General Physiology
Second semester 2024
Lecture 30
Regulation of Energy Balance and , Food Intake , Body Weight and Obesity

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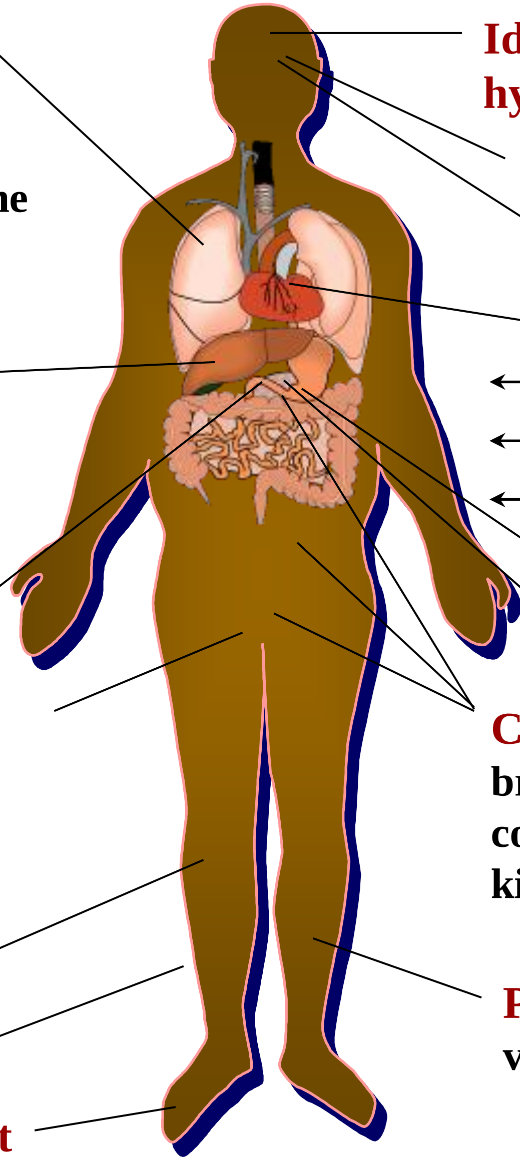
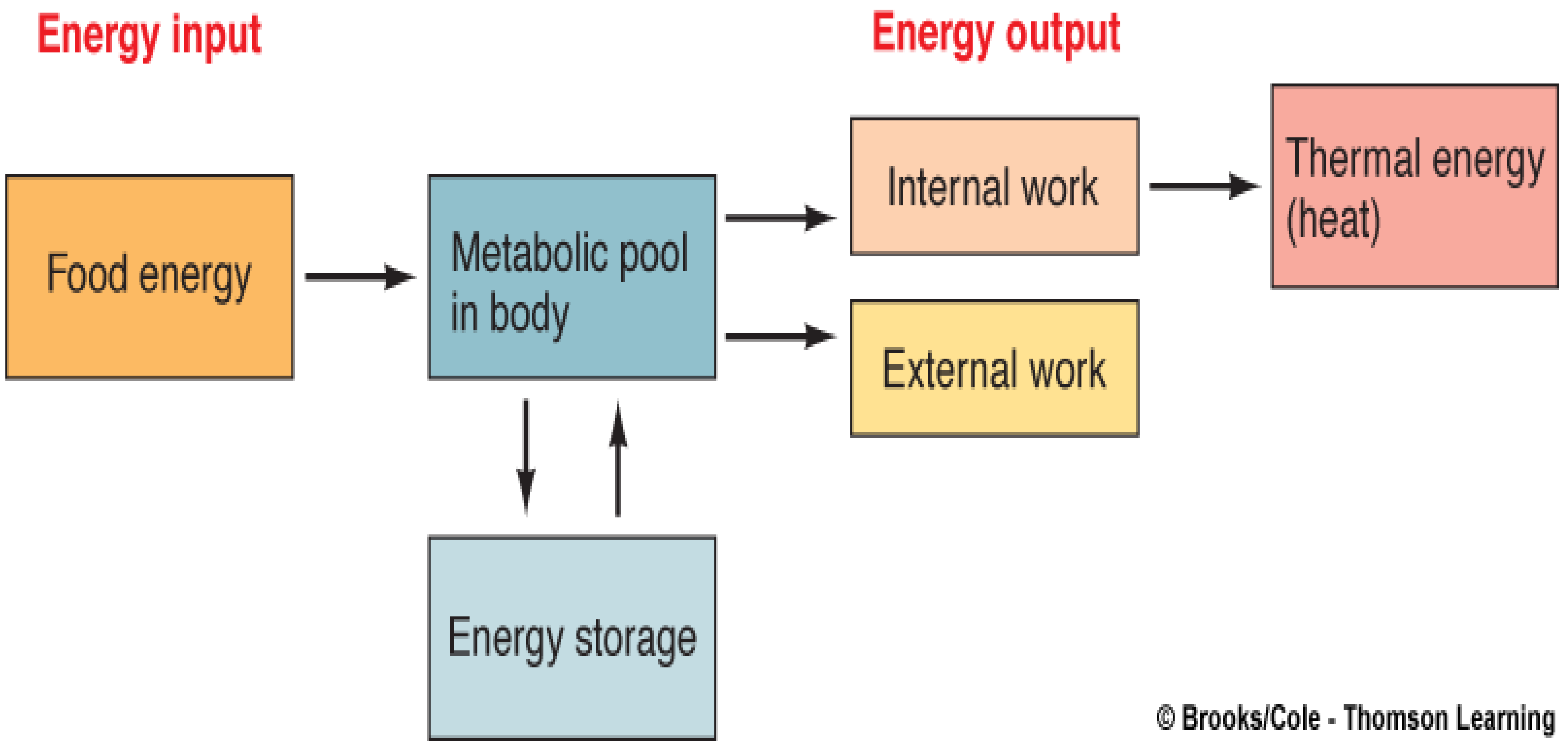
Lecture objectives

- Describe the balance of energy input and output
- Define metabolic rate and list factors affecting metabolic rate
- Describe methods of assessment of metabolic rate
- Describe the neuronal and hormonal regulation of food intake and energy balance
- Define obesity and list main cause of obesity
- Define Inanition, Anorexia, and Cachexia
- List common methods for assessment of obesity

Medical Complications of Obesity



Energy Input and Output



Not more than 25% of nutrient energy is available for work, either external or internal. The remaining 75% is lost as heat.

