Chapter 4: Macronutrient Uptake, Absorption & Transport

The term absorption can have a number of different meanings. Not everything that is taken up into the enterocyte from the lumen of the GI tract will be absorbed, so the term *uptake* refers to compounds being transported into the enterocyte. *Absorption* means that a compound is transported from the enterocyte into the bloodstream for circulation throughout the body. Under most circumstances, compounds that are taken up into the enterocytes will then be absorbed into the bloodstream. After this chapter, hopefully this distinction between these terms will be clear. After later micronutrient chapters, hopefully you will understand the reason for emphasizing this distinction.

Sections:
- 4.1 Crypts of Lieberkuhn & Enterocyte Maturation
- 4.2 Absorptive Lineup & Cell Membranes
- 4.3 Transport Mechanisms Used for Uptake and Absorption
- 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

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 defining uptake and absorption processes. *Crypts of Lieberkuhn* are pits located between the 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

\[^1\]
The crypts of Lieberkuhn (often referred to simply as crypts) are similar to the gastric pits in the stomach. The crypts contain stem cells at their bases that can produce a number of different cell types, including enterocytes. From these stem cells, immature enterocyte cells are formed. As they mature, the enterocytes rise, or migrate up, the villi. Thus, the tips 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, while 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 (they contain proteins and lipids) 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.](image)
Thus, we define absorption as reaching the bloodstream, because some compounds taken up into enterocytes will not always make it into the bloodstream. So remember, uptake is moving from the GI tract into the enterocyte, and absorption is moving from the enterocyte into the bloodstream.

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 lyssolecithin (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.
In order to be taken up by the enterocytes, these compounds must now cross the cell (plasma) membrane, which is a **phospholipid bilayer**. In the cell membrane, the **hydrophilic heads** of the phospholipids point into the lumen of the GI tract, as well as towards the interior of the cell, while the **hydrophobic tails** are on the interior of the plasma membrane. This is depicted in the diagram below.

![Diagram of plasma membrane](image)

Figure 4.22 Plasma membrane of a cell

In addition to phospholipids, the cell membrane also contains proteins, cholesterol, and carbohydrates in addition to the phospholipids. Membrane proteins, such as channels, pumps, pores, and carriers are important for the transport of some compounds across the cell membrane. Figure 4.23 and two videos below do a nice job of illustrating the components of the cell membrane.
Figure 4.23 Cell membrane

**Required Web Links**

**Video:** Cell Membrane (1:27)

**Video:** Voyage Inside the Cell: Membrane (1:23)

**References & Links**


**Videos**

Cell Membrane - [http://www.youtube.com/watch?v=owEgqrq51zY](http://www.youtube.com/watch?v=owEgqrq51zY)

Voyage Inside the Cell: Membrane - [http://www.youtube.com/watch?v=GW0lqf4Fqpg](http://www.youtube.com/watch?v=GW0lqf4Fqpg)
4.3 Transport Mechanisms Used for Uptake and Absorption

There are a number of different transport mechanisms utilized by your body for the uptake of nutrients into cells, and absorption into the bloodstream. These mechanisms can be classified as being either passive transport or active transport. The difference between the two types of transport 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 (high to low concentration). Active transport requires energy to move against the concentration gradient (low to high concentration).

A concentration gradient is a result of an unequal distribution of solutes within a solution. A solute is what is dissolved in a solvent in a solution. The more solute a region has, the higher the its concentration, while the less solute a region has, the lower the its concentration. Moving with the gradient is moving from a region of higher concentration to an area of lower concentration. Moving against the gradient is moving from an area of lower concentration to an area of higher concentration.

Figure 4.31 Movement with and against a concentration gradient.

Because our cells are surrounded by fluids containing varying amounts of solute, our body cells can experience concentration gradients across the plasma membrane. Hypertonic refers to a situation when the cell is surrounded by a solution that contains more solute than inside the cell. Hypotonic refers to a situation when the cell is surrounded by a solution containing less solutes than inside the cell. Isotonic refers to a situation when the cell is surrounded by a solution containing the same number of solutes that inside the cell. Figure 4.32 demonstrates these well.
Figure 4.32 Tonicity across the plasma membrane of cells.

The energy for active transport is provided by adenosine triphosphate (ATP), which is the energy currency in the body. Tri- means three, thus ATP is adenosine (composed of an adenine and a ribose) with three phosphate groups bonded to it, as shown below.

