Ministry of Health of Belarus
Gomel State Medical University

Department of Orthopedic, Trauma and military field surgery
with the course of Anesthesiology and Critical Care Medicine

Been approved by the Department of
№ __ "___" _____2019

Head of the department: MD, PhD Julia Cherniakova

SUBJECT: "General anesthesia. Inhalation general anesthesia. "

Educational and methodical development
For 4th year students of medical faculty

Author: MD, PhD,
Lyzikova TV

Gomel, 2019

Methodical development is designed for practical training by teacher. It provides:
I. Relevance of the topic
II. Purpose of the lesson
III. Tasks
IV. Basic Forums
V. Recommended Reading
VI. Questions for self-preparation
VII. Self-study
VIII. Clinical problems and test control

I. Relevance of the topic

Inhalational general anesthesia is the most common type of pain relief. It is achieved by introducing volatile or gaseous anesthetics into the body. Accordingly, inhalation can only be called the method of anesthesia, when the anesthetic is absorbed through the respiratory tract. Currently used substances for inhalation anesthesia is much less toxic than the previous ones used, and also much more efficient and manageable. In addition, modern anesthesia and respiratory equipment can significantly reduce their intra-operative consumption through the use of so-called "low-flow" anesthetic technique.

II. Purpose of the lesson

Study the features of the general inhalation anesthesia, the development of methodologies for the general inhalation anesthesia.

III. Tasks

The student should know:

- The essence of the method of inhalation anesthesia;
- The variety, the advantages and disadvantages of inhalation anesthesia;
- Features of a mask method of inhalation anesthesia;
- Method of endotracheal inhalation anesthesia: equipment for endotracheal anesthesia, the technique of intubation;
- Complications during laryngoscopy and intubation of the trachea and bronchi.

The student should be able to:

- To hold mask ventilation;
- Perform the Safar method;
- Determine the stage of anesthesia by Gvedel;

- To define the parameters of mechanical ventilation (respiratory rate, tidal volume);
- Evaluate the effectiveness of anesthesia;
- To justify the choice of drugs for inhalation anesthesia.

IV. Sections, studied before that are needed for the session

1. Anatomy of the respiratory system,
2. Normal and pathological physiology of the respiratory system;
3. Pharmacology of inhaled anesthetics.

V. Recommended Reading

Books on anatomy, normal and pathological physiology, anesthesiology for medical students.

Suggested Reading on lessons

Main Reading

1. Lectures;
2. Bunyatyan, AA Anaesthesia and Intensive Care / AA Bunyatyan [and others] Ed. Ed. AA Buniatian. - M., Medicine. - 1997. - 565 p.;
3. Dale, OA Anaesthesia and Intensive Care / O. Valley [and others] Ed. Ed. OA Valley - M., Medicine - 2008. - 574 p.

Further Reading

1. Barash, P. Clinical Anesthesiology. / P. Barash, B.Kullen. - M., 2004. - S. 104-113.
2. Morgan Jr.., J. Edward. Clinical Anesthesiology: in 3 vols 1. / J. Edward Morgan Jr.., Magid S. Michael. - Moscow, 2005. - S. 66-256.
3. Eytkenhed, AR Leadership in anesthesiology. / AR Eytkenhed, G. Smith. - M., 2007. - S. 415-432.
4. Gelfand, BR Anaesthesia and Intensive Care. / B.R.Gelfand. - M., 2006. - S. 258-263.

VI. Questions for self-preparation

Questions on basic knowledge

1. Anatomy of the upper respiratory tract;
2. Anatomical and physiological characteristics of the upper respiratory tract infections in children;

3. The structure of the trachea-bronchial tree;
4. Blood circulation in the lungs;
5. Mechanics of breathing. Regulation of respiration;
6. Ventilation-perfusion ratio.

Questions on this topic:
1. Anatomy and physiology of nociceptive and antinociceptive system (way of pain sensitivity, pain mediators);
2. Effect of pain on the function of organs and systems (circulatory, respiratory, gastrointestinal, urinary tract, endocrine system, blood, immune system, central nervous system);
3. Theories of anesthesia;
4. Types of modern general anesthesia, the components of general anesthesia;
5. The clinics, stages of general anesthesia;
6. Inhalational general anesthesia. Mask and endotracheal general anesthesia. The method of application, indications, contraindications;
7. Inhaled anesthetics. The concept of minimum alveolar ventilation (MAV), its distribution in the body, the solubility in lipids and blood;
8. Clinical and pharmacological characteristics of inhaled anesthetics: ether, nitrous oxide, halothane, isoflurane, sevoflurane, desflurane, enflurane.

Topics UIRS
1. One-lung intubation technique, indications for its use.
2. Methods of "low-flow" inhalation anesthesia
Teaching tools for organization of self study of students
1. Computer database;
2. Tasks, test control, tasks for self study of students;
3. Thematics of the sick
4. Medical history, anesthetic records of patients;
5. Training films;
6. The equipment needed to perform tracheal intubation and mask ventilation.

VII. Training Material
Pain is a subjective feeling of the individual, including sensory, emotional, and behavioral aspects, caused by actual or probable tissue damage. There is

considerable individual variability in the perception of pain, which is defined by sex and age of the patient, genetic, and socio-cultural factors. System of perception and transmission of pain signals called nociceptive (from the Latin «noci» - harm, damage, injury). Antinociceptive system - functional opposite - controls the activities of the structures nociceptive system.

Nociceptive system (the scheme of the pain impulse)

Nociceptors – are receptors, most of them are free nerve endings of unmyelinated fibers, perceiving thermal, mechanical and chemical-mechanical effects. They are characterized by a high activation threshold. Nociceptors are located both in somatic tissues and the internal organs.

Pain is conducted through the Three-neuron pathway that transmit nociceptive stimulus from the periphery to the cerebral cortex.

1st neurons - their bodies are in the spinal nodes located in the intervertebral foramen. Each neuron has one axon, which is divided into two branches:

- One supplies the peripheral tissues;
- The other - in the dorsal root is sent to the posterior horn of spinal cord and ends with the second synapse on cells of neurons.

