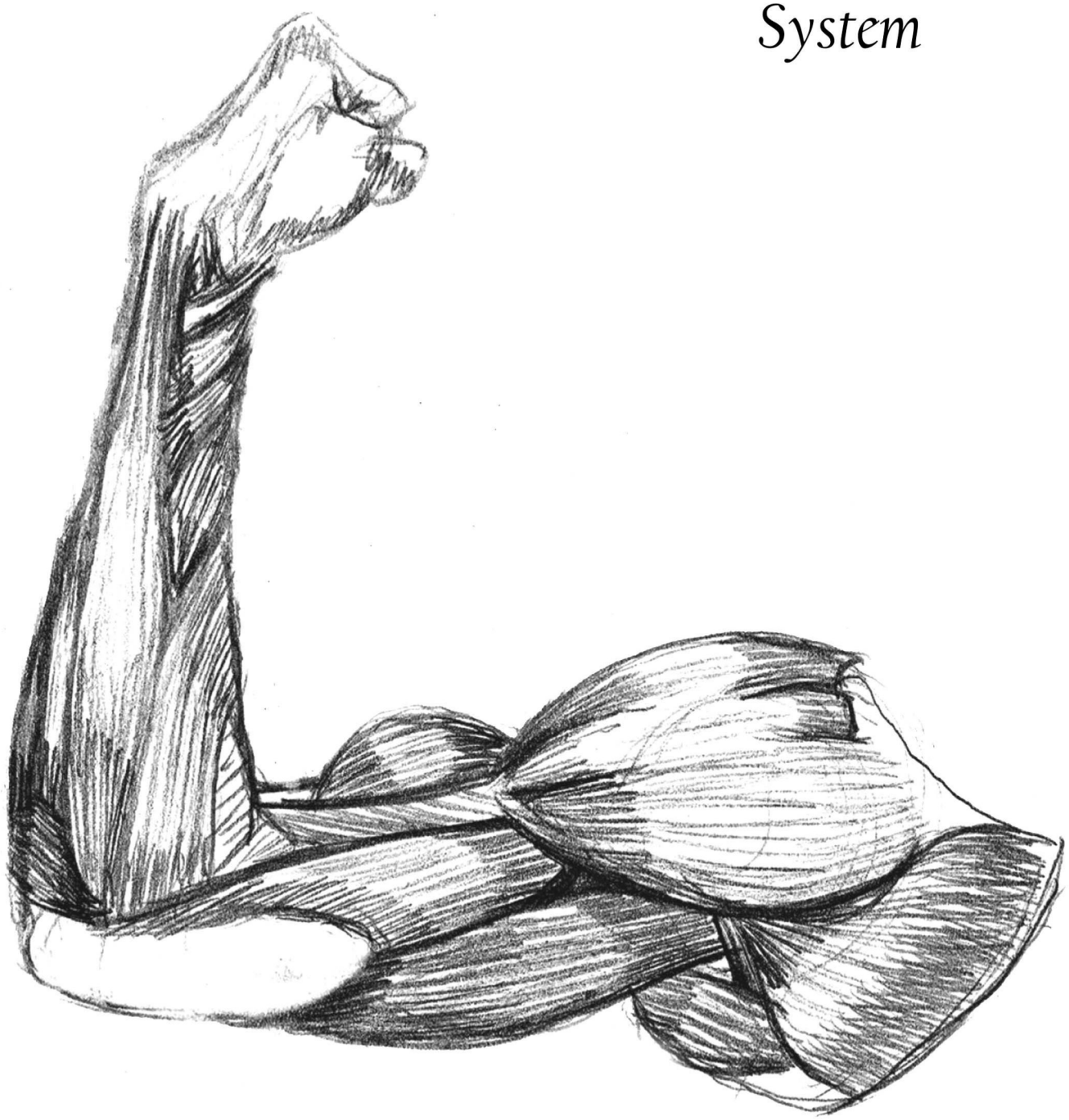
Medical Committee
The University of Jordan

The Skin and MUSCULOSKELETAL System



PHARMACOLOGY

SLIDES ☐
SHEET ■
LECTURE # 6

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Local Anesthetics & Muscle Relaxants

Local Anesthetics

*introduction:

- People started using local anesthetics before thousands of years ago, especially; Indian-americans in middle and South America, they used to chew leaves of coca plant, as psycholeptic agents, they are CNS stimulants.

-In 1860; they extracted cocaine from it, because it is CNS stimulant and causes physical and psychological effects.

- They caused numbness in tongue and mouth.

