



NATIONAL UNIVERSITY OF PHARMACY

The Department Of Pharmacology



SIDE EFFECTS OF DRUGS AFFECTING CNS



Lecturer :
prof. Shchekina C.G.

Classification of psycho- and neurotropic medicines

<i>CNS DEPRESSANTS</i>	<i>CNS STIMULANTS</i>
HYPNOTIC MEDICINES ANTICONVULSANTS MEDICINES FOR PARKINSONISM TREATMENT <u>Psycholeptics</u> NEUROLEPTICS TRANQUILIZERS SEDATIVE MEDICINES	ADAPTOGENS ANALEPTICS <u>Psychotonic medicines</u> PSYCHOMOTOR STIMULANTS ANTIDEPRESSANTS NOOTROPIC MEDICINES

Neuroleptics (antipsychotic medicines) are psychotropic medicines that are able to reveal the inhibitory action on the CNS (without consciousness disturbing): eliminate hallucinations, delirium and stop the psychomotor excitation.

Classification

Derivatives of phenothiazine	Derivatives of butyrophenone	Derivatives of thioxanthene, dibenzodiazepine*, benzamide**
Chlorpromazine Levomepromazine Perphenazine hydrochloride	Droperidol Haloperidol	Chlorprothixene Sulpyrid** Closapine*

NEUROLEPTICS

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graph TD; A[NEUROLEPTICS] --> B[A. "typical"]; A --> C[B. "atypical"];
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A. “typical” (causing the extrapyramidal disorders):

- derivatives of phenothiazine
- derivatives of thioxanthene
- derivatives of butyrophenone

B. “atypical” (don’t cause the extrapyramidal disorders)

- derivatives of benzamide
- derivatives of dibenzodiazepine

Glossary

- ***Extrapyramidal disorders (drug-induced parkinsonism)*** – bounds to inhibition of the mediator activity of postsynaptic dopamine D2-receptors and disbalance: ↑ glutamat, acetylcholine and ↓ dophamine. Appearing: hypokinesy and rigidity, tremor.
- ***Neuroleptic malignant syndrome (NMS)*** - a rare and dangerous complication of neuroleptic therapy: hyperthermia, extrapyramidal and autonomic disorders, pulmonary edema that may lead to death.
- ***Akathisia*** - an irresistible need to move to reduce internal discomfort.
- ***Dystonia*** - dyskinetic movement disorders due to the disturbances of muscle tone.

The mechanism of sides effects of neuroleptics

- In accordance with the A. Carlson's dopaminergic hypothesis, for which he was awarded the Nobel Prize in 2000, the blockade of D2-dopamine receptors is the primary mechanism of the antipsychotic effect.
- This mechanism underlies many of the side effects of neuroleptics.
- In addition, neuroleptics block the α -adrenergic receptors, the M-cholinergic receptors, H1-histamine and 5-HT2-serotonin receptors in the reticular formation, the nuclei of the midbrain, the limbic system, the hypothalamus.

Constipation
Dry mouth
Disturbances of vision
Impairment of urination

The influence on the psyche

The side effects of antipsychotic medicines

Brain cortex
Limbic system

The blockade of M-cholinoreceptors

Mesolimbic pathway

Neuroleptics

The blockade of D₂-dopamine receptors

Nigrostriatal pathway

Basal ganglia (striatum)

The blockade of α-adrenoreceptors

Tuberoinfundibular pathway

Movement disorders

Hypophysis

Parkinsonism
Akinesia
Dyskinesia

↑Prolactin
Endocrine disorders
Gynecomastia
Galactorrhea
Dysfunction of the menstrual cycle
Impotency
Body weight increase

Orthostatic hypotension
Hypothermia

The blockade of serotonin and histamine receptors

Typical side effects	The mechanism of side effect	Contraindications
<ul style="list-style-type: none"> ◆ Extrapyrarnidal disorders (drug-induced parkinsonism), akinesia, dyskinesia, akathisia ◆ Orthostatic hypotension ◆ Toxic retinopathy ◆ The reduction of the secretion and intestinal motility, constipation, dry mouth, difficulty urination, necrosis of the intestinal wall of the colon ◆ Hyperthermia 	<ul style="list-style-type: none"> ◆ The blockade of dopaminergic subcortical structures of the brain (substantia nigra, striatum, and the limbic system and thalamus) ◆ The blockade of α-adreno-receptors ◆ The affinity of the phenothiazine derivatives to melanin, and their accumulation in the retinal pigment epithelium ◆ The inhibition of M-cholinergic transmission ◆ Disturbances of thermoregulation at the level of the hypothalamus. Anticholinergic influence, decrease the secretion of sweat glands. 	<ul style="list-style-type: none"> ▶ Parkinsonism, epilepsy, depression, CNS inhibition, systemic brain diseases, craniocerebral trauma ▶ Hypotension ▶ Closed-angle glaucoma ▶ Atony, benign hyperplasia of prostate (BHP)