2nd neurons - their bodies are in the rear horns of the spinal cord. Most of the second neuron axons are directed to the opposite side of the spinal cord through the front of the white spike, they are included in spinal-thalamic way and reaches the thalamus, the reticular formation, the raphe nuclei and central gray matter. The axons of the second neuron ends with synapse on cells of thalamic nuclei.

In addition, the axons of neurons 2 switch on the motor neurons of the anterior horn, which provides a reflex muscle activity (physiological and pathological) for pain stimuli, as well as sympathetic neurons, which provides autonomic responses to pain (vasoconstriction, spasm of smooth muscle, the release of cathecholamines).

3rd neurons - bodies are located in the thalamus, their axons are sent to the postcentral gyrus of the cerebral cortex, where a feeling of pain is formed and its localized in the anterior cingulate gyrus, which is mediated by the emotional component of pain, in the reticular formation and the limbic system.

Stages of pain sensitivity in the central nervous system:

Transduction - turning the damaging effects of an electrical pulse (ie, formation of the primary nociceptive impulses);
Transmission - transmission of the pain impulse along the afferent fibers of the damaged area in the spinal cord;
Modulation - to change the nature of the information in the spinal cord;
Perception - processing of nociceptive information in the cerebral cortex, the formation of feelings and emotional components of pain.

Antinociceptive system
Antinociceptive system weakens upward flow of pain impulses and intensity of pain. It is represented by a complex of structures that have a downward effect on the inhibitory transmission of pain stimuli (nucleus of the midbrain, the nucleus of the medulla oblongata). Carried downward through inhibition of serotonergic, noradrenergic, GABA-ergic and opioidergic systems (this explains the analgesic effect of antidepressants that block the neuronal capture of noradrenaline and serotonin). One of the mechanisms of suppression of endogenous pain caused by activation of opioid receptors by endogenous opioids (endorphins, enkephalins, donorfin). Endorphins and enkephalins are produced in the tissues of the body, react with opiate receptors and inhibit the sensation of pain, as well as changing the number of autonomic and emotional responses.

At present we know 5 types of opioid receptors:
1. Mu (μ) - are located in the structures of the brain and spinal cord. Stimulation of these receptors causes the following effects:
- Supraspinal analgesia;
- Physical dependence;
- Respiratory depression;
- Inhibition of gastrointestinal motility;
- Bradycardia;
- Sedation.
2. Kappa (κ) - are located in the brain and spinal cord. Their stimulation causes the following effects:
- Spinal analgesia;
- Pronounced sedation;
- Miosis;

- Inhibition of the release of antidiuretic hormone (ADH).
3. Delta (δ) - mainly localized in the brain, the effects of stimulation are:
- Spinal analgesia (significant level is below);
- Euphoria, perhaps hallucinations;
- Physical dependence;
- Respiratory depression;
- Nausea.
4. Sigma (σ) - the exact location is unknown, some authors believe that they are not true opiate receptors (as opioid receptor antagonist naloxone has no effect on them), as a result of stimulation observed:
- Dysphoria, hallucinations;
- Tachycardia;
- Respiratory depression;
- Hypotension.
5. Epsilon (ε) - currently not well understood.
The analgesic effect is mediated primarily μ - and κ-receptors, but to a greater extent μ-receptors.
Normally, the body has a constant balance between nociceptive and antinociceptive systems. Antinociceptive system is always a certain level of activation: a constant concentration of endorphins, enkephalins, serotonin, catecholamines, a certain degree of neuronal activity of the antinociceptive system. In this case, the pain may occur not only when you activate the nociceptive system, but also when level of functional antinociceptive system decreased.

The body's reaction to pain

Pain syndrome is a generalized response to the pain of the body and is characterized by activation of metabolic processes, the voltage of the endocrine, cardiovascular and respiratory systems to the stress level. Systemic effects of pain:
Cardiovascular system: the rise of blood pressure, tachycardia, an increase in total peripheral vascular resistance (SVR), and myocardial oxygen demand;
Respiratory system: reducing the depth of breathing, decrease in tidal volume (TV), the occurrence of ineffective cough and risk of atelectasis;
GIT: increase sphincter tone, decreased intestinal motility;
Urinary system: an increase in sphincter tone (urinary retention);
Coagulation system: increased platelet aggregation, inhibition of fibrinolysis;

Immunity: the development of lymphopenia, inhibition of the reticuloendothelial system, as a result - increased risk of infectious complications;
Endocrine organs: the increase in the concentration of catabolic hormones, reducing the concentration of anabolic hormones (insulin, testosterone), increasing the concentration of cortisol, renin, aldosterone, angiotensin and antidiuretic hormone (sodium retention, water and a secondary increase in extracellular space);
CNS: the emergence of anxiety, sleep disorders, depression (in continuous pain).

General anesthesia (narcosis)
Anesthesia - a condition caused by the influence of drugs on the central nervous system, characterized by the temporary shutdown of consciousness, pain sensitivity and a certain degree of muscle relaxation.
Types of anesthesia:
1) Inhalation;
2) Non-inhalation;
3) Multi-balanced (a combination of the first two methods).

Components of general anesthesia:
- Hypnosis;
- Amnesia;
- Pain Management;
- Myorelaxation;
- Autonomic correction;
- Maintenance of organ function and homeostasis.

