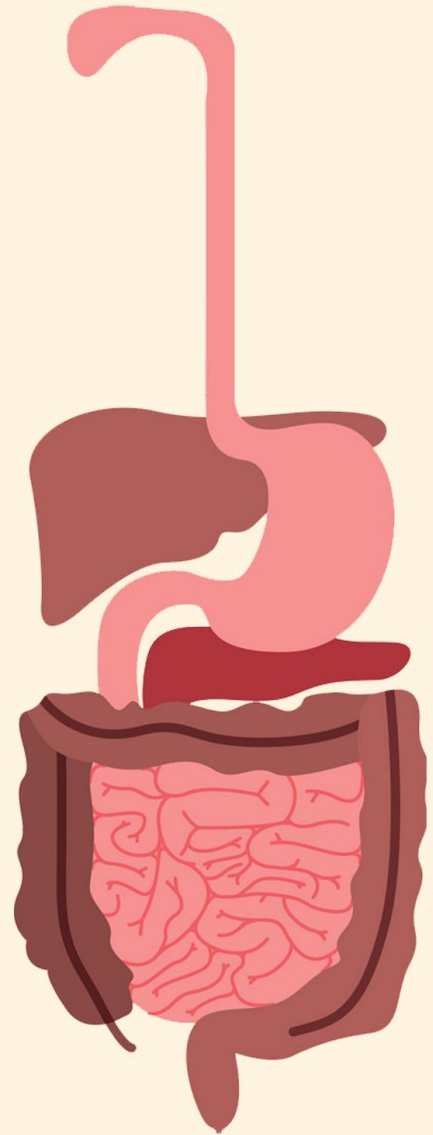




physiology
faculty of medicine - JU2017

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2nd system - GI



Measuring metabolic rate:

There are two main methods for the measurement of metabolic rate:

1-Direct method (direct Calorimetry): direct measurement of heat (Kcal/hour) using a calorimeter. The calorimeter is a device which has water flowing through it at a constant rate. When water passes through the calorimeter, its temperature is changed. So you know the initial temperature of water and the final temperature of water after it passes through the calorimeter. Now you can measure the heat taken by the flow of water and you can measure the metabolic rate.[EXTRA: It is the device used to calculate the heat changes in chemical reactions and it helps in knowing if the reaction is endergonic or exergonic.]. This method is not convenient because it requires long time, so other methods were made.

2- Indirect method: using the amount of oxygen consumed to measure the rate of heat production. For each liter of oxygen consumed, we are generating 4.8 Cal (when cal is written Cal (with a capital (c)), it means Kcal). This is called the energy equivalent of oxygen. The indirect method could be either a closed method (by using the spirometer) or an open method.

a) Closed method (spirometer):

Closed method means that we are using a closed system to measure the metabolic rate such as the spirometer. The spirometer has an inverted cylinder over a water bath. We place a known amount of pure oxygen and let a person respire (breathe) through the device. After some time, we measure the amount of oxygen left in the spirometer to know how much oxygen that person has consumed and then we can calculate the metabolic rate using the energy equivalent of oxygen (1liter=4.8Cal). In the spirometer, there is another device to collect CO₂ produced during respiration so that it will not affect the volume of oxygen in the device. For example: a spirometer contains 10 liters of oxygen. We bring a person to respire through it. After five minutes, we measure the oxygen to find that there are nine liters of oxygen left. This means that the person consumed one liter of oxygen in five minutes. By using the energy equivalent of oxygen: 1liter*4.8Cal*12=57Cal/hour. We multiplied by 12 because the time was five minutes, and we usually

calculate the metabolic rate per hour (1 liter per 5 minutes = 12 liters per hour). So the metabolic rate is 57 Cal/hour. **For more** standardization, because people have differences in their bodies (big body, small body...), we divide it by the surface area of the person's body. We get the surface area of the body by using certain methods (measuring the height, weight, gender... in a specific way). If the person has a surface area of 1.7m^2 , we divide 57 over 1.7 which equals 35 Cal/hour/ m^2 (this unit can also be written as $\text{Cal}\cdot\text{hour}^{-1}\cdot\text{m}^{-2}$).

b) Open method:

Open method means that we are using an open system to measure the metabolic rate. We know that the concentration of oxygen in the atmosphere is 20% (20 liter of oxygen per 100 liter of air). So we let a person respire and we collect the expired air and measure the concentration of oxygen in it. For example: if we find that the expired air has 17% oxygen concentration (17 liters of oxygen per 100 liter of air), this means that the person consumed 3 liters of oxygen. Then we can measure the metabolic rate by using the same method (using the energy equivalent of oxygen and then dividing the result over the body surface area for standardization).