Typical side effect	The mechanism of side effect	Contraindications
<ul style="list-style-type: none"> ◆ Body weight increase ◆ Sedative action ◆ Agranulocytosis ◆ Photosensitization ◆ Sexual dysfunction (erection and ejaculation) ◆ Neuroendocrine disorders (hyperprolactinemia) 	<ul style="list-style-type: none"> ◆ The result of hypersecretion of antidiuretic hormone ◆ The result of the inhibition of dopamine and histamine receptors ◆ Toxic effect on myeloid elements of the bone marrow ◆ The production cytotoxic products under UV irradiation ◆ α-adrenergic blockade ◆ \uparrow prolactine in hypophysis 	<ul style="list-style-type: none"> ▶ Hypertension, atherosclerosis, valvular heart disease, heart failure ▶ Agranulocytosis, leukopenia ▶ Hypersensibility ▶ Endocrine disorders

Factors that increase the side effects

- **The combined administration with antidepressants increases the risk of NMS development.**
- **Neuroleptics are incompatible with α -adrenoblockers.**
- **Alcohol enhances the cardiotoxic effect of neuroleptics.**
- **The therapy by sedative antipsychotics leads to the development of insomnia.**
- **Haloperidol is incompatible with adrenaline h/chl, sombrevine; it decreases the effects of indirect-acting anticoagulants.**
- **The combined application of phenothiazines with anticonvulsants - ↓ seizure threshold.**

Factors that decrease the side effects

- It is necessary to control the blood, prothrombin index, liver function, kidney and blood pressure with long-term neuroleptics treatment.
- Anticholinergic medicines, amantadine are used for the prevention of Parkinson's disease at the NMS.
- Droperidol is used only in a hospital, analeptics and sympathomimetics should be used while reducing blood pressure.

Doctor and pharmacist, remember!

Phenothiazine derivatives are characterized by a high index of sensitization in direct contact with the drug (in medical stuff it is 60%).

Hyperthermia during the treatment with phenothiazines is an early sign of NMS → removal of the drug.

TRANQUILIZERS

(ANXIOLYTICS, ATARACTICS)

Tranquilizers (in Latin *tranquillare* is “to make calm”) – are medicines that remove selectively fear, anxiety, emotional tension, increased restlessness and are used mainly in neuroses and the related states.

Classification

Derivatives of benzodiazepine	Derivatives of other chemical groups
Diazepam Alprazolam Medazepam Lorazepam Chlordiazepoxide Gidazepam Dipotassium clorazepate	Hydroxysine Trimetosine Benactyzine

Glossary

- *Amnestic syndrome* – an impairment of memory.
- *Anterograde amnesia* – a memory loss after the beginning of the disease.
- *Porphyria* – the bouts of intestinal colic, polyneuritis, paralysis, mental disorders, convulsions.

Typical side effects	The mechanism of side effect	Contraindications
<p>CNS: irritability, headache, dizziness, confusion, anterograde amnesia, muscle weakness, staggering when walking, addiction, withdrawal syndrome, depression, hallucinations, drug dependence, porphyria</p>	<p>◆ The result of their GABA-, serotonin-, dopamine- и noradrenergic action (derivatives of benzodiazepine)</p> <p>◆ Derivatives of diphenylmethane – the result of their central cholinolytic action (the blockade of M-cholinoreceptors of reticular formation).</p> <p>◆ Withdrawal syndrome - the restructuring in the GABA-benzodiazepine receptor complex, ↓ inhibitory mechanisms.</p>	<ul style="list-style-type: none"> ▶ Depression ▶ Myasthenia ▶ Driving transport ▶ Chronic alcoholism