Theory of anesthesia. At present there is no theory of anesthesia, clearly defining the mechanism of action of narcotic anesthetics. In chronological order, the basic theory can be summarized as follows:
1. Coagulation theory (Claude Bernard, 1875);
2. Lipoid theory (Meyer and Overton, 1899 - 1901);
3. The theory of "strangulation of nerve cells" (Verworn, 1912);
4. Adsorption theory (boundary voltage) (Traube, 1904 - 1913. Warburg, 1914 - 1918);
5. Theory of water microcrystals (Pauling, 1961);

6. Membrane Theory (Hobér, 1907 Winterstein, 1916) - has been widely used in recent years. It explains the development of anesthesia, anesthetic effect on the mechanisms of polarization and depolarization of the cell membranes of neurons.
In the period of organism anesthetic there is a certain regularity (staging) in the change of consciousness, breathing and circulation. Therefore, providing a certain stage, describing the depth of anesthesia.
Stage of anesthesia described by Gvedel *to ether anesthesia* in 1937. This classification is to be modified by I.S.Zhorov is the main and currently:
Stage analgesia (I): the patient is conscious, but slowed down, asleep, responds to questions in monosyllables. No superficial pain sensitivity, but tactile and thermal sensitivity saved. During this period, you can do the short-term interventions (opening phlegmon, abscesses, diagnostic studies).
Excitation stage (II): in this stage of the braking points of the cerebral cortex, while the subcortical centers are in a state of excitement: Consciousness is absent, expressed motor and language stimulation. Patients screaming, trying to get up from the operating table. Integuments hyperemic, frequent pulse, blood pressure increased. The pupil is wide, but reacts to light, watery notes. Often, there are cough, increased bronchial secretions, possible vomiting. Surgical procedures on the background of excitation cannot be carried out.
Surgical stage (III):
Level III, 1: the patient calm, steady breathing, blood pressure and heart rate reach the original values. The pupil begins to narrow, reaction to light is preserved. Observed smooth movement of the eyeballs, eccentric their location. Preserved corneal and pharyngeal-laryngeal reflexes. Muscle tone is saved, so an abdominal operation is difficult.
Level III, 2: a movement of the eyeballs stops, they are located in a central position. Pupils are beginning to gradually expand, the reaction of the pupil to light decreases. Corneal and pharyngeal-laryngeal reflexes are weakened and the end of the second level disappears. Breathing is calm, steady, blood pressure and pulse were normal. Begins lowering muscle tone, which allows abdominal surgery. Anesthesia usually performed at the level III, 1 - III, 2.
Level III, 3 - level of deep anesthesia. Dilated pupils, only respond to strong light stimulus, corneal reflex is absent. During this period, there is complete relaxation of skeletal muscles, including the intercostal muscles. Breathing becomes shallow, diaphragmatic. As a result of relaxation of the muscles of the lower jaw and the

tongue sinks closes the entrance to the larynx, leading to respiratory failure. To prevent this complication is necessary to bring the lower jaw forward and keep it in that position (reception Safar). Pulse at this level is frequent, reduced cardiac filling, blood pressure is reduced. Anesthetization at this level is dangerous for the patient's life.

Level III, 4: maximum mydriasis with no response to the light, the cornea is dull and dry. Breathing is shallow, at the expense of movement of the diaphragm due to paralysis of intercostal muscles. Thready pulse, frequent, low blood pressure or not is determined. Deepen anesthesia to the fourth level is dangerous for the patient's life, as it can stop breathing and circulation.

Stage of revival (IV). As soon as shutting down the drug, the concentration of anesthetic in the blood decreases, the patient in the reverse order goes through all stages of anesthesia and awakening occurs.

Inhalation anesthesia

Inhalation anesthesia - type of anesthesia in which the anesthetic is absorbed through the respiratory tract. Conduct inhalation anesthesia can be a mask and endotracheal way. Endotracheal way shown at the risk of aspiration during surgery on the abdominal and thoracic cavities, on the head and neck. For a brief time ¬ nepolostnyh interventions acceptable masked inhalation anesthesia.

The method of mask inhalation anesthesia

Face mask ensures the supply of breathing gas from the breathing circuit to the patient by creating a tight contact with a patient. Edge of the mask with soft rim and adapts to any face shape. Aperture mask attached to the breathing circuit through connector. There are many types of facial masks. Transparent case allows you to monitor exhaled moist mixture and immediately noticed the appearance of vomiting. Black rubber mask is usually sufficient plasticity, which allows a good fit it in atypical facial bone structures.

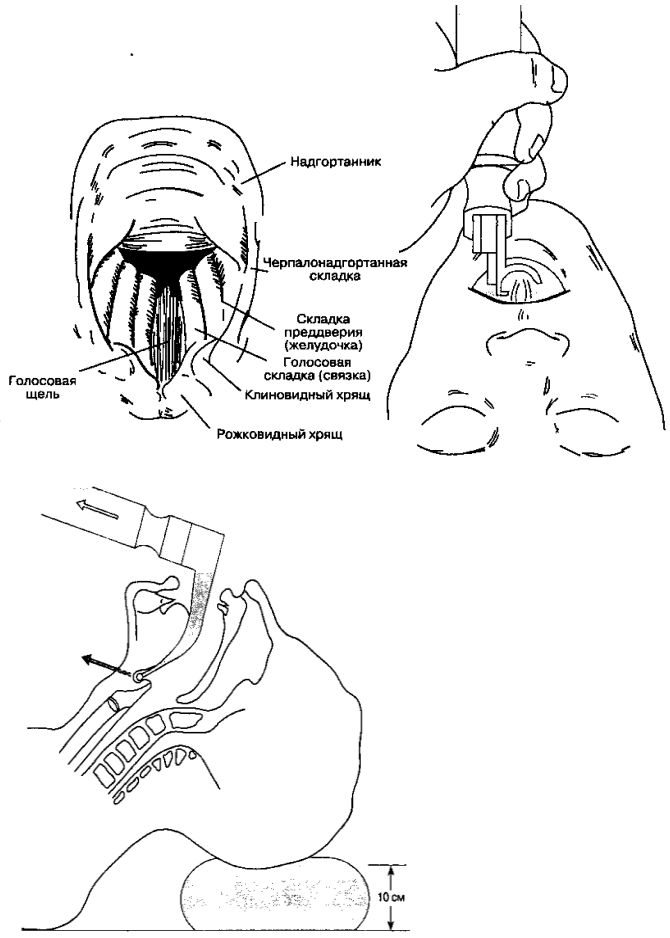
Methods of endotracheal inhalation anesthesia.

