Introduction to the Biochemistry of Digestion, Absorption and Detoxification

Digestion is the chemical breakdown of large food molecules into smaller molecules that can be used by cells. The breakdown occurs when certain specific enzymes are mixed with the food.

Main components of food are:

Carbohydrates

1. **Monosaccharides** or simple sugars are either hexoses (6-carbon) like glucose, galactose and fructose, or pentoses (5-carbon) like ribose. These are the breakdown products of more complex carbohydrates and can be efficiently absorbed across the wall of the digestive tube and transported into blood.

2. **Disaccharides** are simply two monosaccharides linked together by a glycosidic bond. The disaccharides most important in nutrition and digestion are:
   - lactose or "milk sugar": glucose + galactose
   - sucrose or "table sugar": glucose + fructose
   - maltose: glucose + glucose
   - Oligosaccharides are relatively short chains of monosaccharides which typically are intermediates in the breakdown of polysaccharides to monosaccharides.

3. **Polysaccharides**:
   - Starch is a major plant storage form of glucose. It occurs in two forms:
   - alpha-amylose, in which the glucoses are linked together in straight chains,
• and amylopectin, in which the glucose chains are highly branched. Except for the branch points of amylopectin, the glucose monomers in starch are linked via alpha(1->4) glycosidic bonds, which, in the digestive tract of mammals, are hydrolyzed by amylases.

• Dietary fibers (Cellulose) is the other major plant carbohydrate. It is the major constituent of plant cell walls, and more than half of the organic carbon on earth is found in cellulose. Cellulose is composed of unbranched, linear chains of D-glucose molecules, linked to one another by beta(1->4) glycosidic bonds, which no vertebrate has the capacity to enzymatically digest.

Overview of carbohydrate digestion. **Digestion** of the carbohydrates occurs first, followed by **absorption** of monosaccharides. Subsequent **metabolic** reactions occur after the sugars are absorbed.
Clinical cases in carbohydrate digestion and absorption:

1. **Deria Voider** is a 20-year-old exchange student from Nigeria who has noted gastrointestinal bloating, abdominal cramps, and intermittent diarrhea ever since arriving in the United States 6 months earlier. A careful history shows that these symptoms occur most commonly about 45 minutes to 1 hour after eating breakfast but may occur after other meals as well. Dairy products, not a part of Deria’s diet in Nigeria, were identified as the probable offending agent because her gastrointestinal symptoms disappeared when milk and milk products were eliminated from her diet.

2. **Ann Sulin**’s fasting and postprandial blood glucose levels are frequently above the normal range in spite of good compliance with insulin therapy. Her physician has referred her to a dietician skilled in training diabetic patients in the successful application of an appropriate American Diabetes Association diet. As part of the program, Ms. Sulin is asked to incorporate foods containing fiber into her diet, such as whole grains (e.g., wheat, oats, corn), legumes (e.g., peas, beans, lentils), tubers (e.g., potatoes, peanuts), and fruits.

3. **Nona Melos** (no sweets) is a 7-month-old baby girl, the second child born to unrelated parents. Her mother had a healthy, full-term pregnancy, and Nona’s birth weight was normal. She did not respond well to breastfeeding and was changed entirely to a formula based on cow’s milk at 4 weeks. Between 7 and 12 weeks of age, she was admitted to the hospital twice with a history of screaming after feeding but was discharged after observation without a specific diagnosis. Elimination of cow’s milk from her diet did not relieve her symptoms; Nona’s mother reported that the screaming bouts were worse after Nona drank juice and that Nona frequently had gas and a distended abdomen. At 7 months she was still thriving (weight above 97th percentile) with no abnormal findings on physical examination. A stool sample was taken.
Proteins

Proteins are polymers of amino acids linked together by peptide bonds. Chain length varies tremendously and many dietary proteins have been modified after translation by addition of carbohydrate (glycoproteins) or lipid (lipoprotein) moieties. Very short proteins, typically 3 to 10 amino acids in length, are called peptides.

