , vit K juga tidak terabsorbsi → hepar gagal membentuk substansi koagulan.

Role of liver in clotting



- **The Liver Removes or Excretes Drugs, Hormones, and Other Substances.**
  - ❖ Liver mampu mendetoksifikasi dan mengeksresi obat-obat ke dalam empedu, yaitu sulfonamides, penicillin, ampicillin, and erythromycin.
  - ❖ Beberapa hormon, thyroxine dan semua hormon steroid (estrogen, cortisol, and aldosterone) → dirubah dan dieksresi dari liver
  - ❖ Liver damage → akumulasi 1 atau lebih hormon → overaktivitas sistem hormonal

BILIARY SECRETIONS

- Formed by hepatocytes (250-1100 ml/day)
- Secreted continuously, stored in gallbladder during interdigestive period.
- Released into the duodenum during digestive period, triggered by CCK
- CCK cause relaxation of spincter oddi, and contraction of gallbladder.

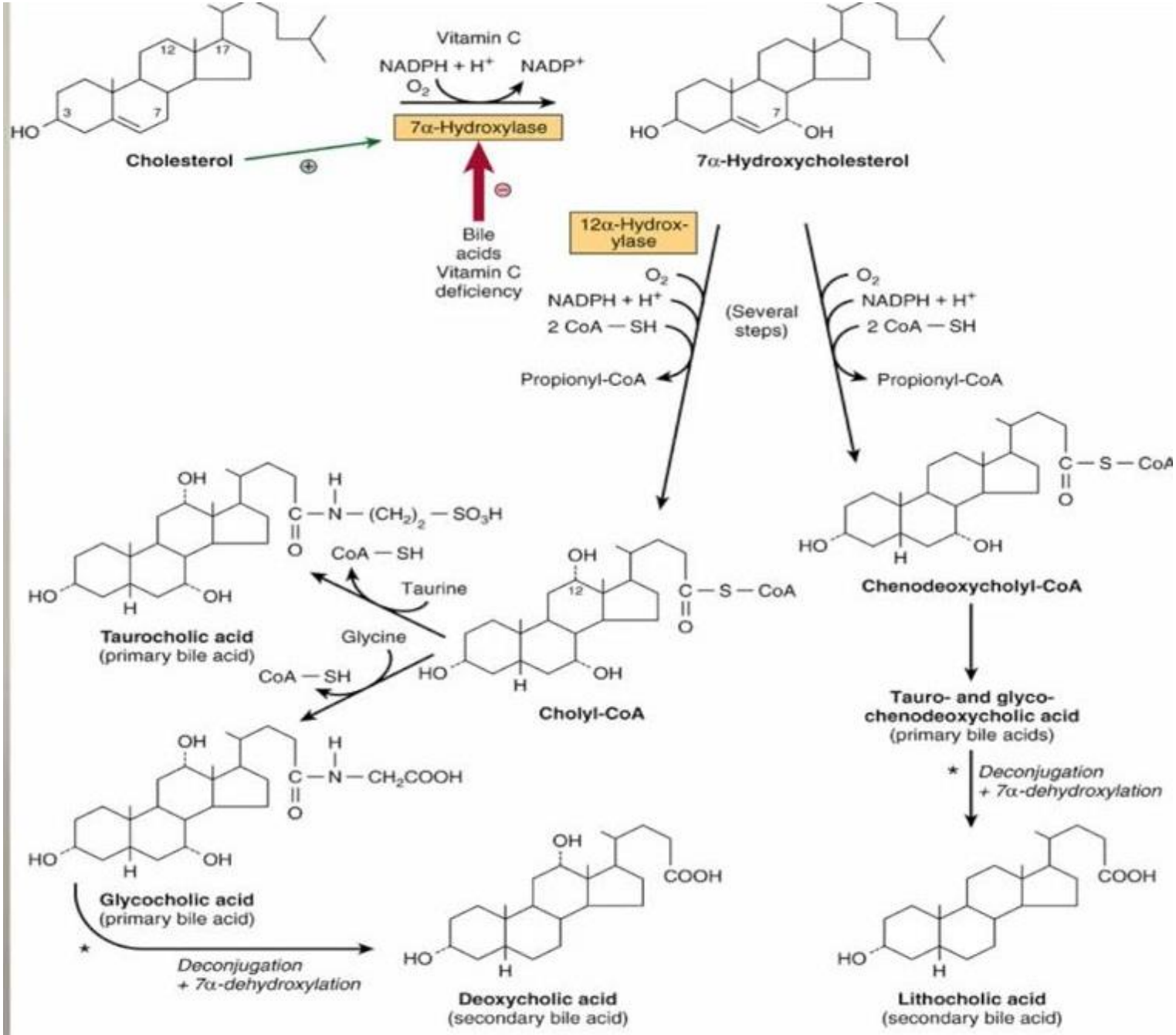
COMPOTITION OF BILE (1)

1. Bile acids **:**

(primary bile acids) synthesized from cholesterol and converted form → *bile salt* by the hepatocytes, and

(secondary bile acids) formed by deconjugation and dehydroxylation of primary bile salt by intestinal bacteria.

Bile syntesis



Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's Illustrated Biochemistry, 29th Edition*: www.accessmedicine.com

- Setelah disintesis, asam empedu segera dikonjugasi menjadi as amino, glisin, taurin melalui amidasi.
- Di usus, beberapa as.empedu mengalami dekonjugasi oleh aktivitas flora usus (enzim 7α-dehydroxylase) → menjadi as.empedu sekunder **deoxycholic acid** (DCA) and **lithocholic acid** (LCA).
- DCA is reabsorbed in the colon. Most LCA is excreted into feces and small amount of LCA is circulated to the liver and rapidly conjugated by sulfation and/or amidation and excreted into bile.

COMPOTITION OF BILE (2)

2. Bile pigments **:**

bilirubin and biliverdin **(two principal bile pigments), formed from hemoglobin responsible for the golden yellow color of the bile**

Urobilin**, metabolized from bilirubin by intestinal bacteria. Responsible for the brown color of the stool**

COMPOTITION OF BILE (3)