Typical side effects	The mechanism of side effect	Contraindications
Constipation, dyspepsia, dry mouth, tachycardia urinary retention	◆ the result of peripheral cholinolytic action (the predominance of the sympathetic system).	▶ Obstructive diseases of the GIT, megacolon ▶ BHP, kidneys diseases



Factors that increase the side effects

- ▶ **Tranquilizers mustn't be combined with MAO inhibitors, phenothiazine derivatives, alcohol, CNS depressants.**
- ▶ **Fatty food increases absorption of lipid soluble diazepam and enhances its effect.**
- ▶ **The simultaneous use of tranquilizers with amidopyridine, β -adrenoblockers, reserpine, cardiac glycosides can cause bradycardia.**
- ▶ **The concurrent use of tranquilizers and other psycholeptics, anticonvulsants, antihistamines potentiate the CNS depression.**

Factors that decrease the side effects

- ► *Diazepam* can not be mixed in the same syringe with other drugs and can not be administered intra-arterial.
- ► *Hydroxyzine* accumulates → the dose must be reduced in renal failure.
- ► *Dipotassium clorazepate* is prescribed in half doses for elderly patients.
- ► *Chlordiazepoxide* has a great affinity to the protein, displacing connection with any drug, it can increase its concentration in the blood in a free form.

SEDATIVE MEDICINES

Sedative medicines (in Latin *sedatio* is “calming”) are medicines that cause a moderate sedative effect as a result of decrease of the CNS excitability and its reactivity to different stimuli.

Classification of medicines

Medicines of the plant origin	Bromides* and combined medicines
Persen Valerian extract Motherwort herb tincture Novo-passit	Sodium bromide * Corvalol Valocormide

<i>Side effects</i>	→ <i>Contraindications</i>
Decrease of the mental and physical activity, feeling of fatigue, drowsiness	Activities that require rapid psychomotor reactions

The peculiarity of sedative medicines is the low toxicity (lack of serious side effects); it allows using them widely in the ambulatory practice, especially while treating aged patients.

However, if they are used for a long time, bromine-containing medicines cause bromism that is characterized by such symptoms as drowsiness, general inhibition, memory impairment, apathy, decrease of potency, lacrimation, cough, rhinitis, appearance of rash on the skin.

The treatment of bromism is the following: stoppage of drug administration immediately; using of a great amount of sodium chloride (up to 20 g a day) and abundant drinking.

HYPNOTIC MEDICINES



- **Hypnotics** - are medicines that are able to restore the process of falling asleep, duration and depth of sleep if these processes are disturbed.

Classification of medicines

Derivatives of benzodiazepine, barbituric acid*	Derivatives of cyclopyrrolone, imidazopyridine*, methylbutamide**	Combined medicines, Sedative medicines *
Nitrazepam Phenobarbital*	Zopiclone Zolpidem* Bromisoval **	Reladorm (cyclobarbital+ diazepam) Sodium bromide * Corvalol*

The typical side effects	The mechanism of side effect	Contraindications
<p>CNS: “after (post-) action” syndrom (fatigue, muscle weakness, loss of coordination, drowsiness, headache, depression, memory loss), disorder of the sleep structure, paralysis of respiratory and vasomotor centers, porphyria, habituation, addiction, psychosis, seizures, withdrawal symptoms, apathy and aggression.</p> <p>Accumulation (bromides, barbiturates)</p>	<ul style="list-style-type: none"> ◆ Impair activating signal of reticular formation on the cerebral cortex. ◆ Interact with benzodiazepine and barbiturate receptors in the limbic system → ↑ activity of GABA-system. ◆ Barbiturates lower oxygen demand by neurons and violations of the cytochrome system, which leads to ↓ ACh and the transmission of nerve impulses in the central nervous system. 	<ul style="list-style-type: none"> ▶ Hyperkinesies ▶ Psychosis ▶ Cerebral traumas ▶ Sevier depression

Factors that increase the side effects

- **Barbiturates should not be taken during pregnancy (cross the placenta), lactation. They cause drowsiness and provoke bleeding in newborns.**
- **Sulfonamides and NSAIDs displace barbiturates from its binding with proteins and thus increase the toxicity of barbiturates.**
- **Barbiturates are the inducers of microsomal liver enzymes, so their co-administration with anticoagulants, corticosteroids, oral contraceptives, vitamin D, anticonvulsants is danger.**
- **Barbiturates are incompatible with the cardiac glycosides and reduce the activity of antibiotics.**

Factors that decrease the side effects

- ***Hypnotics*** are used 30 minutes before sleep in minimal effective dose.
- Benzodiazepines → a risk of drug dependence is lower than barbiturates.
- The intake of ***benzodiazepines*** should not be exceeded 14 days.
- The prevention of the syndrome "return, abstinence, nightmares" - the phasing out of hypnotics.
- The intake of ***sodium bromide and hypnotics*** → should refrain from activities that require concentration.
- NaCl (10-20 grams per day) and water (3.5 L) should be taken when bromism.

