Local anesthetics

Local anesthetics (LA)

- cause temporary loss of sensation in a limited area (absence of pain sensation) by local reversible inhibition of sensory neurons
- other senses are often affected as well

  - sensitivity of nerve fibres to LA:

  vegetative > sensory > motoric nerve fibres

- in sensory fibers the perception of heat is blocked first, later the perception of pain stimuli, and then the touch also
- at higher concentrations the loss of muscle power can be achieved as well (e.g.local anesthetic regional nerve blockade)

Sensitive nerve system

- types of somatosensory nerve fibres - signals from skin receptors and from skeletal muscles and joints, etc.

- protopathic perception (sensing pain, pressure, heat, or cold in a nonspecific manner)
- epicritic perception (permits the discrimination and the topographic localization of the finer degrees of touch and temperature stimuli)
- and proprioception (sense of the movements and position of the body independent of vision)

LA - mechanism of action

- penetration into sensitive nerve fibres
- blockade of voltage-gated sodium channels responsible for fast depolarization along nerves

- binding on the inner side of the nerve membrane, and preventing Na^+ ions flow

other effects:

- vasodilation (sympathetic nerve fibres blockade)
- class I antiarrhythmic drugs (influence on Na^+ channels in myocardium)

LA - chemical structure

- amphiphilic substances:
- aromatic group is lipophilic
- nitrogen group is hydrophilic (ionizable)

  - connected via **ester** or **amide** bond

  (ester-type and amide-type of LA; exception - benzocaine)
- LA are weak bases, pK_a = 8-9
- their efficacy depends on pH – ionized/non-ionized

- higher pH = increased efficacy– more molecules are non-ionized = increased penetration to nerve fibres
- low pH = less effective, e.g. in tissues with inflammation

LA - pharmacokinetics

- **absorption** - depends on drug concentration, on the site of administration, dose, blood perfusion and physical-chemical properties of drug

- **distribution** – in the whole body, deposits in adipose tissues, amides strong binding to plasma proteins

- **biotransformation** – plasmatic esterases are involved (fast, ester LA) or hepatic metabolism via CYP (slower, amide LA)

- **excretion** of metabolites - kidneys

Vasoconstrictory agents

- additives for lowering systemic toxicity
- compensation of vasodilation induced by LA
- shortening time of onset
- increased duration of analgesia (delayed diffusion of LA)

in acral parts with caution – risk of ischemic necrosis

adrenaline, ev. noradrenaline, derivatives of vasopressin

LA - administration routes delivery techniques

- **topical (surface) anesthesia** - transdermal penetration of LA
  - solution, gel, cream
  - mucosa, cornea, esophagus, respiratory tract, decubitus
  - often used in urology (catheterization) and before other painful instrumental procedures

- **infiltration anesthesia**

  subcutanous, submucosal, intraarticular
  - blocks nerve conduction near their site of administration
  - low concentrations of LA and vasoconstrictory agents
  - often used for minor surgical and dental procedures

LA - delivery techniques

- **conduction anesthesia**

  - peripheral - local anesthetic nerve block

  single treatments, multiple injections over a period of time, or continuous infusions

  - central - always without a vasoconstrictory agent
  - **epidural anesthesia**
  - **subarachnoideal anesthesia (spinal)**

LA - delivery techniques

central conduction anesthesia <contd>

- **epidural anesthesia**
  - postoperative analgesia, analgesia in obstetrics
  - regional anesthesia (cervical, thoracic, or lumbar)

- **subarachnoideal anesthesia** (spinal block)
  - intrathecal administration of LA, must be injected below L2 to avoid piercing the spinal cord
  - limited to procedures involving most structures below the upper abdomen.
  - without vasoconstrictory agent

LA - delivery techniques

- **intravenous regional anesthesia (Bier block)**
  - trimecaine 1%
  - lidocaine 0,5 %

  - for surgical procedures on extremities
  - quick onset and inhibition of motor functions
  - exsanguination of the limb (elevation + tourniquets)
  - procedures max. up to 2 hrs (risk of ischaemia)
  - no postoperative analgesia

Ester type of LA

cocaine

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

Ester types of LA

procaine

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

tetracaine

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

benzocaine ethyl ester of p-aminobenzoic acid (PABA)

- only for topical anesthesia of oral cavity, ear and throat (available in combination with antiseptics, OTC drugs)

Amide types of LA

trimecaine

- universal, for all types of local anesthesia
- used also as the class I antiarrhythmic drug

lidocaine (syn. xylocaine and lignocaine)

- universal LA for surface, infiltration and conduction anesthesia
- class I antiarrhythmic drug

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

Amide type of LA

mepivacaine

- in dentistry, in patients with KI of catecholamines

articaine

- used in dentistry
- fast onset, long effect

bupivacaine

- all typer of local anesthesia
- cardiotoxic

levobupivacaine

- lower cardiovascular toxicity and neurotoxicity

Amide type of LA

ropivacaine

- amide type of anesthetic
- for all types of anesthesia except subarachnoidal

prilocaine

- surface anesthesia EMLA
- spinal anesthesia for short surgical procedures

cinchocaine (dibucaine)