Intratracheal inhalation anesthesia delivery breathing gas from the breathing circuit to the patient through the endotracheal tube.

There are two ways to tracheal intubation: 1) orotraheal intubation under the control of direct laryngoscopy, 2) nasotraheal intubation under the control of direct laryngoscopy. The most common technique is the first version of endotracheal intubation.

Orotraheal intubation: laryngoscopy is usually performed by the nondominant hand (for most people is the left hand). The patient's mouth open, tongue moves to the left and lift the blade up to the vault of the pharynx. The tip of the curved blade is introduced into vallekula (small hole located on the front surface of the epiglottis), whereas the direct tip should immediately lift the epiglottis. After these manipulations open glottis and the entrance to the trachea. His right hand under the control of the endotracheal tube is introduced into the glottis and promote it to the disappearance of the vocal cords inflatable cuff. Immediately after intubation is necessary to perform auscultation of the lungs and in the epigastrium, and assess carpnographic curve to confirm the position of the tube in the trachea. If the tube is

in the trachea, it is fixed in position tapes or adhesive plaster.



Nasotraheal intubation: - endotracheal tube is introduced into the oropharynx through the nose. Intubation is used more passable nasal passage (through which air flows better). Endotracheal tube moistened and applied to the lower nasal passage. The tube is then gently pushing until its end is in sight in the oropharynx. Under the control of the laryngoscope tube carried through the open glottis. Sometimes, for a tube through the vocal cords need to manipulate Magil tongs.

Advantages of general endotracheal anesthesia:

1. Airway Management, regardless of the operating position of the patient, the possibility of rehabilitation of the respiratory tract;
2. Reliable isolation of the gastrointestinal tract of a patient airway, which prevents aspiration and the development of severe respiratory damage by gastric contents (Mendelson's syndrome);

3. Optimal conditions for mechanical ventilation, which ensures adequate gas exchange, oxygen transport and utilization of organs and tissues of the patient;
4. The use of muscle relaxants, allows you to perform abdominal surgery.

Disadvantages general endotracheal anesthesia:
The relative complexity. However, given that the endotracheal anesthesia is carried out, as a rule, by experienced professionals, is hardly appropriate to consider it a disadvantage.
Contraindications of general endotracheal anesthesia:
- There are no absolute contraindications;
- Relative contraindications may be related to structural features of the facial skeleton and neck (limited mobility of the lower jaw, neck short inactive, moved back lower jaw forward of the large upper teeth, combined with a large upper jaw, etc.).

Inhalation anesthetics

Inhalation anesthetics are primarily intended for shutdown of consciousness. But at the same time they can have a significant analgesic effect (nitrous oxide) or cause myorelaxation (sevoflurane). Rapid development of the narcotic effect, the depth of anesthesia, the rate of awakening depends on many factors, including the leading role are:

- ✓ anesthetic partial pressure in the breathing mixture;
- ✓ volume of alveolar ventilation;
- ✓ diffusion capacity of the alveolar-capillary membrane;
- ✓ the amount of blood flow in the lungs, the blood circulation conditions in general;
- ✓ alveolar-arterial gradient of partial pressures of general anesthesia;
- ✓ its water and fat soluble.

In the mechanism of absorption and distribution in the body of inhaled anesthetics to distinguish between two phases - the pulmonary and circulatory. In the pulmonary phase of creating the desired concentration of anesthetic in the pulmonary alveoli by the value of its partial pressure in the breathing mixture. In the circulatory phase of the anesthetic is absorbed by blood and transfer it to the tissues. Of particular importance is a property of an anesthetic, as the solubility in blood. Depends on the coefficient of solubility time of administration of anesthesia

and the rate of awakening. With the increase in this ratio increases the induction time and slows down out of the state of general anesthesia. With a low voltage coefficient of solubility of the anesthetic in the blood increases rapidly, accompanied by a reduction in the introduction of anesthesia and awakening. The distribution of the anesthetic in the tissues depends on the fat-soluble, the gradient of the partial pressures in the blood and tissues and vascularity of the latter. In the initial period of anesthesia anesthetic is absorbed in the first well-vascularized organs and tissues (brain, heart, liver, kidneys, muscles). Adipose tissue, despite the high rate of solubility of anesthetic saturated slowly because of poor blood supply.

Quantitative measurement principle narcotic effect of inhaled anesthetics conducted based on the amount of minimum alveolar anesthetic concentration (MAC). MAC - the minimum alveolar concentration in a phase of saturation (steady-state), which is sufficient to prevent reaction 50% of patients on standard surgical stimulus (skin incision). MAC values enable us to establish the relationship between the dose of anesthetic and narcotic effect on the basis of determining the concentration of volatile agent in the alveolar air.

PREPARATIONS

In Western countries, is common to use one of the five volatile liquid anesthetic - desflurane, enflurane, halothane (halothane), isoflurane and sevoflurane and nitrous oxide, a gas.

Desflurane

Physical properties. Colorless substance is not flammable. The boiling point of desflurane 23,5 ° C, a vapor pressure of 88.5 kPa (664 mmhg) at 20 ° C, which does not allow to use the standard evaporator. Developed a special vaporizer that requires a source of electricity for heating and circulating the drug. MAC desflurane approximately 6% oxygen (3% to 60% mixture of nitrous oxide). Of essential, but less pungent odor compared with isoflurane.

Accumulation and distribution. The distribution coefficient of blood / gas desflurane about 0.42, almost the same as that for nitrous oxide. Therefore, also be a rapid change in the depth of anesthesia, and the rate of recovery of consciousness after application of the anesthetic is higher than with any other inhaled medicines.