3. Phospholipids **(prymarily lecithin)**

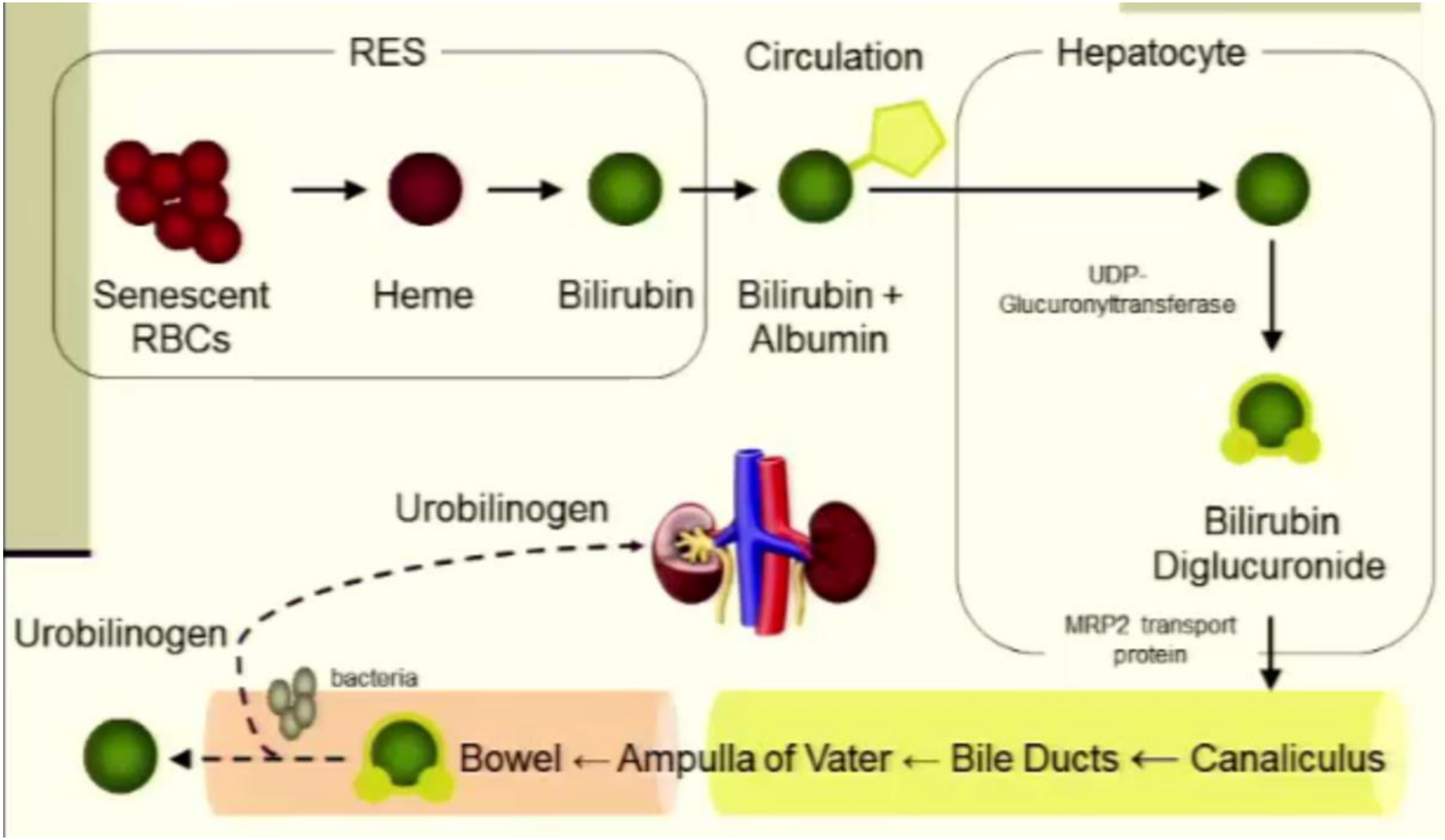
solubilized by the bile salt micelles

4. Cholesterol

is important of bile, because it is one of the few ways in which cholesterol regulation

5. electrolytes

Metabolisme Bilirubin



BILIRUBIN METABOLISM

1. Bilirubin transport across sinusoids
2. Binding to glutathione S-transferases (GSTs or Ligandins)
3. Conversion to glucuronides by transfer of glucuronic acid from UDP-glucuronic acid (UDP-glucuronosyltransferase)
4. Transport across canalicular membrane by ATP-dependent transport (MRP2)

Breakdown of RBC's in RE cells

HEME

Heme oxygenase

CO

Biliverdin

Biliverdin Reductase

BILIRUBIN

Excreted into the biliary tract and subsequently into the intestine

Released into circulation where bilirubin is tightly but reversibly bound to albumin

BILIRUBIN METABOLISM

- Formation of bilirubin

  is yellowish pigment formed as an end product of hemoglobin catabolism.
- Jaundice

  is yellowing of the skin due to **the accumulation of bilirubin within the tissues**, may result from : excess production of bilirubin, or obstruction of the bile ducts or the liver cells preventing the secretion of bilirubin.

FUNCTION OF THE BILE

- **Digestion and absoption of fat**
  help to emulsify of the large fat particle
  aid to absorption of fat through the intestinal mucosal membrane
- **Excretion of several important waste products from the blood (bilirubin) and excess of cholesterol**

ENTEROHEPATIC CIRCULATION

- The circulation of bile salt from the liver to the small intestine and back again.
- Necessary, because limited poll of bile salt to help breakdown and absorption fats
- 90% - 95% absorbed only in the terminal ileum
- *Bayangkan bila tdk ada sirkulasi enterohepatik! Sifat bile salt dalam feses adalah menarik air&Na shg menyebabkan watery diarrhea, so harus ada reabsorbsi bile salt kembali ke hepar*

Enterohepatic circulation of bile salts

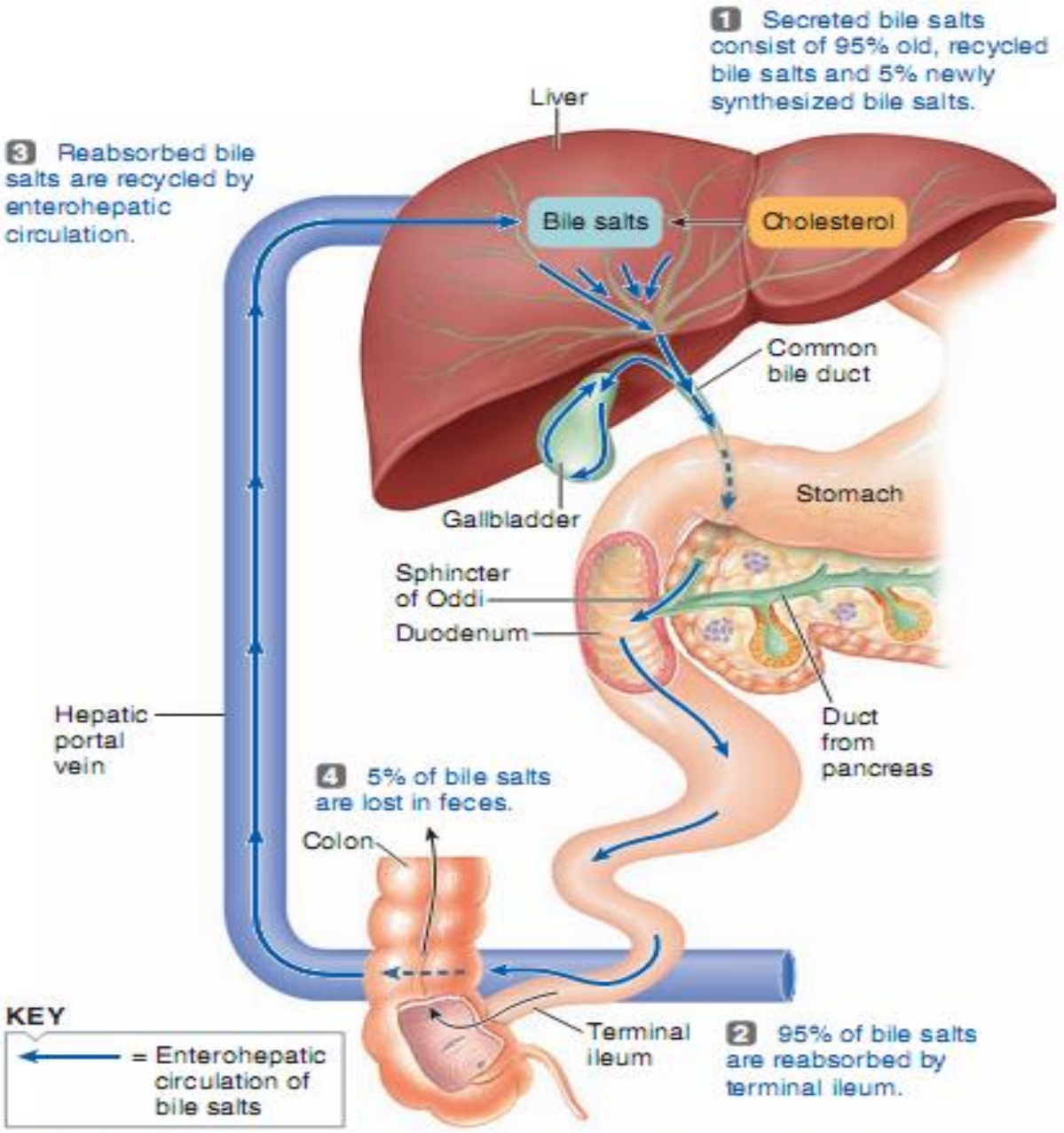
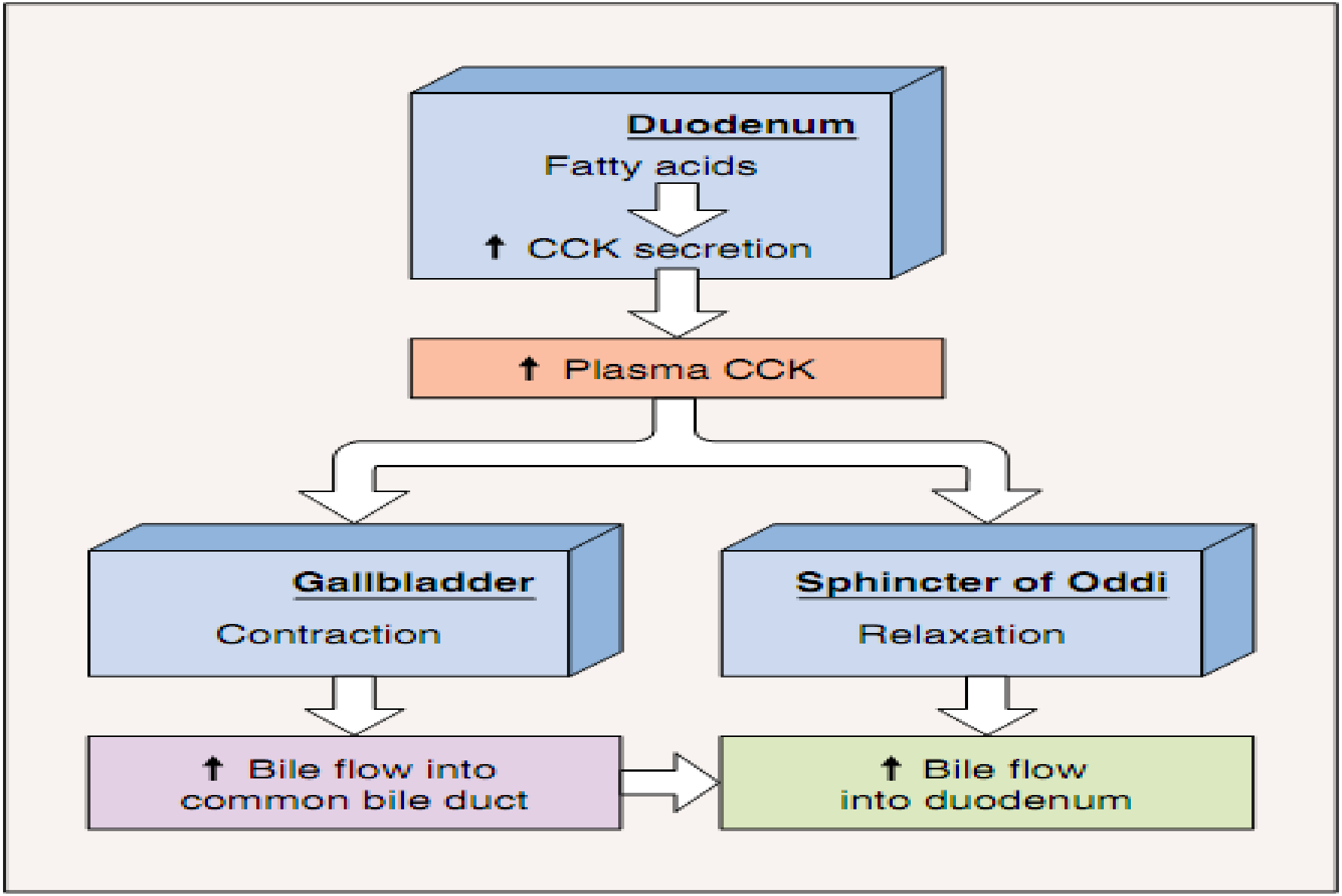