Doctor and pharmacist, remember!

- During syndrome "return" - ↑ risk of stroke and myocardial infarction.
- The content of ***bromides*** in the blood (1 mg / ml) → chronic toxicity, 2-3 mg / ml - severe CNS disorders.
- ***Zopiclone*** and ***zolpidem*** do not cause syndrome "after (post-) action" do not disturb the phases of sleep.
- Arrhythmia, stenocardia, the pain are observed in the phase of "rapid" sleep; asthma attack, heart stoppage - "slow" sleep.

ANTICONVULSANTS

Anticonvulsants – are drugs that prevent or reduce the frequency and intensity of seizures and their corresponding equivalents (behavioral, autonomic dysfunction, and others.) that are observed in various forms of epilepsy.

Classification

Benzodiazepines	Valproates	Barbiturates
Diazepam Clonazepam	Valproic acid	Benzobarbital Phenobarbital
Succinimides	Iminostilbens	Others
Ethosuccimide	Carbamazepine	Tolperizone

Glossary

- **Ataxia** - the loss of full control of bodily movements.
- **Dystonia** – is a dyskinetic movement disorders due to disturbances of muscle tone.
- **Porphyria** – is a disease accompanied by bouts of intestinal colic, polyneuritis, paralysis, mental disorders, seizures.
- **Diplopia** – is a disorders of vision, when an object is seen double.
- **Tremor** – is an involuntary, stereotypical rhythmic oscillatory movement of the entire body or its parts.

The typical side effects	The mechanism of side effects	Contraindications
<ul style="list-style-type: none"> ● CNS: <i>addiction, increased seizures, worsening mental state, CNS depression, drowsiness, headache, ataxia, dystonia, confusion</i> ● Porphyria ● Megaloblastic anemia, thrombocytopenia ● Hepatotoxicity 	<p>↑ GABA in CNS, ↓ consumption of oxygen by nerve cells and the exciting action of aminoacids (glutamate and aspartate) on CNS, the blockade of Na + Ca ++ membrane channels.</p> <hr/> <p>The increase d-aminolevulinic acid and porphobilinogen in the liver and urine.</p> <p>-----</p> <p>The antagonism of folic acid.</p> <hr/> <p>The result of mitochondrial cytophathy and fatty liver dystrophy.</p>	<ul style="list-style-type: none"> ▶ myasthenia ▶ craniocerebral trauma ▶ impairment of cerebral circulation ▶ porphyria ▶ diseases of hematopoietic system ▶ liver diseases

Factors that increase the side effects

- CNS depressants increase the action of *phenobarbital*.
- *Barbiturates, phenytoin, carbamazepine* increase the activity of microsomal liver enzymes. The combination with *carbamazepine, nialamide, furazolidone, tetracycline* increases of the side effects.
- The combined administration of *carbamazepine* with valproic acid → the possibility of coma development.
- Long-term use of *anticonvulsants* is a risk factor for cancer of the genital organs.

Factors that decrease the side effects

- Discontinuation of the medicines should be gradually (the possibility of status epilepticus)
- Replace the drug correctly: a gradual reduction of the dose of the old medicines and an increase of the dose a new one.

Doctors and pharmacists, remember!

- The side effects of anticonvulsants are the hematological and metabolic complications (from 7 up to 25%).
- A hypersensitivity to barbiturates have got 1-3% of the patients, which may be accompanied by ↑ intracranial pressure and cerebral edema.
- Particularly dangerous side effects (*phenobarbital, carbamazepine, ethosuximide*):
 - Changes in blood formula;
 - A psychological state;
 - Ataxia;
 - Disturbances the function of liver or kidneys;
 - Bone marrow suppression.

