4. ABSORPTION

**ABSORPTION MECHANISMS**

Once the digestive process is completed, the nutrients have to be transferred across the digestive tract epithelium into the extracellular space. The nutrients eventually make their way into circulation for distribution throughout the body. Absorption can take place by several means (Fig. 4-1). It can be carried out by active transport and passive diffusion. Some elements such as water are absorbed exclusively by diffusion using osmotic forces. Ions can enter enterocytes by diffusion, but may need to be transported actively to the extracellular space.

<table>
<thead>
<tr>
<th><strong>Absorption</strong></th>
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<tbody>
<tr>
<td>• Nutrients can be absorbed by</td>
</tr>
<tr>
<td>o Active transport</td>
</tr>
<tr>
<td>o Diffusion</td>
</tr>
<tr>
<td>• Water is absorbed entirely by diffusion (osmosis)</td>
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<tr>
<td>o It can also be secreted that way</td>
</tr>
<tr>
<td>• Ions diffuse into enterocytes and are transported to extracellular space</td>
</tr>
<tr>
<td>• Molecules move across membranes following gradient</td>
</tr>
<tr>
<td>o Concentration (to lower)</td>
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<tr>
<td>o Electric (to opposite charge)</td>
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**Active transport**

There are several active transport mechanisms (Fig. 4-2).

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Molecules move across membranes following concentration gradients, thus moving from more concentrated to less concentrated pools. They also can follow electric gradients whereby they move to areas of opposite charge.

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**Transport mechanisms**

- **Active transport uses metabolic energy**
  - Na⁺, K⁺, ATPase pump
    - Creates an intracellular electronegative environment
    - Lowers Na⁺ concentration
- **Co-transport or symport**
  - Carries two Na⁺ and one glucose
  - Depends on Na⁺ gradient
- **Exchangers or antiports**
  - Switches Na⁺ for H⁺
  - Uses Na⁺ gradients

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One uses metabolic energy in the form of ATP to drive Na⁺ and K⁺. The ATPase pump creates an intracellular electronegative environment by lowering the concentration of Na⁺ as a result of being pumped out into the extracellular space. By pumping Na⁺ out, K⁺ is brought into the cell. To prevent accumulation of intracellular K⁺, the cell has leak channels that permit the escape of K⁺ into the extracellular space (Fig. 4-3).

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**Figure 4-1. Basic mechanism of absorption**

**Figure 4-2. Mechanisms of active transport used in absorption of nutrients**

**Figure 4-3. Mechanism of co-transport of materials into the enterocytes using sodium gradient created by ATP driven sodium pump**
Co-transport
A second mechanism called co-transport or symport consists of using the lower Na⁺ concentration in the cell to attract two Na⁺, while at the same time attracting a third molecule, which could be a monosaccharide or an amino acid. A special membrane-bound protein binds all three components in the outside of the cell. As the Na⁺ enters into the cell, it flips the protein and internalizes the desired molecule. Upon release of the Na⁺, the protein changes its conformation and releases the molecule inside the cell. Finally, the empty molecule reverts to its original position, ready to pick up more cargo outside the cell (Fig. 4-3).

Antiports
The third mechanism of transport is the use of exchangers or antiports. In these cases, a Na⁺ is exchanged with an H⁺ generating a Na⁺ gradient, which is used to move molecules across the cell membrane.

CARBOHYDRATE ABSORPTION
All glucose molecules are internalized using the co-transport system, using a Na⁺ gradient. The passage of glucose from the epithelial cell to the extracellular space is done through facilitated diffusion via leak channels of the basolateral membrane (Fig. 4-4).

Galactose is absorbed using the same mechanism of Na⁺ co-transport that permits the absorption of glucose (Figs. 4-3, 4-5). Fructose, however, operates in a different manner. Fructose is internalized by facilitated diffusion.

This is a much slower system than the co-transport, thus less fructose can be absorbed in a given time. Once fructose is in the cell, it is phosphorylated and converted to glucose before it is released into the extracellular space (Fig. 4-5).

The flow of materials in the small intestine has different velocities depending on the position within the lumen of the intestine. Molecules in the center move faster than those closer to the wall (Fig. 4-6).

In order to be able to internalize the carbohydrates, membranous digestion has to take place. For the membrane bound enzymes to work, the sugars have to be in the area of the unstirred water layer where they can
then get into the glycocalix. Once attached to the digestive enzymes, the molecules of monosaccharides are in very close proximity with the apical epithelial membrane where the co-transport system or facilitated diffusion takes place.