**Figure 4.33 Structure of adenosine triphosphate (ATP)**

**Phosphorylation** is the formation of a phosphate bond. **Dephosphorylation** is the removal of a phosphate bond. Phosphorylation is an anabolic process that requires energy. Dephosphorylation is a catabolic process that releases energy. Thus, energy is required to add phosphates to ATP, while energy is released through removing phosphates from ATP. Figure 4.34 depicts this process.
Figure 4.34 The ATP Cycle demonstrating the processes of phosphorylation and dephosphorylation.

Subsections:

- 4.31 Passive Transport Mechanisms
- 4.32 Active Transport Mechanisms

References & Links

1. https://userscontent2.emaze.com/images/92312f55-f2da-4d80-a1c3-657851b8e450/bf6e4c6e-7a39-406f-aac7-b422321028a5.jpg

4.31 Passive Transport Mechanisms

There are three forms of passive transport involved in uptake and absorption of nutrients in the body:

1. Simple Diffusion
2. Osmosis
3. Facilitated Diffusion

1. Simple Diffusion

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

Osmosis is similar to simple diffusion, but water moves instead of solutes. In osmosis water molecules move from an area of lower solute concentration to an area of higher solute concentration 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.

**Required 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.

![Figure 4.313 Effect of salt solution concentration on red blood cells](image)

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 transport is similar to diffusion in that it also moves *with* the concentration gradient (higher concentration to lower concentration). While it requires no energy, it does require a *carrier protein* to transport the solute across the membrane. Figure 4.314 and Required Video Link do a nice job of illustrating facilitated diffusion.
4.32 Active Transport Mechanisms

There are two forms of active transport:

1. Active Carrier Transport
2. Endocytosis

1. Active Carrier Transport

Active carrier transport (sometimes referred to as secondary active transport) is similar to facilitated diffusion in that it utilizes a protein carrier. However, energy is also required to move compounds against their concentration gradient (lower to higher concentration). Figure 4.321 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

Required Web Link
Video: Active Transport (0:21)

2. Endocytosis

Endocytosis is the engulfing of particles, or fluids, to be taken up into the cell. If a particle is endocytosed, this process is referred to as phagocytosis. If a fluid is endocytosed, this process is referred to as pinocytosis. Whenever a receptor located on the membrane is used to assist in engulfing an extracellular component, it is known as receptor mediated endocytosis. These processes are shown in Figure 4.322.

Figure 4.322 Different types of endocytosis
The following video does a really nice job of showing how endocytosis occurs.

**Required Web Link**

**Video: Endocytosis (0:35)**

**References & Links**


**Videos**

Active Transport - [http://www.youtube.com/watch?v=STzOiRqzzL4](http://www.youtube.com/watch?v=STzOiRqzzL4)

Endocytosis - [http://www.youtube.com/watch?v=4gLtk8Yc1Zc](http://www.youtube.com/watch?v=4gLtk8Yc1Zc)

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### 4.4 Carbohydrate Uptake, Absorption, Transport & Liver Uptake

Monosaccharides (glucose, galactose, and fructose) are taken up into the enterocyte by two processes. Glucose and galactose are taken up by the sodium-glucose cotransporter 1 (SGLT1, active carrier transport). The cotransporter part of the name of this transporter means that it also transports sodium along with glucose or galactose. Fructose is taken up by facilitated diffusion through glucose transporter 5 (GLUT5). There are 12 glucose transporters that are named GLUT 1-12, and all use facilitated diffusion to transport various monosaccharides.

The different GLUTs have different functions and are expressed at high levels in different tissues. Thus, the intestine might be high in GLUT5, but not in GLUT12.

Once inside the enterocyte, all three monosaccharides are then transported out of the enterocyte and into capillaries or lacteals (absorption) through GLUT2 as shown in Figure 4.41\(^1\).
The capillaries and lacteals are located within each villus as shown below. Capillaries are the smallest blood vessels in the body, while lacteals are also small vessels but are part of the lymphatic system, as will be described further in a later subsection.
The following video does a nice job of illustrating capillaries and lacteal and provides some basic detail on uptake into enterocytes and absorption into capillaries/lacteals.

