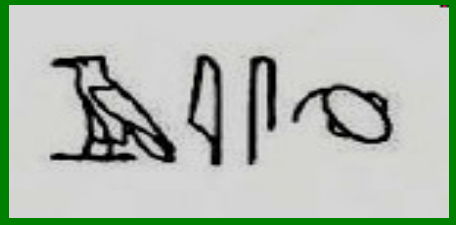
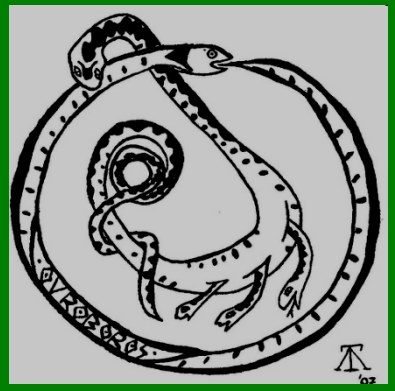
Image source: http://schools-wikipedia.org/2006/wp/b/Brain.htm



▶ Substances

that influence CNS and VNS activity



▶ Substances

with antihistaminic activity

Image source: http://farm4.static.flickr.com/3378/3224932185_01c27e0206.jpg

C.6.
C.7.
/S.II.

Romeo T. Cristina®

Mandatory recollections

CNS consists of:

- brain and
- spinal cord

It is involved in:

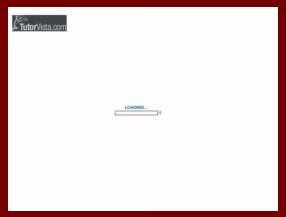
- controlling and coordinating movement,
- memory and
- consciousness.

CNS functional unit = neuron that consists of:

- neuron cell body
- dendrites and
- axon.

The nervous impulse in the neurons can be :

- blocked,
- converted from single pulse to repetitive pulse;
- amplified by the interaction with other neurons.



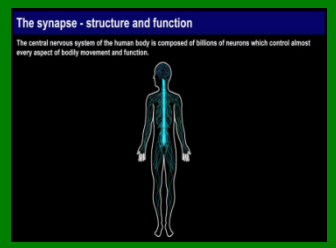
Synapse chimique ionotrope

The transmission of the nerve impulses from one neuron to another = through synapses.

There are two types of synapses:

- electrical = the impulse is directly transmitted from one neuron to another;
- chemical = uses chemical structures for the same purpose.
- Currently, there are known over 40 substances that have the role of neurotransmitters, and the most important are: acetylcholine, norepinephrine, dopamine, gamma-aminobutyric acid - GABA, etc.).

The main role of medication = specific



to change the levels of nerve transmission

Result:

▼

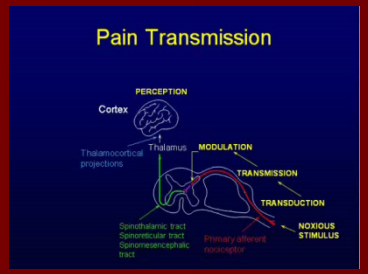
- blocking / pulse amplification or
- to act over different cell types and tissues (including CNS) using a more or less known mechanisms.

The main CNS barrier is

the blood-brain barrier, that is less permeable to large molecules or hydrosoluble substances.

Essential elements

about pain



Pain = is a unwanted sensiting mechanism with a perpetual nature and it's not a physical entity.

Pain: is caused by the cerebral cortex activity.

Pain's perception depends also on:

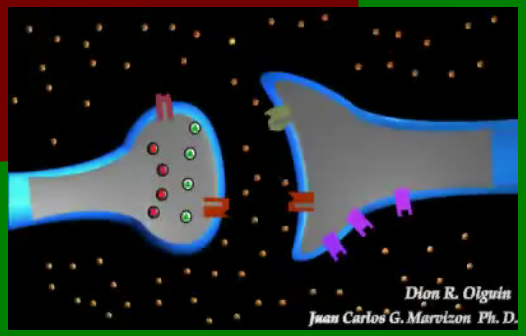
the existence of specific receptors for pain that are distributed through the body: visceral and somatic, skin, muscles, bones, joints and fascia etc.

The Phases of Nociceptive Pain

Anesthesia can be:

- Chemical (medicated) or
- Physical (sensitive nerve damage)
- Action: local or general
- The administration path can be:
- Injectable: i.v., s.c., i.m., i.p., intraosseous, intrarahidian, i.articular.
- percutaneous,
- oral
- rectal and
- respiratory.

The role of therapy:



- applying means and / or methods in order to:
- to restrict
- to eliminate pain,
- to determine muscle relaxation,
- to facilitate examination,
- to the application of investigations or surgical procedures,
- to support vital functions during an operatorion
- the painful stimulus = can cause tissue destruction

CNS

depressants

Principles of anesthesiology therapy

Pre-anesthesia

During this early stage the aim is to:

- Calm the animal,
- Reduce pain,
- Minimize the secondary reflections of VNS and
- to reduce the dose of general anesthetic.

The medication will be administered with:

- 15-45 min. before general anesthesia

The pre-anesthetic medication
-classes of drugs used in pre-anesthesia

Nr.	Class	Recommended substances
1	Tranquilizers - sedatives	Acepromazine Diazepam Droperidol Azaperone
2	Hypnotic - sedatives	Pentobarbital Chloralhydrate
3	Opioids	Morphine Meperidine
4	a_2 - adrenergic agonists	Xylazine Detomidine
5	Dissociative	Ketamine
6	Parasimpaticolitics	Atropine Glycopyrrolate

Anesthesia

- drugs used in the AG, more commonly administered by inhalation or injection, rarely p.o. or rectal.
- the medication's role is to temporarily suspend animal motility and sensitivity.

The main classes of drugs used in general anesthesia

Nr.	Class	Exemples
1	Hipnotics-sedatives	Very short action: Thiopental Short action: Pentobarbital
2	Dissociative	Ketamine
3	Opioids	Morphine, Oxymorphine, Fentanyl, Alfentanyl
4	Tranquilizers - sedatives	Benzodiazepine
5	Other classes	Guaifenesin, Propofol, Etomidate, Saffan

Post-anesthesia

Post-anesthetic recovery, immediately after administration, in case of inhalant path = quick recovery, the animal feels pain, which delays his healing.

Undesirable effects of the post-anesthetic period

Nr.	Localization	Effects
1	Circulatory system	arterial hypotension arterial hypertension cardiac arrhythmias
2	Respiratory system	Hypoxemia Hypoventilation
3	Organism	Pain Delays in awakening from anesthesia
4	CNS & PNS	Excitation phase Seizures, tetany
5	Thermoregulatory system	Hypothermia Hyperthermia
6	Digestive system (CNS)	Vomiturition & vomit

Assessment of body's response to anesthesia

Stage	Installation and evolution of the body's response
I.	a. stage of analgesia and amnesia b. period between analgesia and loss of consciousness c. voluntary response rejecting the volatile anesthetic d. disappearance of pain sensation and facial muscle control (human)
II.	a. stage of delirium, involuntary excitations / of uninhibited actions (urination, defecation) b. the period between loss of consciousness and the appearance of automatic respiration c. the narcotic sleep
III.	a. surgical stage b. the period between automatic and uncontrolled breathing c. the 4 plans of anesthesia: I: *easy surgical intervention, with short duration* II: *medium lasting intervention,* III: *long lasting intervention* IV: *very long lasting intervention*
IV.	a. The stage of respiratory paralysis or overdose b. The interval between the cardiac and respiratory arrest

Inhalant

anesthetic

From the point of view of the chemical structure, there is a very heterogeneous group of substances

Volatile anesthetics have simple structure = from one to four carbon atoms, often halogenated with F, Br or Cl ions.

The concentrations of inhaled anesthetic needed for the induction or maintenance of anesthesia have real practical importance, but do not offer precise indications on anesthetic potency.

This is due to the fact that concentrations in the CNS are not directly proportional with the inhaled concentration.

Due to the fact that the alveolar concentration at equilibrium is closer to the concentration from the brain,

The measurement unit of potency of an inhaled anesthetic = *Minimum Alveolar Concentration (MAC)*

This unit is defined as the lowest concentration of anesthetic present in the alveolar air at the time of equilibrium (between the inspired alveolar air, blood and brain).

MAC values are used to express the safety of the inhaled anesthetic.

Physiological considerations

Inhalant anesthetics = drugs that can cross the hematoencephalic barrier of the animals.

In animals, researches have shown that the barriers: blood - CSF and blood-brain have very similar permeability for the inhaled anesthetics and to other organic compounds given their similarity in terms of pharmacology.

The inhalant anesthetics action on the cortex will be: brutal and fast, instaled a few seconds after inhalation.

For a direct effect on its cell, a drug must enter the extracellular fluid of the CNS.

If it is orally administered, its molecules must:

- resist to the enzymatic and chemical attack of the stomach,
- to cross the intestinal wall,
- to pass the liver,
- to resist the enzymatic degradation from blood,
- to remain non-ionized in plasma,
- to remain unattached to plasma proteins and
- to pass the blood brain barrier.

The blood-brain barrier = almost impermeable to macromolecules but permeable to many drugs and metabolites: eg. procaine, caffeine, opiates, levodopamin, cyanides, etc.

The blood-CSF and blood-brain barrier,

They are so effective, that, for example, radiolabeled potassium administered i.v or i.p., will reach a steady state with potassium into the brain and CSF after 18-24 hours.

Blood

can be considered a reservoir for these agents, having the ability to take significant amounts of anesthetic and „delay'' its brutal penetration into the CNS.

An advantage of inhalation narcosis compared to injection techniques arises from the fact that:

duration and depth of anesthesia can be adjusted according to the requirements of the surgery, (installation speed is easily achievable by increasing the induction dose).

Installing narcosis = continuous, uniform, multistage process.

In the first stage,

- alveolar tension increases rapidly,
- is the result of narcotic penetration into the lung.

Consequently,

- equilibrium in blood capillaries and
- distribution toward tissues,
- venous blood, containing lower concentrations of anesthetic, will return to the lungs where it will be rebalancing with the alveolar air.

In practice,

- the solubility of the anesthetic in the blood will be the one that determines the speed of the equilibrium (tissue-blood or brain-blood solubility coefficients for most anesthetics are 1,0-1,5).
- Inhalent narcotics are substances with a maximum depressant activity on CNS.
- Alveolar growth rate will slow down, while tissue saturation continues.
- The amount of gas required to saturate tissue is highly variable from one anesthetic to another.

- After this, at 10-15 min. from administration it can almost be seen a voltage equalization of the gray matter, with the one from the alveolar air.
- Adipose tissue may be an exception, given the lipophilic character of the inhaled agents.
- For example, methoxyflurane is taken up by adipose tissue and then is slowly released by the end of anesthesia.
- Without doubt the agents with rapid kinetics (e.g. isoflurane) are very advantageous, but on *unskillful* hands, this feature can be dangerous = leads to respiratory paralysis accompanied by a specific cardiac manifestation.

Presentation of the main characteristics of inhalant anesthetics, those used in veterinary medicine

Category	Ether	Chloroform	Halothane	Methoxyflurane	Enflurane	Isoflurane
General structure	$C_2H_5OC_2H_5$ diethylether	$CHCl_3$ Methane chloride	$CF_3CHBrCl$ halogenated ethane	$CHCl_2CF_2OCH_3$ halogenated ether	$CHCl_2CF_2OCH_3$ halogenated ether	$CHCl_2CF_2OCH_3$ halogenated ether
Melting point	35	61	50	105	57	48,5
Concentration in the inspired air	5-15	1-3	1-3	1-3	1,5-4,0	1-2
Minimum alveolar concentration. (MAC%)	1,9-3,0	0,70	0,75-0,90	0,23 (dog) 0,16 (human)	1,6-2,2	1,2
Partition coefficient: Blood-Gas	12,1	?	2,3	12,0	1,9	1,3
Induction of narcosis	Slow	Fast	Fast	Slow	Very fast	Very fast
Recovery from anesthesia	Slow	Fast	Fast	Slow	Fast	Very fast
Partition coefficient Oil-Gas	65	aprox. 250	224	970	98	99

Pharmacology

stages of narcosis

Analyzing the stadial installation of narcosis, we notice that it is accompanied by skeletal muscle relaxation.