**PROTEIN ABSORPTION**

The absorption of protein is very similar to that of carbohydrates. The main difference is that at the end of the membranous digestion there are still many di and tripeptides, which can be absorbed into the enterocytes. These peptides are hydrolyzed by enzymes located inside the enterocytes and the individual amino acids released by passive diffusion, through the basolateral membrane into the extracellular space (Figs. 4-7, 4-8).

**LIPID ABSORPTION**

The mechanism for lipid absorption is a little more complex than that of carbohydrates or proteins. After digestion is completed, we find micelles in the lumen of the small intestine. The micelle contacts the apical membrane of the enterocytes. The monoglycerides, as well as the cholesterol and vitamin A, diffuse from the micelle into the enterocyte. The free fatty acids have to be carried out by a series of membrane bound proteins called fatty acid binding proteins (Figs. 4-9, 4-10).

### Protein absorption

- Similar to carbohydrates
- Also di and tripeptides internalized into enterocytes
- Digested by internal enzymes
- Released to extracellular space as free amino acids

**Figure 4-7. General aspects of protein absorption**

### Lipid absorption in the jejunum

- Micelles contact enterocytes
- Most lipid components diffuse into enterocyte
  - Monoglycerides
  - Cholesterol
  - Vitamin A
- Free fatty acids are transported by membrane bound proteins
  - Fatty acid binding protein
- Bile acids continue in lumen

**Figure 4-9. Steps in lipid absorption**

- What is left of the micelle, in the lumen of the small intestine, are the bile salts which are immediately reused.

**Figure 4-10. Transfer of lipids from a micelle to the inside of the enterocyte by active transport and diffusion**
in the formation of new micelles during the digestive process.

Eventually, the bile salts reach the ileum where they are absorbed by a Na\(^+\) co-transport system and routed through the portal vasculature directly to the liver. In the liver, they are recycled into the lumen of the intestine or to the gallbladder forming the previously described enterohepatic circulation (Fig. 4-10). After the incorporation of all digested components into the enterocyte, the fatty acids and monoglycerides are transported to the endoplasmic reticulum where they are reconverted to triglycerides (Fig. 4-11).

**Enterohepatic circulation**

- BA reach the ileum
- BA are absorbed by Na\(^+\) co-transport system
- BA routed through the portal vasculature directly to the liver
- BA recycled into gallbladder

![Figure 4-11. Routes followed by bile acids (BA)](image)

**Reconstitution**

- Fatty acids, monoglycerides are converted into triglycerides
  - Endoplasmic reticulum
- Cholesterol is re-esterified
- Packed into chylomicrons
  - Core cholesterol ester and triglycerides
  - Surface phospholipids, cholesterol and proteins (water soluble)

![Figure 4-12. Formation of chylomicrons](image)

Here the cholesterol is re-esterified and all of these are packed into chylomicrons (Fig. 4-12); in such a way that the cholesterol esters and the triglycerides form the core, which is surrounded by phospholipids, cholesterol and proteins. The entire surface component makes the chylomicron water-soluble (Fig. 4-13).

The chylomicrons (Fig. 4-14) are released through the basolateral membrane into the extracellular space where they are picked up in the lymphatics to reach the thoracic duct which empties into the vena cava. High concentrations of chylomicrons, as a result of a fatty meal, can generate lipemia or a white colour in plasma (Fig. 4-15).

![Figure 4-13. Formation of chylomicrons in the enterocytes](image)

![Figure 4-14. Composition of a chylomicron](image)
LIPOPROTEINS

Chylomicrons are one of the five types of lipoproteins which are used to transport lipids of dietary origin within the aqueous medium of circulation. They are by far the largest complex out of all of them. The others, in descending size, are the very low density lipoproteins (VLDL), the intermediate density lipoproteins (IDL), the low density lipoproteins (LDL) and finally the high density lipoproteins (HDL). All of these are of liver origin and they are characterized by having one molecule in their surface of a specific apolipoprotein B-100 (APOB100).

Once in circulation the chylomicrons acquires apolipoprotein C-II (APOC2) and apolipoprotein E (APOE) from HDL and discards most of its triglycerides and cholesterol into the liver, cardiac and skeletal muscle and of course the adipose tissue. The role of the apolipoprotein is to make the chylomicron soluble in water however, some of them like APOC2 are cofactors, and thus they facilitate the action of lipoprotein lipase (LPL) which is the enzyme responsible for removing triglycerides from the chylomicrons into the different tissues.