Metabolism. In the body is metabolized approximately 0.02% of inhaled desflurane.
Respiratory system. Causes respiratory depression in the same way that isoflurane, with increasing concentrations up to 1.5 MAC. The product is irritating to the upper respiratory tract, especially at higher concentrations of more than 6%. For this reason, desflurane is not recommended for inhalational induction of anesthesia, during which may cough, breath holding, and laryngospasm.
Cardio-vascular system. First, develop a dose-dependent decrease in total systemic vascular resistance, myocardial contractility, and mean arterial pressure. Heart rate remained unchanged at low steady-state concentrations, but increases when they rise. Cardiac output tends to remain at a constant level. The second variant effects on the cardiovascular system is observed with the rapid increase of inhaled concentrations of more than 1 MAC. If sedation is not used, the sympathetic activity increases, leading to an increase in heart rate and mean arterial pressure. Desflurane as isoflurane and sevoflurane, usually increases the sensitivity of the myocardium to catecholamines.
Central nervous system. The EEG is observed dose-related depression, does not cause seizure activity, reduces the resistance of cerebral vessels and increases intracranial pressure, depending on the dose.
Musculoskeletal system. Leads to a dose-dependent muscle relaxation, enhances the action of muscle relaxants, can trigger malignant hyperthermia.
Desfluranes advantages over other inhaled anesthetics:
• low solubility in blood, which can be closely monitored anesthesia and recovery from it;
• minimal metabolism in the body, the absence of toxic effects on the liver and kidneys;
Disadvantages of desflurane:
• Inability to use for inhalation induction because of irritation to the respiratory tract;
• tachycardia at high concentrations;
• The need for a special evaporator, the high cost.

Enflurane

Physical properties. Clear, colorless volatile anesthetic with a pleasant ethereal odor. In clinical concentrations does not ignite. MAC enflurane 1.68% oxygen and 0.57% in 70% nitrous oxide.
Accumulation and distribution. Solubility ratio blood / gas for enflurane is 1.9. This figure is between halothane and isoflurane. Therefore, the induction of anesthesia and waking up after it faster than with halothane, isoflurane but slower, desflurane and sevoflurane.
Metabolism. About 2.5% of the absorbed dose is metabolized mainly to fluoride.
The respiratory system. Enflurane has no irritant, does not increase salivation and bronchial secretion, induction of anesthesia so runs smoothly and relatively quickly. Along with other inhaled anesthetics enflurane causes dose-related depression of alveolar ventilation with a reduction in tidal volume and an increase in respiratory rate.
Cardio-vascular system. Causes dose-related depression of myocardial contractility and decreased cardiac output. Due to a slight decrease in systemic vascular resistance, blood pressure decreases with increasing dose. Since enflurane (in contrast to halothane) has no central vagal activity, hypotension accompanied by reflex tachycardia. During anesthesia enfluranom myocardial sensitivity to catecholamines is increased to a much lesser extent than with halothane.
Uterus. With increasing doses of enflurane relaxes myometrium.
CNS. Enflurane in the transition from moderate to high concentrations (greater than 3%) causes epileptiform activity. Occasionally occur twitching face and upper extremities. You should avoid the use of enflurane in patients with epilepsy.
Musculoskeletal system. Relaxes the muscles. Potentiates the effect of nondepolarizing muscle relaxants are more than halothane. Can trigger malignant hyperthermia.
Hepatotoxicity. Liver is extremely unusual.
Enfluranes advantages:
• low risk of liver dysfunction;
• Low probability of arrhythmias.
Enfluranes disadvantages:
• seizure activity in the EEG;

Halothane

Colorless liquid with a relatively pleasant odor. At the light. In the presence of moisture destroys aluminum, tin, lead, magnesium, and various alloys. This anesthetic should be stored in closed containers away from heat and light.
Accumulation and distribution. Solubility ratio blood / gas from halothane is 2.5 and is the largest among all modern inhaled anesthetics. Like all other volatile anesthetics halothane for induction is usually used at a pressure at concentrations exceeding the MAC in 2 or 3 times, the concentration of respirable lower after a stable level of anesthesia. MAC halothane in oxygen is about 0.8% (0.29% in 70% nitrous oxide). Recovery of consciousness after halothane anesthesia is slower than with other inhaled drugs, because of the high solubility of the blood / gas.
Metabolism. Approximately 20% of halothane is metabolized in the liver. The end products are excreted in the urine. A small proportion of the drug undergoes biotransformation replacement, especially in hypoxemia and while taking drugs that induce microsomal enzymes, such as phenobarbital. Regenerative pathway can lead to the formation of reactive compounds and fluorides.
Respiratory system. Halothane does not cause irritation to the respiratory tract, comfortable breathing during induction of anesthesia. Causes a rapid loss of gag and cough reflexes, inhibits salivation and bronchial secretions. With increasing depth of halothane anesthesia increases RaCO2. Considered anesthetic causes a decrease in the activity of the mucociliary clearance. This effect contributes to the retention of phlegm in the postoperative period. Halothane prevents bronchoconstriction and reduces airway resistance, probably by central inhibition of the reflex bronchoconstriction and β-adrenomimeticheskim action on the bronchi-trivial muscle.
Cardio-vascular system. Causes a significant decrease in myocardial contractility, decreased heart rate, decrease in cardiac output and blood pressure. To correct bradycardia prescribe atropine. During anesthesia anesthetic often considered Arrhythmias that occur much more frequently than with other inhaled drugs.
Central nervous system. Increased cerebral blood flow and intracranial pressure. There is no seizure activity in the EEG.
Gastro-intestinal tract. Inhibited peristalsis. Severe postoperative nausea and vomiting is rare.
Uterus. The drug relaxes the myometrium and can cause bleeding after childbirth.

Skeletal muscle. Leads to a relaxation of the skeletal muscles, potentiates the action of non-depolarizing muscle relaxant. Can trigger malignant hyperthermia in susceptible individuals.

Hepatotoxicity. After halothane anesthesia, two types of dysfunction. The first, more benign, associated with impaired liver enzymes. Disturbances are transient in nature, mostly settled in a few days. The second type of liver disorders is extremely rare, takes the form of severe jaundice leads to fulminant hepatic necrosis. In this case, the mortality rate is 30% to 70%. The probability of this type of disorder increases with repeated use of halothane.

