Human Phys PCB4701

Digestion part 2 Pancreas

RED DOT

Exocrine Pancreas and digestive secretions

[endocrine = Islets of Langerhans - alpha & beta cells, secrete glucagon & insulin]

Acinar cells in acini.
Each acinus is a single layer of epithelial cells that secretes into lumen of ductules which flow into pancreatic duct (which merges with common bile duct).

Pancreatic Juice
Bicarbonate (HC03-) + enzymes, esp. amylase; trypsin (protease) and lipase.

Bicarbonate Secretion
Neutralizes stomach acid.
Lining of ductules use carbonic anhydrase to produce HCO3- & H+; HCO3- exchanged for Cl- in the lumen, while H+ exchanged for Na+ in the blood.
Cl- diffuses into lumen through cystic fibrosis CFTR channel.

Enzyme Secretion
Inactive enzymes stored in zymogen granules in acinar cells (prevent self-digestion).
Zymogens dumped into ductule. Enzymes activated in the duodenum.

- Brush border enterokinase converts trypsinogen to trypsin.
- Trypsin converts inactive zymogens to active digestive enzymes.

acinus raspberry
-zyme related to enzymes (from Greek “to leaven”)

Figure 18.25

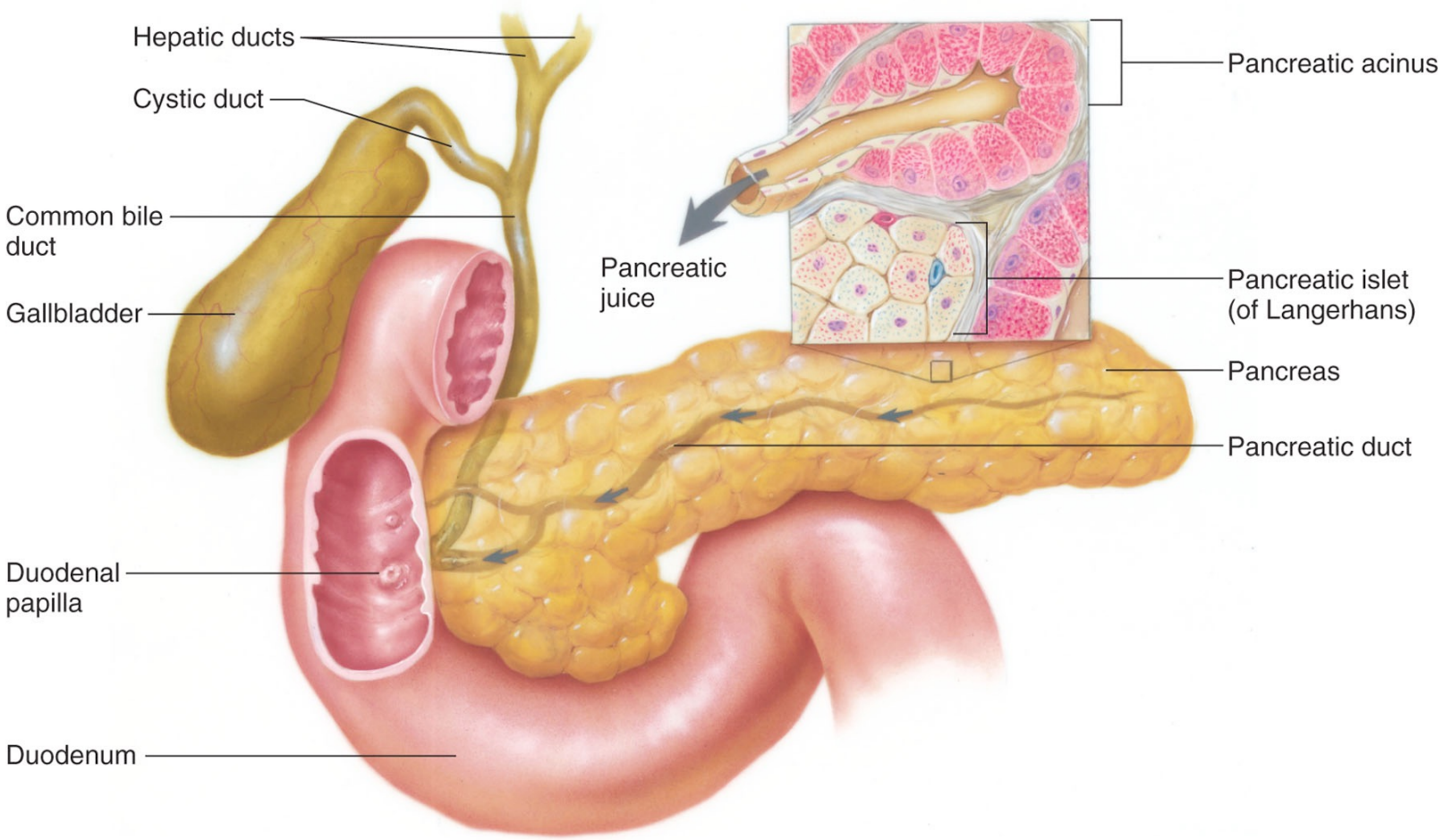

Hepatic ducts
Cystic duct
Common bile duct
Gallbladder
Duodenal papilla
Duodenum
Pancreatic juice
Pancreatic acinus
Pancreatic islet (of Langerhans)
Pancreas
Pancreatic duct

Figure 18.27a

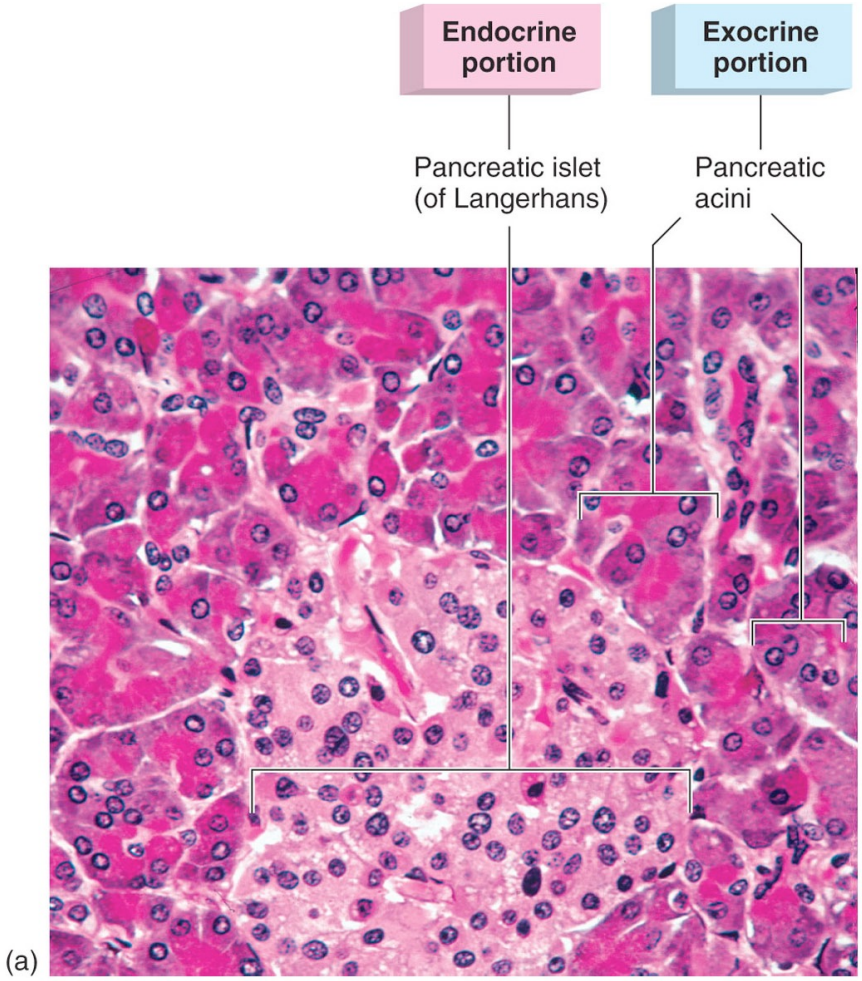
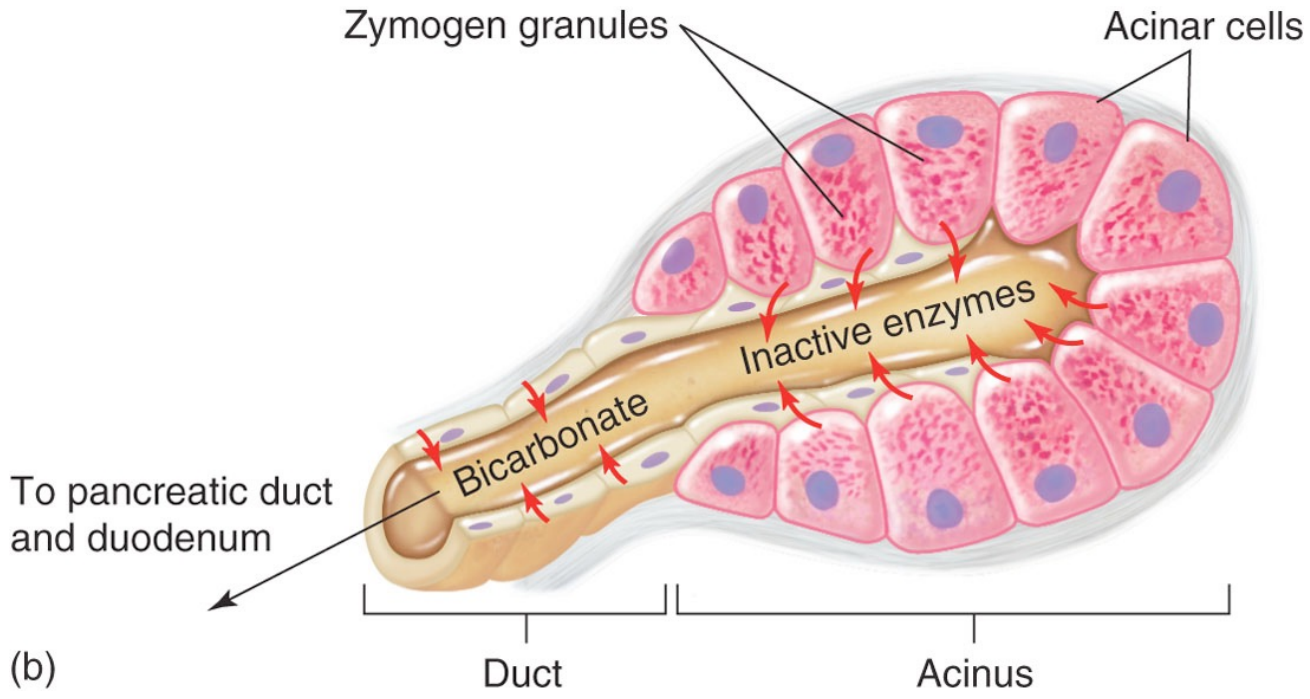


Figure 18.27b

Exocrine Pancreas: Acinar cells



-zyme related to enzymes (from Greek “to leaven”)

Figure 18.28

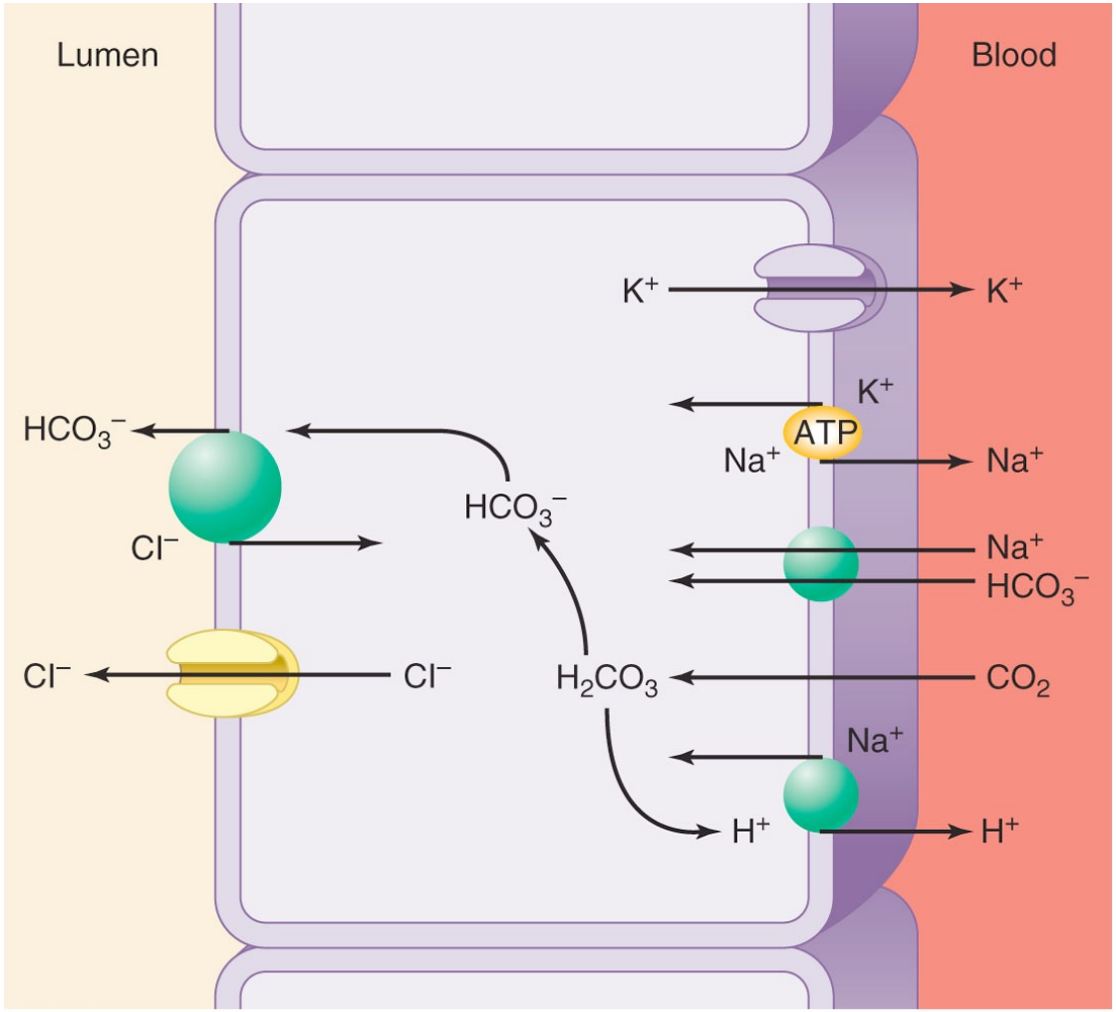

Lumen
Blood
K+
K+
K+
ATP
Na+
Na+
HCO3−
HCO3−
Cl−
Na+
HCO3−
Cl−
Cl−
H2CO3
CO2
Na+
H+
H+

