Local anesthetics

This study material is recommended specifically for practical courses from Pharmacology II for students of general medicine and stomatology. These brief notes could be used to prepare for the lesson and as a base for own notes during courses. Addititonal explanations and information are given in single lessons.

Local anesthetics

- drugs evoking local reversible anesthesy by inhibition of sensory neurons

Sensitivity of neuronal fibres to LA:

vegetative > sensory > motoric

in sensory fibers the perception of heat is blocked first, then pain perception follows and last sensations inhibited is touch

LA mode of action

LA penetrates the neuronal fiber and block Na^+ channels

Other effects:

- vasodilation (sympathetic fibres blockade)
- antidysrhytmic activity (influence on Na^+ channels in myocardium)

LA chemical structure

LA are amphiphilic substances:

- aromatic group is lipophilic
- nitrogen moiety is hydrophilic (ionizable)

  nitrogen and aromatic moite are connect via **esteric** or **amide** bound

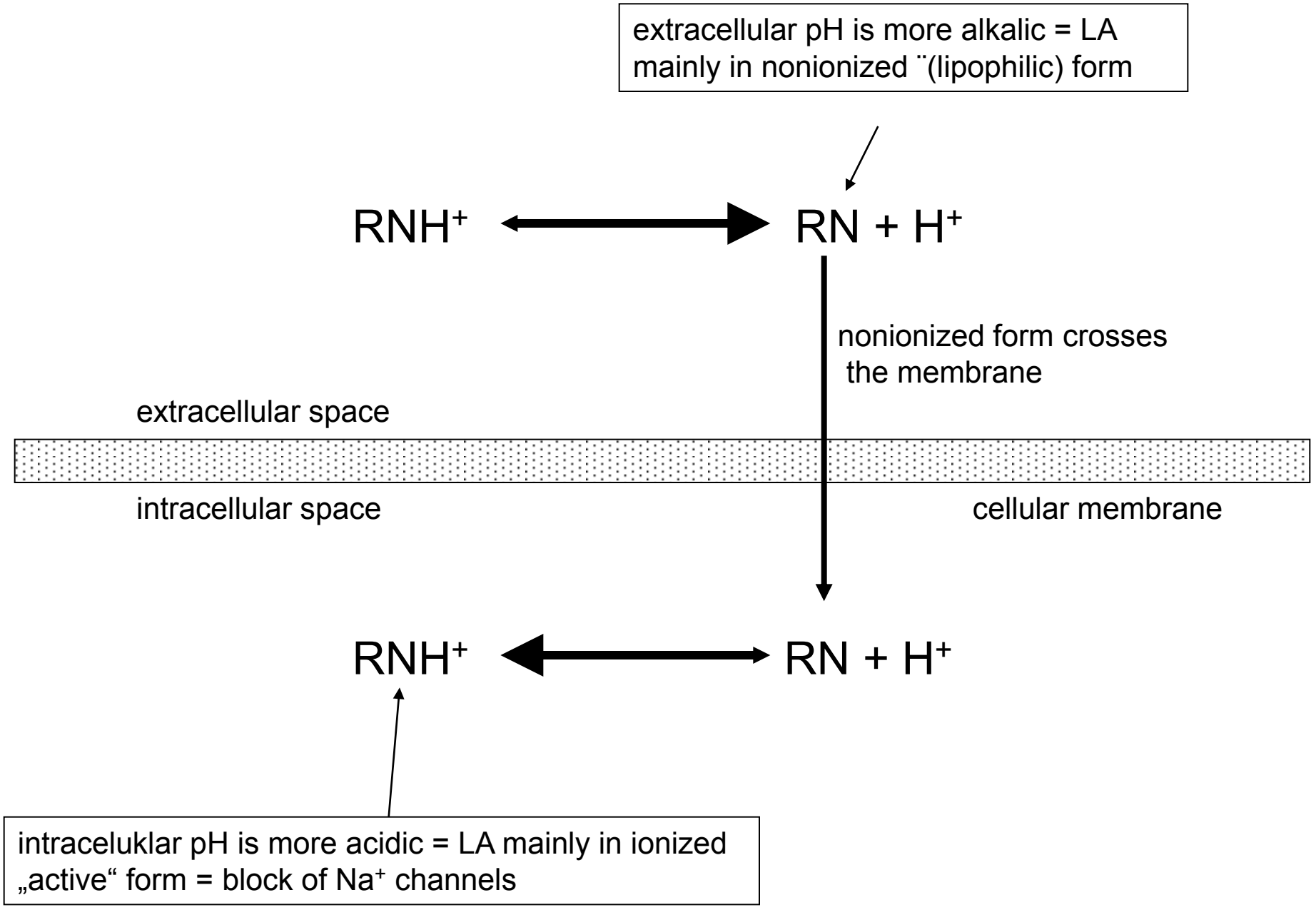
  (classification to esteric and amide LA)