Committee on the safe use of medicines (Committee on Safety of Medicines) offered the following recommendations for halothane anesthesia:

• Avoid re-use of halothane during the 3-months, except aggravating medical circumstances;

• information about the history of unexplained jaundice or hyperthermia after previous halothane anesthesia considered an absolute contraindication to further use of the drug in this patient.

The main advantages of halothane:

• smooth induction;

• minimal stimulation of salivation and bronchial secretion, bronchodilation.

Disadvantages of halothane:

• arrhythmia;

• The risk of hepatotoxicity, especially with repeated use;

• slow awakening compared to other newer drugs.

Isoflurane

Physical properties. A colorless, volatile liquid with a pungent odor. The compound is stable, does not react with metals and other substances. MAC of isoflurane is 1.15% oxygen and 0.56% in 70% nitrous oxide.

Accumulation and distribution. The anesthetic has a low solubility coefficient blood / gas, equal to 1.4, respectively alveolar concentration quickly reaches equilibrium with the inspired concentration. However, the rate of induction is limited bite vapor treatment.

Metabolism. Approximately 0.17% of the absorbed dose is metabolized. Due to the minimal biotransformation found only very low concentrations of fluoride ions in the serum, so hepatotoxicity and nephrotoxicity of the least likely.
Respiratory system. Causes dose-dependent respiratory depression, tidal volume decreases and respiratory rate increases. Irritating to respiratory system, which complicates the introduction of anesthesia.
Cardio-vascular system. Cardiac output is reduced to a lesser degree than the action of halothane and enflurane. Due to the reduction in systemic vascular resistance develops systemic hypotension. Arrhythmias are rare, because the sensitivity of myocardium to catecholamines increased slightly. It is shown that the drug affects the small arterioles (theoretically lead to the syndrome of "steal" the coronary arteries), but the impact has no clinical manifestations.
Uterus. Influences on the pregnant uterus like halothane and enfluranu.
Central nervous system. Low concentrations of isoflurane have no effect on cerebral blood flow in normocapnia. In this respect, the drug is superior enflurane and halothane, which cause dilation of cerebral blood vessels. However, the high concentration of anesthetic in the inspired mixture leads to vasodilation and increased cerebral blood flow. There is no seizure activity in the EEG.
Muscle relaxation. Isoflurane promotes dose-dependent decrease in neuromuscular conduction and potentiates the action of non-depolarizing muscle relaxant.
Advantages of isoflurane:
• rapid awakening;
• minimal biotransformation with a small chance of hepatotoxicity and nephrotoxicity;
• Very low risk of arrhythmias;
• muscle relaxation.
Disadvantages:
• strong odor, making inhalation induction proceeds relatively unpleasant, especially in children.

Sevoflurane
Physical properties. Non-flammable, has a pleasant smell. The distribution coefficient of blood / gas is 0.69, which is half the relative solubility of isoflurane (1.43), and the closest to desfluranu (0.42) and nitrous oxide (0.44). MAC

sevoflurane in adults is in the range 1.7-2% oxygen and 0.66% in 60% nitrous oxide. Chemically stable.

Accumulation and distribution. Characterized by a low partition coefficient blood / gas, for this reason, the rate of equalization of concentration in the alveoli and the inspired mixture is higher than that of halothane, enflurane, but less than desflurane. Does not irritate the upper respiratory tract and, therefore, the rate of administration of anesthesia is higher in comparison with the other inhaled anesthetics.

Metabolism. Approximately 5% of the absorbed dose is metabolized in the liver. Sevoflurane biotransformation catalyzed by cytochrome P450 isoform, which is activated by phenobarbital, isoniazid, ethanol.

Respiratory system. Does not irritate the upper respiratory tract. Causes dose-dependent respiratory depression, due to respiratory depression of spinal neurons and diaphragm contractility. Relaxes the smooth muscles of the bronchi, but not as effective as halothane.

Cardio-vascular system. Lowers blood pressure mainly by reducing peripheral vascular resistance, the use of standard doses of anesthetic cardiac output is maintained at an adequate level. Sevoflurane does not increase the sensitivity of the myocardium to exogenous catecholamines. Coronary arteries dilate less and the syndrome of "steal" is not shown. The drug reduces myocardial oxygen demand, as it causes the decrease in heart rate.

Central nervous system. Increases intracranial pressure at high concentrations in the breathing mix, but the effect is minimal at 0.5-1.0 MAC. Decreases metabolism of the brain. There is no sign of excitement in the EEG.

Urinary system. The absence of nephrotoxicity, renal blood flow remains at the initial level.

Musculoskeletal system. Potentiates the action of non-depolarizing neuromuscular blocking agents, can initiate malignant hyperthermia.

Use in obstetrics. For information about using the drug in obstetric practice is limited.

Sevoflurane a new drug for inhalation anesthesia, which, compared to other volatile anesthetics, has several advantages:

• Fast and smooth induction of anesthesia;

• rapid awakening;

Disadvantages of sevoflurane:
• theory - the body's potentially toxic metabolites;
• relative cost.

Nitrous oxide (N2O)

Physical properties. Colorless gas with a pleasant smell, not irritating the respiratory tract, the critical temperature of vaporization - 36,5 ° C, and the critical pressure - 72.6 bar, non-flammable, but will support combustion in the absence of oxygen.

Pharmacology. Good analgesic, but a weak anesthetic. This is explained by the fact that the MAC is 105%. Because during anesthesia FiO2 ratio should be maintained at no less than 0.3, a nitrous oxide is not sufficient to achieve adequate depth of anesthesia in all but the most severe cases, and in this connection the gas is commonly used in conjunction with other drugs. For nitrous oxide has low solubility ratio blood / gas (0.47 at 37 ° C), for this reason, and inspiratory alveolar concentration balanced by very quickly. Not metabolized and is excreted unchanged.

