

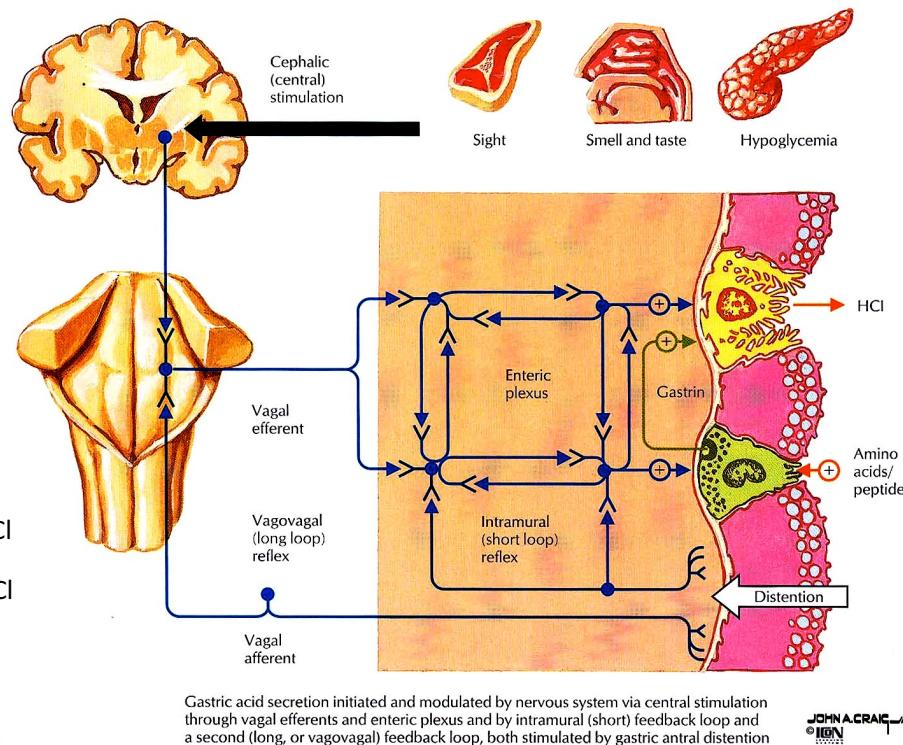
## Système digestif Régulation neuro-endocrine de la sécrétion gastrique Relation cerveau-tube digestif

Phase céphalique SNC

Phase gastrique neuro-endocrine

Voie neurocrine: Nerf vague  $\rightarrow$  ACh  $\rightarrow$  HCl

Voie endocrine: Cellule G  $\rightarrow$  Gastrine  $\rightarrow$  HCl

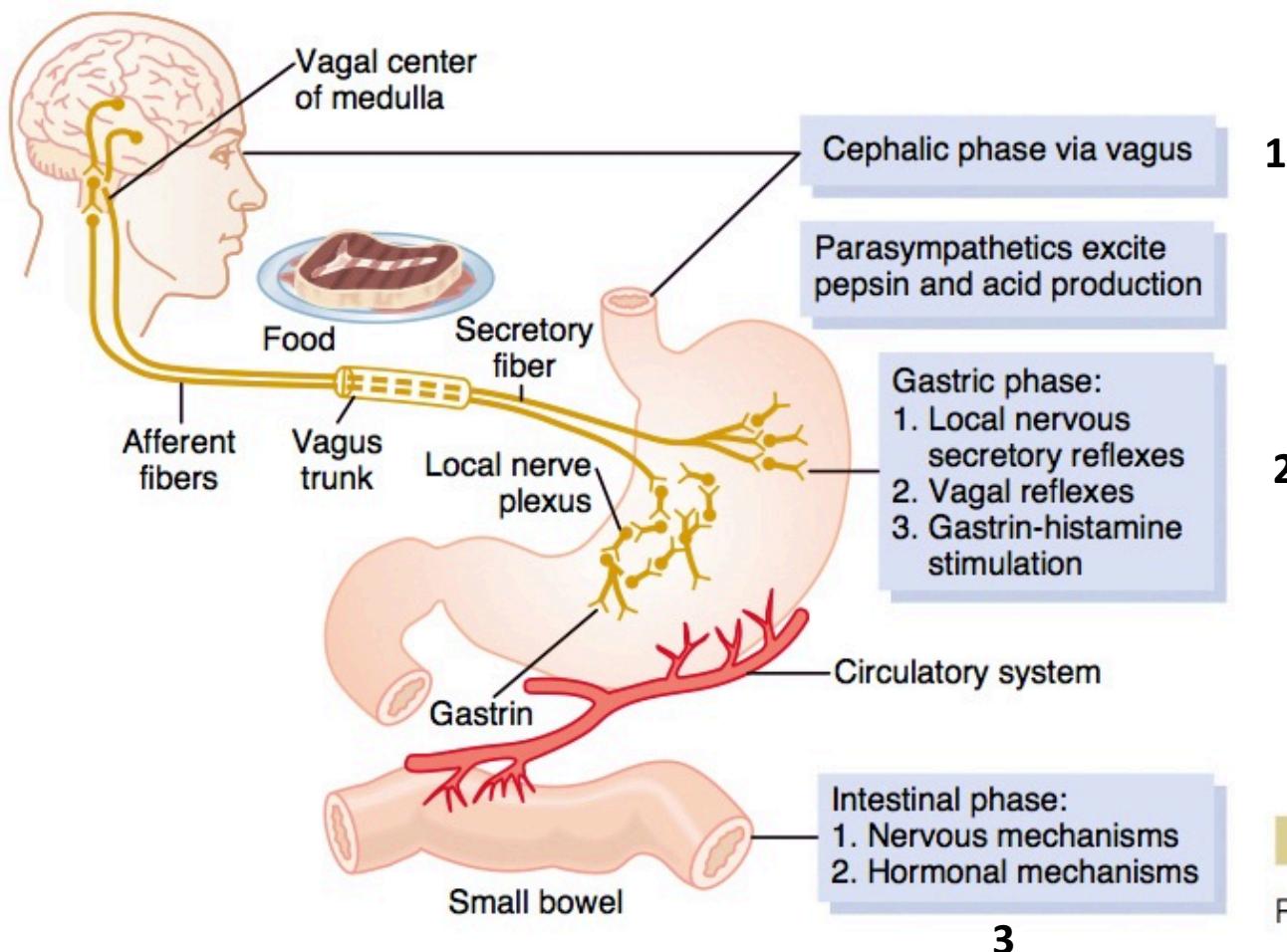


**FIGURE 7.13 VAGAL CONTROL OF GASTRIC SECRETION**

Gastric secretion, in response to sight, smell, taste, and chewing of food, is initiated and modulated by the vagus nerves of the autonomic nervous system. This initial stimulation of secretomotor activity is referred to as the "cephalic phase." The vagal stimulation

acts via the enteric nervous system to initiate gastric secretion of acid (HCl) and gastrin. The presence of acid, amino acids, and peptides, as well as gastric distension, effectively stimulates the next phase of gastric secretion, termed the "gastric phase."

## Système digestif 3 phases de la sécrétion gastrique et leurs régulations



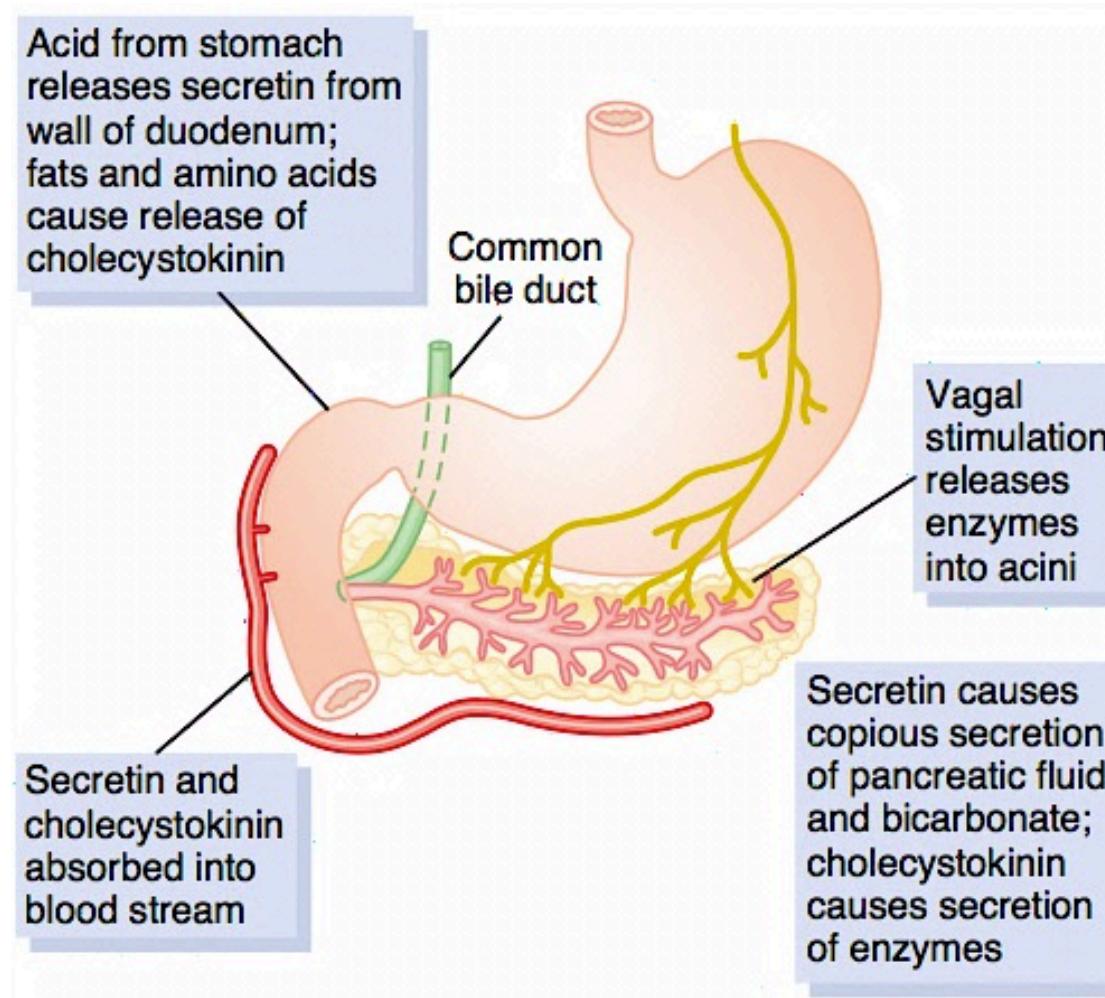
**Figure 64-7**

Phases of gastric secretion and their regulation.

## Système digestif Régulation de la sécrétion pancréatique

HCl → sécrétine

Graisses +  
Ac. aminés  
→ CCK



sécrétine →  $\text{HCO}_3^-$

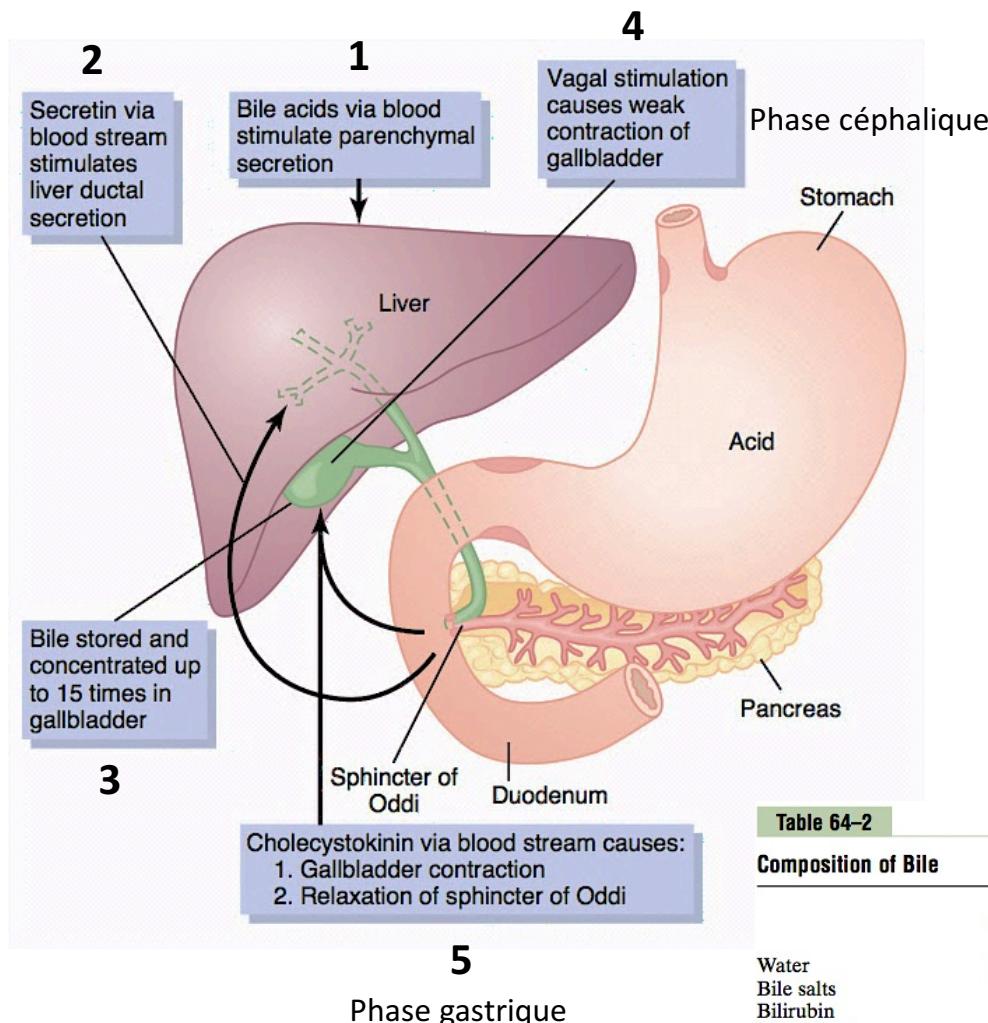
CCK → enzymes digestion  

- trypsinogène
- amylase
- lipase

**Figure 64-10**

Regulation of pancreatic secretion.

## Système digestif Régulation de la sécrétion biliaire

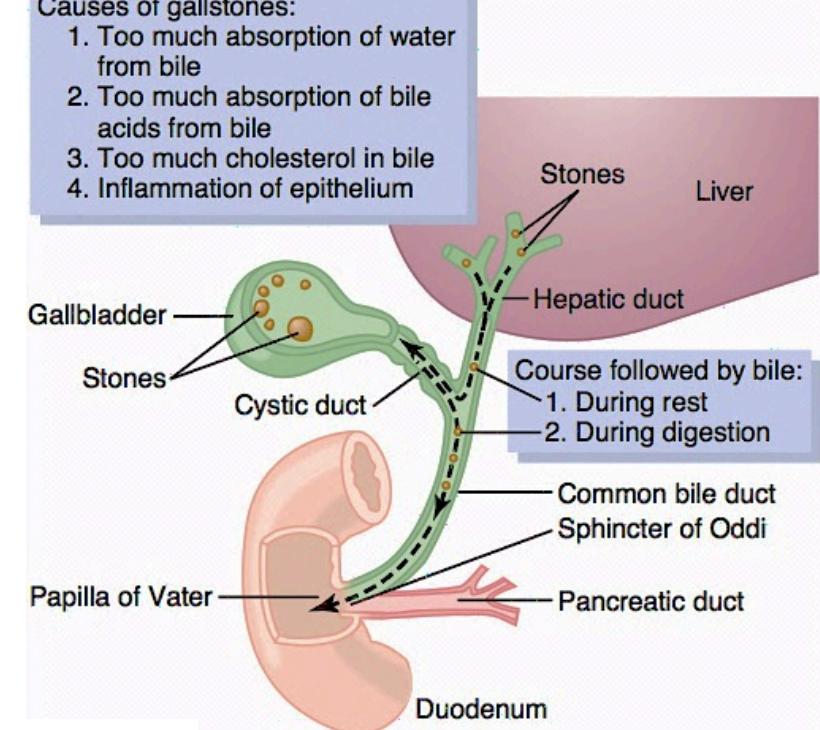


**Table 64-2**  
**Composition of Bile**

	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 <sup>+</sup>	145.04 mEq/L	130 mEq/L
K <sup>+</sup>	5 mEq/L	12 mEq/L
Ca <sup>++</sup>	5 mEq/L	23 mEq/L
Cl <sup>-</sup>	100 mEq/L	25 mEq/L
HCO <sub>3</sub> <sup>-</sup>	28 mEq/L	10 mEq/L

**Causes of gallstones:**

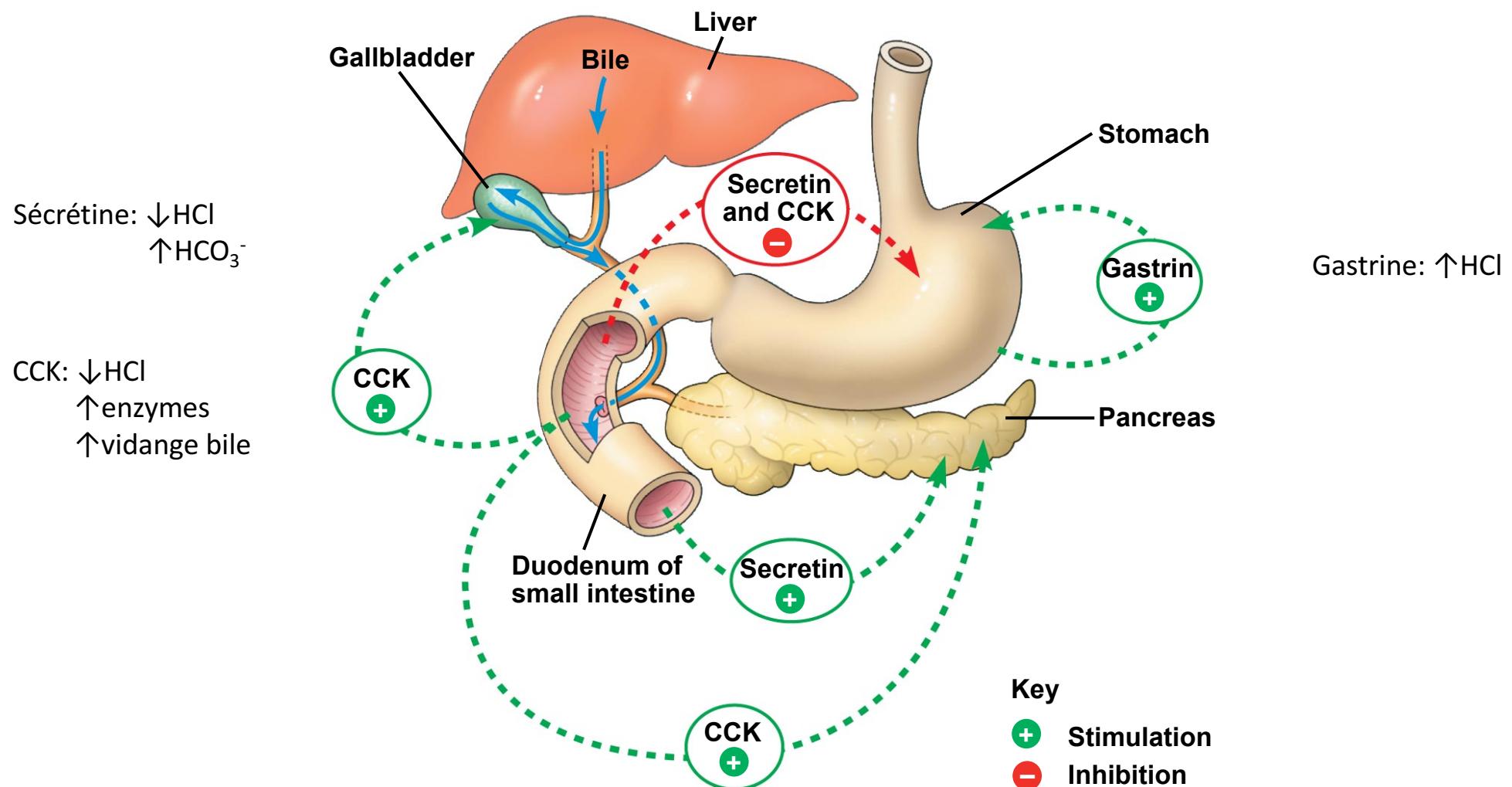
1. Too much absorption of water from bile
2. Too much absorption of bile acids from bile
3. Too much cholesterol in bile
4. Inflammation of epithelium