**Required Web Link**
**Video: Absorption in the Small Intestine**

The capillaries in the small intestine join with the portal vein (a.k.a. hepatic portal vein), which transports monosaccharides directly to the liver. The figure below shows the portal vein and all the smaller vessels from the stomach, small intestine, and large intestine that feed into it.

![Portal Vein](image)

**Figure 4.43 The portal vein transports monosaccharides and amino acids to the liver**

In the liver, galactose and fructose are completely taken up by the hepatocytes, while only 30-40% of glucose is taken up (more on this shortly.) The monosaccharides are phosphorylated by their respective kinase enzymes forming galactose-1-phosphate, fructose-1-phosphate, and glucose-6-phosphate as shown in Figure 4.44.
Galactose-1-phosphate, fructose-1-phosphate, and glucose-6-phosphate are important for energy (ATP) production by cells as they can all enter glycolysis directly, or after undergoing conversion to another molecule. This will be covered in greater detail in Chapter 6.

References & Links

Video
Absorption in the Small Intestine - http://www.youtube.com/watch?v=P1sDOJM65Bc

4.5 Glycemic Response, Insulin, & Glucagon

If only 30-40% of glucose is being taken up by the liver, then what happens to the rest? How the body handles the rise in blood glucose after a meal is referred to as the glycemic response. The pancreas senses the blood glucose levels and responds appropriately. After a meal, the pancreatic beta-cells sense that glucose levels are high and secrete the hormone insulin, as shown in Figure 4.51.
Thus, as can be seen in the following figure, blood insulin levels peak and drop with blood glucose levels over the course of a day.

Blood glucose and insulin levels rise following carbohydrate consumption, and they drop after tissues have taken up the glucose from the blood (described below). Higher than normal blood sugar levels are referred to as **hyperglycemia**, while lower than normal blood sugar levels are known as **hypoglycemia**.
Insulin travels through the bloodstream to the muscle and adipose cells. There, insulin binds to the insulin receptor located within the cell membrane of the muscle and adipose cells. This causes GLUT4 transporters that are in vesicles inside the cell to move to the cell surface as shown below.

The movement of the GLUT4 to the cell surface allows glucose to enter muscle cells and adipocytes (fat cells). The glucose is then phosphorylated to glucose-6-phosphate by hexokinase (different enzyme but same function as glucokinase in liver) to maintain gradient.
**Glucagon** is a hormone that has the opposite action of insulin. Glucagon is secreted from the **alpha-cells** of the pancreas when they sense that blood glucose levels are low, as shown below.

![Figure 4.55 Glucagon secretion from pancreatic alpha-cells in response to low blood glucose levels.](image)

Glucagon binds to the glucagon receptors located in the cell membrane of hepatocytes, which causes the breakdown of the glycogen stored in the hepatocytes to glucose (glycogenolysis) as illustrated below.

![Figure 4.56 Glucagon binding to its receptor leads to the breakdown of glycogen to glucose.](image)
This glucose is then released into circulation which causes blood glucose levels to rise as shown below.

Figure 4.57 Glucagon leads to the release of glucose from the liver.

Subsections:
- 4.51 Diabetes
- 4.52 Glycemic Index
- 4.53 Glycemic Load

References & Links
2. [http://en.wikipedia.org/wiki/File:Suckale08_fig3_glucose_insulin_day.jpg](http://en.wikipedia.org/wiki/File:Suckale08_fig3_glucose_insulin_day.jpg)

### 4.51 Diabetes

**Diabetes** is a condition of chronically high blood sugar levels. The prevalence of diabetes in the US has been rapidly increasing; the link below provides some statistics about prevalence.

<table>
<thead>
<tr>
<th>Required Web Link</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diabetes Statistics</strong></td>
</tr>
</tbody>
</table>

There are 2 forms of diabetes: Type 1 and Type 2.
In **Type 1 diabetes**, not enough insulin is produced, as shown in the figure below.

![Type 1 diabetes diagram](image1)

**Figure 4.512 Type 1 diabetes**

Without insulin, GLUT4 does not move to the surface of muscle and adipose cells, meaning glucose will not be taken up into these cells. This results in an increase in the amount of glucose remaining in circulation (i.e. increased blood sugar.)

Type 1 diabetes was previously known as juvenile-onset, or insulin-dependent diabetes and is estimated to account for 5-10% of diabetes cases. Type 1 diabetics receive insulin through injections or pumps to manage their blood sugar.

