3 Macronutrient Digestion*

You probably don't think too much about what actually happens to the taco you eat for lunch. This section will describe in depth how that taco is digested. The desired end result for the learner will be an integrated understanding of the process. This will require higher levels of thinking, but will prove to be well worth it in the end.

Sections:

3.1 Digestion at a Glance
3.2 Mouth to the Stomach
3.3 Stomach
3.4 Small Intestine
3.5 Macronutrient Digestion Review
3.6 Large Intestine

References and Links

Students – I included the entire chapter so that you get a full picture of the process – this is MORE reading than required but may of you asked for the complete textbook. I have noted key terms to study and made note of sections NOT to spend a lot of time on.

Dr von Castel-Roberts
3.1 Digestion at a Glance

Digestion is the process of breaking down food to be absorbed or excreted. The gastrointestinal (GI, digestive) tract, the passage through which our food travels, is a "tube within a tube." The trunk of our body is the outer tube and the GI tract is the interior tube, as shown below. Thus, even though the GI tract is within the body, the actual interior of the tract is technically outside of the body. This is because the contents have to be absorbed into the body. If it's not absorbed, it will be excreted and never enter the body itself.

Figure 3.11 The digestive tract, also known as the gastrointestinal tract, is a "tube within a tube"

A number of organs are involved in digestion, which collectively are referred to as the digestive system.
The organs that form the gastrointestinal tract (mouth, esophagus, stomach, small intestine, large intestine (aka colon), rectum, and anus) come into direct contact with the food or digestive content.

The journey through the gastrointestinal tract starts in the mouth and ends in the anus as shown below:
Know this order if the tract

Mouth --> Esophagus --> Stomach --> Small Intestine --> Large Intestine --> Rectum --> Anus

In addition to the GI tract, there are digestion accessory organs (salivary glands, pancreas, gallbladder, and liver) that play an integral role in digestion. The accessory organs do not come directly in contact with food or digestive content.

Figure 3.14 Digestion accessory organs

There are a number of enzymes that are involved in digestion. We will go through each one in detail, but this table should help give an overview of which enzymes are active at each location of the GI tract.

Table 3.11 Digestive enzymes

<table>
<thead>
<tr>
<th>Location</th>
<th>Enzyme/Coenzyme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mouth</td>
<td>Salivary amylase</td>
</tr>
<tr>
<td></td>
<td>Lingual lipase</td>
</tr>
<tr>
<td></td>
<td>Lysozyme</td>
</tr>
<tr>
<td>Stomach</td>
<td>pepsin</td>
</tr>
<tr>
<td></td>
<td>gastric lipase</td>
</tr>
</tbody>
</table>
Check Yourself
Name the organs that are involved in digestion but are *not* part of the GI tract.

References & Links

Videos
Enzymes and Digestion - http://www.youtube.com/watch?v=bNMsnHqxszc
3.2 Mouth to the Stomach

Digestion begins in the mouth, both mechanically and chemically. Mechanical digestion is called mastication, or the chewing and grinding of food into smaller pieces. The salivary glands release saliva, mucus, and the enzymes, salivary amylase and lysozyme.

Figure 3.21 The mouth

Salivary amylase cleaves the alpha 1-4 glycosidic bonds in the starch molecules, amylose and amylopectin. However, salivary amylase cannot cleave the branch points in amylopectin where there are alpha 1-6 glycosidic bonds, as shown in the figure below. Overall this enzyme accounts for a minor amount of carbohydrate digestion.

Figure 3.22 Enzymatic action of salivary amylase. Purple arrows point to alpha 1-4 glycosidic bonds that can be cleaved. The yellow arrows point to the alpha 1-6 glycosidic bonds that cannot be cleaved.
Lysozyme helps break down bacteria cell walls to prevent a possible infection. Another enzyme, lingual lipase, is also released in the mouth. Although it is released in the mouth, it is most active in the stomach where it preferentially cleaves short-chain fatty acids in the sn-3 position. Lingual lipase has a small role in digestion in adults, but may be important for infants to help break down triglycerides in breast milk.

Check Yourself

What macronutrients are digested in our mouth? By what enzymes?

Swallowing

Now that the food has been thoroughly chewed and formed into a bolus, it can proceed down the throat to the next stop in digestion. It will move down the pharynx where it reaches a "fork in the road", with the larynx as one road and the esophagus as the other. The esophagus road leads to the stomach; this is the direction that food should go. The other road, through the larynx, leads to the trachea and ultimately the lungs. This is definitely not where you want your food or drink going, as this is the pathway for the air you breathe.

Key terms:
Bolus
Epiglottis

Fortunately, our body was designed in such a way that a small tissue, called the epiglottis, covers the opening to the trachea. It directs the food down the correct road as shown below.
Esophagus

Before being correctly guided into the esophagus, the bolus of food will travel through the upper esophageal sphincter. Sphincters are circular muscles that are found throughout the gastrointestinal tract that essentially serve as gates between the different sections. Once in the esophagus, wavelike muscular movements, known as peristalsis, occur, as shown in the animation & video in the links below.

