Odesa National Medical University
Department of General and Clinical Pharmacology and Pharmacognosy

PSYCHOTROPIC PREPARATIONS THAT SUPPRESS CNS (NEUROLEPTICS, TRANQUILIZERS, PSYCHSEDATIVES)

NEUROLEPTICS (ANTIPSYCHOTICS) –

neuron – nerve; lepticos – hold

Psychotropic agents that inhibit CNS, remove hallucinations, delusion without inhibition of conciseness

5 signs (J. Delay and P. Deniker):

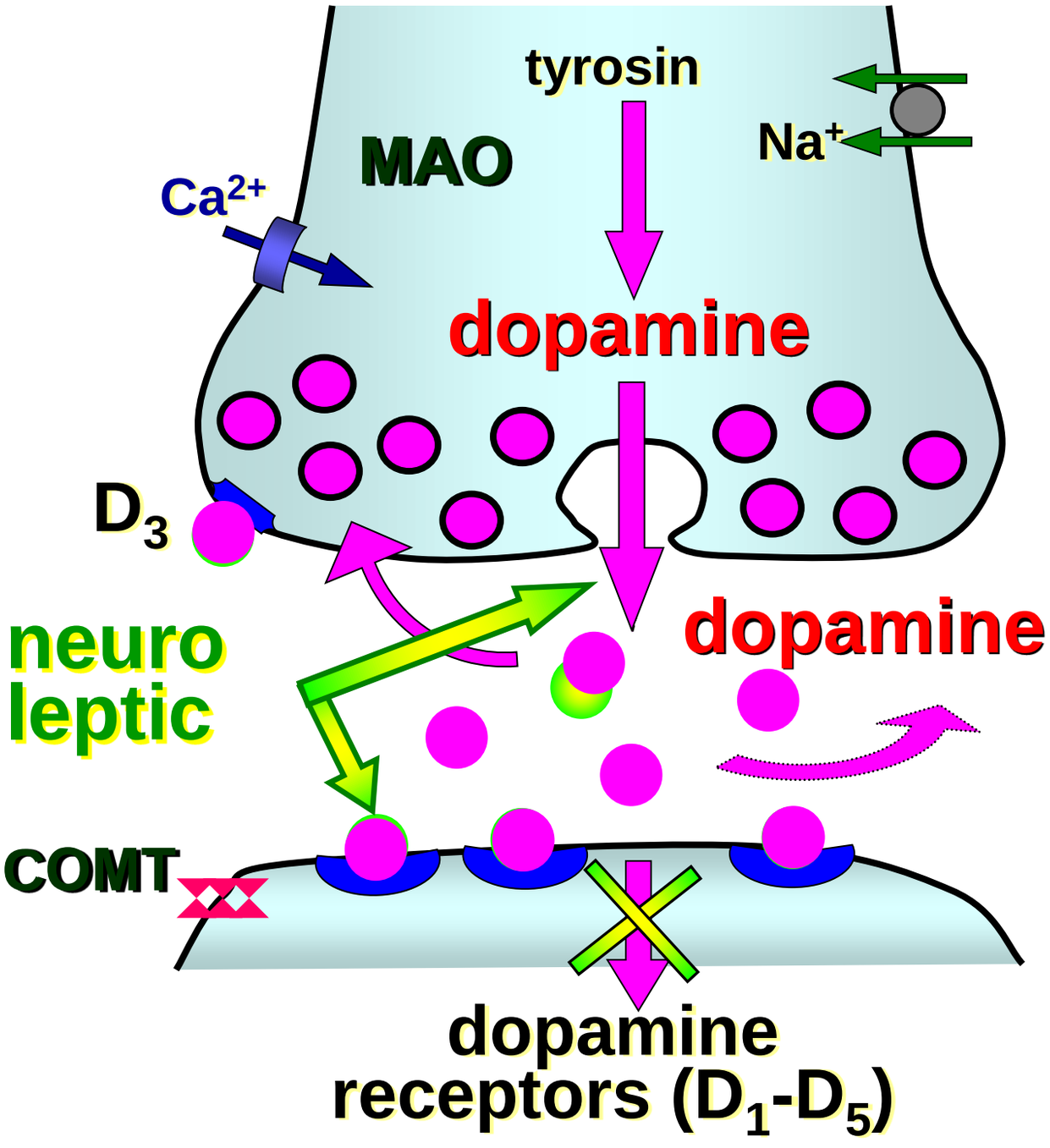
- **remove psychosis (antipsychotic action)**
- **abort psychomotor excitement of different origin**
- **predominantly influence on subcortex structures of the brain**
- **possible psychodysleptic action without hypnotic action**
- **oftenly produce neurologic and neurovegetative reactions**

(3 «H»: hypodynamia, hypothermia, hypotension)