Digestion of proteins. The proteolytic enzymes, pepsin, trypsin, chymotrypsin, elastase, and the carboxypeptidases, are produced as zymogens (the [pro] and [ogen] accompanying the enzyme name) that are activated by cleavage after they enter the gastrointestinal lumen.
Clinical cases in protein digestion and absorption:

1. **Sissy Fibrosa**, a young child with cystic fibrosis, has had repeated bouts of bronchitis caused by *Pseudomonas aeruginosa*. With each of these infections, her response to aerosolized antibiotics has been good. However, her malabsorption of food continues, resulting in foul-smelling, glistening, bulky stools. Her growth records show a slow decline. She is now in the 24th percentile for height and the 20th percentile for weight. She is often listless and irritable, and she tires easily. When her pediatrician discovered that her levels of the serum proteins albumin, transferrin, and thyroid hormone binding prealbumin (transthyretin) were low to low-normal (indicating protein malnutrition), Sissy was given enteric-coated microspheres of pancreatic enzymes. Almost immediately, the character of Sissy’s stools became more normal and she began gaining weight. In the next 6 months, her growth curves showed improvement, and she seemed brighter, more active, and less irritable.

2. For the first few months after a painful episode of renal colic, during which he passed a kidney stone, **Cal Kulis** had faithfully maintained a high daily fluid intake and had taken the medication required to increase the pH of his urine. Because he has cystinuria, these measures were necessary to increase the solubility of the large amounts of cystine present in his urine and, thereby, to prevent further formation of kidney stones (calculi). With time, however, he became increasingly complacent about his preventive program. After failing to take his medication for a month, he experienced another severe episode of renal colic with grossly bloody urine. Fortunately, he passed the stone spontaneously, after which he vowed to faithfully comply with therapy. His mother heard that some dietary amino acids were not absorbed in patients with cystinuria and asked whether any dietary changes would reduce Cal's chances of developing additional renal stones.
**Lipids**

Fatty acids are present in only small amounts in animal and plant tissues, but are the building blocks of many important complex lipids. True fatty acids possess a long hydrocarbon chain terminating in a carboxyl group. Nearly all fatty acids have an even number of carbons and have chains between 14 and 22 carbons in length. The principle differences among the many fatty acids are the length of the chain (usually 16 or 18 carbons) and the positions of unsaturated or double bonds.

The most abundant storage form of fat in animals and plants, and hence the most important dietary lipid, is triglyceride. A molecule of triglyceride is composed of a molecule of glycerol in which each of the three carbons is linked through an ester bond to a fatty acid. Triglycerides cannot be efficiently absorbed, and are enzymatically digested by pancreatic lipase into a 2-monoglyceride and two free fatty acids, all of which can be absorbed. Other lipases hydrolyse a triglyceride into glycerol and three fatty acids.

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\text{fats} \rightarrow \text{fatty acids and glycerol}
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\[
\begin{align*}
\text{fats} & \quad \text{lipase - pancreas} \\
\text{glycerol} & \quad + \\
\text{fatty acids} &
\end{align*}
\]
Clinical cases in lipid digestion and absorption:

1. **Will Michael** had several episodes of mild back and lower extremity pain over the last year, probably caused by minor sickle cell crises. He then developed severe right upper abdominal pain radiating to his lower right chest and his right flank 36 hours before admission to the emergency room. He states that the pain is not like his usual crisis pain. Intractable vomiting began 12 hours after the onset of these new symptoms. He reports that his urine is the color of iced tea and his stool now has a light clay color. On physical examination, his body temperature is slightly elevated, and his heart rate is rapid. The whites of his eyes (the sclerae) are obviously jaundiced (a yellow discoloration caused by the accumulation of bilirubin pigment). He is exquisitely tender to pressure over his right upper abdomen. The emergency room physician suspects that Michael is not in sickle cell crisis but instead has either acute cholecystitis (gallbladder inflammation) or a gallstone lodged in his common bile duct, causing cholestasis (the inability of the bile from the liver to reach his small intestine). His hemoglobin level was low at 7.6 mg/dL (reference range _12–16) but unchanged from his baseline 3 months earlier. His serum total bilirubin level was 3.2 mg/dL (reference range _ 0.2–1.0), and his direct (conjugated) bilirubin level was 0.9 mg/dL (reference range _0 –0.2). Intravenous fluids were started, he was not allowed to take anything by mouth, a nasogastric tube was passed and placed on constant suction, and symptomatic therapy was started for pain and nausea. When his condition had stabilized, Michael was sent for an ultrasonographic (ultrasound) study of his upper abdomen.

