Drugs that act in the central nervous system
Psychotropic drugs

- Drugs for narcosis
- Hypnotic and antiseizures drugs
- Neuroleptic
- Tranquilizers
- Sedative drugs
- Analgesics (narcotic, non-narcotic)
- Psychostimulants
- Antidepressants
- Nootropic drugs
- Analeptic
- Adaptogens
Drugs for narcosis

Narcosis – (from the Greek narkosis – numbness, rigidity)

condition which is characterized by

- loss of consciousness
- pain feelings
- depression of reflexes
- relaxation of skeletal muscles
- postnarcosis amnesia
Drugs for narcosis

Characteristics of the ideal anesthetic

- Rapid, pleasant induction and recovery of anesthesia
- Rapid changes in the depth of anesthesia
- Adequate skeletal muscle relaxation to perform surgery
- Production of amnesia
- Ability to provide analgesia
- A wide safety margin
- Nontoxic
Types of general anesthetics: 

Inhalation Anesthetics:

- gases: 
  *Nitrogenium oxydulatum*

- volatile liquids:
  *Aether pro narcosi, Ftorotanum, Halotanum*

Inhalation anesthetics have advantages over intravenous agents in that the depth of anesthesia can be changed rapidly by altering the inhaled concentration and, because of their rapid elimination, they do not contribute to postoperative respiratory depression.
Ether for narcosis

Narcosis develops after 10-20 min, stage of excitation - 10-20 min, strongly expressed after-narcosis depression, high width of narcosis action

Side effects and complications

- bright stage of excitation
- Increasing of tone of n. vagi
- Increasing of secretion of salivary, bronchial glands, coughing; laryngospasm, bronchospasm, vomiting with the following aspiration of the masses bradycardia, stop of heart beat
- Increasing of tone of sympathetic nervous system
- Tachycardia, hyperglycemia
Ftorotan (galotan)

Power of narcosis action of ftorotan is higher than of ether, it has a large width of narcosis action, doesn’t irritate mucous membranes of breath tracts, doesn’t cause laryngeal and bronchial spasm, speed of development of narcosis – 3-5 min., after narcosis depression is not expressed

Side effects and complications

- hypotension and heart stop,
- sensibilization (increased sensitivity) of myocardium towards catecholamines
- acute damage of liver – halothane hepatitis,
- teratogenic action
Nitrogen oxide

Small power and width of narcosis action, stage of excitation is present, quick entry and exit from narcosis (1-2 min)

**Administration** as an analgesic:
- pregnancy,
- teeth extraction,
- bandaging in case of burns,
- cleaning and revisions of wounds,
- traumas, burns,
- attacks of stenocardia and myocardium infarction,
- colics,
- pain relieving in post-operative period
Intravenous Anesthetics:

Short-acting drugs (10-15 min):
- Ketaminum (Kalipsol, Ketanest)
- Propofol (Diprivan)
- Propanididum (Sombrevin)

Drugs with medium duration of action (20-50 min):
- Thiopental-natrium

Long-acting drugs:
- Natrii oxybutyras

Cause rapid loss of consciousness and induction is pleasant. However, they produce little muscle relaxation and frequently do not obtund reflexes adequately. Repeated administration results in accumulation and prolongs the recovery time. Since these agents have little if any analgesic activity, they are seldom used alone except in brief minor procedures.
Thiopental-natrium

After administration of the drug narcosis develops in 1-2 min., awakening occurs in 20-30 min.

**Administration**

- introduction narcosis,
- basis narcosis,
- mononarcosis in case of short-lasting operative interventions (dentistry, gynecology, traumatology),
- anti-seizure drug.

**Side effects**

- cough, laryngeal and bronchial spasm
  - in case of rapid introduction – depression of centers of medulla oblongata

In case of contact of the drug with skin, it’s separation may occur, contact with nervous trunk or near it – nonreversible paralysis, contact with an artery – thrombosis with the following gangrene of the extremity
PREANESTHETIC MEDICATION

Can foster an uncomplicated anesthetic and operative course by involving the rapidity and smoothness of induction, reducing anxiety, providing analgesia and amnesia, and compensating for the salivation, bradycardia, and other side effects of anesthesia. Agents used as premedication, include sedatives, opioids, tranquilizers, and anticholinergic agents.
Drugs use for premedication

M-cholinoblockers
- *Atropini sulfas*
  - Decrease secretion of salivary glands
  - Prophylaxis of laryngo- and bronchospasm
  - Prophylaxis of vagotony

Narcotic analgesics
- *Morphini hydrochloridum, Promedolom*
  - Potentiation of drugs for nacrosis