In **Type 2 diabetes**, the body produces enough insulin, but the person's body is resistant to it. In Type 2 diabetics the binding of insulin to its receptor does not cause GLUT4 to move to the surface of the muscle and adipose cells as it normally should, thus no glucose will be taken up by these cells.

![Type 2 diabetes diagram](image2)

**Figure 4.513 Type 2 diabetes**
Type 2 diabetes accounts for 90-95% of diabetes cases, and was once known as non-insulin-dependent diabetes or adult-onset diabetes\(^1\). However, with the increasing rates of obesity, many younger people are being diagnosed with Type 2, making the adult-onset distinction no longer appropriate. Some people with Type 2 diabetes can control their condition with a diet and exercise regimen. This regimen improves their insulin sensitivity, or their response to the body’s own insulin. Others with Type 2 diabetes must receive insulin. These individuals are producing enough insulin, but are so resistant to it that more is needed for glucose to be taken up by their muscle and adipose cells.

The video below illustrates Type 2 diabetes.

<table>
<thead>
<tr>
<th>Required Web Link</th>
</tr>
</thead>
<tbody>
<tr>
<td>Video: Understanding Type 2 Diabetes (3:45)</td>
</tr>
</tbody>
</table>

**References & Links**


**Link**


**Video**

Understanding Type 2 Diabetes - [https://www.youtube.com/watch?v=JAjZv41iUJJ](https://www.youtube.com/watch?v=JAjZv41iUJJ)

### 4.52 Glycemic Index

Research has indicated that hyperglycemia is associated with chronic diseases and obesity. As a result, measures of the glycemic response to food consumption have been developed so that people can choose foods with a smaller glycemic response. The first measure developed for this purpose was the glycemic index. The **glycemic index** is the relative change in blood glucose after consumption of 50 g of carbohydrate in a test food compared to 50 g of carbohydrates of a reference food (white bread or glucose). Thus, high glycemic index foods will produce a greater rise in blood glucose concentrations compared to low glycemic index foods, as shown in Figure 4.521.
As a general guideline, a glycemic index that is 70 or greater is high, 56-69 is medium, and 55 and below is low. A stop light graphical presentation has been designed to emphasize the consumption of the low glycemic index foods while cautioning against the consumption of too many high glycemic index foods. The main problem with the glycemic index is that it does not take into account serving sizes. Let's take popcorn (glycemic index 89-127) as an example. A “serving size” of popcorn is 20 g, 11 g of which is carbohydrate. This is equal to approximately 2.5 cups of popcorn. Thus, a person would have to consume over 11 cups of popcorn to consume 50 g of carbohydrate needed for the glycemic index measurement. Another example is watermelon, which has a
glycemic index of 103, with a 120 g serving containing only 6 g of carbohydrates\(^3\). To consume the 50 g needed for glycemic index measurement, a person would need to consume over 1000 g (1 kg or 2.2 lbs.) of watermelon. Assuming this is all watermelon flesh (no rind), this would be over 6.5 cups of watermelon\(^4\).

The website glycemicindex.com (link provided below) contains a database you can search to see the glycemic index and glycemic load (covered in the next section) of various foods. The database also contains detail on how the measurement was done, and more information on the product itself. The top link below will take you to this website. The second link is to another database that contains the same information that might be easier for some people to use. However, please note that in the second link the glycemic loads are calculated using 100 g serving sizes for all foods. This might not be the actual serving size for all foods, which is what is typically used, so it is important to keep this in mind.

**Required Web Links**

Glycemicindex.com

Glycemic Index & Glycemic Load of Foods

**References & Links**

1. [http://upload.wikimedia.org/wikipedia/commons/e/ec/Glycemic.png](http://upload.wikimedia.org/wikipedia/commons/e/ec/Glycemic.png)
2. [www.glycemicindex.com](http://www.glycemicindex.com)

**Links**


Glycemic Index & Glycemic Load of Foods - [http://dietgrail.com/gid/](http://dietgrail.com/gid/)

### 4.53 Glycemic Load

To incorporate serving size into the calculation, another measure known as the **glycemic load** has been developed. It is calculated as shown below:
Thus, for most people, the glycemic load is a more meaningful measure of the glycemic impact of different foods. Considering the two previous examples from the glycemic index section, their glycemic loads would be:

**Popcorn:**
Glycemic load = \( \frac{89-127 \times 11}{100} = 9.79-13.97 \)

**Watermelon:**
Glycemic load = \( \frac{103 \times 6}{100} = 6.18 \)

As a general guideline for glycemic loads of foods: 20 or above is high, 11-19 is medium, and 10 or below is low\(^1,2\).

