physiology

faculty of medicine - JU2017

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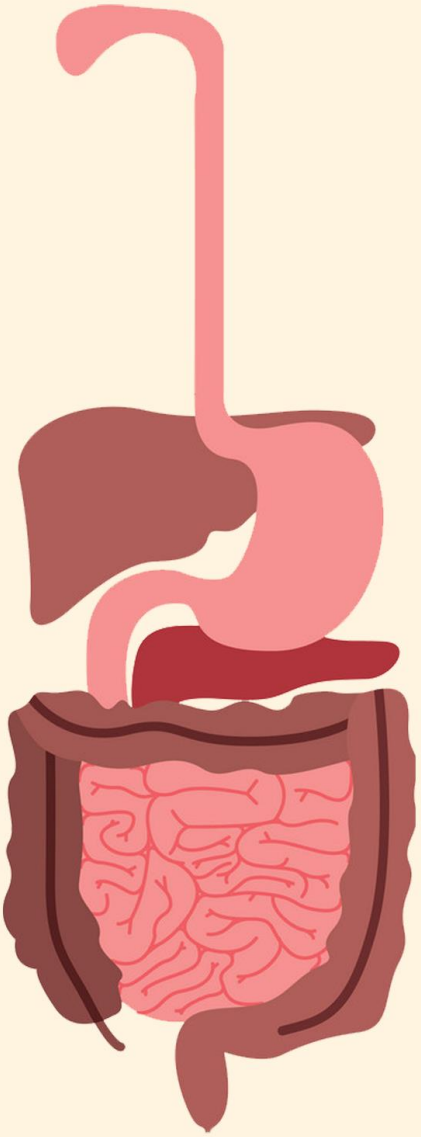
CorrectedBy	Saif yamin



2nd system - GI

Quick review of some points from the last lecture :

Lipid digestion: first of all, we have emulsification with the help of bile salts, and by this process Micelles are formed to increase surface area of lipid droplets.

After that digestion of triglycerides happens by attacking at carbon #1 and #3, we get 2 fatty acids and one monoglyceride, then once the micelles become in contact with the membrane, absorption happens to these molecules by simple diffusion to absorptive cells, followed by reforming triglycerides.

Also, we have lipoproteins which later become chylomicrons by aggregating more lipids, then these chylomicrons get expelled out of the cell by exocytosis (because they are big particles) and once they got expelled out these particles cannot be dissolved in the blood, but we have lymphatic vessels that take these particles away with the help of lymphatic circulation and then they are introduced to the blood slowly through the thoracic duct, then the liver takes them from the blood.

Now let's get into the lecture's main subjects.

Absorption of water and electrolytes

A) Absorption of Na+

We have a lot of carriers at the luminal membrane, to get these carriers to function we need to keep low concentration of sodium inside the cell. How? We have Na+/K+ pumps at the basolateral membrane, these pumps **actively** transport Na+ from inside the cell toward interstitial fluid.

After we have increased the Na+ concentration in the interstitial fluid we increased the positive charges there, so this will attract the negatively charged particles (like chloride) from the lumen by transcellular potential which is more positive at the interstitial fluid. This will increase the osmolarity attracting water inside.

Potassium moves in a passive way according to the electro-chemical gradient. At the level of small intestines, this gradient favour absorption of K+, but at the level of the colon this gradient favour secretion of K+. For sodium, The absorption is greatest in duodenum and decreases caudad.

The effect of aldosterone:

a hormone secreted by adrenal glands after dehydration. This hormone increases Na+ absorption by enhancing the enzymes and transport mechanisms of Na+. This hormone is important mainly in the colon.

In this way it conserves water and Na+ from loss with feces mainly when there is a need for Na+ and water in dehydration.

***Cl-**:

- Absorbed mainly in the upper part of the small intestine (duodenum and jejunum). Cl- moves in passive diffusion when an electrical gradient is established by the absorption of Na+.

Calcium absorption mechanism

- It binds to a protein at the brush border membrane (may be a carrier).
- Once Ca++ is inside it binds to a cytosolic Ca++ binding protein called *calbindin* Which transports Ca++ across the cell.