**Figure 64-12**

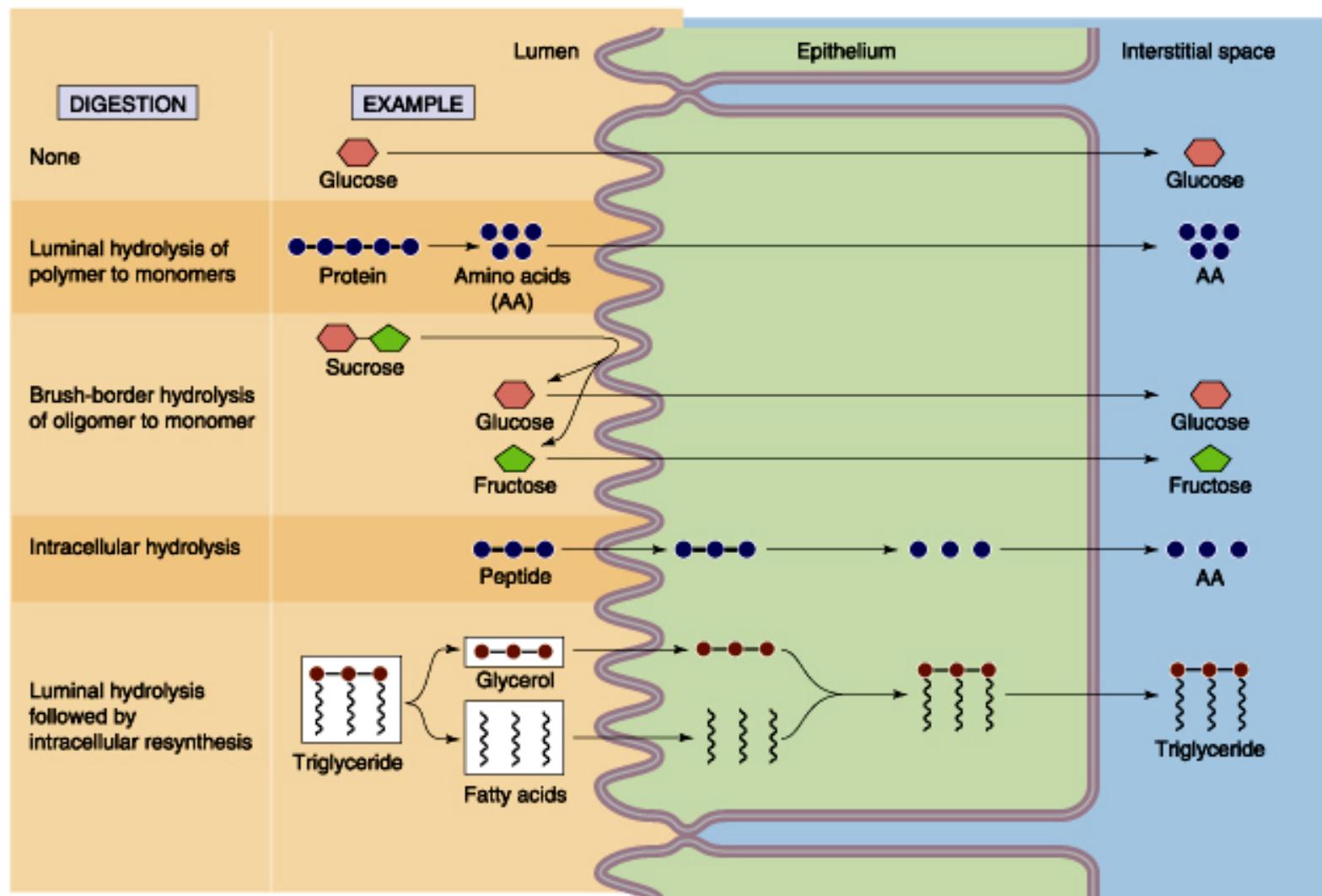
Formation of gallstones.

## Système digestif Régulation neuro-endocrine de la sécrétion digestive



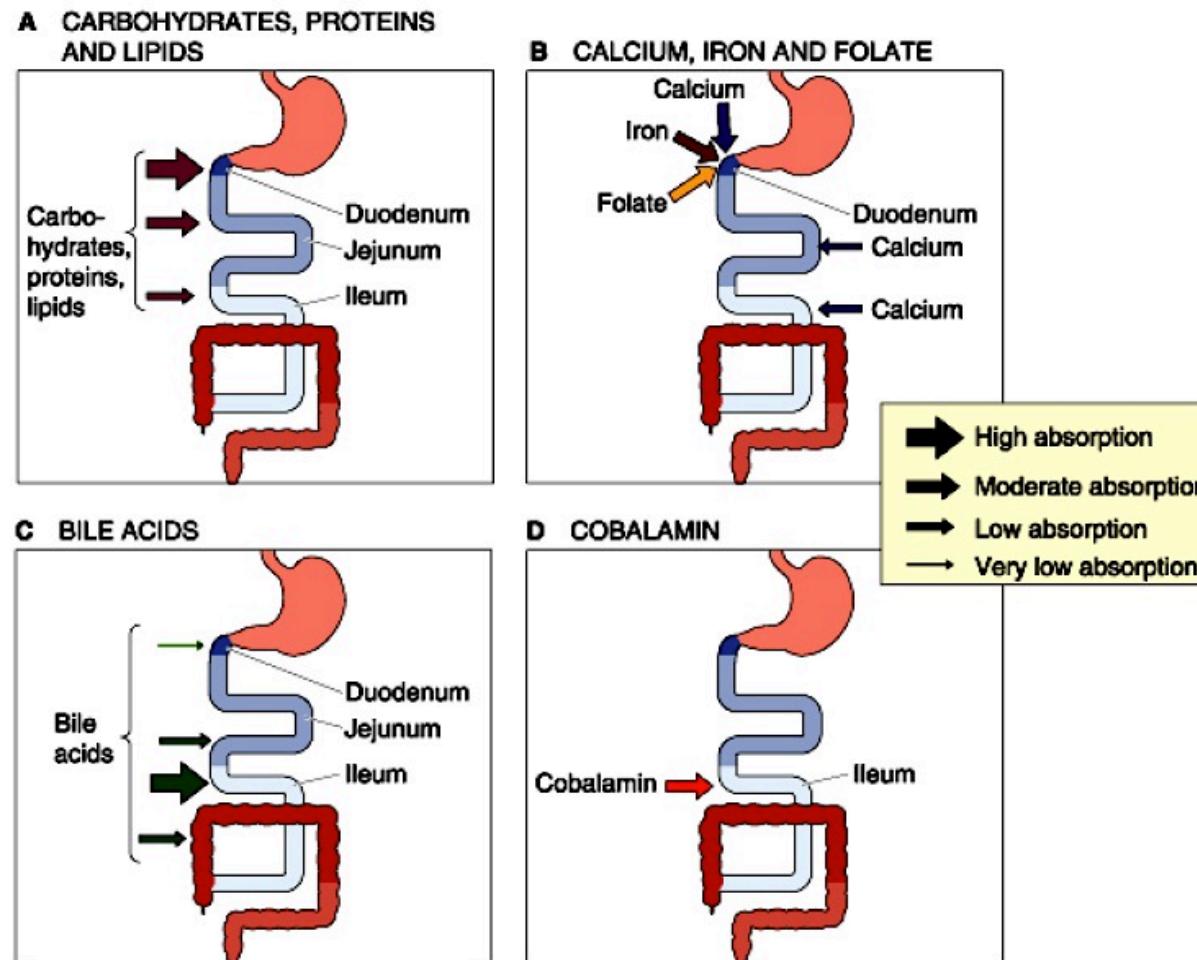
Copyright © 2008 Pearson Education, Inc., publishing as Pearson Benjamin Cummings.

## Système digestif Mécanismes généraux de la digestion



**Système digestif Mécanismes généraux de la digestion**

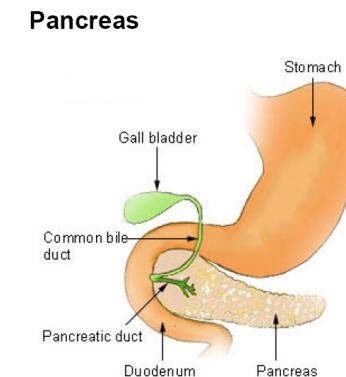
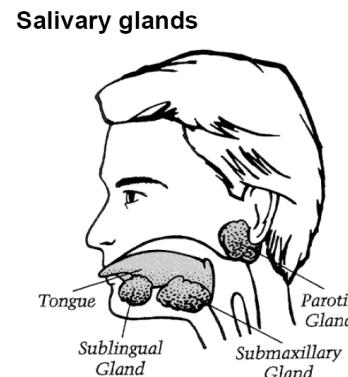
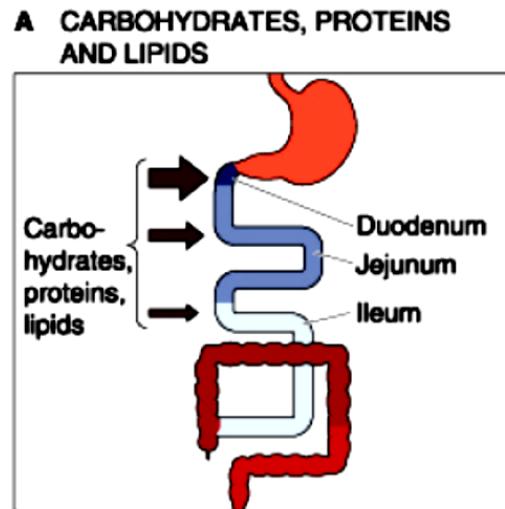
# Les sites de l'absorption des nutriments



## Système digestif Digestion des précurseurs des sucres et leur absorption

### Les hydrates de carbone dans notre alimentation

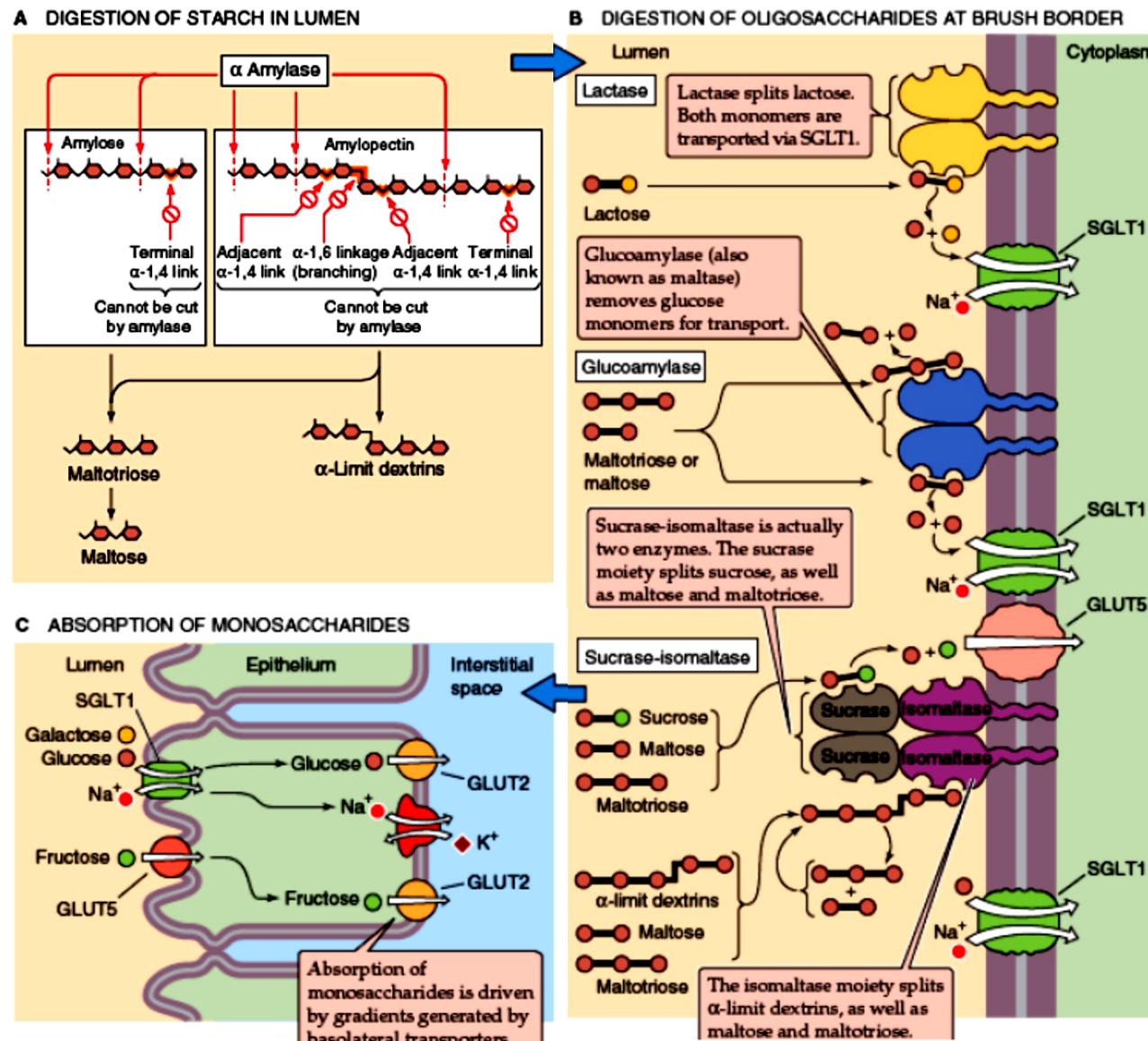
- 5-10% Monosaccharides => directement absorbables *fructose, glucose*
- 30-40% Oligosaccharides => nécessitent la digestion *sucrose, maltose*
- 45-60% Polysaccharides => nécessitent la digestion *amidon, amylose*  $\alpha$ -1,4,  $\alpha$ -1,6
- var. Fibres  $\beta$ -1,4 => non digestes (éventuellement par bactéries)



Secretion of:	
mucus:	lubrication and binding of masticated bolus
electrolytes:	solubilize dry food: tasted
$\alpha$ -amylase:	initiates starch digestion
factors:	protecting against bacteria and caries

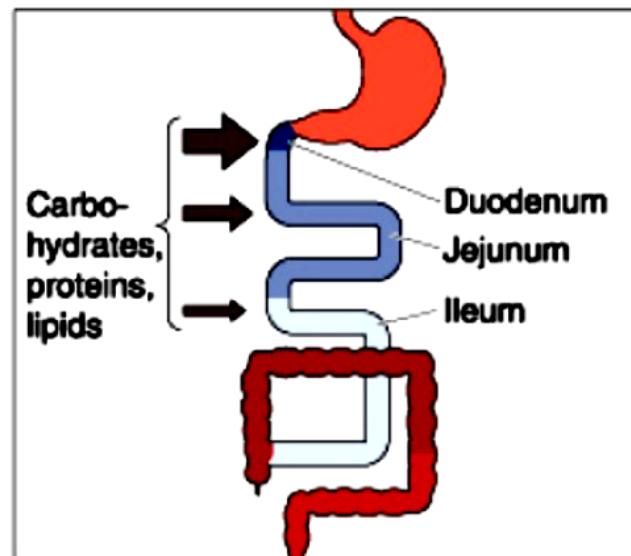
	Secretion of:
Endocrine	hormones that regulate blood glucose levels: Insuline, Glucagon
Exocrine	bicarbonate that neutralises acid chyme coming from stomach enzymes that break down digestible foods: trypsinogen, amylase, lipase

## Système digestif Digestion des sucres dans l'intestin grêle



## Système digestif Absorption des acides aminés et des petits peptides

### A CARBOHYDRATES, PROTEINS AND LIPIDS

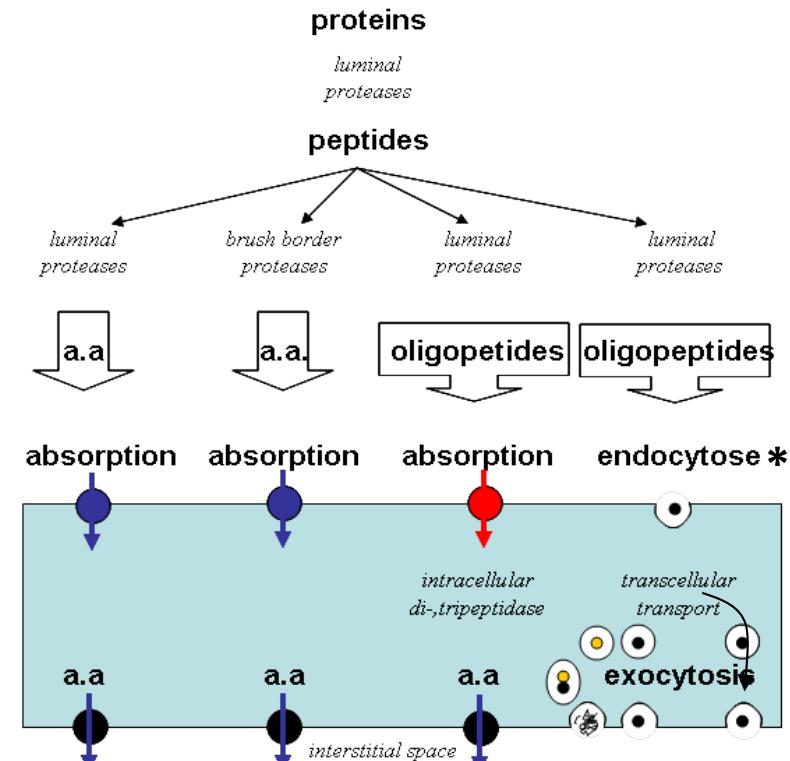


70 - 100 gr / j

10 – 15% coûts énergétiques pour l'apport

+ 30-50 gr de protéines endogènes

### 4 absorption pathways



\* neonatal period

**Les protéases luminales sont sécrétées en tant que proenzymes**

Estomac : Pepsinogène  $\rightarrow$  pH < 2.0  $\sim$  pepsine

Pancréas: Trypsinogène

$\rightarrow$  entéropeptidase + trypsine  $\rightarrow$  trypsine (antitrypsine présente dans le pancréas)