Basal metabolic rate: it is the metabolic rate measured under basal conditions. It is used to standardize and decrease errors in tests. The basal conditions are:

- 1- No food for at least 12 hours before the measurement (food increases metabolic rate, and we don't want that to happen).
- 2- Measurement after a night of restful sleep.
- 3- No exercise for at least one hour before the test, because exercising causes the body to consume its stored oxygen so you need to time for the body to restore oxygen.
- 4- Elimination of all factors that may cause excitement (exam stress for example).
- 5- Comfortable temperature during measurement (22°C) because temperature can change the metabolic activity (cold temperature increases the metabolic activity).

Factors affecting metabolic rate: factors that alter basal metabolic rate:

- 1- Exercise: an exercising person has higher metabolic rate than a person not exercising.
- 2- Daily activities: a person who is sitting on a chair all the day has low metabolic activity.
- 3- Age: metabolic activity decreases with age (kids have the highest metabolic rate).
- 4- Sleep: it decreases the metabolic rate.
- 5- Climate: cold climates have people with higher metabolic rate than people in hot climates.
- 6- Fever: a person with fever has higher metabolic rate because he needs more oxygen than normal.
- 7- Malnutrition: it reduces the metabolic rate because the body is trying to reserve nutrients.
- 8- Specific dynamic action (diet): if you put a person on a protein diet, he will have higher metabolic rate compared to putting him on carbohydrate diet. This is because some amino acids increase the metabolic rate by specific dynamic actions.
- 9- Hormones:
 - a) Thyroid hormone: increases the metabolic rate.
 - b) Sex hormones: increase the metabolic rate. Male sex hormones have higher effect in increasing the metabolic rate (10%-15%) than female sex hormones.
 - c) Growth hormone: increases metabolic rate.
- 10- Sympathetic stimulation: high sympathetic stimulation means higher metabolic rate.

Regulation of food intake

Every type of food has a specific amount of energy (calories):

1g of Protein → 4 calories AND 1g of carbohydrates → 4 calories AND 1g of fat → 9 calories

- **Food intake=energy expenditure** : the body tries to make you eat according to the used energy. So if you worked a lot and you are tired, you have used a lot of energy so you will feel hungry and eat to compensate for the used energy. On the other hand, if you are resting and didn't use a lot of energy, you will not feel hungry and will not eat because there is no energy to be compensated. This balance is called **neutral balance** (calories in=calories out). Some people eat too much, this is called **positive balance** (calories in>calories out). Some people eat too little, this is called **negative balance** (calories in<calories out).

To maintain the normal store of protein we need an intake of about 30-55grams/day. If for a long time some constituents of food stuff are lacking, it will generate some diseases. The absence of proteins from the diet for a long time may result in a syndrome known as *Kwashiorkor*. This is a protein deficiency syndrome characterized by (failure to grow, lethargy "laziness" , mental depression and hypoproteinic edema) that may result from insufficient intake of proteins.

Regulation of food intake

-**Hypothalamic control**: the hypothalamus has two centers that regulate the amount of food: 1- Feeding center. 2- Satiety "fullness" center.

** The Feeding center and Satiety center receive signals from the body about the status of food storage and the need of the cells, that will result in stimulation or inhibition of food intake.

Stimulation of the lateral hypothalamus will result in an excess of feeding (hyperphagia). While stimulation of the ventromedial nuclei of the hypothalamus will cause satiety feeling. The destruction of these centers will induce an opposite effect of their stimulation. Thus the feeding center tell us to eat while the satiety center tell us to stop eating.

-Amygdala: if the Amygdala is destroyed, this will result in eating anything the person is seeing (soil, sawdust...), this is known as *psychic blindness*. So the Amygdala regulates the quality of food.

-Prefrontal cortex: it is involved in the regulation of choice of food (appetite).

Note: amygdala and prefrontal cortex are involved in regulation of the quality of eaten food. On the other hand, the feeding center and satiety center are involved in the regulation of quantity of food eaten.

Theories of food intake regulation:

1-Long term regulatory mechanisms: there are many theories regarding the long term regulatory mechanisms.

- a) Glucostatic theory: it states that glucose level is the stimulus for eating ($\uparrow$ glucose $\rightarrow$ $\downarrow$ eating). This is not true because diabetic patients have elevated blood sugar and they eat a lot. So this theory has been modified to become: *the availability of glucose for cellular energy is the stimulus to eat or not*. In diabetic patients, glucose is not available for cellular energy even if it's found in high amounts.

When you eat, blood glucose level increases so insulin is produced to lower it. What insulin does is transport glucose from the blood to the cells, and when cells have a lot of glucose, they are producing a lot of ATP. So this is a stimulation to stop eating.

- b) Lipostatic theory: this theory states that the presence of fat products in the blood such as keto acids and some fatty acids act to inhibit feeding. This theory is also related by other studies to the amount of fat in adipocytes. If the adipocyte is filled with fat, it is stimulated to produce an endocrine hormone called *Leptin* which acts on receptors on the hypothalamic centers to reduce food intake. Leptin is transcribed by a gene called Ob gene (obesity gene). If there is a defect in this gene, Leptin will be defective and the person might become obese. This defect in the gene can be inherited. That is why obesity can run in the family.