Figure 16-15 Enterohepatic circulation of bile salts. Most bile salts are recycled between the liver and small intestine through the enterohepatic circulation (*blue arrows*). After participating in fat digestion and absorption, most bile salts are reabsorbed by active transport in the terminal ileum and returned through the hepatic portal vein to the liver, which resecretes them in the bile.

Regulation of bile entry into the small intestine



CILINICAL IMPLICATION

- **Any condition that disrupts enterohepatic circulation (ileal resection or small intestinal diseases : sprue or Crohn's disease) leads to malabsorption of fat and fat soluble vitamins.**
- **The clinical manifestation : steathorrea and nutritional deficiency.**
- **Increasing in fecal losses of bile salt result in watery diarrhea, bile salt inhibit water and Na absorption**

LIVER AS ENDOCRINE FUNCTION

- Secrete IGF I and somatomedin in response to growth hormone
- Forms T3 from T4
- Secrete angiotensinogen
- Activation of vitamin D
- Secrete erytropoetin (10-15 %)

GALLBLADDER

- **FUNCTION :**

  Storage : stores and concentrates during interdigestive periode.

  contraction : during digestive periode, the gallbladder contracts, emptying the content into the duodenum

- **CONTROL :**
  - **fat and protein digestion product → CCK → gallbladder contraction**
  - **vagal stimulation during cephalic and gastric phase**

Sekresi Empedu oleh Hepar; fungsi traktus bilier

- Sekresi empedu N (600-1000 ml/hari)
- Empedu mempunyai 2 fungsi penting:

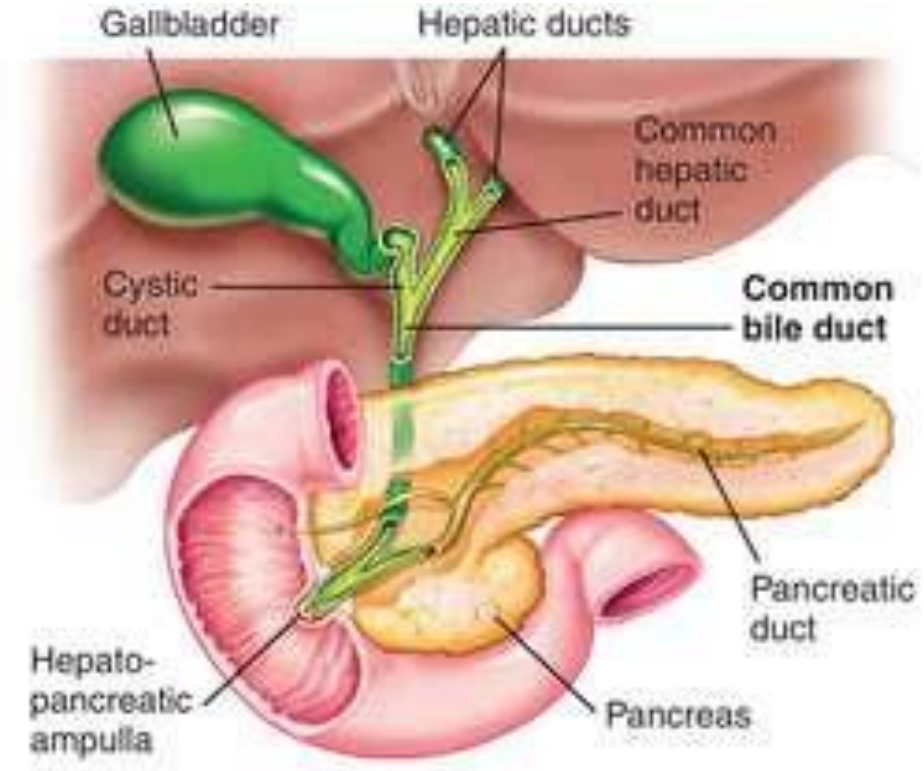
1).Pencernaan dan absorbsi lemak melalui :

- Emulsifikasi partikel lemak besar menjadi partikel-partikel lebih kecil sehingga dapat dicerna oleh enzim lipase pankreas
- Membantu absorbsi produk akhir lemak

2).Empedu sebagai media untuk mengeksresi bilirubin, suatu produk akhir penghancuran hemoglobin, dan berlebihnya kolesterol.

Anatomi-fisiologi sekresi empedu

- Empedu disekresi dalam 2 tahap oleh hati:
- Disekresi oleh sel hepatosit (sekresi awal mengandung as.empedu, kolesterol, dan zat organik lainnya)
  → kanalikuli



- Dalam perjalanan melalui duktus-duktus biliaris tahap ke-2, ditambahkan ke dalam sekresi empedu yang pertama berupa larutan ion Na + ion Bic.Nat encer yang disekresi oleh sel epitel sekretoris yang ada di duktulus dan duktus
- Sekresi tersebut dirangsang oleh sekretin

Penyimpanan dan pemekatan empedu di kandung empedu

- Empedu yg disekresi oleh hepatosit akan disimpan di kandung empedu dan dipekatkan dengan cara mengabsorbsi Na, Cl, air dan elektrolit lainnya, → memekatkan kolesterol, garam empedu, lesitin, dan bilirubin.
- Vol.maks kandung empedu : 30-60 ml, sekresi dari hepatosit dalam 12 jam (450 ml)
- Normalnya dapat memekatkan 5-20X lipat

Komposisi Empedu

Composition of Bile

	Liver Bile	Gallbladder Bile
Water	97.5 g/dl	92 g/dl
Bile salts	1.1 g/dl	6 g/dl
Bilirubin	0.04 g/dl	0.3 g/dl
Cholesterol	0.1 g/dl	0.3 to 0.9 g/dl
Fatty acids	0.12 g/dl	0.3 to 1.2 g/dl
Lecithin	0.04 g/dl	0.3 g/dl
Na^+	145.04 mEq/L	130 mEq/L
K^+	5 mEq/L	12 mEq/L
Ca^{++}	5 mEq/L	23 mEq/L
Cl^-	100 mEq/L	25 mEq/L
HCO_3^-	28 mEq/L	10 mEq/L