Figure 18.29

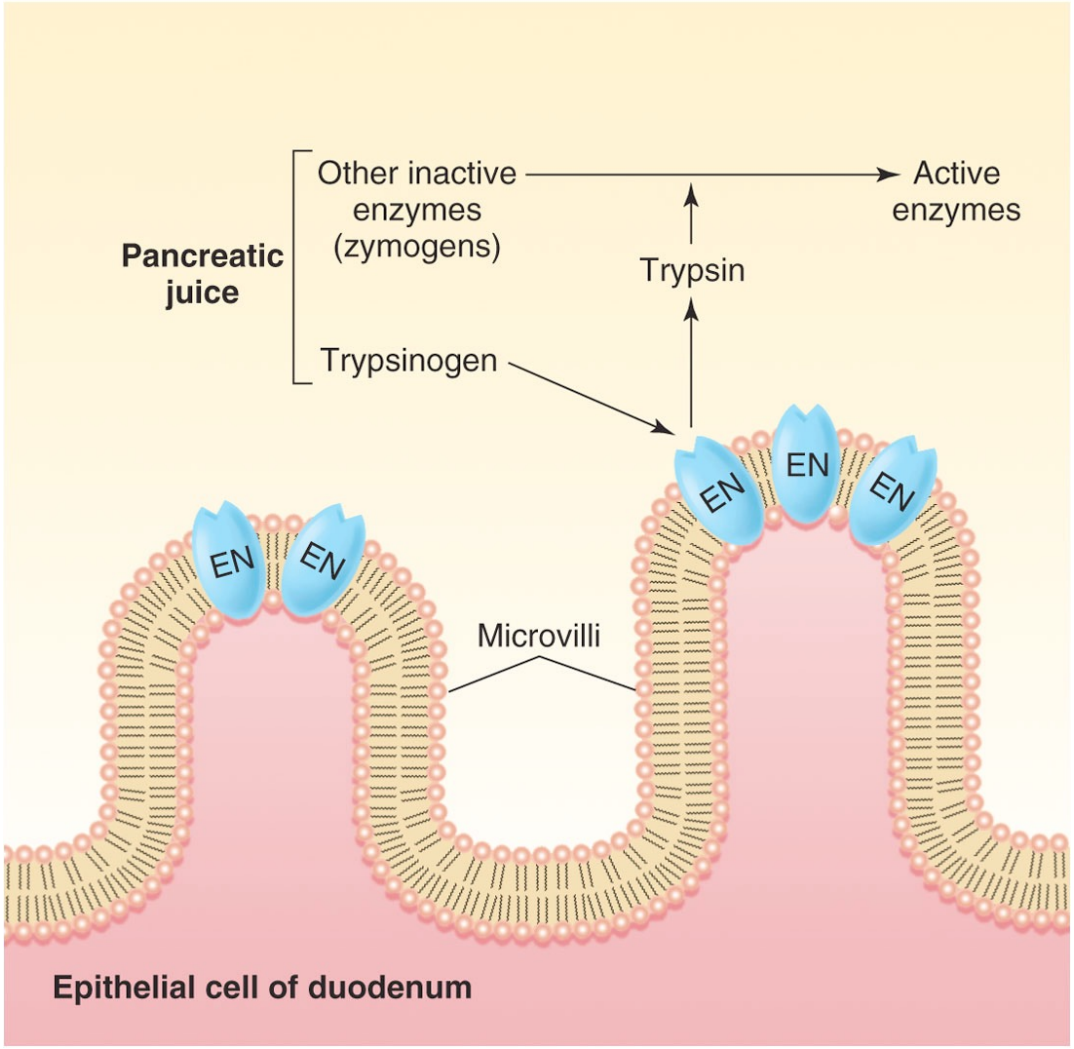

Pancreatic juice
Other inactive enzymes (zymogens)
Active enzymes
Trypsin
Trypsinogen
EN
EN
EN
EN
EN
Microvilli
Epithelial cell of duodenum

Table 18.4

Pancreatic enzymes digest many types of macromolecules: proteins, lipids, starch, nucleic acids

Table 18.4 | Enzymes Contained in Pancreatic Juice

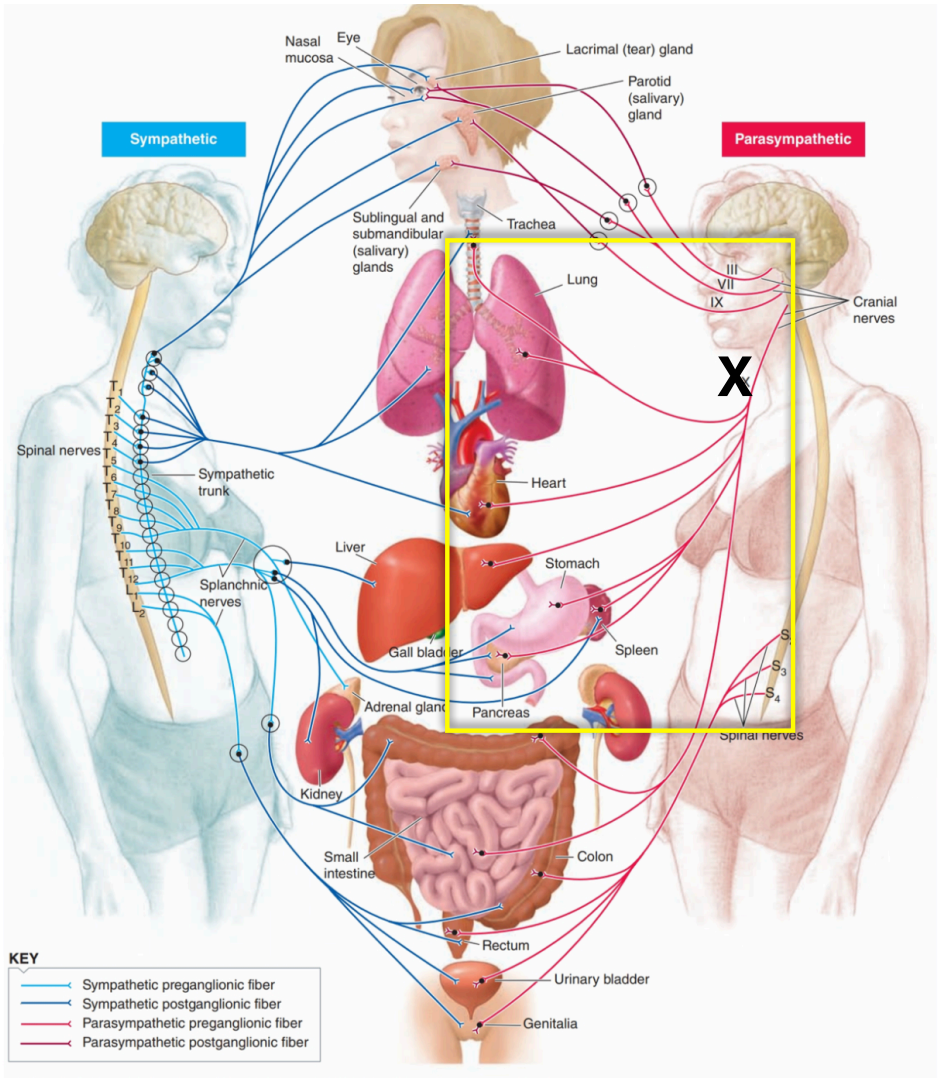
Enzyme	Zymogen	Activator	Action
Trypsin	Trypsinogen	Enterokinase	Cleaves internal peptide bonds
Chymotrypsin	Chymotrypsinogen	Trypsin	Cleaves internal peptide bonds
Elastase	Proelastase	Trypsin	Cleaves internal peptide bonds
Carboxypeptidase	Procarboxypeptidase	Trypsin	Cleaves last amino acid from carboxyl-terminal end of polypeptide
Phospholipase	Prophospholipase	Trypsin	Cleaves fatty acids from phospholipids such as lecithin
Lipase	None	None	Cleaves fatty acids from glycerol
Amylase	None	None	Digests starch to maltose and short chains of glucose molecules
Cholesterolesterase	None	None	Releases cholesterol from its bonds with other molecules
Ribonuclease	None	None	Cleaves RNA to form short chains
Deoxyribonuclease	None	None	Cleaves DNA to form short chains

Regulation of Pancreatic Secretion

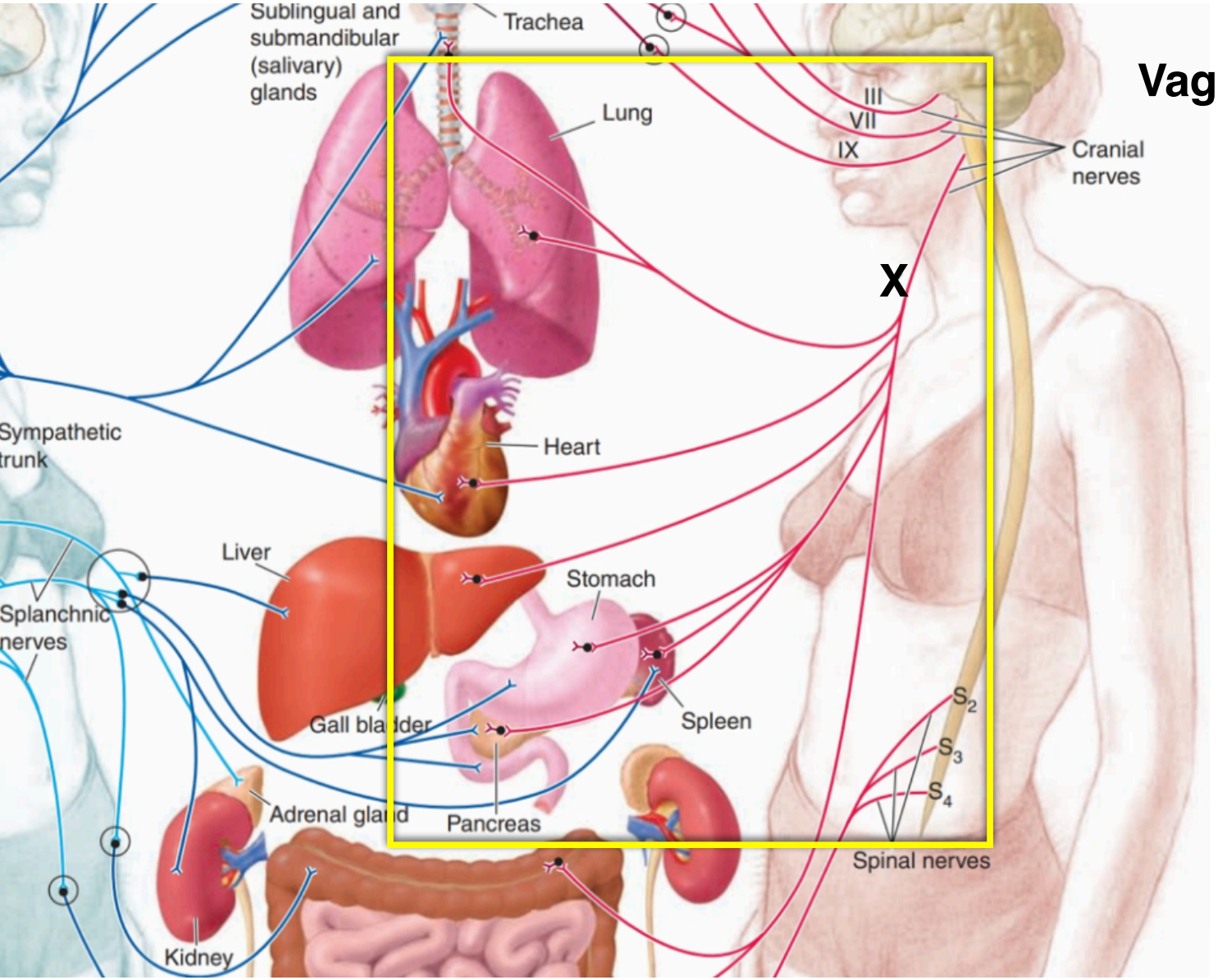
Cholecystokinin
Presence of fat, protein in duodenum causes secretion of CCK into blood. CCK causes pancreatic juice secretion (and gall bladder contraction).

