Disorders of metabolism

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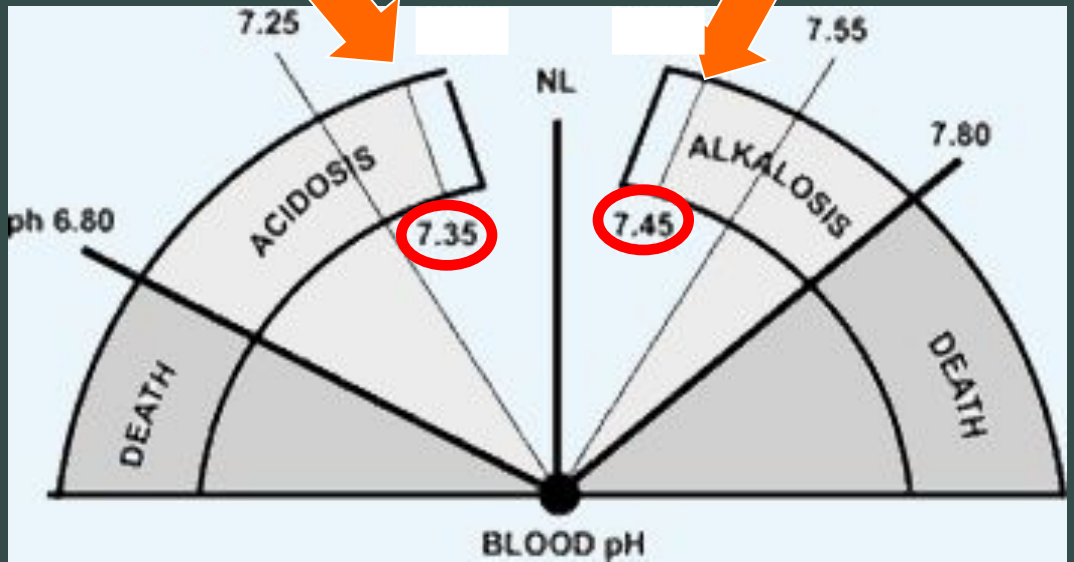
ABB regulation

Acidosis
pH < 7.35

Alkalosis
pH > 7.45



Blood buffer systems

Bicarbonate buffer system

the most mobile (can be regulated by lungs and kidneys) 7-9% of general blood buffer capacity .

Proteins, especially **hemoglobin** (oxy-hemoglobin and reduced hemoglobin)

the most powerful buffer system.

The Phosphate Buffer System

5% of total capacity

works mainly in intra-cellular fluids and urine

Physiological mechanisms of ABB regulation

Respiratory system

regulation of the $_{P}CO_2$ and, hence, H_2CO_3 of the blood

Kidneys

acidogenesis, ammoniogenesis, Berliner's exchange, excretion of phosphates

GIT

stomach HCL, intestinal content, ammonia in liver

Respiratory acidosis

Reason: hypoventilation of lungs (obturation of respiratory tract, pulmonary edema, □ of respiratory center , problems with respiratory muscles and thoracic chest)

Compensatory mechanisms:

- Acute - □ frequency and depth of respiration.
- Long-term
  - hemoglobin buffer (5-10 minutes)
  - renal acidogenesis (3-5 days).

The effects of high pCO_2

- spasm of peripheral arterioles, □ of BP
- □ urine formation.
- brain vessels dilate, □ spinal fluid and □ of intracranial pressure □headache
- sedative effect on nervous system.
- activation of vagal nerve (bradycardia, spasm of bronchial muscles, □ mucus secretion) – vicious circle

Metabolic acidosis

Reasons:

- failure of the kidneys to excrete the metabolic acids (uremia)
- loss of bases from GIT (diarrhea, loss of pancreatic secretions)
- **exogenous acidosis** :
  - long excessive consumption of sour food
  - poisoning with acids

Metabolic acidosis

Formation of excess of metabolic acids in the body:

Ketoacidosis*:* accumulation of keton bodies (diabetes mellitus).

Lactate-acidosis: physical overload, severe hypoxia, permanent fever, liver failure

Compensation:

- ↑ pulmonary ventilation.
- Protein and hemoglobin buffer (accumulate H^+).
- Acidogenesis, reabsorbtion of bases in kidneys. ↓urine pH

Acidosis clinical manifestation

- depression of the central nervous system (from disorientation to coma).
- □ blood vessels tone, □ brain and heart circulation (circulatory hypoxia)
- Kussmaul respiration (metabolic acidosis)
- □ pulmonary ventilation in respiratory acidosis.
- □ K in plasma □arrhythmia
- decalcification of tissues

Respiratory alkalosis

Reason - hyperventilation:

- excitation of respiratory center (brain inflammation or edema)
- reflex stimulation of respiratory center (pneumonia, pneumosclerosis, altitude and mountain disease)
- incorrect artificial respiration.