Web Links

- Peristalsis Animation
- Video: Peristalsis (0:57)

Recognise the job of sphincters - know there is one at the top and one at the bottom of the esophagus.
Key term = peristalsis

At the end of the esophagus the bolus will encounter the lower esophageal sphincter. This sphincter keeps the harmful acids of the stomach out of the esophagus. However, in many people this sphincter is leaky, which allows stomach acid to reflux, or creep up, the esophagus. Stomach acid is very acidic (has a low pH). The ruler below will give you an idea of just how acidic the stomach is. Notice that the pH of gastric (term used to describe the stomach) fluid is lower (more acidic) than any of the listed items besides battery acid.
The leaking of the very acidic gastric contents results in a burning sensation, commonly referred to as "heartburn." If this occurs more than twice per week and is more severe, the person may have gastroesophageal reflux disease (GERD). The following videos explain more about these conditions.

**Web Links**

**Video:** Acid Reflux (1:28)

**Video:** GERD 101 (0.55)

**Table 3.21 Review of Chemical Digestion in the Mouth**

<table>
<thead>
<tr>
<th>Macronutrient</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrates</td>
<td>Salivary amylase cleaves 1,4-glycosidic bonds</td>
</tr>
<tr>
<td>Lipids</td>
<td>Release of lingual lipase</td>
</tr>
<tr>
<td>Protein</td>
<td>None</td>
</tr>
</tbody>
</table>

**References & Links**

3.3 Stomach

After going through the lower esophageal sphincter, the food enters the stomach. Our stomach is involved in both chemical and mechanical digestion. Mechanical digestion occurs as the stomach churns and grinds food into a semisolid substance called chyme (partially digested food).

The lining of the stomach is made up of different layers of tissue. The mucosa is the outermost layer (closest to stomach cavity) as shown in the figure below.

**Stomach**

![Stomach Diagram]

Figure 3.31 The anatomy of the stomach\(^1\)

The mucosa is not a flat surface. Instead, its surface is lined by gastric pits, as shown in the figure below.

**Key terms**

- Mucosa
- Chyme
Gastric pits are indentations in the stomach's surface that are lined by four different types of cells.

The following video is a nice introduction to gastric pits and talks about chief and parietal cells that are covered in more detail below.

Web Link

Video: Gastric Pits (0:56)
At the bottom of the gastric pit are the G cells that secrete the hormone gastrin. Gastrin stimulates the parietal and chief cells that are found above the G cells. The chief cells secrete the zymogen pepsinogen and the enzyme gastric lipase. A zymogen is an inactive precursor of an enzyme that must be cleaved or altered to form the active enzyme. The parietal cells secrete hydrochloric acid (HCl), which lowers the pH of the gastric juice (water + enzymes + acid). The HCl inactivates salivary amylase and catalyzes the conversion of pepsinogen to pepsin. Finally, the top of the pits are the neck cells that secrete mucus to prevent the gastric juice from digesting or damaging the stomach mucosa. The table below summarizes the actions of the different cells in the gastric pits.

**Table 3.41 Cells involved in the digestive processes in the stomach**

<table>
<thead>
<tr>
<th>Type of Cell</th>
<th>Secrete</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neck</td>
<td>Mucus</td>
</tr>
<tr>
<td>Chief</td>
<td>Pepsinogen and gastric lipase</td>
</tr>
<tr>
<td>Parieta</td>
<td>HCl</td>
</tr>
<tr>
<td>G</td>
<td>Gastrin</td>
</tr>
</tbody>
</table>

The figure below shows the action of all these different secretions in the stomach.

![Figure 3.34 The action of gastric secretions in the stomach](image)

To reiterate, the figure above illustrates that the neck cells of the gastric pits secrete mucus to protect the mucosa of the stomach from essentially digesting itself. Gastrin from the G cells stimulates the parietal and chief cells to secrete HCl and enzymes, respectively.

The HCl in the stomach denatures salivary amylase and other proteins by breaking down the structure and, thus, the function of it. HCl also converts pepsinogen to the active enzyme...
pepsin. Pepsin is a protease, meaning that it cleaves bonds in proteins. It breaks down the proteins in food into individual peptides (shorter segments of amino acids). The other enzyme that is active in the stomach is gastric lipase. This enzyme preferentially cleaves the sn-3 position of triglycerides to produce 1,2-diglyceride and a free fatty acid, as shown below. It is responsible for up to 20% of triglyceride digestion.

![Figure 3.35 Gastric Lipase action results in production of 1,2-diglyceride and a free fatty acid](image)

The chyme will then leave the stomach and enter the small intestine via the pyloric sphincter (shown below).

![Figure 3.36 Cross section of the stomach showing the pyloric sphincter](image)

<table>
<thead>
<tr>
<th>Table 3.32 Summary of chemical digestion in the stomach</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chemical or Enzyme</strong></td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td>Gastrin</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Compound</td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>HCl</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Pepsin</td>
</tr>
<tr>
<td>Gastric lipase</td>
</tr>
</tbody>
</table>

**References & Links**

**Video**
Gastric Pits - http://www.youtube.com/watch?v=6hquzCXYiNg
3.4 Small Intestine

The small intestine is the primary site of digestion. It is divided into three sections: the duodenum, jejunum, and ileum (shown below). After leaving the stomach, the first part of the small intestine that chyme will encounter is the duodenum.