Chymotrypsinogène

$\rightarrow$  trypsine  $\rightarrow$  chymotrypsine

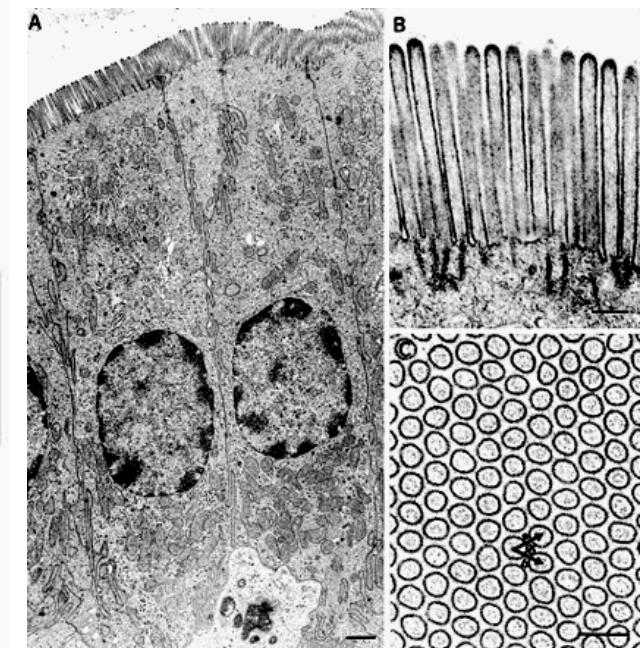
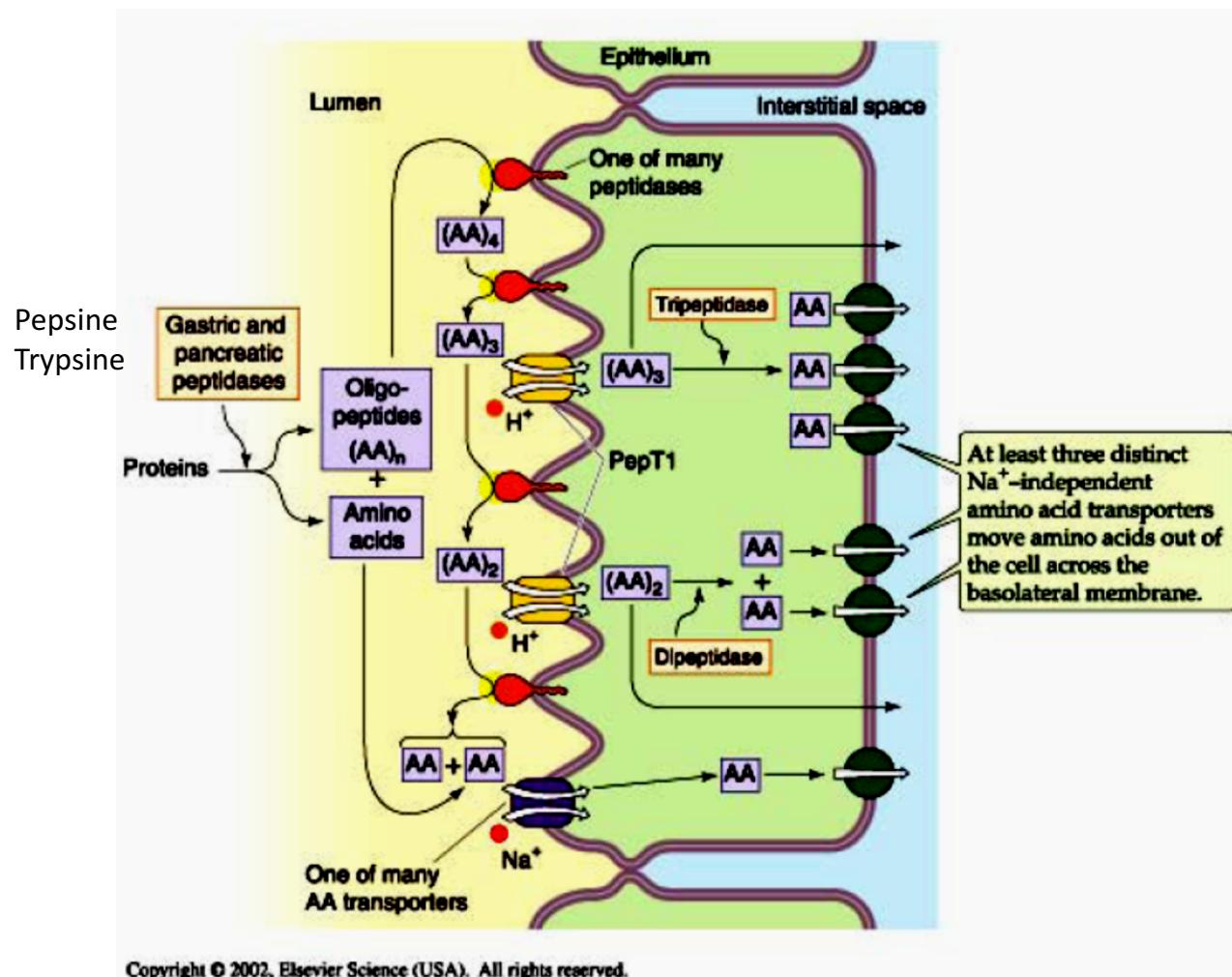
Proélastase

$\rightarrow$  trypsine  $\rightarrow$  élastase

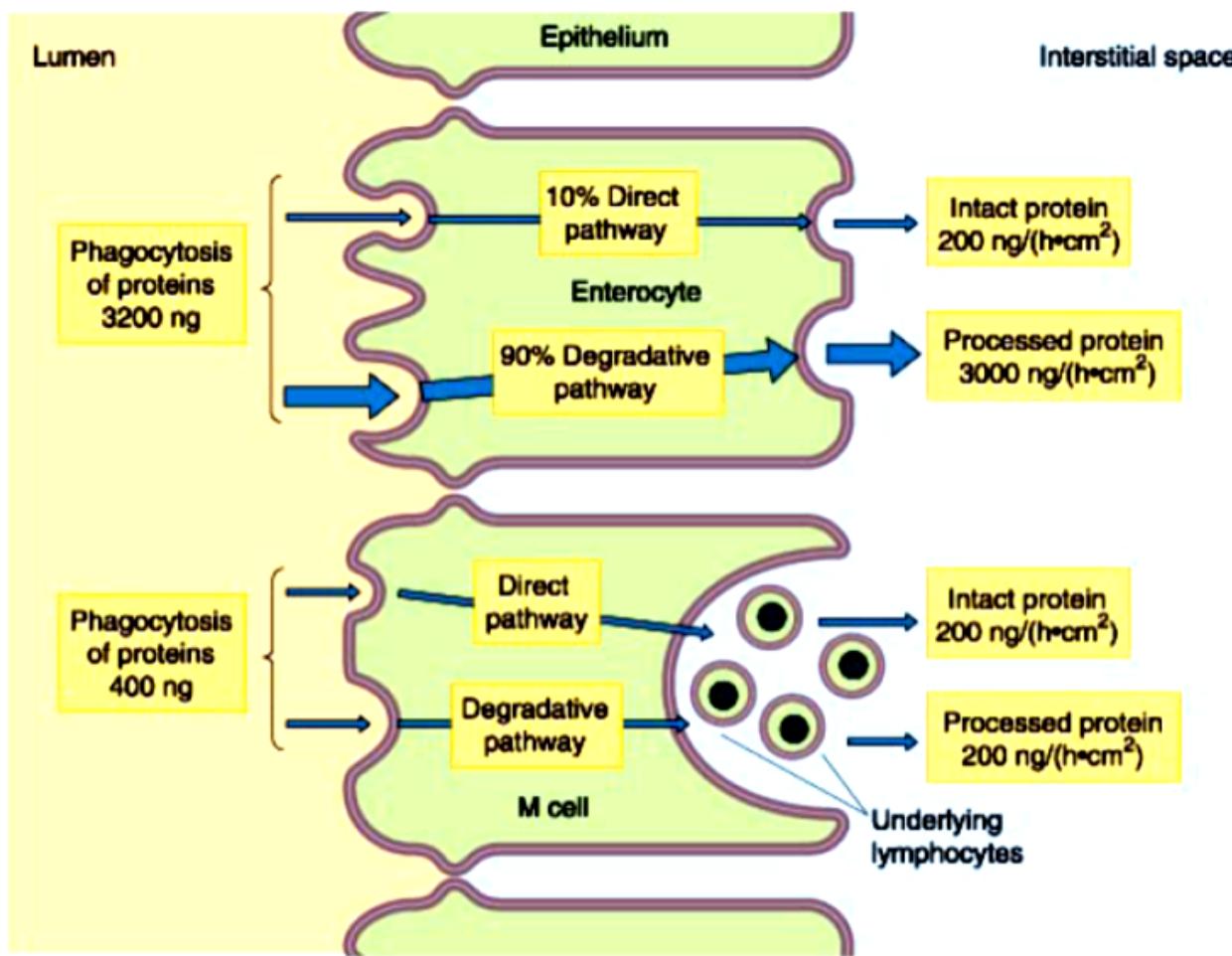
Procarboxypeptidase A et B

$\rightarrow$  trypsine  $\rightarrow$  carboxypeptidase A et B

## Système digestif Absorption des acides aminés et des petits peptides

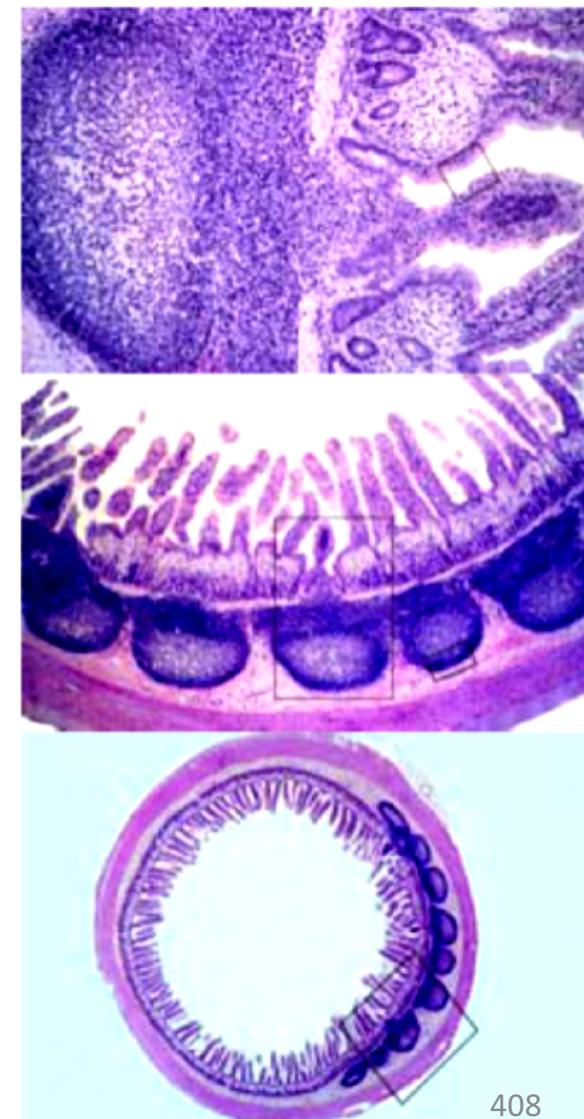


## Système digestif Absorption des acides aminés et des petits peptides



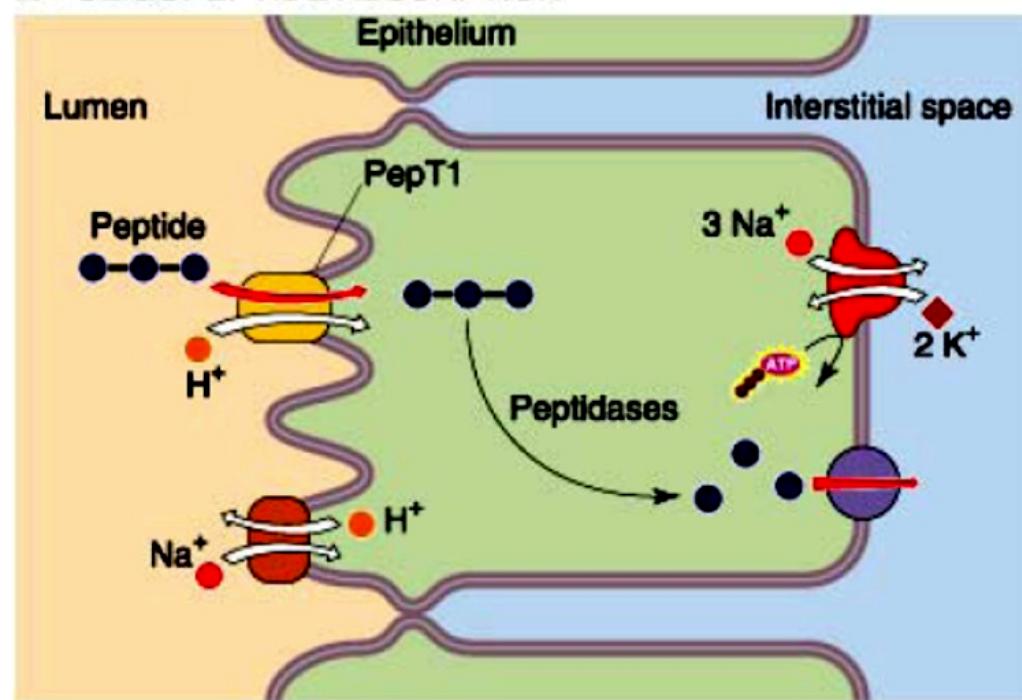
Copyright © 2002, Elsevier Science (USA). All rights reserved.

Peyer's patches →

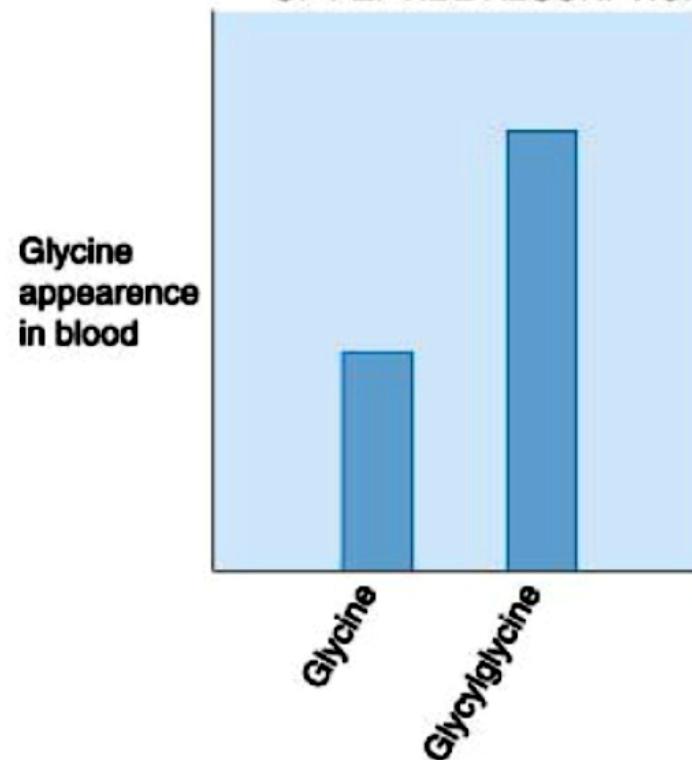


## Système digestif Absorption des acides aminés et des petits peptides

### A OLIGOPEPTIDE ABSORPTION



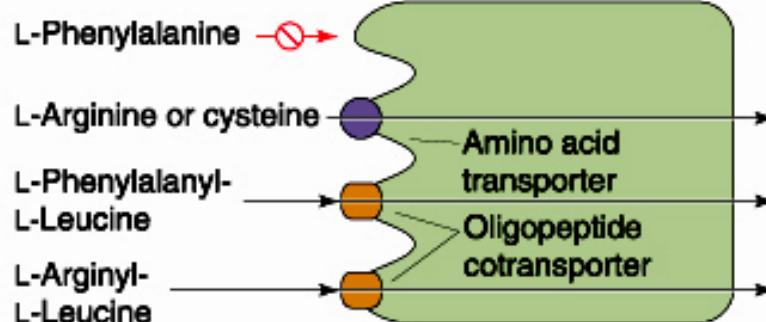
### B "KINETIC ADVANTAGE" OF PEPTIDE ABSORPTION



Copyright © 2002, Elsevier Science (USA). All rights reserved.

## Système digestif Absorption des acides aminés et petits peptides

### A HARTNUP DISEASE



### Exemple

### B CYSTINURIA

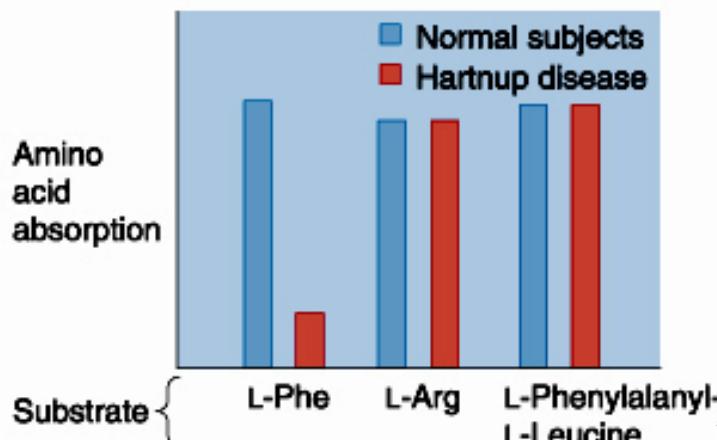
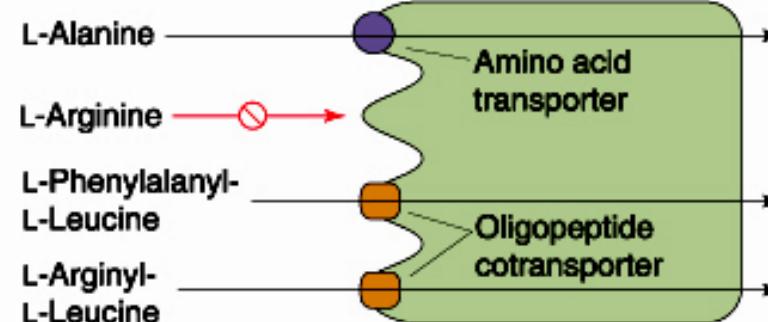
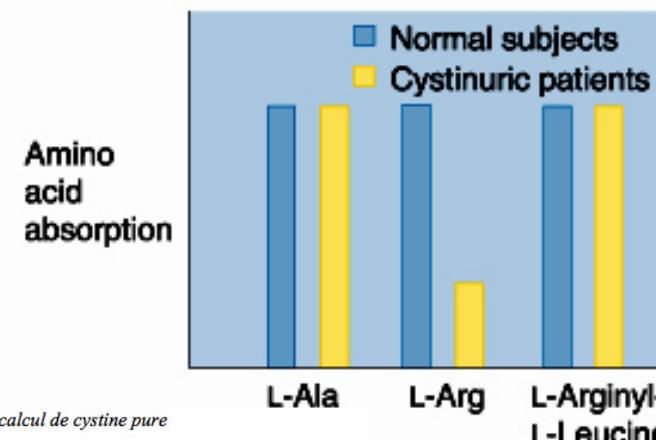


Figure 1 : calcul de cystine pure

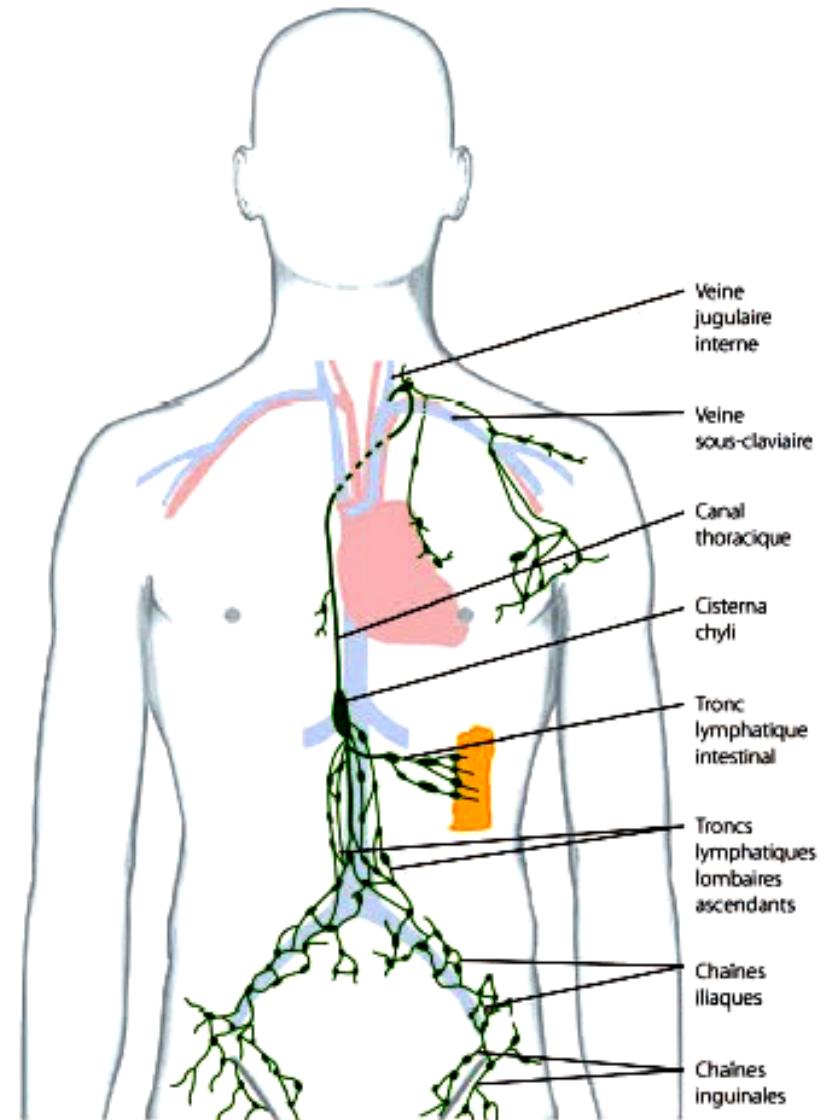
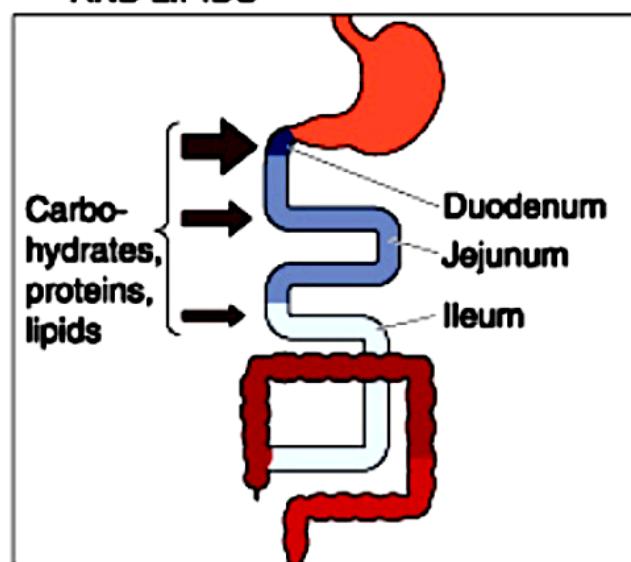


Copyright © 2002, Elsevier Science (USA). All rights reserved.

