Gastrointestinal Physiology

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Summary

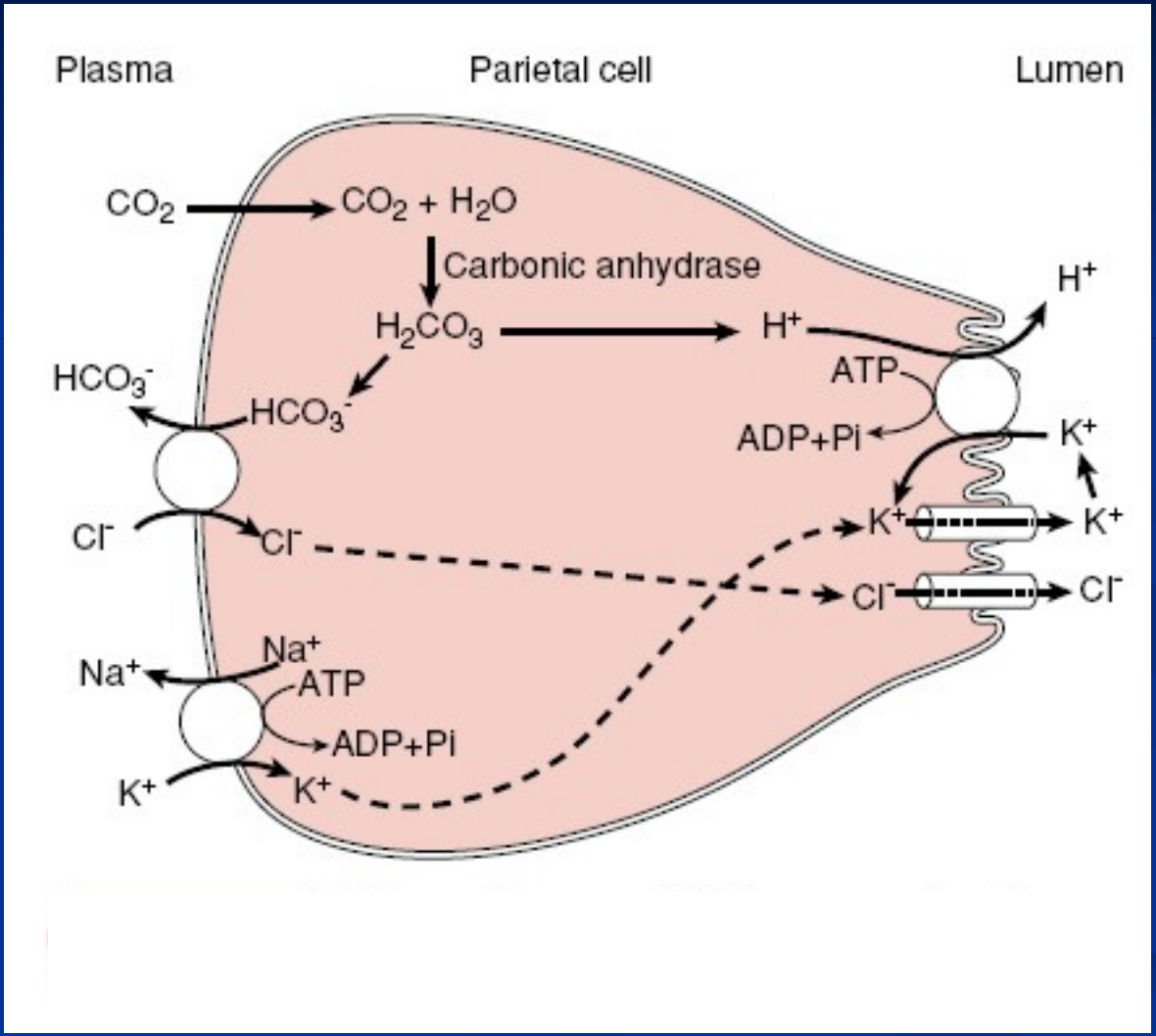
- GI secretions esp. gastric acid production
- GI hormones
- GI complications in the critically ill (and acid suppression in ICU)
- Jaundice and gallstones

How is acid produced in the stomach?