Compensation:

- Decrease of pulmonary ventilation
- Excretion of bases with urine

Metabolic alkalosis

Reasons:

- Diuretic drugs – reabsorption of Na; loss of H^+ and K^+
- Excessive use of sodium bicarbonate (treatment of gastritis or peptic ulcer).
- Loss of Cl ions - excessive vomiting of gastric contents.
- Excess of aldosterone (see diuretic drugs)

Clinical manifestation of alkalosis

- ↓ pCO_2 – spasm of brain vessels and dilation of peripheral vessels → collapse → ↓kidney function
- ↓ Ca - muscles tetany (tonic spasm).
- ↓ K – muscles paralysis (respiratory , intestinal obstruction)
- overexcitability of the nervous system:
  - CNS – nervousness, excitation,
- ↑ affinity of oxygen to hemoglobin → tissue hypoxia and cellular acidosis

Water (Fluid) Balance Disorders

Hypohydration symptoms (2-15% of body weight)

- □ of blood circulating volume
- weight loss of the patient
- strong thirst, dry mouth
- □ saliva, tears production
- □ urine output
- □ skin elasticity
- eye collapse and abnormal vision.
- □ of blood viscosity (hemoconcentration)

Water (Fluid) Balance Disorders

Hypohydration symptoms

- Nervous system disorders:
  - headache, dizziness,
  - disorders of consciousness, inability to speak, illusions
- Hypoxia of mixed type:
  - due to disturbances in blood flow (circulatory hypoxia),
  - decrease in lungs perfusion (respiratory hypoxia),
  - metabolic disturbances in organs (tissue hypoxia).
- breathing and tachycardia

Hypohydration causes

hypoosmolar	isoosmolar	hyperosmolar
excessive sweating continuous diarrhea and vomiting Addison's disease polyuria	initial stage of acute blood loss extensive burns bacterial dysentery cholera stenosis of pylorus	water intake drinking sea water in hypohydration hyperthermia, hyperpyretic fever. prolonged ALV with insufficiently moistened gaseous mixture
low	normal	high

concentration of electrolytes in blood plasma (osmotic pressure)

Hyperhydration causes

hypoosmolar	isoosmolar	hyperosmolar
□water intake + □ function of the kidneys treatment of hypohydration with pure water and low osmotic solutions increase of ADH production	infusion of a great amount of isotonic solutions congestive heart failure hypoproteinemia chronic lymphostasis	infusion of the hyperosmolar solutions acute renal failure (□ salt excretion) forced intake of sea water hyperaldosteronism
low	normal	high

concentration of electrolytes in blood plasma (osmotic pressure)

Hyperhydration symptoms

- □ blood circulating volume and ABP
- heart overload
- general edema (cardiac failure and hypoproteinemia)
- polyuria (in absence of kidney diseases)

Water intoxication (severe cases) :

- pulmonary edema
- brain edema (headache, inadequate behavior, disorders of consciousness)
- nausea, vomiting (intracranial hypertension)
- hemolysis of erythrocytes.

Edema

- Accumulation of excess fluid:
  - in intercellular space
  - body cavities (hydrothorax, hydropericardium and hydroperitoneum (ascites))
- generalized (anasarca) or local disorder
- inflammatory (exudate) or non-inflammatory (transudate) origin

Edema mechanisms

- □ capillary hydrostatic pressure (high venous BP – local, systemic)
- Alterations in oncotic pressure (low albumin content - problems with intake, digestion, synthesis, loss)
- Impaired lymph flow (filariasis, trauma, surgery, tumors)
- Renal retention of Na and water (impaired kidney function)

Starvation

Forms of starvation:

- Total (absolute) – deprivation of food and water
- Complete – deprivation only of food, but not water
- Incomplete – restriction of food intake.
- Partial – decreased intake of proteins, lipids, carbohydrates, minerals, vitamins.

Starvation

- Exogenous:
  - voluntary starvation
  - involuntary (social and economical problems)
  - eating disorders (Anorexia nervosa)
- Endogenous:
  - malabsorption syndrome
  - chronic wasting disorders (cancer, heart failure)
  - increased catabolism (DM, thyrotoxicosis)
  - increased metabolic demands

Stage 1. Early starvation

blood glucose glucagon glycogenolysis

Glycogen stores are depleted in 12 to 24 hours.