Energy input

- The energy in ingested food constitutes *energy input* to the body.
- Chemical energy locked in the bonds that hold the atoms together in nutrient molecules is released when these molecules are broken down in the body.
- Cells capture a portion of this nutrient energy in the high energy phosphate bonds of adenosine triphosphate (ATP)
- Energy harvested from biochemical processing of ingested nutrients is either used immediately to perform biological work or stored in the body for later use as needed during periods when food is not being digested and absorbed

Energy output

Energy output or *expenditure* by the body falls into two categories:

- **External work**
- is the energy expended when skeletal muscles contract to move external objects or to move the body in relation to the environment
- **Internal work** constitutes all other forms of biological energy expenditure that do not accomplish mechanical work outside the body.

Energy output

Internal work encompasses two types of energy-dependent activities

(1) skeletal muscle activity used for purposes other than external work, such as the contractions associated with postural maintenance and shivering,

(2) all energy-expending activities that must go on all the time just to sustain life. the "metabolic cost of living."

- work of pumping blood and breathing,
- the energy required for active transport of critical materials across plasma membranes
- energy used during synthetic reactions essential for the life maintenance, repair, and growth of cellular structures (metabolic cost of living.) "

Content of Foods in Kcal

Carbohydrate	Protein	Fat
~ 4 kcal/gram	~ 4 kcal/gram	~ 9 kcal/gram
~ 45%, American diet	~ 15%, American diet	~ 40%, American diet

For a 2000 kcal/day diet, the approximate kcalories and weight consumed per food per day are:

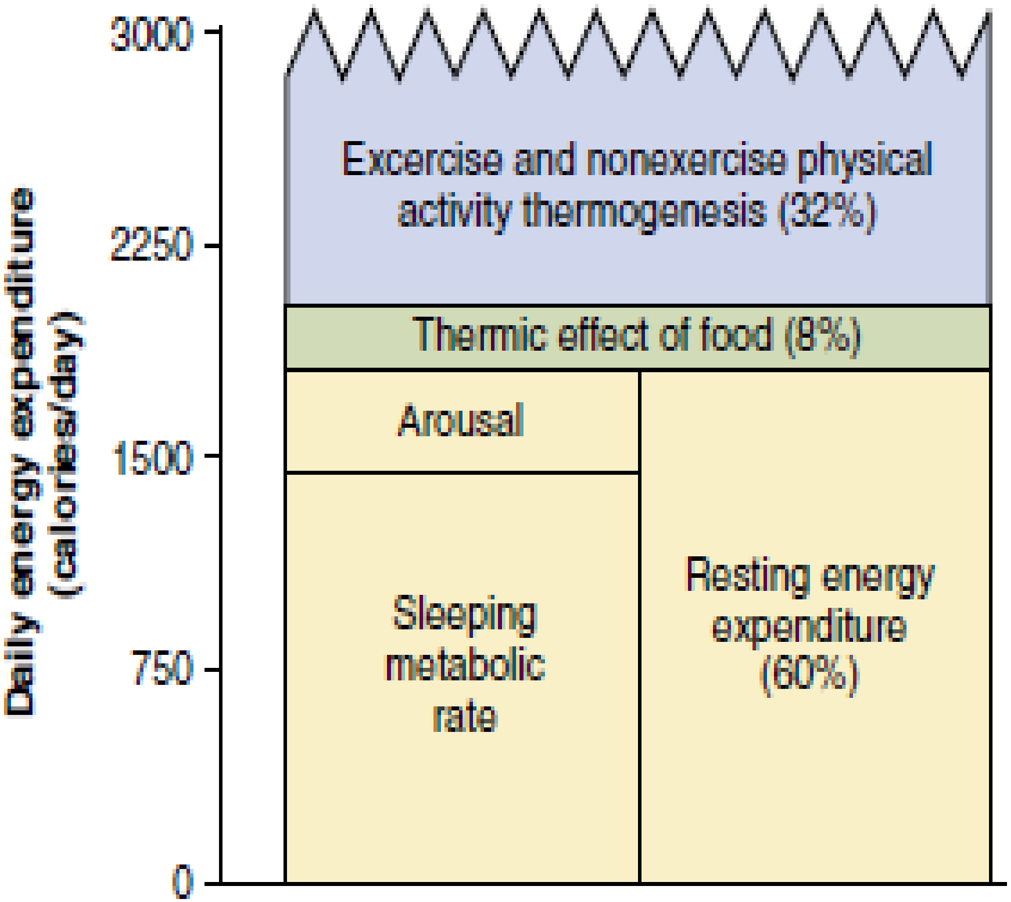
900 kcal	300 kcal	800 kcal
~ 225 grams *	~ 75 grams *	~ 89 grams
or 7.9 oz. *	or 2.64 oz. *	or 3.14 oz.

Overall Energy Requirements for Daily Activities

- An average man who weighs 70 kilograms and lies in bed all day uses about 1650 Calories of energy.
- The process of eating and digesting food increases the amount of energy used each day by an additional 200 or more Calories, so the same man lying in bed and eating a reasonable diet requires a dietary intake of about 1850 Calories per day. If he sits in a chair all day without exercising, his total energy requirement reaches 2000 to 2250 Calories.(SDA)
- Therefore, the daily energy requirement for a very sedentary man performing only essential functions is about 2000 Calories.
- The amount of energy used to perform daily physical activities is normally about 25% of the total energy expenditure, but it can vary markedly in different individuals, depending on the type and amount of physical activity
- In general, over a 24-hour period, a person performing heavy labor can achieve a maximal rate of energy utilization as great as 6000 to 7000 Calories, or as much as 3.5 times the energy used under conditions of no physical activity

Average daily energy expenditure and components of energy usage in a 70-kg person in energy balance and ingesting approximately 3000 Calories per day.