In terms of pharmacodynamics, the phases that can be identified are:

1. Apparent excitation & analgesia

(also known as the subcortical „rebellion")

- installed after narcotics arrive in CNS
- cerebral cortex = depressed
- will be eliminated its coordinating role on subcortical centers.

Are depressed: the inhibitor and pain centers

Remain free: excitatory centers, dominating the behavior of the animal.

Apparent excitation is well observed in: horses, carnassiers and large ruminants

In swine the excitation phase is short, and in birds is missing.

2. Superficial narcosis phase:

In this phase the narcotics depress:

- initially: encephalon
- then: spinal cord,
- finally: rachidian bulb.

Respiration and blood pressure = diminished.

At this stage you can perform small surgical operations.

3. Profound narcosis phase

- the narcotic reaches the maximum quota and *significant reflexes disappear.*
- first part of the profound narcosis is the one required, now being able to perform *laborious operations..*
- last part of narcosis needs to be avoided, because the risk of installation of the respiratory syncope exists

The inhalent anesthetics substances are classified into:

- gaseous
- volatile and
- non volatile.

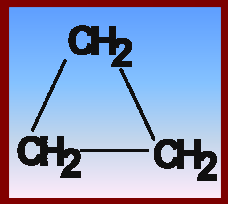
Gaseous narcotic

substances

Nitrogen protoxide (N_2O)
(nitrogen monoxide, nitrous oxide, illariant gas)

- liquefiable, produces rapid narcosis= appreciable anesthesia
- partition coefficient = 0.47 very low compared to: methoxyflurane and halothane.
- accordingly: alveolar and encephalic concentrations of protoxide will fluctuate more in induction phase and in recovery from narcosis.
- very safe anesthetic, non-irritable, without side effects.
- in some species, variable sensitivity, disadvantages:
  - low potency,
  - week muscular relaxation,
  - hypoxia diffusion and also the
  - so-called “second gas effect”.

Cyclopropane



The simplest saturated cyclic hydrocarbon – liquefiable gas, great anesthetic.

Disadvantage: inflammable and explosive= less used.

For administration in: closed systems, rarely half-closed.

Often associated with: oxygen and barbiturates.

Atropine administration consecutively cyclopropane narcosis is totally contraindicated = increases the incidence of cardiac dysrythmia.

Another disadvantage = increased capillary fragility (may induce haemorrhage at the incision site).

Therapeutic gases

Oxygen

- inhaled air represented 21% by oxygen ,
- Hypoxia = the decrease of inspired air at the level of pulmonary alveoli , blood and tissues.
- Hypoxemia = the decrease below the normal limits of the O_2 value at the level of hemoglobin, and
- Hyperoxia = increase over the normal limits of O_2 inspired quantity.

Causes:

► **Pre-pulmonary:**

- low concentration of atmospheric oxygen
- upper airway obstruction;

►**Pulmonary:**

- pulmonary edema;

►**Post-pulmonary:**

- inadequate transport of oxygen,
- hemoglobin reduction, anemia, hyperthermia, etc.
- the oxygen is used in: correction of hypoxemia, hypoxia and as a diluent in the use of inhaled anesthetics.
- in terrestrial atmosphere: 0,03%
- physiological role in : hypo or hypercapnia.

Volatile narcotic substances

Inhalation anesthetics with MV utilization

They are liquid, but at room temperatures **volatilizes easily.**

Advantages:

Gradation of narcosis, **being able to be stopped at any time.**

1st Group	**Frequently used:** • Halothane • Isoflurane **Rarely used:** • Enflurane • Methoxyflurane • Ether
2nd Group	**New:** • Desflurane • Sevoflurane
3rd Group	**Old:** • Chloroform • Cyclopropane • Fluroxene • Trichloroethylene

Other advantages:

- administering the exact needed dose,
- pulmonary ventilation can be controlled and arterial oxygenation improved.

In narcosis: preventing decompensated form of deep narcosis.

Accidents solved by:

- artificial respiration, cardio excitants, sympathomimetics.

Preparing for surgery = emptying the rectum and bladder.

- Function: of solubility, anesthetic = absorbed and distributed into the body.

Recovery from anesthesia is done by:

- elimination of anesthetic in the brain,
- ceasing anesthetic administration and
- oxygen administration.

Only a small part of anesthetic (0.004%) is metabolized and excreted in urine and faeces.

In addition to the effect of general anesthetic, inhalational agents produce side effects to the animal organism:

- reversible depression of CNS, unknown mechanism;
- bronchodilation, bronchospasm, decreases alveolar ventilation;
- myocardium depression (contractility, arterial pressure);
- reduces blood flow or hepatotoxicity (halothane);
- reduces blood flow= decreases renal filtering capacity;
- skeletal muscles = relaxation (due to CNS depression).

Chloroform (*Cloroformium pro narcosi*)

- clear liquid, colorless, volatile, sweet-smelling.
- high density, over 1.47.
- should not get into the mouth or stomach of omnivorous = triggers vomiting.
- infiltration and fatty degeneration of liver and heart.
- in *cats* and *ruminants* due to the rapid installation of hyperemia and hypersecretion = ab ingestis bronchopneumonia.
- in low concentrations (0.3-0.5%), an excellent anti-emetics.
- in organism decomposes, penetrates in lipids = meat is improper for consumption (5-7days).

- In *bovines* = gaseous indigestion, *sheep* and *goats* are more resistant.
- well taken by *horses,* but *prenarcosis* with chloral hydrate in association with barbiturates is required.
- *dogs* are most resistant ► *prenarcosis* with morphine - atropine and/or other neuroplegic-barbiturates it is recommended
- *pigs* supports well narcosis with chloroform, as well as birds.
- in euthanasia in dogs: i.c. or iv = 10ml / animal.

Ethyl ether

- clear, colorless liquid, with vapors heavier than air.
- inflammable, low density = 0.71-0.72, highly lipid-soluble.

Acts locally as chloroform: first effect = irritating, analgesic and local anesthetic.

In: small surgical interventions (in the absence of alternatives).

Ethyl chloride (Kelen)

- clear, colorless liquid, volatile, inflammable, characteristic odor,
- boils at 12-13°C; preserved in hermetically sealed ampoules.
- produces rapid and superficial anesthesia, of short duration.
- in high doses = toxic.
- is the most recommended substance used for local administration in bruises.

Halothane (Narcotane, Fluotane, Ftorotane)

- photosensitive, clear, colorless liquid , with high density;
- reduced conservability, being kept in brown bottles.
- has the greatest potential of narcotics.
- not irritate for mucosa.
- does not transmit odor to meat.
- associated with: nitrous protoxide and oxygen.
- before narcosis neuroplegia needs to be assured!
- great narcotic in: swine, chickens and dogs.

Non-volatile narcotics

Advantages

- Acts faster than inhalations when is administered i.v.
- produce very weak excitation, so severe contention isn't necessary .
- fast eliminated, easy to administrate, in big animals.
- allow the examination and the approach of respiratory tract;
- can be used in capturing animals;
- profitable, does not require special equipment, difficult to transport

Disadvantages

- level and depth of anesthesia is difficult to control;
- metabolization time is longer
- overdosing or underdosing risks are higher.

With volatile narcotics= superficial narcosis, further ► non-volatile narcotics = acts longer.

acts gradually in comparison to hypnotics, depending on dose.

In small doses= hypnotic and in high doses= narcotic.

Chloralhydrate

- colorless crystals, melon odor, slightly soluble in water.
- irritant for tissues, not administered i.m., s.c., just strictly i.v.
- per os and *per rectum* administered up to 4% in mucilage.
- best deep narcosis = chloralhydrate + magnesium sulfate, i.v. (solvents: Distilled water, sodium citrate, 1% and glucose solution 25%)
- dose: 0.1g/kg.bw, effect = 20-120 min.
- instant awakening with: cocaine 0.3g/20ml distilled water in horse.
- well supported by pigs where apparent excitation doesn't occur.
- injected i.p.: 0.25g/kgbw, sol.5%, narcosis lasts 2 h.
- well supported by dogs, the apparent excitation phase is intense.
- utilized in strychnine intoxication: 0.3g/kg bw, sol. of 10%.
- also as: hypnotic, sedative, antispasmotic, anticonvulsant and vasodilatator in encephalitis, colic, meningitis, distemper.

Chloralose

- condensation product of chloralhydrate with glucose.
- the least toxic and irritating mixture.
- white crystalline powder, soluble only in hot water.
- in small ruminants = concentration 1% i.v., and
- In dog = appreciable narcosis, without apparent excitation, with reflex persistence, most often in concentrations of 0,5-1% = increaces the reflex activity!

Ethyl alcohol

- induction of apparent excitation with depression of pain centers.
- in moderate dose = apparent excitation = superficial narcosis

Urethane

- white powder, odorless, very soluble in water,
- good lasting narcotic in laboratory animals.
- in dog the effect occurs after 1-1,5 h and lasts 24-36 h;
- hypnotic: 5–10%,
- narcotic: 10–20%.

Ketalar (ketamine)

- non-volatile narcotic, profound analgesia and superficial sleep.
- administered i.v. or i.m.
- tremors, tonic spasms and seizures after administration = fewer in comparison to other anesthetics.
- stimulate heart activity but
- does not produce respiratory depression (hypoxia).
- determine: sialorrhoea and increased secretion of tracheobronchial glands, being indicated premedication with atropine.
- considered non-volatile narcotic because in practice it is used hydrochloride salt = slightly soluble in water.
- produces: profound analgesia and superficial sleep.
- i.v. = fast effect, with short–term up to 15 min.
- It is preferred in emergencies, as a short-term narcotic.

Epontol (Sombrevin)

- phenoxyacetic amide.
- used i.v. = superficial general anesthesia accompanied by transient hypotension, hypopnea, hypoventilation.
- recovery from narcosis = rapid in goats, longer in dogs.
- Used in 0.5% i.v. solution.

Hypnotics

- Cannot be net differentiated from non-volatile narcotic, are called so because it depresses the CNS = installs *the physiologic sleep type*
- Action: less intense;
- Favorises: nutrient exchanges in nervous tissue = inhibition of protection, but regulates also chemical shifts from the body.
- Hypnotics are slowly eliminated, anticonvulsant activity.
- The long effect, in therapeutic doses, does not produce unapparent excitation or cardio-respiratory disorders.
- in small dose= sedative activity (reduce spontaneous motor activity and response to external stimuli).
- high dosage= sleep
- exaggerated doses= acute intoxications, profound narcosis, coma, exitus.

Barbituric acid derivatives

- poorly soluble in water, slowly absorbed;
- delayed installation of the pharmacodynamic effect;
- cortex and subcortical depressor, depending on dose has a soothing, hypnotic or narcotic role.
- anticonvulsivants, being antagonist to the CNS excitation ;
- antispasmodics, towards smooth muscle of: blood vessels, intestines, uterus;
- antidiuretics, acting centrally, indirectly, by decreasing blood flow velocity.

Duration of action of the classic barbiturates

Barbituric	Duration of action
Phenobarbital	Short
Barbital	
Amobarbital	Medium
Pentobarbital	Long
Secobarbital	
Thiopental	Long
Thialbarbital	

Side effects

are different, depending on the site of action:

- respiratory system= slightly depression, in cat = accentuated;
- circulatory system= tachycardia;
- gastro-intestinal = reduces motility;
- renal and hepatic = significant changes are not not produced.
- uterus = just at the time of parturition = decreased motility;
- in fetus = complete inhibition of the contraction of the respiratory muscles without maternal hypoxia phenomena;
- skeletal muscles relaxes without being anesthetized.

Veronal (Barbital)

- diethylbarbituric acid under the form of colorless crystals de cristale incolore or powder, odorless, bitter taste, soluble in water.
- as: sedative and hypnotic in: epilepsy, eclampsia, nervous form of distemper: 0.05-0.30g = long lasting sleep.

Commercials: *Veropirin* (contains aminophenazone, having analgesic, antipyretic, anti-migraine, poor psychomotor).

Sodium barbital (Medinal)

- officinal, stored in Separanda, administered iv.

Phenobarbital (Luminal)

- colorless crystals or crystalline powder, white, with bitter taste, soluble in alcohol. Stored in *Separanda*, it is officinal.