Key Terms:
Duodenum
Jejunum
Ileum

Figure 3.41 Three sections of the small intestine

The small intestine consists of many layers, which can be seen in the cross section below.

Key terms:
Chyme
Lumen

Figure 3.42 Cross section of the small intestine

Examining these layers closer, we are going to focus on the epithelium, which comes into contact with the chyme and is responsible for absorption. The area contained within the epithelium is the lumen (area considered outside the body).
The organization of the small intestine is in such a way that it contains circular folds and finger-like projections known as villi. The folds and villi are shown in the next few figures.

Figure 3.43 Cross section of small intestine with the structures labeled

Figure 3.44 Folds in the small intestine

Key concept - muscular movement controls the movement of digested food

Key term = villi
Figure 3.45 Villi in the small intestine

Figure 3.46 Villi line the surface of the small intestine

If we were to zoom in even closer, we would be able to see that enterocytes (small intestine absorptive cells) line villi as shown below.
Figure 3.47 Enterocytes line villi

The side, or membrane, of the enterocyte that faces the lumen is not smooth either. It is lined with microvilli, and is known as the brush border (aka apical) membrane, as shown below.

Figure 3.48 Enterocyte, or small intestinal absorptive cell is lined with microvilli. This lined surface is referred to as the brush border membrane

Together these features (folds + villi + microvilli) increase the surface area ~600 times versus if it was a smooth tube. More surface area leads to more contact with the enterocytes and thus, increased absorption.

Going even closer, we discover that the surface of the microvilli is covered by the hair-like glycocalyx, which is glycoproteins and carbohydrates as shown below.
Now that we’ve set up the anatomy of the small intestine, the following subsections go through the its different digestive processes.

Subsections:

3.41 Digestive Hormones, Accessory Organs, & Secretions
3.42 Carbohydrate Digestion in the Small Intestine
3.43 Protein Digestion in the Small Intestine
3.44 Lipid Digestion in the Small Intestine

References & Links
1. http://commons.wikimedia.org/wiki/Image:Illu_small_intestine_catal%C3%A0.png
3.41 Digestive Hormones, Accessory Organs, & Secretions

Before we go into the digestive details of the small intestine, it is important that you have a basic understanding of the anatomy and physiology of the following digestion accessory organs: pancreas, liver, and gallbladder. Digestion accessory organs assist in digestion, but are not part of the gastrointestinal tract. How are these organs involved?

Upon entering the duodenum, the chyme causes the release of two hormones from the small intestine: secretin and cholecystokinin (CCK, previously known as pancreozymin) in response to acid and fat, respectively. These hormones have multiple effects on different tissues. In the pancreas, secretin stimulates the secretion of bicarbonate (HCO₃⁻), while CCK stimulates the secretion of digestive enzymes. The bicarbonate and digestive enzymes released together are collectively known as pancreatic juice, which travels to the small intestine, as shown below.

![Figure 3.411](image_url) The hormones secretin and CCK stimulate the pancreas to secrete pancreatic juice.

In addition, CCK also stimulates the contraction of the gallbladder causing the secretion of bile into the duodenum.

Pancreas  Key terms: Insulin, glucagon

The pancreas is found behind the stomach and has two different portions. It has an endocrine (hormone-producing) portion that contains alpha and beta cells that secrete the hormones glucagon and insulin, respectively. However, the vast majority of the pancreas is made up of acini, or acinar cells, that are responsible for producing pancreatic juice. The following video does a nice job of showing and explaining the function of the different pancreatic cells.

Web Link

*Video: Dual Role of the Pancreas (2:05)*
Bicarbonate is a base (high pH) meaning that it can help neutralize acid. You can find sodium bicarbonate (NaHCO₃, baking soda) on the ruler below to get an idea of its pH.

![pH of some common items](image)

Figure 3.412 pH of some common items²

The main digestive enzymes in pancreatic juice are listed in the table below. Their function will be discussed further in later subsections.

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Understand main grouping of enzymes: Lipase, amylase, protease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatic alpha-amylase</td>
<td></td>
</tr>
<tr>
<td>Proteases</td>
<td></td>
</tr>
<tr>
<td>Pancreatic Lipase &amp; Procolipase*</td>
<td></td>
</tr>
<tr>
<td>Phospholipase A₂</td>
<td></td>
</tr>
<tr>
<td>Cholesterol Esterase</td>
<td></td>
</tr>
</tbody>
</table>

*Not an enzyme

Liver  Understand liver's very important role in nutrient processing overall

The liver is the largest internal and most metabolically active organ in the body. The figure below shows the liver and the accessory organs position relative to the stomach.
The liver is made up two major types of cells. The primary liver cells are hepatocytes, which carry out most of the liver’s functions. Hepatic is another term for liver. For example, if you are going to refer to liver concentrations of a certain nutrient, these are often reported as hepatic concentrations. The other major cell type is the hepatic stellate (aka Ito) cells. These are fat storing cells in the liver. These two cell types are depicted below.