Vagus Nerve
Vagus activates cholinergic receptors on acinar cells to cause pancreatic juice secretion.
(Vagus can also activate islet cells to cause insulin release).

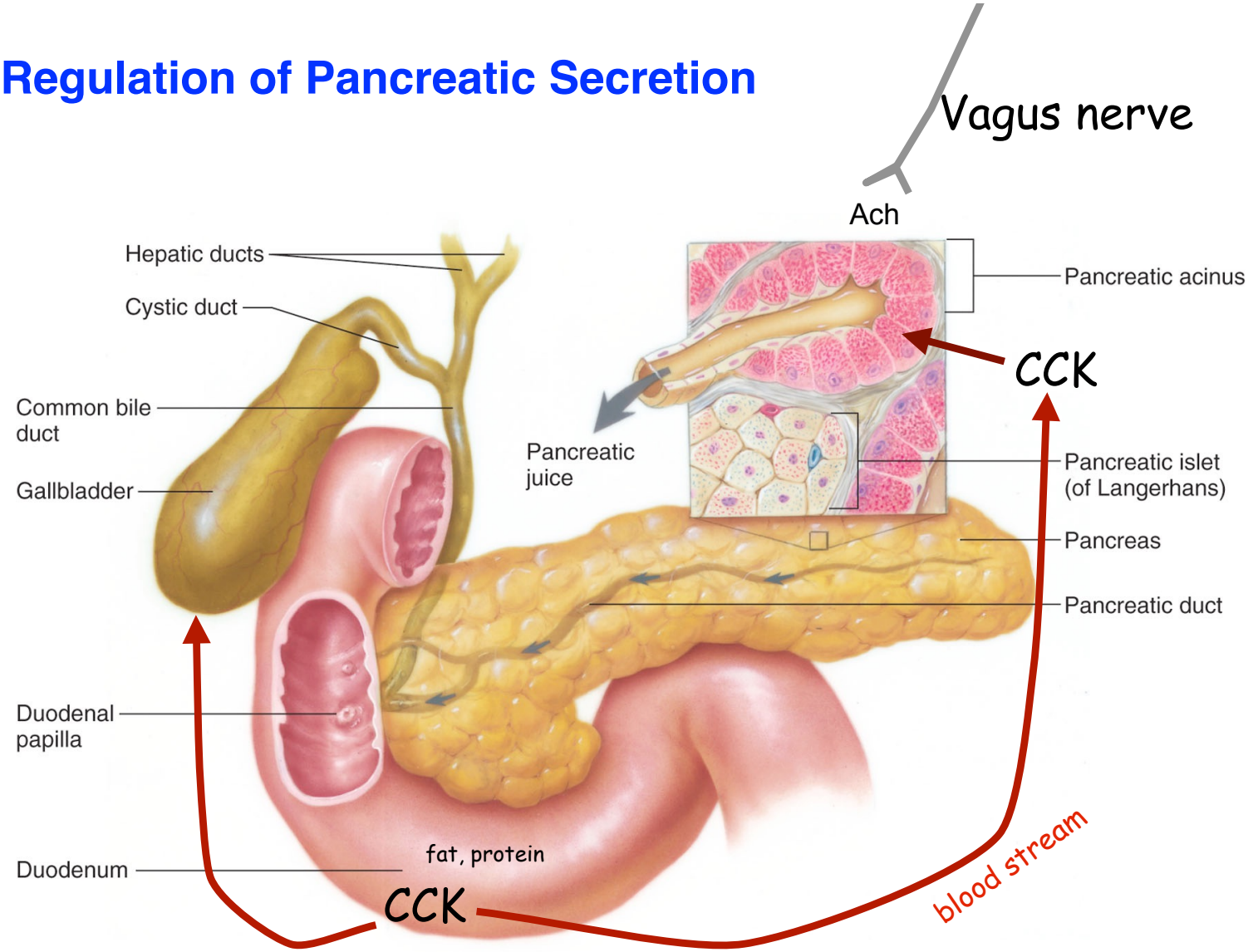
Vagus Nerve (X)



Vagus Nerve (X)



Regulation of Pancreatic Secretion



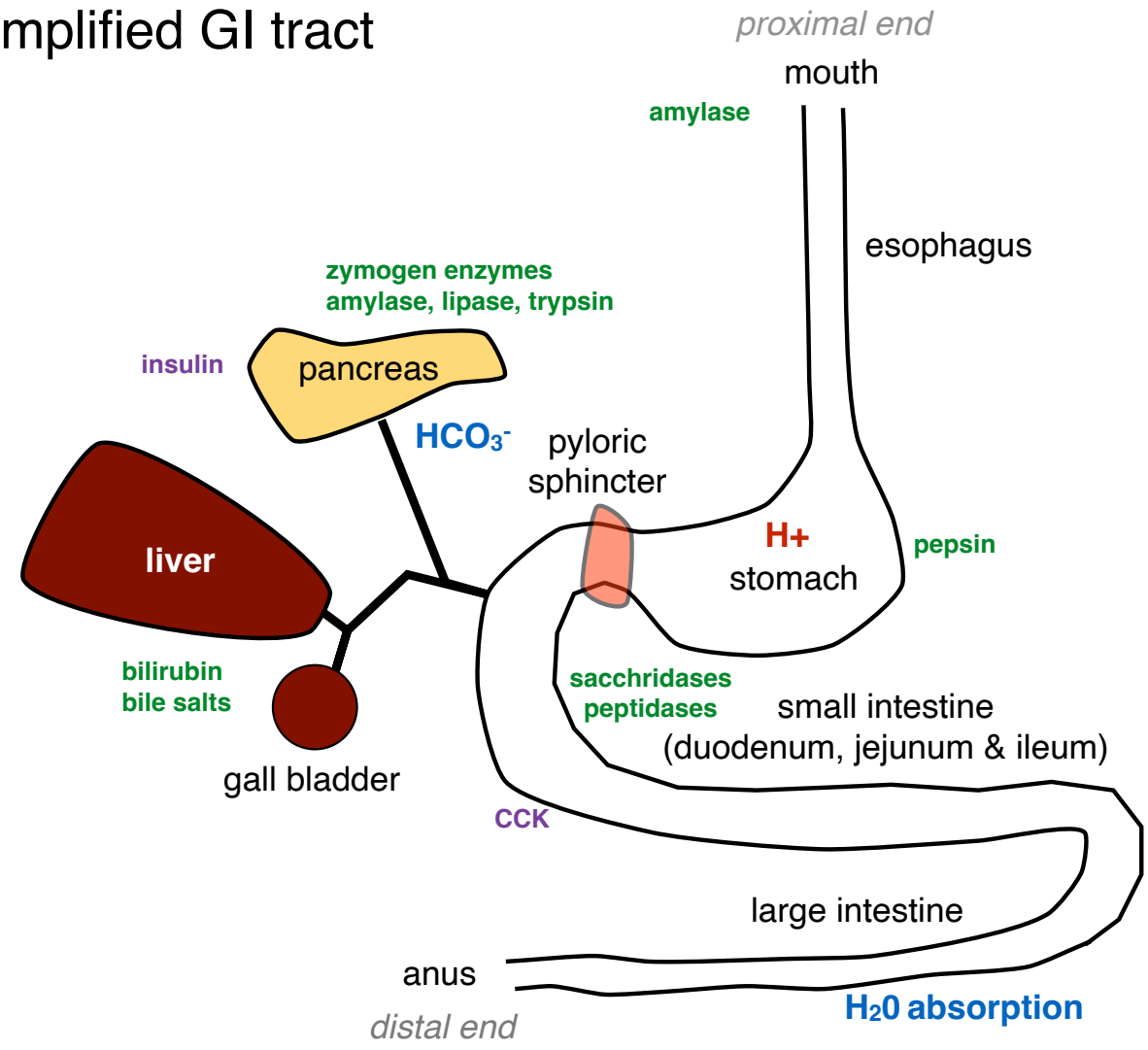
Summary of Digestive Enzymes

know amylase, pepsin, trypsin, enterokinase. Recognize other types by prefix name

Table 18.7 | Characteristics of the Major Digestive Enzymes

Enzyme	Site of Action	Source	Substrate	Optimum pH	Product(s)
Salivary amylase	Mouth	Saliva	Starch	6.7	Maltose
Pepsin	Stomach	Gastric glands	Protein	1.6–2.4	Shorter polypeptides
Pancreatic amylase	Duodenum	Pancreatic juice	Starch	6.7–7.0	Maltose, maltriose, and oligosaccharides
Trypsin, chymotrypsin, carboxypeptidase	Small intestine	Pancreatic juice	Polypeptides	8.0	Amino acids, dipeptides, and tripeptides
Pancreatic lipase	Small intestine	Pancreatic juice	Triglycerides	8.0	Fatty acids and monoglycerides
Maltase	Small intestine	Brush border of epithelial cells	Maltose	5.0–7.0	Glucose
Sucrase	Small intestine	Brush border of epithelial cells	Sucrose	5.0–7.0	Glucose + fructose
Lactase	Small intestine	Brush border of epithelial cells	Lactose	5.8–6.2	Glucose + galactose
Aminopeptidase	Small intestine	Brush border of epithelial cells	Polypeptides	8.0	Amino acids, dipeptides, tripeptides

Simplified GI tract



Endocrine Pancreas and Glucose Homeostasis

Blood glucose maintained at ~ 100 mg/100 ml

After meals, glucose from blood stored in liver and muscles as **glycogen** (a branched starch)

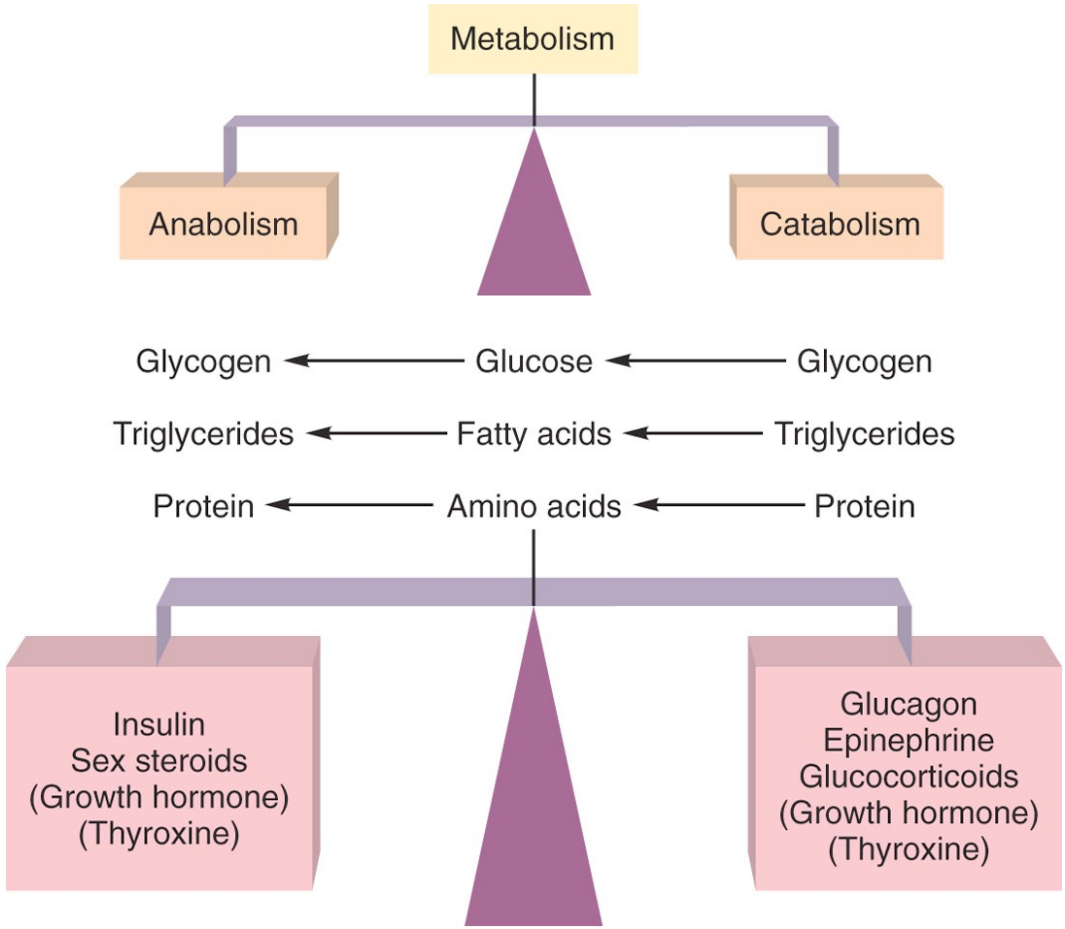
Between meals, glycogen broken down to glucose (**gluconeogenesis**) and released from liver into blood

Glucose regulated by pancreatic hormones, epinephrine, glucocorticoids (cortisol), thyroid hormone etc.