MEDICINES FOR PARKINSONISM

TREATMENT

Classification

Anticholinergic (cholinolytic) ones	Dopaminergic ones
Trihexiphenydil	Levodopa
Triperiden	Selegiline
Diphenyltropine h/chl	Nacom
	Gludantane
	Bromocriptine
	Madopar
	Amantadine
	Entacapone

Glossary

- ***Hyperkinesia*** – is an increase in muscular activity that can result in excessive abnormal movements, excessive normal movements, or a combination of both.
- ***"Cheese syndrome"*** – is an abrupt ↑ blood pressure and the exacerbation of ischemic heart disease when the receiving the food containing tyramine (a cheese, a cream).
- ***"The phenomenon of wear"*** - a progressive decrease the effectiveness of levodopa, due to the reducing sensitivity of D-receptors to levodopa.
- ***The phenomenon of "on-off"*** - a periodic fluctuation of the reaction of the patients to levodopa.

The typical side effects	The mechanism of the side effects	Contraindications
<ul style="list-style-type: none"> ● CNS: hyperkinesia, movement disorders, psychosis, hallucinations, ataxia, chorea, weakness ● Dry mouth, dizziness, tachycardia ● Hyperthermia ● Blood: agranulocytosis, leukopenia, thrombocytopenia 	<ul style="list-style-type: none"> ● Stimulation of dopamine receptors ● The central and peripheral cholinolytic action ● ↓ secretion of sweat glands and heat emission 	<ul style="list-style-type: none"> ▶ Mental disorders, epilepsy, diseases of CNS ▶ Cardio-vascular disease ▶ Diseases of blood system

Factors that increase the side effects

- The age is over 60 years (*trihexyphenidyl*).
- Psychoses, neuroses (*dopaminergic drugs*).
- Liver and kidneys diseases (*all medicines*).
- The combined administration of *dopaminergic drugs* and *MAO inhibitors causes* an abrupt arterial hypertension; *tricyclic antidepressants, MAO inhibitors* cause hyperthermia.
- The overdose of *bromocriptine* and food containing tyramine leads to "cheese syndrome".

Factors that decrease the side effects

- Dose reduction, the abolition of anticholinergic drugs.
- The medicines should be taken by short breaks of 1-2 days per week.
- Bromocriptine shouldn't be used in the patients with heart diseases, peripheral circulatory disorders, with acromegaly or gastric ulcer.
- The blood pressure control is in the first days of the bromocriptine treatment

Doctors and pharmacists, remember!

- Deep phase dystonia can be developed at the late stage of Parkinson's disease (dystonia - improvement - dystonia).
- The *levodopa* action begins next week, the maximum effect develops within 1 month.
- The combination of levodopa and cholinolytic agents → ↓ the therapeutical effect of *levodopa*.

MEDICINES STIMULATING THE CENTRAL NERVOUS SYSTEM

- **Analeptics** (in Greek *analepticos* means “recovery, reviving”) - are medicines stimulating inhibited vitally important centres of the medulla oblongata (respiratory and vasomotor ones) due to decrease of the excitability threshold of these centres.
- **Psychomotor stimulants** – are medicines that increase mental and physical activity.

Classification

Analeptics	Psychomotor stimulants
Caffeine sodium benzoate	Caffeine sodium benzoate
Bemegrade	Amphetamine sulphate
Nicethamide	Mesocarb
Sulphocamphocaine	Feprosidine hydrochloride
Ethimizole	
Cytisine	

ANALEPTICS

Typical side effects	The mechanism of side effect	Contraindications
<p>CNS: ▶ ↑ convulsive readiness, anxiety, insomnia, tremors</p> <p>CVS: tachycardia, ↑ blood pressure</p>	<p>▶ Excitation of motor areas of the cerebral cortex excitation MTI</p> <p>▶ Excitation of vaso-motor center</p> <p>▶ Disorders of the central reciprocal inhibition of antagonist muscles</p>	<p>▶ Psychosis, agitation, epilepsy, anxiety and depression</p> <p>▶ Organic heart disease, hypertension, atherosclerosis</p> <p>▶ Convulsive states</p>