Specific dynamicaction (**SDA**), also known as **thermic effect of food** (**TEF**) or **dietary induced thermogenesis** (**DIT**), is the amount of energy expenditure above the basal metabolic rate due to the cost of processing food for use and storage



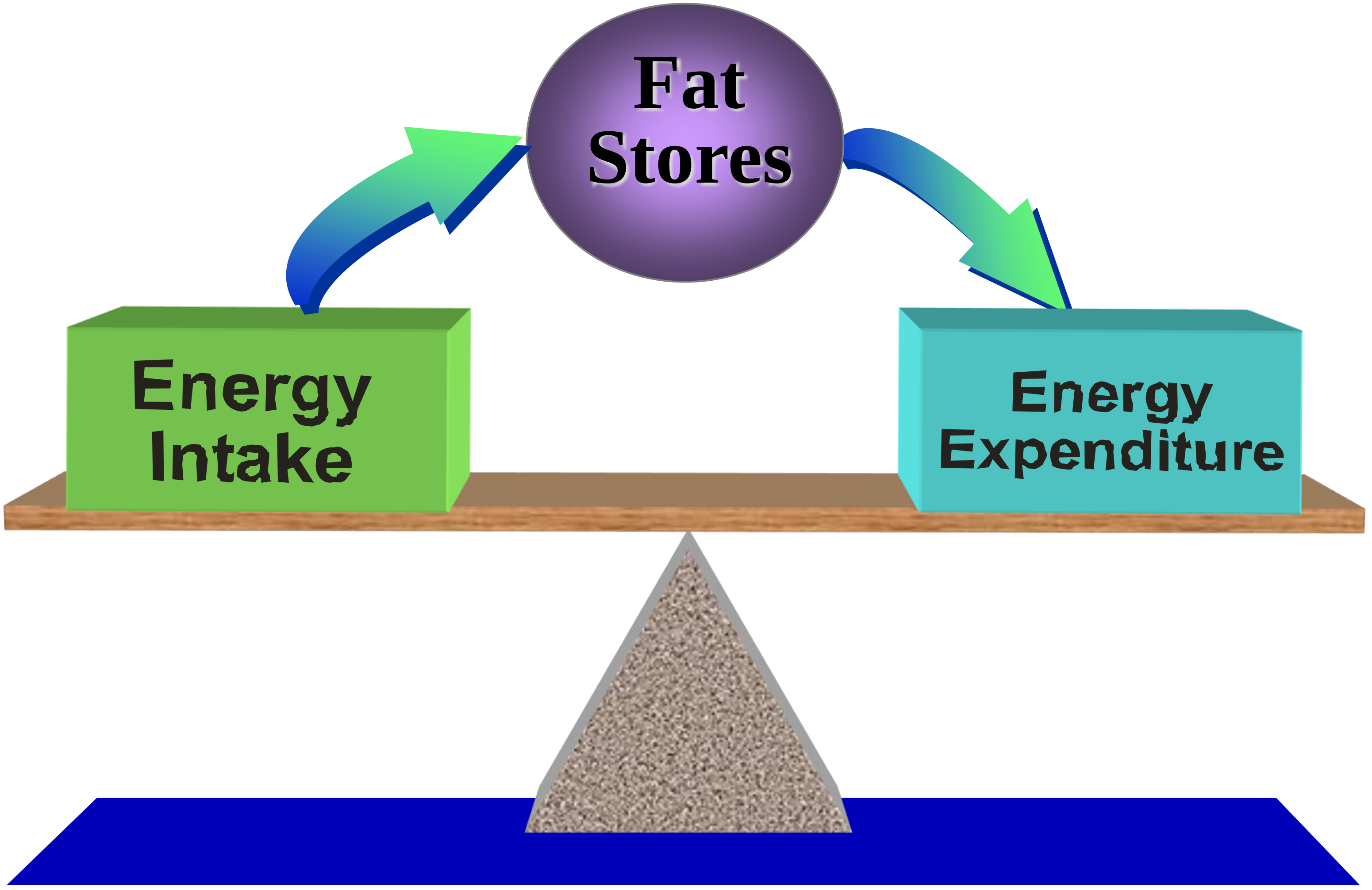
ENERGY BALANCE

Neutral energy balance. If the amount of energy in food intake exactly equals the amount of energy expended in performing external work plus the basal internal energy expenditure that eventually appears as body heat, then energy input and output are exactly in balance, and body weight remains constant.

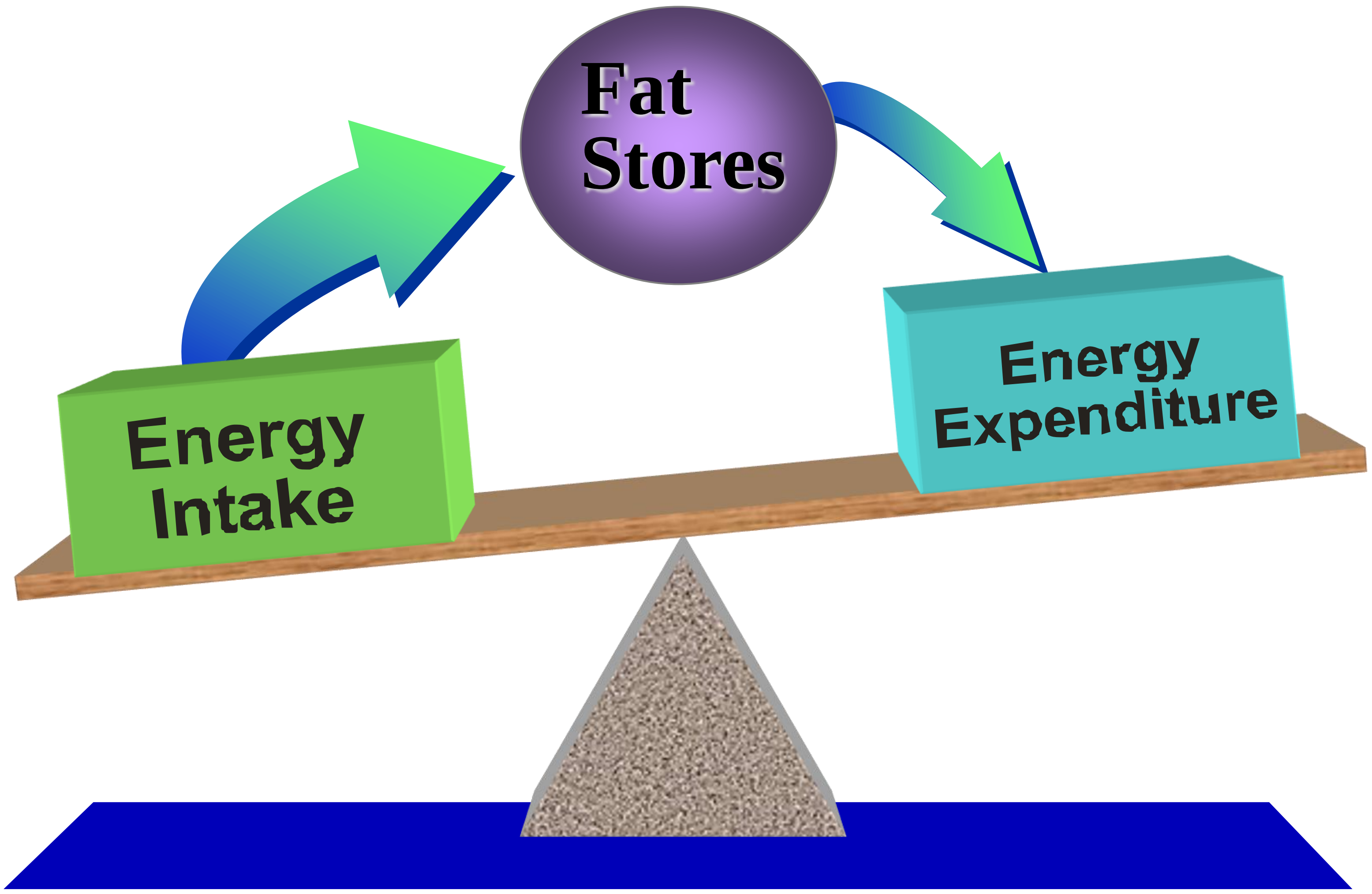
Positive energy balance. If the amount of energy in food intake is greater than the amount of energy expended, the extra energy taken in but not used is stored in the body, primarily as adipose tissue, so body weight increases