Pengosongan kandung empedu – Peran CCK

- 30 menit setelah makan (t.u lemak) → kandung empedu dikosongkan
- Pengosongan tjd krn kontraksi ritmis dinding kandung empedu + relaksasi sfingter Oddi
- Makanan berlemak → mukosa duodenum → pelepasan CCK → aliran darah → kontraksi kandung empedu + relaksasi sfingter Oddi → empedu di lepas ke duodenum

Regulation of Bile Release

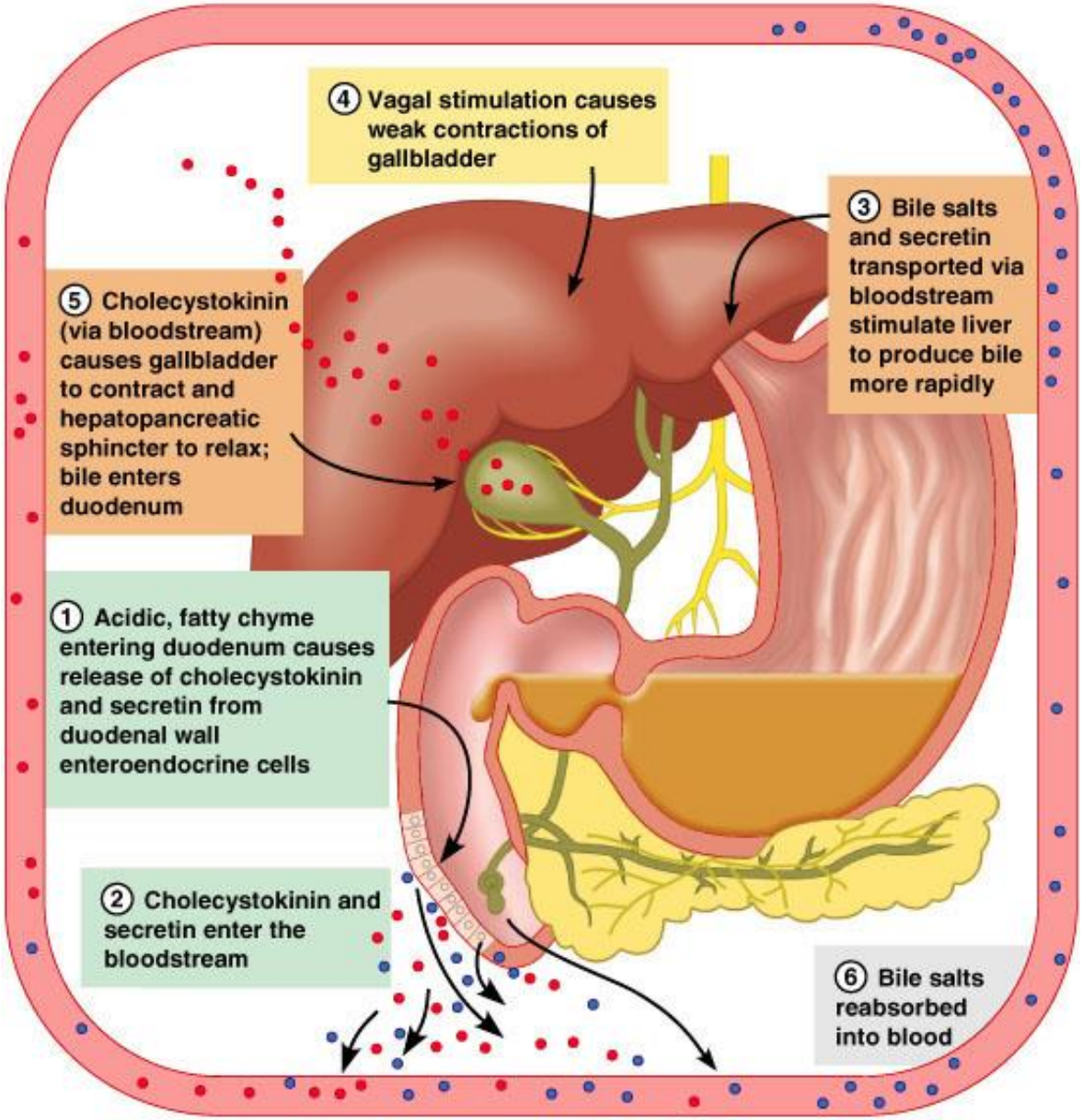


Figure 23.25

PANKREAS
- Sekresi Pankreas

- Enzim digestif pankreas disekresi oleh asinus pankreas
- Na.Bic.nat disekresi dari **ductus** asinus
- Produk enzim dan Na.Bic.nat → duct.pankreatikus → papila vater yg dikelilingi spincter oddi.
- Sekresi pankreas dikeluarkan sbg respon thd kimus. **Sekresinya bergantung isi kimus**

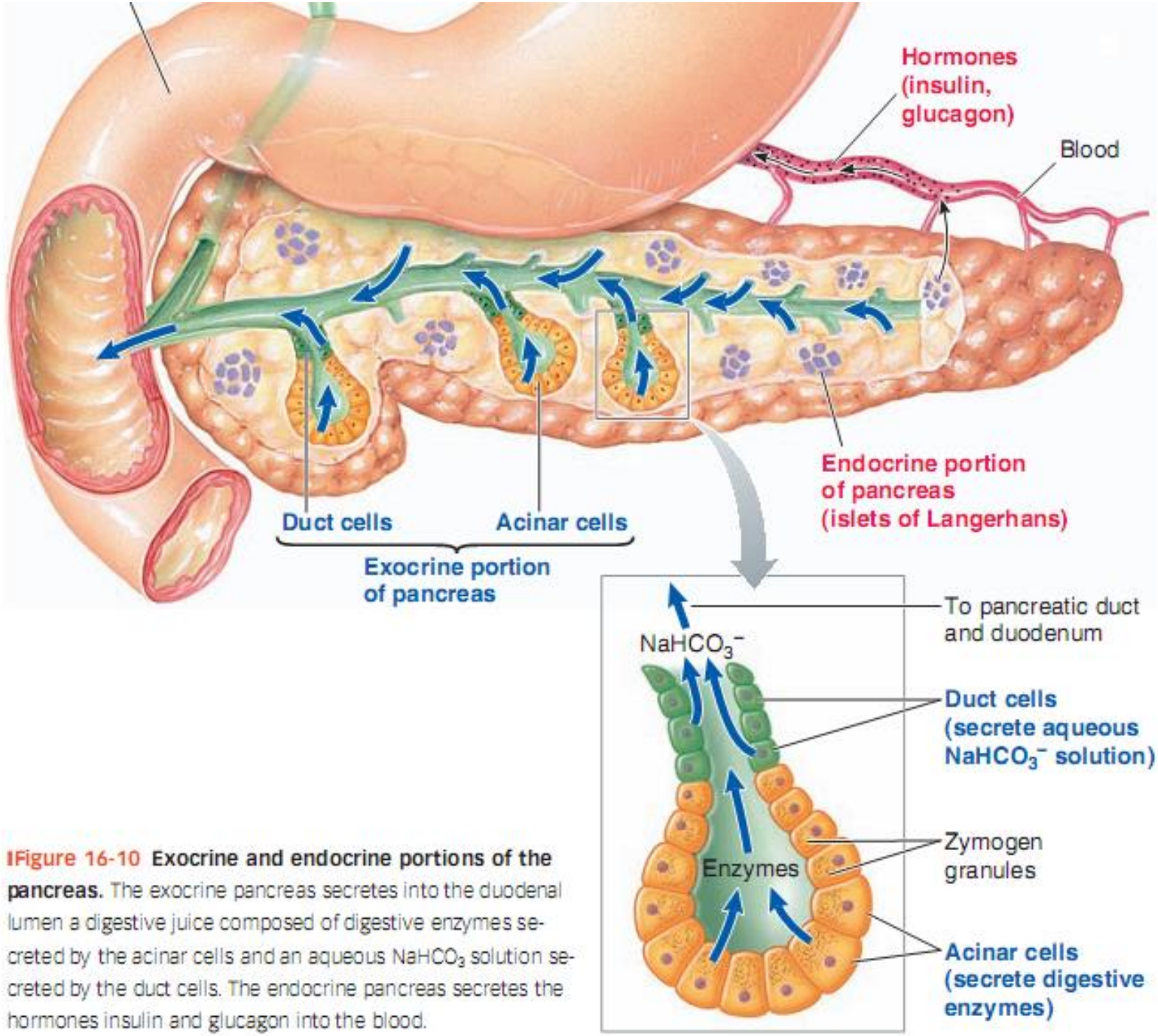


Figure 16-10 Exocrine and endocrine portions of the pancreas. The exocrine pancreas secretes into the duodenal lumen a digestive juice composed of digestive enzymes secreted by the acinar cells and an aqueous $NaHCO_3$ solution secreted by the duct cells. The endocrine pancreas secretes the hormones insulin and glucagon into the blood.