Amobarbital (Amytal)

- used sodium salt, very hygroscopic, odorless, bitter taste, slightly soluble in water. Stored is Separanda.
- 0,1 g. tablets, action: sedative, hypnotic, with a duration of action: 4-6 hours.

Hexobarbital (Hexenal)

- used sodium salt, crystalline powder, white, bitter taste.
- stored in *Separanda*.
- is used most often as 'Chemical restraint'.

Pentothal (Thiopental, Trapanal, Nesdonal)

- general anesthetic qualities, the apparent excitation phase is minimal, moderate analgesia and poor myorelaxation.
- very short post-narcotic sleep, in horses= missing.

Pernocton (Sonbuttal)

- it is used both basic substance as well as sodium salt.
- administered i.v., sol. 10%, maximum 1 ml/min.
- superficial narcosis = excellent 1-3 h, especially in dogs.
- if morphine is administered, apparent excitation is missing.

Cyclobarbital (Phanodorm)

- white crystals or powder, bitter taste and odorless.
- great solubility in water.

Eunarcon (Pronarcon)

- sodium salt , in 10% solution, i.v., slowly.
- doesn't give apparent excitation, narcosis = 15 min.
- dose: 0,01-0,02 g/kgc in pigs and 0,03 g/kgc in dog.

Cyclobarbital (Fanadorm)

- Crystals, white powder, bitter taste, odorless, high solubility in water. Is: officinal, short-term hypnotic. In the 0.2 g /tablet.

Brevinarcon (Inactin, Venobarbital)

- sodium salt, produces short-term general anesthesia.
- i.v. the effect appears after 15-20 sec. and lasts: 15-20 min.
- Dose: 0.010-0.020 g/kgc at larg e animals and of: 0.020-0.040 in dog.

Tialbarbital (Intranarcon, Chemital)

- 10% solutions with i.v. administration.
- General anesthesia: in 10-15 min., without apparent excitation.
- Dose: 0.02-0,04 g/kgc., in cat: 0,01 g/kgc.
- at LA is associated with *Anavenol* = general anesthesia acting on spinal cord.

Baytinal

- Very efficient sodium salt in dogs: 0,05 g/kgc.

Propofol

- administered i.v. continuous or in bolus,
- Insoluble in water, commercialized under the form of emulsion.

Etomidate

- administered i.v. = rapid induce anesthesia.

Guaifenesine

- potentiates barbitures.
- muscle relaxation= blocking nerve impulse transmission.

Alehezine

- steroid,
- induces rapidly short-term anesthesia without complications.

Phencyclidine

-corneal and pupillary reflexes does not disappear, induces stage 1 and 2 of anesthesia, but not stage 3.

- depending on the species, it produces depression or stimulation of the CNS.

Tiletamine

- similar to Ketamine, but the anesthesia = 3 times longer.

Urethane

- lately used only in laboratory animals,
- long-term anesthesia. Produces liver damage.

Propanidine

- rarely used in animals, more frequently in humans.
- muscle spasms and uncoordinated movements,
- recovery from anesthesia = rapidly (9 min.).

Magnesium

derivatives

Acts hypnotic or narcotic due to the contained cations.

- the salt administered p.o. is hardly absorbed, therefore the depressant effects are not present.

- when using therapeutic doses, via other pathways, depresses : encephalon and spinal cord = direct or indirect inhibitor of the skeletal muscle ► stopping the contraction stimulus to the motor plates.

- ions increase the sensitivity of the heart, the action of acetylcholine, causing hypotension.

Magnesium sulfate

- action: hypnotic or sedative;

- in rabbits 5ml 25% = profound narcosis, without excitation, appears: after 30-35 min., lasts: 2-20 h.

- recommended in colic = saturated solutions 64-65%, i.v.

- in euthanasia, in dogs and cats = 5-15g saturated solution.

Analgesic

substances

Relieve pain by:

- depressing pain centers,
- thalamo-subcortical pathway, responsible for transmission of pain and other centers.
- other activities: antipyretic, antiphlogistic, hypotensive, bechic

Opium (Laudanum, Meconium)

- is air dried latex originated from immature capsules of *Papaver somniferum*.
- the composition of opium contains: alkaloids, mucilaginous substances, resins and other indifferent compounds.

The active constituents of opium are 24 alkaloids, of which only morphine and codeine are used in medicine.

There are also endogenous opioid substances that have the role to temporarily block the sensation of pain or stress:

- ***β endorphins***
- ***enkephalins***
- ***dynorphins***

Alkaloids derive from: *phenanthrene and isoquinoline.*

The phenanthrene group includes:

morphine, dionine, thebaine, heroin, apomorphine.

The isoquinoline group includes:

papaverine , narcotine, narceine.

In general, the phenanthrene group acts: on the CNS and the others on: smooth muscles, as antispasmodic or on the respiratory and cough centers , as depressors.

Powdered opium contains 11% morphine, stored in Venena

It is used in the form of pills and bowls.

Opium tincture containing 1% morphine and is recommended as a beverage, with 2-3 times greater doses than the opium.

Opium contains between 10 and 10,5% morphine.

In animals = changing behavior (depression or excitation), vomiting in some species, and in other inhibits this sensation (e.g. in pig and bird)

Hexapon

- injectable aqueous solution, 1-2% concentration, in 1 ml. ampoules.
- is: powerful analgesic and euphoric.

Opium concentrate (Pantopon, Omnopon)

- contains 50% morphine and is not officinal.

Morphine hydrochloride

- phenanthrene, needle crystals, silky, light yellowish-white powder, odorless, bitter taste.

Action - *depresses* the nervous centers on one side and *excites* the other nervous centers on the other side.

Anticholinesterase = as *indirectly parasympathomimetic.*

Produces: vomiting and defecation that can be countered with a parasympatholytic (e.g. Atropine).

Acts as a *sympathomimetic* substance, because it is an *adrenalin-secretory substance.*

Main effects:

- inhibites the cough center,
- body temperature changes depending on species and dose:
- hypothermia: *rabbit, dog, monkey;*
- hyperthermia: *cat, goat, cow and horse;*
- increased doses = hypothermia *in rabbits;*
- low doses = hyperthermia *in pig, rats and mice.*
- mydriasis: *monkeys, cat, sheep and horse.*
- myosis: *dog, rat, rabbit and human..*
- respiratory center: initially stimulated, and then, due to CNS depression, the respiratory center is depressed.
- causes increased heart rate,
- a slight increase in urine output
- blocks gastrointestinal motility = constipation
- stimulates: growth hormone and prolactin release.

Long-term administrations = *morphinomania* due to the formation into the organism of an *antagonist factor* towards an alkaloid, a new dose is therefore more necessary to produce the same effect.

Morphinan analgesia occurs quickly and lasts for hours, the alkaloid being *neutralized* by the liver and *excreted* by the kidneys.

- in cat = dramatic excitation, rabiforme crises;
- same effect: in pigs and ruminants.

Morphine hydrochloride = in the adjuvant treatment of non-spastic colic..

In dog is used in the production of narcosis.

Morphine - *antidote* for intoxications by plants containing atropine = anticholinesterase parasympathomimetic effect.

Hydromorphone Hydrochloride

- white powder, crystalline, odorless, photo-sensible, water soluble, stored at *Venena*.
- as analgesic, but is more euphoric than morphine.

Codeine hydrochloride

- needle crystal, white powder, bitter taste, soluble in water in a ratio 1:25.

Ethylmorphine hydrochloride

- white, crystallized powder, bitter taste;
- officinal in Separanda. It is the ethyl ether of the morphine.

Used also in ophthalmology, iritis, conjunctivitis, blepharitis, in eye drops 2-5%.

Heroine

- *semisynthetic crystalline powder, white, odorless, bitter taste, slightly soluble in water and alcohol.*
- prompt analgesic activity,
- not as intense as in the case of morphine.
- Heroinomania is worse than morphinomania!

Apomorphine

- morphine without a water molecule.
- does not possess analgesic activity but has expectorant activity in small doses and emetic in large doses.

New synthetic products

Mialgin (Lidol, Pethidine, Dolantin, Dencerol, Meperidine)

- synthetic substituent of morphine, most used: hydrochloride.
- white powder with bitter taste.

Sintalgon (Dolofin, Polaridon, Amidone, Fenadon)

- crystalline, white, bitter, soluble in water;
- analgesic activity similar to morphine, more intense, but much less depressant on respiratory system.
- moderate antispasmodic action;
- induces excito-parasimpatico-central effect, therefore is associated with parasimpaticolitice.

Fentanyl (Sublimaze)

- white powder, soluble in water.
- much powerful but much shorter analgesic activity than the morphine's.
- in NLA (neuroleptanalgesia) is associated with Droperidol.

Dosage in dog: 0,1 mg i.v. and 0,5 i.m.

Recent studies on this group brought to light other related compounds , with similar effects, but with amplified analgesic activity, with activitate analgezică amplificată, with particular use in NLA.

These are:

- Alfentanyl,
- Carfentanyl,
- Remifentanyl,
- Sufentanyl.

Pentazocine (Fortral, Talwin)

- energical analgesic , two times less intense than morphine,
- doesn't cause addiction, has also a central sedative role.

Isoquinoline

derivatives

Narcotine (Noscapine)

- energetic antitussive effect and stimulant on respiratory centers.
- *antagonist to morphine.*
- duration of action: 4 hours. In dogs, the dose is 2-10 mg/animal

The preparation *Tusan* can be under the form of tablets 0,01–0,05 g, being bechic, weak vasodilator. Stimulates respiration.

Papaverine

- the most important derivative of opium.
- the antispasmodic effect increases over the contracted muscles of vessels, including the coronary arteries
- p.o. = slightly anesthetic activity, reduced central analgesia. Is marketed under the form of injectable solutions in ampoules of 1ml 4% and tablets of 0,1-0,2g.
- acts: antispasmodic directly on smooth muscles of all organs , (seems like the pre-stomachs are not relaxed).
- potentiate morphine.

Antagonist

opioid drugs

The antagonists cancel the effects of opioid drugs:

- Naloxone
- Diprenorphine
- Levallorfan
- Naltrexone and
- Nalmefene.

Role: occupy and / or removes the analgesic substances from the receptors = their effect diminishes to extinction.

Antipyretic

substances

Causes:

lowering the temperature : depression of the thermoregulation center from the brain and then of the vasomotor center = peripheral vasodilatation, heat radiation (but not in normothermia).

Fever:

Mechanism for the body's protection, that's why antipyretics are administered only in exaggerated hyperthermia, harmful to health.

Natural antipyretics = analgesics = depresses pain centers;

also= stimulates *diaphoresis.*

in addition, salicylic acid derivatives, = etiotrope;

Another derivatives (e.g. quinine) = intracellular oxidation inhibitors.

Pyrazolone derivates

Weaker antithermic agents but with important analgesic qualities.

Phenazone (Antipyrin, Analgesin)

- crystalline, white powder, colorless blades, bitter taste, soluble in water, alcohol, chloroform. It is officinal.
- causes incompatibilities, prescribed alone!
- on general pathway = antipyretic effect for: 2-4h.
- rapid analgesic effect after a few minutes.
- antirheumatic and
- antispasmodic.

In large animals: *per os*, 15-30g, in medium sized animals 2-5g, and in dog and cat: 0,2-2g.

Salipyrin

- phenazone salicylate salt. It is officinal.
- under the form of crystalline powder, white, bitter, soluble in water.

Aminophenazone (Pyramidon, Amidopyrine)

- is a dimethylaminopyrine,
- colorless crystals, white crystalline powder, odorless, bitter taste.
- excellent antirheumatic, better than salicylic acid;
- does not produce gastrointestinal disturbances.

Noraminophenazone (Algocalmin, Novalgin, Metamizol)

- white-yellowish powder, bitter, soluble in boiled and cooled water.
- great analgesic, twice more intensely than aminophenazone;
- spasmolytic, antipyretic and antiimmflamatory.

Isopyrine (Reumazol, Butalgin)

- crystalline powder, white-yellowish, slightly bitter. Is officinal.

Derivates of salicylic acid

Are: *antipyretic, analgesic and antirheumatic,*

This is due to the fact that they have an antiphlogistic activity produced by the corticosteroids secreted by the adrenal gland.