Pancreatic Islets of Langerhans
alpha cells secrete **glucagon** to **raise** blood glucose by gluconeogenesis
beta cells secrete **insulin** to **lower** blood glucose by tissue uptake

glyco- related to glucose
(h)emia - related to blood
euglycemia - normal blood glucose level
hyperglycemia - elevated blood glucose
hypoglycemia - lowered blood glucose
insula - island (so insulin is hormone from pancreatic islets)

Figure 19.6


Metabolism
Anabolism
Catabolism
Glycogen
Glucose
Glycogen
Triglycerides
Fatty acids
Triglycerides
Protein
Amino acids
Protein
Insulin
Sex steroids
(Growth hormone)
(Thyroxine)
Glucagon
Epinephrine
Glucocorticoids
(Growth hormone)
(Thyroxine)

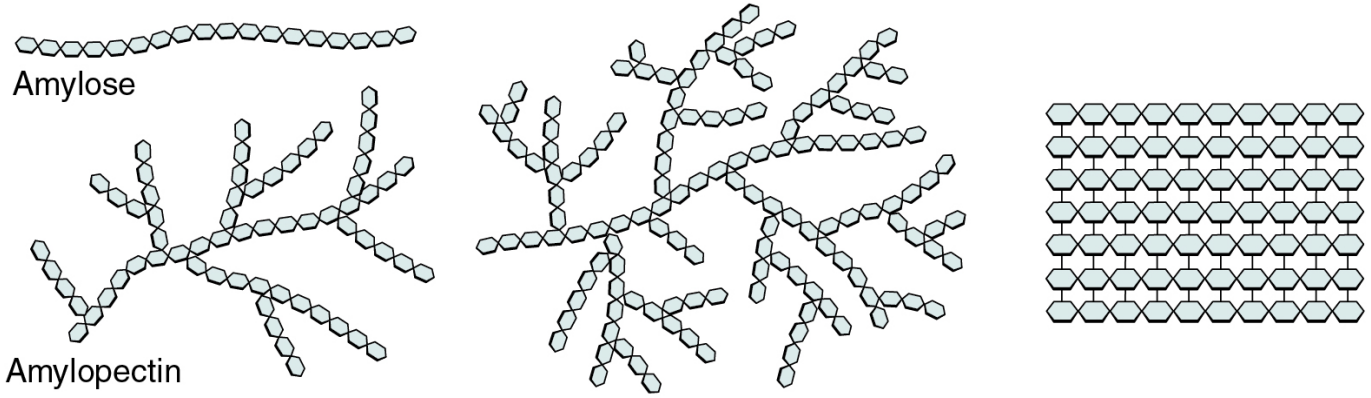
Time of Check	Goal plasma blood glucose ranges for people without diabetes	Goal plasma blood glucose ranges for people with diabetes
Before breakfast (fasting)	< 100	70 - 130
Before lunch, supper and snack	< 110	70 - 130
Two hours after meals	< 140	< 180
Bedtime	< 120	90- 150
A1C (also called glycosylated hemoglobin A1c, HbA1c or glycohemoglobin A1c)	< 6%	< 7%

Effects of Hypoglycemia

100 mg/ml	euglycemic
70 mg/ml	glucagon, epinephrine release
60 mg/ml	sympathetic activation: anxiety, heart rate, sweating, tremor
50 mg/ml	hunger, dizziness, blurred vision, difficulty thinking, faintness

Mitrakou et al. Hierarchy of glycemic thresholds for counterregulatory hormone secretion, symptoms, and cerebral dysfunction. Am J Physiol 260:E67-E74, 1991

Glucose Polymers

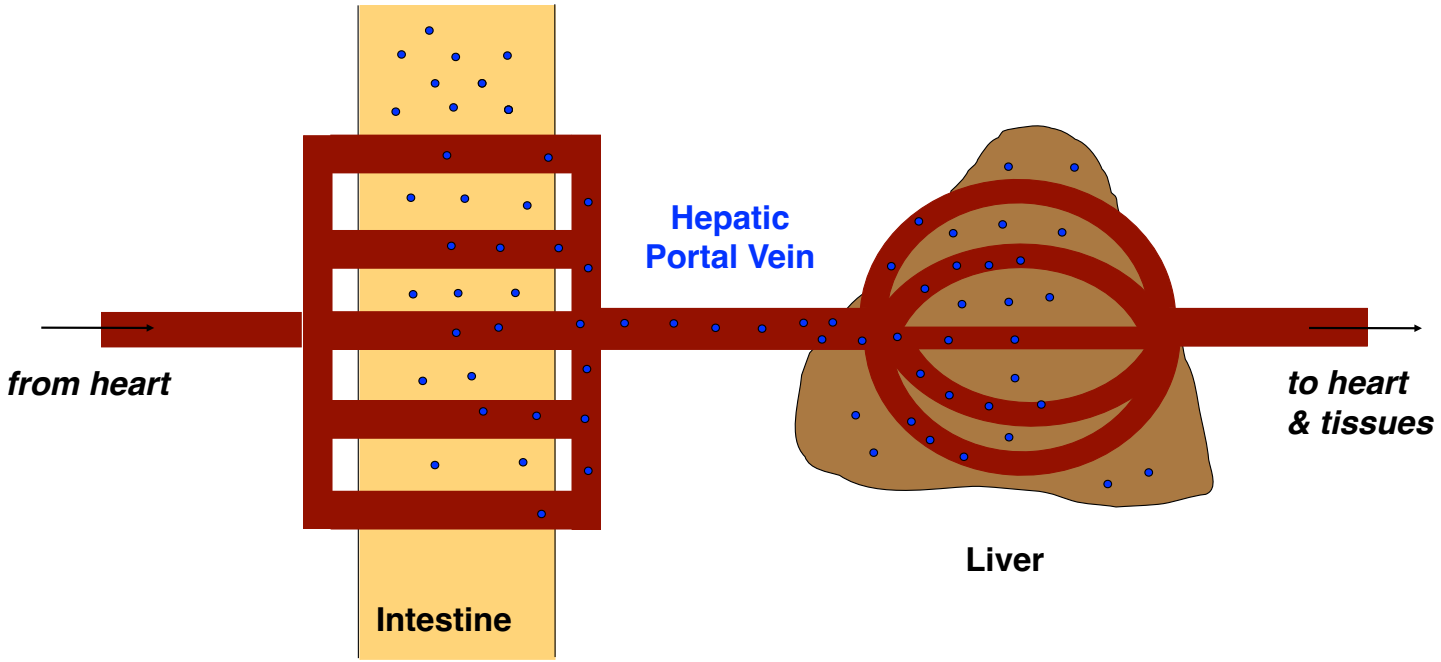


Starch **Glycogen** **Cellulose (fiber)**

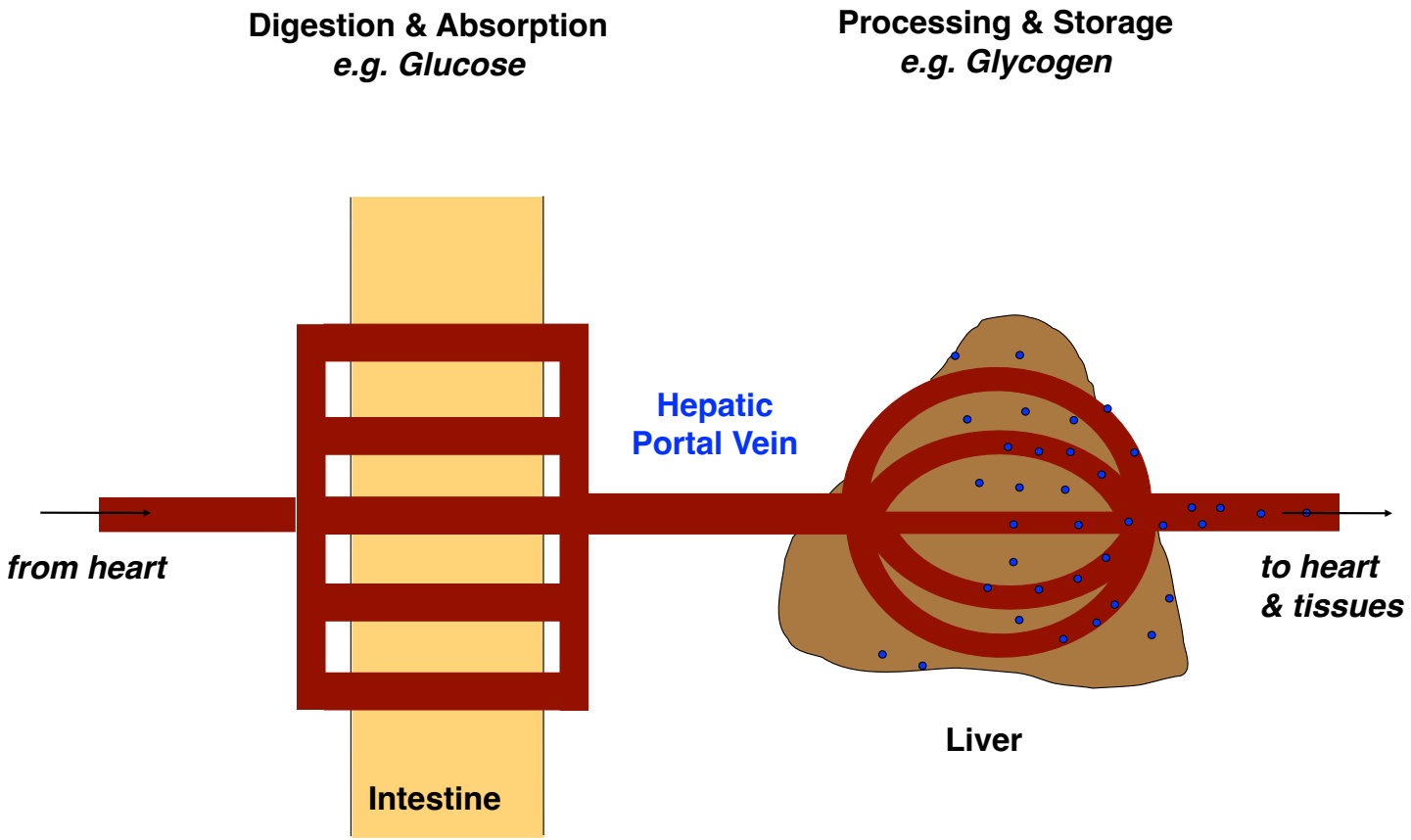
http://cnx.org/content/m46008/latest/?collection=col11540/latest