Enzim digesti pankreas

Sekresinya mengandung multiple enzim untuk mencerna KH, protein, lemak dan sekresi Na.bic.nat

Enzim pankreas utk digesti protein :

- **Tripsin** & chimotripsin : protein → peptida
- Carboxipolipeptidase : peptida → a.amino

Enzim pankreas utk digesti KH :

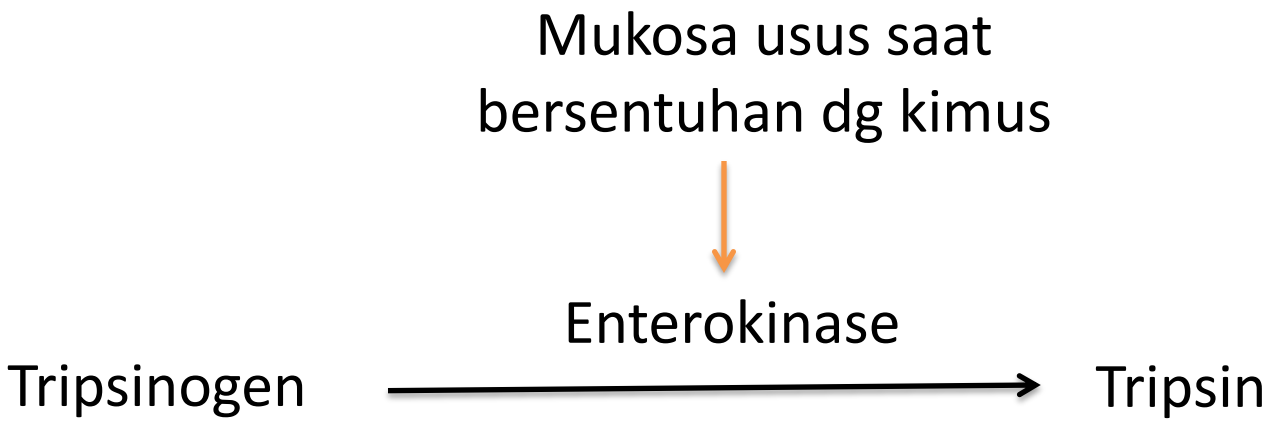
- Amilase pankreas : hidrolisis ikatan α 1-4 glikosida → disakarida & trisakarida

Enzim pankreas utk digesti lemak:

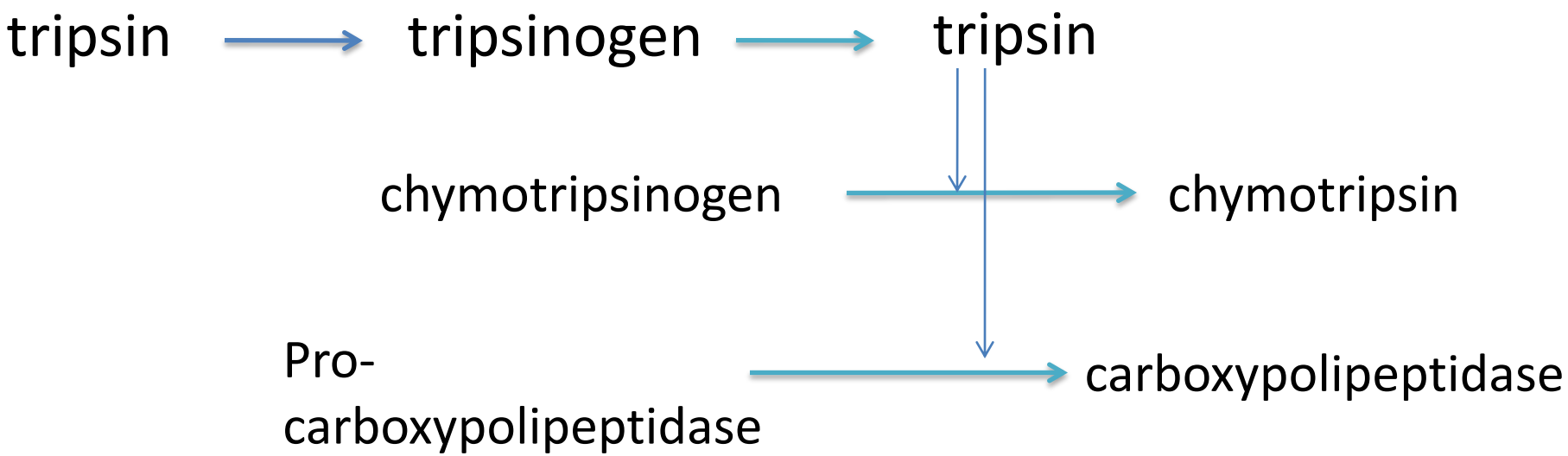
- Lipase pankreas : lemak → as.lemak & monogliserida
- Kolesterol esterase : hidrolisis ester kolesterol
- Fosfolipase : fosfolipid → as. lemak

Sekresi pankreas dalam bentuk zymogen (tdk aktif)→ tripsinogen, chimotripsinogen, procarboxypolipeptidase

- Akan aktif saat tersekresi di usus
- Enterokinase (enzim Brush border) mengaktifkan zymogen pancreas



- Tripsinogen juga diaktifkan scr autokatalitik



Sekresi inhibitor tripsin

- **Sel asinus pankreas** juga mensekresi substansi inhibitor tripsin secara bersamaan dg enzim2 proteolitik pankreas
- **Inhibitor tripsin** berfungsi **mencegah aktivasi** tripsin di dalam sel sekretorik, ductus, maupun asinus pankreas sehingga enzim2 proteolitik tidak akan mencerna pankreas