![Figure 4.531 Food glycemic load classifications\(^1,2\)](image)

Putting it all together, popcorn and watermelon have high glycemic indexes, but medium and low glycemic loads, respectively.
You can also use the top two links below to find the glycemic loads of foods. However, please note that in the second link the glycemic loads are calculated using 100g serving sizes for all foods. This might not be the actual serving size for all foods, which is what is typically used, so it is important to keep this in mind. The third link is to the NutritionData estimated glycemic load tool that is pretty good at estimating the glycemic loads of foods, even if actual glycemic indexes have not been measured.

**Required Web Links**
- Glycemicindex.com
- Glycemic Index & Glycemic Load of Foods
- Estimated Glycemic Load

**References & Links**
1. [http://www.mendosa.com/gilists.htm](http://www.mendosa.com/gilists.htm)

**Links**

### 4.6 Protein Uptake, Absorption, Transport & Liver Uptake

There are a number of similarities between carbohydrate and protein uptake, absorption, transport, and uptake by the liver. Hopefully after this section you will understand these similarities.

Over 60% of all amino acids are taken up into the enterocyte as di- and tripeptides through the PepT1 transporter (active carrier transport). Individual amino acids are taken up through a variety of amino acid transporters. Once inside the enterocyte, peptidases cleave the peptides to individual amino acids. These cleaved amino acids, along with those that were taken up as individual amino acids, are moved into the capillary by another variety of amino acid transporters (some are the same as on the brush border, some are different).
The capillary inside a villus is shown below.

Like monosaccharides, amino acids are transported directly to the liver through the portal vein.
Amino acids are taken up into the hepatocyte through a variety of amino acid transporters. The amino acids can then be used to either make proteins, or are broken down to produce glucose, as will be described in Chapter 6.

References & Links

Videos
Absorption in the Small Intestine - http://www.youtube.com/watch?v=P1sDOJM65Bc
4.7 Lipid Uptake, Absorption & Transport

Once mixed micelles reach the brush border of the enterocyte, two different lipid uptake mechanisms are believed to occur, but lipid uptake is not completely understood. One mechanism is that individual components of micelles may diffuse across the enterocyte. Otherwise, it is believed that some components may be taken up through unresolved transporters. For example, cholesterol transporters have been identified, but their overall mechanism of absorption is not well understood. The individual compounds are taken up as shown below.

![Figure 4.71 Uptake of mixed micelle components into the enterocyte](image)

Once inside the enterocyte, there are different fates for fatty acids, depending on their length. Short- and medium-chain fatty acids move through the enterocyte by simple diffusion and enter circulation through the capillaries; they are transported by the protein albumin. They will be carried to the liver by the portal vein, like monosaccharides and amino acids. Long-chain fatty acids, 2-monoglyceride, lysolecithin, and cholesterol will be re-esterified forming triglycerides, phosphatidylcholine, and cholesterol esters, respectively. These re-esterified lipids are then packaged into chylomicrons, which are lipoproteins, that are described in further detail in the next section. These chylomicrons are too large to fit through the pores in the capillaries, but they can fit through the larger fenestrations (openings) in the lacteal.
Lacteals (shown below) are small vessels that feed into the lymphatic system. Thus, the chylomicrons enter the lacteals and enter into lymphatic circulation.

The lymphatic system is a system similar to the circulatory system in that it contains vessels that transport fluid. However, instead of blood, the lymphatic system contains a clear fluid known as lymph. There are a number of lymph nodes (small glands) within the lymphatic system that play a key role in the body’s immune system. The figure below shows the lymphatic system.
The lymphatic system enters general circulation through the thoracic duct that enters the left subclavian vein as shown below. In this case that means that it is not directed to the liver like other components that have been absorbed.
Figure 4.75 The thoracic duct is where the lymphatic system enters circulation.

The animation below is an overview of lipid digestion, uptake, and initial transport.