How is HCl produced by the stomach?

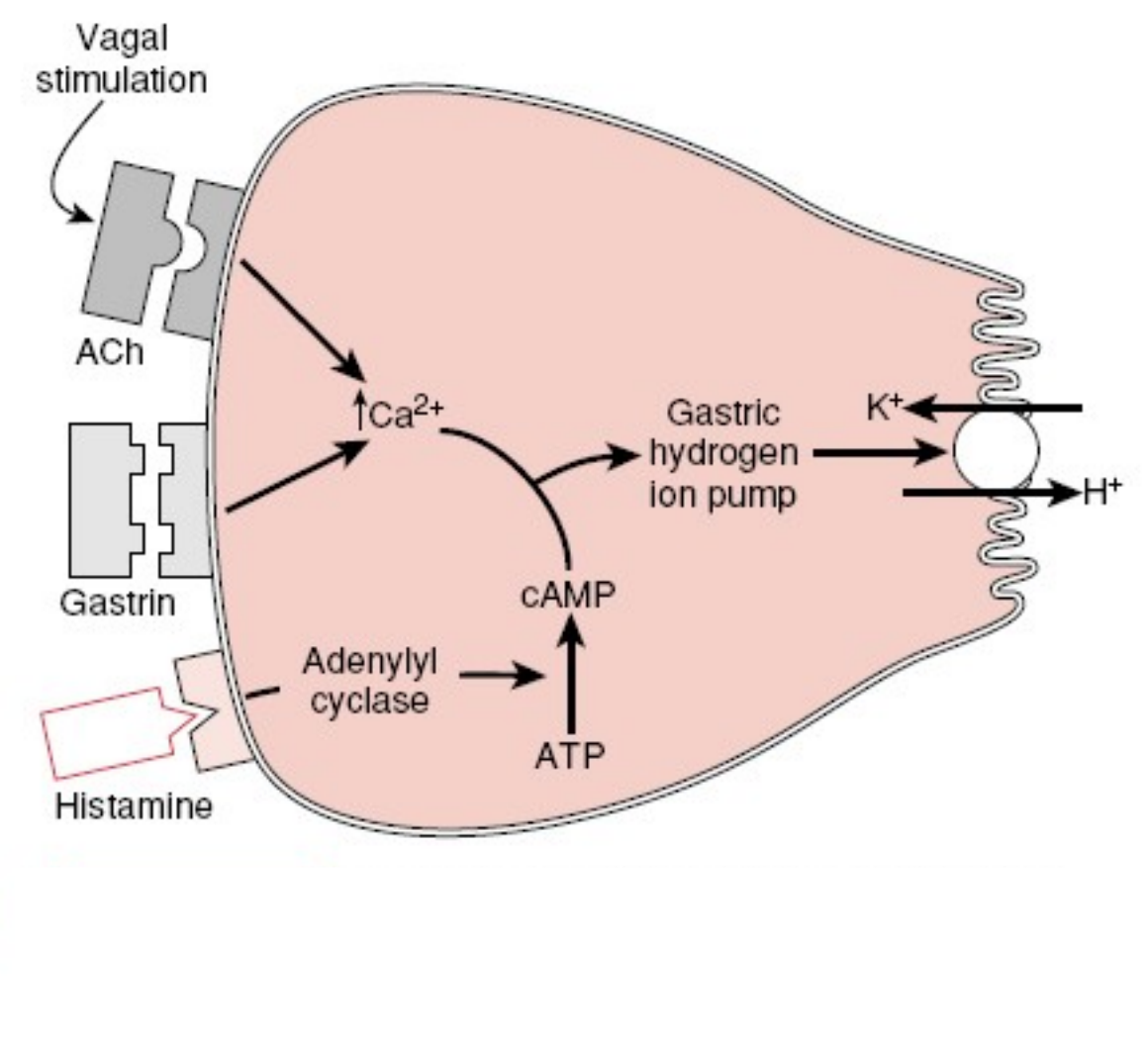
- Food (peptide fragments) stimulate the release of gastrin by antral G cells
- Enterochromaffin-like cells release histamine
- Parietal cells are stimulated by histamine to secrete H+

Mechanism of HCl Secretion



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Potentiation of Secretion



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What is the function of gastrointestinal hormones?