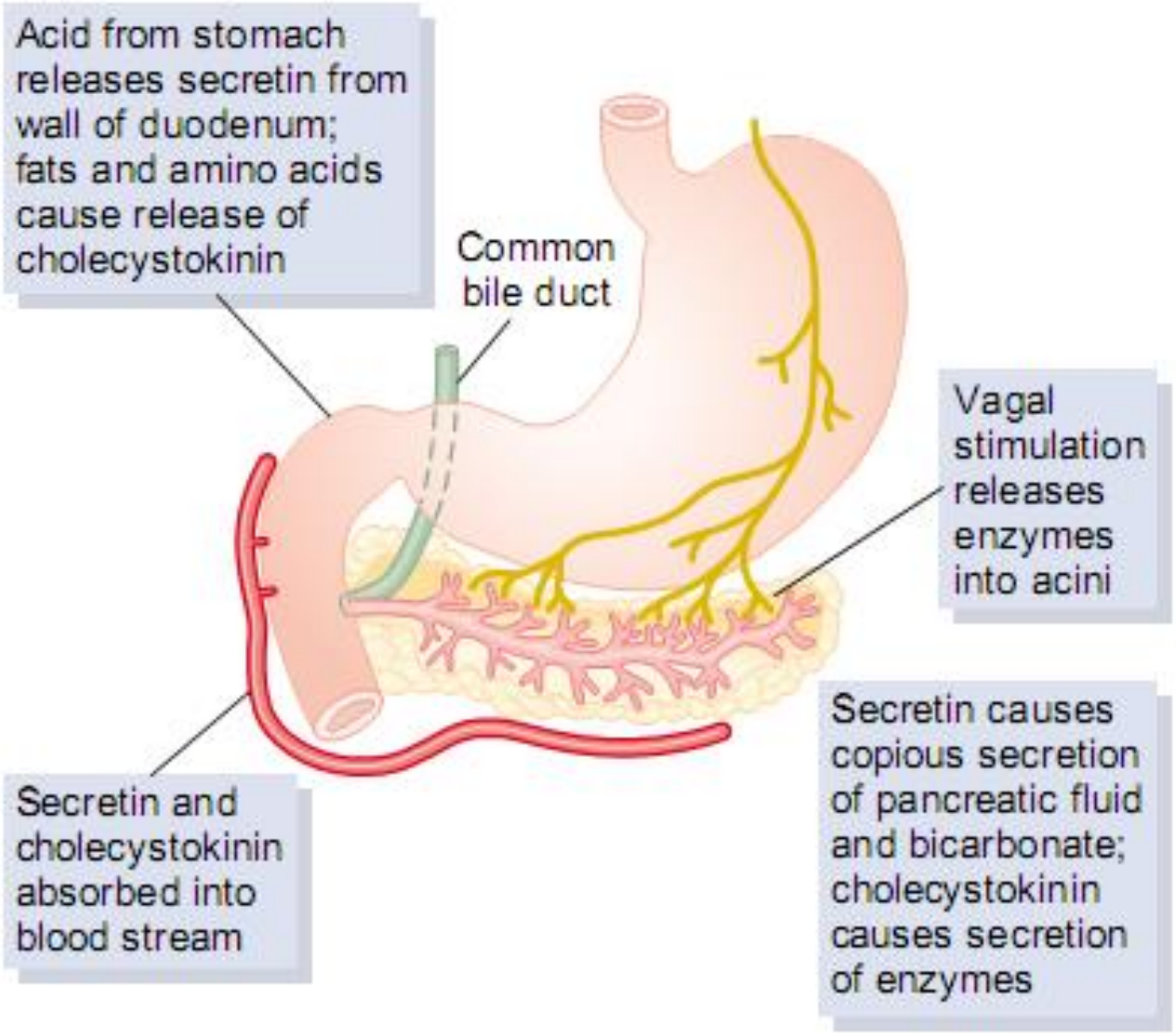
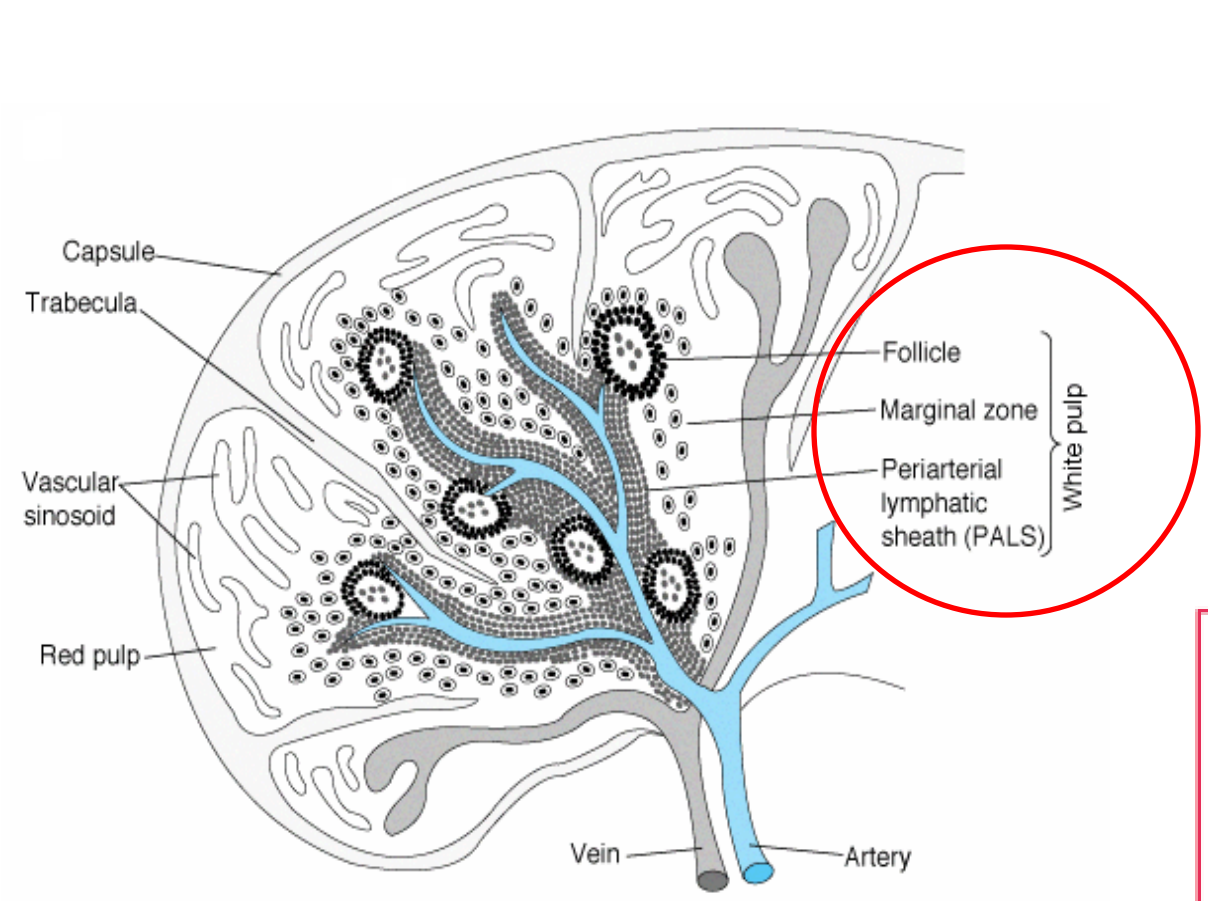
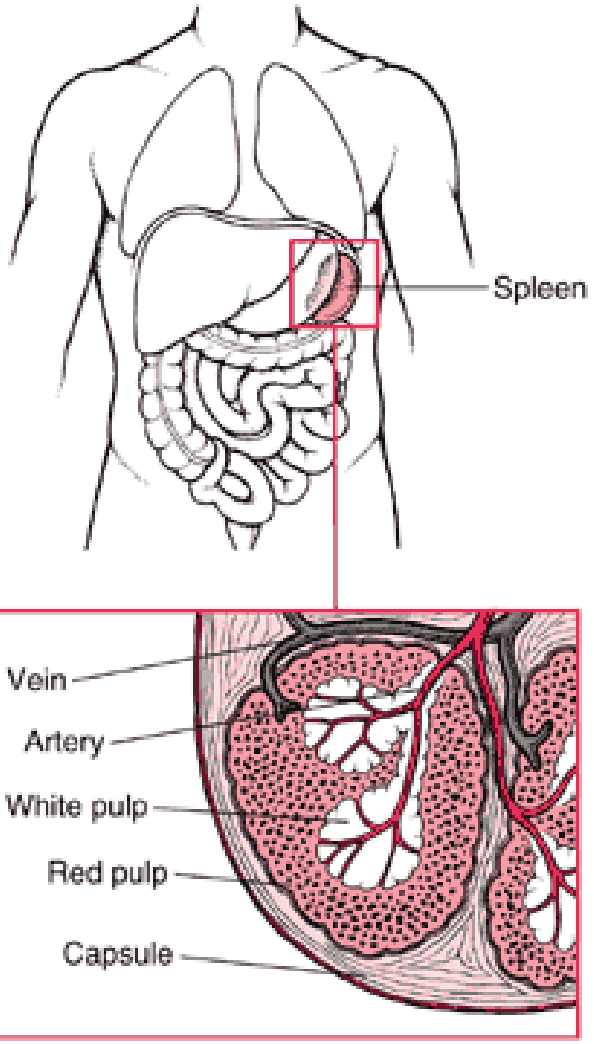