Under the control of ACTH = elaborated by the anterior pituitary.

To this is added the action of inhibition of hyaluronidase and the proteolytic processes to diminish the histamine release.

Salicylic acid

- intensely irritating to the mucosa, producing nozee and vomiting.
- needle like crystal, odorless, sweet-sour taste, soluble in water
- externally: antipruritic, keratolytic, even caustic.
- and as: antiseptic and fungicide în 5-20% alcohol solutions (in dermatomycosis) and 2-5% powdery mixtures .

Lassari paste: 2g salicylic acid, 25g zinc oxide and excipient,

- used in scleroderma and bleime.

Sodium salicylate

- effect: antithermic, analgesic, antirheumatic, only after the release of salicylic acid.
- antirheumatic: i.v. sol. 20%.
- used as: sclerosant of varicose veins.

Methyl salicylate

- methylic ether of salicylic acid
- colorless liquid, characteristic aromatic odor.
- in: tendonitis, myalgias and in articular rheumatism in horses.

Salicylamide

- needle like crystals, colorless or crystalline powder, white, pinkish-yellowish, odorless, bitter taste, soluble in water.

Acetylsalicylic acid (Aspro, Colfarit)

- Colorless crystals, acicular, fine powder. Is officinal.
- sour taste, odorless, hydrolyze in moist air, soluble in water.
- Incompatible with: Urotropin, alkalis, antipyrine, piramidon.
- 0,5g tablets, effervescent tablets, buffered with sodium citrate.
- Are not discomposed in the stomach but in the intestine, from which it is absorbed as such or in the form of other salicylates.
- very strong antipyretic action = peripheral vasodilatation, followed by profuse sweating.
- Intens analgesic and week antirheumatic.
- The cat is sensitive to acetylsalicylic acid!

Aniline derivatives

Aniline is antipyretic and analgesic, it also has a toxic potential!

Antifebrin (Acetanilide)

- white, glossy and crystalline blades, white powder;
- odorless, bitter, slightly burner.
- incompatible with: antipyrin, chloralhydrate, resorcinol, thymol, piperazine salts.
- the most powerful antipyretic, used more frequently in large animals.

Phenacetin

- crystalline, white, bitter, solubilizează foarte greu în apă, oficinală.
- activity: antipyretic, analgesic, anti-inflammatory, week psychomotor, antimigraine.

Paracetamol
(Panadol, Acetophen, Acetaminophen)

- hydroxy-acetanilide,
- metabolite of phenacetin and antifebrin.
- crystalline, white, odorless, bitter powder, less soluble in water.
- tablets= 0,3-0,5g and suppositories = 125-250 mg
- low toxicity;
- but= energetic antipyretic.

Quinoline derivatives

Atofal (Cincophen)

- excelent antipyretic, cholagogue, anti-rheumatic in dog.

Quinine

one of the alkaloids from *Chinae cortex.*

- human: antimalarial, etiotrop, antipyretic, analgesic symptomatic
- active analgesic in case of neuralgia.
- high doses: stimulates the pregnant uterus = spasms (h).

Acalor (Chinoseptol, Antigermin, Germicid)

- mixture: oxyquinidine sulfate + aminophenazone.
- under the form of tablets: 0,5g and suppositories 0,2g.
- great antipyretic and analgesic, şi analgezic, often associated with caffeine,
- into the body, the tablets hydrolyzes in components.

Local anesthetic

substances

Substances that interact with the nervous endings and temporary suspend their function =local insensitivity.

Occurs: paralysis at the site of application, at the PNS level.

Drugs that form this group= elective for fibers and sensitive endings.

Local anesthetics should be:

- nonirritant,
- nontoxic,
- with an more reduced activity compared to cocaine standard.

Mechanism of action:

- decreased permeability of the nervous fibers towards water and ions,
- decreasing concentrations of calcium ions,
- changing ratio: elimination CO_2 / consumption O_2
- histological modifications of: myelin sheath and axons.

first local anesthetic = cocaine, in 1905 = procaine.
present = < 50 drugs with a local anesthetic effect.

depending on the nerve or the innervated area they can produce:

- blockage of the autonomic nervous system.
- anesthesia and / or skeletal muscle paralysis.

Chemical= two groups of local anesthetics:

a. amino esters:
- procaine, chlorprocaine and tetracaine;

b. amino amides:
- lidocaine, mepivacaine, bupivacaine, and ropivacaine.
- in practice: alleviating interventions and treating disorders,
- often A.L. replaces narcosis, complicated and dangerous.

In practice: used, in particular, neutral or acid salts (hydrochloride): in moderately alkaline medium decomposes = soluble anesthetic base (differentiated by suitable salts that are soluble in water) = drugs pass easily from the aqueous environment into lipoids from the peripheral nerves.

In acidic media (e.g. cases of inflammatory foci) the drug does not hydrolyze and therefore the liposoluble anesthetic base is not released = null or weak effect.

In alkaline media the local anesthetic effect = low: is formed voluminous particles of substances incapable to penetrate the nerve sheath, sometimes the base itself decomposes.

Use of local anesthetics

Anesthetic	Skin or mucosa	Local infiltrations	Peripheral nerves	Intravenous	Epidural	Spinal
Procaine	No	Yes	Yes	No	No	Yes
Chlorprocaine	No	Yes	Yes	No	Yes	No
Tetracaine	Yes	No	No	No	No	Yes
Lidocaine	Yes	Yes	Yes	Yes	Yes	Yes
Mepivacaine	No	Yes	Yes	No	Yes	No
Bupivacaine	No	Yes	Yes	Yes	Yes	Yes
Etidocaine	No	Yes	Yes	No	Yes	No
Prilocaine	No	Yes	Yes	Yes	Yes	No
Ropivacaine	No	Yes	Yes	No	Yes	Yes

Essentially the local anesthesia is of several types:

- of surface = of mucosa.
- of infiltration = through an anatomical layer and
- regional = on the nerve path.

There are many forms

- epidural and
- subarachnoid

Cocaine

- alkaloid, originated from the leaves of plants belonging to the *Eritroxilaceae* family.
- considered the best local anesthetic of surface (mucosa, muscle, skin)
- on the nerves path it determines insensibility of the anatomic region innervated buy them.
- recommended in: ophthalmology, O.R.L., local anesthetic eye drops (1-2%);
- local vasoconstrictor.
- antipruritic activity in eczema (in ointments 2-3%).
- relieves the pain produced by burns.

- administered in the conjunctival sac it produces active mydriasis;
- has parasimpatico-mimetic antiamino oxidase activity;
- the action lasts 10 minutes.
- considered the best local anesthetic of surface (mucous, muscle, skin).
- from the injection site the substance is absorbed, decomposes partly in the liver, the rest will result in moderate doses of excitement, tachypnea, mydriasis, seizures, and finally even blocking the respiratory center and death by asphyxiation.

Equines = more sensible than large ruminants (reverse as in morphine).

In human, excitement is accompanied by euphoria, subjective sensations of great amplitude. Produces *cocainomania.*

Cocaine's succedaneous does not produce mania!

- the succedaneous substances are frequently used for the diagnosis of lameness,
- in this situation is not associated with adrenaline that could prolong unwanted anesthetic activity.

Anestesine
(Benzocaine, Norcaine, Ethophorm)

- crystalline powder, white or colorless crystals, odorless.
- weak bitter taste, on the tongue it produces transient anesthesia.
- very effective in antipruritic local applications ,
- has the form of powder, suppositories or 3-10% ointments.

Procaine(Novocaine)

- white powder, crystalline, odorless, bitter taste
- is considered the best local anesthetic of all types of anesthetic.

Denervin

- contains: phenol, glycerin, lasting analgesic.
- administration: on the nerve path by integrating of myelin.

Gerovital H_3

- contains: procaine hydrochloride, benzoic acid, potassium metasulfite, sodium phosphate.

Panthocaine (Tetracaine, Dicaine)

- local anesthetic stronger than procaine, but toxic.
- always associated with adrenaline.
- in the form of a 0.5-1% solution.

Tutocaine

- effective local anesthetic for mucous;
- associated with adrenaline;
- in the form of 1-2% solutions.

Maxicaine (Parethoxycaine)

- related to procaine;
- advantages: effective action even on mucous membranes,
- it is not antagonist to sulphonamides.
- does not produce local vasodilatation!

Stovaine (Amylocaine)

- local anesthesia similar to cocaine;
- lower toxicity.

Xiline (Lindocaine, Xilocaine)

- not i.v.! = 5-6 times higher toxicity than procaine.
- ampoules: 1-2-4%, 2-10ml, spray 10%: mucosal and skin anesthesia

Carbocaine (Mepivacaine)

- similar to Xilin, being the derivative of acetanilide.
-the hydrochloride salt is used.
- has stronger activity than Xilin.
- the only local anesthetic that causes vasoconstriction!
- in the form of 0,5-1% solutions.

Percaine (Sovcaine, Dibucaine, Supercaine)

- it is considered the most active local anesthetic
-20 times stronger than procaine.
- it's even more toxic than cocaine, toxicity: 4mg/kgc.
- long-term anesthesia
- It's not recommended when diagnosting limps.

Tranquilizers (neuroleptics)

History

In 1950 was introduced the first veterinary tranquilizers (phenothiazine derivatives).

Tranquilizers are called neuroleptics because their main action is calming CNS.

Phenothiazine derivatives

Main action = blocking dopamine (neurotransmitters);

Effect: sedation through CNS depression and through the connection with the cerebral cortex

- decreases spontaneously the motor activity of the animal;

High dose = animals remain in fixed positions for long periods.

Chlorpromazine

blocks central receptors of catecholamines

Promazine

widely used in all species

exception: farm (rent) animals !

Acepromazine

- widely used.
- more potent effect than chlorpromazine and promazine

Prochlorpremazine

- great antiemetic effect,
- but the sedative effect is quite low.

Trimeprazine

- in addition to the sedative effects has
- also antipruritic, anticonvulsant and antihistaminic effect.

α-2 adrenergic antagonists

Action: sedative, analgesic, relaxant over the muscle.,
Discovered in 1981 stimulates the central α2 adrenergic receptors.

Xylazine

- potent antagonistic substance.

Detomidine

- sedative and analgesic more potent than Xylazine,
- **causes:** decreased cardiac contractility as Xylazine..

Medetomidine

- the strongest substance in this group.
- produces: sedation, muscle relaxation and analgesia.

Yohimbine

- **induces:** sedation and analgesia,
- **used:** as an antagonist in combined anesthesia with Xylazine.

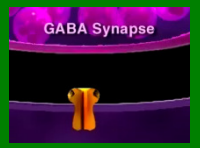
Tolazoline

- Xylazine antagonist,
- but with a tranquilizing effect more potent than the yohimbine

Benzodiazepine derivatives

So far, it is not known the intimate mechanism of action.

Increasing the action of neurotransmitter: gamma - amino butyric acid (GABA) = hypnosis, sedation, anxiolytic effect, anticonvulsant and muscle relaxation.



Diazepam

- insoluble in water produces behavioral disinhibition ("taming"), changing behavior,
- muscle relaxant effect, anticonvulsant, anxiolytic, hypnotic, somnolence, and ataxia.

Clonazepam

- similar to diazepam,
- has also an anticonvulsant action but lower than phenobarbital.
- tolerance within a week (as in diazepam)!

Midazolam

- soluble in water. Similar effects to those of diazepam.

Flumazenil

- a benzodiazepine competitive antagonist.

Butyrophenone derivatives

- Similar neuroleptics to phenothiazines, but
- the predominant effect is to block the dopaminic receptor

Droperidol

- when used on dogs it is 400 times more activ than chlorpromazine.
- its a strong antiemetic.
- duration of action= approximately 2 hours.
- drug of first choice in traumatic shock.
- decreases also blood pressure.

Azaperone

- great neuroleptic for swine.
- in: reducing stress from: transport, weaning, establishing the lots, surgery, etc.

Anticonvulsants

Rapid depolarization of neuronal membrane =

- alters the function of the potassium-calcium pump,
- changes the permeability of the cell membrane,
- changes the concentration of the inhibitory or excitatory neuronal substance
- changes cellular metabolism.