Cardio-vascular system. Nitrous oxide stimulates the sympathetic nervous system, which explains its effect on blood circulation: blood pressure, cardiac output and heart rate did not change or increased slightly due to increased concentrations of catecholamines. Causes narrowing of the pulmonary artery, which increases pulmonary vascular resistance and leads to increased pressure in the right atrium. Despite the narrowing of blood vessels of the skin, and total peripheral vascular resistance (SVR) is changed slightly.

The respiratory system. Causes tachypnea and reduced breathing capacity, the total effect - a slight change in minute volume and PaCO2 alone. Hypoxic drive, ie an increase in ventilation in response to arterial hypoxemia, mediated by peripheral chemoreceptors in the carotid corpuscles, significantly inhibited the use of nitrous oxide, even in low concentrations. This can lead to serious complications occur in patients in the postoperative recovery room, it is not always possible to quickly detect hypoxemia.

Central nervous system. Nitrous oxide increases cerebral blood flow, causing a rise in intracranial pressure. Increases oxygen consumption by the brain.

Neuromuscular conduction. Does not cause a noticeable muscle relaxation, on the contrary, in high concentrations causes stiffness of skeletal muscles. Does not cause malignant hyperthermia.
Kidney. Reduces renal blood flow due to increased renal vascular resistance. This reduces the glomerular filtration rate and urine output.
Liver. Reduces blood flow to the liver, but to a lesser extent than other inhaled anesthetics.
Biotransformation and toxicity. During awakening almost all nitrous oxide is removed through the lungs. A small amount diffuses through the skin. Less than 0.01% is set foot into the body anesthetic biotransformation that occurs in the gastrointestinal tract and is the restoration of the substance under the action of anaerobic bacteria. Irreversibly oxidizing the cobalt atom in vitamin B12, nitrous oxide inhibits B12-dependent enzymes. These enzymes include methionine, required for the formation of myelin, and thymidylate involved in DNA synthesis. Prolonged exposure to anesthetic degree ¬ critical concentration of nitrous oxide causes bone marrow depression (megaloblastic anemia), and even neurological deficit (peripheral neuropathy and funicular myelosis). Nitrous oxide reduces the immunological resistance to infection by inhibiting chemotaxis and motility of polymorphonuclear leukocytes.
Teratogenic effects. Currently, there is no consensus on this issue, but it is recommended to avoid its use in early pregnancy.
Effect of concentration. Nitrous oxide is more soluble in blood than molecular nitrogen. Thus, the amount of anesthetic entering the pulmonary capillary bed of the alveoli exceeds nitrogen moving in the opposite direction. As a result, the total amount of the remaining alveolar gas is reduced and their relative concentrations increase. Investigation of the process:
- The higher the concentration of inhaled nitric oxide and the more concentrated anesthetic remaining in the alveoli.
- At high concentrations of the drug in the inspired mixture reduces the amount of gases in the alveoli, which causes an increase PACO2. Equilibration with the blood concentrations of pulmonary capillaries increases PaCO2.
Effect of the second gas. When nitrous oxide is used in high concentrations, but the joint with a second anesthetic, the volume of alveolar gas emissions reduced by the absorption of nitrous oxide, which contributes to the alveolar concentration of the

second inhalation anesthetic and faster equilibration with its inspiratory concentration. Second gas effect also leads to a slight increase PACO2 and PaCO2.

Side effects of nitrous oxide

Diffusion hypoxia. At the end of anesthesia, when the inspired gas mixture, consisting of nitrous oxide and oxygen is substituted by nitrogen and oxygen, can develop hypoxemia due to the fact that the amount of nitrous oxide, diffused from the venous blood into the alveoli, greatly exceeds the amount of nitrogen, is directed to the pulmonary capillaries (the opposite of the effect of concentration). Accordingly, alveolar gases are diluted nitrous oxide, which leads to lower PaO2 and PaCO2. In healthy individuals the diffusion hypoxia relatively brief, but can last up to 10 minutes at the end of anesthesia. The use of oxygen at this stage mandatory event, aimed at preventing hemoglobin oxygen desaturation.

Impact on the closed cavity filled with gas. When the content of nitrous oxide in the blood comes into equilibrium with closed air-containing cavities within the body, the amount entering the cavity of nitrous oxide exceeds the amount of nitrogen diffuses back. Consequently, the space with elastic walls expand, for example, pleural, peritoneal cavity or lumen of the digestive tract. If the expansion of the cavity is not possible (eg, sinuses, middle ear), increases the pressure inside it. These changes complicate the operation of the middle ear and the eardrum. When nitrous oxide is used in concentrations of 75%, the volume of space can be increased to three or even four times in 30 minutes.

A short list of the physical properties of inhaled anesthetics

	Halothane	***Isoflu***	***Enflur***	***Desfl***	***Sev***	***N_2O***
MAC, %	0.75	1.2	1.8	6	2	105
MAC when breathing 70% N2O	0.29	0.56	0.57	2.5	0.66	-
% Biotransformation	20	0.2	2	<0.1	3 -5	0.01
Blood/gas	2.4	1.4	1.9	0.45	0.6	0,47
Fat/gas	224	98	98.5	28	47	-

Clinical pharmacology of inhaled anesthetics

	N_2O	***Halotha***	***Enflura***	***Isoflurane***	***Desflurane***	***Sevoflura***

		ne	***ne***			***ne***
Circulatory system						
BP	±	↓↓	↓↓	↓↓	↓↓	↓
HR	±	↓	↑	↑	± or ↑	↑
ОПСС	±	±	↓	↓↓	↓↓	↓
Cardiac output[1]	±	↓	↓↓	±	± or ↓	↓
Respiratory system						
Respiratory volume	↓	↓↓	↓↓	↓↓	↓	↓
Frequency of breathing	↑	↑↑	↑↑	↑	↑	↑
$PaCO_2$ at rest	±	↑	↑↑	↑	↑↑	↑
$PaCO_2$ in overload	↑	↑	↑↑	↑	↑↑	↑
CNS						
Brain circulation	↑	↑↑	↑	↑	↑	↑
Intracranial pressure	↑	↑↑	↑↑	↑	↑	↑
Metabolic requirement of brain[2]	↑	↓	↓	↓↓	↓↓	↓↓
Seizures	↓	↓	↑	↓	↓	↓
Neuro-muscular conductivity						
Non-depolarised blockage[3]	↑	↑↑	↑↑↑	↑↑↑	↑↑↑	↑↑
Kidney						
Renal circulation	↓↓	↓↓	↓↓	↓↓	↓	↓
Glomerular filtration rate	↓↓	↓↓	↓↓	↓↓	?	?
Diuresis	↓↓	↓↓	↓↓	↓↓	?	?
Liver						
Circulation in liver	↓	↓↓	↓↓	↓	↓	↓
Metabolism[4]	0,004 %	15-20%	2-5 %	0,2 %	< 0, 1 %	2-3 %