PSYCHOMOTOR STIMULANTS

The typical side effects	The mechanism of side effects	Contraindications
<p>CNS: tremor, convulsions, coma, bleeding in the brain, addiction, euphoria, withdrawal, psychosis, hallucinations, extrapyramidal disorder (<i>amphetamines</i>)</p> <p>▶ Hyperglycemia (<i>caffeine</i>)</p> <p>▶ Hyperventilation, dyspnea (<i>caffeine, ethimizole</i>)</p>	<p>▶ ↑ the concentration of catecholamines in the brain tissue, the stimulation of adrenergic and dopaminergic receptors</p> <p>▶ Withdrawal syndrom - the result of the depletion of monoamines in the CNS</p> <p>▶ Extrapyramidal disorders is a result of the blockade of dopaminergic system</p> <p>▶ Stimulation of adrenaline (hormone mobilizes liver glycogen)</p> <p>▶ Stimulation of the respiratory center</p>	<p>Psychosis, agitation, epilepsy, anxiety, depression, insomnia, brain diseases</p> <p>Diabetes mellitus</p> <p>Bronchial asthma</p>

Factors that increase the side effects

- **Amphetamine** is contraindicated in pregnancy and lactation (congenital defects of mouth in newborns)
- The combined administration of **amphetamine** and barbiturates, benzodiazepines ↑ hypermobility.
- Tricyclic antidepressants and alcohol ↑ level of **amphetamine** in the blood.
- The use of high doses of **amphetamine** leads to the development of mental depression.
- The abrupt discontinuation of **caffeine** → ↓ central nervous system, drowsiness, depression.

Factors that decrease the side effects

- **Amphetamine** is eliminated slowly → the accumulation phenomenon.
- **Amphetamines** are not used with MAO inhibitors or earlier than 14 days after discontinuation → the development of AG.
- **Sulphocamphocaine** should be applied gently for the patients with low blood pressure → the possibility of hypotensive action of procaine.

Doctors and pharmacists, remember!

- **Psychomotor stimulants** should be taken in large doses in a sharp inhibition of CNS.
- **Caffeine** is characterized by large range of the drug therapeutic action. Many painkillers contain caffeine (askophen, citramone etc.) → addiction with prolonged use. It is strong stimulator of HCl.
- **Amphetamine** is released only by prescription (the development of drug addiction), the possibility of "paradoxical reaction" (in 5-10% of cases) – sedation.

ANTIDEPRESSANTS

Antidepressants (thymoleptics) – are psychotropic medicines, which remove mainly the depressive mood or depression, they can stimulate the interest to the life, activity and optimism.

Classification

Tricyclic, tetracyclic* agents	MAO inhibitors (reversible, irreversible*)	Selective inhibitors of serotonin re-uptake	Plant origin, others*
Mianserine* Amitriptyline Doxepin Imipramine Maprotiline Clomipramine	Nialamide* Pyrazidol Befol	Fluoxetine Sertraline Nefazodone Paroxetine Fluvoxamin	Hyperycin Amixide* Thianeptine* Mirtazapine*

Glossary

- ***Tremor*** – an involuntary stereotypical rhythmic oscillatory movement of the entire body or its parts.
- ***Paresthesia*** - a disturbances of the sensitivity, characterized by tingling, burning, creeping sensation.
- ***Agitation*** - a motor excitation.
- ***Delirium*** - an acute mental disorder characterized by a dimming of consciousness with a predominance of visual hallucinations, illusions, delirium, motor excitation.
- ***Ataxia*** - the loss of full control of bodily movements.

The typical side effects	The mechanism of side effects	Contraindications
<p>▶ CNS: anxiety, headache, confusion, tremors, convulsions, paresthesias, hallucinations, delirium, withdrawal syndrome, ataxia, amnestic syndrome</p> <p>▶ Sedation, drowsiness, ↓ BP</p> <p>▶ Visual impairment, dry mouth, constipation, urinary difficulty</p>	<p>▶ The accumulation of NA and the excitation of central and peripheral serotonin receptors</p> <p>▶ The blockade of H₁-histaminic and α₁-adrenoreceptors</p> <p>▶ The blockade of M-cholinoreceptors</p>	<p>◆ Mania, epilepsy, insomnia</p> <p>◆ Hypotension, work that requires concentration.</p> <p>◆ Glaucoma, constipation, benign hyperplasia of prostate gland, atony</p>