CLASSIFICATION OF NEUROLEPTICS

- derivatives of **phenothiazins** (typical neuroleptics)
  - ✓ ***alyphyatic*** – **chlorprominazin (aminazin), levomepromazin**
  - ✓ ***piperazin*** – **ethaperazinн, triphtazin**
  - ✓ ***piperidin*** – **neuleptil**
- derivatives of **buterophenone** – **haloperidol, droperidol**
- derivatives of **benzamid** – **sulpirid, metoclopramid**
- derivatives of **piperidin** – **fluspirilen, pimosid**
- derivatives of **different chemical groups** – **reserpin, clozepin, olenzepin etc**

MECHANISM OF ACTION OF NEUROLEPTICS



Main dopaminergic routes
Mesolimbic and mesocortical systems (antipsychotic action, mental depression)
Hypothalamus-pituitary (hypothermia, ↑ prolactin)
Extrapyramidal system (symptoms of parkinsonism)
Trigger zone of vomiting center (antiemetic effect)

SPECTRUM OF PSYCHOTROPIC ACTION OF NEUROLEPTICS

chlorpromazin – $\alpha > 5\text{-}HT_2 \geq D_2 > D_1$

haloperidol – $D_2 > D_1 = D_4 > \alpha_1 > 5\text{-}HT_2$

antipsychotic

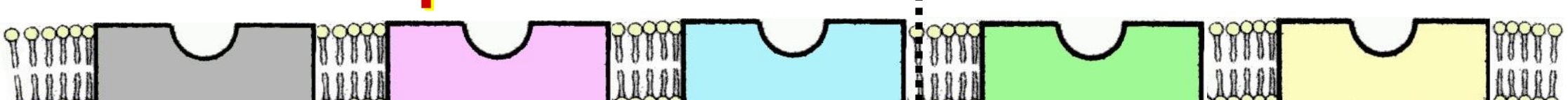
sedatives:

droperidol > aminazin > chlorprotixen > clozepin > neuleptil

antipsychotics:

haloperidol > pimozid > fluspirilen > triftazin > etaperazin > sulpirid

neuroleptic



H_1- M- α- $D_{1,2,3,4,5}$- $5HT_2$-

PHARMACODYNAMICS OF NEUROLEPTICS

neuroleptic (sedative)

- ✓ apathy, drowsiness, lethargy
- ✓ depression of initiative, “paralysis” of will, emotional indifference to environment
- ✓ inhibition of motor activity
- ✓ quick onset of action
- ✓ vegetative disturbances (collaptoid reaction etc), especially at the beginning of treatment

antipsychotic

- ✓ removing of persistent changes of personality and asocial features of behaviour
- ✓ removing of hallucination, delirium
- ✓ enhancement of motives and initiative, interest to surrounding
- ✓ develops in 1–2 weeks
- ✓ extrapyramidal disorders (increasing during the therapy course)

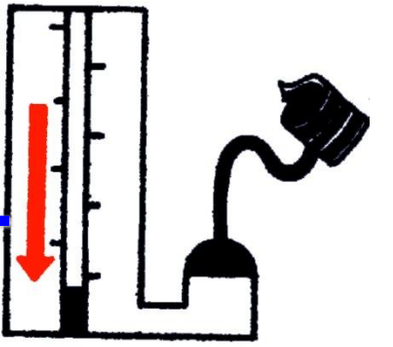
PHARMACODYNAMICS OF NEUROLEPTICS

CNS:

- **hypothermia** (↓ the center of heat release because of blockade of α-adreno- and serotonin receptors of hypothalamus + dilatation of the skin vessels)
- **hypodynamia** (muscular tone as a result of activating influence of reticular formation and spinal cord through α-adrenoblockade)
- **anti-vomiting** (anti-emetic) **and anti-hiccup effects** (blockade of D_2-receptors of the trigger zone of the vomiting center)
- **disorders in the motor sphere with systematic intake:** parkinsonism, acute dystonia, tardive dyskinesia, etc. (D_2-receptors blockade of extrapyramidal system)
- **potentiation of anaesthesia and analgesia, especially with sedatives** (blockade of α-adrenoreceptors of the reticular formation and ↓activating influence on the cerebral cortex)

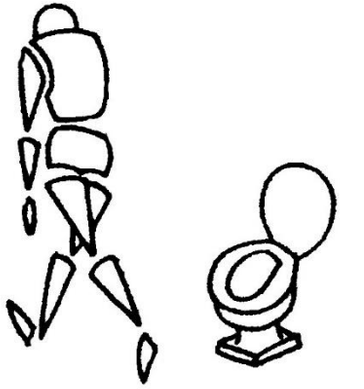
PHARMACODYNAMICS OF NEUROLEPTICS

Vegetative reactions:



- acute hypotension, ↑ HR
- ↓ tone of hollow organs, motility and GIT secretion
- disturbance of accommodation, dry mouth

Endocrinic and other disorders:



- ↑ prolactin, ↓ gonadotropins, estrogens, gestagens
- in women — amenorea, ↑ libido; in men — gynecomastia, impotence
- ↓ STH, ACTH, ADH, oxytocin
- ↑ melanostimulating hormone
- ↑ appetite and body weight antiallergic and antipruritic action (H_1-receptors blockade)

PHARMACOKINETICS OF NEUROLEPTICS

Administration: **with oral administration absorption is unpredictable (first pass metabolism, change of GIT motility because of cholinolytic action; partial biotransformation in the intestine), bioavailability – 30-60 %; at I.M. – ↑ in 10-40 times, but also is unpredictable (precipitation in the muscle)**

Plasma protein binding: **90-95 %**

Distribution: **accumulate in tissues of the brain, lungs and other well vascularized organs; penetrate well through the BBB, placenta; penetrate well through the BBB, placenta!**

Biotransformation: **takes place by various ways (oxidization, conjugation) not only in the liver, but also in the lungs, brain, kidneys and intestine with formation of active and nonactive metabolites**

Excretion: **via the kidneys and bile mainly as nonactive metabolites; *T ½:* in majority – 20-40 hrs ⇒ there are slow-release forms –flushpirilen, pimozide (4-20 days)**

APPLICATION OF NEUROLEPTICS

- schizophrenia
- attack (relapse) of endogenous psychoses with delirium, hallucinations, aggressiveness
- acute psychical disorders (psychologic traumatic situations, traumas)
- delirium, abstinence syndrome — haloperidol, sedative neuroleptics
- neuroleptanalgesia — haloperidol, droperidol in combination with opioids (fentanyl) and premedication
- vomiting of the central origin, hiccup (chemotherapy of oncologic patients) — pimozide, haloperidol, etaperazine

APPLICATION OF NEUROLEPTICS

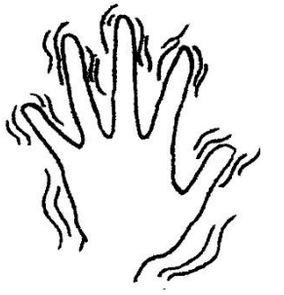
- shock (traumatic and burn) — droperidol, aminazine
- hypertensive crisis — levomepromazine, droperidol, aminazine
- hyperthermia (resistant to NSAIDs) — aminazine
- vegetoneuroses (ischemic heart disease (IHD), peptic ulcer, climax) — sulpiride, thioridazine
- neurodermatosis (pruritis) — aminazine, levomepromazine, chlorprotixen
- migraine — sulpiride
- in gastroenterology — metoclopramide

ADVERSE EFFECTS OF NEUROLEPTICS

- “behavioral” affects like “pseudodepressions” (flaccidity, lack of initiative, indifference, etc.)
- as a result of dopamine blockade extrapyramidal disorders (neuroleptic syndrome):

  at the early stages: parkinsonism (rigidity, tremor)

  at the late stages (in months and years), tardive dyskenesis (winking, spasm of eyelids, choreoatetosis as usual in women)



- malignant neuroleptic syndrome (malignant hyperthermias) — rigidity of muscles, high temperature, arrhythmia, coma

ADVERSE EFFECTS OF NEUROLEPTICS

- collapse (α-adrenoblockage)
- M-cholinolytic action (dryness of mouth, mydriasis, urine retention, constipation etc.)
- endocrinic disturbance:
  - ✓ «castration effect» (dopamine blockade ⇒ ↑ prolactin,↓ gonadotropic hormones, in women galactorrhea, amenorrhea, in men gynecomastia, ↓ libido, importance)

- hepatotoxicity (cholestatic hepatitis)
- cardiotoxicity
- allergic reaction (rush, hemolysis, agranulocytosis)
- corneal and lenticular opacity (20-30 %)
- teratogenic, embryo-, fetotoxic action
- local irriation (phenothiazinese)

TRANQUILIZERS (ANXIOLYTICS)

tranquillium — rest; *anxious* — warried, frightened
ataractics (ataraxia — coolness*)*

– depriming psychotropic drugs, selectively removing emotional instability, anxiety, fear (phobia), tension

HISTORY OF CREATION

1954 г. a new tranquilizer meprobamate was introduced in the USA

1957 г. swiss scientists synthesized the first tranquilizer from a series of derivatives of 1,4-benzodiazepine — chlordiazepoxide (elenium)

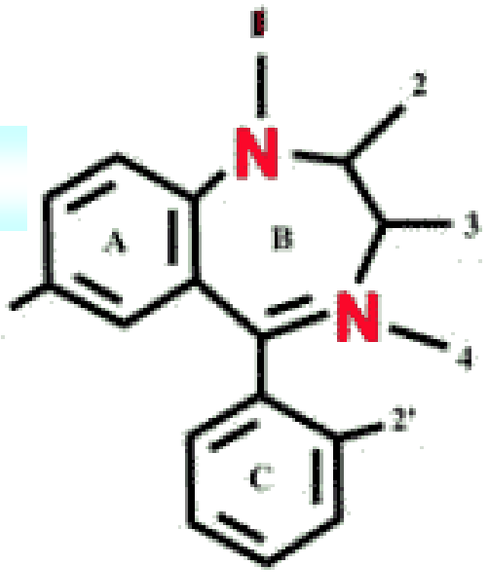
1963 г. diazepam (valium) was applied

CLASSIFICATIONS OF TRANQUILIZERS

historically:

- **I generation**: meprobamate, hydroxizine (atharax), amizil, (benactizine), mebicar, etc.
- **II generation**: benzodiazepine derivatives (chlordiazepoxide, diazepam, etc.)
- **III generation**: buspirone, etc.

according to chemical structure:



- **benzodiazepine derivatives (typical)**– chlordiazepoxide, diazepam, phenazepam, lorazepam, flunitrazepam, alprazolam, etc.)
- **different chemical groups (atypical)** – buspirone, mebicar, amizyl, trioxaxine, oxalidine, meprobamate, etc

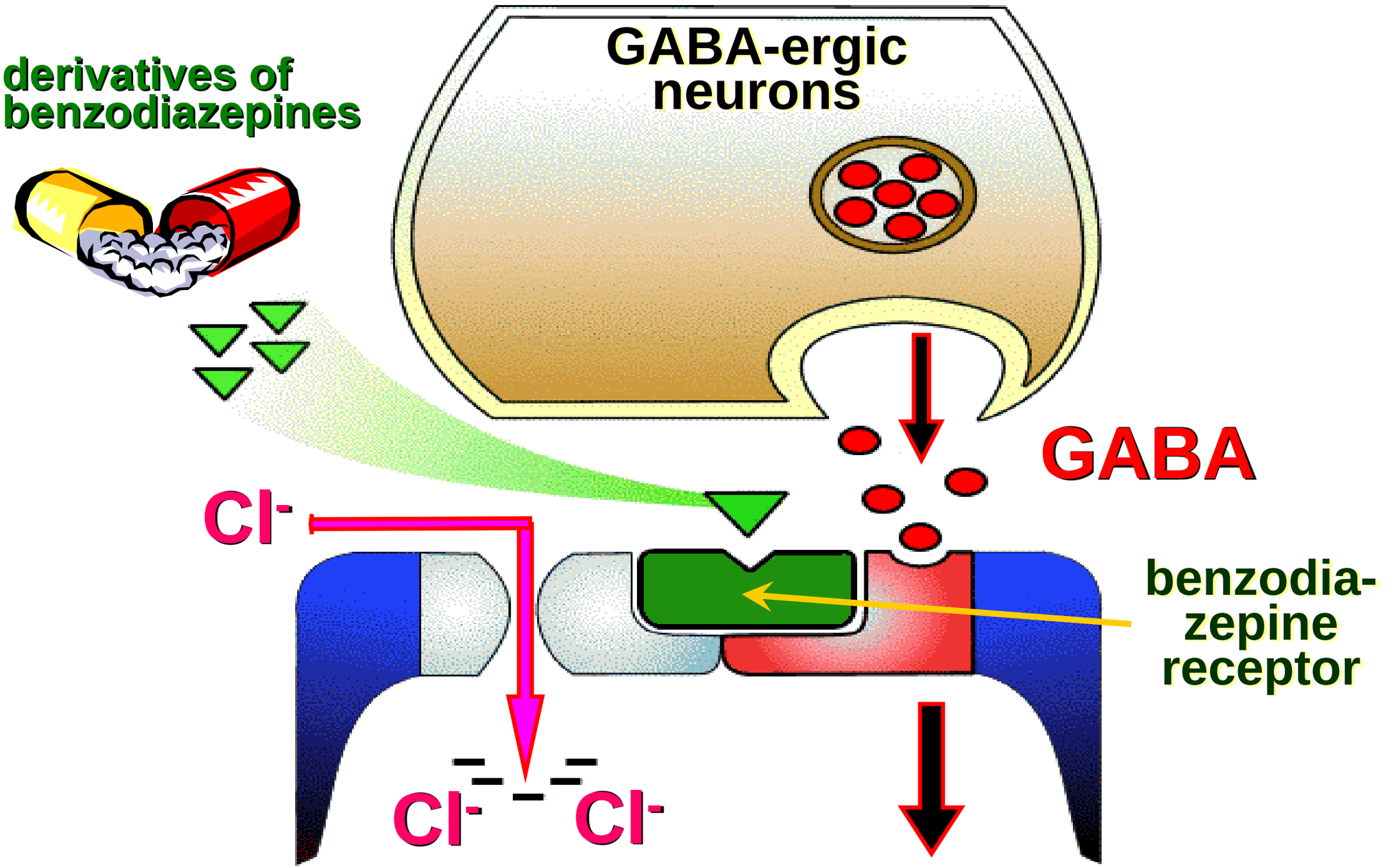
SPECTRUM OF TRANQUILIZERS' PHARMACOLOGICAL EFFECTS

- anxiolytic (reduction of anxiety + stress-protective + antiphobic)
- sedative
- hypnotic
- myorelaxant
- anticonvulsant
- vegetostabilizing
- amnestic (anterograde amnesia)
- activate action of hypnotics, narcotic analgesics, alcohol

according to spectrum of action:

- sedative («major», night) – nitrazepam, flurazepam, diazepam, phenazepam, etc.
- daily («minor») – mezapam, gidazepam, buspirone, mebicar

MECHANISM OF BENZODIAZEPINES ACTION



PHARMACODYNAMICS OF BENZODIAZEPINES

- benzodiazepine → stimulation of BZ-receptor of the
- complex GABAA-receptor-chlorionic channel ⇒
- ↑ sensitivity of GABA-receptors to GABA ⇒
- ↑ the rate of chlorine channels opening, which ↑ the entering current of Cl- ⇒
- hyperpolarization of the neuron postsynaptic membrane ⇒
- ↑GABA-transmission ⇒ inhibition process development in definite departments of the CNS (limbic system, cerebral cortex, hypothalamus, thalamus, reticular formation, spinal cord, etc.)
- ⇒suppressing effect on the emotional sphere (anxiolytic, sedative-hypnotic, amnestic), motor and vegetative systems (myorelaxation, relief of seizures, vegetostabilization)

PECULIARITIES OF BENZODIAZEPINES' CLINICAL ACTION

- **with pronounced anxiolytic effect — phenazepam, diazepam, lorazepam, alprazolam, etc.; *moderate* — chlordiazepoxide, gidazepam, oxazepam, etc.; *"daily"* (anxioselectivity with activating component) — medazepam, tophizopam, gidazepam, etc.**
- **with pronounced hypno-sedative effect — nitrazepam, flunitrazepam, phenazepam, diazepam, lorazepam, chlordeazepoxide, oxazepam, triazolam, midazolam, etc.**
- **with pronounced anticonvulsant effect — clonazepam, diazepam, phenazepam, lorazepam, nitrozepam**

PHARMACOKINETICS OF BENZODIAZEPINES

T ½ depend on:

- ✓ **age (in newborns — 31, infants — 8–14, a 24–72, aged — 100 hrs)**
- ✓ **concomitant diseases of the liver, kidneys, etc.**

according to duration of action:

- **short acting ($T_{1/2}$ upto 6 hrs): triazolam, medazolam**
- **intermediate ($T_{1/2}$ – 6-24 hrs): lorazepam, oxazepam, flunitrazepam, etc.**
- **long acting ($T_{1/2}$ more than 24 hrs): nitrazepam, phenazepam, diazepam, flurazepam (prodrug, T1/2 ≈ 100 hrs), etc.**

APPLICATION OF TRANQUILIZERS

- all the kinds of phobic disorders (neuroses, psychopathy, accompanied with alertness, fear, emotional stress, etc.) - phenazepam, alprazolam, lorazepam
- anxiety with a background of depressive conditions of various genesis — with antidepressants alprazolam, lorazepam, oxazepam
- endogenic psychiatric diseases (schizophrenia) — diazepam, phenazepam, etc.
- acute conditions (psychomotor agitation, alcohol abstinence, delirium) — diazepam, phenazepam
- in somatic diseases therapy (IHD, peptic ulcer, hypertension, cholecystitis, bronchial asthma, etc.)

APPLICATION OF TRANQUILIZERS

- sleep disorders — nitrazepam, phenazepam
- epilepsy, epileptic status, seizures of various genesis, tetanus — clonazepam, diazepam, etc.
- neurologic disorders accompanied with muscular hypertonus — diazepam, lorazepam
- for premedication and anesthesia (atharalgesia — diazepam + phentanyl), during the postoperative period — flunitrazepam, midazolam, diazepam, etc.
- acute reactive stress conditions in healthy people in extreme situations (but not with everyday stress)

ADVERSE EFFECTS OF TRANQUILIZERS

- **"behavioral" reactions: ↓ apprehensive and psychomotor processes, disturbance of orientation, anterograde amnesia**
- **after-effect (hangover), especially in elderly people (dose-dependent hypersedation, dysco-ordination of movement)**
- **"paradoxal" reactions: movement anxiety, nightmares, ↑ aggressiveness, inadequate conduction (in children, elderly and mentally ill patients)**
- **tolerance**
- **drug dependence (psychic and/or physical) neuroses-like. The risk of arising with administration for more than 6 months, especially high doses**

ADVERSE EFFECTS OF TRANQUILIZERS

- rebound syndrome
- ↓ myocardial contractility, hypotension (diazepam, lorazepam with parenteral introduction in elderly people)
- moderate depressive influence on the respiratory center (in pulmonary patients)
- dry mouth, dyspepsia, ↑ appetite, ↑ intraocular pressure, impotence; seldom allergy, hematologic changes (leukopenia)
- teratogenic, embryo- and fetotoxic action