2. **Al Martini** has continued to abuse alcohol and to eat poorly. After a particularly heavy intake of vodka, a steady severe pain began in his upper mid-abdomen. This pain spread to the left upper quadrant and eventually radiated to his mid-back. He began vomiting nonbloody material and was brought to the hospital emergency room with fever, a rapid heart beat, and a mild reduction in blood pressure. On physical examination, he was dehydrated and tender to pressure over the upper abdomen. His vomitus and stool were both negative for occult blood. Blood samples were sent to the laboratory for a variety of hematologic and chemical tests, including a measurement of serum amylase and lipase, digestive enzymes normally secreted from the exocrine pancreas through the pancreatic ducts into the lumen of the small intestine.
The process of digestion produces glucose, amino acids, glycerol, and fatty acids (see above). The energy in glucose is used to produce ATP via the reactions of glycolysis, cellular respiration, and the electron transport system (see diagram below). The body uses amino acids to construct proteins. Excess amino acids can be used to synthesize pyruvate, acetyl CoA, and alpha ketogluterate, which enters the Krebs cycle. Glycerol and fatty acids can be converted to pyruvate and Acetyl CoA and then enter cellular respiration.
Mouth
Chewing breaks food into smaller particles so that chemical digestion can occur faster.

- **Enzymes:** *Salivary amylase* breaks starch (a polysaccharide) down to maltose (a disaccharide).
- Bicarbonate ions in saliva act as buffers, maintaining a pH between 6.5 and 7.5.
- Mucins (mucous) lubricate and help hold chewed food together in a clump called a bolus.

Stomach
The stomach stores up to 2 liters of food. Gastric glands within the stomach produce secretions called *gastric juice.*
The muscular walls of the stomach contract vigorously to mix food with gastric juice, producing a mixture called *chyme.*

**Gastric juice**
- **Pepsinogen** is converted to pepsin, which digests proteins. Pepsinogen production is stimulated by the presence of gastrin in the blood.
- **HCl**
  Hydrochloric acid (HCl) converts pepsinogen to *pepsin* which breaks down proteins to peptides. HCl maintains a pH in the stomach of approximately 2.0.
  It also dissolves food and kills microorganisms.

*Mucous* protects the stomach from HCl and pepsin.

**Secretion of Gastric Juice: Gastrin** is a hormone that stimulates the stomach to secrete gastric juice.

Duodenum
The duodenum is the first part of the small intestine.
Chyme enters in tiny spurts. At this point, proteins and carbohydrates are only partially digested and lipid digestion has not begun.
Pancreas
The pancreas acts as an exocrine gland by producing *pancreatic juice* which empties into the small intestine via a duct. The pancreas also acts as an endocrine gland to produce insulin.

- **Pancreatic Juice**
  Pancreatic juice contains sodium bicarbonate which neutralizes the acidic material from the stomach.
  - *Pancreatic amylase* digests starch to maltose.
  - *Trypsin* and *Chymotrypsin* digest proteins to peptides. Like pepsin (produced in the stomach), they are specific for certain amino acids, not all of them. They therefore produce peptides.
  - *Lipase* digests fats to glycerol and fatty acids.