The liver's major role in digestion is to produce bile. This is a greenish-yellow fluid that is composed primarily of bile acids, but also contains cholesterol, phospholipids, and the pigments bilirubin and biliverdin. Bile acids are synthesized from cholesterol. The two primary bile acids are chenodeoxycholic acid and cholic acid. In the same way that fatty acids are found in the form of salts, these bile acids can also be found as salts. These salts have an (-ate) ending, as shown below.
Bile acids, much like phospholipids, have a hydrophobic and hydrophilic end. This makes them excellent emulsifiers that are instrumental in fat digestion. Bile is then transported to the gallbladder.

Understand: Bile made in liver, stored in Gallbladder and what Gallbladder bile does

The gallbladder is a small, sac-like organ found just off the liver (see figures above). Its primary function is to store and concentrate bile made by the liver. The bile is then transported to the duodenum through the common bile duct (Figure 3.412).

Why do we need bile?

Bile is important because fat is hydrophobic and the environment in the lumen of the small intestine is watery. In addition, there is an unstirred water layer that fat must cross to reach the enterocytes in order to be absorbed.
Here triglycerides form large triglyceride droplets to keep the interaction with the watery environment to a minimum. This is inefficient for digestion, because enzymes cannot access the interior of the droplet. Bile acts as an emulsifier, or detergent. It, along with phospholipids, forms smaller triglyceride droplets that increased access for triglyceride digestive enzymes, as indicated below.

![Diagram showing triglyceride droplets and bile emulsifiers](image)

These are also called Micelles

Figure 3.417 Bile acids and phospholipids facilitate the production of smaller triglyceride droplets

Secretin and CCK also control the production and secretion of bile. Secretin stimulates the flow of bile from the liver to the gallbladder. CCK stimulates the gallbladder to contract, causing bile to be secreted into the duodenum, as shown below.
Figure 3.418 Secretion stimulates bile flow from liver; CCK stimulates the gallbladder to contract.  

**References & Links**  
4. http://www.comparative-hepatology.com/content/6/1/7  

**Video**  
Dual Role of the Pancreas - http://www.youtube.com/watch?v=jOH2MU00g1M
3.42 Carbohydrate Digestion in the Small Intestine

The small intestine is the primary site of carbohydrate digestion. Pancreatic alpha-amylase is the primary carbohydrate digesting enzyme. Pancreatic alpha-amylase, like salivary amylase, cleaves the alpha 1-4 glycosidic bonds of carbohydrates, reducing them to simpler carbohydrates, such as glucose, maltose, maltotriose, and dextrins (oligosaccharides containing 1 or more alpha 1-6 glycosidic bonds). Pancreatic amylase is also unable to cleave the branch point alpha 1-6 bonds.

![Figure 3.421 The function of pancreatic amylase](http://example.com/figure3.421.png)

![Figure 3.422 Products of pancreatic amylase](http://example.com/figure3.422.png)

The pancreatic amylase products, along with the disaccharides sucrose and lactose, then move to the surface of the enterocyte. Here, there are disaccharidase enzymes (lactase, sucrase, maltase) on the outside of the enterocyte. Enzymes, like these, that are on the outside of cell walls are referred to as ectoenzymes. Individual monosaccharides are formed when lactase cleaves lactose, sucrase cleaves sucrose, and maltase cleaves maltose. There is also another brush border enzyme, alpha-dextrinase. This enzyme cleaves alpha 1-6 glycosidic bonds in dextrins, primarily the branch point bonds in amylpectin. The products from these brush border enzymes are the single monosaccharides glucose, fructose, and galactose that are ready for absorption into the enterocyte.
Figure 3.423 Disaccharidases on the outside of the enterocyte.

**References & Links**
3.43 Protein Digestion in the Small Intestine

The small intestine is the major site of protein digestion by proteases (enzymes that cleave proteins). The pancreas secretes a number of proteases as zymogens into the duodenum where they must be activated before they can cleave peptide bonds. This activation occurs through an activation cascade. A cascade is a series of reactions in which one step activates the next in a sequence that results in an amplification of the response. An example of a cascade is shown below.

Key terms: Protease, zymogen again a lot of extra detail, but do note: enzymes for protein digestion are inactive until needed and why this is important

Figure 3.431 An example of a cascade, with one event leading to many more events

In this example, A activates B, B activates C, D, & E, C activates F & G, D activates H & I, and E activates K & L. Cascades also help to serve as control points for certain process. In the protease cascade, the activation of B is really important because it starts the cascade.

The protease/collipase activation scheme starts with the enzyme enteropeptidase (secreted from the intestinal brush border) that converts trypsinogen to trypsin. Trypsin can activate all the proteases (including itself) and collipase (involved in fat digestion) as shown in the 2 figures below.
The products of the action of the proteases on proteins are dipeptides, tripeptides, and individual amino acids, as shown below.
At the brush border, much like disaccharidases, there are peptidases that cleave some peptides down to amino acids. Not all peptides are cleaved to individual amino acid, because small peptides can be taken up into the enterocyte, thus, the peptides do not need to be completely broken down to individual amino acids. Thus the end products of protein digestion are primarily dipeptides and tripeptides, along with individual amino acids\(^1\).