  Exception– benzocaine without ionizabe group

LA are weak alkalis, pK_a = 8-9, LA efficacy depends on tissue pH – ionized/unionized ratio

Higher pH = increased efficacy– more molecules are unionized and increased penetration to neurons

Less effective in tissues with lower pH (inflammation) tkáni – ionized molecules do not penetrate into neurons


extracellular pH is more alkalic = LA
mainly in nonionized ¨(lipophilic) form
RNH+
RN + H+
nonionized form crosses
the membrane
extracellular space
intracellular space
cellular membrane
RNH+
RN + H+
intraceluklar pH is more acidic = LA mainly in ionized
„active“ form = block of Na+ channels

LA pharmacokinetics

- absorption - depends on concentration of drug on the site of administration, dose, blood perfusion and phys.-chem. properties of drug
- distribution – in the whole body, deposits in adipose tissue, amides strong binding to plasma proteins
- biotransformation – plasmatic esterases are involved (fast, ester LA) or hepatic metabolism by CYP (slower amides)
- excretion of metabolites - kidneys

Vazoconstrictors

- to decrease LA systemic toxicity
- to compensate induced vasodilation
- to prolong and increase LA efficacy

careful in acral body parts – risk of ischemic necrosis!

epinephrine (most often in conc. 1:200 000), or norepinephrine or naphazoline

LA routes of administration

Superficial anesthesia (topical)

LA in solutions, gels, ointments

mucosas, cornea, oesophagus, respiratory tract, ...

Infiltration anesthesia

subcutaneous, intradermal, intramuscular

block of thin fibres in the site of administration – low LA concentrations + vasoconstrictors

LA routes of administration

Conduction anesthesia

epidural anesthesia – special case of conduction an.

(regional anesth.– used for block of neurve fascicles incl. epidural an.)

Subarachnoideal anesthesia

(intratintrathecal, spinal, lumbal anesthesy) LA administered into the spinal canal, ALWAYS WITHOUT VASOCONSTRICTORS!)

Intravenous regional anesthesia (Bier block)

Ester LA

cocaine

- first known AL (medical use from 1884)
- natural compound, isolated from leaves of *Erythroxylon coca*
- also central psychostimulant with high risk of addiction
- for superficial anesthesia (today rarely for LA for paracentesis – Bonain‘s solution IPP blue stripe)

Ester LA

procaine

- the oldest sythetic LA (1905)
- slow onset, short duration
- for infiltration and conduction anesthesia (hardly penetrates skin)

tetracaine

- fast onset
- high systemic toxicity – only for superficial anesthesia of oral cavity and throat(combined with chlorhexidine)

benzocaine

- only for superficial anesthesia of oral cavity and throat (in combination with antiseptics)

Amide LA

trimecaine

- universal, for all types of anesthesia
- used as antiarhythmic agent too

lidocaine

- universal LA for superficial, infiltration and conduction anesthesia
- used as antiarhythmic agent too

doses of trimecaine and lidocaine must be halved in patents treated with betalytics, Ca^{2+} channel blockers and in epileptics!

Amide LA

mepivacaine

- in stomatology, namely in patients not tolerating vasoconstrictors

bupivacaine

- all typer of local anesthesia
- highly cardiotoxic

levobupivacaine

- similar to bupivacaine

prilocaine

- only for topical anesthesia

Amide LA

ropivacaine

- all types of anesthesia except subarachnoid.