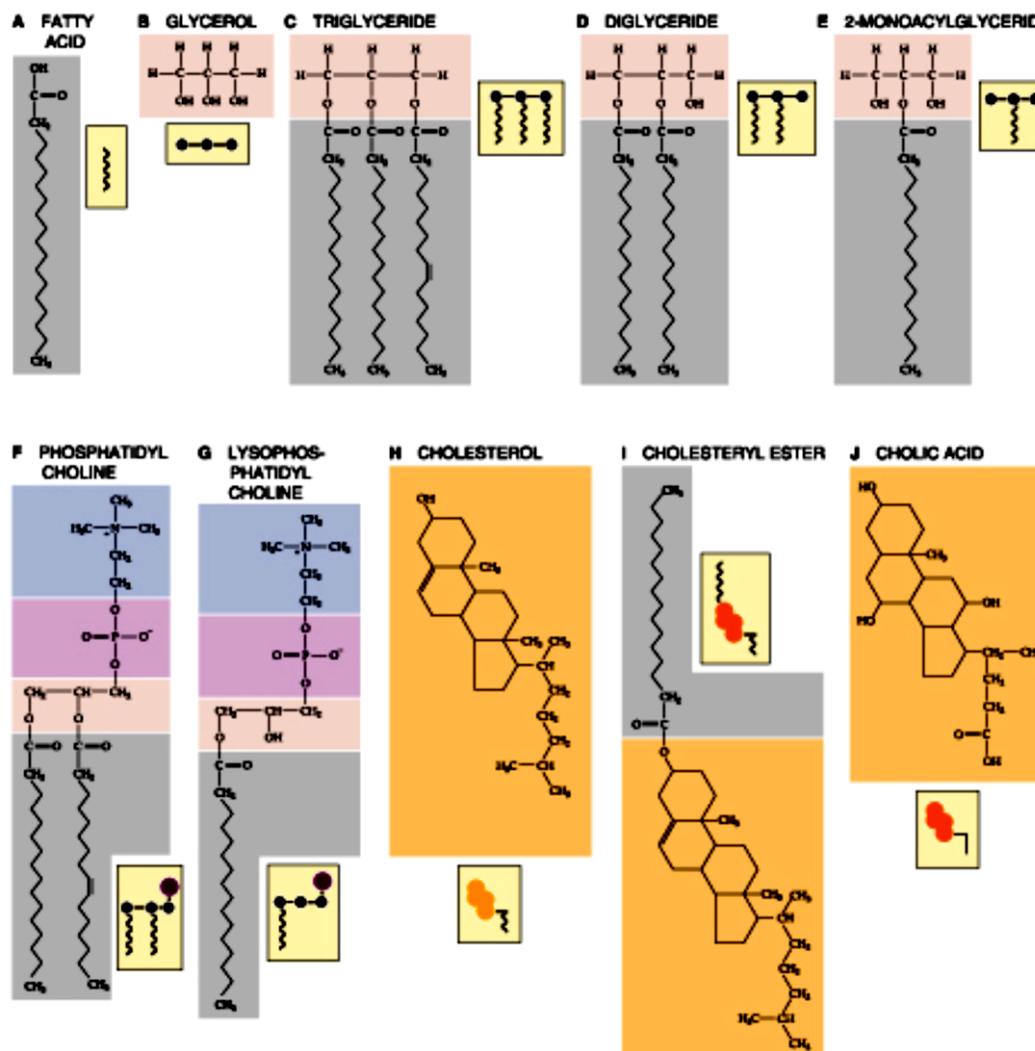


## Système digestif   Absorption des corps gras

### A CARBOHYDRATES, PROTEINS AND LIPIDS



## Système digestif Structure générale des lipides



140 g de graisses/ jour

90 % sont des triglycérides [C]

5 % sont des phospholipides [F; G]

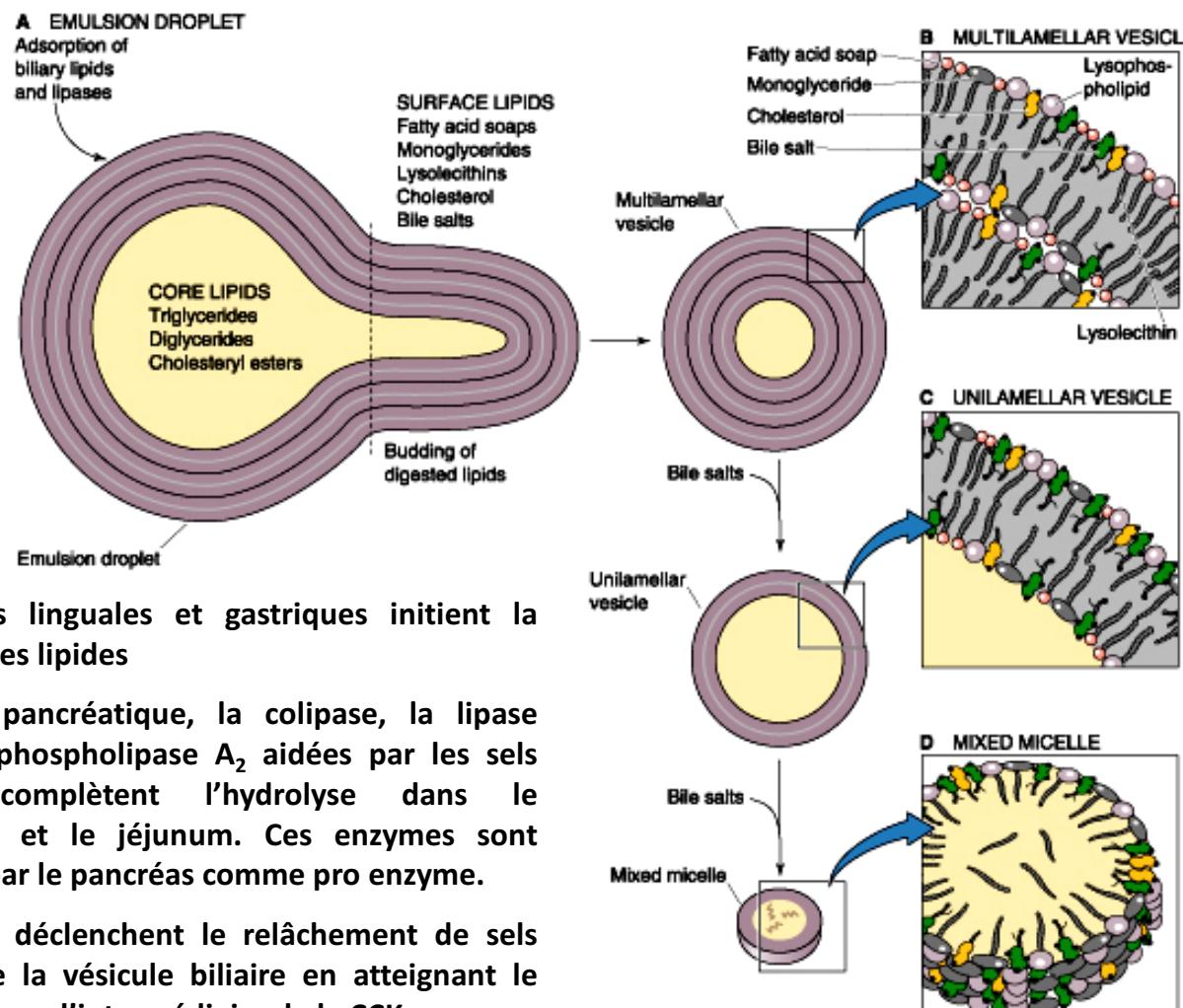
0.6% est du cholestérol estérifié [I]

AG Saturés/insaturés > graisses animales  
< graisses végétales

Liaison saturée: nombre max de liaison simple –H

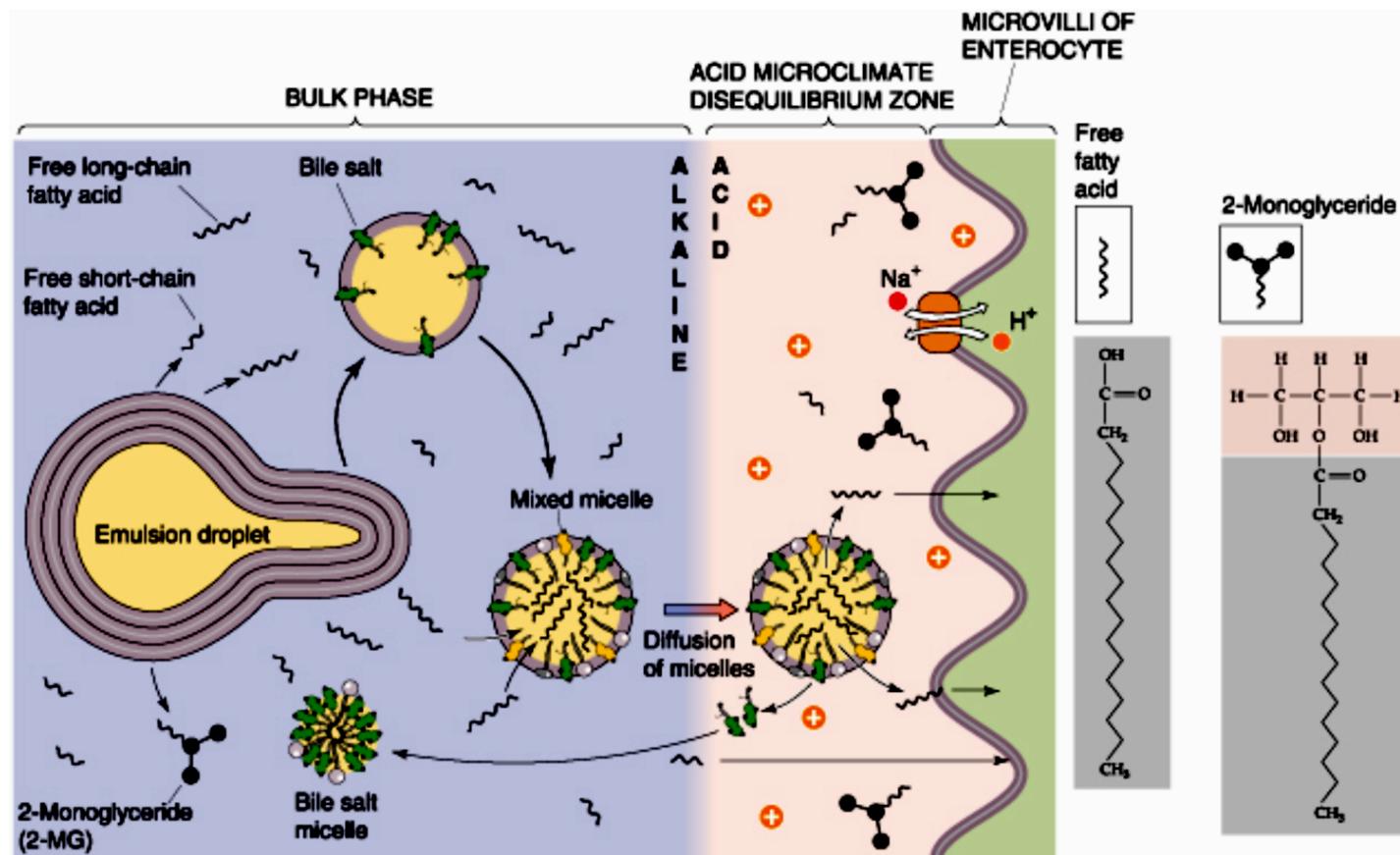
Liaison insaturée: double liaison =

## Système digestif Effets des sels biliaires sur la composition des lobules lipidiques



- Les lipases linguaes et gastriques initient la digestion des lipides
- La lipase pancréatique, la colipase, la lipase lactée, la phospholipase A<sub>2</sub> aidées par les sels biliaires complètent l'hydrolyse dans le duodénum et le jéjunum. Ces enzymes sont sécrétées par le pancréas comme pro enzyme.
- Les lipides déclenchent le relâchement de sels biliaires de la vésicule biliaire en atteignant le duodénum par l'intermédiaire de la CCK

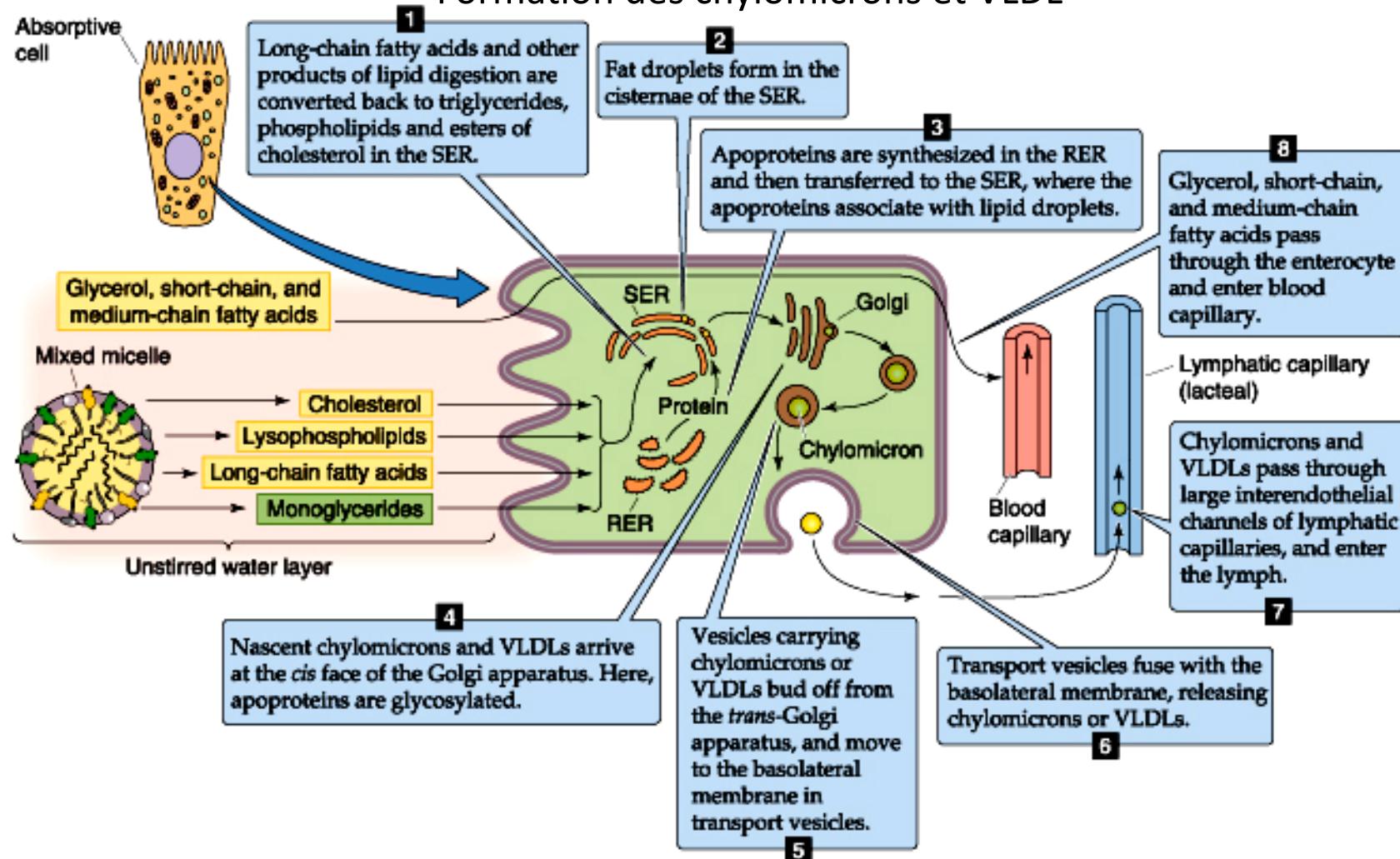
## Système digestif Organisation moléculaire de l'absorption des lipides



**Capture:**

**l'acidification titre les lipides les rendant neutres**  
**=> diffusion facilitée**  
**=> facilite l'incorporation membranaire**

## Système digestif Organisation générale de l'absorption des lipides Formation des chylomicrons et VLDL



## Système digestif Absorption de l' $H_2O$ et du $Na^+$ dans le tube digestif

### Principes généraux

- 1) L'eau est réabsorbée par un transport isomotique et entièrement par diffusion**
- 2) Le  $Na^+$  est transporté activement**

30 gr/jour de  $Na^+$  sont sécrétés par le tube digestif

5-8 gr/jour sont présents dans la nourriture

=> pour garder l'équilibre le tube digestif doit en réabsorber 25-35 gr/jour

=> régulation comme dans les reins avec l'aldostérone qui stimule la capture de  $Na^+$  => colon

La diarrhée peut provoquer d'importantes pertes de  $Na^+$  en quelques heures!!!