Digestion & Absorption
e.g. Glucose

Processing & Storage



after meals, glucose taken up by liver and stored as glycogen



between meals, glycogen -> glucose
and released into blood

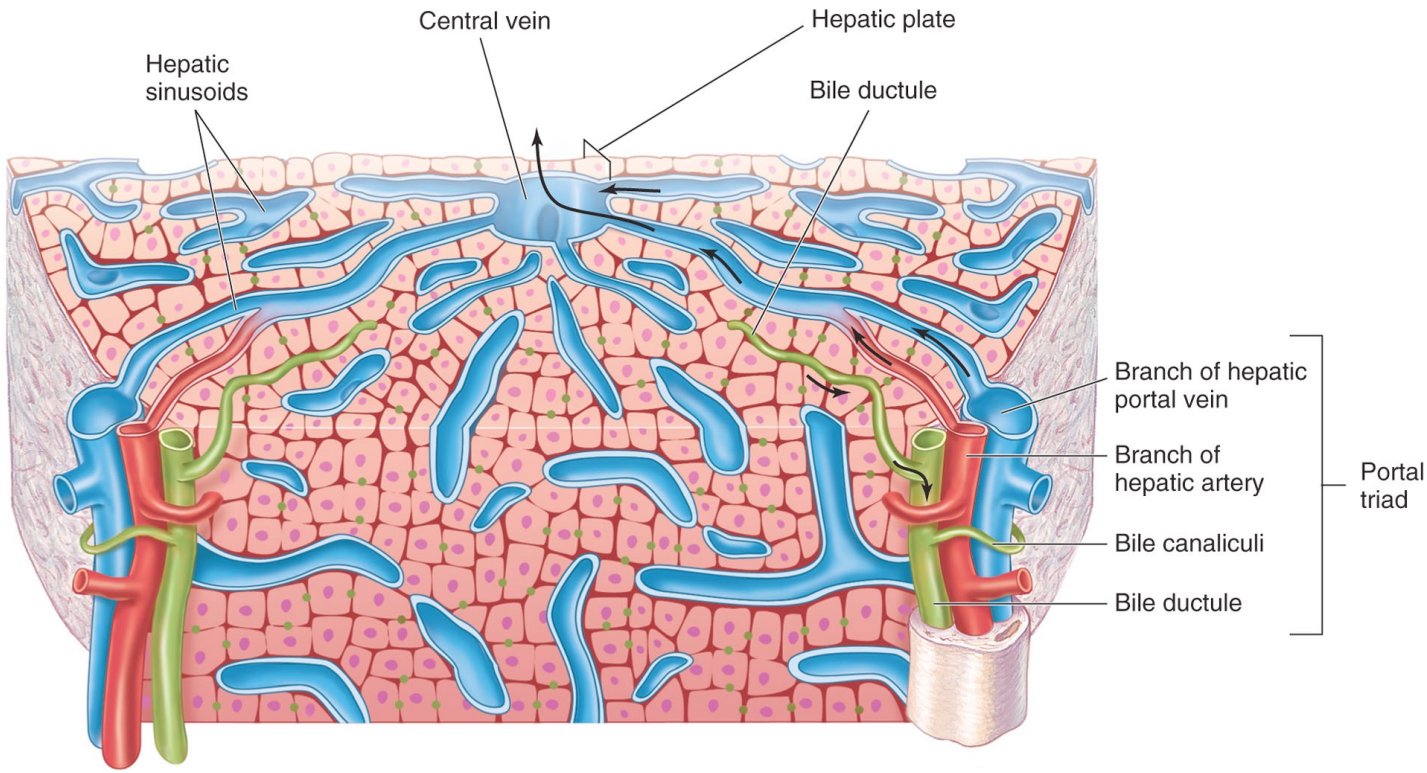
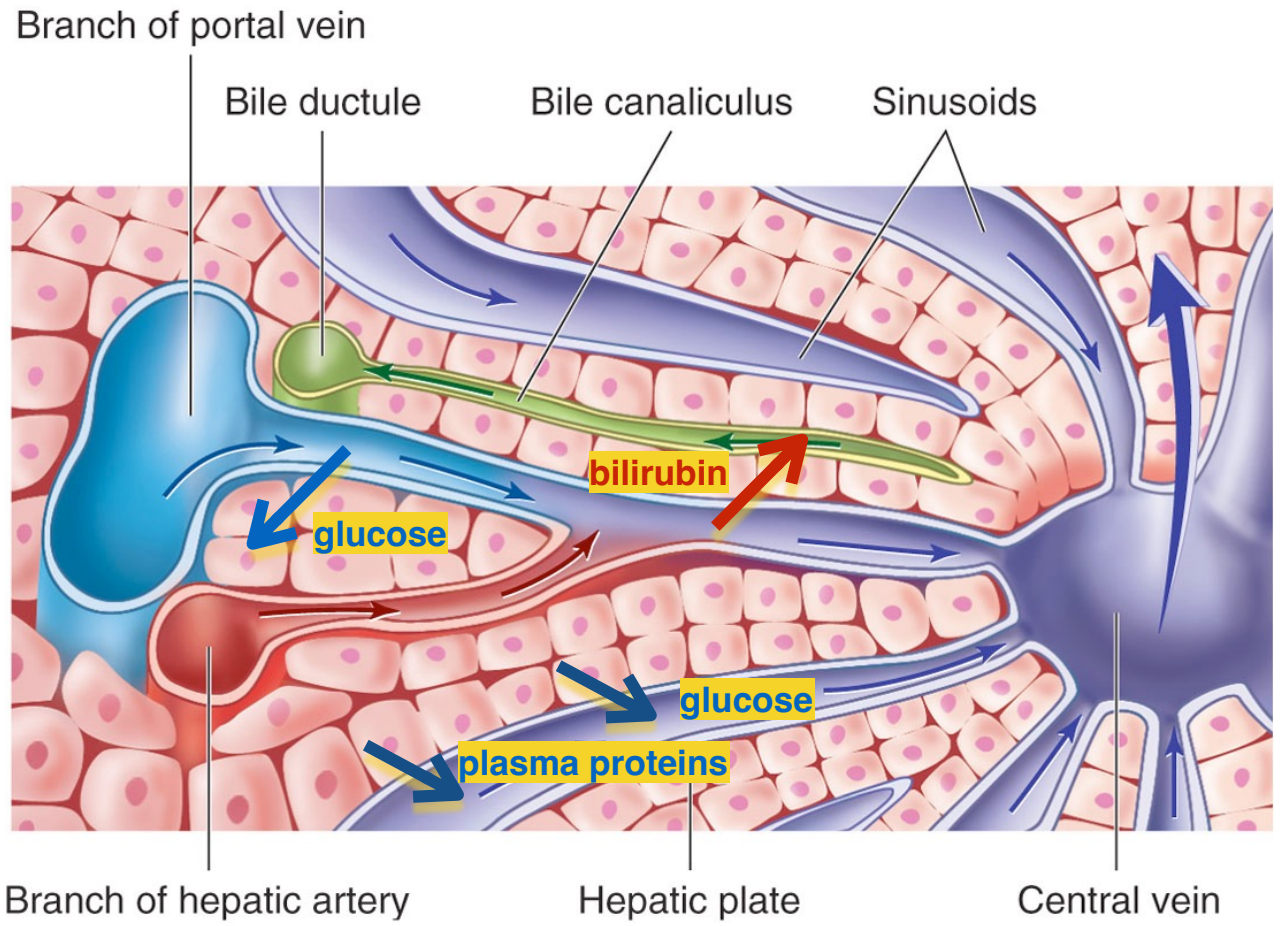
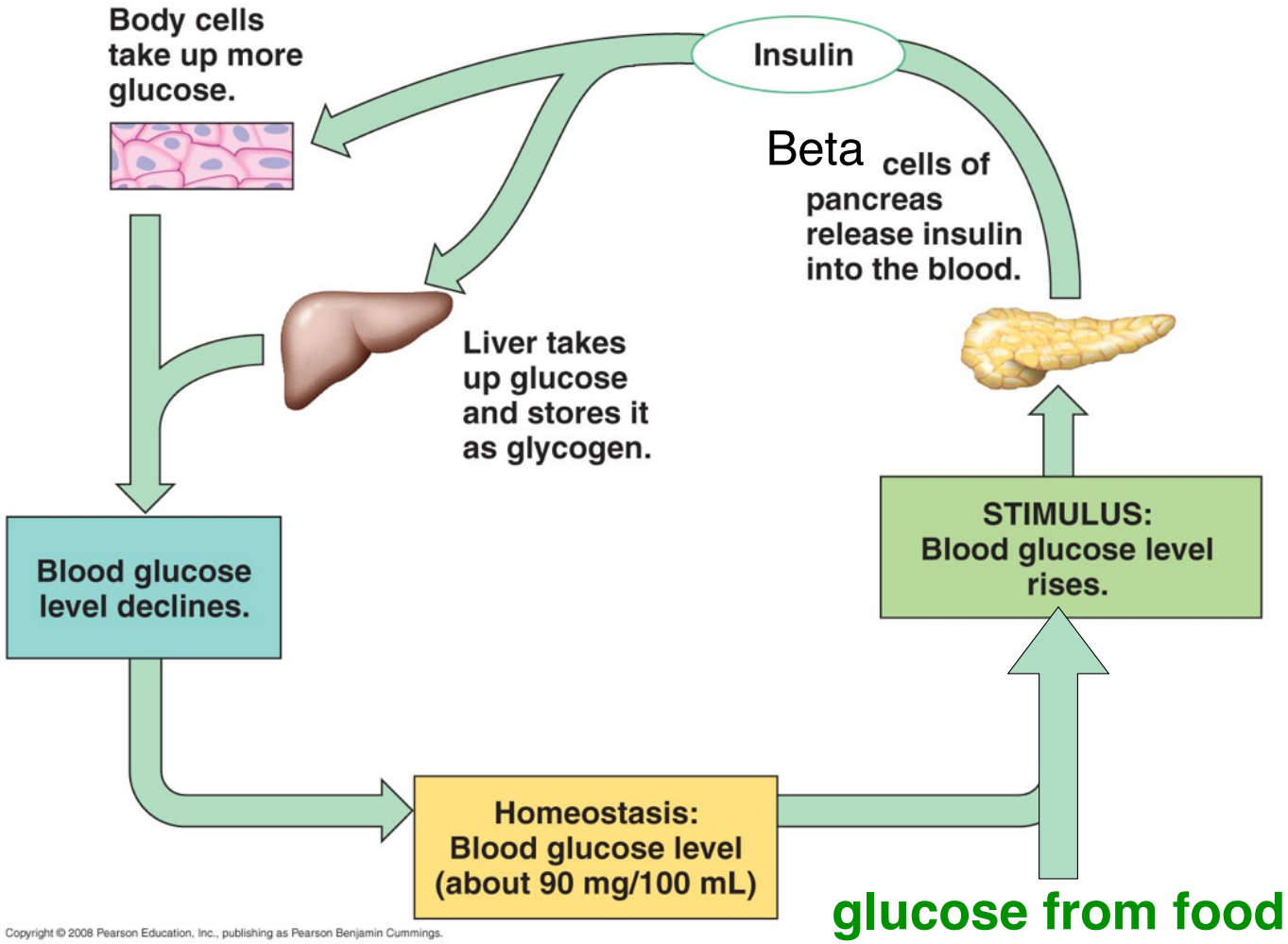

Central vein
Hepatic plate
Hepatic sinusoids
Bile ductule
Branch of hepatic portal vein
Branch of hepatic artery
Bile canaliculi
Bile ductule
Portal triad