- gluconeogenesis (aminoacids, fatty acids)
  - Glucose - only for brain nutrition
  - Other tissues use ketone bodies (product of incomplete oxidation of fatty acids)

BMR in the beginning of the stage

in the end -

- patient's weight loss - maximal;

Stage 2 Prolonged starvation

- □ protein catabolism
- high lipolysis + □ muscle oxidation of ketone bodies = accumulation of ketone bodies

Ketone bodies become the main fuel for the brain

Body's activity is decreased:

- □ energy expenditure, body $T^{0,}$ heart rate, BP and respiration
- □ brain activity (apathy, low memory)
- □ proteins synthesis, □ activity of immune system
- skeletal and respiratory muscles progressive weakness.
- atrophy of GIT organs

Stage 3 Terminal phase

- Lipid stores of body are completely depleted (97-100%), loss of 40-50% body weight
- Then protein store of inner organs, muscles, cell membranes, blood are used for energy needs.

Clinical features:

- Fluid and electrolyte imbalance, dehydration and edema
- Severe cardiac arrhythmias
- Loss of neural control upon the body (paralysis)
- Patient's death

Obesity

Excessive accumulation and storage of fat in the body.

Body mass index (BMI) - weight/height (in kg/m^2).

- Normal BMI - 19 to 25 kg/m^2.
  - 25-30 - overweight or obesity 1^{st} stage.
  - 30-40 - obesity 2^{nd} stage
  - over 40 - 3^{rd} stage (morbid obesity)

Obesity classification

General and local obesity.

- Local obesity - central or peripheral.
- Central obesity (upper body obesity) – fat accumulation in the abdominal area (males)
  - waist/hip ratio > 0,8 – females, >1,0 - males
  - levels of circulating free fatty acids, overload of liver
  - risk of negative consequences.
- Peripheral obesity (lower body obesity) – subcutaneous fat in gluteal –femoral zone (females).

Obesity classification

- Hyperplastic obesity - □ number of fat cells.
  - massive obesity & early age of development.
- Hypertrophic obesity – normal number and □ size of fat
  - moderate obesity in adults.
- Mixed obesity - □ of fat cell size and amount.
  - When all the existing fat cells are filled with lipids new cell are formed
  - the number of fat cells can't be decreased by diet and weight loss

Obesity classification

Primary obesity - leptin deficiency or decreased function.

- 20% obese patients - absolute leptin deficiency.
- 80% of people with primary - relative leptin deficiency
  - Leptin - protein hormone, synthesized by adipocytes
    - signals to the brain about satiety
    - ↓ synthesis of neuropeptide Y (which stimulate appetite)
    - □ energy expenditure.

Secondary obesity due to:

- ↓ energy expenditure
- ↓ triglycerides use as energy source;
- □ lipids synthesis (□ insulin or glucocorticoids, ↓ thyroid hormones.

Obesity pathogenesis

Neural mechanisms:

- Central (psychogenic) mechanism:
  - food addiction.
- Hypothalamic mechanism:
  - synthesis of neuropeptide Y

Endocrine mechanisms:

- Absolute or relative leptin deficiency ;
- Low thyroid hormones (↓ lypolysis, BMR and energy expenditure);
- High glucocorticoids (lipogenesis);
- High insulin (lipogenesis).

Obesity Consequences

Insulin Resistance and Type 2 Diabetes Mellitus

weight gain insulin resistance type 2 DM

Atherosclerosis and Cardiovascular Disease

- obesity causes hyperlipidemia (LDL,VLDL)
- obesity causes hypertension
  - peripheral resistance,
  - cardiac output,
  - sympathetic nervous system tone,
  - salt sensitivity and salt retention.
- **Increased risk of myocardial infarction and stroke.**

Obesity Consequences

Pulmonary Disease

- obesity hypoventilation syndrome
- ↓ oxygen and carbon dioxide during sleep = obstructive sleep apnea
  - ↓ chest wall mobility,
  - work of breathing,
  - minute ventilation (due to high BMR),
  - ↓ total lung capacity and functional residual capacity.

Obesity Consequences

Gallstones

- □ secretion of cholesterol, supersaturation of bile.

Cancer

- increased rates of sex hormones conversion in adipose tissue.

Bone and Joint Disease

- osteoarthritis because due to joints overload with large body weight.
- □ incidence of gout.