**Required Web Link**

**Animation: Lipid Digestion, Uptake, and Transport**

**Subsection:**

- 4.71 Lipoproteins

**References & Links**


**Link**

[http://www.wiley.com/college/grosvenor/0470197587/animations/Animation_Lipid_Digestion_and_Absorption/Energy/media/content/dig/anima/dig5a/frameset.htm](http://www.wiley.com/college/grosvenor/0470197587/animations/Animation_Lipid_Digestion_and_Absorption/Energy/media/content/dig/anima/dig5a/frameset.htm)

**Videos**

Lymphatic system - [http://www.youtube.com/watch?v=qTXTDqvPnRk](http://www.youtube.com/watch?v=qTXTDqvPnRk)
Lymph Movement - [https://www.youtube.com/watch?v=ZdYxx4CHb-A](https://www.youtube.com/watch?v=ZdYxx4CHb-A)
4.71 Lipoproteins

**Lipoproteins**, as the name suggests, are complexes of lipids and protein. The proteins within a lipoprotein are called **apolipoproteins** (a.k.a. apoproteins). There are a number of different apolipoproteins that are abbreviated apo-, then an identifying letter (i.e. Apo A) as shown in the chylomicron below.

Figure 4.71 Chylomicron structure

The following video does a nice job of illustrating the different lipoprotein components.

**Required Web Link**
**Video: Lipoproteins (0:28)**

There are a number of lipoproteins in the body. They differ by the apolipoproteins they contain, size (diameter), density, and composition. Table 4.711 below shows the difference in density and diameter of different lipoproteins. Notice that as diameter decreases, density increases.

Table 4.711 The density and diameter of different lipoproteins

<table>
<thead>
<tr>
<th>Lipoprotein</th>
<th>Density (g/dL)</th>
<th>Diameter (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chylomicrons</td>
<td>0.95</td>
<td>75-1200</td>
</tr>
<tr>
<td>VLDL (very low-density lipoproteins)</td>
<td>0.95-1.006</td>
<td>30-80</td>
</tr>
<tr>
<td>IDL (intermediate-density lipoproteins)</td>
<td>1.006-1.019</td>
<td>25-35</td>
</tr>
<tr>
<td>LDL (low-density lipoproteins)</td>
<td>1.019-1.063</td>
<td>18-25</td>
</tr>
<tr>
<td>HDL (high-density lipoproteins)</td>
<td>1.063-1.21</td>
<td>5-12</td>
</tr>
</tbody>
</table>
This inverse relationship is a result of the larger lipoproteins being composed of a higher percentage of triglyceride and a lower percentage of protein as shown below.

Figure 4.712 Composition of lipoproteins

Protein is denser than triglyceride (this is why muscle weighs more than fat). Thus, the higher the protein/lower triglyceride composition, the higher the density of the lipoprotein. Many of the lipoproteins are named based on their densities (i.e. very low-density lipoproteins).

As described in the last subsection, the lipoproteins released from the small intestine are chylomicrons. The video below does a nice job of showing, describing, and illustrating how chylomicrons are constructed and function.

Required Web Link
Video: Chylomicrons (0:55)

The endothelial cells that line blood vessels, especially in the muscle and adipose tissue, contain the enzyme lipoprotein lipase (LPL). LPL cleaves the fatty acids from lipoprotein triglycerides so that the fatty acids can be taken up into tissues. Figure 4.713 illustrates how endothelial cells are in contact with the blood that flows through the lumen of blood vessels.
Figure 4.713 Lining of a blood vessel. The lumen is where the blood would be flowing, thus endothelial cells are those that are in contact with blood.

LPL cleaves fatty acids from the triglycerides in the chylomicron, decreasing the amount of triglyceride in the lipoprotein. This lipoprotein with less triglycerides becomes what is known as a chylomicron remnant, as shown in Figure 4.714.

Figure 4.714 The cleavage of triglycerides by LPL from a chylomicron leads to the formation of a chylomicron remnant.

Now in the form of a chylomicron remnant, the digested lipid components originally packaged into the chylomicron are directed to the liver where the chylomicron remnant is pulled into the hepatocytes. This process of clearing chylomicrons from the blood takes 2-10 hours after a
meal\(^2\). This is why people must fast 12 hours before having their blood lipids (triglycerides, HDL, LDL, etc.) measured. This fast allows all the chylomicrons and chylomicron remnants to be cleared before blood is taken. However, whether patients should be asked to fast has been questioned as described in the link below.