Absorptive cells form a protein structure called **calbindin**, this structure have the ability to bind to calcium, and by binding of more calcium to it, the concentration of free calcium decreases, so when we have low concentration of free calcium we have gradient, and because of having this gradient we get more calcium absorbed by simple diffusion at the luminal membrane to compensate the shortage of calcium. But at the basolateral membrane we have pumps for calcium which can transport calcium toward the interstitial fluid.

How can we increase calcium absorption at the level of absorptive cells?

-By **Vitamin D and Parathyroid hormone**, which increase the expression of calbindin, and by increasing that we get more calcium binding to calbindin and that will decrease free calcium concentration and as we said earlier this will cause more absorption of calcium

Iron absorption mechanism

Iron is mostly absorbed in the Ferrous form (**Fe^{+2}**) at the level of the upper part of small intestine, and you can enhance iron absorption by taking vitamin C. Also, taking more phosphates, oxalates or phytic acid (that's found in cereals) in the diet and pancreatic juice , inhibits the absorption of iron.

Conversion of iron from ferric (Fe^{+3}) to ferrous and vice versa is possible by changing the pH of the media. So, in **alkaline media we get more transformation into ferric (Fe^{+3})** and in **acidic media we get more transformation into ferrous (Fe^{+2})** (which is more soluble).

- The detailed mechanisms of iron absorption are still unsettled. Some believe that there is an active transport at the lumenal membrane. Other theory for iron transport is by secreting a globular protein from the epithelial cells known as apoferritin. This protein binds to Fe++ → ferritin. This complex of protein and iron is transported into the cell by receptor mediated endocytosis.

- Then iron stored in the epithelial cell in the form of ferritin, then transported into the blood where it binds trasnferrin as needed.

- If **NOT** needed, iron is lost when cells are desquamated. This mechanism prevents excess iron from entering the blood and causing toxic effects. This process is known as **Mucosal Block**.

What stimulates iron transporting and absorption?

Imagine that all transferrin molecules are bound to iron, this indicates that there is no need for iron in the body and there is no transporting of iron from enterocytes to the interstitial fluid.

If there was consumption of iron somewhere in the body, that means some transferrin molecules are becoming available to be loaded with iron, and we are activating the process of transporting iron from inside the enterocytes to the interstitial fluid.

Patients with thalassemia suffer from high amounts of RBCs destructed (Anaemia), so they take high amounts of blood. Because they have high destruction of RBCs, iron is released and deposited in their tissues especially in the skin, liver and lung, and their skin appears grey, and they die early.

So, our body cannot store iron except for small amounts in the liver in the form of ferritin, and as we said the body reabsorb iron only if it is needed, and because of that we have mucosal block of iron absorption phenomenon to protect us from iron deposition in tissues which will destroy them.

Vitamins absorption

We have water soluble vitamins and lipid soluble vitamins. Some of the water soluble vitamins are absorbed passively and some actively.

Most vitamins are absorbed in the upper part of the small intestines, but vitamin B_{12} is absorbed in the ileum. We have special mechanism for the absorption of **vitamin B_{12} which needs intrinsic factors secreted by the oxyntic cells of the stomach.**

water soluble vitamins are absorbed passively except vitamin C, vitamin B_1, and vitamin B_{12}.

Lipid soluble vitamins (A, D, E, K) are absorbed in the same route as lipids. So, any problem related to the absorption of lipids will result in deficiency in these vitamins.

People have steatorrhea (high lipid amounts in feces) may develop deficiency in one or more of these lipid soluble vitamins.

Vitamin K is related to coagulation of blood.
Vitamin D is related to Calcium homeostasis.
Vitamin A is related to regeneration of skin and retina.
Vitamin E is related to regeneration of cells in general.

After the process of absorption, all eaten material enter the metabolic pool to supply the body with energy we need by chemical burning in our cells (mainly in the liver), to get chemical transformations, and we use the chemical energy that resulted in the form of micro energetic molecules (ATP, GTP,…), and we use these molecules for the body to work and for metabolic processes.

Types of work:

1- Chemical works: building of cellular components, secretions, etc.

2- Mechanical works: muscle contractions, heart pumping, etc.

3- Electrical works: nerve conduction, resting potential (by maintaining the activity of Na+/K+ pumps and other pumps).

Can we measure all metabolic transformations that are taking place in the body?