Antihistaminic
- *Dimedrolom, Suprastinum*
  - Prophylaxis of allergic reactions

Tranquilizers
- *Sibasonum*
  - Decrease of anxiety, potentiation of nacrosis
NEUROLEPTANALGESIA – special type of general analgesia which include neuroleptic (droperidol) and narcotic analgesic (fentanyl). Combined drug is talamonal

Main peculiarities
- Low toxicity
- Potent antishock action
- Evident antivomiting effect
- Stability of hemodynamics
- Rapid onset (1-3 min), rapid termination of action (20-30 min)

Usage:
- Extensive traumas, burns (the prophylactic of pain shock)
- Myocardium infarction
- Initial narcosis
Hypnotic drugs

These drugs are able to cause sedation (with concomitant relief of anxiety) or to encourage sleep.

**Chemical classes of sedative-hypnotics**

**Barbiturates:** Hexobarbital, Phenobarbital, Thiopental.

**Benzodiazepines:** Chlordiazepoxide, Diazepam, Nitrazepam, Oxazepam

**Carbamates:** Meprobamate

**Quinazolones:** Methaqualone

**Alcohols:** Ethanol
Indication for usage of hypnotic drugs

- For relief of anxiety
- For sedation and amnesia before medical and surgical procedures
- Treatment of epilepsy and seizure states.
- Premedication prior to anesthesia
- Intravenous administration, as a component of balanced anesthesia
- For control of ethanol or other sedative hypnotic withdrawal states
- For muscle relaxation in specific neuromuscular disorders
Adverse effects of hypnotic drugs

- **CNS** – drowsiness, impaired concentration, mental and physical sluggishness

- **Drug hangover**: hypnotic doses produce a feeling of tiredness well after the patient awakes. This drug hangover leads to impaired ability to function normally for many hours after waking. Occasionally, nausea and dizziness occurs.

**Precautions.** Barbiturates induce the P-450 system and therefore may decrease the effect of drug that metabolized by these hepatic enzymes.

- **Addiction.** Abrupt withdrawal from barbiturates may cause tremors, anxiety, weakness, restlessness, nausea and cardiac arrest.

- **Drug dependence** (physiological and psychological). Poisoning leads to severe depression of respiration and central cardiovascular depression.
Antiseizure drugs

Antiepileptic
Carbamazepinum (Finlepsin, Tegretol)
Ethosuximidum (Suxilep)
Natrii valproas (Convulex)

Antiparkinsonic
Dopaniergic system activators
Levodopa
Midantanum
Nakom

Central cholininoblockers
Cyclodolum (Parkopan)
Neuroleptics

Neuroleptic drugs (also called antischizophrenic drugs) are the group of sedative medicines with potent antipsychotic activity (they can remove delirium, hallucinations, psychomotor anxiety).

They also influence on the vegetative nervous system functions (BP, temperature, etc.) and after long-term using cause parkinsonism (extrapyramidal disorders).
Classification of neuroleptics by chemical structure

Derivatives of phenotiazine: *aminasine, triflazine, etaperasine,*

Derivatives of tioxantrene: *chlorprotixen*

Derivatives of butyrophenon: *haloperidol, droperidol*

Derivatives of piperasine-dibenzodiazepine: *clozapine*

Derivatives of indole: *reserpin, sulpyrid (eglonil)*
Neuroleptics

“Typical” – derivatives of phenotiazine, tioxanthen, butyrophenon – they cause disorders of extrapyramidal system function – syndrome of parkinsonism

“Atypical” – derivatives of indole, piperasine-dibenzodiazepine – they cause those negative reactions very rarely
The mechanism of action of neuroleptics

1. Block a adreno-, dopamino-, cholino-, histamino- and serotoninergic receptors.

Typical antipsychotics block postsynaptic dopamine receptors in the limbic system and increase dopamine turnover by blockade of the D2 receptor. The decrease in dopamine neurotransmission has been correlated to the antipsychotic effects of the phenothiazines. This D2 blockade is also responsible for their extrapyramidal and antiemetic effects.

2. Decrease the permeability of cell membranes for electrolytes

3. They inhibit the enzyme tyrosine-hydroxylase, which convert aminoacid tyrosine to DOPA, one of the precursors of main mediators dopamine and norepinephrine.

4. They inhibit the calmoduline activity. This enzyme converts Ca^{++} into its active form, and influence on the main processes in the cells.