Negative energy balance. If the energy derived from food intake is less than the body's immediate energy requirements, the body must use stored energy to supply energy needs, and body weight decreases accordingly.

Intake and Expenditure are Balanced



Obesity Is Caused by Long-Term Positive Energy Balance



The metabolic rate is the rate of energy use.

- The rate at which energy is expended by the body during both external and internal work is known as the **metabolic rate**:
- Metabolic rate = energy expenditure/unit of time
- Because most of the body's energy expenditure eventually appears as heat, the metabolic rate is normally expressed in terms of the rate of heat production in kilocalories per hour.
- The basic unit of heat energy is the **calorie,** which is the amount of heat required to raise the temperature of 1 g of H2O by 1°C.
- This unit is too small to be convenient when discussing the human body because of the magnitude of heat involved, so the **kilocalorie** or **Calorie,** which is equivalent to 1000 calories, is used.

Basal Metabolic Rate

- This minimum level of energy required to exist is called the *basal metabolic rate* (BMR) and accounts for about 50% to 70% of the daily energy expenditure in most sedentary persons
- The **basal metabolic rate (BMR)** is a reflection of the minimal rate of internal energy expenditure.
- The usual method for determining BMR is to measure the rate of oxygen utilization over a given period under the following conditions:
- The person must not have eaten food for at least 12 hours. to avoid **diet-induced thermogenesis (Specific dynamic action)** or the obligatory, short-lived (less than 12-hour) rise in metabolic rate that occurs as a result of the increased metabolic activity associated with processing and storing ingested nutrients
- The BMR is determined after a night of restful sleep.
- All psychic and physical factors that cause excitement must be eliminated.
- The temperature of the air must be comfortable and between 68°F and 80°F (in In a room at a comfortable temperature in the thermoneutral zone)

Basal Metabolic Rate

- No strenuous activity is performed for at least 1 hour before the test
- The person should be at mental rest to minimize skeletal muscle tone (people “tense up” when they are nervous) and to prevent a rise in epinephrine, a hormone secreted in response to stress that increases metabolic rate.
- The BMR normally averages about 65 to 70 Calories per hour in an average 70-kilogram man
- The BMR of a man of average size is about 2000 kcal/d
- The BMR is expressed as a percentage increase or decrease above or below a standard normal values.
- Thus, a value of +65 means that the individual's BMR is 65% above the standard for that age and sex.

FACTORS AFFECTING THE METABOLIC RATE

- Height, weight, and surface area
- Sex Males have higher metabolic rate than female due to larger muscle mass
- Age : Much of the decline in BMR with increasing age is probably related to loss of muscle mass and replacement of muscle with adipose tissue, which has a lower rate of metabolism
- Muscular exertion
- Recent ingestion of food (Specific dynamic action)
- Circulating levels of thyroid hormones
- Circulating epinephrine and norepinephrine levels
- High or low environmental temperature
- Growth Reproduction , Lactation
- Body temperature Increased body temperature during fever increases basal metabolic rate

FACTORS AFFECTING THE METABOLIC RATE

Male Sex Hormone Increases Metabolic Rate. The male sex hormone testosterone can increase the metabolic rate about 10% to 15%. The female sex hormones may increase the BMR a small amount, but usually not enough to be significant. Much of this effect of the male sex hormone is related to its anabolic effect to increase skeletal muscle mass.

Growth Hormone Increases Metabolic Rate. Growth hormone can increase the metabolic rate by stimulating cellular metabolism and by increasing skeletal muscle mass.