**Required Web Link**
*Should you fast before a cholesterol test?*

After the chylomicron remnant has entered the hepatocytes, it is broken down to its individual components (triglycerides, cholesterol, protein etc.). In the liver, VLDL are produced, similar to how chylomicrons are produced in the small intestine. The individual components are packaged into VLDL and secreted into circulation as shown below.

Figure 4.715 Chylomicron remnants are taken up by the liver. The liver secretes VLDL that contain cholesterol (C)

Like it does to chylomicrons, LPL cleaves fatty acids from triglycerides in VLDL, forming the smaller IDL (aka VLDL remnant). Further action of LPL on IDL results in the formation of LDL. The C in Figures 4.715 and 4.716 represents cholesterol, which is not increasing; rather, since triglyceride is being removed, it constitutes a greater percentage of particle mass of lipoproteins. As a result, LDL is composed mostly of cholesterol, as depicted in Figure 4.716.
LDL contains a specific apolipoprotein (Apo B100) that binds to LDL receptors on the surface of target tissues. The LDL are then endocytosed into the target tissue and broken down to cholesterol and amino acids.

HDL are made up of mostly protein and are derived from the liver and intestine. HDL participates in reverse cholesterol transport, which is the transport of cholesterol back to the liver. HDL picks up cholesterol from tissues/blood vessels and returns it to the liver itself or transfers it to other lipoproteins returning to the liver.
The animation under the transport button in the following link does a really nice job of going through the process of lipoprotein transport.

Required Web Link
Lipoprotein Animation

You are probably familiar with HDL and LDL being referred to as "good cholesterol" and "bad cholesterol," respectively. This is an oversimplification to help the public interpret their blood lipid values, because cholesterol is cholesterol; it's not good or bad. LDL and HDL are lipoproteins, and as a result you can't consume good or bad cholesterol, you consume cholesterol. A more appropriate descriptor for these lipoproteins would be HDL "good cholesterol transporter" and LDL "bad cholesterol transporter."

What's so bad about LDL?
LDL enters the endothelium where it is oxidized. This oxidized LDL is engulfed by white blood cells (macrophages), leading to the formation of what are known as foam cells. The foam cells eventually accumulate so much LDL that they die and accumulate, forming a fatty streak. From there, the fatty streak, which is the beginning stages of a lesion, can continue to grow until it blocks the artery. This can result in a myocardial infarction (heart attack) or a stroke. HDL is good in that it scavenges cholesterol from other lipoproteins or cells and returns it to the liver. The figure below shows the formation of the fatty streak and how this can progress to a point where it greatly alters blood flow.
The video below does an excellent job of illustrating this process. However, there are two caveats to point out. First, it incorrectly refers to cholesterol (LDL-C etc.), and second, it is clearly made by a drug company, so keep these factors in mind. The second link below is the American Heart Association’s simple animation of how atherosclerosis develops.

Required Web Links

Video: Atherosclerosis (5:36)
Cholesterol and CAD

Despite what you learned above about HDL, a recent study questions its importance in preventing cardiovascular disease. It found that people who have genetic variations that lead to higher HDL levels were not at decreased risk of developing cardiovascular disease. You can read more about this interesting finding in the first link below. In addition, another recent study is questioning whether saturated fat is associated with an increased risk of cardiovascular disease.
The following video gives a general overview of macronutrient digestion, uptake, and absorption.

References & Links

Links

Videos
Lipoproteins - [https://www.youtube.com/watch?v=x-4ZQaiZry8](https://www.youtube.com/watch?v=x-4ZQaiZry8)
Chylomicrons - [http://www.youtube.com/watch?v=hRx_i9npTDU](http://www.youtube.com/watch?v=hRx_i9npTDU)
LDL Receptor - [http://www.youtube.com/watch?v=XPguyN7dcbE](http://www.youtube.com/watch?v=XPguyN7dcbE)
Atherosclerosis - [http://www.youtube.com/watch?v=fLohn7ZesKs&feature=rec-HM-r2](http://www.youtube.com/watch?v=fLohn7ZesKs&feature=rec-HM-r2)
Small Intestine - [http://www.youtube.com/watch?v=P1sDOJM65Bc](http://www.youtube.com/watch?v=P1sDOJM65Bc)