References & Links

### 3.44 Lipid Digestion in the Small Intestine

The small intestine is the major site for lipid digestion. There are specific enzymes for the digestion of triglycerides, phospholipids, and cleavage of esters from cholesterol. We will look at each in this section.

#### Triglycerides

The pancreas secretes pancreatic lipase into the duodenum as part of pancreatic juice. This major triglyceride digestion enzyme preferentially cleaves the sn-1 and sn-3 fatty acids from triglycerides. This cleavage results in the formation of a 2-monoglyceride and two free fatty acids as shown below.

**Figure 3.441** Pancreatic lipase cleaves the sn-1 and sn-3 fatty acids of triglycerides

**Figure 3.442** The products of pancreatic lipase are a 2-monoglyceride and two free fatty acids

To assist lipase, colipase serves as an anchor point to help lipase attach to the triglyceride droplet.
Colipase helps anchor lipase to the triglyceride droplet

**Phospholipids**

The enzyme phospholipase A$_2$ cleaves the C-2 fatty acid of lecithin, producing lysolecithin and a free fatty acid.

**Cholesterol Esters**

The fatty acid in cholesterol esters is cleaved by the enzyme, cholesterol esterase, producing cholesterol and a free fatty acid.
Figure 3.446 Cholesterol esterase cleaves fatty acids off of cholesterol

Figure 3.447 Products of cholesterol esterase

**Formation of Mixed Micelles**

If nothing else happened at this point, the 2-monoglycerides and fatty acids produced by pancreatic lipase would form micelles. The hydrophilic heads would be outward and the fatty acids would be buried on the interior. These micelles are not sufficiently water-soluble to cross the unstirred water layer to get to the brush border of enterocytes. Thus, mixed micelles are formed containing cholesterol, bile acids, and lysolecithin in addition to the 2-monoglycerides and fatty acids, as illustrated below¹.
Mixed micelles are more water-soluble, allowing them to cross the unstirred water layer to the brush border of enterocytes for absorption.

References & Links
3.5 Macronutrient Digestion Review

The following figures review the digestion of the different macronutrients.

**Carbohydrate Digestion**

![Carbohydrate Digestion Diagram](image1)

Figure 3.51 Review of carbohydrate digestion

**Protein Digestion**

![Protein Digestion Diagram](image2)

Figure 3.52 Review of protein digestion

**Lipid Digestion**
After digestion we are left with the products below that are ready for uptake into the enterocyte.
Figure 3.55 Macronutrient digestion products ready for uptake into the enterocyte

References & Links
3.6 The Large Intestine

We have reached a fork in the road. We could follow the uptake of the digested compounds into the enterocyte or we could finish following what has escaped digestion and is going to continue into the large intestine. Obviously from the title of this section we are going to do the latter. As we learned previously, fiber is a crude term for what has survived digestion and has reached the large intestine.

The ileocecal valve is the sphincter between the ileum and the large intestine. This name should make more sense as we go through the anatomy of the large intestine.

The large intestine consists of the colon, the rectum, and the anus. The colon can be further divided into the cecum (hence the -cecal in ileocecal valve, ileo- refers to ileum), ascending colon, transverse colon, descending colon, and sigmoid colon as shown below.
The large intestine is responsible for absorbing remaining water and electrolytes (sodium, potassium, and chloride). It also forms and excretes feces. The large intestine contains large amounts of microorganisms like those shown in the figure below.

The large intestine can also be referred to as the gut. There are a large number of microorganisms found throughout the gastrointestinal tract that collectively are referred to as the flora, microflora, biota, or microbiota. Technically, microbiota is the preferred term because flora means "pertaining to plants". There are 10 times more microorganisms in the gastrointestinal tract than cells in the whole human body. As can be seen in the figure below,
the density of microorganisms increases as you move down the digestive tract.

Figure 3.65 Relative amount of bacteria in selected locations of the GI tract. cfu/ml = colony forming unit, a measure of the number of live microorganisms in 1 mL of digestive sample $^5,^6$

As described in the fiber sections, there are two different fates for fiber once it reaches the large intestine. The fermentable, viscous fiber is fermented by bacteria. Fermentation is the metabolism of compounds by the microorganisms in the gut. An example of fermentation is the utilization of the oligosaccharides raffinose and stachyose by microorganisms that results in the production of gas, which can lead to flatulence. Also, some bile acids are fermented by microorganisms to form secondary bile acids that can be reabsorbed. These secondary bile acids represent approximately 20% of the total bile acids in our body. Fermentable fibers can be used to form short-chain fatty acids that can then be absorbed and used by the body. The nonfermentable, nonviscous fiber is not really altered and will be a component of feces, that is then excreted through the rectum and anus. This process involves both an internal and external sphincter that are shown in figure 3.63 above.

Subsection:

3.61 Probiotics & Prebiotics

References & Links
4 Macronutrient Uptake, Absorption, & Transport

The term absorption can have a number of different meanings. For clarity, when we refer to absorption, this is the uptake of a compound into the body's circulation. Thus, if something is taken up into the enterocyte, it is not necessarily absorbed. Hopefully after this chapter, the reasoning for this distinction will be clear.