After the chylomicron has been stripped of the triglycerides and cholesterol, the HDL re-uptakes the APOC2. The other two apolipoproteins, APOB48 and APOE remain in the chylomicrons and serve as the agonists to be recognized by the liver cells’ receptors in order to internalize them and break them down.

The other lipoproteins are made by the liver and released into circulation. Very low density lipoproteins (VLDL) are smaller lipoproteins than chylomicrons. They become the most important transport mechanism for all lipids, including triglycerides, phospholipids, cholesterol and its esterified version, cholesterol ester.

As the chylomicrons did, VLDL also obtain APOC-II and APOE from HDL. Then they can deliver their contents to different tissues in the organism with the support of LPL. After getting rid of some of the lipids, the VLDL again exchange with the HDL giving back APOC2, phospholipids and triglycerides in exchange for cholesteryl esters. As the VLDL delivers their triglycerides content, they become IDL. IDL are smaller than VLDL and about half of them are reabsorbed in the liver and are catabolized. The rest remain in circulation and they discard the APOE from their surface. As the IDL continue in circulation, they continue delivering triglycerides. Once the composition of the IDL is made up of more cholesterol than triglycerides, they become what is called low density lipoproteins (LDL) or “Bad cholesterol”. These lipoproteins have then only apolipoprotein B-100. The LDL are internalized into cells by a receptor mediated endocytosis and their contents are used for cell structure, or as substrate for other compounds such as steroid hormones.

LDL carries and easily delivers cholesterol into the arteries, hence the name “bad cholesterol”. The cholesterol released into the arteries forms agglomerations called plaques which reduce the flexibility of the arteries and reduce their internal diameter, thus increasing propensity for heart attacks, stroke and general vascular disease.

The HDL are the smaller lipoproteins that have a high percentage of proteins. That characteristic gives the lipoprotein its high density. HDL appears to have the capacity to harvest and remove cholesterol from arteries, thus their denomination of “good cholesterol”. The cholesterol that is harvested is then delivered to the liver, where it can be catabolized or exported to organs which use cholesterol as a precursor of other compounds such as the ovaries, testis, and adrenals. Removing cholesterol from the arteries reduces the chances of cardiovascular disease, stroke and heart attack.

WATER AND ELECTROLYTES ABSORPTION

The absorption of water takes place by osmosis and may follow the paracellular route (moves between the cells...
through the tight junctions) or the intracellular route (enters the cell through the apical membrane and leaves the cell to the extracellular space through the basolateral membrane). Usually, when the nutrients are absorbed and diffused into the intercellular space (monosaccharides, amino acids, and chylomicrons) they create an osmotic gradient which brings water from the ingesta.

When these particles enter the capillaries, they again create an osmotic pressure which attracts water into the villi microcirculation. (Figs. 4-16, 4-17).

**Water absorption**

- **Trans cellular absorption**
- **By osmotic pressure**
  - Created by other absorbed solutes (food)
- **Then diffuses into the capillary**
- **Under pressure can leave to the intestinal lumen via tight junctions (paracellular)**

![Figure 4-16. Mechanism of water absorption](image)

![Figure 4-17. Absorption of water in the intestine](image)

Furthermore, within the villi there is a counter-current transfer of water from the incoming arterial blood to the closely apposed venous return. This generates a more concentrated blood at the tip of the villi, where water is drawn by osmosis from the extracellular space. This process is similar to that used in the kidney. In the villi, the concentration at the entry point is 300 mOsm while at the tip it may reach a concentration of 600 mOsm (Fig. 4-18).

![Figure 4-18. Counter current mechanism of water absorption](image)

All the water absorption takes place in a transcellular manner (Fig. 4-19).

![Figure 4-19. Trans cellular absorption of water by enterocytes](image)

Under abnormal conditions, when there is an inflammation and there is more extracellular water, the reverse process is created by transporting water from the extracellular space to the lumen of the intestine. This transport takes place exclusively through the paracellular route (Fig. 4-20).
Water is also secreted by the endothelial cells in the crypt area. Usually, the majority of the ingested and secreted water is absorbed by the small intestine, leaving a relatively small amount to be excreted in the feces. A disruption in this balance causes diarrhoea.

Figure 4-20. Paracellular release of water into the lumen of the intestine