- surface (topical) anesthesia
- (spinal anesthesia)

LA - according to their efficacy

- weak

  procaine, benzocaine

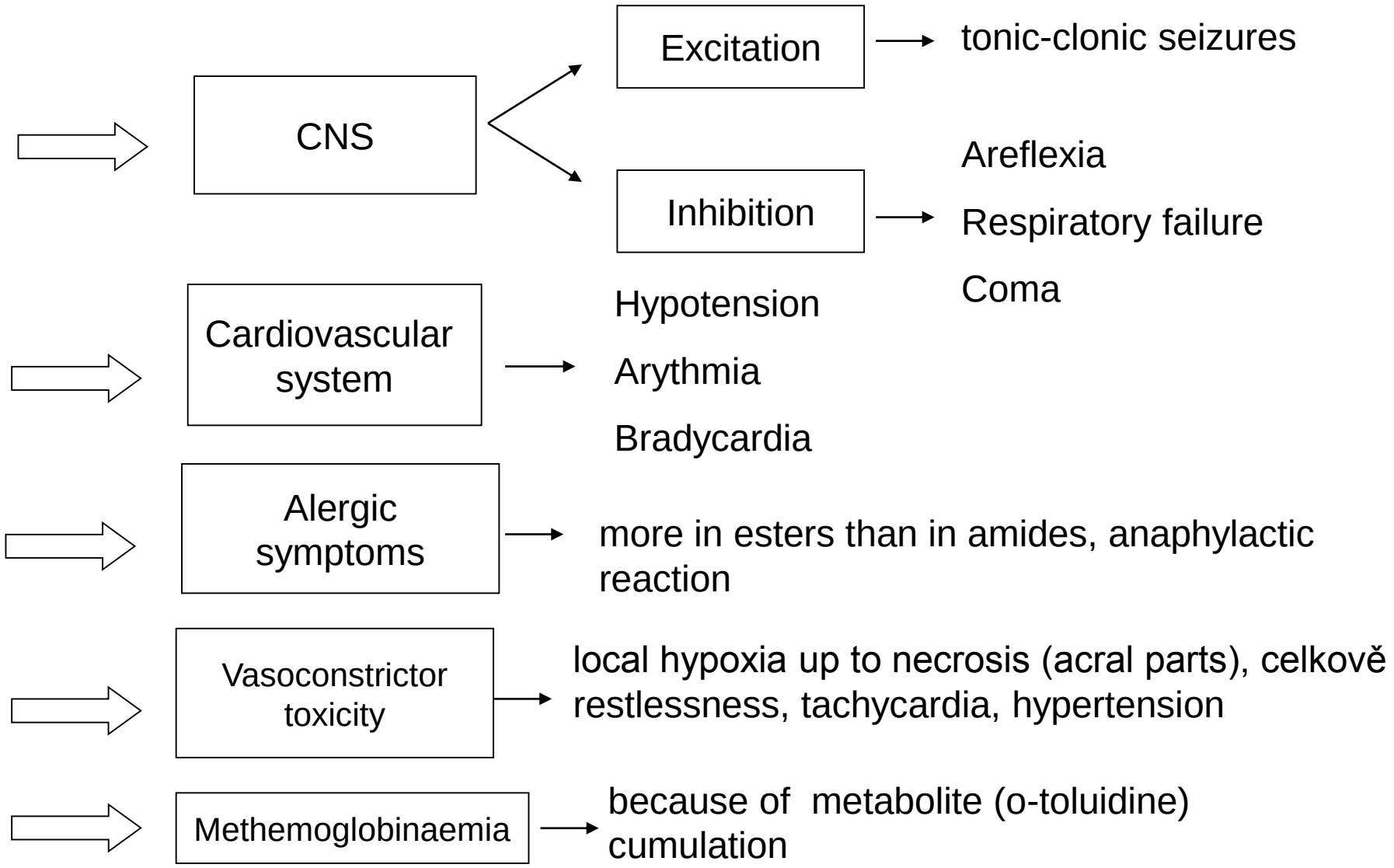
- intermediate

  trimecaine, lidocaine

- strong

  tetracaine, articaine, bupivacaine, ropivacaine

Toxic effects of LA



Alergic and anaphylactic reaction to LA

symptoms:

- pruritus
- urticaria
- swellings
- anaphylactic shock- restlessness, anxiety, breathlessness, vomiting
- Quincke‘s oedema – without inflammation, fast onset in face, affecting lips, face and throat (suffocation!!)

therapy:

- adrenaline 1mg in 10 ml of saline i.v.
- oxygen and infusion 5% glucose with noradrenaline
- hydrocortisone i.v.
- antihistamines
- in case of respiratory failure, keep free airways, artificial respiratory ventilation

Systemic toxic reaction to LA

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

- restlessness, hand tingling, hot or cold, nausea, vertigo, cold sweat
- tachypnoe
- tremor, fasciculations, 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 adrenaline i.v. if critical decrease of BP
- resuscitation in respiratory and cardiac failure