Figure 18.19

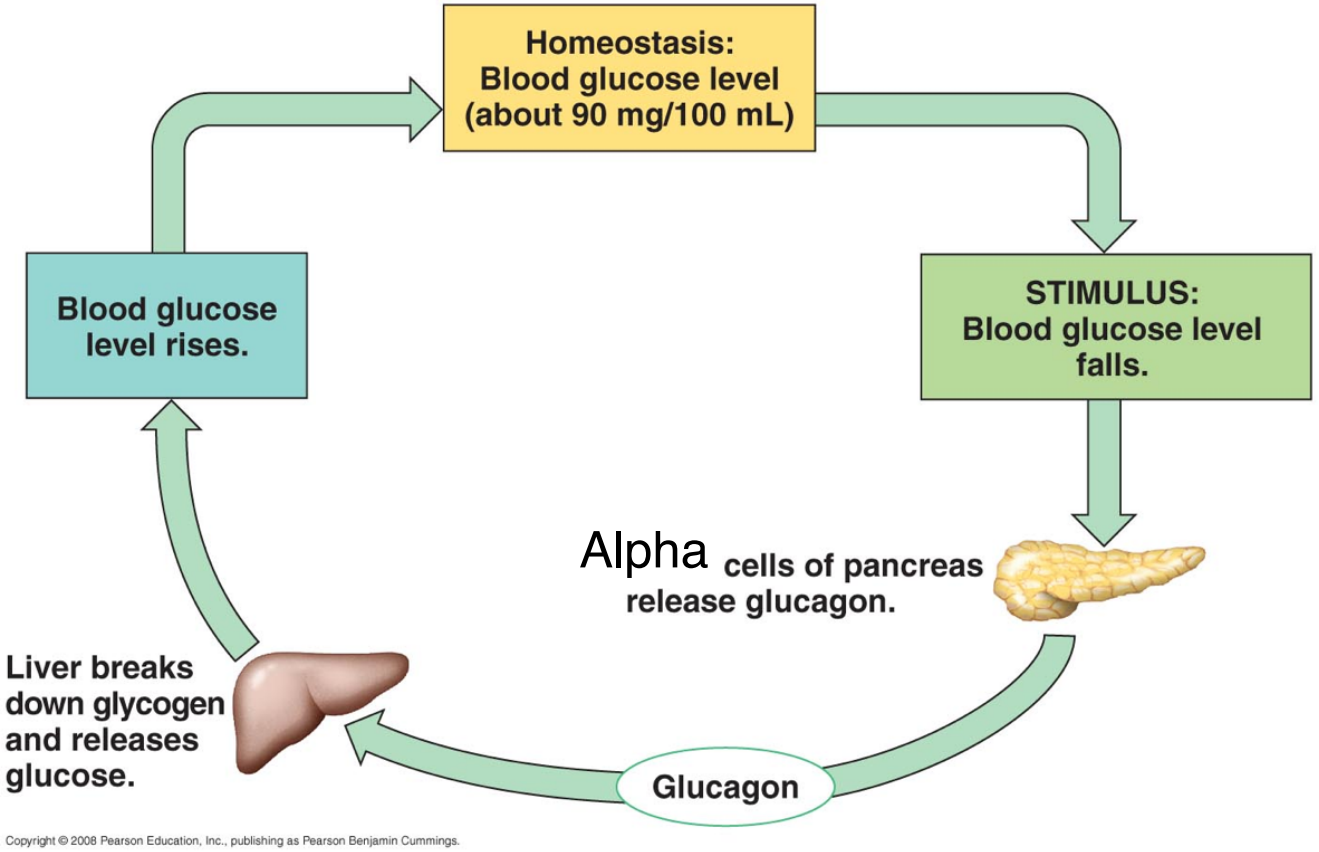
Figure 18.20

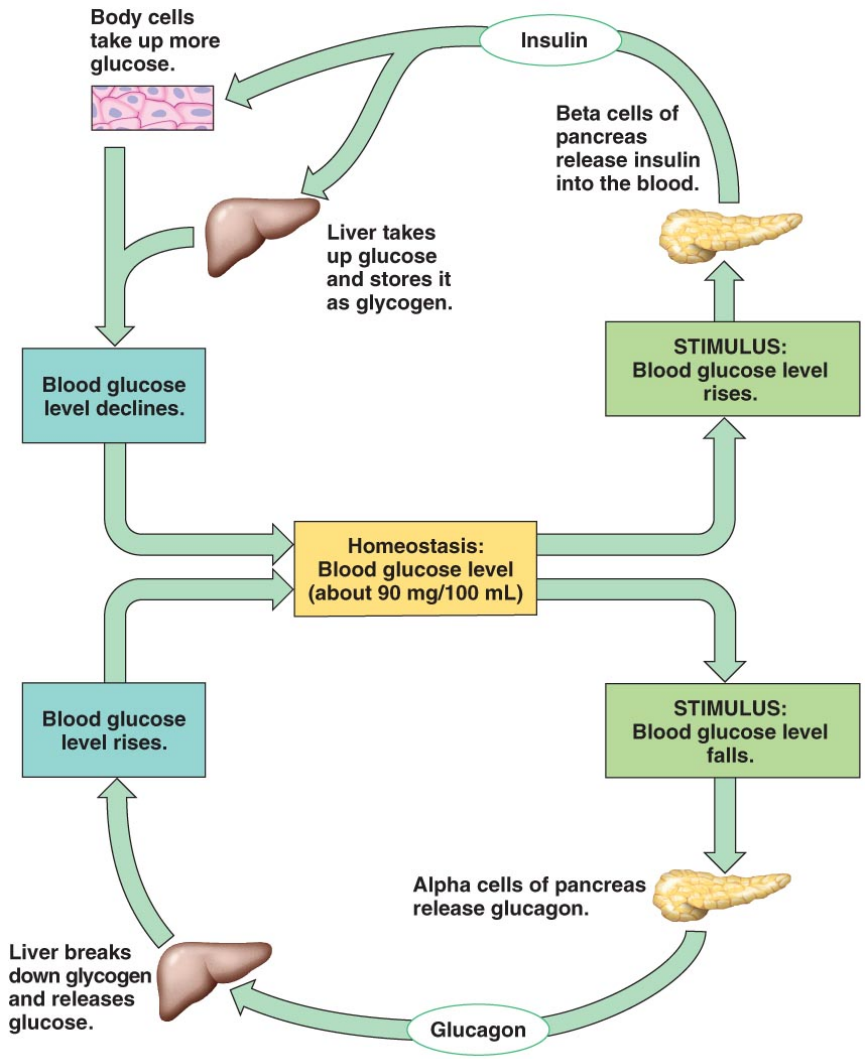

Branch of portal vein
Bile ductule
Bile canaliculus
Sinusoids
bilirubin
glucose
glucose
plasma proteins
Branch of hepatic artery
Hepatic plate
Central vein

Insulin: hormone that decreases blood glucose levels

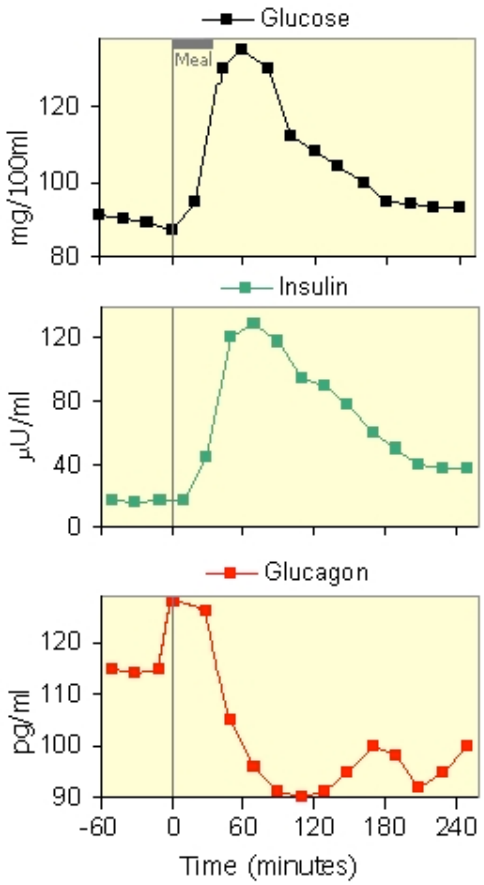


Glucagon: hormone that increases blood glucose levels





Insulin & Glucose profile after a meal



http://www.ncbi.nlm.nih.gov/books/NBK1671/

Regulation of Beta Cells: increase insulin secretion

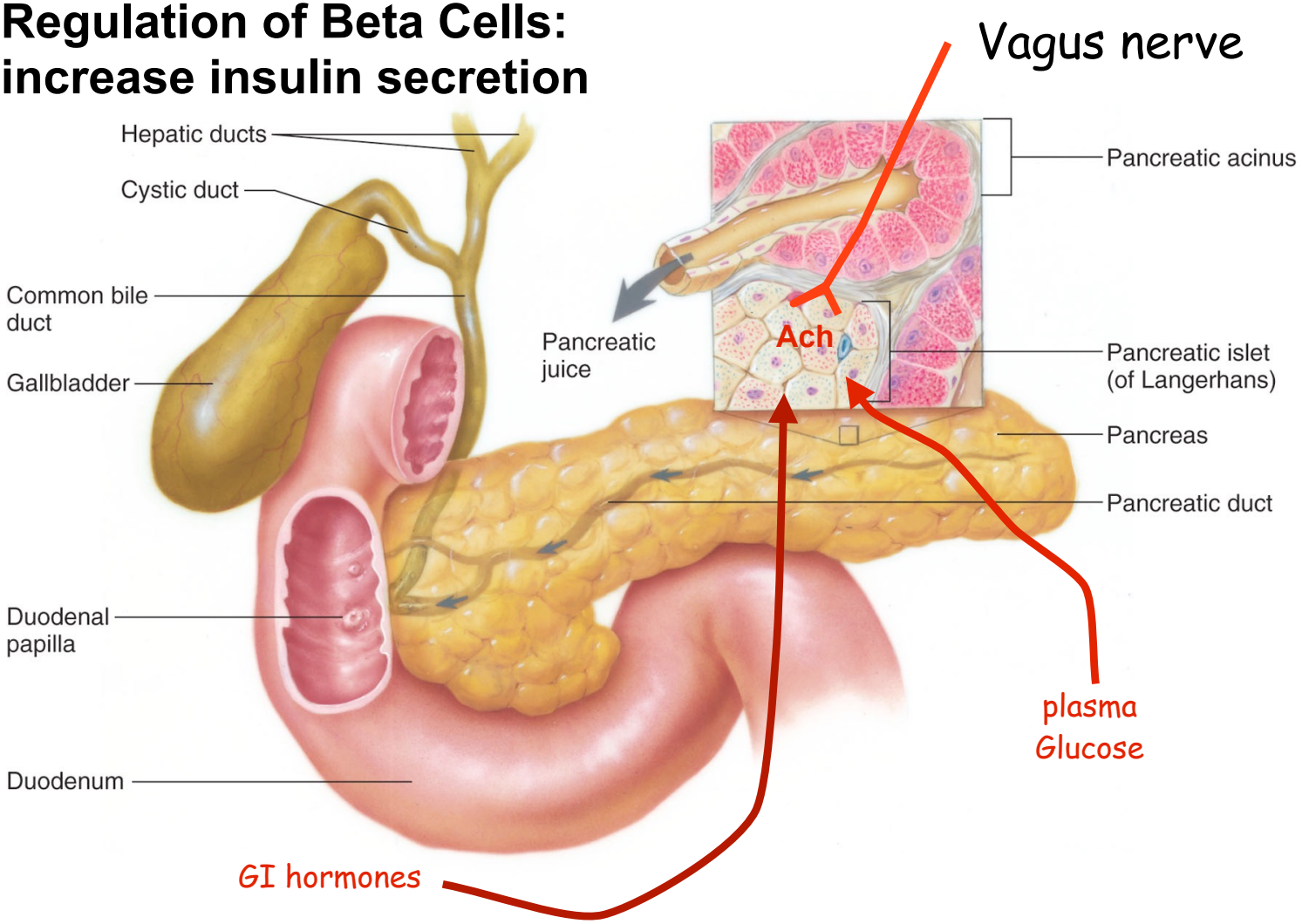


Figure 18.25

alpha cells secrete **glucagon** to **raise** blood glucose by gluconeogenesis

beta cells secrete **insulin** to **lower** blood glucose by tissue uptake

insulin and glucagon have opposite effects on glucose uptake/ glucose storage in target tissues

Exocrine Pancreas: beta cells secrete insulin

↑glucose -> ↑ATP -> close K+ channels

-> Depolarization -> open Ca++ channels

-> ↑insulin secretion

Target tissues: Insulin increases glucose uptake

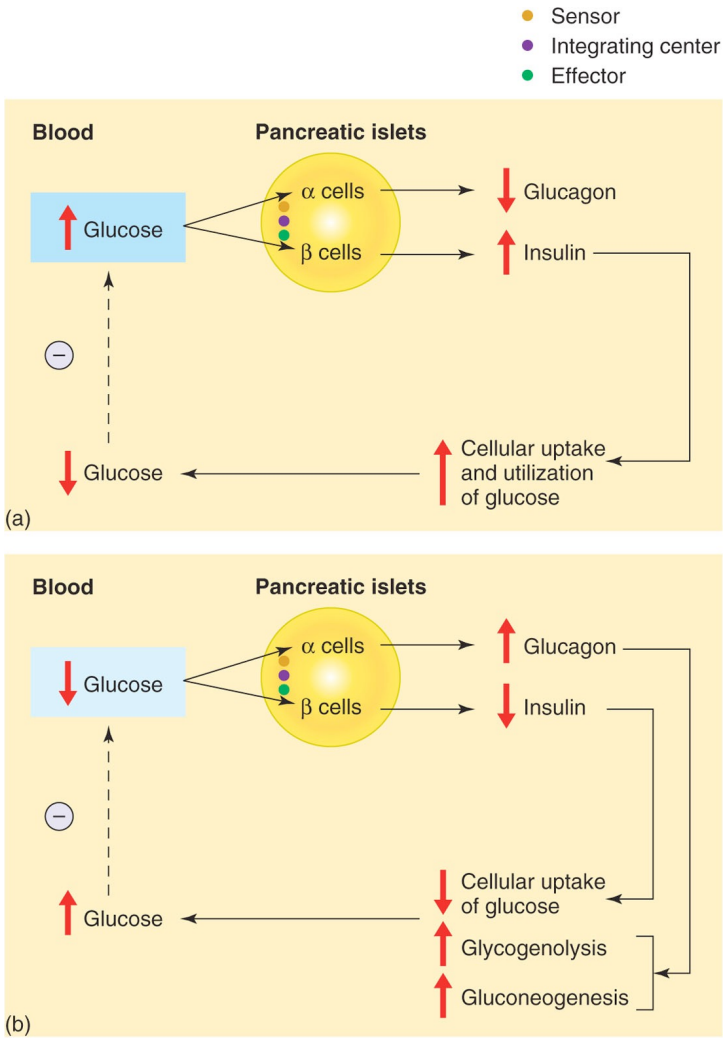
insulin -> insulin receptor (tyrosine kinase)

-> insertion of glucose transporters into cell membrane

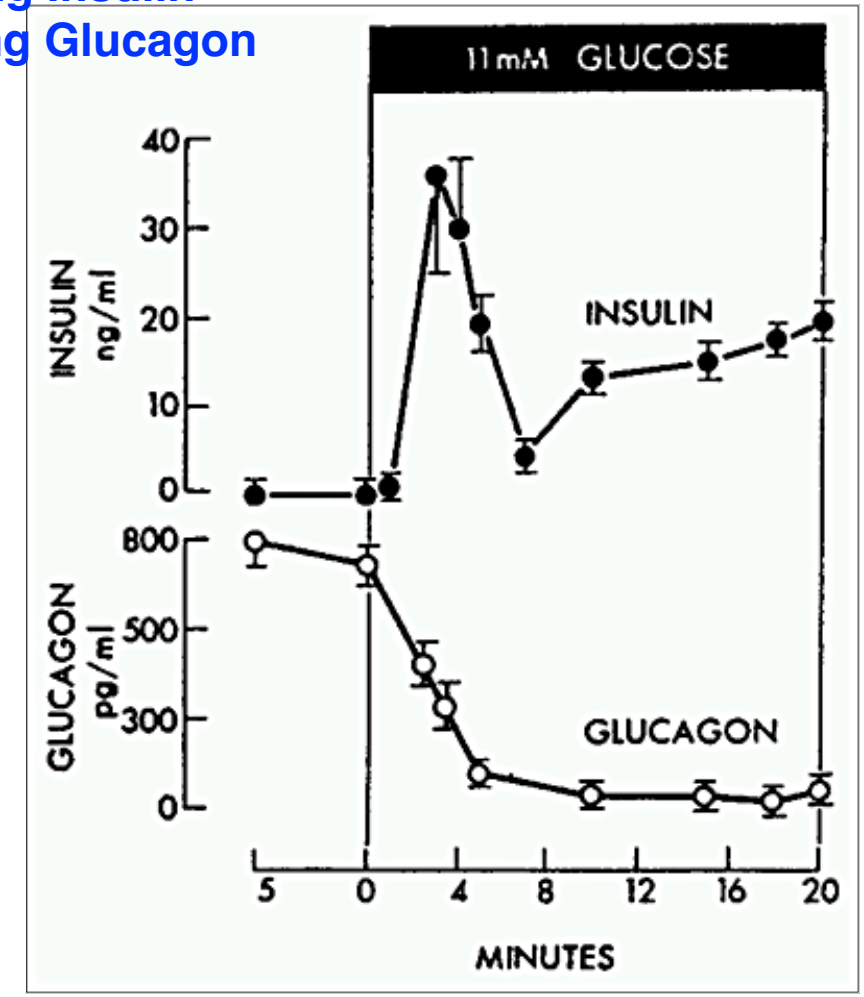
-> ↑ glucose uptake

(also stimulates glycogen synthesis enzymes)