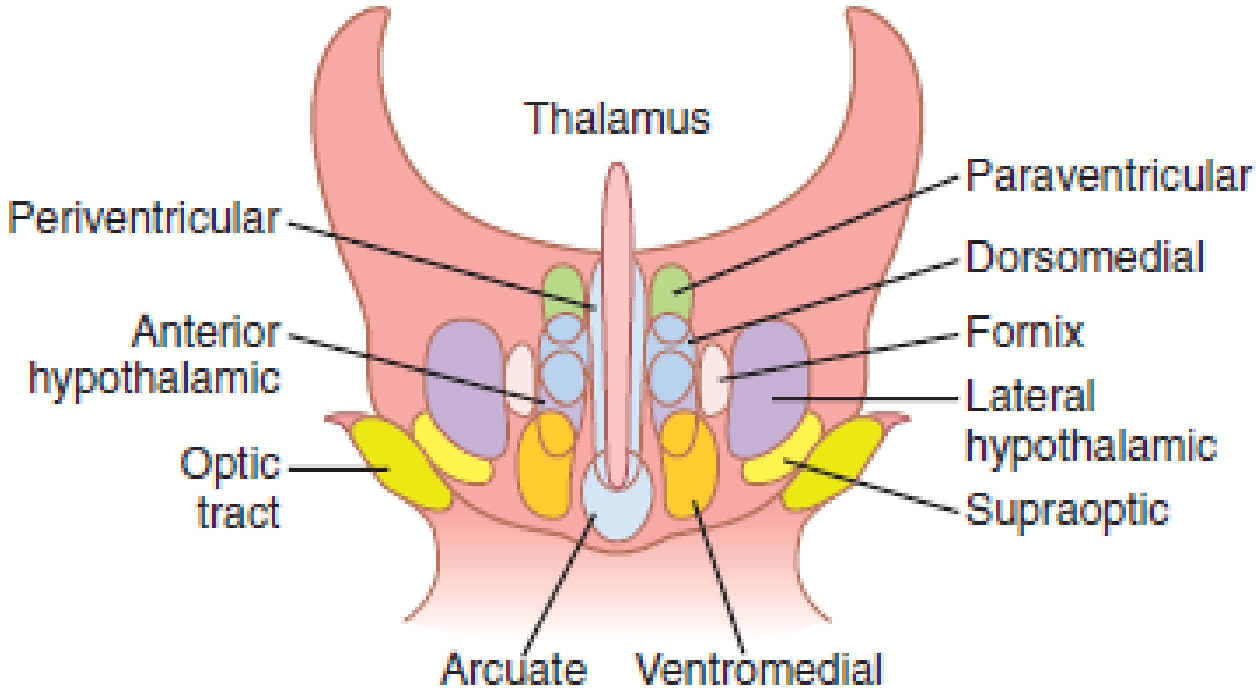
Sleep Decreases Metabolic Rate. The metabolic rate decreases 10% to 15% below normal during sleep. This decreases is due to two principal factors

(1) decreased tone

(2) decreased activity of the central nervous system.

Control of food intake and energy balance

Coronal view of the hypothalamus, showing the mediolateral positions of the respective hypothalamic nuclei.



Control of food intake”

Hypothalamus controls hunger and satiety.

- lateral nuclei serve as a feeding center (lesions cause *inanition*)
- ventromedial nuclei serve as the satiety center

  and inhibits the feeding center (lesions cause *hyperphagia*)
- paraventricular, dorsomedial, and arcuate nuclei

  play important roles

Brain stem : NST satiety center ?

- Feeding is modulated by higher centers (e.g. amygdala and prefrontal cortex) and Neurohumoral signals from the GI and adipose tissue

Role of arcuate nucleus

- Arcuate nucleus pathways involved in control of food
- Orexigenic pathway (appetite-stimulating) neurons release the following neurotransmitters
- Agouti-related peptide (AgRP)
- and Neuropeptide Y (NPY) releasing neurons

Anorexigenic (appetite-suppressant) pathways neurons release the following neurotransmitters

Cocaine- and amphetamine-regulated transcript (CART) and proopiomelanocortin (POMC) neurotransmitters. (Alpha melanocyte stimulating hormone)

Control of food intake

Both neuronal populations innervate the paraventricular nucleus (PVN), which, in turn, sends signals to other areas of the hypothalamus

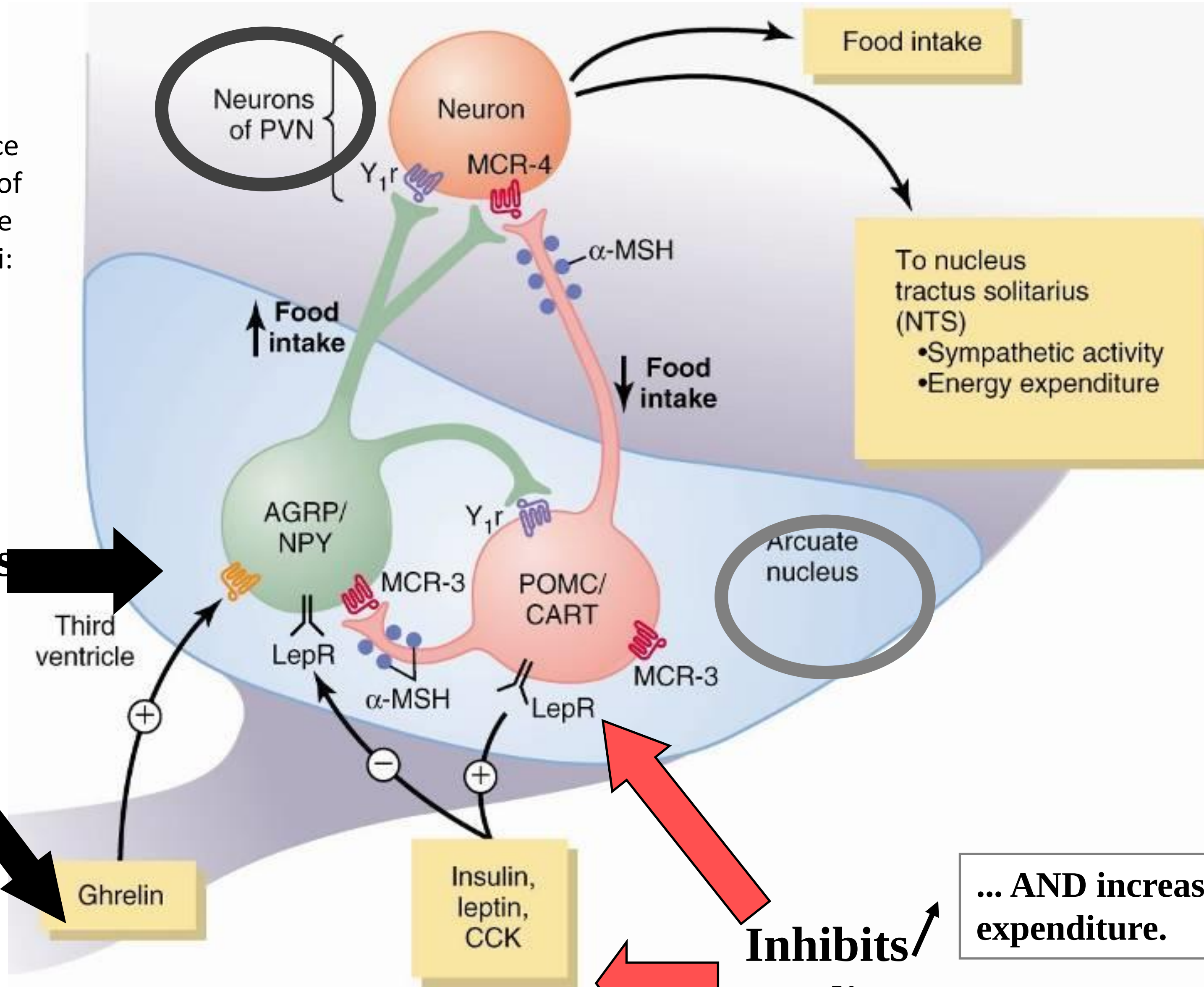
These include hypothalamic areas such as the ventromedial nucleus, dorsomedial nucleus, and the lateral hypothalamic area, which modulate this control system.