GI Hormones

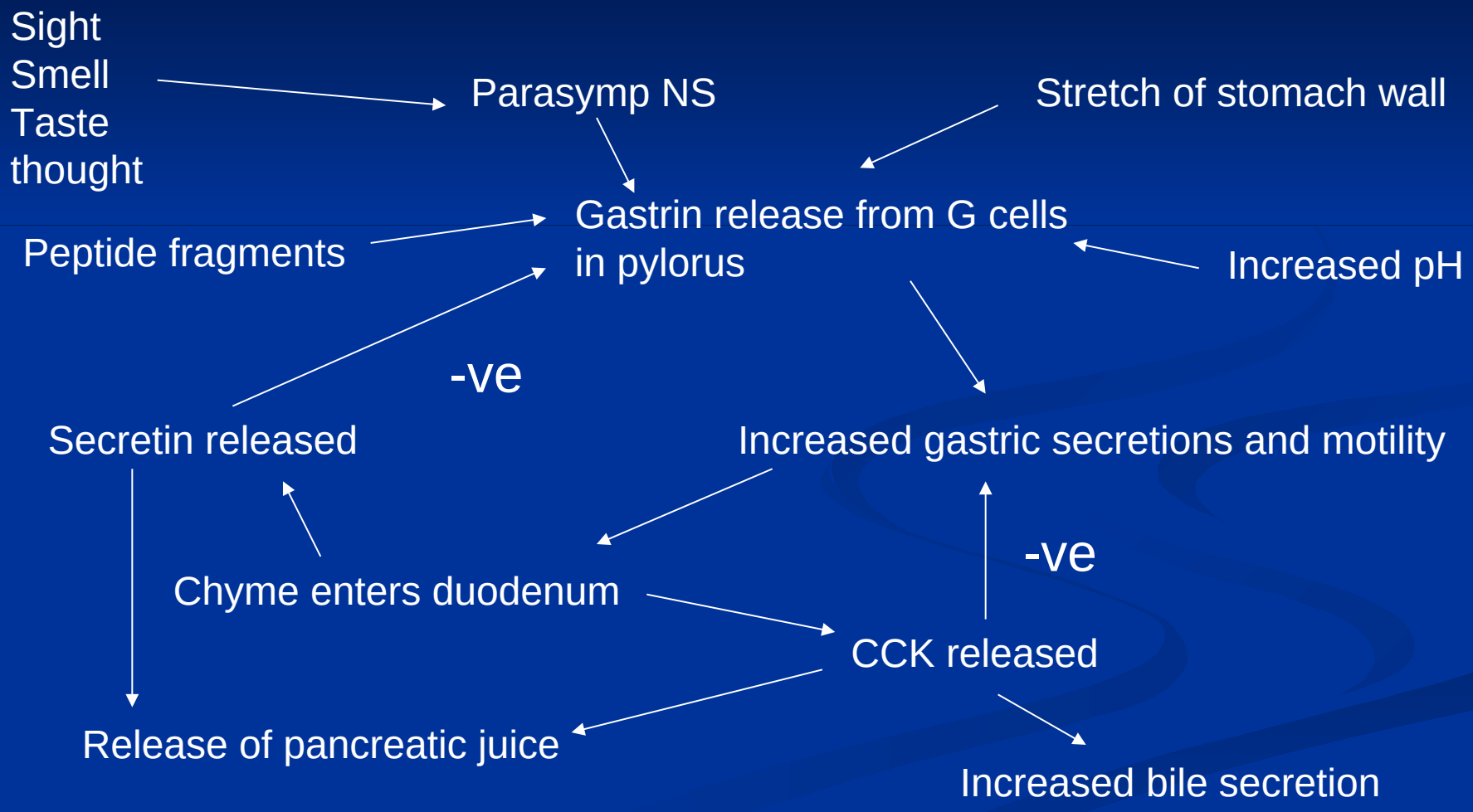
- Gastrin
  - Increases HCl, pepsinogen and intrinsic factor secretion by parietal cells
  - Increases gastric motility
  - Increased levels – gastrinoma, small bowel resection, hypochlorhydria
  - Inhibited by low pH, somatostatin