The convulsive crisis can be:

- primary (genetic) or secondary (acquired).
- general or local (focalized)

The origin of these seizures is in the cerebral cortex.

Epilepsy and other disorders with similar symptoms are due to:

- lesions or CNS tumors, head trauma,
- exogenous or endogenous toxics,
- electrolyte imbalance, hypoglycemia, renal failure, hepatic disease..

The convulsive crisis are triggered by

4 mechanisms:

1. Alteration of the functional neuronal membrane = excessive depolarization;
2. Decreased inhibitory neurotransmitters (GABA);
3. Increased excitatory neurotransmitters (glutamate);
4. Alteration of extracellular concentrations of potassium and calcium;

Epilepsy can be controlled, but cannot be treated.

In dogs epilepsy can be controlled in 60-70% of cases, with a lifetime treatment.

Phenobarbital

- depresses the motor center of the cerebral cortex,
- one of the most potent anticonvulsant drugs.

Pentobarbital

- administered i.v.,
- the most effective drug used in dogs with epilepsy when other drugs fail to give the expected results.
- pentobarbital needs to be administered with caution.

Primidone

- similar to phenobarbital, higher hepatotoxicity.

Phenytoin

- depresses the motor center of the cerebral cortex,
- but does not affect the sensory area of the cortex.

CNS excitants

Analeptics

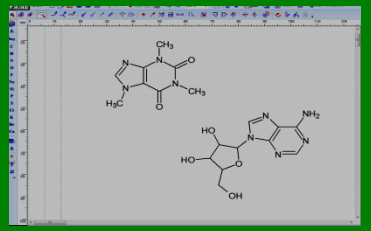
A large number of drugs cause CNS stimulation.

- some can be used for the therapeutic effect,
- others are considered toxic (e.g. nicotine, strychnine).

They excite the neuraxis, but after a period of time depression is installed.

Some excitations act on:

- encephalon: caffeine, pentetrazole,
- bulb: camphor, lobelline,
- marrow: strychnine.



In high doses all CNS stimulants are toxic.

They cause: convulsions, exhaustion, paralysis deadly.

Therapeutic doses = reestablish the debilitated functions of the nervous centers with great importance for the organism, this is the reason why they are cardiovascular and respiratory analeptics.

In addition they have a cardio excitatory function.

Methylxanthine derivatives

These derivatives include:

- caffein - 1% - in coffee beans,
- theophylline - 3% - in tea leaves and
- theobromine.

Effect:

- CNS stimulant,
- coronary vasodilator and
- diuretic.

most important for the veterinary medicine: *caffeine*

Caffeine (Guaranine, Theine)

- the alkaloid is in:
- coffee beans *(Coffea arabica),*
- tea leaves (*Thea sinensis),*
- cola seeds (*Cola nitida*),
- cocoa seeds(*Theobroma cacao*).
- excites: respiratory, vasomotor and depressed vagal centers,
- increases: cortical neuronal excitability, improving psycho functions (increases intellectual effort), especially when the CNS is depressed.
- in overworking = backfire = paradoxical effects;
- excites: respiratory, vasomotor, vagal centers, when they are depressed.
- high doses: excite the spinal cord, increased reflex activity.

- high dose = renal vasoconstriction = coffeine, unrealiable diuretic.
- blood pressure = influenced by the stimulation of the vasomotor center and through the vasodilatation by stimulating the vagal centers.
- excites the thermoregulatory center : in therapeutic dose the temperature increases with 0,5 ºC, and in high doses, with 1-2ºC.
- p.o. increases reflexivity and though vagus the gastrointestinal secretomotor function, acting antispasmodic towards the intestinal smooth muscle.
- exerts the same action also on the bronchial muscles.
- in spite of her low toxicity, in high doses = intoxications: restlessness, hyperreflexia, palpitations, death: heart stopping in systole.
- as: cardiovascular and respiratory analeptic in exhausted animals, infectious diseases: 2-8g at AM and 0,1-0,5g in dog.
-often used: 25% sodium benzoic caffeine.
- in collapse is injected at AM, i.v., 5g in 40ml distillated water.

Camphor

- on healthy individuals doesn't work, but in animals with respiratory, cardiovascular disorders or in the case of superior nervous centers depression = stimulatory effects.
- compared to caffeine, enhances the breathing amplitude, less its rhythmicity.
- favorable effect on the heart in 15 min. after s.c. injection or i.m. and lasts for hours.
- action: reflex, injection site being the starting point, as well as direct, acting on the CNS and heart.
- by stimulating the depressed vasomotor center and the cardiac labor center, blood pressure is restored.
- antifebrile action= vasodilatation.
- antiseptic and diaphoretic action. It has low toxic effects.
- renal excretion and bronchial glands: diuresis and expectoration.
- used *10-20% camphor oil, 2-3 times / day..*
- in i.v. administration using isotonic chloride solution.

Pentetrazole (Cardiazole; Penthazol)

-10% solution, in 5-10 ml. ampoules.

- administered i.m., s.c. or i.v., even p.o. in certain cases .
- rapidly inactivated into the body, must be administered 1-2 hours. It is not cumulative.
- small doses, stimulants: CNS, cardiovascular, respiratory.
- best antagonistic toward narcotics and hypnotics, the animals wake up instantly.
- high doses i.v. = clonic convulsions.

Nicetamid (Coramide; Cordiamine)

-25% solution.

- safe stimulant of the respiratory center,
- not cardioexcitant.

Strychnine

- alkaloid that, is found in the seeds of various species of Strychnos, along with *brucine* and *vomicine*
- incompatible with: alkaline solutions, iodine, tannin, oxidants.
- acts: by increasing the excitability of the modulator system from marrow (represented by intercalary neurons).
- also stimulates blood pressure and respiration.
- high doses: preconvulsiv stage, exaggerating reflectivity, intense hyperesthesia and disorder in the nervous coordination.
- high electivity for medullary neurons and less for the cortical ones.
- by stimulating the vasomotor center, vasoconstrictor, peripheral vasodilator, cerebral and coronary = increased pressure.

Morphine is contraindicated, due to its synergy with strychnine.

Doxapram

- used to stimulate the medullary respiratory center in the post-anesthetic period.
- the minute-respiratory volume increases at 1 min. after administration with 200%.

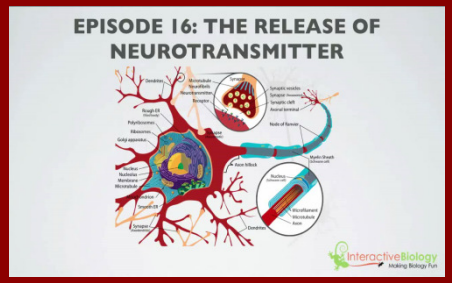
4-aminopyridine

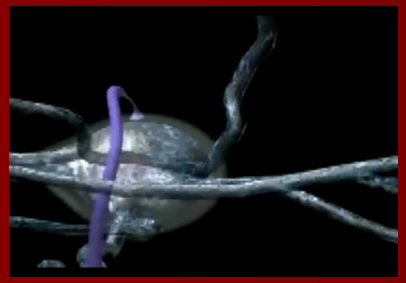
- CNS stimulant, but overdoses cause seizures.
- in: the treatment of paralysis caused by C. *botulinum*

Tolazoline

- adrenergic blockers, sympathomimetic,
- antihistaminic and antihypertensive
- xylazine and ketamine antagonist.

Antidepressants





Most states of malaise in animals have been extrapolated to humans having little importance in MV.

Action: blocks the recycling of the presynaptic biogenic amines at the levels of the neurotransmitter receptors in the brain = increasing concentration = extension of the CNS stimulant action.

Imipramine, Clomipramine, Doxepine

- medicines for human use
- medication can be used in animals with malaise state

Behavioral

medication

It is assumed that the serotonin is a neurotransmitter that plays an important role in behavioral disorders in animals.

With VM use can be enumerated two groups:

- antipsychotics
- anxiolytics

In human psychoses = serious brain disorders characterized by hallucinations, speech disturbances, etc.

In animals = similar events may be suspected.

Medications used in veterinary medicine as antipsychotic :

- chlorpromazine,
- acepromazine,
- promazine,
- haloperidol,
- phenothiazine derivatives.

Serotonin = synthesized in the brain from tryptophan, in the presence of GABA, (inhibitory neurotransmitter in the CNS)

GABA is preformed of glutamate (an excitatory neurotransmitter like acetylcholine).

Increased glutamate = behavioral disorders: aggression, impulsivity and phenomena of schizophrenia.

It can be used as anxiolytics :

- diazepam,
- oxazepam,
- lorazepam, etc.

Euthanasia

in veterinary medicine

Although, generally avoided, euthanasia has shown, many times its utility, in extreme situations, traumatizing, severe, hopeless, especially, when the owners are emotionally tied to their animals.

Euthanasia means using processes that permit suppression of life followed by an easy death and , without any type of pain.

Regardless of the method used, the ethical principles of veterinary medicine must be respected!

Euthanasia is practiced in the following situations:

- shortening the suffering of animals with incurable disease,
- appearance of infectious disease or
- most often, at the owner's request.

The methods used to produce euthanasia:

- direct or indirect hypoxemia;
- direct depression of vital neurons;
- physical destruction of nervous tissue.

The treaty of Amsterdam relating to protection and welfare of animals and animal testing (Directive 86/609/EEC) indicates the desiderata of euthanasia:

- death without pain;
- time required to install the loss of consciousness;
- personal security;
- unwanted psychological stress (its magnitude);
- irreversibility of the process;
- emotional effect on the operator and observer;
- economicity;
- tissue modifications;
- access to medicines, potential for abuse.

Choosing the most suitable method of euthanasia depends on:

- species
- number of animals
- economic criteria, available equipment.

If the meat of the animals is used in consummation then atunci you can not use substances that have remanence in tissues, being dangerous to the consumer.

- In VM are accepted three concepts of euthanasia:

1. inhaled;
2. medicated;
3. with physical means.

Euthanasia in horse and ruminants:

Barbitures in high doses are suitable for euthanasia,

often used is: Pentobarbital sodium salt

Comercial: Nembutal, Narcoren, Eutha: 50-100mg/kgc.

- s.a. diluted in 1.000ml water and administered i.v.

Pentobarbital, in combination with magnesium sulfate and chloralhydrate corresponds also to euthanasia.
Phenobarbital, can substitute pentobarbital!

Other barbitures, even if effective, are uneconomical.

T-61 (Hoechst)

- association: local anesthetic, a narcotic and a curarizant.
- 1ml contains: 0,2mg embutramide, 0,05mg mebezonium iodide and 5mg tetracaine hydrochloride.

Administered strictly i.v.

In: SUA, Canada, Europa, euthanasia in horses and ruminants.

Used for euthanasia in:

cat, dog: 0,3ml/kg i.v.

large animals: 4-6ml/50kg, i.v.

Chloralhydrate

20% aqueous solution administered iv, can be given alone only to euthanize large animals.

Euthanasia in pig

- Barbitures in large doses i.v. = accepted method in pigs.
- This method is not suitable for. a large number of animals.
- The combination: chloralhydrate + magnesium sulfate+ pentobarbital = eliminates the side effects (e.g. dyspnea, convulsions)

In inhaled euthanasia, carbon dioxide is indicated:

Inhalation of CO_2 60%, in45 sec. = loss of consciousness + respiratory arrest, in 5 minutes.

Used in slaughterhouses, but has a number of *disadvantages:*

- excitation signs,
- vocalization about 40 seconds before loss of consciousness,
- the only method used where meat is given to consumption!

Euthanasia in birds

Barbitures

In accepted increased doses, can not be applied in mass.

Chloroform

In euthanasia of small birds (parrots),

effective, inexpensive and non-flammable.

imbibes a pad with chloroform and place it together with the bird under a glass bell jar.

Carbon dioxide

For mass euthanasia of birds, in closed spaces.

Euthanasia in dogs

Barbitures: 50-100 mg/kg body, are used for this purpose.

After premedication with a neuroleptic (e.g. propionilpromazine 0.5 mg / kg., i.m) = death without pain with saturated solution of magnesium sulphate: 10-30mg/animal (i.v).