Note:

↑ - increase;

↓ - decrease; ± - no change; ? – Unknown; ([1])- background ventilation.

([2])-metabolic requirements of the brain are increased if enflurane causes seizures.

(^{3})-Anesthetics likely prolong and depolarizing block, but this effect has no clinical significance.
(^{4})- often released to the blood of the anesthetic, which is metabolized.

VIII. Self-study

Task number one

Place the inhalation anesthetics in increasing order since the introduction of anesthesia and awakening.

Task number two

Compare inhalation anesthetics on the effect on hemodynamics.

IX. Clinical problem:

Objective number one

Girl, 5 years without comorbidities than significant obesity, was admitted to herniotomy for inguinal hernia. After standard induction of anesthesia and tracheal intubation, mechanical ventilation is translated with a tidal volume of 7 ml / kg and a frequency of 16 to 1 min. Despite the inhalation of 2% halothane in 50% nitrous oxide there was tachycardia (145 beats / min) and mild hypertension (140/90 mmHg). In order to deepen the anesthesia put fentanyl (3 mg / kg). Despite this, tachycardia and hypertension continues to grow, joined frequent ventricular extrasystoles. What to think about the differential diagnosis of hemodynamic abnormalities in this patient? Which technical problems be causing these complications.

Objective number two

The girl at the age of 7 years has been directed to the operation adenoidectomy. Parents reported that she snores during sleep and often wakes up. Body weight was 30 kg. In addition to enlarged tonsils, other pathology was identified. After induction of anesthesia with halothane with nitrous oxide, oxygen and succinyl-choline. To open the baby's mouth in order to perform laryngoscopy was impossible. Started marked tachycardia, hyperthermia, increase CO2 exhalation. Your assumption about the cause of the incident, the tactics?

Test control:

1. The major components of general anesthesia include:

a) sleep;
b) analgesia;
c) hyporeflexia;
d) muscle relaxation;
e) the control of functions of vital organs.

2. Inhalational general anesthesia:
a) is the least toxic to the patient and operating personnel;
b) a more manageable compared to other types of general anesthesia;
c) should not be combined with intravenous anesthetics;
d) not to be used in thoracic surgery.

3. Inhaled anesthetics:
a) leads to reversible depression of affererent fibers of synaptic transmission in the central nervous system;
b) causes thalamoneocortical depression;
c) act on peripheral pain receptors;
d) inhibits the limbic system of the brain.

4. The fastest introduction of anesthesia occurs by inhalation:
a) halothane;
b) isoflurane;
c) nitrous oxide;
d) sevoflurane.

5. The depth of anesthesia induced by inhalation anesthetic, depends on the following factors, except:
a) the concentration of anesthetic in the blood;
b) the minimum alveolar concentration;
c) the solubility of the anesthetic in the blood;
d) the structure of an anesthetic agent.

6. A mask inhalation anesthesia is shown:
a) for short non cavital operations;
b) during surgery on the abdominal cavity;

c) operations on the head and neck;
d) at the risk of aspiration.

7. The onset of surgical stage of ether anesthesia is most easily determined by:
a) the disappearance of the ciliary reflex;
b) the size of the pupil;
c) the movement of the eyes;
d) beginning of rhythmic breathing;
e) the disappearance of the corneal reflex.

8. The halogenic inhalation anesthetics are:
a) desflurane;
b) sevoflurane;
c) ether;
d) halothane;
e) nitrous oxide.

9. Performing abdominal operations is possible in the which phase of anesthesia by Gvedelu:
a) II;
b) III 1;
a) III 2;
d) IV.

10. Trigger of malignant hyperthermia is caused:
a) succinylcholine;
b) nitrous oxide;
c) halothane;
d) sevoflurane.

Response
Objective number one

Should exclude hypercapnia and hypoxia, which cause symptoms of increased sympathetic activity. Common cause of intraoperative tachycardia and hypertension is a surface anesthetic.
Cause hypoxia and hypercapnia may be incorrect connection elements breathing circuit. In addition, disruption of the valve guides is increasing the "dead space" and recycling of carbon dioxide. Depletion sorbent direction breathing gas to bypass the canister leads to increase recycling at low flow of fresh mixture.
Objective number two
The patient developed a malignant hyperthermia (MH). The frequency of G in children 1 in 15000 - 50000, and in adults 1 in 50,000 - 100,000 patients. MH is inherited in an autosomal - dominant type. It is now believed that the major pathophysiological mechanism in G is the release of excess potassium from the sarcoplasmic reticulum. Accumulation of excess potassium in the cytoplasm of muscle cells triggers a chain hypermetabolic responses that include activation of contractile elements of heat, oxygen uptake, CO2 and lactate formation and the final destruction of the cells with the release of intracellular contents (CreatinineKinase, K +, Ca + +, and myoglobin. Classic trigger factors - volatile anesthetics and succinylcholine.
Tactics aimed at combating hyperthermia, maintain ventilation and elimination of CO2.
Test control:
1) - a, b, c, d, e;
2) – b; 3) – a; 4) – d; 5) – d;
6) – a; 7) – c; 8) - a, b, d;
9) - c, 10) - a, c, d.