Brain circuits integrate information from the NTS and multiple hypothalamic nuclei to regulate overall body wight homeostasis

Beyond the Arcuate Nucleus

- Two hypothalamic areas are richly supplied by axons from the NPY and melanocortin-secreting neurons of the arcuate nucleus.
- These second-order neuronal areas involved in energy balance and food intake are the **lateral hypothalamic area (LHA)** and **paraventricular nucleus (PVN)**.
- The LHA and PVN release chemical messengers in response to input from the arcuate nucleus neurons. These messengers act downstream from the NPY and melanocortin signals to regulate appetite.
- The LHA produces **orexins** (ore-EKS-ins), which are potent stimulators for appetite and food of food intake (*orexis* means "appetite").
- Melanocortins inhibit the release of appetite-enhancing orexins.
- By contrast, the PVN releases chemical messengers, for example, **corticotropin-releasing hormone**, that decrease appetite and food intake.

Control of energy balance by two types of neurons of the arcuate nuclei:



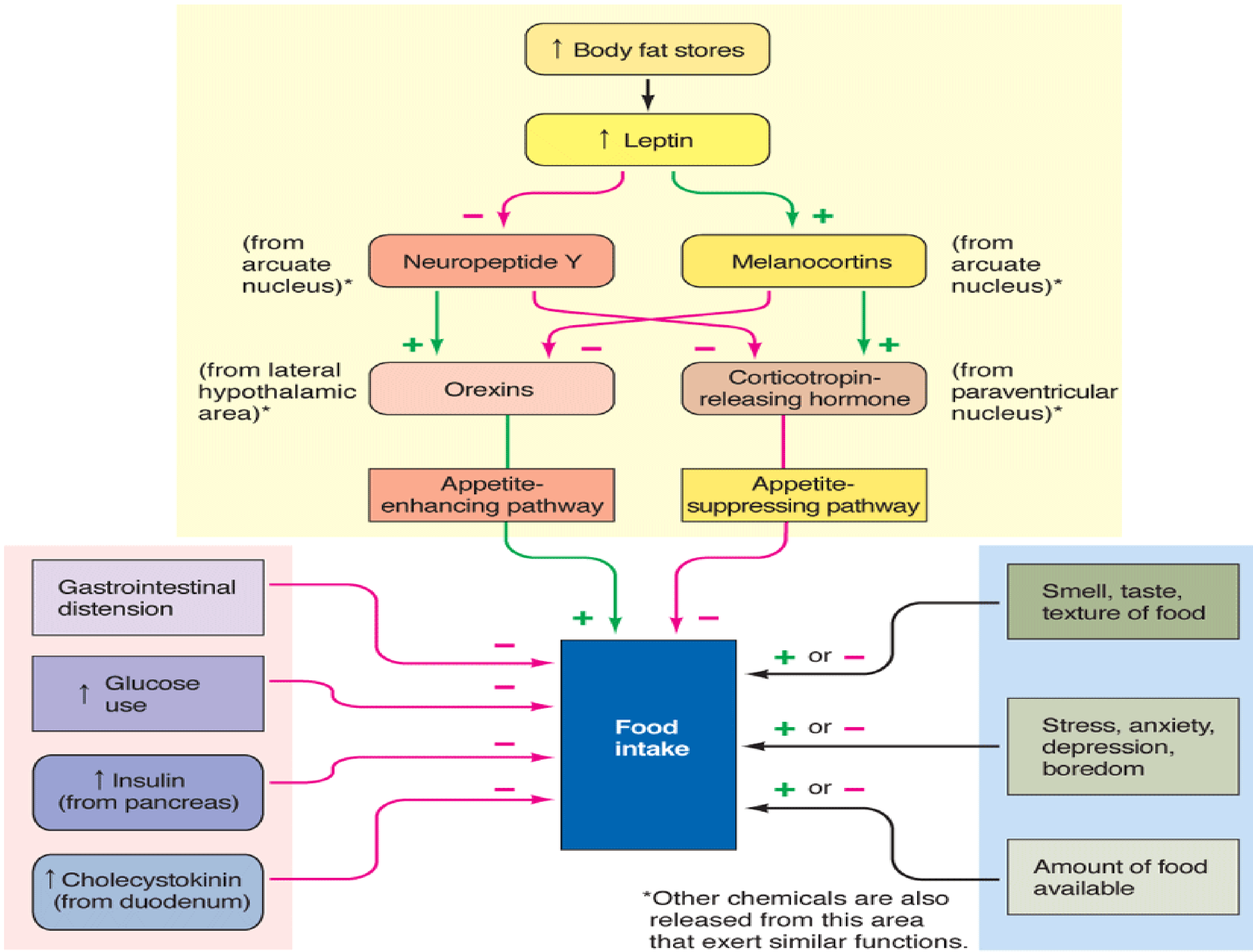
Stimulates Feeding

Inhibits Feeding

... AND increases energy expenditure.

Figure 71-2

Control of food intake



Satiety signals important in short-term control of the timing and size of meals

Adipose tissue-related signals important in long-term matching of food intake to energy expenditure to control body weight

Psychosocial and environmental factors that influence food intake

Regulatory Inputs to the Arcuate Nucleus in Long- Term Maintenance of Energy Balance: Leptin and Insulin

- Adipose tissue secretes several hormones, collectively termed **adipokines,** that play important roles in energy balance and metabolism

- One of the most important adipokines is **leptin,** a hormone essential for normal body-weight regulation (*leptin* means “thin”). The amount of leptin in the blood is an excellent indicator of the total amount of triglyceride fat stored in adipose tissue: The larger the fat stores, the more leptin released into the blood.