Sections:

4.1 Crypts of Lieberkuhn & Enterocyte Maturation
4.2 Absorptive Lineup & Cell Membranes
4.3 Types of Cell Uptake/Transport
4.4 Carbohydrate Uptake, Absorption, Transport, & Liver Uptake
4.5 Protein Uptake, Absorption, Transport, & Liver Uptake
4.6 Lipid Uptake, Absorption & Transport
4.7 Glycemic Response, Insulin, & Glucagon

Just like CH 3 I will note sections and terms to know and what is extra
You do not need CH 4.4-4.7
4.1 Crypts of Lieberkuhn & Enterocyte Maturation

There are some additional anatomical and physiological features of the small intestine that are important to understand before we start talking about absorption. Crypts of Lieberkuhn are pits between villi as pointed out by the green arrow in the figure below.

![Figure 4.11 A crypt of Lieberkuhn is the pit between the villi in the small intestine as pointed out by the green arrow](image)

The crypts of Lieberkuhn (often referred to as crypts to shorten name) are similar to the gastric pits in the stomach. In the crypts are stem cells that can produce a number of different cell types, including enterocytes. Thus, immature enterocyte cells are formed that mature as they rise or migrate up the villi. Thus, the tips at the top of villi are where the mature, fully functioning enterocytes are located, as represented by the purple cells in the figure below.

![Figure 4.12 Crypts are represented by green arrows, fully mature enterocytes are represented by the purple cells at the top of the villi](image)

This maturation and migration is a continuous process. The life cycle of an enterocyte is 72 hours once it enters the villus from the crypt. At the top, enterocytes are sloughed off, and, unless they are digested (contain proteins and lipid) and components are taken up by
enterocytes still on villi, they will be excreted in feces as depicted in the figure below.

Figure 4.13 Enterocytes sloughed off the villus. Unless these cells are digested and their components are taken up by other enterocytes on the villus, they will be excreted in feces.

Thus, we define absorption as reaching body circulation, because compounds taken up into enterocytes might not make it into body circulation, and thus are not necessarily absorbed.

References & Links
4.2 Uptake Lineup & Cell Membranes

Having completed digestion in the small intestine, a number of compounds are ready for uptake into the enterocyte. The figure below shows the macronutrient uptake lineup, or what is ready to be taken up into the enterocyte.

![Figure 4.21 The macronutrient uptake lineup](image)

From lipids, we have the lysolecithin (from phospholipid), 2-monoglyceride (from triglycerides), fatty acids, and cholesterol. From protein, there are small peptides (di- and tripeptides) and amino acids. From carbohydrates, only the monosaccharides glucose, galactose, and fructose will be taken up. The other macronutrient, water, has not been discussed so far because it does not undergo digestion.

However, these compounds must now cross the plasma (cell) membrane, which is a phospholipid bilayer. In the cell membrane, the hydrophilic heads of the phospholipids point into the lumen as well as towards the interior of the cell, while the tails are on the interior of the plasma membrane as shown below.

![Figure 4.22 Plasma membrane of a cell](image)
The plasma membrane contains proteins, cholesterol, and carbohydrates in addition to the phospholipids. Membrane proteins, such as channels and pumps, are important for the transport of some compounds across the cell membrane. The figure and two videos below do a nice job of illustrating the components of the cell membrane.

![Cell membrane components diagram](image)

Figure 4.23 Cell membrane

**Web Links**

- Video: Cell Membrane (1:27)
- Video: Voyage inside the cell: Membrane (1:23)

**References & Links**

4.3 Types of Cell Uptake/Transport

There are a number of different forms of uptake/transport utilized by your body. These can be classified as passive or active. The difference between the two is whether energy is required and whether they move with or against a concentration gradient. Passive transport does not require energy and moves with a concentration gradient. Active transport requires energy to move against the concentration gradient.

The energy for active uptake/transport is provided by adenosine triphosphate (ATP), which is the energy currency in the body. ATP stores energy in its high-energy phosphate bonds. The structures of adenosine and phosphate are shown below.

![Figure 4.31 Structures of adenosine (left) and phosphate (right)](image)

Tri- means three, so ATP is adenosine with three phosphate groups bonded to it, as shown below.

![Figure 4.32 Structure of adenosine triphosphate (ATP)](image)
4.31 Passive Uptake/Transport

There are three forms of passive uptake/transport:

1. Simple Diffusion
2. Osmosis
3. Facilitated Diffusion

Below is more information of each type of uptake/transport.

1. Simple Diffusion

Simple diffusion is the movement of solutes from an area of higher concentration (with the concentration gradient) to an area of lower concentration without the help of a protein, as shown below.

![Figure 4.311 Simple diffusion](image)

2. Osmosis

Osmosis is similar to simple diffusion, but water moves instead of solutes. In osmosis water molecules move from an area of lower concentration to an area of higher concentration of solute as shown below. The effect of this movement is to dilute the area of higher concentration.
The following videos do a nice job of illustrating osmosis.

**Web Links**

- Video: Osmosis (0:47)
- Video: Osmosis in the Kitchen (0:58)

Another example illustrating osmosis is the red blood cells in different solutions shown below.