GI hormones
Inhibitory effect on stomach

- Cholecystokinin CCK
  - Stimulates gallbladder contraction
  - Delays gastric emptying
- Secretin (produced in small intestine)
  - Stimulates pancreatic secretion
  - Reduces gastric acid production

How is digestion controlled?

Control of digestive activity



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Why don't gastric acid and enzymes attack the mucosa?

Protection of digestive system

- Tight junctions between epithelial cells
- Mucus secretion
- Enzymes produced in inactive forms

What GI complications may occur in the critically ill?

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GI complications in the critically ill

- Stress-related mucosal damage is very common
- Clinically relevant haemorrhage occurs in 1-4%
- Causes
  - Acid/pepsin erosion and ulceration
  - Bacterial translocation (SIRS and MODS)
- Consequences – mucosal ischaemia, reperfusion injury etc

How can we minimise GI complications in the critically ill?

Acid suppression in ICU

- H2 blockers
- PPIs – block H2 receptors, gastrin release and cholinergic-mediated H+ release
- Maintenance of splanchnic oxygenation (NB vasopressin)
- Sucralfate (mucosal protection)
- Enteral nutrition

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Enteral Nutrition

Advantages

- ⇩ Metabolic stress
- ⇧ Nitrogen balance
- Better glycemic control
- ⇧ Visceral protein synthesis
- Mucosa barrier function
- ⇧ GALT, fewer infections
- ⇧ Variety of nutrients
- ⇧ Visceral blood flow
- ⇧ Anastomotic strength
- Cost effective

Disadvantages

- GI dysmotility
- Aspiration risk
- Distention
- Diarrhea
- Gut ischemia
- Access difficulty
- ? Underfeeding

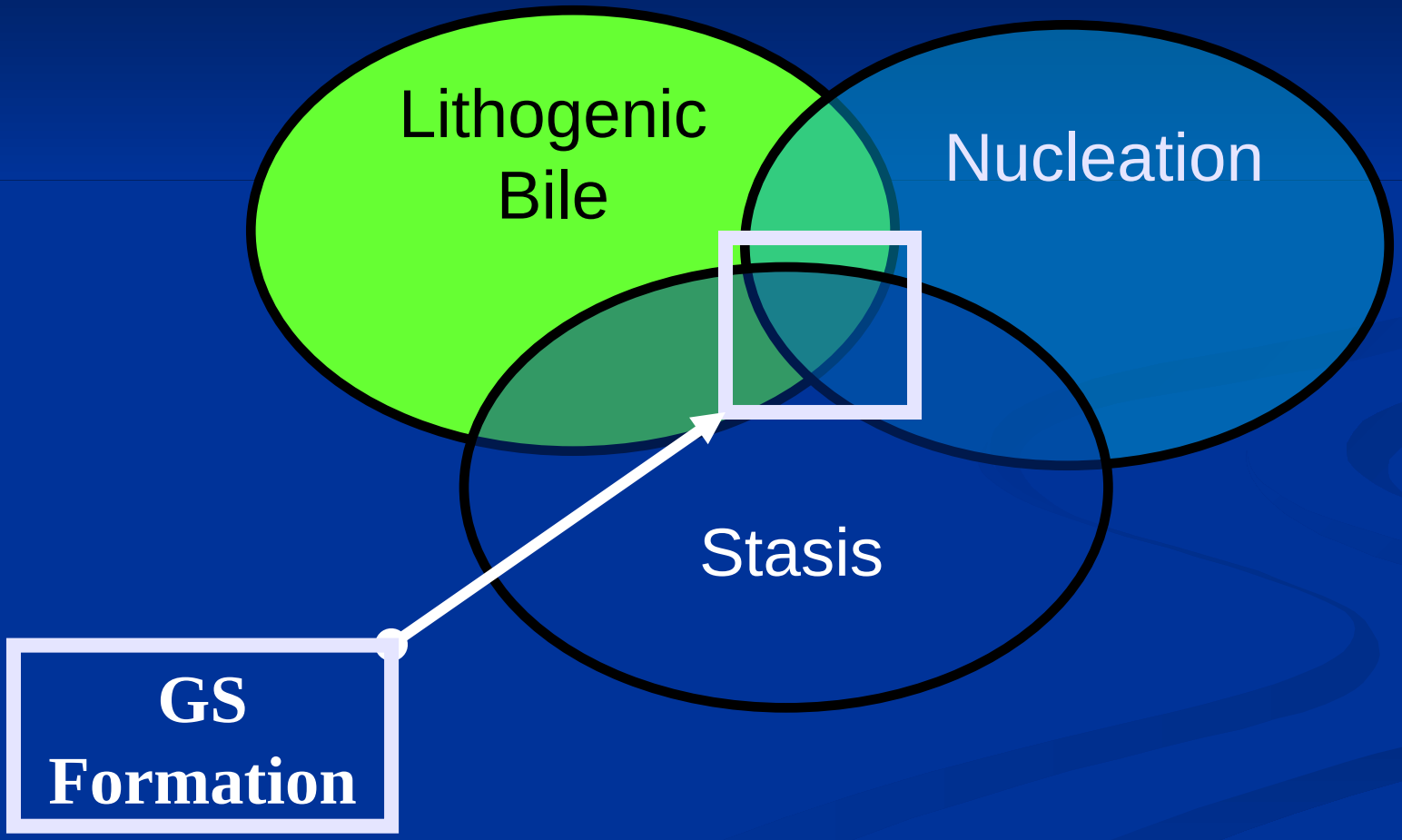
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How are gallstones formed?