Figure 11.31


Sensor
Integrating center
Effector
Blood
Pancreatic islets
Glucose
α cells
β cells
Glucagon
Insulin
Glucose
Cellular uptake and utilization of glucose
(a)
Blood
Pancreatic islets
Glucose
α cells
β cells
Glucagon
Insulin
Glucose
Cellular uptake of glucose
Glycogenolysis
Gluconeogenesis
(b)

Glucose as signal to islet cells
-> Pancreas starts secreting Insulin
-> Pancreas stops secreting Glucagon



Pancreatic Beta Cell:
responds to plasma glucose by secreting insulin

↑Glucose -> ↑ATP
-> close K+ channels
-> Depolarization
-> open Ca++ channels
-> ↑insulin secretion

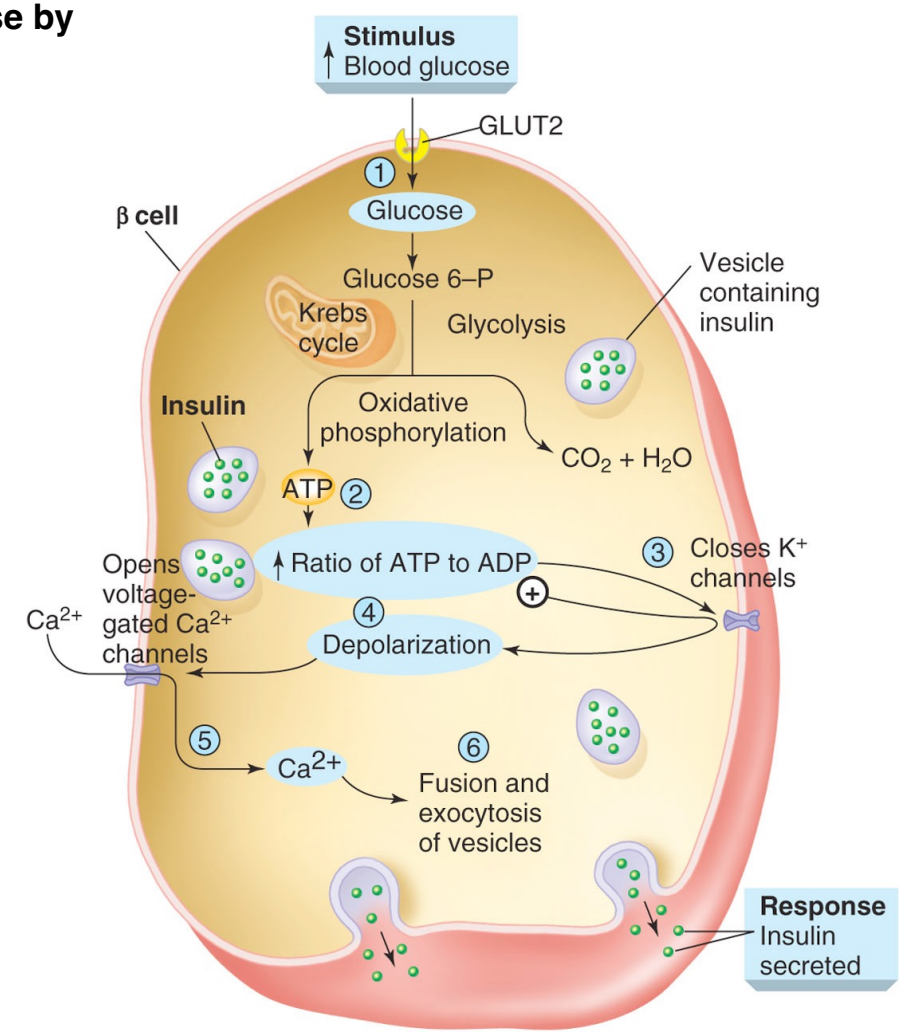


Figure 19.8

Figure 19.7

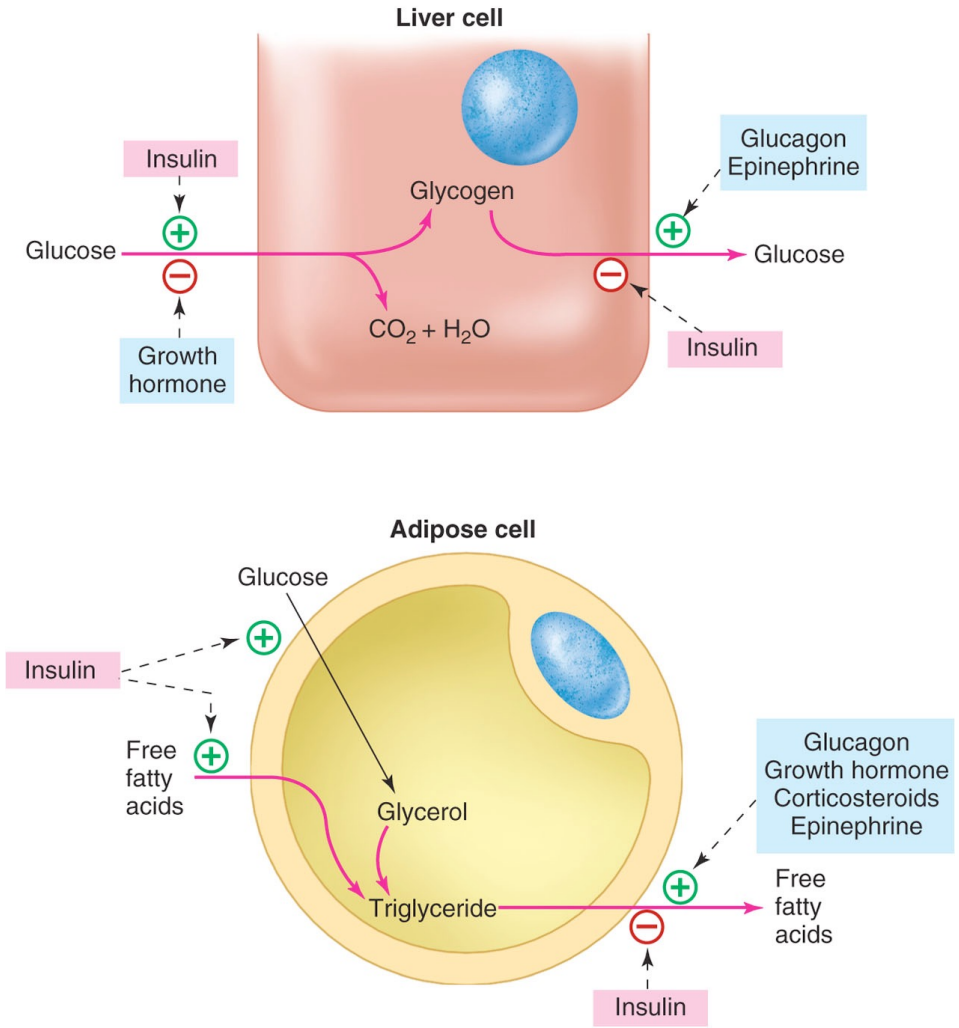

Liver cell
Insulin
Glucose
Growth hormone
Glycogen
$CO_2 + H_2O$
Glucagon
Epinephrine
Glucose
Insulin
Adipose cell
Glucose
Insulin
Free fatty acids
Glycerol
Triglyceride
Glucagon
Growth hormone
Corticosteroids
Epinephrine
Free fatty acids
Insulin

Figure 11.30

Liver/Muscle/Adipose Cells:
responds to plasma insulin by moving glucose transporters to the membrane and taking up plasma glucose

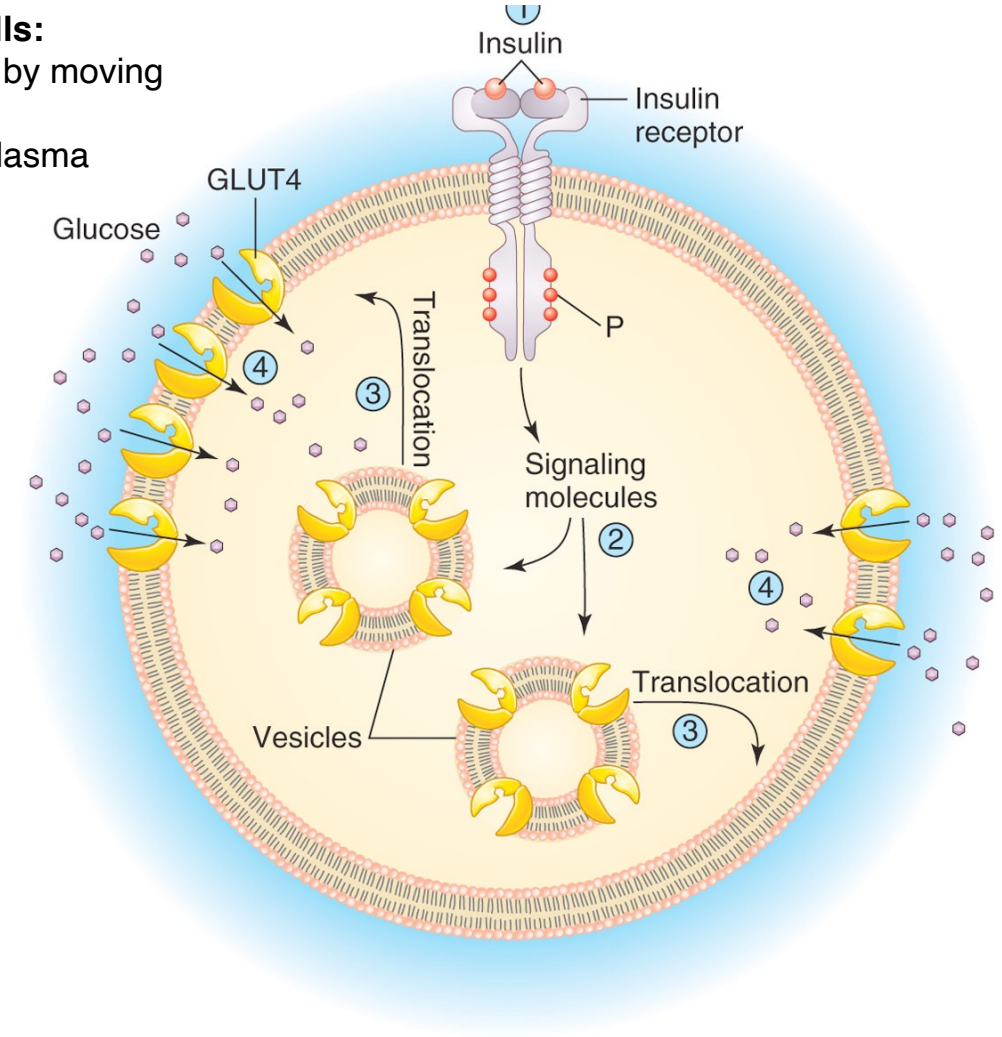


Table 19.4

Table 19.4 | Endocrine Regulation of Metabolism

Hormone	Blood Glucose	Carbohydrate Metabolism	Protein Metabolism	Lipid Metabolism
Insulin	Decreased	↑ Glycogen formation ↓ Glycogenolysis ↓ Gluconeogenesis	↑ Protein synthesis	↑ Lipogenesis ↓ Lipolysis ↓ Ketogenesis
Glucagon	Increased	↓ Glycogen formation ↑ Glycogenolysis ↑ Gluconeogenesis	No direct effect	↑ Lipolysis ↑ Ketogenesis
Growth hormone	Increased	↑ Glycogenolysis ↑ Gluconeogenesis ↓ Glucose utilization	↑ Protein synthesis	↓ Lipogenesis ↑ Lipolysis ↑ Ketogenesis
Glucocorticoids (hydrocortisone)	Increased	↑ Glycogen formation ↑ Gluconeogenesis	↓ Protein synthesis	↓ Lipogenesis ↑ Lipolysis ↑ Ketogenesis
Epinephrine	Increased	↓ Glycogen formation ↑ Glycogenolysis ↑ Gluconeogenesis	No direct effect	↑ Lipolysis ↑ Ketogenesis
Thyroid hormones	No effect	↑ Glucose utilization	↑ Protein synthesis	No direct effect

Diabetes Mellitus (sweet urine)

Elevated glucose causes excess urine production & excess glucose in urine.
Chronically elevated glucose (**hyperglycemia**) has toxic effects on kidney, retina, nerves, peripheral tissues.