*mechanism of Action:

-Mainly Local anesthetics block Na-channels in meylinated and unmyelinated nerves (by mechanical means), so they block action potential.

*Examples on this group:

1-Procaine 2-Cocaine 3-Tetracaine=Amethocaine 4-Cinchocaine

5-Lidocaine=Lignocaine 6-Prilocaine 7-Bupivacaine 8-Benzocaine

-The most common one is Lidocaine (Lignocaine), also it is mainly used as antiarrhythmic drugs.

*Classification of local anesthetics:

1) Surface Anesthesia:

- Applied mainly on the skin or mucus membrane (ear, eye, nose, mouth, bladder, rectum, **bronical tree: using spray suspended particles whether they are on solid or gas forms**), then they get absorbed and interfere with pain sensory transmission.

-Mainly they are used to do procedures without causing pain.

-Sometimes we use them for: burn or injury or small procedures (surgery).

-Not effective for skin! Because these drugs can't pass through the striated layers of the epidermis and can't get absorbed so they don't reach nerves.

-**EMLA: (eutectic mixture of local Anesthetics)** application to the skin which is mixture of Lidocaine and Prilocaine.

From Wiki:

* Lidocaine/prilocaine is a eutectic mixture of equal quantities (by weight) of lidocaine and prilocaine.

*EMLA: trade name

-Main drugs used for this purpose: Lidocaine, Tetracaine (Amethocaine), dibucaine, benzocaine.

-Adverse effects:

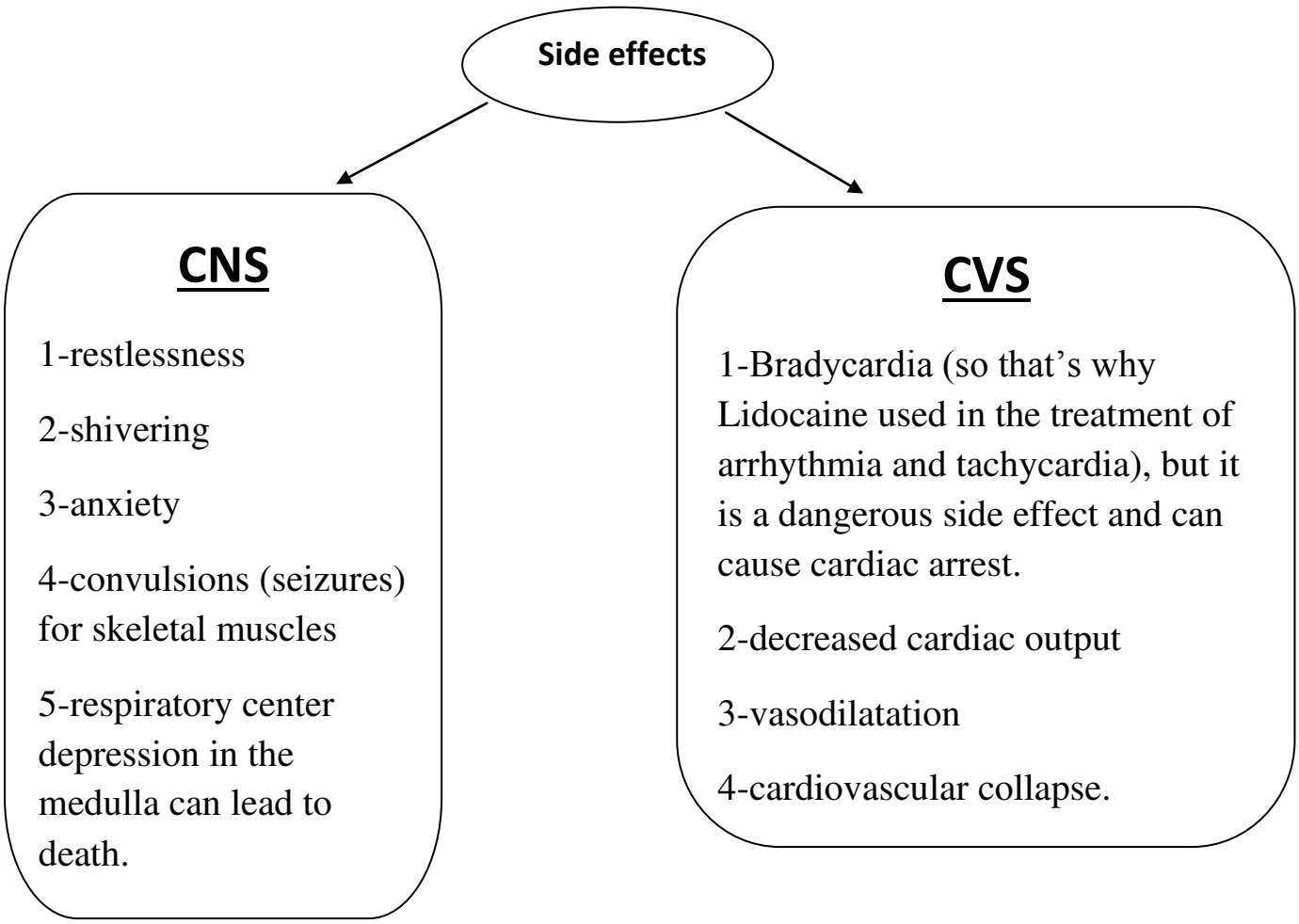
#Locally on the site it is so rare, nearly there are no side effects because it doesn't get absorbed, maybe there is a simple rash, itching, irritation, numbness and so on due to local anesthetics.