Euthanasia in cat

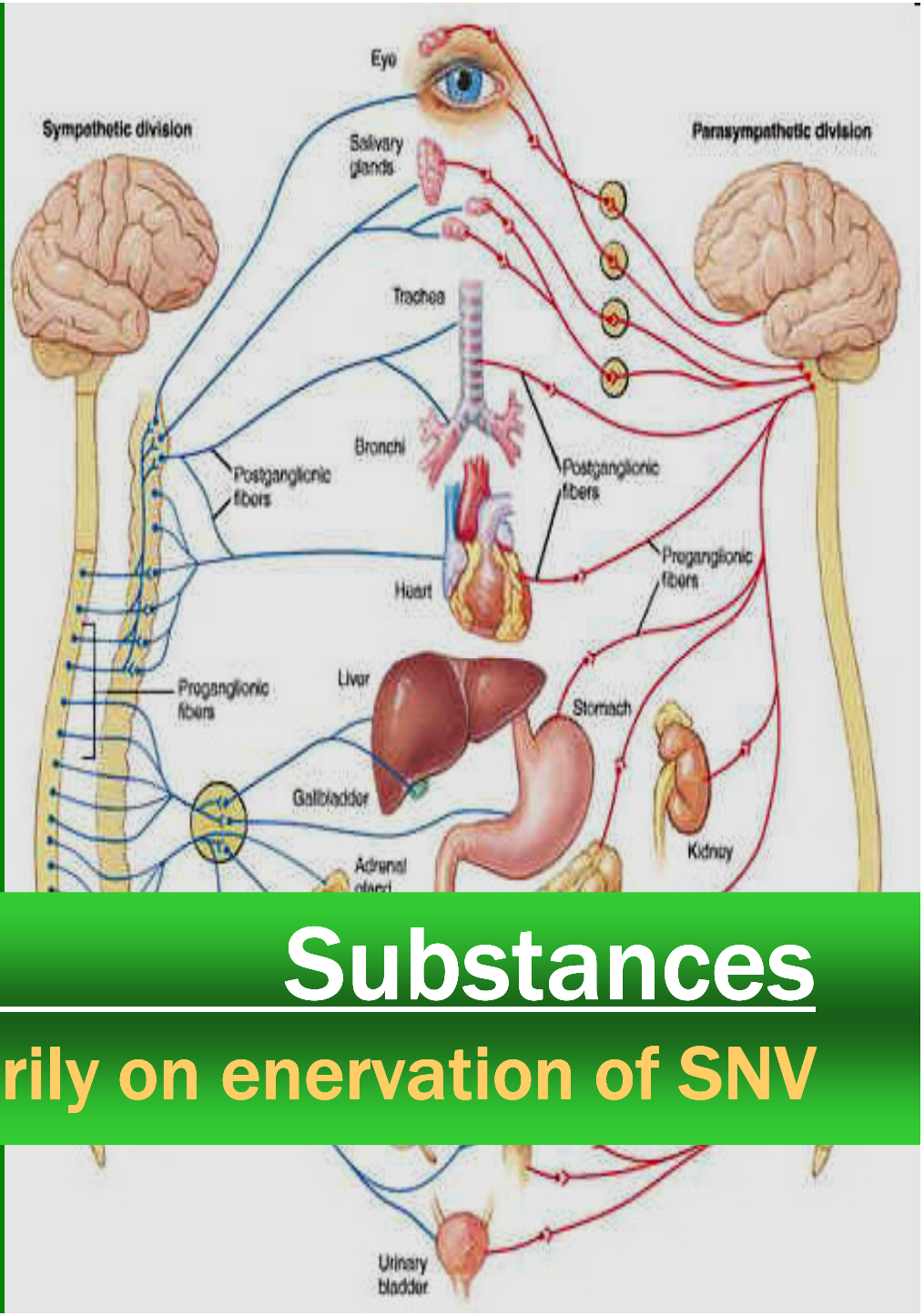
rapidly i.v barbitures. : 100-150mg/kgb, aqueous sol. 10% = rapid death.

- Premedication with neuroleptic and then with barbitures 200mg/kgb i.p. or i.pulmonary = certain effect.

In newborns

By injection of 5-10ml ether or chloroform, in the brain.

Chloroform can be used by inhalation.



Substances

acting primarily on enervation of SNV

Morphological V.N.S. - two segments:

- sympathetic,
- parasympathetic.

Vegetative depending on the biochemical system:

- cholinergic;
- adrenergic;
- purinergic;
- histaminergic;
- triptaminergic.

For pharmacology, the most important are:
cholinergic and *adrenergic* systems.

Cholinergic systems- sensible to acetylcholine.
Adrenergic systems– sensible to catecholamines.

Drugs from this category:
- similar effects to those of chemical mediators,
- they work on morphofunctional elements innervated by parasympathetic or sympathetic,
- others produce the same action, but by another way (using cholinesterase or monoamine oxidase).

First factor= destroys acetylcholine,

second= sympatine,

effects = is the result of the indirect action on the vegetative system

Inhibitory effects (blocking mediators) produce:

- parasympatholytic
- sympatholytic

Biochemical systems:

Besides mimetic and lytic of the vegetative exists also substances that act on the synapses of the autonomic ganglia.

Acts on the cholinreactive systems.

After their sensitivity are divided into:

cholinereactive muscarinic systems

☞ sensible to muscarinic and blocked by atropine;

muscarine-cholinereactive systems

☞ in heart and intestines (postganglionic cholinergic fibers);

nicotinamid-cholinereactive systems

☞ sensible to small doses of nicotine, blocked by high doses of nicotine and curarine.

Nicotine-cholinreactive systems

in: vegetative ganglion cells, some cells of the adrenal (medullary zone), striated skeletal muscle, carotid sinus, post-pituitary lobe.

Nicotine reactive systems from:

striated muscle - blocked by curarine;

vegetative ganglia - are not blocked by curarine;

Carotid sinus and post-pituitary lobe- blocked by substances from the tetraethyl ammonium group;

Parasympathomimetics

-alkaloids or synthetic product (contain nitrogen).

The pharmacodynamic effect is identical to that produced by electrical excitation of parasympathic nerve (vagus, common oculomotor, pelvic).

- It produces:
  - hypotension, bronchial hypersecretion;
  - gastrointestinal hyperperistaltism, bradycardia;
  - increased smooth muscle contraction.
- Parasympathics mimetics are used as:
  - purgative;
  - stimulators of rumination
  - emetic

Acetylcholine

- mediator of PSy, choline ester (ammonium derivative)

In therapeutic dose it produces:

- bradycardia;
- peripheral vasodilatation;
- hypotension;

Vasoperif (Carbachol, Doryl)

- carbonic ester of choline (chlorinated derivative)
- in: gastrointestinal atony, prestomach, some dystocia, retention and as vasodilatator.

Not used in: acute gastric overload, advanced gestation in old animals and / or exhausted.

Pilocarpine

Alkaloid - *Pilocarpus* leaf extract (Fam. Rutaceae).

Officinal- hydrochloride pilocarpine

Activity: predominantly hypersecretory in the salivary and bronchial gland, less at the pancreas and intestine level.

One of the best alternatives in combating: edema, dropsy, acute laminitis, purgative and ruminant,

In feline, large and small ruminants : = bronchial secretions exaggeration = ab ingestis bronchopneumonia.

High doses = nervous system excitation, abortion, worsening of the cardio-pulmonary condition.

Eserine (physostigmine)

- tropical liana alkaloid of *Physostigma*;
- officinal: salicylate salt;
- is an: *indirect parasympatho-mimetic*
- **Effects:** on the gastrointestinal smooth muscle, eyes and uterus.
- In gestating: induces abortion;
- best miotic under the form of instillations into the conjunctival sac!
- in 0,5-1% solutions, miosis lasting up to 24 h.

Miostin (neostigmine)

- synthetic anticholinesterase substance;
- one of the best stimulants of the smooth muscles.

Arecoline

- alkaloid obtained from the seeds of *Areca.*
- acts: directly on the elements innervated by Psy
- the action: 30 min. = defecations, bradycardia, miosis, sweating
- less hypersecretory than Pilocarpine;
- Stimulates motility better than Eserine;
- do not use when dealing with colic caused by torsion!
- to use only in colic caused by indigestion!
- the intoxications are controlled by atropine.

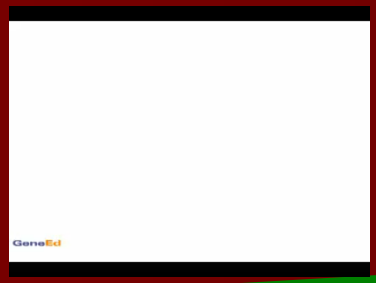
Parasympatholytics (vagolytics)

Parasympathomimetic antagonist producing:

- tachycardia,
- hypertension,
- hyposecretion,
- hypoperistaltism,
- mydriasis,
- ocular hypertension.

Atropine

- alkaloid, contains tropane nucleus and is found in *Solanaceae.*
- in practice: sulfuric atropine
- crystalline powder, white, colorless crystals, odorless, bitter (very toxic), very soluble in water.
- incompatible with: iodine, iodides, tannin, adrenaline coloring substances. Stored at *Venena!*



- CNS stimulant;
- parasympatholytic effect = due to preventing the action of acetylcholine on the active choline biochemical systems from different anatomical structures.
- quickly absorbed, even on skin, from the s.c connective tissue.
- high doses on CNS, after powerful excitation, paralysis and death by asphyxiation.

The lytic action: especially on the organs innervated by the vagus.

Intoxications: excitement, anger, dry mouth and nose

(main sign to identify fraud in horses!)

Atropine- recommended for:

- its antispasmodic qualities;
- differential diagnosis in heart disease;
- diminishing secretions;
- antidote: intoxications with parasympathomimetics, OP;
- in: s.c. injections, in colic in horses;
- in: ophthalmology are used instillations with 1% solution.
- in the form of ampoules 1-5ml., 0,25-1%.

Tropicamide

- in ophthalmology;
- rapid mydriatic: effect in 20 min. and disappears after 5-6 h.

Cyclopentolate

Its is used the hydrochloride salt for its mydriatic action, max. 24 h.

Scopolamine (hyoscine)

- officinal: scopolamine *hydrobromide,* stored at Venena.
- incompatible with: iodine, silver salts, tannins, alkaloids.
- resembles atropine in +: analgesic, reassuring, therefore, often associated with opioids.
- strong mydriasis: short term;
- one of the best medication to combat motion sickness, vertigo, in hyperexcitation, myalgia, neuralgia!

Scobutil (Buscopan)

- derivative of scopolamine.
- less intense on: salivary secretions sweat, heart and eye.
- properties: antisecretory, digestive antispasmodic, weak ganglioplegic

Sympathomimetics

- in general, aromatic amines;
- acts upon existent adenoreactive biochemical systems in the cardiovascular apparatus, intestinal and bronchial smooth muscles, iris, spleen, uterus, salivary and digestive gland, in equine sweat gland.
- relaxes the contracted smooth muscle;
- produces active mydriasis and CNS excitation.

Noradrenalin

- vasoconstrictor substance,
- produces: short-term hypertension;
- advantages= vasoconstriction is not followed by vasodilatation.
- very effective in capillary hemorrhages!

Commercials:

Noratrinal (bitartrate) 2-4‰ sol, i.m., i.v., local.

Naohazoline (Rinofug, Privine)

- hydrochloride salt, officinal, microcrystalline powder, yellowish, odorless, bitter, slightly soluble.
- officinal: nose drops with the hydrochloride form of 0,1%.
- rapid and prolonged vasoconstrictor in: rhinitis, sinusitis, as nasal instillation, but no more than 10 days,
- over 10 days: risk of mucosal necrosis!

Phenylephrine (Usophrin, Mezaton)

- of synthesis, vasoconstrictor for all territories,
- the effect is reduced 4-5 times as in adrenaline, the duration= double;
- hypertensive, local vasoconstrictor for the nasal mucosa, in 0,25% solution.

Astmopent (Alupent)

- synthetic substance, beta-stimulant,
- long acting bronchodilator, p.o. and aerosols.

Isoprenaline (Bronhodilatin, Isupren, Novodrin)

- beta stimulator, very good bronchodilator.
- tablets and aerosol solution 0,5%.

