Anatomy of Digestive System
Peristalsis
Stomach and Acid Secretion
Liver and Bile Secretion

Pancreas and pancreatic juice
Pancreas and glucose regulation (19.3 & 19.4)

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 (HCO3-) + 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.

Acinar: raspberry
- zyme: related to enzymes (from Greek "to leaven")
Exocrine Pancreas: Acinar cells

- Zymogen granules
- Bicarbonate
- Inactive enzymes
- Acinar cells

To pancreatic duct and duodenum
Pancreatic enzymes digest many types of macromolecules: proteins, lipids, starch, nucleic acids

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Zymogen</th>
<th>Activator</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trypsin</td>
<td>Trypsinogen</td>
<td>Enterokinase</td>
<td>Cleaves internal peptide bonds</td>
</tr>
<tr>
<td>Chymotrypsin</td>
<td>Chymotrypsinogen</td>
<td>Trypsin</td>
<td>Cleaves internal peptide bonds</td>
</tr>
<tr>
<td>Elastase</td>
<td>Proelastase</td>
<td>Trypsin</td>
<td>Cleaves internal peptide bonds</td>
</tr>
<tr>
<td>Carboxypeptidase</td>
<td>Procarboxypeptidase</td>
<td>Trypsin</td>
<td>Cleaves last amino acid from carboxyl-terminal end</td>
</tr>
<tr>
<td>Phospholipase</td>
<td>Phospholipase</td>
<td>Trypsin</td>
<td>Cleaves fatty acids from phospholipids such as lecithin</td>
</tr>
<tr>
<td>Lipase</td>
<td>None</td>
<td>None</td>
<td>Cleaves fatty acids from glycerol</td>
</tr>
<tr>
<td>Amylase</td>
<td>None</td>
<td>None</td>
<td>Digests starch to maltose and short chains of glucose</td>
</tr>
<tr>
<td>Cholesterol esterase</td>
<td>None</td>
<td>None</td>
<td>Releases cholesterol from its bonds with other molecules</td>
</tr>
<tr>
<td>Ribonuclease</td>
<td>None</td>
<td>None</td>
<td>Cleaves RNA to form short chains</td>
</tr>
<tr>
<td>Deoxyribonuclease</td>
<td>None</td>
<td>None</td>
<td>Cleaves DNA to form short chains</td>
</tr>
</tbody>
</table>
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.)

---

**Summary of Digestive Enzymes**

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

<table>
<thead>
<tr>
<th>Table 18.7</th>
<th>Characteristics of the Major Digestive Enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme</td>
<td>Site of Action</td>
</tr>
<tr>
<td>Salivary amylase</td>
<td>Mouth</td>
</tr>
<tr>
<td>Pepsin</td>
<td>Stomach</td>
</tr>
<tr>
<td>Pancreatic amylase</td>
<td>Duodenum</td>
</tr>
<tr>
<td>Trypsin, chymotrypsin, carboxypeptidase</td>
<td>Small intestine</td>
</tr>
<tr>
<td>Pancreatic lipase</td>
<td>Small intestine</td>
</tr>
<tr>
<td>Maltase</td>
<td>Small intestine</td>
</tr>
<tr>
<td>Sucrase</td>
<td>Small intestine</td>
</tr>
<tr>
<td>Lactase</td>
<td>Small intestine</td>
</tr>
<tr>
<td>Aminopeptidase</td>
<td>Small intestine</td>
</tr>
</tbody>
</table>
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
hemia-related to blood
euglycemia - normal blood glucose level
hypoglycemia - lowered blood glucose
hyperglycemia - elevated blood glucose
insula - island (as insulin is hormone from pancreatic islets)
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
Glucose Polymers

- Amylose
- Amylopectin

Starch  
Glycogen  
Cellulose (fiber)

Digestion & Absorption  
e.g. Glucose

Processing & Storage

Hepatic Portal Vein  
Liver

to heart & tissues

from heart

Intestine

Liver

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

Digested & Absorption  
e.g. Glucose

Processing & Storage

Hepatic Portal Vein  
Liver

to heart & tissues

from heart

Intestine

between meals, glycogen → glucose and released into blood
Insulin: hormone that decreases blood glucose levels

Body cells take up more glucose.

Liver takes up glucose and stores it as glycogen.

Beta cells of pancreas release insulin into the blood.

Homeostasis: Blood glucose level (about 90 mg/100 mL)

Blood glucose level declines.

STIMULUS: Blood glucose level rises.

Glucose from food

Glucagon: hormone that increases blood glucose levels

Homeostasis: Blood glucose level (about 90 mg/100 mL)

Blood glucose level rises.

STIMULUS: Blood glucose level falls.

Liver breaks down glycogen and releases glucose.

Alpha cells of pancreas release glucagon.

Glucagon

Body cells take up more glucose.

Liver takes up glucose and stores it as glycogen.

Beta cells of pancreas release insulin into the blood.

Homeostasis: Blood glucose level (about 90 mg/100 mL)

Blood glucose level declines.

STIMULUS: Blood glucose level rises.

Alpha cells of pancreas release glucagon.
Insulin & Glucose profile after a meal

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

Regulation of Beta Cells:
increase insulin secretion

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

Table 19.4

<table>
<thead>
<tr>
<th>Hormones</th>
<th>Blood Glucose</th>
<th>Carbohydrate Metabolism</th>
<th>Protein Metabolism</th>
<th>Lipid Metabolism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin</td>
<td>Decreased</td>
<td>T Glycogen formation</td>
<td>T Protein synthesis</td>
<td>T Lipogenesis</td>
</tr>
<tr>
<td>Glucagon</td>
<td>Increased</td>
<td>J Glucagon formation</td>
<td>No direct effect</td>
<td>J Lipogenesis</td>
</tr>
<tr>
<td>Growth hormone</td>
<td>Increased</td>
<td>T Glycogen formation</td>
<td>T Protein synthesis</td>
<td>T Lipogenesis</td>
</tr>
<tr>
<td>Glucocorticoids (hydrocortisone)</td>
<td>Increased</td>
<td>T Glucocorticoids</td>
<td>T Protein synthesis</td>
<td>T Lipogenesis</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>Increased</td>
<td>T Glucagon formation</td>
<td>T Protein synthesis</td>
<td>T Lipogenesis</td>
</tr>
<tr>
<td>Thyroid hormones</td>
<td>No effect</td>
<td>T Glucocorticoids</td>
<td>No direct effect</td>
<td>T Lipogenesis</td>
</tr>
</tbody>
</table>
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
Type II Diabetes: obesity causes insulin receptors to stop functioning

Body cells take up more glucose.

Insulin

Beta cells of pancreas release insulin into the blood.

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.