But if it gets absorbed and it goes to the systemic circulation it may cause serious side effects; this case happens when:

A) There is a large area of skin that has been covered with surface anesthetics; particularly in children especially babies because the absorption from their skin is faster.

B) High concentration of local anesthesia; like large amount to the skin so significant amount will get absorbed then it goes to the systemic circulation.

#The main side effects in (A + B) will be on:



2) Infiltration anesthesia:

- It is directly injected in the tissue, here you are closer to the nerve receptors, passing the skin and the injection will be around the nerve terminal and branches.

-This type is used in minor surgery; e.g.: in big toe procedure to the nail there, or abscess and in other small procedures (up to 15 min).

-In Past; squint was done by the ophthalmologist in the eye, they used local anesthesia but nowadays they use generalized Anesthesia. Because they used to believe that general anesthesia was dangerous because the patient here loses consciousness, however, sometimes local anesthesia is more dangerous.

-The toxicity is much due to the effect of the drug at the site of administration, the toxicity is mainly due to the absorption of the drug "when it is transferred from the site of injection to the systemic circulation ". ⇨

So if we need to inhibit or decrease the absorption of this type: we should administer vasoconstrictive substance; and as a consequence of constriction to the blood vessels, the amount reaching the systemic circulation will be hindered.

⇨ These drugs like: adrenaline, vasotensin* (*the sheet writer and the correction are not sure of this name) or such substances (catecholamines).

-This will help by prolonging the effect of the drug at the site of operation, also preventing the drug from reaching the systemic circulation and thus hindering or reducing the side effects.

-DON'T use vasoconstrictive drugs in the operation of toes or fingers; that's because there will be severe constriction and may cause tissue death (gangrene).

-Adverse effects:

Same as we mentioned above about CNS and CVS.

3) Intravenous regional anesthesia:

-How is it considered local and is given IV? We put an inflatable cuff (glove) around the arm for example and blow it so you prevent the return of the blood back to the systemic circulation then it will act locally, as we know there are anastomoses between veins, but this process shouldn't be applied for long time (up to 20 min) to prevent damage to the limb.

-Mainly it is used in operation to the limbs (arm, forearms, leg...)

- You block the veins without blocking the arteries as they carry the nutrients.

-Drugs used:

A) Lidocaine is known to have a short half-life and action when it's given orally, it will not reach the systemic circulation, high first pass effect almost 100%.

B) Prilocaine.

-Toxicity: it is very risky as they cause CNS and CVS effects. And this could happen when we remove the cuff prematurely.

4) Nerve block anesthesia:

-We search for the trunk of the nerve and inject anesthesia around the stem of the nerve

-Example on it: in the brachial plexus in cases of cancer for example, in the intercostal nerves, or in dental nerves (most).

-Sometimes it is very dangerous, and patients could die.

- The drug may get absorbed or the patient may have hypersensitivity, so you have to be aware that such injection of lidocaine is a serious procedure.

-Shouldn't be given in the nerve itself ~ causing paralysis.

5) Spinal anesthesia:

- It is injected in the spinal cord in the lumber or cervical regions (moving parts), placed inside the CSF, and it can cause allergy or change in the environment around the nerves in the spinal cord and plexuses.

-Act on the spinal cord and spinal roots.

-It is used when patients can't tolerate general anesthesia.

-It is used in: abdomen, leg, pelvic surgeries.

-this type could be dangerous and cause paralysis, it must be absolutely sterile to prevent any serious infections to CSF.