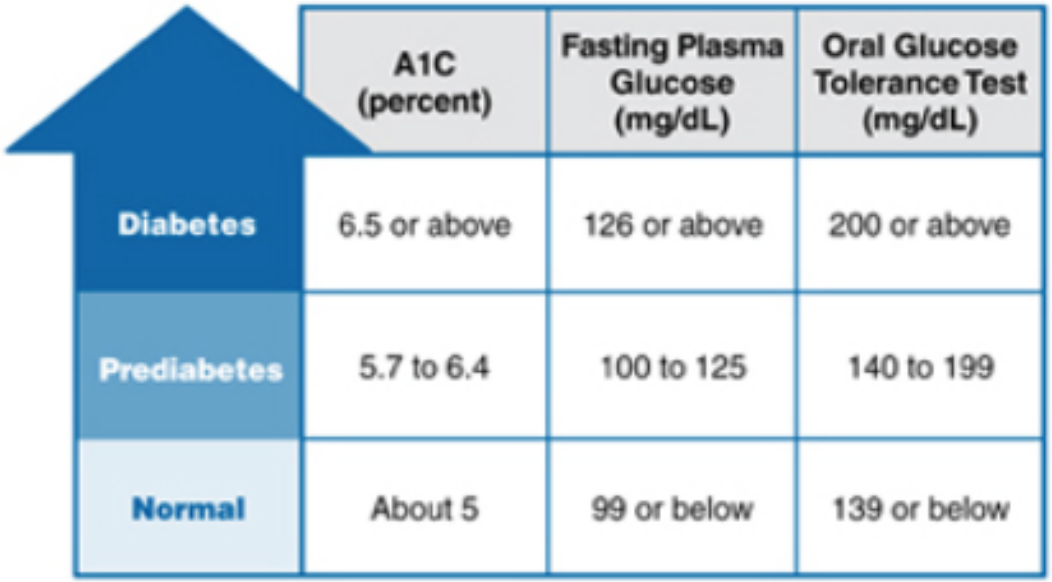
Type 1 Diabetes
autoimmune disease, often appears in childhood.
Immune system attacks & kills beta cells of pancreas, so **no insulin produced**; glucose levels remain high, little glucose stored.

-> Hypoinsulinemia, can be treated with exogenous insulin

Type 2 Diabetes
Unknown cause, related to genes and obesity; appears in midlife. Target cells become **unresponsive to insulin** (insulin resistance), so pancreas produces excessive insulin (but blood glucose remains high); eventually beta cells stop working

-> Functional Hypoinsulinemia, in later stages exogenous insulin does not help

Blood Test Levels for Diagnosis of Diabetes and Prediabetes



	A1C (percent)	Fasting Plasma Glucose (mg/dL)	Oral Glucose Tolerance Test (mg/dL)
Diabetes	6.5 or above	126 or above	200 or above
Prediabetes	5.7 to 6.4	100 to 125	140 to 199
Normal	About 5	99 or below	139 or below

Definitions: mg = milligram, dL = deciliter
For all three tests, within the prediabetes range, the higher the test result, the greater the risk of diabetes.

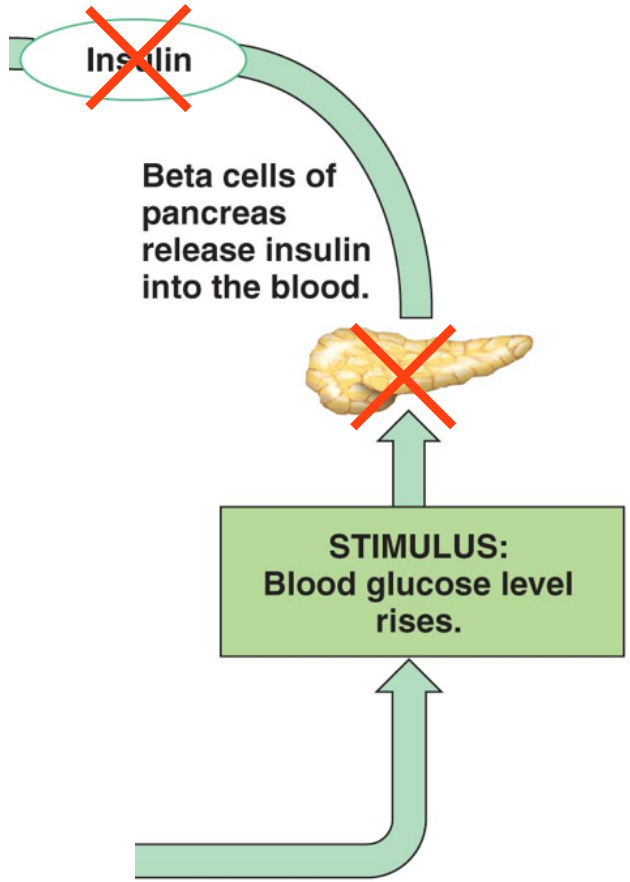
Source: Adapted from American Diabetes Association. Standards of medical care in diabetes—2012. *Diabetes Care.* 2012;35(Supp 1):S12, table 2.

Type I Diabetes: beta cells die, so no insulin

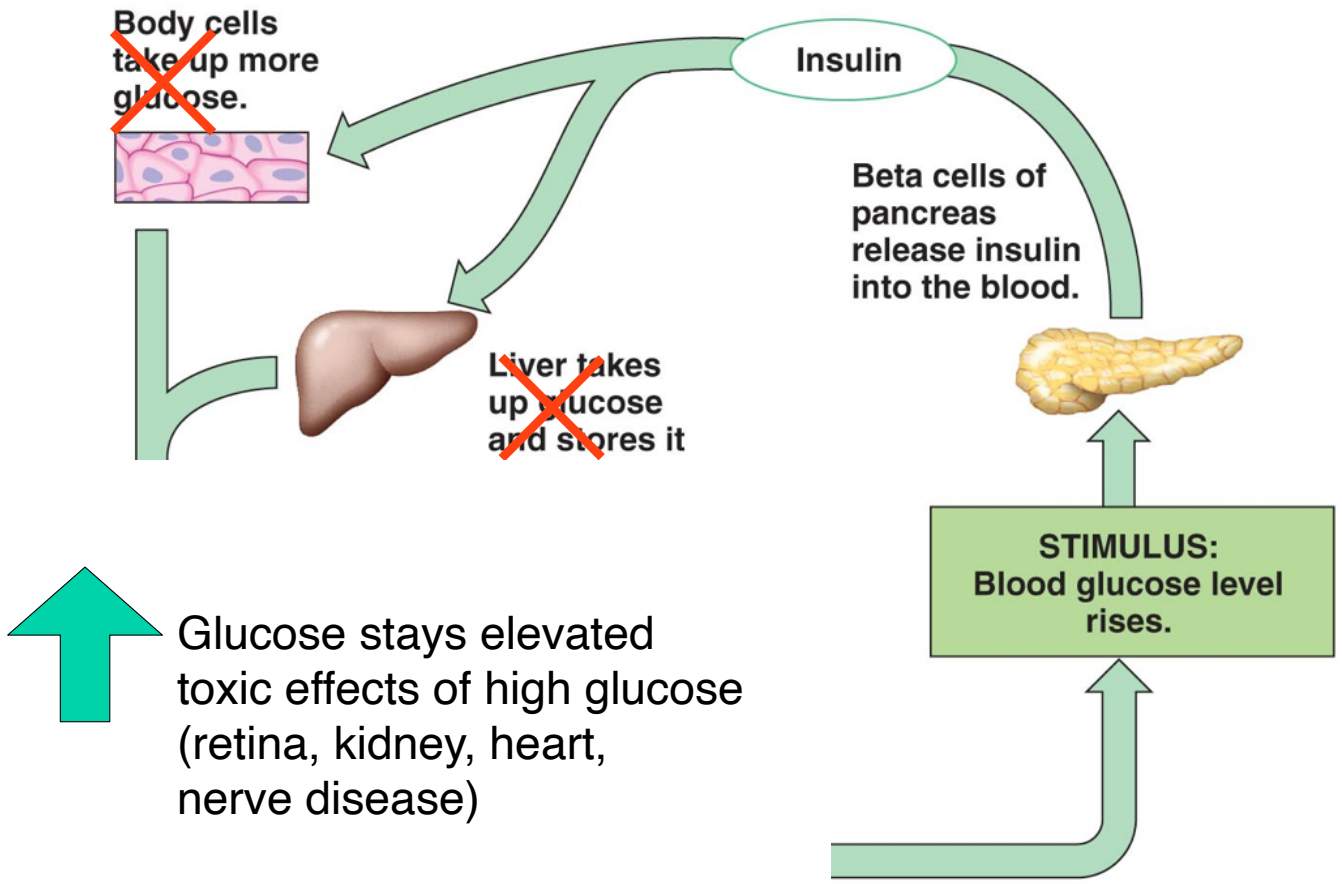
Diabetes Mellitus (sweet urine)

Glucose stays elevated
toxic effects of high glucose
(retina, kidney, heart,
nerve disease)

Glucose lost in urine
hypoglycemia
body weight loss



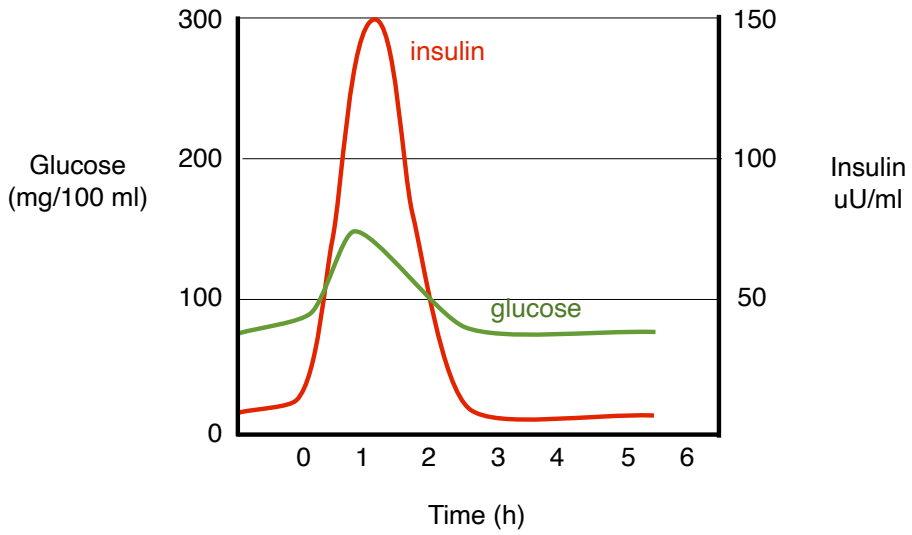
Type II Diabetes: obesity causes insulin receptors to stop functioning



Glucose stays elevated
toxic effects of high glucose
(retina, kidney, heart,
nerve disease)

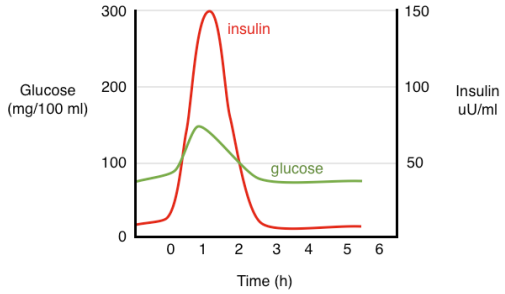
Glucose Tolerance Test: Normal

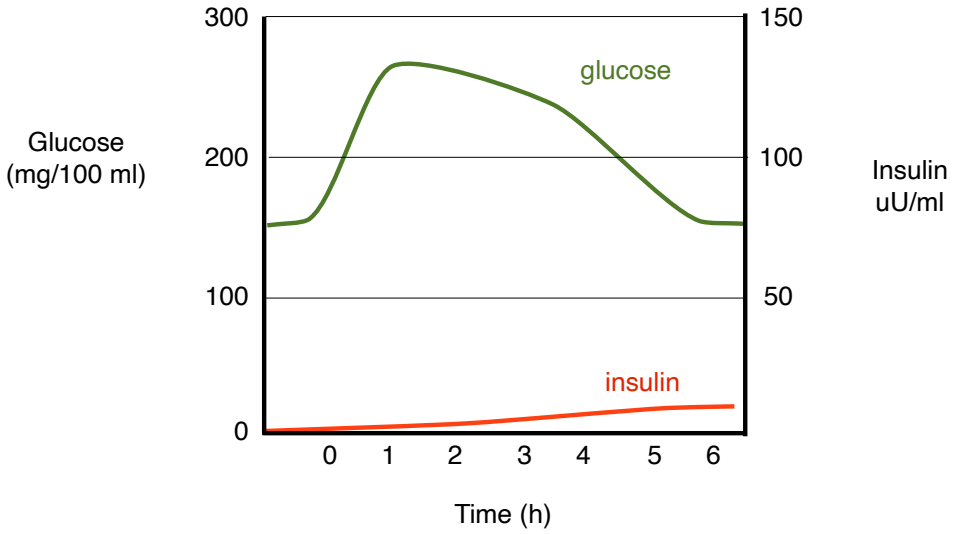
glucose absorption causes spike of insulin release to restore blood glucose to 100 mg/100 ml



Glucose Tolerance Test: Type 1 Diabetes

Lack of insulin causes chronically elevated glucose and prolonged rise after ingesting glucose





Glucose Tolerance Test: Type 2 Diabetes (early stage)

Insulin resistance causes prolonged rise in insulin & glucose after ingesting glucose