Figure 64–10

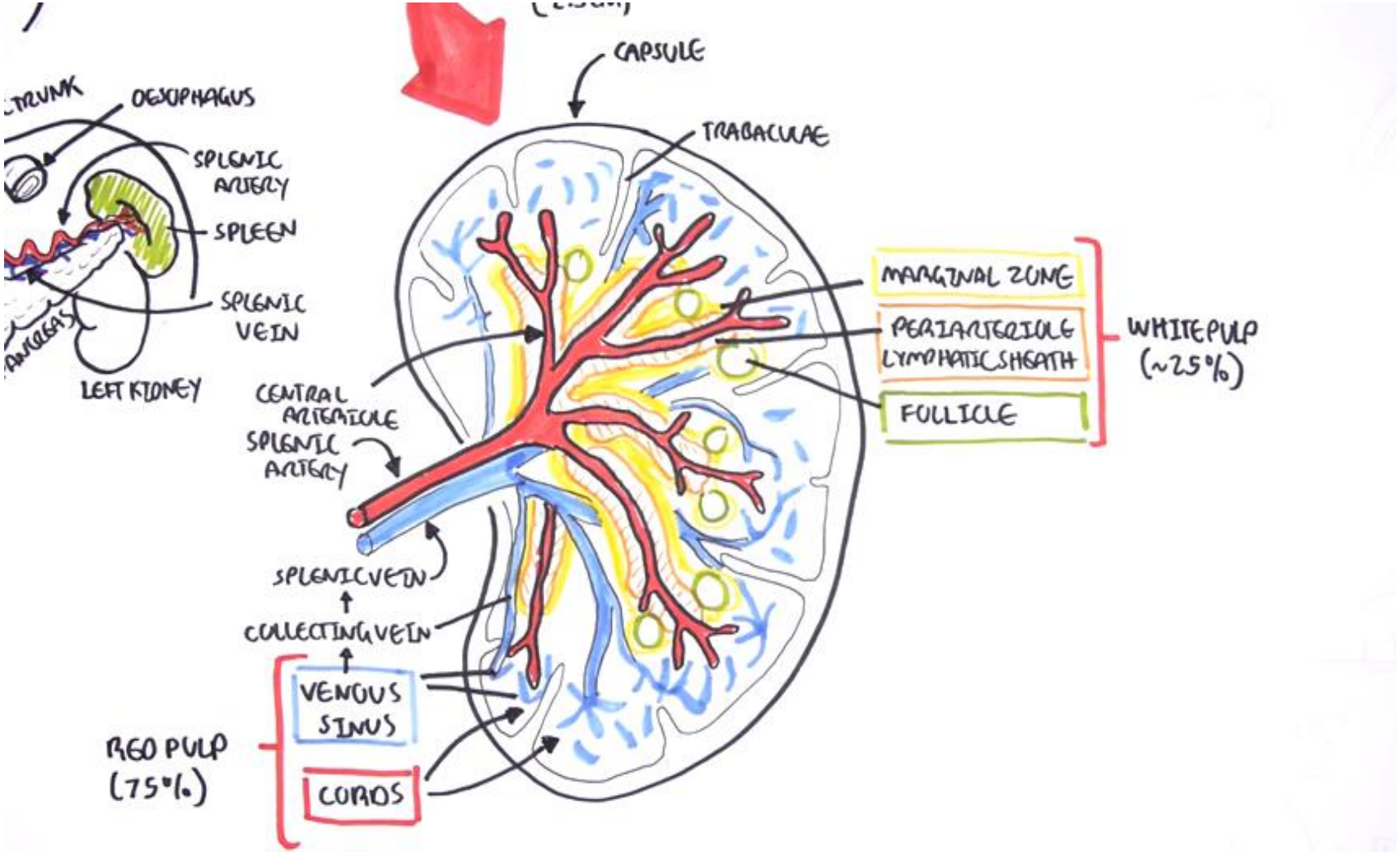
Regulation of pancreatic secretion.

Physiology of Spleen





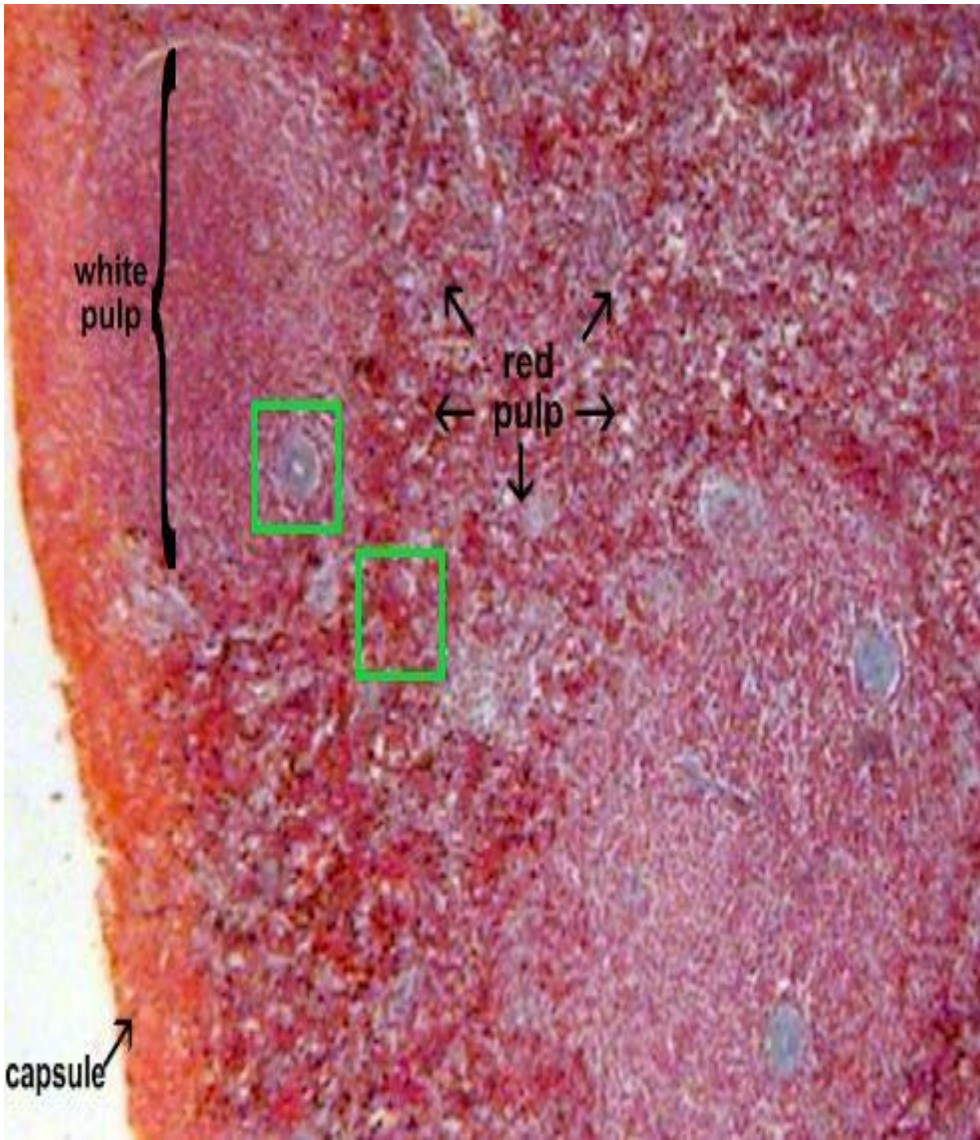
White pulp : contain many immune cell
Follicle contain many B cell


CAPSULE
TRABECULAE
OESOPHAGUS
SPLENIC ARTERY
SPLEEN
SPLENIC VEIN
LEFT KIDNEY
MARGINAL ZONE
PERIARTERIOLE LYMPHATIC SHEATH
FOLLICLE
WHITE PULP (~25%)
CENTRAL ARTERIOLE
SPLENIC ARTERY
SPLENIC VEIN
COLLECTING VEIN
VENOUS SINUS
CORDS
RED PULP (75%)

Spleen Structure

The **white pulp** is circular in structure and is made up mainly of **lymphocytes**. It functions in a manner similar to the nodules of the lymph node.

The **red pulp** surrounds the white pulp and contains mainly **red blood cells and macrophages**. The main function of the red pulp is to phagocytize old red blood cells.