According to the law of energy (energy can neither be created nor destroyed; rather, it can only be transformed from one form to another), after chemical transformation in the body we get ATP, which will release energy (heat) when being used in chemical reactions.

In fact, we can measure the heat produced by the body. So, when we measure the heat we can get an estimate for the metabolic transformations that take place in the body.

To get formation of ATP we have 2 pathways: Aerobic and Anaerobic, and the amount of energy produced by the anaerobic is much less than that of the aerobic pathways.

Respiratory Quotient (RQ)

The amount of CO_2 produced by metabolic processes to the amount of consumed O_2.

$$Respiratory\ Quotient = \frac{volume\ of\ carbon\ dioxide\ per\ unit\ time}{volume\ of\ oxygen\ per\ unit\ time}$$

By degradation of one glucose molecule, 6 oxygen molecules are used, So, according to the following equation we can know the amount of CO_2 produced:

$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$

If we use **glucose** as the only source for energy, RQ will be 1 ($6CO_2/6O_2$).

If we use **fats** as the only source for energy, RQ will be around 0.7, and for **proteins** it's 0.8

RQ for brain is almost 1, because it's main source of energy is glucose. In diabetic patients, if you measure RQ for their whole body it will be around 0.7 because fat is the main source for their energy.

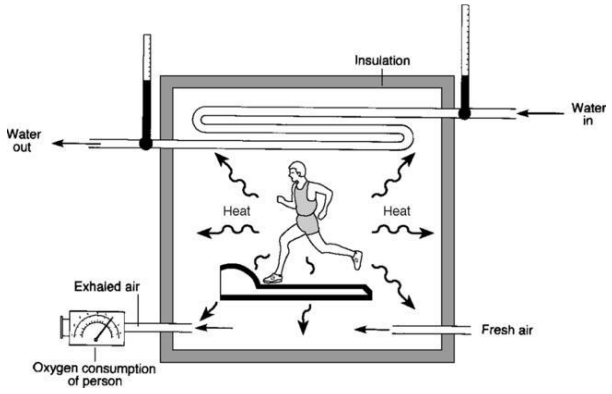
Metabolic Rate

If you measure the amount of heat which is produced by a body, you can get an estimate for the metabolic transformations that took place in that body. The unit of measuring heat is **calories**, and we have to measure the amount of heat per time unit (hour) in the previous case.

So, the metabolic rate is **the amount of heat produce by the body (calories) per time unit (hour).** This gives an estimate for the whole metabolic transformations in the body.

We have 2 methods for measuring the metabolic rate: Direct and indirect calorimetry.

Direct calorimetry

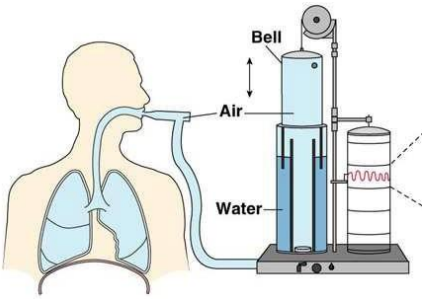


In this method we can see how much heat the body produce, so when you place a running or chilling person in a closed and insulated chamber, and you have a flowing of water in and out of the chamber, and you measure the temperature of the water that is getting in and the water getting out, you don't have the same temperature, actually you have higher temperature. The difference in the temperature is the heat which is released from the body and gained by water. If you know the flow rate of water per time unit and you know the number of calories which is gained by water at the same time, you can calculate by a direct way the amount of heat which is produced by the body.

This process is complicated and not so practical because the person stays in the chamber for a long time and you can't have high amount of flowing water.

Indirect calorimetry

By measuring the amount of consumed oxygen or produced CO_2. We can measure the amount of consumed oxygen by **Spirometer.**



With this device we create a closed system between the lungs and the spirometer, so at any time the person inhales air from the cylinder of the device and exhales air back to the cylinder. In the way of expiration, the device is linked to another device which can adsorb all CO_2, what remains in the spirometer is oxygen which is inhaled by the person and so on.

After few minutes, you do not find the same volume of oxygen, it's actually getting less with time, so if you know the amount of oxygen consumed per time unit then you can proceed with calculations. **It was found that for each 1 liter of O_2 consumption, 4.8 calories are generated. This is called the energy equivalent of oxygen.**

The heat produced is calculated as the amount of heat/m2 surface body/hour