**potentiellement mortel!**

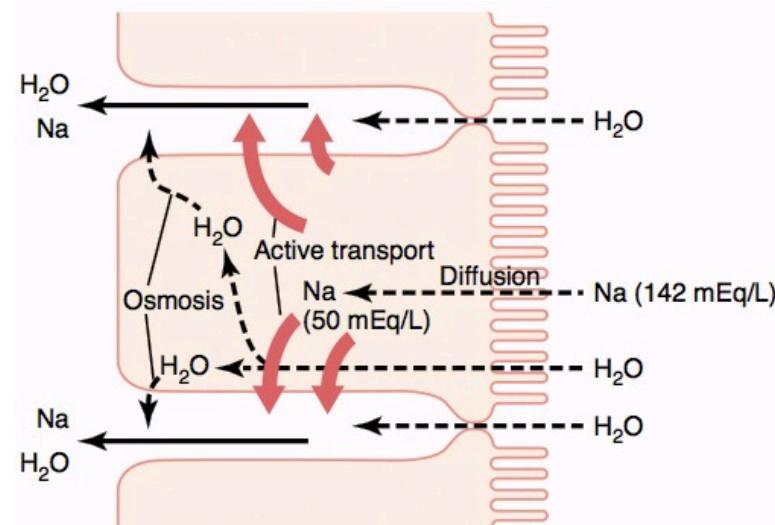
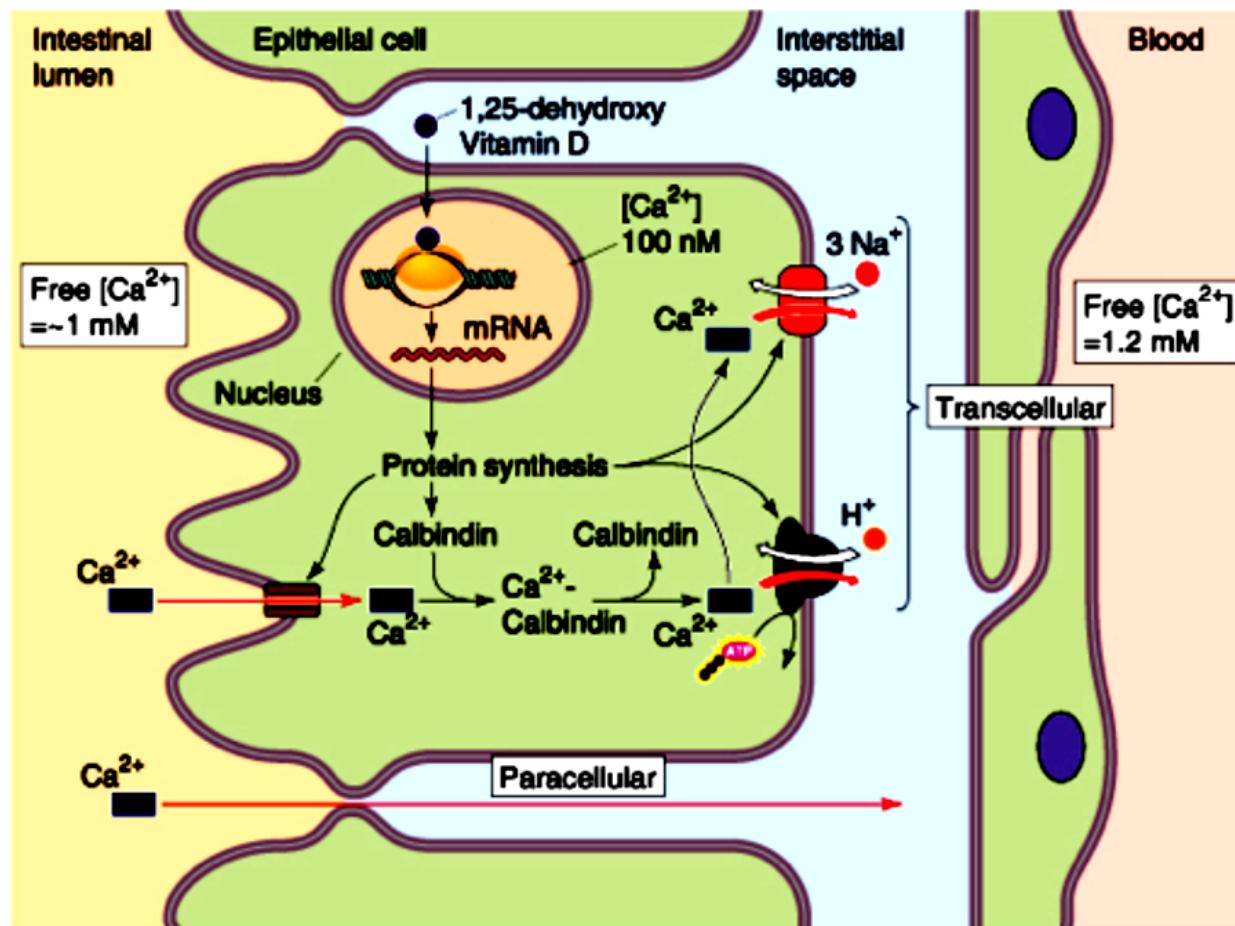


Figure 65-8

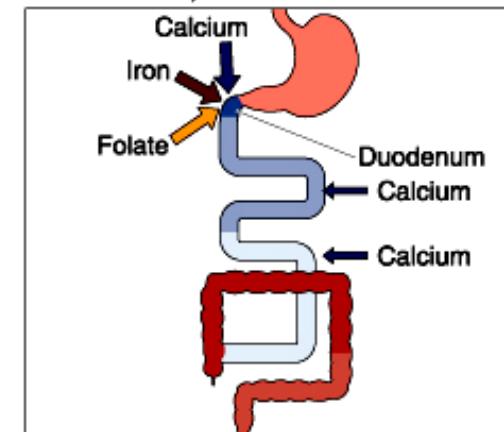
Absorption of sodium through the intestinal epithelium. Note also osmotic absorption of water—that is, water “follows” sodium through the epithelial membrane.

## Système digestif Régulation de l'absorption du Ca<sup>++</sup> par le duodénum



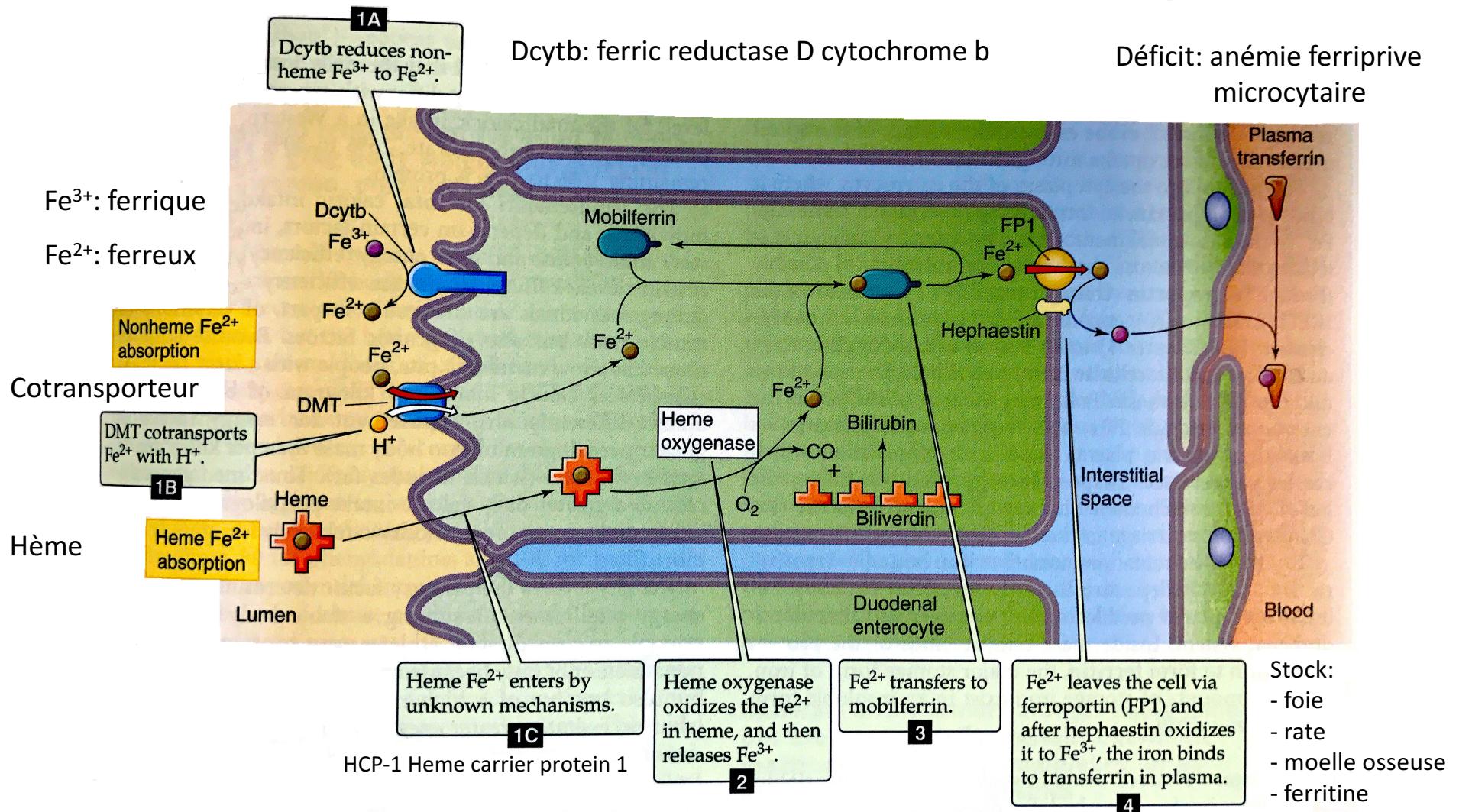
Ca<sup>++</sup> Messager intracellulaire  
par. ex. contraction musculaire

### B CALCIUM, IRON AND FOLATE



forme active de la vitamine D (1,25 dihydroxy vitamine D)

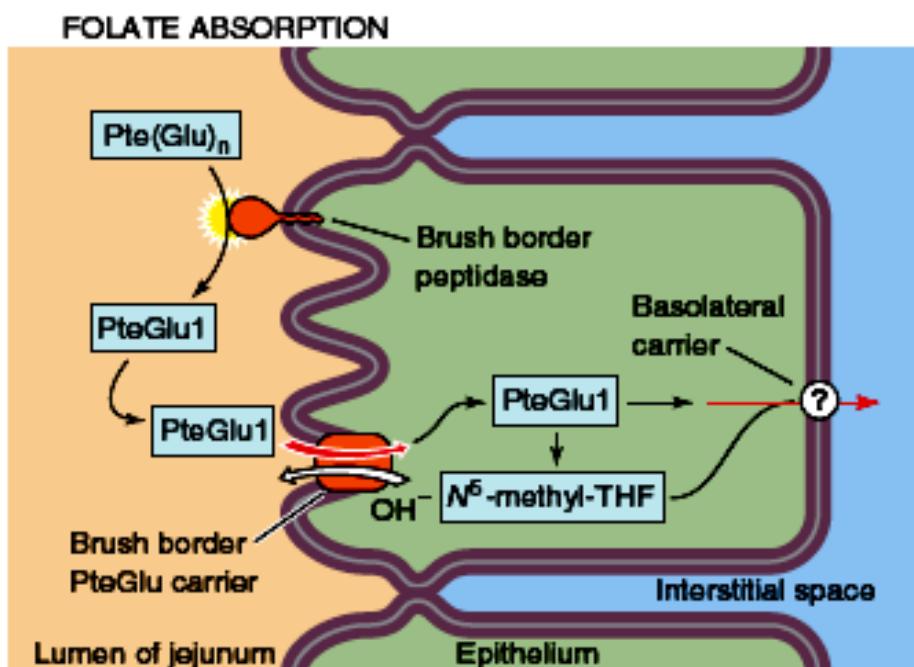
## Système digestif Régulation de l'absorption du Fe<sup>++</sup>



10-15 mg/jour aliments [10% ingéré → absorbé]

DMT= divalent metal transporter 1

## Système digestif Capture de l'acide folique dans l'intestin



Pte(Glu)<sub>n</sub> = pteroylpolyglutamates

PteGlu1 = pteroylglutamic acid

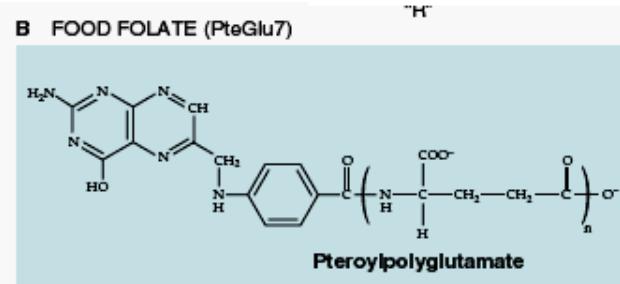
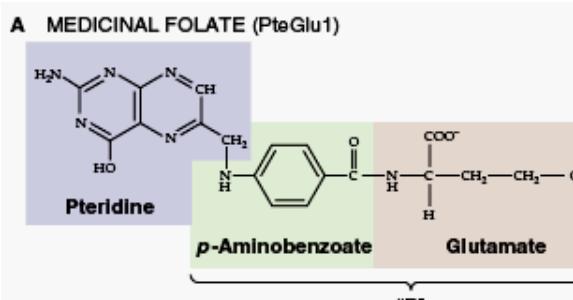
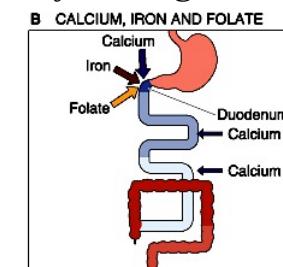
Folate: Vit. B9

**Facteur important pour la synthèse de thymine et de purine\* de l'ADN \*Adénine-Guanine**

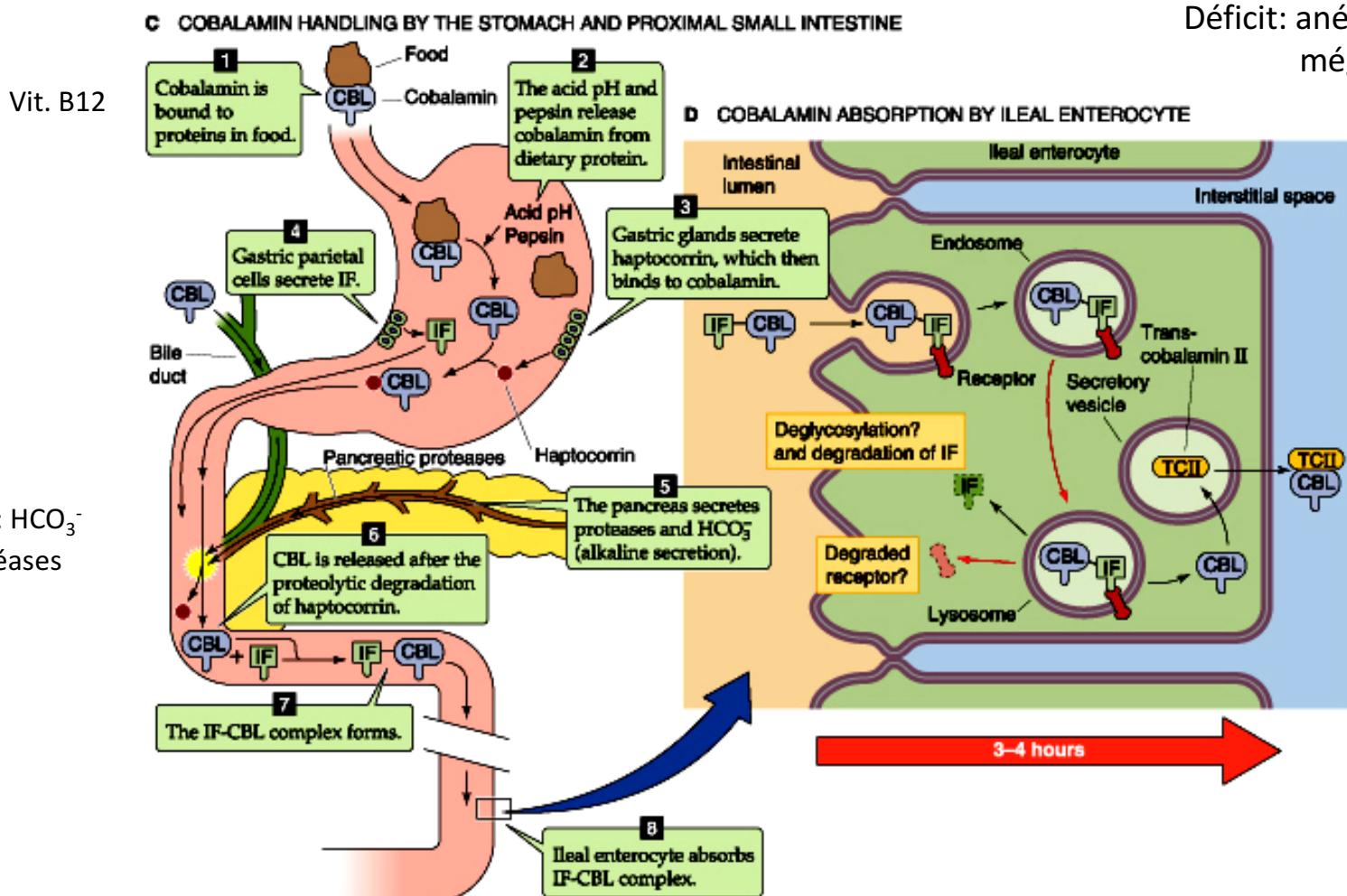
- 200µg / jour
- affecte initialement les cellules à taux rapide de renouvellement: moelle osseuse

⇒ anémie mégaloblastique

Sources: foie, végétaux



## Système digestif Absorption de la vitamine B12



Déficit: anémie pernicieuse  
mégloblastique

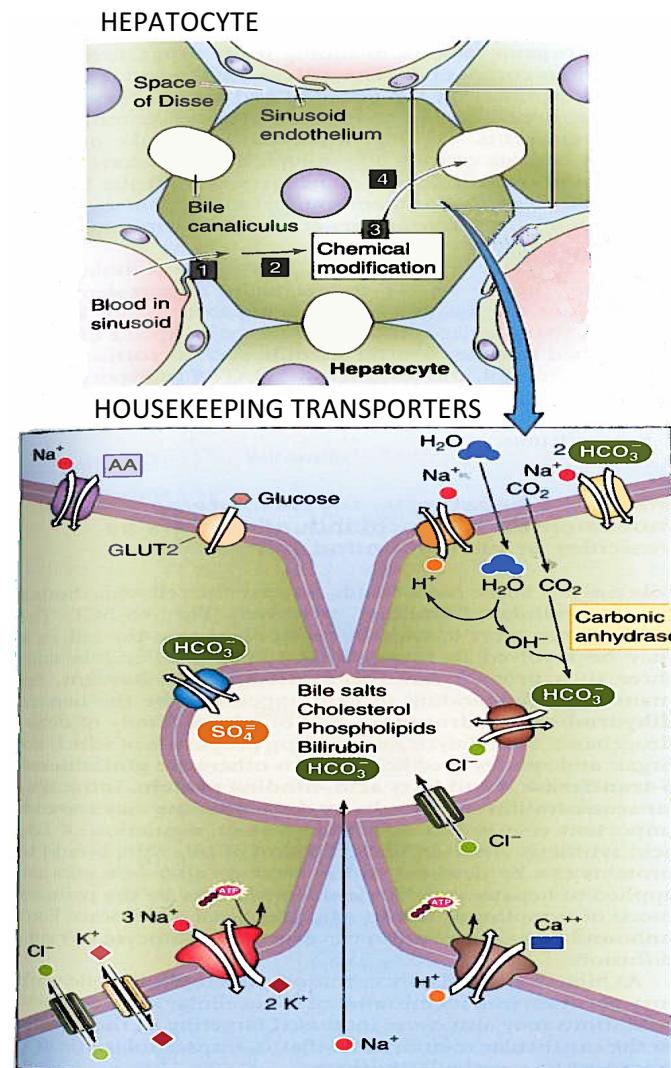
Sécrétine:  $\text{HCO}_3^-$   
CCK: protéases

Vitamine hydrosoluble  
→ cycle Krebs  
→ synthèse purines  
→ myéline du SNC  
→ synthèse GR

Copyright © 2002, Elsevier Science (USA). All rights reserved.

intrinsic factor (IF). cobalamin (CBL). transcobalamin II (TCII)

## Système digestif Transport dans les hépatocytes



### A, Les hépatocytes traitent les composés en 4 étapes:

- (1) extraction du sang au travers de la membrane basolatérale (i.e., sinusoïdale);
- (2) transport intracellulaire;
- (3) contrôle la modification ou dégradation chimique
- (4) exporte dans la bile au travers de la membrane apicale (i.e., canaliculaire).