Bamethan (Butedrin)

- beta stimulant, vasodilator, strongly hypotensive;
- in: syndrome of peripheral ischemia, frostbite, arterial spasm, postoperative vascular disorders, renal disorders;
- tablets and ampoules of 1ml, 5%.

Adrenaline (Epinephrine, Suprarenin)

- adrenal extract, from bone marrow, natural product = levorotatory
- officinal: obtained synthetic, the product is racemic.
- crystalline, odorless, bitter (toxic), photosensitive, sparingly soluble.
- oxidized to heat and light.
- stored at Venena!
- on general path: vasoconstriction in the splachnic territory, over the arterioles of the cutis, but skeletal muscle capillaries dilates

intoxication = exaggerated tachycardia, pulmonary edema , pale mucosa, collapse, anaphylactic reactions, death.

Sympatol (Vasoton)

- adrenaline molecule without oxydril in its aromatic cycle.
- the best succedanous substance adrenaline, the most harmless!
- a little toxic, heart is not too affected.
- administration: i.m. and s.c.

Amphetaminena (Benzedrine)

- officinal: sulphate salt, white powder, odorless, slightly bitter.
- under the form of tablets;
- excellent excitant of the CNS (in human= euphoria).
- in veterinary medicine is used in encephalomyelitis of the horse.

Ephedrine (Epherit)

- related to adrenaline, levorotatory alkaloid of the Ephedra genus.

The synthetic form= ephetonine = racemic;

- officinal: hydrochloride salt crystalline powder, acicular crystals, colorless, odorless, bitter, soluble, at *Separanda*.

- Acts: indirectly parasympathomimetic through: amine oxidase inhibition through sympatine, produced at the sympathetic endings.

-installs: vasoconstriction, vasodilatation, bronchodilation, hypertension, CNS excitation, stimulating the heart and the striated muscles.

Not destroyed in the digestive tract, is well absorbed, as well as in the s.c. tissue.

Sympatholytics

prevents: sympathic or sympathomimetic activity by blocking the adrenoreactive systems.

especially: elements innervated by vasoconstrictors with alpha receptors.

Guanethidine (Ismelin)

- remarkable neurosympatholytic, actually an antiadrenergic.
- produces: arterial hypotension after a latency of 2-5 days,
- effect: 10 days, especially if there is hypotension.

Clonidine (Catapres)

- antiadrenergic imidazole derivative.
- long-acting hypotensive;
- 30–60 min. after installation, for 2-3 h.
- administration: p.o. or i.m.

Methyldopa (Dopegyt)

- sympatholytic, chemical structure similar to DOPA
- modifies catecholamine synthesis, final; methylnorepinephrine will inhibit the central sympathetic = hypertension 6h.

Ergot

- mature sclerotia of *Claviceps purpureea* that develops in the ovary of *Secale cereale*.
- contains: 0,3% alkaloids, expressed by ergotamine tartrate;
- high doses of ergotamine and ergotoxine : vasodilatation through decommissioning adrenoreactive biochemical systems.
- small doses: stimulates uterine and vascular smooth muscle, = vasoconstriction and strong contraction of the uterus.

Ergometrine

- hardly produces vasoconstriction,
- by stimulating uterine muscle contraction = pressed vessels
- effective in combating uterine hemorrhage;
- in: retention of placenta and uterine hemorrhage;
- not used in: stimulation of parturition
- produces spastic contractions ,not undulatory;
- fetal asphyxia or
- uterine rupture.

Tolazoline (Priscol)

-adrenergic receptor blocker

-produces vasodilatation: splachnic, pulmonary, retinal and in cutaneous territories.

Yohimbine

-dextrorotatory alkaloid

- from the peel of *Aspidoderma blanco* and plants of the *Rawfolvia* genus.

Produces vasodilatation:

- abdominal, pelvic and genital: excites the erection center.

Substances that affect
autonomic ganglia (ganglioplegic)

acting on the synapses.

Nicotine substances

- initially produce stimulating effects
- nervous impulse passes to the effector organ then thanks to the extended depolarization, paralysis occurs = depressant effect.
- determines in the first phase paralysis of the ganglionic nicotinic receptors, interrupting the nervous influx.

Nicotine

- pyridine derivative, oily liquid, yellow, characteristic odor.
- in: ruminal atony.

Peracetine

- stimulating action on respiration
- becomes deeper and constant as rhythm
- increased heart rate and blood pressure,
- generally, brief state of excitement.

Lobeline

- piperidine derivative.
- In practice is used chloralhydrate;
- alkaloid, but also prepared synthetically.
- short-term strong excitant, of the respiratory center..

Sparteine

- an alkaloid derived from plants of the *Legume family.*
- respiratory analeptic, antiarrhythmic, good oxytocic.
- in cardiac arrhythmias and obstetrics, carefully.

Cytisine

- white, crystalline, soluble powder;
- alkaloid with intense action on respiration,
- more intense than Lobeline, even in shock.
- administered i.v.

True ganglioplegic substances

Hexamethonium

- has short duration of action.

Trimetaphan (Arfonad)

- sulfide derivative, short ganglioplegic action (5-10 min.).
- determines an appreciable arterial hypotension;
- used in neurosurgery;

Tetraethyl ammonium iodide

- temporarily paralyzing the nicotine-choline-reactive synapses from the autonomic ganglion.

Tripelennamine hydrochloride (Pyribenzamine)

- short duration of action, to medium
- stimulating effects on cows lactation fever, slowly i.v.
- cattle and horses: 0,5 mg/kgb, i.m. every 8 h, with a maximum dose that would not exceed 240 mg.
- in modern antihistamines was attempted exclusion of sedative component such as: terfenadine, astemizole.
- this effect is achieved through the use of substances that can not penetrate the barrier or have low permeability of the H.E barrier.
- CNS depression is not always a disadvantage in vet therapy.

Antihistaminic

substances

Pharmacology of allergies

Allergy = local hypersensitivity reaction,

Anaphylaxis = generalized reaction.

For example: in human and cattle, penicillin allergy is manifested through skin lesions, while the sensitivity of an inhaled atopic allergen is manifested through nasal congestion (fever) and/or bronchoconstriction (asthma).

The allergen can penetrate also p.o. = digestive symptoms;

Allergy symptoms can be reproduced by the administration of histamine, not entirely, because at the allergy installation contributes other factors too: complement or macrophages.

This situation occurs in the case of delayed hypersensitivity reactions (e.g. contact dermatitis), ass opposed to immediate hypersensitivity (e.g. urticaria, rhinitis, bronchoconstriction).

The proportion of reaction depends on:

- the amount of the antigen and
- the type of the participant antibody .

The produced pharmacological effects are determined by:

- distance: site of action- the place where the active substance is released
- factors that influence activity s.a. (e.g. inactivity rate) and
- the type of influenced cell by the active substance

Mediators involved in *immediate hypersensitivity* reactions

Plasmatics	Angiotensin Bradykinin Kalidine Vasoactive intestinal peptide (PIV)
Cellular	Histamine Substance P 5-hydroxytryptamine (5-HT)
Phospholipid precursors	Prostaglandins Leukotrienes Platelet activating factor

The antibodies are found in the globulin fraction of serum proteins (Where are the fractions of distinct immunoglobulin (IG)

Anaphylaxis is the term used to define the a state of shock severe, occurring after the release of histamine in the blood, where it is vehiculated in small grains of basophiles and platelets, in small granulocyte of basophiles and platelets.

The anaphylactic shock is reproduced by:

- repeating the administration of the antiserum produced in different species (heterologous antiserum)
- following the administration of certain drugs.

- in dogs, anaphylaxis = constriction of the hepatic veins
- leads to the repression of the venous blood in portal and liver vessels = intestinal hemorrhage.
- in guinea pigs the dominant symptom is bronchoconstriction.
- Anaphylaxis can be prevented by injecting an antihistaminic before the appearance of histamine in the blood!
- some drugs can determine the release of histamine!

Histamine:

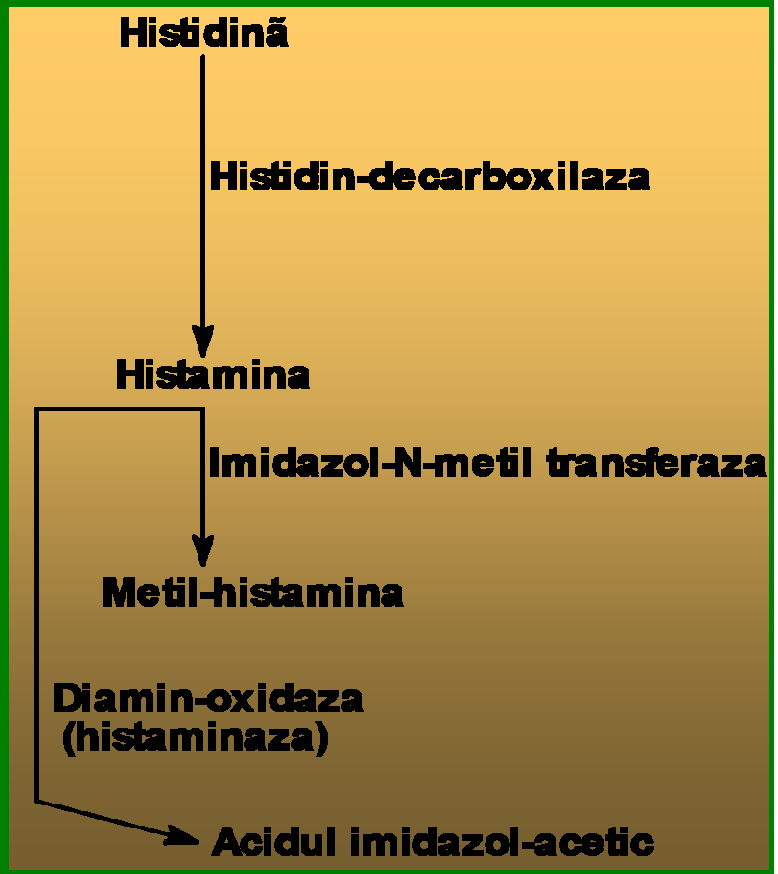
in skin, gastrointestinal mucosa, tissues and in CNS;

Its absorption= restricted by the presence in the g.i. tract wall of enzymes that oxidizes and methylates histamine.

Its inactivation may take place in: liver and kidney.

The main implicated enzymes:

- *diamine oxidase (histaminase) and*
- *imidazol-N-methyl transferase.*



Biosynthesis and degradation of histamine

Action: smooth muscle contraction of:
- digestive tract;
- uterus,
- bronchi;

also leads to smooth muscle contraction of:
- vessels (e.g. hepatic veins of the liver in dogs)
- pulmonary arterioles (in cat)
- relaxation in: venules and small arterioles.

Vasodilatation associated with fluid and protein extravasation, due to increased permeability of venules = decreased blood pressure, hem concentration, tachycardia.

Changing permeability depends on:
- contraction and
- spacing of endothelial cells

administered i.d. = triple response.

1. small vessels from the injection site dilate.

2. neighboring vessels dilate, on the path of an axonal reflex.

3. plasma extravasation : considerably dilated vessel walls,

- the reaction zone becomes edematous and appears higher!

This: overflow, swelling, lifting constitutes triple response, appears after the needle stick (containing histamine).

he medical name to identify the phenomenon: needle rash.

Acts: on the membrane receptors way producing:

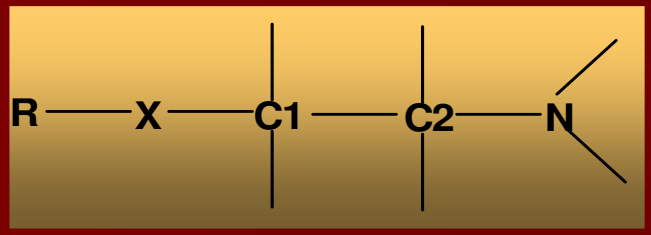
- membrane depolarization and
- raising the concentration of free calcium.
- also causes the accumulation of cAMP

Effects: countered by the use of antagonists:

- pharmacological or
- physiological.

Physiological antagonists are sympathomimetic amines:

- adrenaline
- noradrenaline,
- ephedrine etc.