CLASSIFICATION OF PSYCHOSEDATIVES

- **plant-origin:** valeriana, common motherwort, passiphlora
- **bromides:** potassium and sodium bromide
- **combined:**

valocardin, corvalol (ethyl ether of bromine isovaleric acid + phenobarbital + oil of peppermint + ethanol),

valocormid (extract of valeriana, lily of the valley, belladonna, sodium bromide, mentol),

novopassit etc.

valeriana

motherwort

PSYCHOSEDATIVES

pharmacodynamics

- ↓ excitability of reticular structure, medulla
- oblongata and hypothalamus
- ↑ threshold of neuronal excitability
- ↓ emotional and motive excitation
- ↓ threshold of convulsive activity
- (especially in children)
- adrenolytic activity (↓ ABP, “-” ino-, chronotropic
- effects)
- ↓ afferent impulsation to the cerebral cortex
- spasmolytic action (↓ vessels of the heart and brain,
- ↓ tone of smooth muscles of the intestine)
- potentiation of action of hypnotic drugs

PSYCHOSEDATIVES

indications

- **insomnia** (caused by vegetative disorders)
- **emotional overexcitation**
- **neurotic disorders**
- **angina pectoris with background of neurotic disorders**
- **arrhythmias** (extrasystole, paroxysmal tachycardia)
- **initial stage of hypertension**
- **climacteric disorders**
- **intestinal colic** (especially in children) **инсомния** (на почве вегетативных расстройств)

BROMIDES

adverse effects

- general weakness, fatigue, indifference to surrounding,
- weakening of memory, drowsiness
- irritation of gastric mucous, anorexia, constipation
- excessive sweating
- sexual dysfunction (↓ libido, potentia)
- cumulation ⇒ acute and chronic poisoning (bromism): sleep, apathy, hallucinations, delirium, tremor of eyelids, tongue, hands, speech disorder, conjunctivitis, rhinitis, bronchitis, acne-like rash

bromism treatment

- withdrawal of drug
- antidote — sodium chloride (5–10 g on 3–4 l of liquid)
- diuretics (aminophyllin, ammonium chloride)
- hemodialysis
- symptomatic treatment

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HYPNOTICS.
ANTICONVULSANTS

NORMAL SLEEP

NREM (non-rapid eye movement), orthodox, or slow-wave EEG sleep. NREM sleep progresses through four stages (1-4):

stage 1 - descending drowsiness;

stage 2 - major fraction of non-REM sleep;

stages 3 and 4 - slow-wave sleep

REM (rapid eye movement), paradoxical, or fast-wave EEG sleep.

TYPES OF INSOMNIA:

- ✓ **EMOTIONAL - difficulty in falling asleep**
- ✓ **SENILE – early or frequent awakenings, and remaining unrefreshed after sleep**

THE IDEAL HYPNOTIC DRUG SHOULD:

- ☞ **allow the patient to fall asleep quickly;**
- ☞ **maintain sleep of sufficient quality and duration so that the patient awakes refreshed without a drug hangover, continued sedation or rebound anxiety, should not cause dependence and tolerance;**
- ☞ **have very low toxicity and should not interact with other medications.**

BARBITURATES

Classification

Long-acting (6-10 hrs): phenobarbital

Intermediate-acting(4-6 hrs): pentobarbital, cyclobarbital

Ultra-short-acting (20-30 min): thiopental

Mechanism of action

Barbiturates potentiate GABAinduced chloride currents. Also they suppress high frequency repetitive firing of neurons

Pharmacological effects

CNS: ***all degrees of CNS depression, ranging from mild sedation to general anesthesia including anticonvulsant activity.***

Sleep: ***increase the total sleep time; decrease sleep latency, the number of awakenings, and the durations of REM and slow-wave sleep***

Peripheral Nervous Structures: ***depress transmission in autonomic ganglia***

Respiration: ***depress the respiratory drive***

CVS: ***slight decrease in BP and heart rate***

Liver: ***induce microsomal enzymes. It increases the metabolism of a steroid hormones, vitamins K and D, and barbiturates***

BARBITURATES

Pharmacokinetics

Absorption: **rapid and probably complete**

Distribution: **distributed widely, and readily cross the placenta; the highly lipophilic barbiturates undergo redistribution that limit their action**

Biotransformation: **nearly complete metabolism and/or conjugation of barbiturates in the liver precedes their renal excretion**

Therapeutic uses:

- ***for "sedation"*** **(phenobarbital)**
- ***epilepsy, emergency treatment of convulsions*** **(phenobarbital)**
- ***as intravenous anesthetics*** **(thiopental)**
- ***hyperbilirubinemia in the neonate*** **(phenobarbital)**

Adverse effects:

- ***"after effects" or "hangover"*** **(drowsiness, impairment of judgment)**
- ***paradoxical excitement*** **(among geriatric and debilitated patients)**
- ***potentiate action of alcohol and other CNS depressants***
- ***tolerance*** **(both pharmacokinetic and pharmacodynamic)**
- ***dependence*** **(physical or physiological)**
- ***enhance porphyrin synthesis***

BENZODIAZEPINES (BDZ)

Classification

Long-acting ***($T_{1/2}$>24 hrs) – chlordiazepoxide, diazepam, phenazepam, nitrazepam***

Intermediate-acting($T_{1/2}$=10-20 hrs) – clonazepam, lorazepam, temazepam, alprazolam

Short-acting ($T_{1/2}$=3-8 hrs) – triazolam, midazolam, oxazepam

Mechanism of action

BDZ potentiate GABAergic neurotransmission. Unlike barbiturates, BDZ require GABA to express their effects

Pharmacological effects

CNS – ***sedation, hypnosis, anxiolytic, skeletal muscle relaxation, anticonvulsant effect, anterograde amnesia***

Sleep – ***increase the total sleep time; decrease the time spent in stage 0, 1, 3, 4, the number of awakenings, and the durations of REM sleep; increase time spent in stage 2***

A significant advantage of the BDZ over other CNS depressants (e.g., the barbiturates) is that they possess a much greater separation between the dose that produces sleep and the dose that produces death.

BENZODIAZEPINES (BDZ)

Pharmacokinetics

Absorption: **well absorbed from GI-tract**

Distribution: **BDZ having greater lipid solubility tend to enter the CNS more rapidly; plasma protein binding is 60-95 %**

Biotransformation: **by dealkylation, hydroxylation (phase 1) and conjugation (phase 2) reactions; *most clinically available BDZ are converted in the liver to one or more active metabolites***

Therapeutic uses:

- ***anxiety*** **(diazepam, lorazepam, nitrazepam)**
- ***epilepsy, muscle relaxation and seizures*** **(clonazepam, diazepam, lorazepam)**
- ***insomnia*** **(flurazepam, temazepam, triazolam)**
- ***anesthesia*** **(midazolam)**
- ***withdrawal*** **(diazepam, chlordiazepoxide)**

Adverse effects:

- ***"after-effects"*** **(drowsiness, memory loss, etc)**
- ***paradoxical excitement***
- ***potentiate action of alcohol***
- ***tolerance***
- ***dependence*** **(rebound anxiety and rebound insomnia)**

MISCELLANEOUS SEDATIVE-HYPNOTIC

Other BDZ agonists ***(zolpidem, zopiclon)*** ***- They bind to BDZ receptors and facilitate GABA-mediated inhibition. In usual sedative doses, they preserves stages 3, 4 and has only minor effects on REM sleep. Compared with the BDZ, they have relatively weak anxiolytic, anticonvulsant, and skeletal muscle relaxant properties. Zolpidem*** $T_{1/2}$***=2,5 hrs, zopiclon*** $T_{1/2}$***=1 hr. Zolpidem provides normal 8 hours- sleep; zopiclon is well suited for treatment of sleep onset insomnia***

Antihistamines ***(diphenhydramine, promethazine) - produce sedation, dryness of mucous membranes, and antiemetic activity***

β-blockers ***(propranolol) - can lessen the severity of many of the autonomic responses (tremors, sweating, tachycardia, etc) associated with anxiety***

Antidepressants ***(tricyclic antidepressants, SSRI) - used in the treatment of several anxiety disorders (general anxiety, obsessive-compulsive disorder, and several phobias)***

ANTIEPILEPTIC DRUGS

EPILEPSY is a heterogeneous symptom complex - a chronic disorder characterized by recurrent seizures. Seizures are finite episodes of brain dysfunction resulting from abnormal discharge of cerebral neurons.

CLASSIFICATION OF SEIZURE TYPES:

✓ **PARTIAL (simple, complex, secondarily generalized) - a localized onset of the attack can be ascertained**

✓ **GENERALIZED (tonic-clonic, absence, clonic, myoclonic) - there is no evidence of localized onset.**

DRUGS USED IN EPILEPSY:

☞ **partial and generalized tonic-clonic seizures - phenytoin, carbamazepine, valproate, and phenobarbital**

☞ **absence seizures - clonazepam, valproate, ethosuximide**

☞ **myoclonic seizures – valproate**

☞ **acute seizures – diazepam, lorazepam, phenytoin, phenobarbital, intravenous and inhaled anesthetics, chloral hydrate, myorelaxant etc**

ANTIEPILEPTIC DRUGS

Mechanism of action

blockage of Na^+-channels (carbamazepine, phenytoin, phenobarbital, valproate)

blockage of Ca^{2+}-channels (ethosuximide)

enhancement of GABA-action (phenobarbital, BDZ, tiagabine, vigabatrine)