We will consider the simple example of salt as the solute. If the solution is hypertonic, that means that there is a greater concentration of salt outside (extracellular) the red blood cells.
than within them (intracellular). Water will then move out of the red blood cells to the area of higher salt concentration, resulting in the shriveled red blood cells depicted. Isotonic means that there is no difference between concentrations. There is an equal exchange of water between intracellular and extracellular fluids. Thus, the cells are normal, functioning red blood cells. A hypotonic solution contains a lower extracellular concentration of salt than the red blood cell intracellular fluid. As a result, water enters the red blood cells, possibly causing them to burst.

3. Facilitated Diffusion

The last form of passive absorption is similar to diffusion in that it follows the concentration gradient (higher concentration to lower concentration). However, it requires a carrier protein to transport the solute across the membrane. The following figure and video do a nice job of illustrating facilitated diffusion.

![Facilitated diffusion examples](attachment:image.png)

**Web Link**

*Video: Facilitated Diffusion [0:27]*)

**References & Links**

1. [Osmotic pressure on blood cells diagram](http://en.wikipedia.org/wiki/File:Osmotic_pressure_on_blood_cells_diagram.svg)

**Videos**

Osmosis - [http://www.youtube.com/watch?v=sdiJtDRjQEc](http://www.youtube.com/watch?v=sdiJtDRjQEc)
Osmosis in the Kitchen - [http://www.youtube.com/watch?v=H6N1lIjTmnc&NR=1&feature=fvwp](http://www.youtube.com/watch?v=H6N1lIjTmnc&NR=1&feature=fvwp)
Facilitated Diffusion - [http://www.youtube.com/watch?v=s0p1ztrbXPY](http://www.youtube.com/watch?v=s0p1ztrbXPY)
4.32 Active Uptake/Transport

There are two forms of active uptake/transport:

1. Active Carrier Transport
2. Endocytosis

1. Active Carrier Transport

Active carrier transport is similar to facilitated diffusion in that it utilizes a protein (carrier). However, energy is also used to move compounds against their concentration gradient. The following figure and video do a nice job of illustrating active carrier transport.

![Figure 4.321 Sodium-potassium ATPase (aka sodium-potassium pump) an example of active carrier transport](1)

**Web Link**

[Video: Active Transport (0:21)]

2. Endocytosis

Endocytosis is the engulfing of particles or fluid to be taken up into the cell. If a particle endocytosed, this is referred to as phagocytosis. If a fluid is endocytosed, then this is referred to as pinocytosis as shown below.
Figure 4.322 Different types of endocytosis

The following video does a really nice job of showing how endocytosis occurs.

Web Link

Video: Endocytosis (0:35)

References & Links

Videos
Active Transport - http://www.youtube.com/watch?v=STzOiRqzzL4
Endocytosis - http://www.youtube.com/watch?v=4gLtk8Yc1Zc
5.1 Peptic Ulcers

When the mucus layer of the stomach or duodenum becomes too thin, acid can erode the cells lining these tissues. This results in a lesion known as a peptic ulcer, as shown below.

![Diagram of the stomach and duodenum](image)

Figure 5.11 A peptic ulcer in the duodenum

The first video below illustrates how a peptic ulcer forms. The second link shows what 2 ulcers actually looks like in the stomach.

**Web Links**

**Video:** How a peptic ulcer develops (1:56)
**Video:** Endoscopy of 2 Giant Gastric Ulcers (0:26)

10% of Americans will develop an ulcer in their lifetime. Despite common beliefs, these ulcers are not caused by stress or spicy foods. Most ulcers are believed to be caused by the acid-resistant bacteria, *Helicobacter pylori*. 20% of people <40 years old, and 50% of people >60 years old are infected with this bacteria. *Helicobacter pylori* causes a thinning of the mucus that protects the stomach and duodenum from gastric acid. Prolonged use of nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and naproxen (Aleve) are also a frequent causes of peptic ulcers. NSAIDs inhibit the production of a protective eicosanoid.

**References & Links**


**Videos**

How a peptic ulcer develops - https://www.youtube.com/watch?v=4bXZRgJ-1fk
5.2 Gallstones

It is estimated that up to 1 million Americans are hospitalized annually as a result of gallstones, making it the most common of all digestive diseases\(^1\). Gallstones are formed when bile hardens in the gallbladder. 80% of gallstones are caused by cholesterol precipitation, while 20% are caused by bile pigment precipitation\(^2\). The cause of gallstones is unknown\(^2\). The way in which gallstones are formed is shown in the following video.

The following figure shows a severe case of gallstones.

![Figure 5.21 Gallstones within a dissected gallbladder\(^3\)](image)

Many people don't experience symptoms from gallstones. They are usually discovered during examination for another health condition. However, some people experience an "attack" or pain that results from blockage of the bile ducts. The gallbladder is not essential, so the primary treatment is cholecystectomy, the removal of the gallbladder. Bile then flows directly from the liver into the small intestine.