### B, Les hépatocytes ont une gamme complète de transporteurs pour maintenir

une faible  $[Na^+]_i$

une haute  $[K^+]_i$ ,

une faible  $[Ca^{2+}]_i$ .

De nombreux canaux déterminent le voltage de membrane

Divers transporteurs acide-base régulent le pH intracellulaire

## Système digestif Protéines en circulation d'origine hépatique

### Major Plasma Proteins

Albumin

$\alpha_1$ -Fetoprotein

Plasma fibronectin (an  $\alpha_2$  glycoprotein)

C-reactive protein

$\alpha_2$ -Microglobulin

Various other globulins

### Factors Involved in Hemostasis/Fibrinolysis

Coagulation: fibrinogen and all others except for factor VIII

Inhibitors of coagulation:  $\alpha_1$ -antitrypsin and antithrombin III,  $\alpha_2$ -macroglobulin, protein S, protein C

Fibrinolysis: plasminogen

Inhibitors of fibrinolysis:  $\alpha_2$ -antiplasmin

Complement C3

### Carriage Proteins (“Binding Proteins”)

Ceruloplasmin (p. 1001)

Corticosteroid-binding globulin (CBG, aka transcortin; p. 1053)

GH-binding protein (low affinity form)

Haptoglobin

Hemopexin

IGF-binding proteins (p. 1029)

Retinol-binding protein (p. 1001)

Sex hormone-binding globulin (SHBG; p. 1156)

Thyroid-binding globulin (TBG; p. 1038)

Transferrin

Transthyretin (p. 1038)

Vitamin D-binding protein (p. 1096)

### Prohormones

Angiotensinogen (p. 1059)

### Apolipoproteins

Apo A-I

Apo A-II

Apo A-IV

Apo B-100

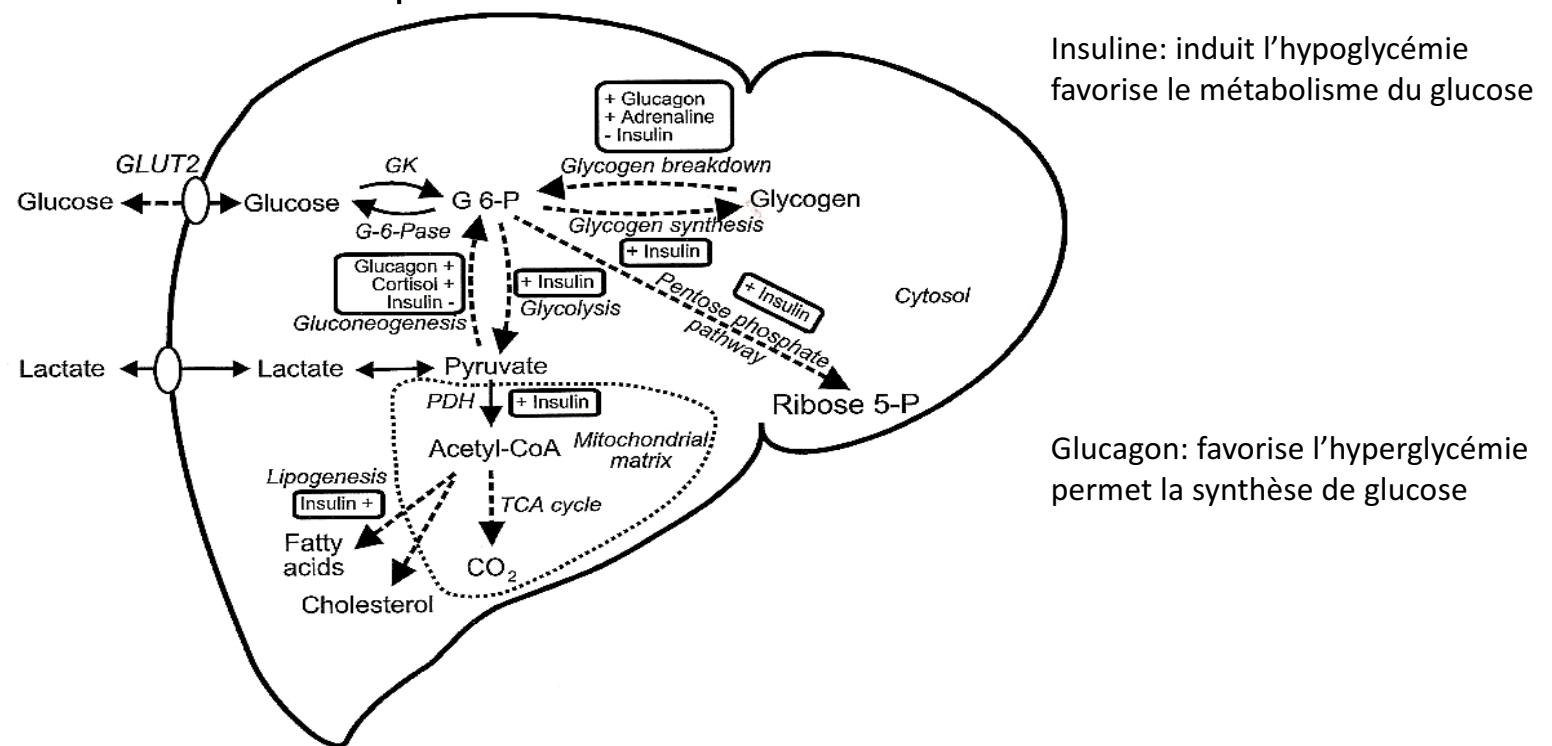
Apo C-II

Apo D

Apo E

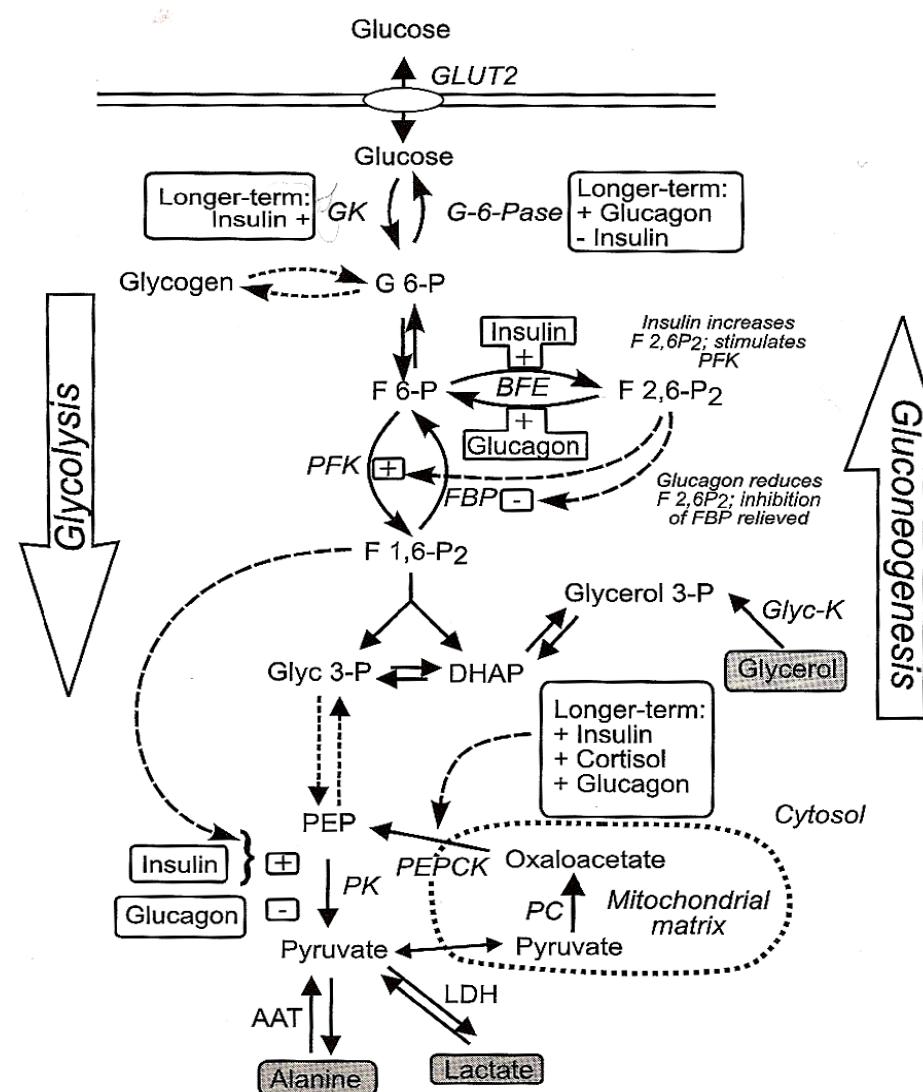
GH, growth hormone; IGF, insulin-like growth factor; TBG, thyroxine-binding globulin.

## Système digestif Métabolisme du glucose et régulation hormonale Gestion par le foie



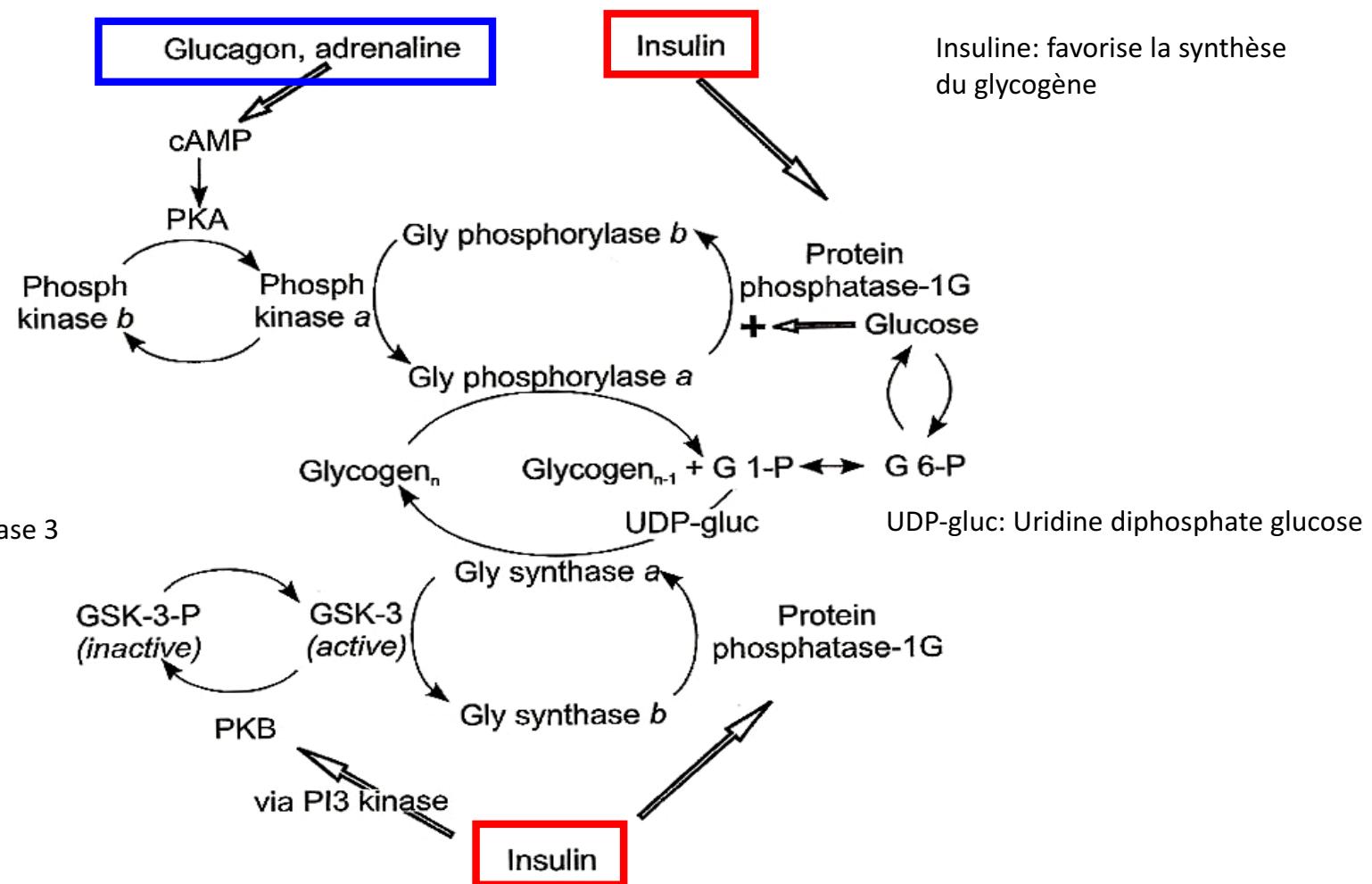
Dashed arrows in pathways indicate multiple enzymatic steps. The dotted shape is the mitochondrial membrane. GLUT2, hepatic glucose transporter (see Box 2.2); G 6-P, glucose 6-phosphate; GK, glucokinase; G-6-Pase, glucose-6-phosphatase; LDH, lactate dehydrogenase; PDH, pyruvate dehydrogenase; Ribose 5-P, ribose 5-phosphate; TCA cycle, tricarboxylic acid (Krebs) cycle. A '+' sign indicates stimulation, a '-' sign inhibition. Note that the pathway for gluconeogenesis is over-simplified (see Box 4.2), and no detail of the pathways of fatty acid and cholesterol synthesis is shown (see Box 4.3).

## Système digestif Métabolisme du glucose dans le foie

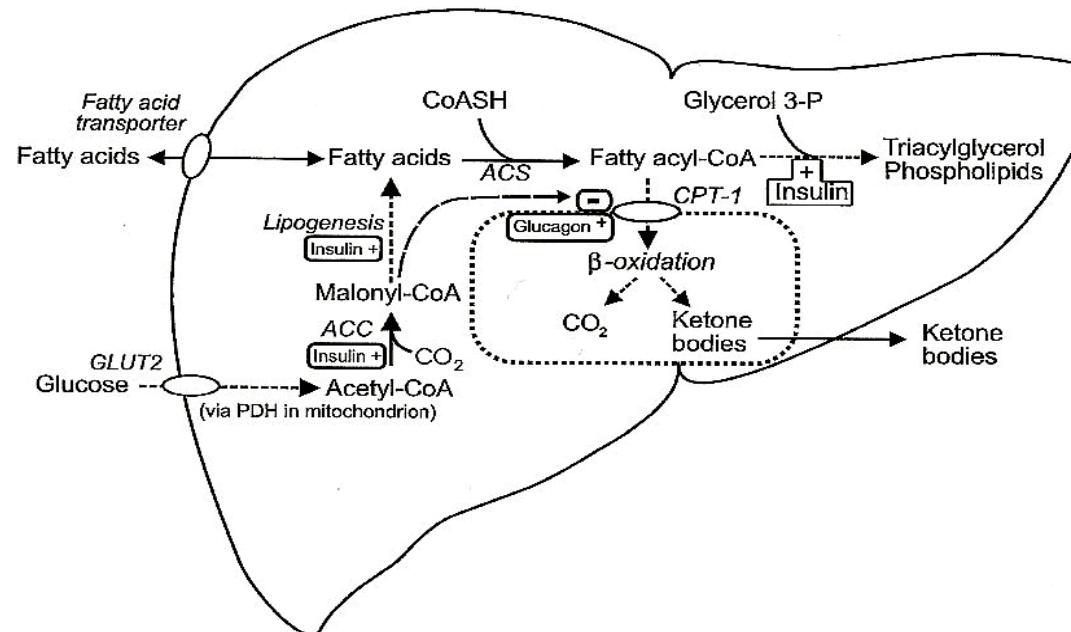


## Système digestif Régulation hormonale: synthèse/dégradation du glycogène

Glucagon: favorise la synthèse de glucose



## Système digestif Métabolisme des acides gras dans le foie



Insuline: favorise la lipogenèse

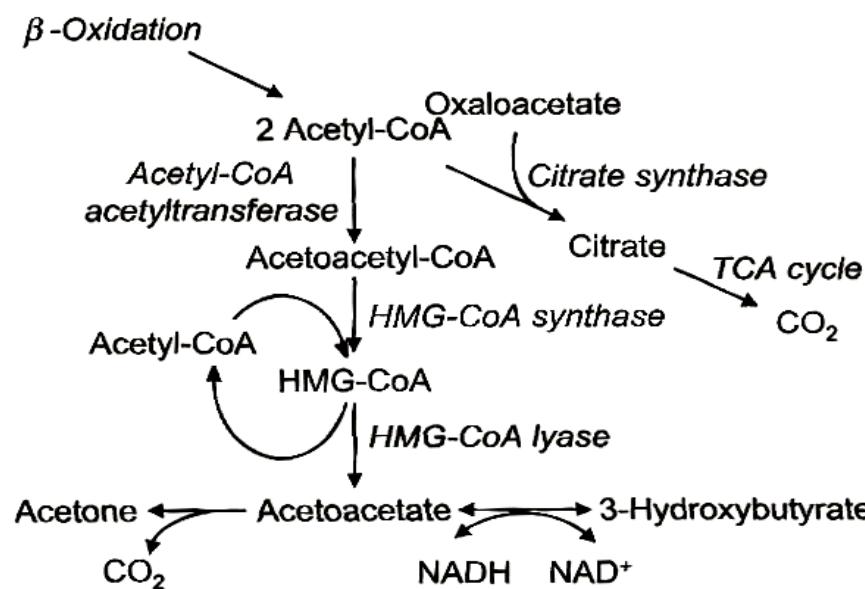
Glucagon: favorise l'oxydation des lipides (lipolyse)

Fatty acids cross the hepatocyte membrane mainly by a carrier-mediated process (see Table 2.4). Inside the liver cell they are transported through the cytosol by binding to specific fatty acid binding proteins, and activated by esterification to coenzyme-A (CoASH) by the enzyme acyl-CoA synthase (ACS). In order to enter the mitochondrion (dotted box) for oxidation in the tricarboxylic acid cycle (TCA cycle), fatty acyl-CoA esters are converted to acyl-carnitine derivatives by the action of carnitine-palmitoyl transferase-1 (CPT-1) (further details on Fig. 4.4). This enzyme is inhibited by malonyl-CoA, an intermediate in the pathway of de novo lipogenesis. Insulin inhibits fatty acid oxidation by (1) increasing the concentration of malonyl-CoA via activation of acetyl-CoA carboxylase (ACC) and (2) stimulating fatty acid esterification to form triacylglycerol. Glucagon increases fatty acid oxidation, possibly by a direct effect on CPT-1. Note that acetyl-CoA formation from glucose is over-simplified: see Fig. 4.5 for further details. PDH, pyruvate dehydrogenase.