5. They decrease the release of exciting aminoacids which can interfered with NMDA receptors and have activating action on the neurons.
The main effect of neuroleptics -

**Antipsychotic** – they reduce main symptoms of psychosis (delirium, hallucination, psychomotor activity).

These drugs also have a calming effect

They keep consciousness
Use of antipsychotic activity of neuroleptics -

Treatment of psychoses

- schizophrenia
- manic-depressive psychosis
- alcoholic psychosis
- reactive psychosis
- psychomotor agitation of different etiology
Other properties and indications for usage of neuroleptics

Drugs with psychosedative action – for potentiation of action of hypnotic, narcotic and nonnarcotic analgesics, drugs for narcosis, local anesthetics

Neuroleptanalgesia

Anti-emetic action (elimination of vomiting of central genesis):
- brain tumors, radial and chemical therapy, intestinal impassability, intoxication with heart glycosides, apomorphine and other drugs

Decreasing of body temperature in case of hypothermia

Decreasing of blood pressure (alpha-adrenoblocking properties – aminasine, droperidol) – in case of hypertensive crisis, lungs edema

Complex treatment of epilepsy (myorelaxation of skeletal muscles) In combination with narcotic analgetics for treatment of chronic pain with severe anxiety.
Extrapyramidal disorders: muscular hypertonus, general constraint, tremor of hands, tongue, mandible, head, seizure contractions of muscles, vegetative crisis (For treatment – cyclodol (levodopa is contraindicated)

- Orthostatic collapse
- Dyspeptic disorders: anorexia, changes of taste
- Abdominal pain
- Damage of the liver (cholestasis)
- Granulocytopenia (especially clozapin)
- Hyperglycemia, dysmenorrhea, galactorrhea, gynecomastia, impotence
- Aminasine has a considerable irritable action
These drugs with sedative action on the CNS have weak antipsychotic and potent antineurotic action (they can remove anxiety disorders, fear, panic, etc). They can acting only in psychically healthy patients.

**Agonists of benzodiazepine receptors:**
- derivatives of benzodiazepine – *Chlozepid, Sibazon, Phenazepam, Hydazepam*

**Agonists of serotonin receptors:** *Buspyrone*

**Drugs with other mechanisms of action:**
- derivatives of diphenilmethan: *Amizyl*
- derivatives of propanedioile: *Meprotan*
Tranquilizers
main types of action

Hypno-sedative
Correct vegetative status
potent anxiolytic (anti-anxiety)
myorelaxant
anticonvulsive
**Indication for usage of tranquilizers**

**Anxiolytic action**
- Treatment of neurosis, accompanied by fear, anxiety, tenseness, increased irritability, insomnia
- In case of headache and heartache of neurotic origin, so called organic neurosis
- In case of abstinence in alcohol and drugs addicts
- In case of diencephal crisis (sibazon)

*Tranquilizers do not eliminate productive symptoms of psychosis!*

**Hypnotic action** – they cause sleep, which is very close to physiological one according to its parameters (Nitrazepam, Phenazepam, Diazepam, Chlozepid)
Indication for usage of tranquilizers

- Depression of CNS – for atharalgesia (*Sibazon*, *Midazolam*)
- Anti-seizure and myorelaxing action (depression of CNS structures, braking polysynaptic spinal reflexes) - *Sibazon*, *Phenazepam*
- In case of seizures of any etiology (epileptic status, tetanus, poisoning with seizure causing poisons) *Sibazon* is introduced i.v (i.m.) – 2-4 ml of 0.5% solution
- To eliminate muscular tension in case of radiculitis, arthritis, myositis bursitis – drugs which practically don’t have myorelaxing properties
Psychological and physical dependence

Prophylaxis: Duration of treatment course should not be more than 2 months

Repeated course – not earlier than after 3 weeks

Sleepiness, reeling walk, retarded reactions

Tranquilizers should not be administered in ambulatories to people whose professions are connected with quick reactions

Paradox reaction of excitation, insomnia

Dizziness, decreasing of libido, disturbances of menstrual cycle

Uncontrolled urination, defecation, ataxia, dysarthria

Acute poisoning in case of overdosing
«Day» tranquilizers

Gidazepam
Mezapam (rudotel)
Grandaxyn (tophizopam)
Trioxazyn
Buspyron
Sedative drugs

Drugs which increase inhibition processes and decrease excitation processes in brain cortex and thus cause calming effect on the CNS

Bromides (KBr, NaBr)

Drugs of plant origin: valerian, dog nettle, melissa, pasiflora etc.

Combine drugs: Corvalolum, Novo-pasit, Persen

They do not cause addiction, somnolence, myorelaxation, ataxia
Indication for usage of sedative drugs

- Neuroses
- Neurasthenia
- Hystéria
- Hyperexcitability
- Insomnia
- Initial stages of hypertony, ischemia, tachycardia
Valeriana
Leonurus quinquelobatus
Mentha piperita
Melissa officinalis L.
Thank you for attention!

Good bye!