Pharmacokinetics

Absorption: **absorption is usually good, with 80-100% of the dose reaching the circulation**

Distribution: **except for phenytoin, the BDZ, and valproic acid antiepileptic drugs are not highly bound to plasma proteins.**

Biotransformation: **the intrinsic ability of the liver to metabolize anticonvulsant drugs is generally low and, with the exception of phenytoin, independent of concentration. For most anticonvulsants, half-lives are greater than 12 hours. Phenobarbital, phenytoin, and carbamazepine are potent inducers of hepatic microsomal enzyme activity; valproate – an inhibitor.**

PHARMACOKINETICS OF ANTIEPILEPTIC DRUGS

	Bioavailabiity, %	Plasma protein binding, %	Elimination, hrs
Valproate sodium	70-100	85-95	8-10
Clona-zepam	100	50-80	24-40
Pheno-barbital	80-95	60	70-100
Diphenin (phenytoin)	95	90-93	15-20
Carbama-zepine	60-85	72-76	25-50
Etho-suximide	90-100	0	30-70

ADVERSE EFFECTS OF ANTIEPILEPTIC AGENTS

Phenytoin

- *nystagmus occurs early, diplopia and ataxia*
- *gingival hyperplasia and hirsutism*
- *coarsening of facial features*
- *mild peripheral neuropathy*

ADVERSE EFFECTS OF ANTIEPILEPTIC AGENTS

Carbamazepine

- *diplopia, ataxia, drowsiness*
- *aplastic anemia, agranulocytosis*

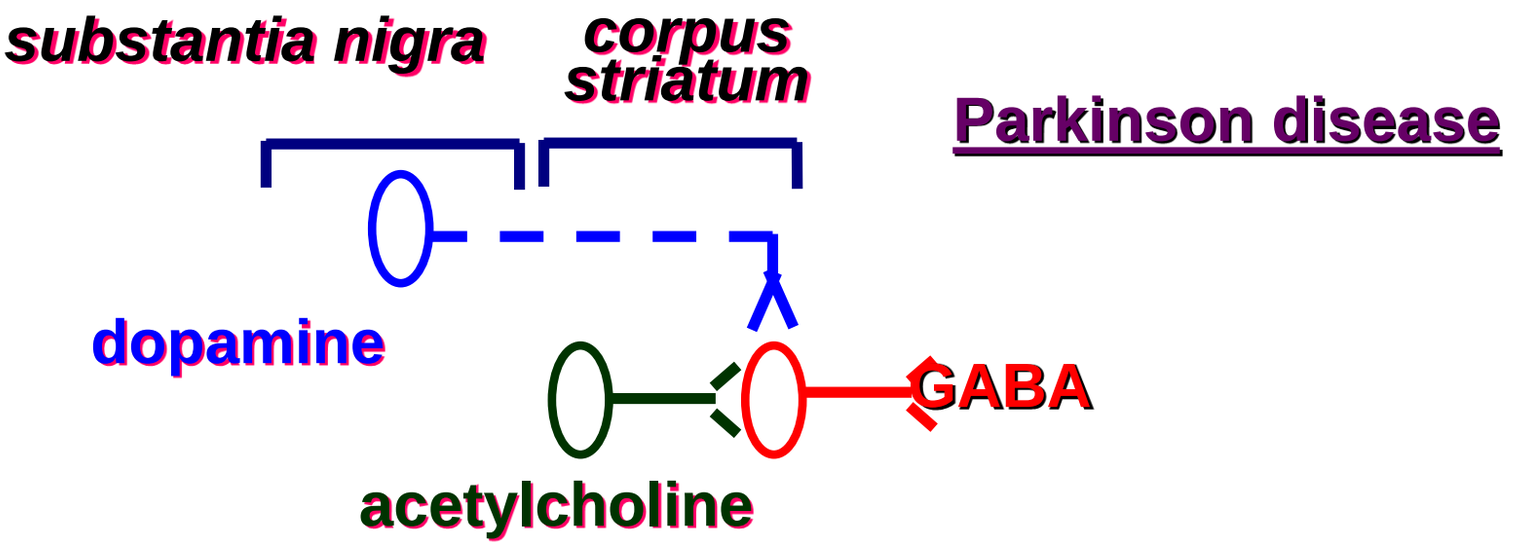
Ethosuximide

- *gastic distress (nausea, vomiting, abdominal pain*
- *fatigue, headache, dizziness, and euphoria*

Sodium valproate

- *abdominal pain and heartburn*
- *sedation, tremor*
- *weight gain, increased appetite, and hair loss*
- *hepatotoxicity*
- *spina bifida*

DRUGS FOR PARKINSON DISEASE TREATMENT



Improving dopamine transmission		Central M-cholinolytics
↑Dopamine synthesis	Dopamine agonists	
Levodopa, Nakom (Levodopa+Carbidopa)	Bromcryptin Midantan	Cyclodol Benztropine