Liver
The liver produces *bile* which is stored in *gallbladder* and sent to the duodenum through a duct.
Bile emulsifies fats (separates it into small droplets) so they can mix with water and be acted upon by enzymes.

**Other Functions of the Liver**
- The liver detoxifies blood from intestines that it receives via the hepatic portal vein.
- The liver stores glucose as glycogen (animal starch) and breaks down glycogen to release glucose as needed. This storage-release process maintains a constant glucose concentration in the blood (0.1%). If glycogen and glucose run short, proteins can be converted to glucose.
- It produces blood proteins.
- It destroys old red blood cells and converts hemoglobin from these cells to bilirubin and biliverdin which are components of bile.
- Ammonia produced by the digestion of proteins is converted to a less toxic compound (urea) by the liver.

Hormones Involved in Digestion
1. **Gastrin**: The presence of food in the stomach stimulates specific receptors which in turn stimulates endocrine cells in the stomach to secrete the hormone *gastrin* into the circulatory system. Gastrin stimulates the stomach to secrete gastric juice.

2. **Secretin**: Secretin is produced by cells of the duodenum. It’s production is stimulated by acid chyme from stomach. It stimulates the pancreas to produce sodium bicarbonate, which neutralizes the acidic chyme. It also stimulates the liver to secrete bile.

3. **CCK (cholecystokinin)**: CCK production is stimulated by the presence of food in the duodenum. It stimulates the gallbladder to release bile and the pancreas to produce pancreatic enzymes.

4. **GIP (Gastric Inhibitory Peptide)**: Food in the duodenum stimulates certain endocrine cells to produce GIP. It has the opposite effects of gastrin; it inhibits gastric glands in the stomach and it inhibits the mixing and churning movement of stomach muscles. This slows the rate of stomach emptying when the duodenum contains food.

**Small Intestine**

The small intestine is approximately 3 m long. Like the stomach, it contains numerous ridges and furrows. In addition, there are numerous projections called **villi** that function to increase the surface area of the intestine. Individual villus cells have **microvilli** which greatly increase absorptive surface area. The total absorptive surface area is equivalent to 500 or 600 square meters.

Each villus contains blood vessels and a **lacteal** (lymph vessel). Peptidases and maltase are embedded within the plasma membrane of the microvilli. **Peptidases** complete the digestion of peptides to amino acids. **Maltase** completes the digestion of disaccharides.

**Absorption:**
The Large Intestine:
It functions in three processes:

- **Recovery of water and electrolytes from ingesta**: By the time ingesta reaches the terminal ileum, roughly 90% of its water has been absorbed, but considerable water and electrolytes like sodium and chloride remain and must be recovered by absorption in the large gut.

- **Formation and storage of feces**: As ingesta is moved through the large intestine, it is dehydrated, mixed with bacteria and mucus, and formed into feces.

- **Microbial fermentation**: The large intestine of all species teems with microbial life. Those microbes produce enzymes capable of digesting many of molecules that to vertebrates are indigestible, cellulose being a premier example. **Absorption**: water, sodium ions and chloride ions

- **Secretion**: bicarbonate ions and mucus

Summary of Digestive Enzymes

The digestive enzymes in the table below are summarized according to type of food that they digest.
### The table below shows digestive enzymes grouped by source of the enzyme.

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>ENZYME</th>
<th>FOOD</th>
<th>PRODUCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>MOUTH (salivary glands)</td>
<td>Salivary amylase</td>
<td>Polysaccharides</td>
<td>Maltose</td>
</tr>
<tr>
<td></td>
<td>Salivary amylase</td>
<td></td>
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<tr>
<td>STOMACH</td>
<td>Pepsin</td>
<td>Proteins</td>
<td>Peptides</td>
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<tr>
<td>PANCREAS</td>
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<tr>
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<td>Trypsin</td>
<td>Proteins</td>
<td>Peptides</td>
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<td>Lipase</td>
<td>Fats</td>
<td>Fatty acids and glycerol</td>
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<td>Peptidases</td>
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