cinchocaine

- highly toxic, just for topic anesthesia

articaine

- fast onset, long duartion
- used mainly in stomatology

Classification with regard to the efficacy

Weak

procaine, benzocaine

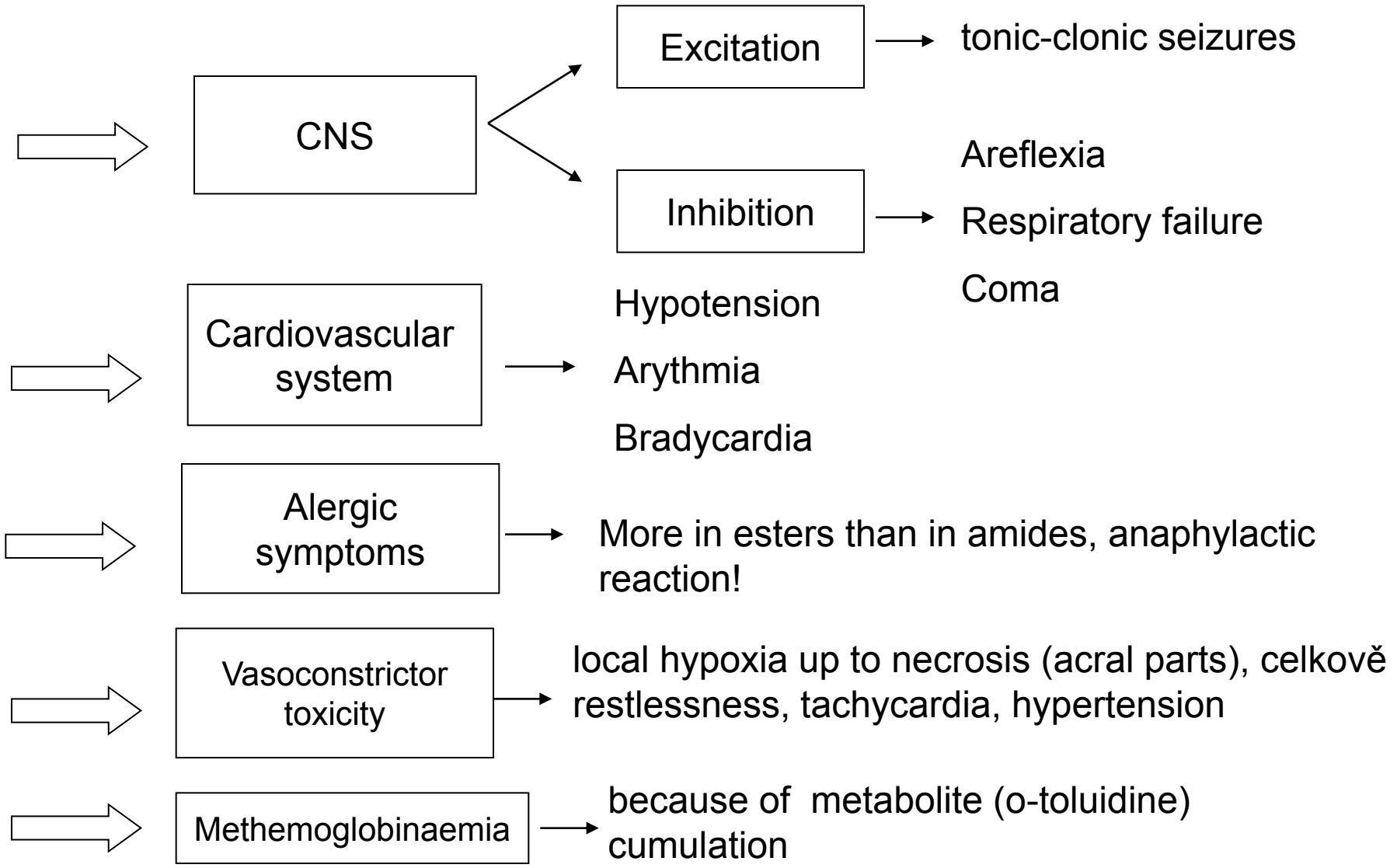
Intermediate

trimecaine, lidocaine

Strong

tetracaine, bupivacaine, articaine, ropivacaine

Toxic effects of LA



LA intoxication

Alergic and anaphylactic reaction

Symptoms:

- pruritus
- urticaria
- swellings
- anaphylactic shock- reslessness, anxiety, breathlessness, vomiting
- Quincke‘s oedema – without inflammation, fast onset in face, affecting lips, face and throat (suffocation!!)
- **Therapy:**
- 1 mg epinephrine in 10 ml of saline i.v.
- oxygen and infusion 5% glucose with norepinephrine
- hydrocortisone i.v.
- antihistamines
- in case of respiratory failure, keep free airways and artificial respiratory ventilation

LA intoxication

Systemic toxic reaction

Symptoms: (most often till 15 min from LA administration):

- resltessness, hand tinglinghot or cold, nausea, vertigo, cold sweat
- tachypnoe
- tremor, fasciculation, seizures
- tachycardia, increased blood pressure in the beginning with the subsequent decrease, unconsciousness, bradycardia
- in the final phase respiratory and cardivascular failure

Therapy:

- lay down patient, oxygen in respiratory insufficiency
- thiopental or diazepam i.v. in seizures
- slow epinephrine i.v. in critical decrease of BP
- resuscitation in respiratory and cardial failure