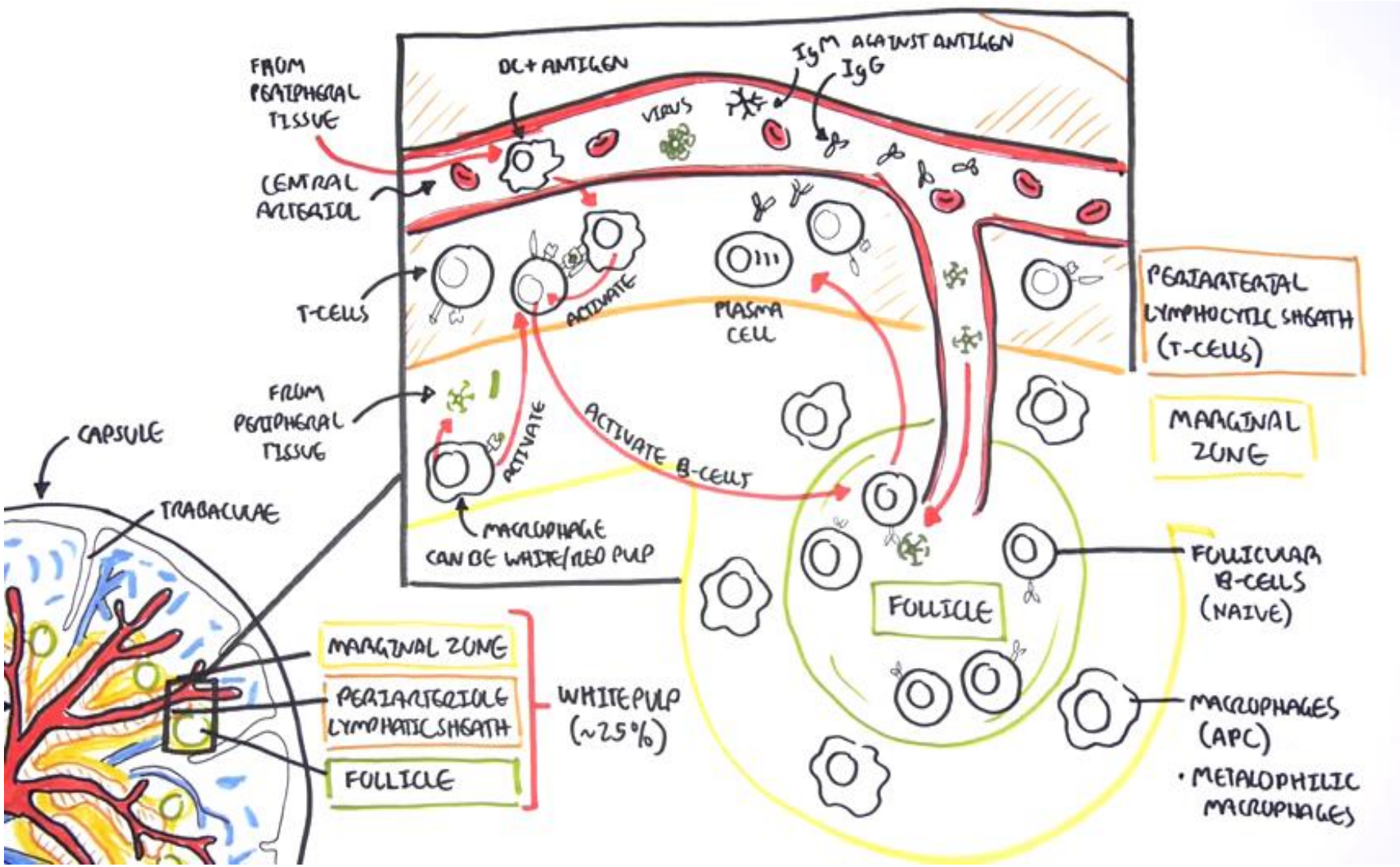
The Spleen

- Largest lymphoid tissue of the body
- Serves two main functions
  - Filters blood to remove damaged/old RBC- red pulp
  - Serves as secondary lymphoid tissue by removing infectious agents and using them to activate lymphocytes- white pulp
- A significant reservoir for T lymphocytes
- Plays an active role in the production of IgM antibodies and complement
- Has significant role in the functional maturation of antibodies

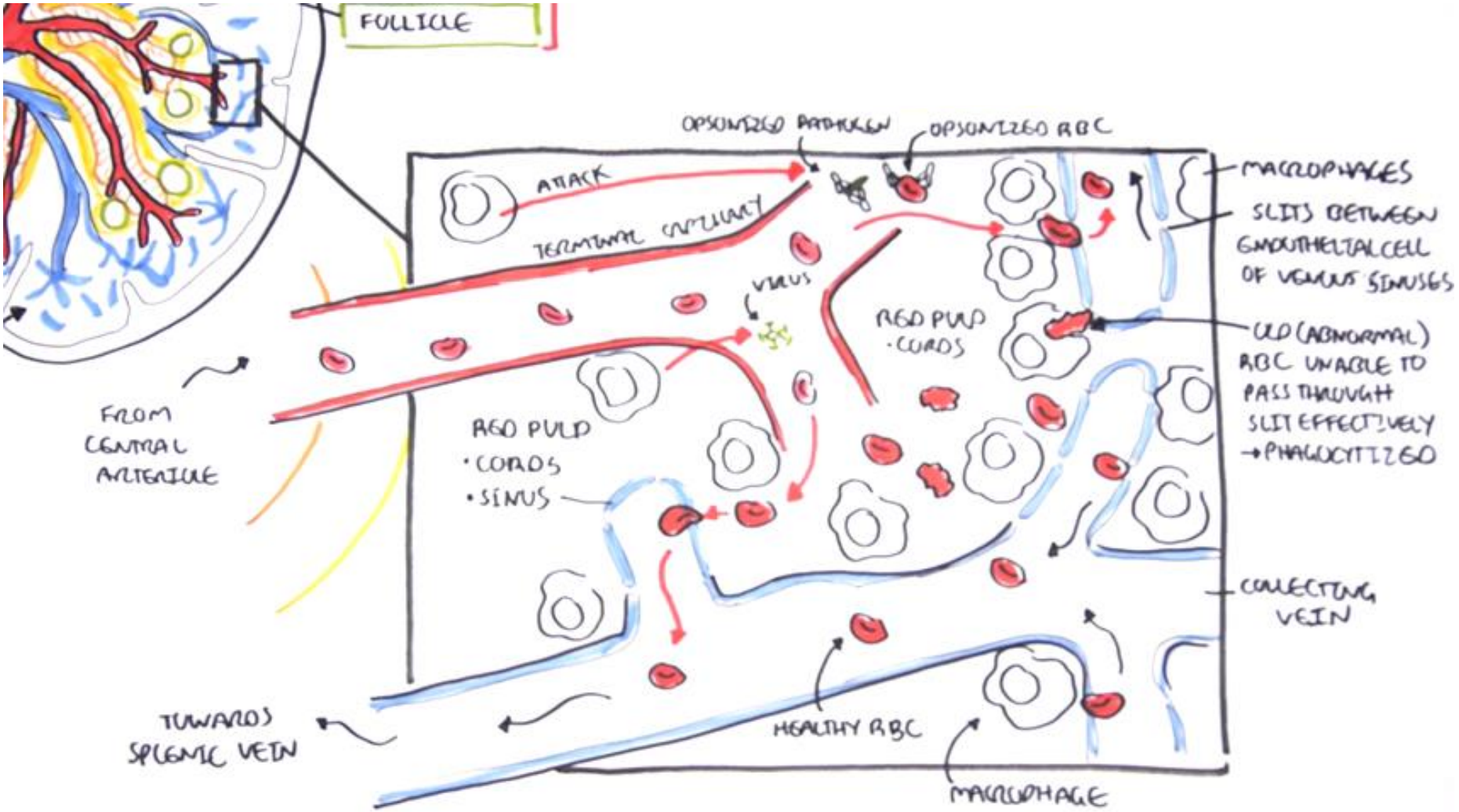
Function of the Spleen

- Immunological functions
  - Main site of opsonic antibody production
  - Especially efficient in removal of encapsulated bacteria
  - Remaining RES may compensate but not in case of encapsulated bacteria
- Filtration
  - Removal of abnormal erythrocytes and intraerythrocytic inclusions and parasitised RBC

White Pulp


FROM PERIPHERAL TISSUE
DC + ANTIGEN
IgM AGAINST ANTIGEN
IgG
VIRUS
CENTRAL ARTERIOL
T-CELLS
ACTIVATE
PLASMA CELL
PERIARTERIAL LYMPHOCYTIC SHEATH (T-CELLS)
FROM PERIPHERAL TISSUE
ACTIVATE
ACTIVATE B-CELLS
MARGINAL ZONE
CAPSULE
TRABECULAE
MACROPHAGE CAN BE WHITE/RED PULP
FOLLICULAR B-CELLS (NAIVE)
FOLLICLE
MARGINAL ZONE
PERIARTERIOLE LYMPHATIC SHEATH
FOLLICLE
WHITE PULP (~25%)
MACROPHAGES (APC)
• METALOPHILIC MACROPHAGES

Red Pulp


FOLLICLE
OPSONIZED ANTIGEN
OPSONIZED RBC
ATTACK
TERMINAL ARTERIOLE
VIRUS
RED PULP
· CORDS
MACROPHAGES
SLITS BETWEEN
ENDOTHELIAL CELL
OF VENOUS SINUSES
OLD (ABNORMAL)
RBC UNABLE TO
PASS THROUGH
SLIT EFFECTIVELY
→ PHAGOCYTIZED
FROM
CENTRAL
ARTERIOLE
RED PULP
· CORDS
· SINUS
COLLECTING
VEIN
TOWARDS
SPLENIC VEIN
HEALTHY RBC
MACROPHAGE

TERIMAKASIH