The typical side effects	The mechanism of side effects	Contraindications
<ul style="list-style-type: none"> ▶ Disturbances of libido, erectile dysfunction, tyramine syndrome, euphoria, hypertension (MAO inhibitors) ▶ Extrapyramidal disorders ▶ Hypotension ▶ Cardiotoxicity ▶ Withdrawal 	<ul style="list-style-type: none"> ▶ The inhibition of MAO-A ▶ The blockade of dopaminergic subcortex (cortex, limbic system) ▶ The inhibition of MAO-B 	<ul style="list-style-type: none"> ▶ Hypertension, disturbances of cerebral circulation ▶ Parkinsonism ▶ Myocardial infarction, heart disease, conduction disorders, atherosclerosis, myocarditis

Factors that increase the side effects

- High doses of antidepressants, the elderly and children's age, diseases of cardiovascular system, liver, kidneys, organic cerebral insufficiency, neoplastic process.
- Foods containing tyramine (the development of "cheese syndrome").
- The concomitant use with terfenadine, astemizole, cisapride may lead to the death.
- *Antidepressants* are not compatible with cholinomimetics, psychomotor stimulants, sympatholytic, anticoagulants, salicylates, phenylbutazone, alcohol.
- *Tricyclic antidepressants* with noradrenalin - arrhythmogenic effect.

Factors that decrease the side effects

- **Prevention of hypersedation – the dose reduction or administration of an antidepressant with less sedative action.**
- **Don't prescribe antidepressant with marked α -adrenoblocking action in patients with cardiovascular diseases for the prevention of orthostatic hypotension.**
- **To prevent cardiotoxicity → administration in low doses, under the control of the ECG.**
- **Bromocriptine (dopamine receptor agonists) up to 60 mg, muscle relaxants, glucocorticoids should be prescribed to correct hyperthermia.**
- **Foods that contain tyramine should be excluded from the diet for the prevention of tyramine syndrome.**

NOOTROPIC MEDICINES and ADAPTOGENS

Nootropic medicines (*noos* means “thinking, mind” and *thropos* is “affinity”) are medicines that improve the mental activity increasing the brain’s resistance to the damaging factors.

Adaptogens are medicines of plant and animal origin that have the general tonic action on the CNS functions, the endocrine system and metabolism. They increase organism’s resistance to the unfavourable environmental factors.

Classification

<i>Nootropic medicines</i>	<i>Adaptogens</i>
Pyracetam	Ginseng root tincture
GABA (Aminalalone)	Pantocrine
Pyritinol	Aralia tincture
Fenibut	Eleutherococcus extract
Picamilone	Schizandra tincture
Meclofenoxate	Citrullin
Sodium oxybutirate	
Hopantenic acid (Pantogam)	

The typical side effects	The mechanism of side effects	Contraindications
<p>▶ CNS: insomnia, agitation, headache, irritability, tremor</p> <p>▶ CVS: increased blood pressure, worsening coronary insufficiency (piracetam), tachycardia (tincture of ginseng root)</p>	<p>▶ The influence on brain neurotransmitter systems (adrenergic, dopaminergic, serotonergic)</p> <p>▶ The result of adrenomimetic processes</p>	<p>▶ Neurosis, myasthenia gravis, agitation, epilepsy, insomnia, psychosis</p> <p>▶ Hypertension, organic heart diseases</p>

Factors that increase the side effects

- ***Aminalton*** ↑ the action and the side effects of hypnotic and anticonvulsive medicines.
- ***Sodium hydroxybutyrate*** ↑ the action of analgesics and medicines for general anesthesia . Hypokalemia may develop with prolonged use. The rapid i/v introduction - stop breathing.
- ***GABA*** ↑ action and the side effects of the benzodiazepines; ***pyritinol*** - penicillamine, medicines containing gold and sulfasalazine; ***fenibut*** - with antiparkinsonian drugs for treatment Parkinson's diseases, neuroleptics, hypnotics, general anesthetic, narcotic analgesic.
- ***Pyracetam*** crosses the placenta and is excreted in breast milk.

Factors that decrease the side effects

- The complications caused by sodium oxybutyrate (jerking limbs and language stimulation) can be stopped by barbiturates, neuroleptics, promedol.
- Bemegride is used to accelerate the elimination of anesthesia induced by *sodium oxybutyrate* use.
- Do not take *adaptogens* in the evening.
- *Sodium hydroxybutyrate* is used with care in hypertension, gestosis.
- *Ginseng preparations* are taken effectively in fall and winter.
- *Citrulline* can be applied during pregnancy.
- *Pantogam* is not recommended to use with psychomotor stimulants and other nootropic medicines with long-term administration.

Thank you for attention!