- The arcuate nucleus is the major site for leptin action. Acting in negative-feedback fashion, increased leptin from burgeoning fat stores serves as a “trim-down” signal. Leptin suppresses appetite, thus decreasing food consumption and promoting weight loss, by inhibiting hypothalamic output of appetite-stimulating NPY and stimulating output of appetite suppressing melanocortins

Long term regulation of food intake Role of leptin and insulin

- Conversely, a decrease in fat stores and the resultant decline in leptin secretion bring about an increase in appetite, leading to weight gain. The leptin signal isgenerally considered the dominant factor responsible for the long-term matching of food intake to energy expenditure so that total body energy content remains balanced and body weight remains constant
- Insulin Had long term regulation of food intake
- Insulin, a hormone secreted by the pancreas in response to a rise in the concentration of glucose and other nutrients in the blood following a meal, stimulates cellular uptake, use, and storage of these nutrients Thus, the increase in insulin secretion that accompanies nutrient abundance, use, and storage appropriately inhibits the NPY-secreting cells of the arcuate nucleus, thus suppressing further food intake
- In addition to the importance of leptin, insulin, and perhaps other so-called **adiposity signals** (signals related to the size of fat stores in adipose tissue) and their downstream mediators in the long-term control of body weight, other factors play a role in controlling the timing and size of meals.

Functions of Leptin

Stimulation of leptin receptors in these hypothalamic nuclei initiates multiple actions that decrease fat storage, including

(1) decreased production in the hypothalamus of appetite stimulators, such as *NPY* and *AGRP*;

(2) *Activation of POMC neurons*, causing release of α-MSH and activation of melanocortin receptors;

(3) increased production in the hypothalamus of substances, such as *corticotropin-releasing hormone*, that decrease food intake;

(4) *increased sympathetic nerve activity* (through neural projections from the hypothalamus to the vasomotor centers), which increases metabolic rate and energy expenditure

(5) *decreased insulin secretion* by the pancreatic beta cells, which decreases energy storage. Thus, leptin is an important means by which the adipose tissue signals the brain that enough energy has been stored and that intake of food is no longer necessary.

Neurotransmitters and hormones that influence feeding

Decrease feeding (anorexogenic)

a-Melanocyte Stimulating hormone (a-MSH)
Insulin
Leptin
Cholecystokinin (CCK), glucagon like peptide
Norepinephrine serotonin ,

Increase feeding (orexogenic)

Neuropeptide Y (NPY)
Agouti related peptide (AGRP)
Endorphins, Endocannabinoids
Cortisol
Ghrelin

Short-Term Regulation of Food Intake

Gastrointestinal Filling Inhibits Feeding

Gastrointestinal Hormonal Factors Suppress Feeding. *CCK,*

Peptide YY (PYY) is secreted from the entire gastrointestinal tract

glucagon-like peptide (GLP),

Ghrelin, a Gastrointestinal Hormone, Increases Feeding. (Hunger hormone)

Oral Receptors Meter Food Intake

Causes of obesity

1. Greater energy intake than energy expenditure
2. Primary and secondary obesity
3. Decreased physical activity and abnormal feeding regulation as causes of obesity
    a. Sedentary lifestyle
    b. Abnormal feeding behavior
    c. Environmental → industrialized countries
    d. Psychological → stress, illness
        - Social

Causes of obesity

3. Childhood over nutrition: increase number of fat cells 3x normal in obese child also number of fat cell increase during puberty.

4. Neurogenic abnormalities: lesions, neurotransmitters, receptors

5. Genetic factors: runs in families 20-25% of cases of obesity maybe caused by genetic factors

6. Neurogenic causes

7. Endocrine cause

Role of Genetics in Obesity?

Gene Mutations

- Leptin gene or leptin receptor mutations (very rare)
- Melanocortin 4 receptor mutations (~4-6% of early onset morbid obesity; not a major cause of adult onset obesity)
- Prader-Willi syndrome (also has many other disorders such as short stature, hypogonadism, hypotonia, hyperphagia); mutations on long arm of chromosome 15

Inanition, Anorexia, and Cachexia

Inanition - the opposite of obesity (extreme weight loss)

- inadequate food supply or loss of appetite

Anorexia - decreased appetite (CNS mechanisms)

- Anorexia nervosa (psychic disorder)

Cachexia - severe metabolic disorder of increased energy use and "wasting" - more than can be explained by decreased food intake alone; anorexia and cachexia often occur together.

- cancer

Thank you for your attention

Methods of Measuring the Basal Metabolic Rate

Direct measurements of heat production:

The person sits in an insulated chamber with water circulating through the walls. The difference in the temperature of the water entering and leaving the chamber reflects the amount of heat liberated by the person and picked up by the water as it passes through the chamber.

Indirect calorimetry

Measures person's O2 uptake per unit of time

Food + O_2 ⟶ CO_2 + H_2O + energy (mostly transformed into heat)

This approximate value, known as the **energy equivalent of O2**, is 4.8 kcal of energy liberated per liter of O2 consumed.

Using this method, the metabolic rate of a person consuming 15 liters/hour of O2 can be estimated

Calculation of metabolic rate using **energy equivalent of O2**

Let us assume that a person consumed 15l/hour Using the energy equiveillance of O2 what the estimated metabolic rate

15 liters/hr 5 O2 consumption

3.48 kilocalories/liter (**energy equivalent of O2**)per liter

energy equivalent of O2 = 15*3.48 =72 kilocalories/hr

Which is the estimated basal metabolic rate per hour

Respiratory Quotient

Respiratory Quotient (Tissues) $= \dfrac{\text{carbon dioxide output}}{\text{oxygen usage}}$

Respiratory Exchange Ratio (Lungs) $= \dfrac{\text{carbon dioxide output}}{\text{oxygen uptake}}$

The two are equal in steady state and usually average approximately 0.8 on a normal diet

Protein metabolism is fairly stable, so *changes* in RQ measured are usually are due to fat/carbos.