References & Links

Video
Gallstones - http://www.youtube.com/watch?v=1q3NxfwSENMI&feature=rec-HM-fresh+div
5.3 Irritable Bowel Syndrome

Up to 20% of Americans may have irritable bowel syndrome (IBS). A syndrome is a group of symptoms, not a disease. In IBS, the colon does not function correctly. The symptoms of IBS are cramping, bloating, gas, diarrhea, and/or constipation. The cause of IBS is unknown\(^1\). Diet changes, stress reduction, and medicine may help manage the condition\(^2\). To learn more about IBS, see the references below.

References & Links
5.4 Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) refers to a number of inflammatory conditions in the intestine. The two most common are Crohn's Disease and ulcerative colitis. These two conditions differ mainly in the areas of the intestine that are affected. Crohn's disease can occur anywhere throughout the GI tract, but most commonly occurs in the last part of the ileum. Crohn's disease may also involve all layers of the intestine\(^1\). Ulcerative colitis are ulcers, or sores, in the lining of the colon and/or rectum\(^2\). It is estimated that up to 1 million people have IBD in the United States. Half of these individuals have Crohn's disease, and the other half have ulcerative colitis\(^3\).

The figures below show the inflammation and swelling that occurs in individuals with Crohn's disease.

![Figure 5.41 Inflamed ileum\(^4\)](image)

![Figure 5.42 Swollen ileum\(^4\)](image)

The exact causes of these two diseases is not known. One hypothesized cause for Crohn's disease is an overactive immune system that results in the chronic inflammation and collateral damage to the cells of the intestine, resulting in formation of lesions.

Crohn's disease and ulcerative colitis present symptoms similar to other gastrointestinal diseases, such as irritable bowel syndrome and GERD. The Inflammatory Bowel Syndrome Self Help and Support Group link below has a nice table that illustrates the overlapping of symptoms, but should not be used as a definitive way to diagnose someone with one of these conditions.
Gastrointestinal Diseases: Similar yet Different Symptoms

References & Links
3. http://www.ccfa.org/info/about/crohns
5.5 Celiac Disease

1 out of every 133 people in the United States has celiac disease\(^1\). People with celiac disease cannot consume the protein, gluten, because it causes their body to generate an autoimmune response (immune cells attack the body's own cells) that causes damage to the villi in the intestine, as shown below.

![Upper Jejunal Mucosal Immunopathology](image)

Figure 5.51 Different stages of of celiac disease\(^2\)

This damage to the villi impairs the absorption of macronutrients and micronutrients from food.

There are a variety of symptoms for celiac disease that vary depending on age and from person to person. For a listing of all symptoms see the link below.

Web Link

What are the symptoms of celiac disease?

What is gluten?

Gluten is a protein that is bound to starch in the endosperm of grains such as:

- Wheat
- Barley
- Rye
- Triticale
Thus, people with celiac disease need to consume a gluten-free diet. The table in the link below shows foods that are allowed to be consumed (gluten-free), as well as foods that need to be avoided or further investigated. The video in the second link is a good overview of celiac disease.

**Web Links**

The gluten-free diet: some examples
Video: Celiac's Disease (2:35)

**References & Links**


**Links**

What are the symptoms of celiacs disease? - http://digestive.niddk.nih.gov/ddiseases/pubs/celiac/#symptoms
The gluten-free diet: some examples - http://digestive.niddk.nih.gov/ddiseases/pubs/celiac/#symptoms

**Video**

Celiac's Disease - http://www.youtube.com/watch?v=EmZczwtsbVc
5.6 Diverticulosis and Diverticulitis

Approximately 10% of people under 40, and 50% of people over 60 years old have a condition known as diverticulosis\textsuperscript{1}. In this condition, diverticula (plural, diverticulum singular), or outpouches, are formed at weak points in the large intestine, primarily in the lowest section of the sigmoid colon, as nicely shown in the figure below and in the video in the web link below.

Figure 5.61 Diverticula on the small intestine\textsuperscript{1}

Web Link

Video: Diverticulosis (1:24)

It is believed that diverticula are formed as a result of a low-fiber diet because people may strain more during bowel movements. Most people with diverticulosis do not know that they have the condition. However, if the pouches become inflamed, then the condition is known as diverticulitis. The most common symptom of this condition is abdominal pain. A liquid diet may be needed until the inflammation is decreased, then fiber is gradually increased\textsuperscript{1}.

References & Links


Video

http://www.youtube.com/watch?v=Mwa1qu9WzMM
5.7 Hemorrhoids

Hemorrhoids are swollen or inflamed veins of the anus or lower rectum. An internal hemorrhoid occurs within the anus, while an external hemorrhoid occurs in the skin surrounding the anus. Symptoms of hemorrhoids include bleeding, pain during bowel movements, and/or itching\(^1\). It is estimated that “about 75% of people will have hemorrhoids at some point in their lives”\(^2\).

![Hemorrhoids Diagram](http://en.wikipedia.org/wiki/File:Hemorrhoid.png)

Figure 5.71 Hemorrhoids\(^3\)

The anus and lower rectum experience high pressure during bowel movements. Thus, hemorrhoids are believed to be caused by straining during bowel movements. To prevent this condition from occurring, it is recommended that people consume a high-fiber diet, drink plenty of water, and exercise to produce regular, large, soft stools. In addition, people should "go" at first urge and not wait until it is more than an urge\(^2\).

References & Links