## Système digestif Formation de corps cétoniques depuis l'acétyl-CoA (cétogenèse)

96

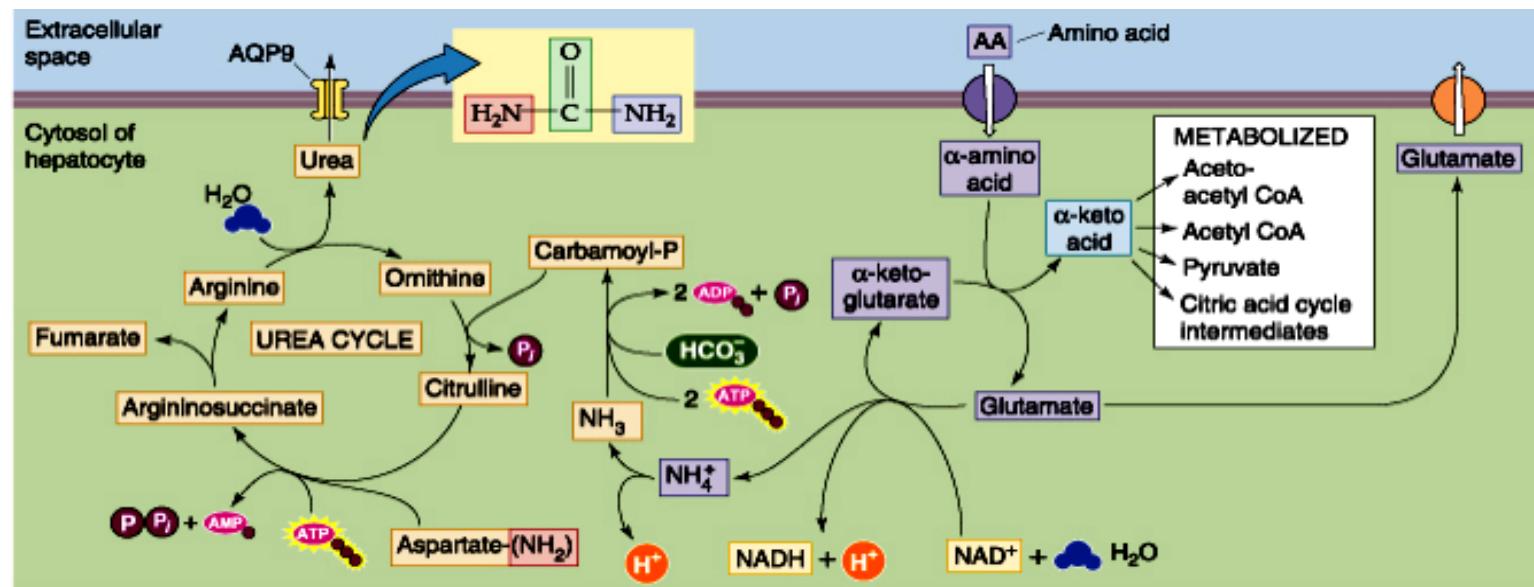
Organs and Tissues



Cétogenèse: déclenchée par le jeûne prolongé; après épuisement des réserves glucidiques et protéiques

This is all located within the mitochondrion. Acetyl-CoA is produced from  $\beta$ -oxidation of fatty acids. It may enter the tricarboxylic acid cycle (TCA cycle) or it may enter the ketogenesis pathway. For the latter, two molecules of acetyl-CoA condense to form acetoacetyl-CoA. A third is added to form 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) in a reaction catalysed by HMG-CoA synthase. This is split to release acetoacetate (a ketone body) and acetyl-CoA. The other major ketone body, 3-hydroxybutyrate, is formed by reduction of acetoacetate. A minor one, acetone, is formed by non-enzymatic breakdown of acetoacetate. The ketone bodies cannot be re-utilised in the liver and are exported into the bloodstream. The major regulation appears to be the delivery of fatty acids to the mitochondrion for oxidation. Beyond that, the availability of oxaloacetate may limit entry of acetyl-CoA into the TCA cycle. HMG-CoA synthase is also regulated by covalent modification (succinylation) by succinyl-CoA, a TCA cycle intermediate. Succinyl-CoA competes with acetyl-CoA and can be displaced when acetyl-CoA concentration is high. Glucagon lowers succinyl-CoA concentration and so stimulates ketogenesis. See Further Reading for more details.

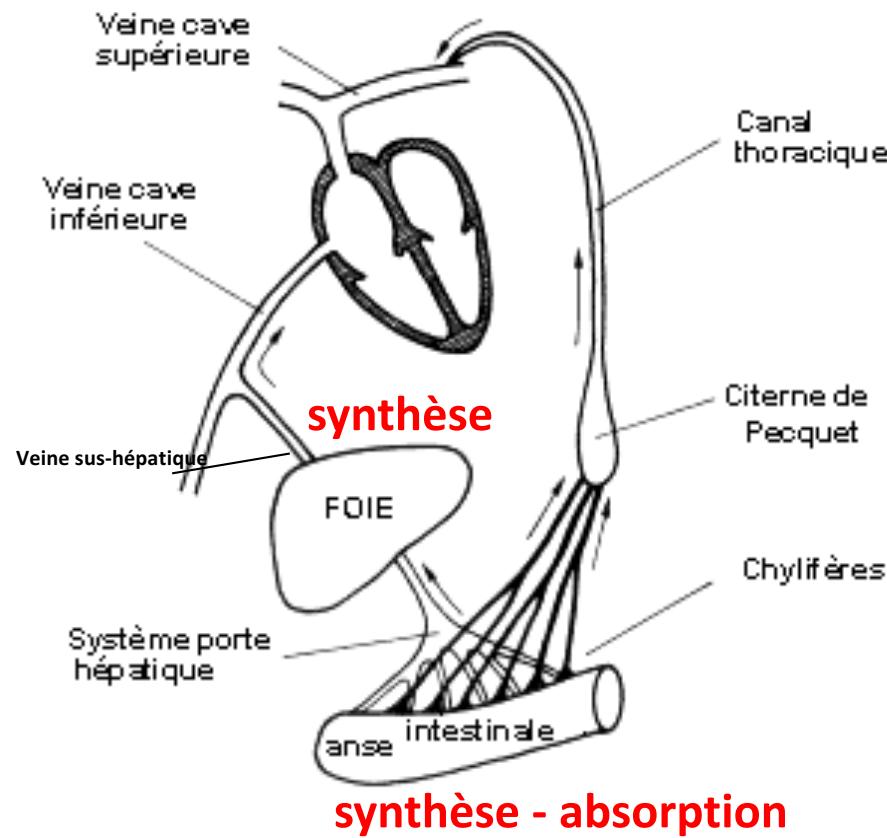
## Système digestif Métabolisme des acides aminés et production d'urée



Copyright © 2002, Elsevier Science (USA). All rights reserved.

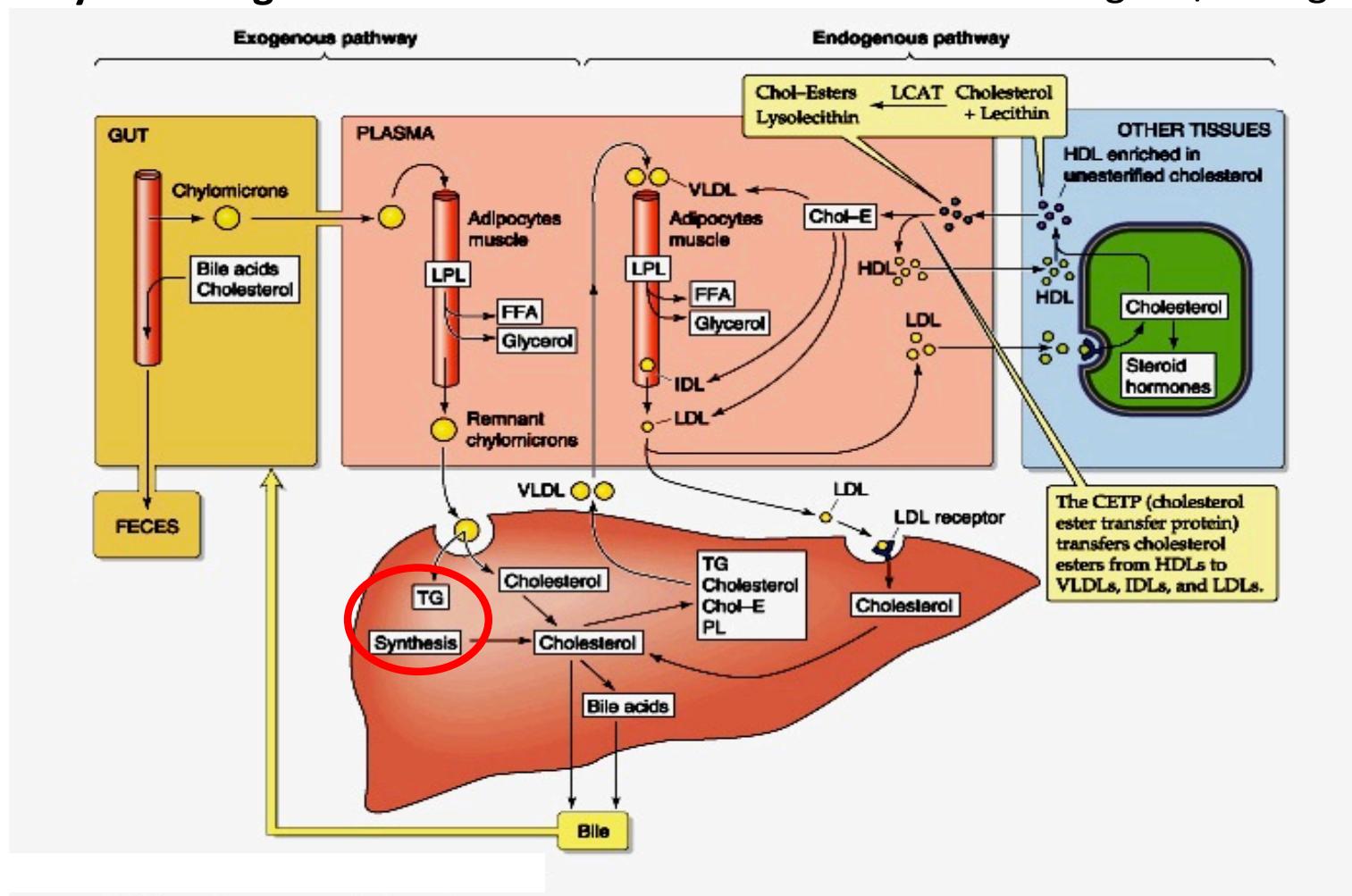
When a hepatocyte takes up an amino acid, it either must use it immediately in protein synthesis or deaminate it. The deamination reaction transfers the amino group of the amino acid to ketoglutarate, yielding glutamate and the corresponding keto acid. Depending on the backbone of the keto acid, it may be metabolized into acetoacetyl CoA, acetyl CoA, pyruvate, or a variety of citric acid cycle intermediates. The  $\text{NH}_4^+$  that results from the regeneration of the -ketoglutarate is **consumed in the urea cycle**. The other amino group of the urea is derived from the amino group of aspartate. The  $\text{C} = \text{O}$  moiety of urea is derived from  $\text{CO}_2$ . The liver then exports the urea, which exits the hepatocyte via AQP9, "aquaporin" 9. CoA, coenzyme A.

## Système digestif    Métabolisme du cholestérol: voies de transport



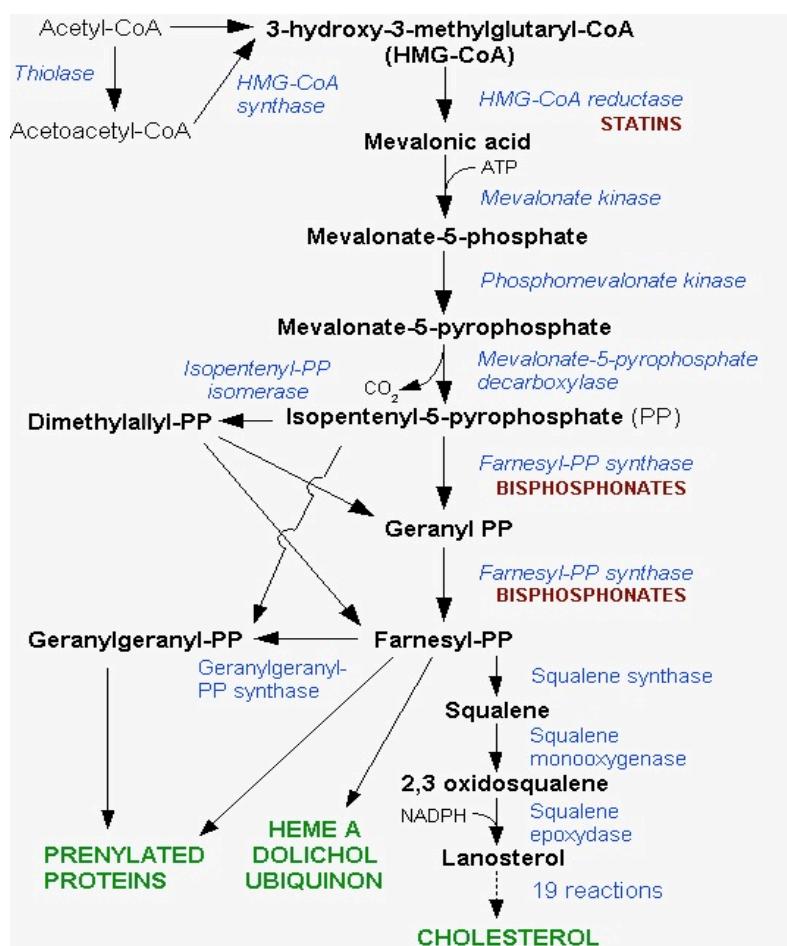
Les deux systèmes de drainage de l'absorption intestinale

## Système digestif Métabolisme du cholestérol: voies exogène/endogène



CETP, cholesteroyl ester transfer protein; Chol-E, cholesteroyl ester; FFA, free fatty acid; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LCAT, lecithin-cholesterol acyltransferase; LDL, low-density lipoprotein; LPL, lipoprotein lipase; PL, phospholipides; VLDL, very-low-density lipoprotein.

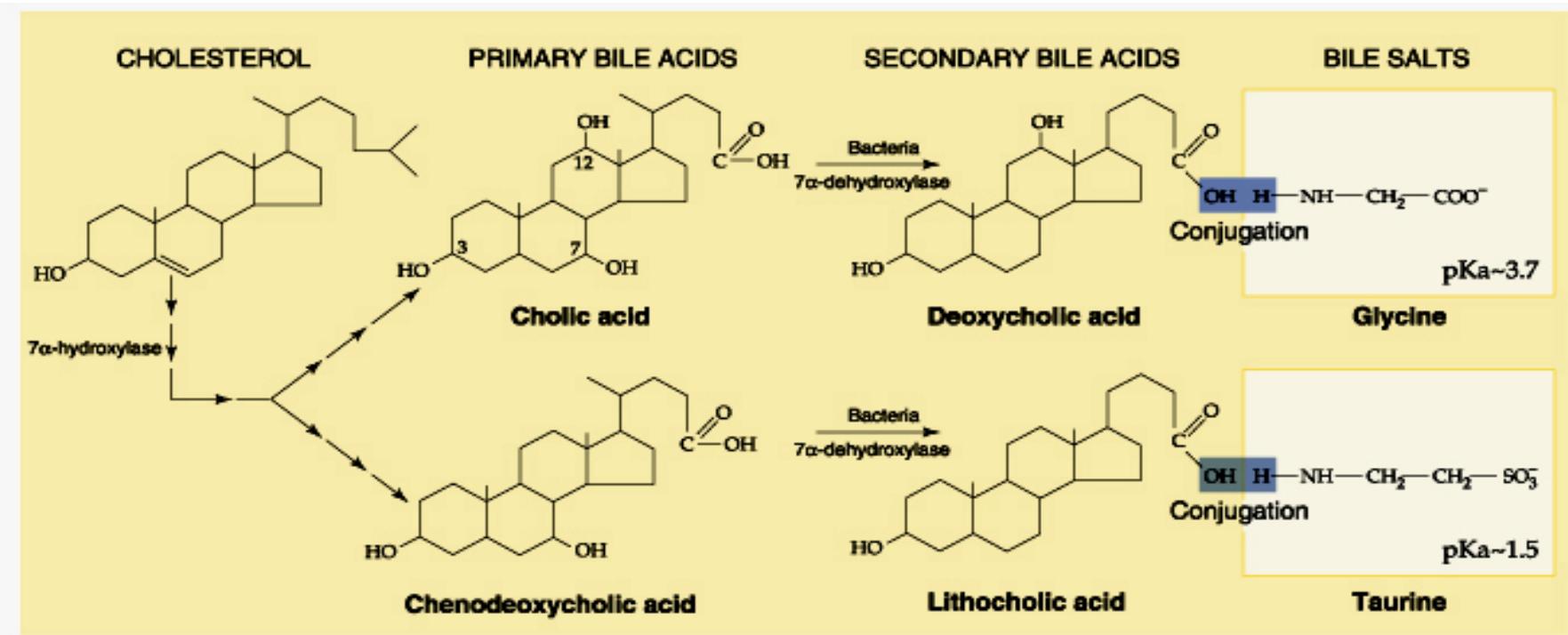
## Système digestif Métabolisme du cholestérol: 3 niveaux de régulation



- La synthèse du cholestérol se fait dans le cytoplasme des cellules du **foie** et de **l'intestin** principalement.
- Il existe **trois niveaux de régulation** du cholestérol, le but étant de diminuer le taux de cholestérol de la cellule quand il est en excès :
  - a) *Le cholestérol libre dans la cellule inhibe la production de ses propres récepteurs membranaires LDLR.* Pour ce faire, il inhibe la transcription du gène qui code les **LDLR**. Par conséquent, le flux entrant de cholestérol dans la cellule est diminué.
  - b) *Le cholestérol libre inhibe la HMG-coA réductase*, ce qui empêche la poursuite de la réaction de synthèse du cholestérol.
  - c) *Enfin, le cholestérol libre stimule l'acyl transférase (ACAT)*, enzyme catalysant son estérification en stéride. Ceci favorise le stockage du cholestérol libre.
- Un équilibre est trouvé avec **la synthèse des acides biliaires** et l'évacuation ainsi du cholestérol

ACAT: Acétyl-CoA acyl transférase

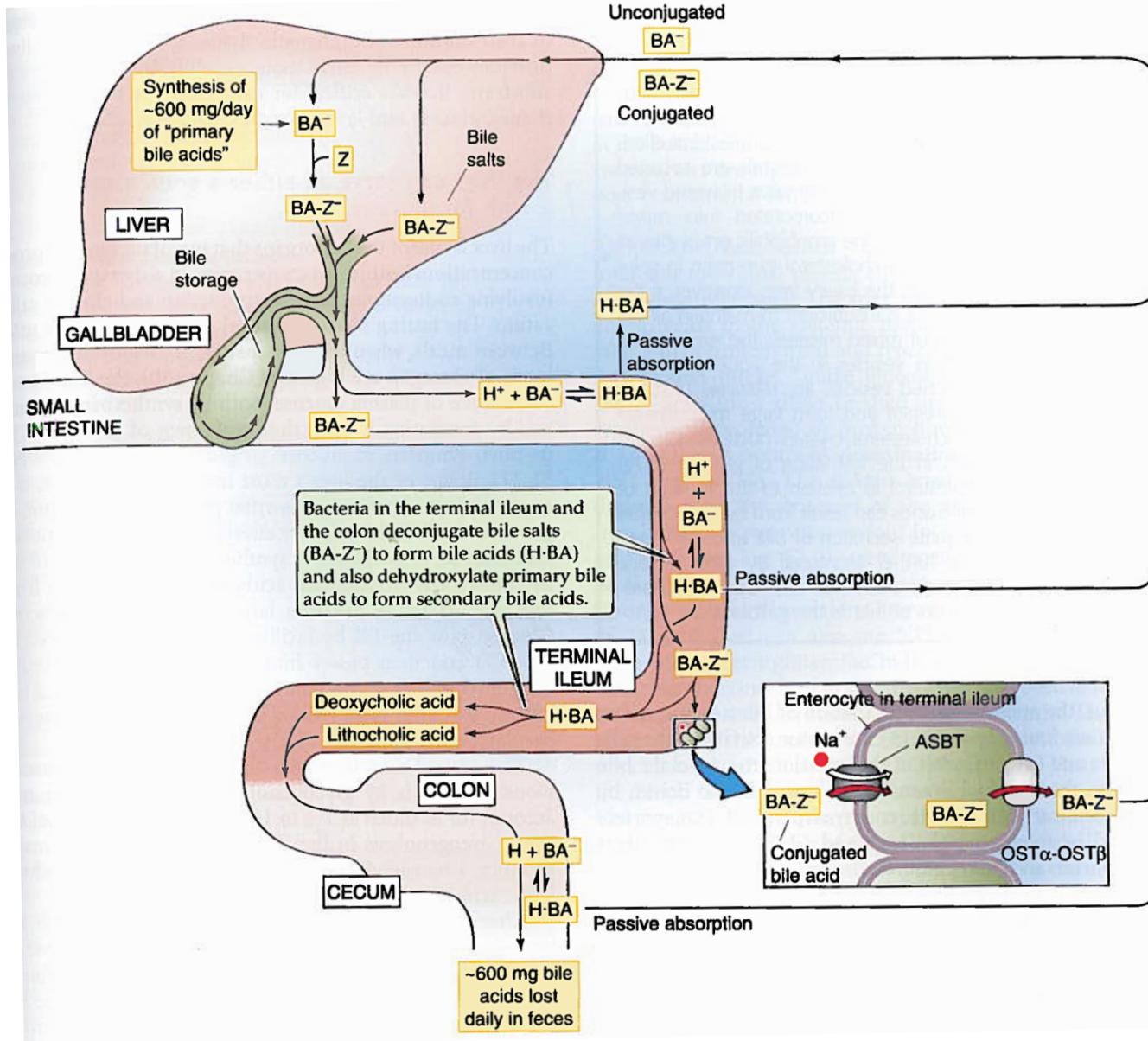
## Système digestif Synthèse d'acides et de sels biliaires



Copyright © 2002, Elsevier Science (USA). All rights reserved.