Gallstone Pathogenesis

Cholesterol and Pigmented GS



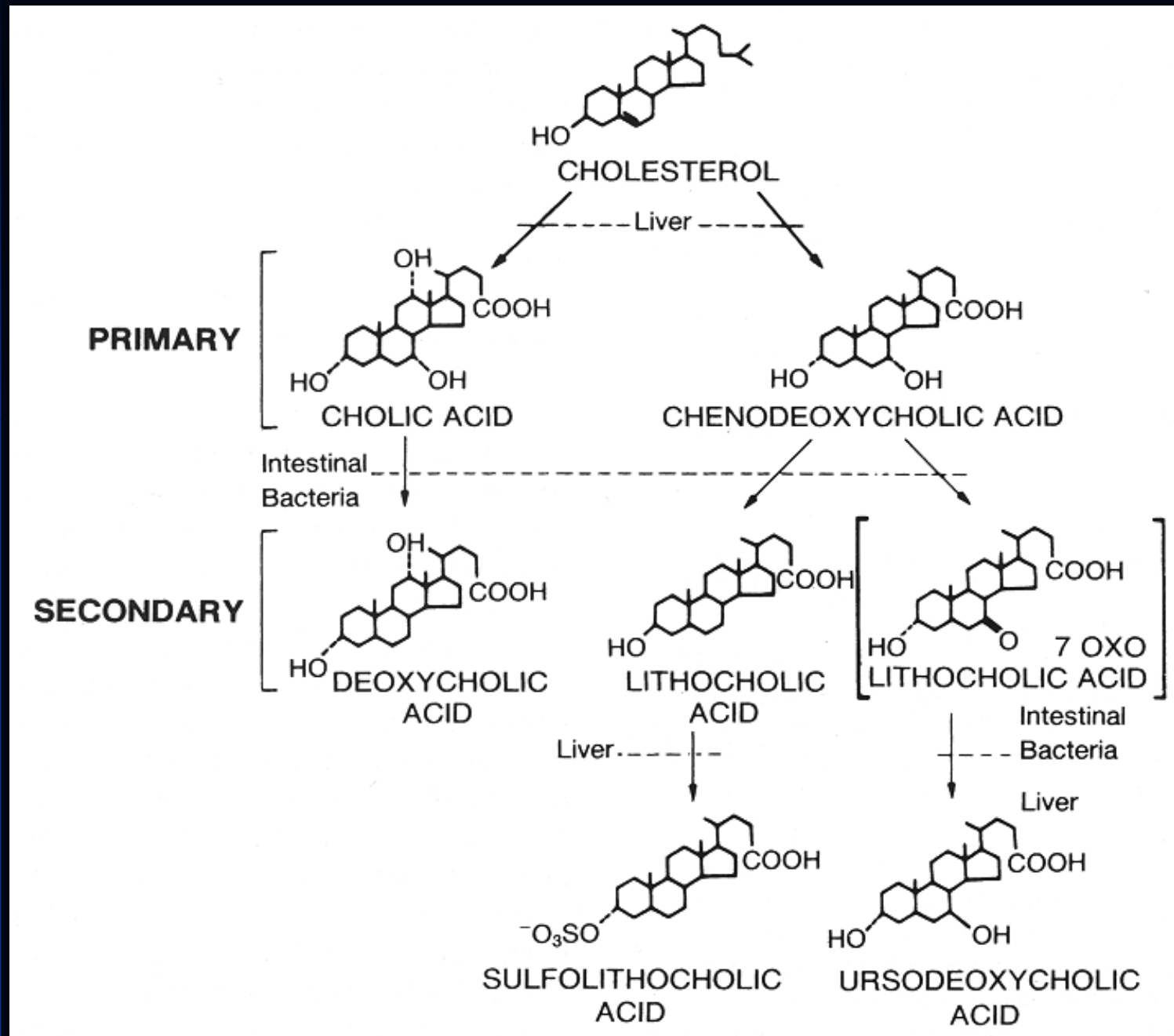
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Cholesterol gallstones