- c) Aminostatic theory: the level of amino acids in the blood can affect eating behaviors.
- d) Thermoregulatory mechanisms: these mechanisms are believed to affect feeding centers in the hypothalamus. In winter people tend to eat more than in the summer, because the body needs higher metabolic rate to keep body temperature at 37°C. So the body requires more nutrients to cover its needs.
- e) Psychosocial factors: some people have customs for eating. For example: some people are used to eating 3 meals per day, so when the time of the second meal comes they will feel hungry. Other people are used to eat 1 meal per day, so when the time of the second meal comes they will not actually care and they will not eat.

2- Short term regulatory mechanisms:

- a) Gastrointestinal filling: Eating will cause distension of the stomach and duodenum and activation of signals that are transmitted by the vagus to suppress the activities of feeding centers and thereby stopping food intake.
- b) Hormonal: eating will cause the release of hormones such as Cholecystikinin, Insulin and GIP (gastric inhibitory peptide). These hormones act to suppress feeding.
- c) Suppression by oral receptors: these are receptors in the pharynx that will suppress feeding according to the amount of food passing through the oral cavity. They sense the number of swallowings (30-50 times) and inhibit feeding according to it.

** The long-term and the short-term factors of regulations are probably sending signals to the hypothalamus. Some neurotransmitters that are released in that area has been known to affect the feeding behaviors. Such as neuropeptide Y, dopamine and serotonin.

Obesity: it is having higher weight than the ideal weight by 20% because of fat. Some people can have higher weight than the ideal weight because of muscles; we can't call these people obese. Obese people usually have *positive balance*, but if their weight stopped increasing they are now on *neutral balance* (but they are still obese).

-Causes of obesity:

1- Neurogenic abnormalities: if hypothalamic receptors have low threshold, they will need less stimulus to inhibit eating which means less eating is needed to stimulate them. The problem is if the receptors have high threshold, they will need a stronger stimulus to inhibit eating which means they will need more eating to stimulate them. Also the number of receptors has an effect. Low number of receptors means that they need a stronger stimulus to inhibit eating compared to when they are at a high number. When there are a lot of receptors, they will need a smaller stimulus to work.

2- Genetic factors: Leptin deficiency (because of the Ob gene) or if the receptors in the hypothalamus are damaged.

3- Psychosocial: if you are invited by a friend, you have to eat.

4- The rate of metabolism: some people eat a lot and they don't get fat and other people eat few and become fat.

5- Childhood over nutrition: some parents force their children to eat even if they are not hungry. This causes adipocytes hyperplasia and the child will have more adipocytes. This means that when he has mature adipocytes, he will need to eat more to fill the adipocytes to produce Leptin. **In the adult, if he over-eats he will hypertrophy of adipocytes.

6- Disorders of the endocrine system: for example hypothyroidism causes low metabolic rate.

7- lack of physical exercise.

-**Treatment**: increase output of energy (exercise), decrease energy input or both. There are surgeries also.

Inanition: the opposite of obesity. It is having weight less than the ideal weight by 10%. These people are always in *negative balance*. Their hypothalamic receptors have low threshold, any small stimulus can cause them to inhibit eating. **Causes**:

1- Psychogenic: anorexia nervosa. Anorexia nervosa is loss of appetite for food because of psychological conditions such as depression.

2- Hypothalamic abnormalities: Destruction of hypothalamic centers by thrombosis may result also in inanition.

Depletion of body stores during starvation: in starvation, the first molecules used for energy are carbohydrates. They are stored in the body as glycogen in the liver. Glycogen is broken down by glycogenolysis to provide glucose needed for energy. This can supply the body for 48-72 hours only. After carbohydrates are finished, the body starts using fat and proteins as a source of energy at the same rate. The body will use fat during starvation by converting them to ketone bodies. The brain uses ketone bodies for energy because they can cross the blood-brain barrier. After 6 weeks, fat is depleted completely and the main source becomes proteins only. Proteins undergo three phases in depletion: the **first phase** is rapid, the **second** is slow and the **third**, which happens before death, is fast. In the **first phase** there is depletion of proteins that are easily mobilized from the protein stores and they are used for gluconeogenesis (proteins and fats are used at the same rate, as mentioned earlier). In the **second phase** the rate of gluconeogenesis is decreased as well as the rate of protein utilization, the body starts to utilize proteins at low rate (preserve functional proteins), and continue to use fat deposits. The **third phase** (after 5 – 6 weeks of starvation) appears after complete depletion of almost all fat stores. So, the body will retain to use proteins at a higher rate. This phase will be followed by death.

***The doctor asked a question at the end of the lecture:**

During high consumption of fat (phase2), what is the RQ (Respiratory quotient) of this person at this stage?

Answer: It is going to be 0.7 because the major source of energy is going to be fat.