-Side effects:

Bradycardia, Hypotension, post-operative urine retention, respiratory depression and death.

6) Epidural anesthesia:

-Most common in pregnancy women who want to deliver without pain.

-The danger is when we want to make synergism between (opiate +local anesthesia) to lower the dose of the local anesthetic in pregnancy, opiates such as

Pethidine or morphine injected passing to the systemic circulation and passing the placenta and reach the fetus "it's a lipid soluble substance", so they will deliver without pain but the infant will be dead. So the application of such drugs is not encouraged.

-Injected in the epidural space blocking spinal cord.

-Drugs used: mainly Lidocaine, bupivacaine.

-side effects:

Bradycardia, Hypotension, depression to the respiratory center mainly to the infants, Urinary Retention.

-To get more effective analgesia, epidural anesthetics drugs are combined with opiates.

Why local anesthesia is considered more dangerous than general anesthesia?

-because local anesthesia is used for short period and in emergency cases usually, so there is no good investigation .But general one is given more properly done by specialist. Also, in the nature of the local anesthesia if they reach the systemic circulation it'll be dangerous. E.g.: Lidocaine concentration shouldn't exceed 2-3 microgram /ml.

Skeletal Muscle Relaxants

*Introduction:

-In South America, Indian-americans used curare-tipped arrows for hunting animals, this substance causes skeletal muscle paralysis.

-It is used in some surgery, when the muscles are contracted, or in convulsions and epilepsy.

-As we know in the neuromuscular junction (NMJ), there is a synaptic cleft, and the neurotransmitter is Acetylcholine, after stimulation comes from the central nervous system the action potential reaches the terminal then Acetylcholine can be released, and binds to its receptors which are (nicotinic receptors) after that it will be metabolized by Acetylcholine esterase producing: choline > reuptaken by the terminals, Acetate > gets destroyed.

*Classification:

-1) Acting pre-synaptically: by inhibiting Acetylcholine synthesis or release

2) Acting post-synaptically: by blocking Acetylcholine receptors.

*Clinical uses:

-There is no medical indication for skeletal muscle relaxants.

-Used as adjunct to general anesthesia, combination; there is a little risk, because it can cause respiratory muscle paralysis and respiratory depression.

*Mechanism of action:

-It works by interfering with the postsynaptic action of acetylcholine, they are divided into two groups:

1) Non-depolarizing drugs: (majority)

-Blocking Acetylcholine receptors -blocking ion channels

2) Depolarizing agents.

*Drugs act as muscle relaxants:

Suxamethonium:

-Most common drug, nicotinic receptor agonist, mainly used by general surgeons to induce intubation? anesthesia beside general anesthesia, before the contraction of the respiratory muscles . We put tube in the larynx for 10-15 min, then give

intravenous to relax the muscles so it prevents muscle reflex in the region of intubation.

-Neuromuscular blockers are clinically useful during surgery to facilitate tracheal intubation and provide complete muscle relaxation at lower anesthetic doses, allowing for more rapid recovery from anesthesia and reducing postoperative respiratory depression. "from book"

Pancuronium , Atracurium, Vecuronium:

-clinical use: are widely used as muscle relaxants in anesthesia
-Type of action: Nicotine receptor antagonists
Transmission block
-Site of Action: Neuromuscular junction.

*Main Side Effects:

Tubocurarine:

-Ganglion blockers - histamine release: A) bronchoconstriction B) hypotension

Suxamethonium:

-Bradycardia -cardiac dysrhythmia due to K+ release
-increase intraocular pressure: if there is an operation for the eye or procedure to remove the lens it is contraindicated because aqueous humour will get out.
-Malignant hyperthermia which is very rare.

Anti-leprosy drugs

-The number of people who are affected by leprosy is around 10 million in the world; mainly in: India

- Causative agent: Mycobacterium (tubercle) leprae.

-Drugs used: Dapson, Rifampicin, clofazimine.

Drugs for leishmanias

-Found in Iraq and Yemen, and Al-ghor. (Jericho Fly or sand fly)

-As we know: cutaneous, visceral, mucocutaneous forms. “Parasite”

-Treatment:

*In skin is self-limited. * It is preferred to give anti-fungal & anti-protozoal drugs (metronidazole “flagyl”, amphotericin B)

☺Special Thanks for who corrects this sheet☺

وَمَا انْتِفَاعُ أَخي الدّنْيَا بِنَاظِرِهِ إذا اسْتَوَتْ عِنْدَهُ الأنْوارُ وَالظُّلَمُ