Most antihistamines = weak base similar to histamine

R: composed of one or more cyclic groups which may be:

- aromatic,
- heterocyclic or
- both.

X: may be embedded (promethazine).

X can be switched with an atom of:

- nitrogen (e.g. tripelennamine);
- oxygen (e.g. diphenhydramine),
- carbon (e.g. chlorpheniramine)

Antihistamines do not prevent:

- formation
- release or
- decomposition of histamine.

but opposes to the effects produced by histamine in the body!

- it snaps on the histaminergic receptors;
- not allowing addition of histamine.

Recommended in:

- allergies,
- rashes,
- serum sickness,
- asthma,
- in acute forms: when large discharge of histamine exist.

Antihistaminic therapy= symptomatic treatment should be continued until the primary cause ceases to act.

If allergies evolves acute and severe, antihistamines act too slow! it is highly recommended to use adrenaline first, followed by p.o. or i.m. administration of an antihistamine.

Systemic therapy should be continued up to 3 days.

The i.v. path carries the risk of cardiac arrest, better to avoid it!

Topical administration may cause skin sensitization!

The condition when antihistamines are effective are associated with:

- allergic congestion,
- edema
- itching (hives)
- allergy serum and
- insect bites.

Side effects:

- CNS depression = due to decrease sedation, during treatment which may have value. Effect that sums with other CNS depression.
- The local anesthetic effect is 3-4 times higher than that of procaine (only if the concentration or therapeutic dose is exceeded).
- G. I. disturbances in monogastric when the p.o. administration. is long.
- Long periods of excitement may occur as a result of the iv administration and may require sedation using barbiturates.
- Interference with allergic diagnostic procedures (eg, tuberculin). Antihistamines should be avoided during such testing.
- Antagonizes the activity of some neurotransmitters: acetylcholine, adrenaline, 5-hydroxytryptamine.

H1 blockers

Antazoline hydrochloride

Compound less active and less locally irritant than other antihistamines, valued in ophthalmology (instillation).

Diphenhydramine hydrochloride

more active, effects occur quickly and the action takes longer.

powerful sedative, antiemetic (used in "motion sickness").

The local anesthetic effect = useful in combating pruritus.

Atropine-like action useful in combating the irritation of the upper respiratory tract.

At: a.m.: 1 mg/kgb, and at A.M.: 0,25-0,5 mg/kgb.

Mepyramine maleate

antihistaminic action time shorter than the previous one,

a weak sedative and local anesthetic.

Chlorpheniramine

- active antihistaminic, sedative effect weaker than diphenhydramine
- The short duration of action has no practical significance if the sustained release is obtained by oral administration.
- Dogs: 0,4-2 mg/kgb, one administration at 12 ore.
- Pheniramine retardation increases activity at 20 hours.

Promethazine chloride (Romergan, Phenergan)

- intermediate action between chlorpheniramine and diphenhydramine.
- the most depressant effect on the central nervous! sedative, hypnotic.
- best effect in preventing motion sickness! Prevent vomiting
- the greatest atropinic effect of all antihistamines!
- horses and cattle: 1,5-2 mg/kgb., in i.m. administration once daily.
- antihistaminic, antiallergic, bechic,
- potentialiser of depressors, psychoplegic, antiparkinsonian.
- In: acute laminitis, dermatitis, hives, anaphylactic accidents.

H2 blockers

Appeared in the 70s. First representative:

Burimamide

is poorly absorbed from the intestinal tract.

Metiamide

produces agranulocytosis.

Cimetidine and Ranitidine

- competitive antagonists of histamine.
- when it is necessary to control the production of acid in the stomach
- in: duodenal ulcer.
- no serious side effects = poor CNS penetration and
- lack of functional importance of other structures than H2 receptors in the stomach lining.

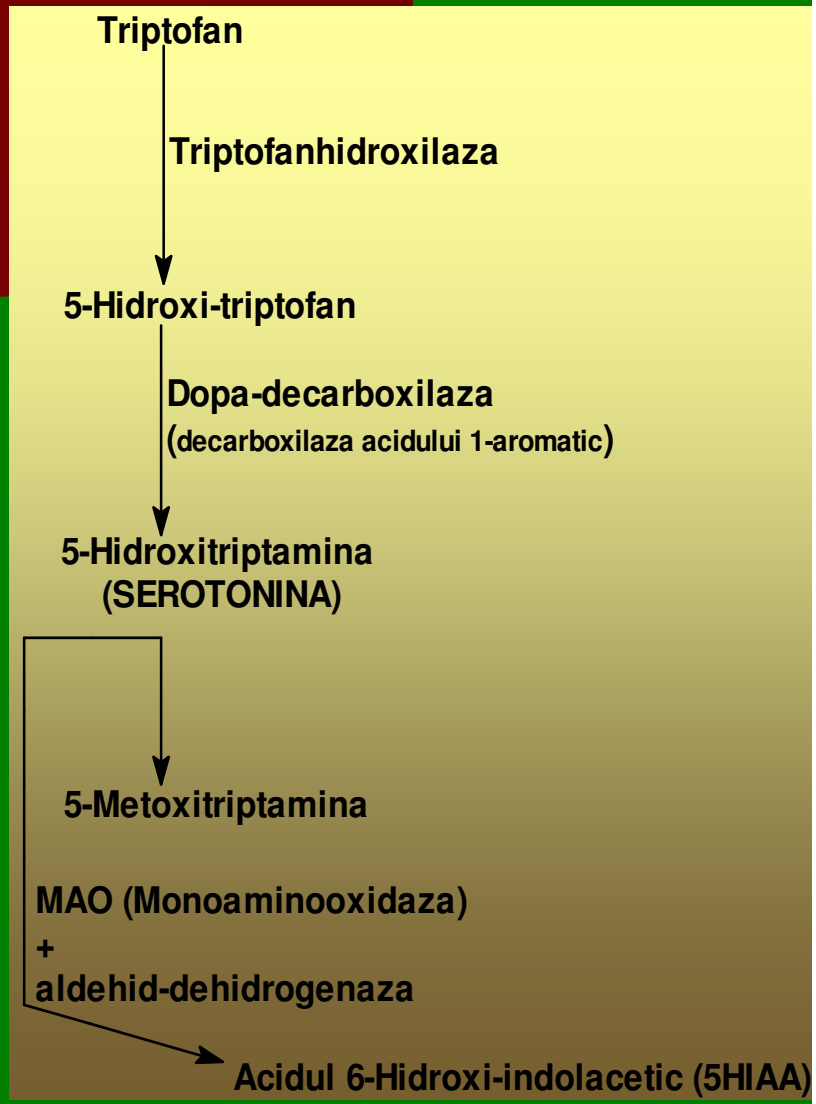
Inhibitors of histamine release

Sodium cromoglycate (Cromolyn Sodium)

- has no antihistaminic effects nor
- smooth muscle relaxant properties but:
- prevents the release of histamine and other mediators involved in lung allergic reactions.
- the effect is mediated through pulmonary mastocytes.
- they cease to degranulate in the presence of antigen.
- calcium entering into mastocytes is not activated as a result of exposure to antigen = it is assumed that the substance limits the availability of calcium for mast cells.

5-hydroxytryptamine (5-HT) (Enteramine, Thrombocytin)

- it is also known as: serotonin or vasotonin
- 5-HT appear in the argentafin cells of the gastrointestinal tract.
- has been identified in mast cells of rats, mice and cattle, species at which is released in anaphylactic reactions.



Reserpine

- liberating activity of noradrenaline and stored 5-HT.
- it is assumed that the depletion of 5-HT in the brain is responsible for reserpine-induced depression.
- 5-HT action = contraction of most smooth muscles in blood vessels but dilates the arterioles = plasma extravasation due to increased permeability.

By direct action = smooth muscle contraction: intestinal, uterine and bronchial tree.

5-hydroxytryptamine antagonists

- used in the control of anaphylaxis of cattles
- the majority members of the ergotamine group (e.g. dihydroergotamine)
- or simple derivatives of lysergic acid (LSD) (lysergic acid diethylamide, methysergide and acid bromolisergic 2).
- in human: hallucinogens in psychotherapy, treatment of migraine and preoperator control of the argentafin tumor tissue..

Cyproheptadine

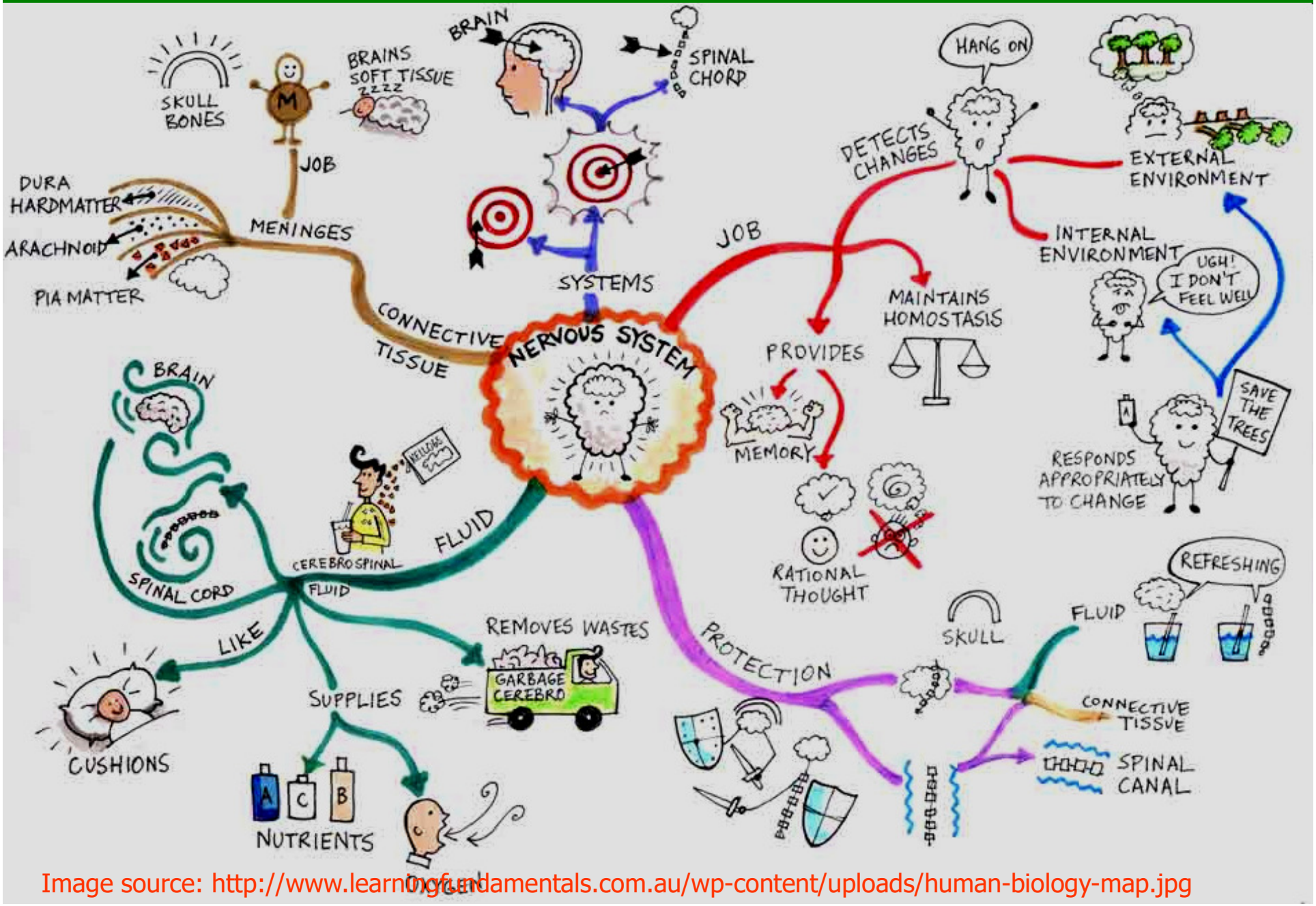
structure that antagonizes competitive histamine and serotonin.

Some antihistamines derivatives of phenothiazine have anti 5-HT effects.

Trimeprazine

used in controlling pruritus of the skin diseases in dogs.

Thank you for your attention !



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