RQs if Burning Pure ….

carbohydrates = 1.0
protein = 0.8
fat = 0.7

RQs:

- Immediately after a meal ~ ? 1.0
- 8-10 hrs after a meal ~ ? 0.7
- diabetes mellitus without insulin ~ ? 0.7

Assessment of obesity

- **Body mass index (BMI)**
- **Skin fold measurement**
- **Waist – hip ratio**
- **Body fat (total & %)**

Stadiometer and weighing machine for BMI measurement

Body Mass Index (**BMI**)

Weight in kg/height in m^2

Example: Body weight= 50 kg

Height= 157.5 cm or 1.58 M,($1.58^2 = 2.5$)

BMI = 50 / 2.5,

BMI = 20

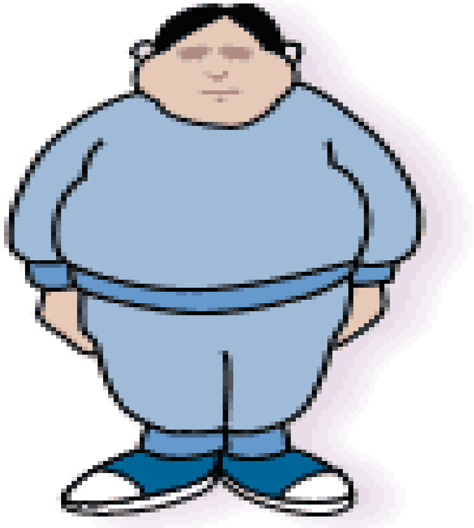
Classification	BMI (kg/m^2)	Risk of co-morbidities
Under weight	< 18.5	Low
Normal range	18.5-24.9	Moderate
Over weight	25-29.9	Mildly increased
Obese	>30	
Class I	30-34.9	Moderate
Class II	35-39.9	Severe
Class III	> 40	Very severe

Central obesity (android obesity)

Fat accumulation around the abdomen (apple)

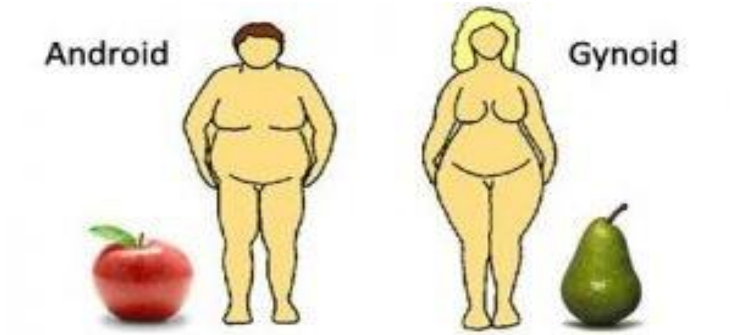
Associated with increase risk of Coronary heart diseases.

Associated with men



Lower body fat (gynoid obesity)

1. Fat accumulation around the hips (pear)
2. Not associated with increase in disease
3. Associated with women

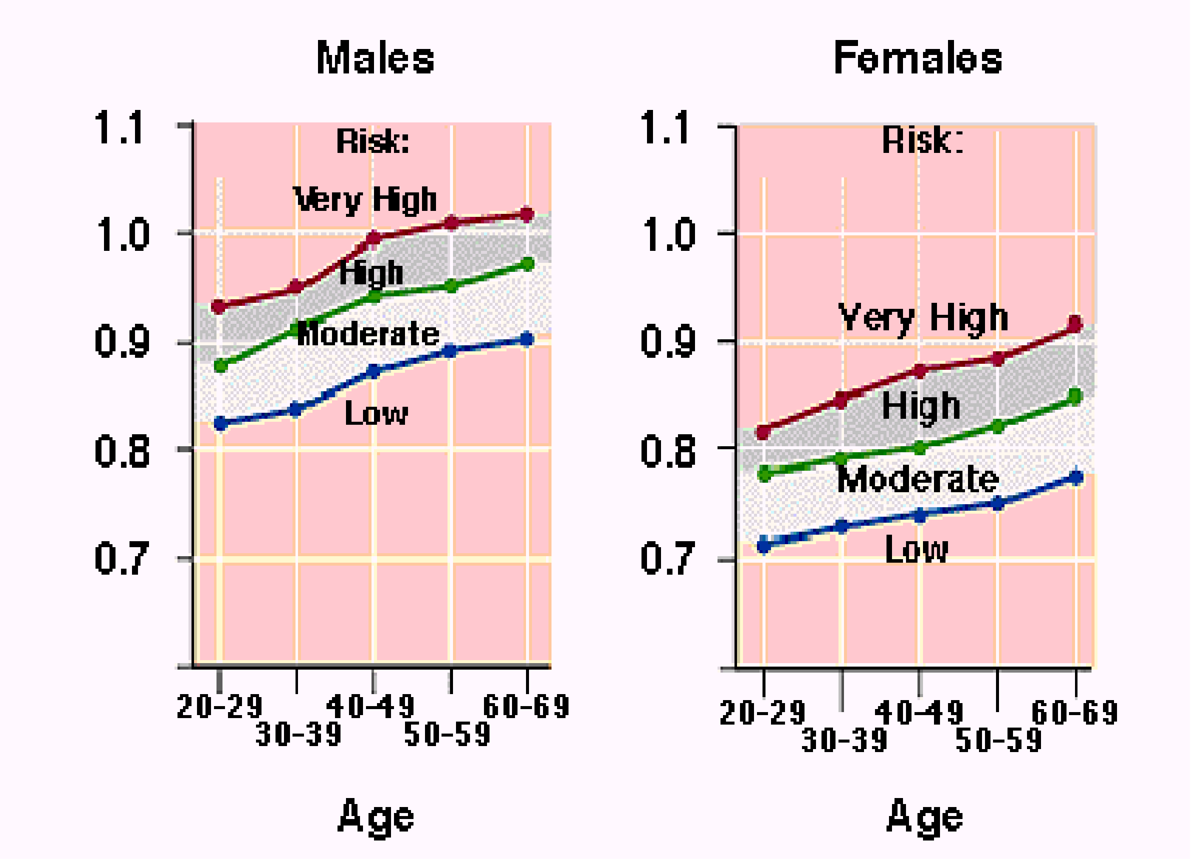


Normal values of Waist to hip ratio

Normal values

WHR <1.0 in a male

WHR < 0.8 in female



Body fat percentage

a. Male 10-25%

b. Female 18-32%

Thank you for following up later on this section