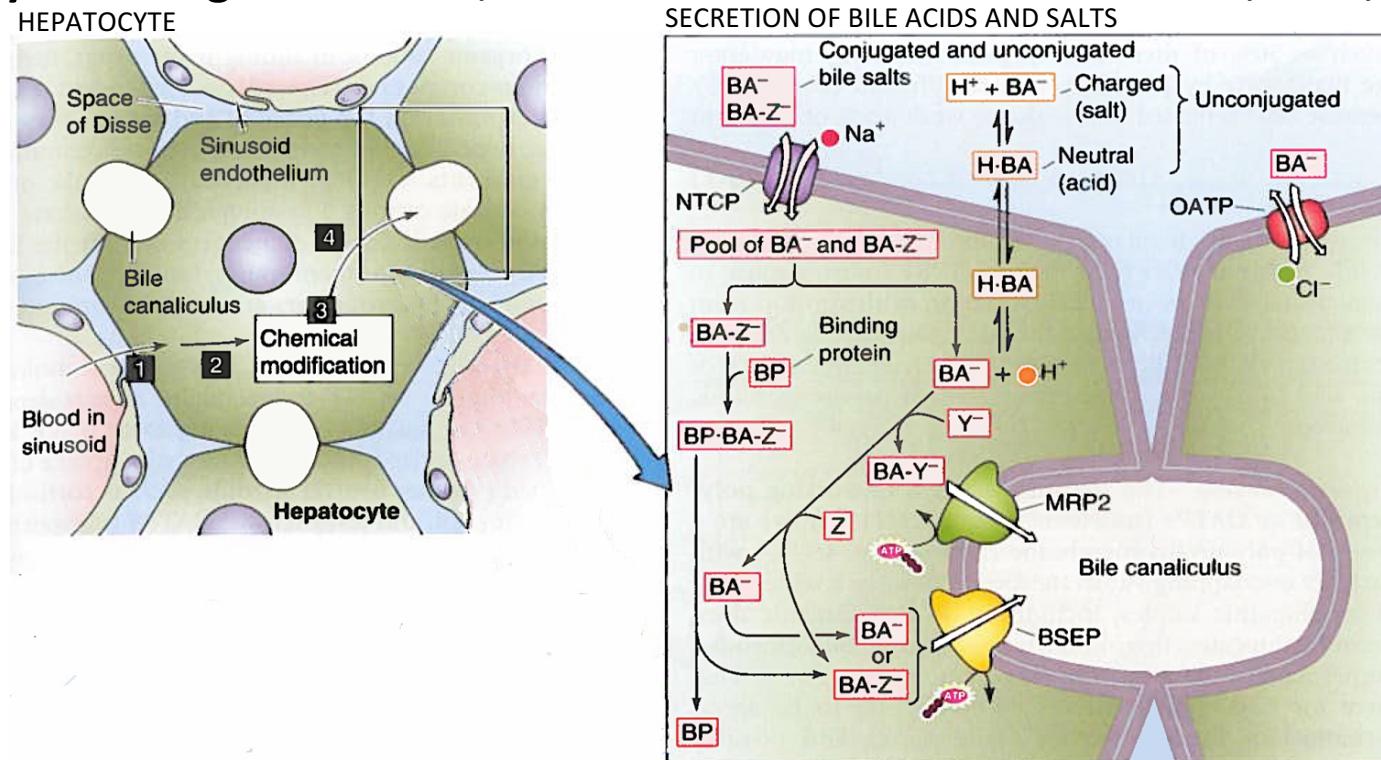
The liver converts cholesterol to the "primary bile acids"-cholic acid and chenodeoxycholic acid-in a series of **14 reactions occurring in four different cellular organelles**. The first reaction is the 7 hydroxylation of cholesterol. In addition, the action of bacteria in the terminal ileum and colon may *dehydroxylate* bile acids, yielding the "secondary bile acids" deoxycholic acid and lithocholic acid. **The hepatocytes conjugate most of the primary bile acids to small molecules such as glycine and taurine (not shown) before secreting them into the bile.** In addition, those secondary bile acids that return to the liver via the enterohepatic circulation may also be conjugated to glycine or taurine, as shown in the figure. The liver may also conjugate some primary and secondary bile acids to sulfate or glucuronate (not shown).

## Système digestif Circulation entérohépatique d'acides biliaires



The **bile acids** that the liver delivers to the duodenum in the bile are primarily **conjugated to taurine or glycine (BA-Z)**. The vast majority of bile acids are reabsorbed as conjugated bile salts (**BA-Z**) in the terminal ileum via an **Na<sup>+</sup>-coupled cotransporter (ASBT)**. Also in the terminal ileum and colon, bacteria deconjugate a small amount of these bile salts to form unconjugated bile acids ( $H-BA \rightleftharpoons H^+ + BA$ ), allowing **HBA to be passively absorbed** by nonionic diffusion. Bacteria in the terminal ileum and colon also dehydroxylate primary bile acids to form secondary bile acids (see next Fig.). Some of these are passively absorbed, and the rest are excreted in the feces. The absorbed bile acids return to the liver via the portal blood and are then taken up into the hepatocyte for resecretion.

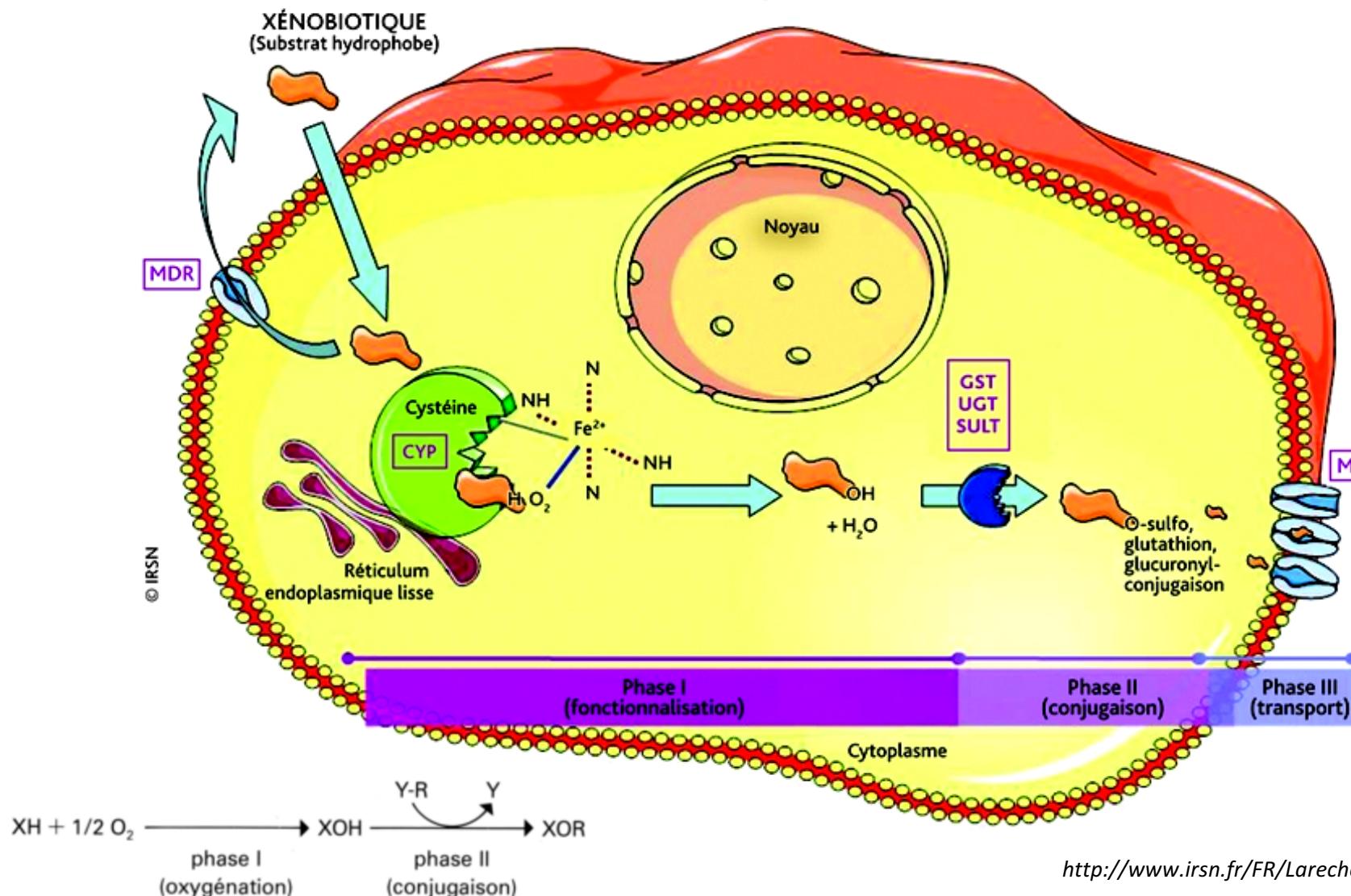
## **Système digestif** Transporteurs d'acides biliaires dans les hépatocytes



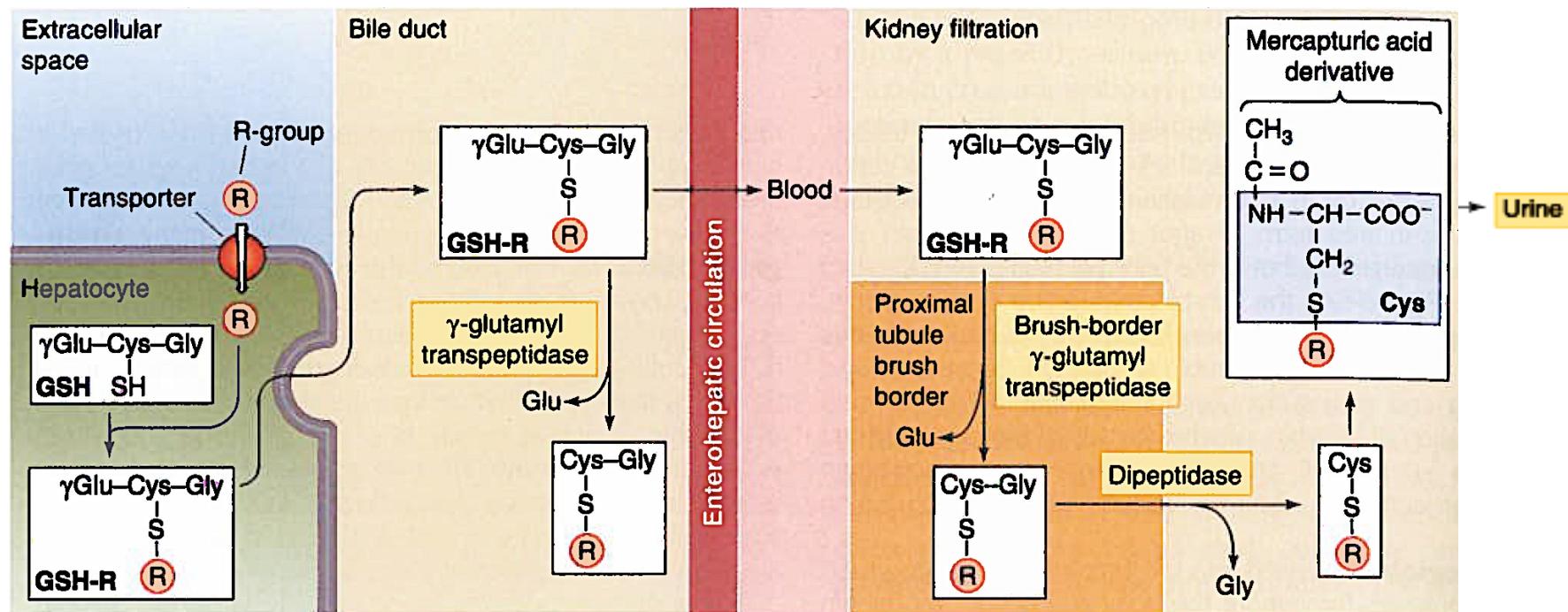
Bile acids can enter the hepatocyte in any of several forms: the unconjugated salt (BA); the neutral, protonated bile acid (HBA); the bile salt conjugated to taurine or glycine (BA-Z, where Z represents taurine or glycine). The three pathways for bile acid entry across the basolateral membrane are the Na<sup>+</sup>-driven transporter NTCP, which prefers BA-Z, but also carries BA; nonionic diffusion of HBA; and the anion exchanger OATP-1. Binding proteins (BP) may ferry conjugated bile acids across the cytoplasm. Some bile acids are conjugated to sulfate or glucuronate (Y); these exit the cell across the canalicular membrane via the MRP2 transporter. Most bile acids are conjugated to glycine or taurine (Z) prior to their extrusion into the bile via BSEP, an ATP-driven member of the ABC class of proteins. *BSEP*, bile salt export pump; *OATP*, organic anion transport protein; *MRP2*, multidrug resistance-associated protein2, Na<sup>+</sup>-taurocholate transporting protein (NTPC)

## Système digestif Fonction de détoxification du foie: 3 phases

### métabolisme des xénobiotiques au niveau cellulaire

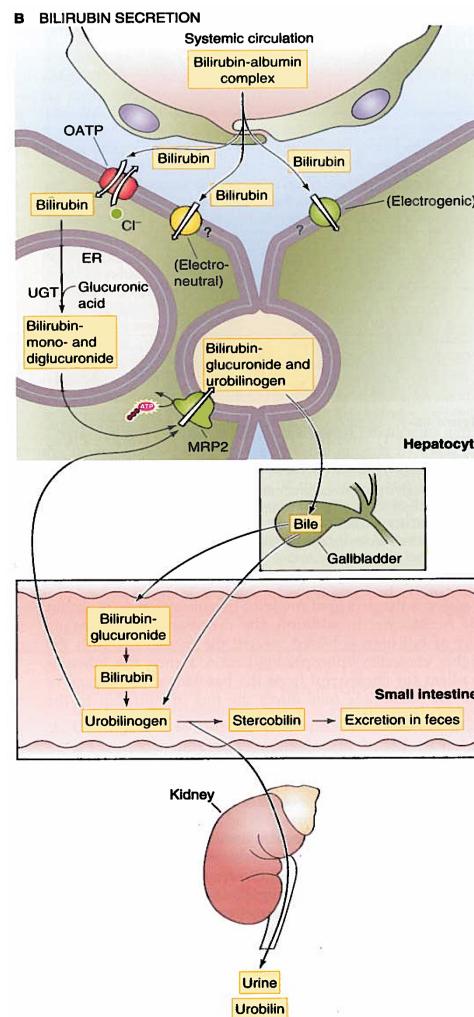
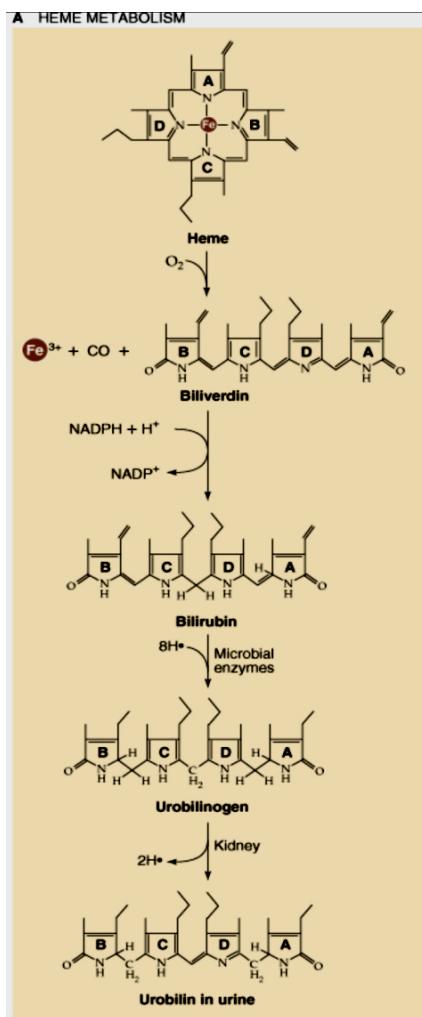


## Système digestif Conjugaison méthathione formation d'acide mercaptourique



The hepatocyte detoxifies compounds by chemically linking ("conjugating") them to small molecules, such as GSH (glutathione), which is a tripeptide. The first step is for glutathione-S-transferase to couple the target compound (R) to the S on the cysteine residue of GSH. After MRP2 transports this GSH conjugate into the canalicular lumen; a  $\gamma$ -glutamyl transpeptidase may remove the terminal glutamate residue. Alternatively, the conjugate may reach the blood and be filtered by the kidney where a  $\gamma$ -glutamyl transpeptidase at the brush border and a dipeptidase generate a cysteine derivative of R. Acetylation yields the mercapturic acid derivative, which appears in the urine. *MRP2, multidrug resistance-associated protein 2.*

## Système digestif Fonction de détoxification du foie: bilirubine de l'hème



**A** **Les macrophages phagocytosent les globules rouges sénescents** et dégradent l'hème en bilirubine, qui transite dans le sang, liée à l'albumine, vers le foie. La conversion en urobilinogène incolore se produit dans l'iléon terminal et le colon, où l'oxydation en uroline jaune à lieu dans les urines.

**B** **L'hépatocyte capture la bilirubine à travers la membrane basolatérale par trois mécanismes et conjuge ensuite la bilirubine avec un ou deux résidus d'acide glucuronique.** La cellule exporte alors cette forme conjuguée de bilirubine dans la bile. Après avoir été sécrété dans la bile, une partie de la bilirubine glucuronide est reconvertisse en bilirubine par des bactéries dans l'iléon terminal et le colon. Cette bilirubine est ensuite convertie en urobilinogène incolore. S'il persiste dans le colon, le composé est ultérieurement converti en stercobiline, qui est le colorant principal des fèces. Si l'urobilinogène rejoint le plasma et est filtré par les reins, il est converti en uroline et donne à l'urine sa couleur jaune caractéristique.

## Système digestif

- Utilisation optimale des aliments
- Extraction de: Hydrates carbone, Acides aminés, Acides gras
- Gestion d' $H_2O$ , Vitamines, Minéraux
- Contrôle et régulation du pH sanguin ( $H^+$ ,  $HCO_3^-$ )
- Organisation linéaire multi-organes
- Régulation locale et centrale
- Contrôlé par Système nerveux central et autonome et par système hormonal