- Cholesterol is synthesised/secreted by the liver and solubilised in bile
- Mechansims of cholesterol GS formation
  - Hypersecretion of cholesterol into bile
  - Hyposecretion of bile acids into bile
  - Nucleation factors
  - Gallbladder mucin
  - Role of gallbladder

Cholesterol Metabolism

- Sources of body cholesterol
  - Diet (Chylomicrons)
  - Synthesis (primarily hepatic)
- Cholesterol is then either:
  - Solubilised and secreted unmodified into bile
  - Converted into **Bile Acids**
  - Stored in the liver as cholesterol esters
  - Shunted to peripheral adipose and skeletal tissues


HO
CHOLESTEROL
Liver
PRIMARY
OH
COOH
HO
OH
CHOLIC ACID
COOH
HO
OH
CHENODEOXYCHOLIC ACID
Intestinal
Bacteria
SECONDARY
OH
COOH
HO
DEOXYCHOLIC
ACID
COOH
HO
LITHOCHOLIC
ACID
COOH
HO
O
7 OXO
LITHOCHOLIC ACID
Liver
Intestinal
Bacteria
Liver
COOH
$^{-}O_3SO$
SULFOLITHOCHOLIC
ACID
COOH
HO
OH
URSODEOXYCHOLIC
ACID

Gallstone formation

- Either
  - Cholesterol **Hyper**-secretion or
  - Bile acid **Hypo**-secretion

Causes of hypersecretion

- Obesity
  - Increased hepatic synthesis
  - Increased dietary cholesterol
- Hormones
  - Oestrogens, OCP's
    - Decreased conversion to cholesterol esters
    - Increased hepatic uptake
- Genetic
  - Increased transport and uptake
  - Decreased 7-alpha-hydroxylase activity (diminshed bile acid production)
- Rapid Weight Loss
  - Mobilization of cholesterol stores
- Advancing Age

Causes of bile acid hyposecretion

- Ileal Disease
  - Loss of enterohepatic circulation of bile acids
- Congenital
  - 12 hydroxylase deficiency, results in decreased production of bile acids
- Cholestatic liver diseases
  - Primary biliary cirrhosis
  - Primary sclerosing cholangitis

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