Pharmacology – Extra Notes

Please pay attention that **only extra notes** will be mentioned

Some of the following notes may seem without any additive value, but since they were mentioned by the Dr. then why not write them down, it'll be more than enough if it helps at least one student ☺

◆ Slides #1

❖ Slide 2:

- Example on regional variation in drug penetration through the skin: penetration of the drug through the palm differs from its penetration through the genital skin.

- Keep in mind: A drug with a greater penetration is not necessarily better since sometimes there may be a risk of systemic absorption. It depends on the drug's purpose: If there is a superficial infection, we don't want the drug to be absorbed systemically.

- What is drug occlusion? The way the drug is dissolved in the formulation, some formulations have good penetration and others do not.

- What is a vehicle? It's a non-active/non-therapeutic component of a drug mixed with the therapeutic ingredient, which determines/designs the way the drug is absorbed into the body (topically, IM, IV…).

❖ Slide 3:

- The vehicle is a lot larger than the drug. Most of the tablets we take are made up of inert substances and only minute amounts of the active ingredient.
- Absorption through the subcutaneous tissue into the systemic circulation is very slow due to its limited blood supply.

❖ Slide 5:

- Tinctures are dyes.
- Wet dressings are bandages.
- Ointments are oily – المراهم -

❖ Slide 7:

- Topical agents: - Used for dermal/skin infections. - Minimally systemic absorption.
- Neomycin & Gentamicin are both very toxic, but luckily, they're mostly used topically and hence not absorbed systemically → no toxicity. But still, an exception is made for Neomycin -which is extremely toxic- as it can be administrated orally for GI sterilization.

❖ Slide 8:

- Pseudomembranous colitis can be treated with Vancomycin.
- Metronidazole is used both for protozoa and bacteria.
- All of the aforementioned drugs are also available for E and T use (Ear and Throat) as well as ophthalmic treatment.

❖ Slide 10:

- Nystatin and Amphocetericin B: oral suspensions are used to treat thrush.

❖ Slide 12:

- Oral agents are used for both oral and systemic infections, they will circulate through the body, but eventually, some portions will reach the skin.
- Prolonged treatment is required for nail infections, why? Since the nail is a dead tissue, and the drug is effective only on germinal layers, we have to wait until the infected nail tissues are fully replaced by new ones –which are not infected-, then we can stop the treatment.

❖ Slide 15:

- Permethrin: highly toxic cream in case of penetration.
- Malathion: irreversible Acetyl cholinesterase inhibitor "organophophate".

❖ Slide 18:

- More melanin = darker skin. If there is an excess of melanin or a deficiency, this indicates a certain disease.
- Depigmented macules of vitiligo: disappearance of melanin pigments from the underlying skin.
- The UV exposure must not be to sun, but a machine (PUVA).

❖ Slide 24:

- Acne is usually present due to blockage of the sebaceous gland.
- Isotretinoin: Vitamin A derivative. It is the last step of acne treatment and is only used for severe forms.
- Teratogenicity is a feature of Isotretinoin: this means that if this preparation is given to a pregnant lady, it'll cause congenital malformation(s) for the fetus.

❖ Slide 26:

- Psoriasis is scaling of the skin.
- Acitretin is a vitamin A derivative.

❖ Slide 28:

- Tazarotene is a vitamin A derivative.

❖ Slide 30:

- Hydrocortisone causes toxicity upon high doses & high absorption.

❖ **Slide 34:**

- The pituitary gland secretes ACTH and the adrenal gland produces secretes, this is suppressed → Suppression of pituitary-adrenal axis.

- Normally, corticosteroids are topical agents, very limited absorption may occur, thus no adverse effects are suspected, but if they were well absorbed upon high doses for example, they'll produce adverse effects. Toxicity depends on the surface area of the organ supplied by the drug. Also, richly supplied areas of skin hold a greater risk.

- Allergic contact dermatitis is a condition that occurs upon contact with clothes, etc, hence the name.

- Allergic contact dermatitis was mentioned in the previous slide -33- as a dermatologic disorder that is responsive to steroids (it is both an indication and a complication); however, some patients are sensitive to corticosteroids, so they'll develop allergic contact dermatitis as a local adverse effect upon usage of these agents.

❖ **Slides 38,39, 40, 41**- each slide a note respectively:

- Humectant activity: softening.
- Podophyllum Resin & Podofilox: good choice for warts. N&V = nausea and vomiting.
- Flurouracil: used as an anti-cancer agent.
- Diclofenac: its trade name is voltaren.

❖ **Slide 44:**

- Minoxidil: given topically locally. Was used in the treatment of high blood pressure.

❖ **Slide 54:**

- There's a relation between developing leprosy and contact with Armadello -حيوان المدرع-.

❖ **Slide 56:**

- RES: Reticulo-Endothelial System

◆ Slides #2

❖ Slides 3,4,5:

- The first two pictures represent the anatomy, physiology and pharmacology of the motor end plate: Ach binds → depolarization (EPP) → Muscle AP → spread to whole muscle via transverse tubules → contraction of muscle as a whole.
- Some drugs prevent AP firing by blocking Ach release, some inhibit depolarization and some inhibit muscle contraction.
- The last picture is of a nicotinic receptor and its units (two alpha, one beta, one gamma, one delta).

❖ Slides 9,10:

- Parenterally since they are lipophobic and hence poorly absorbed.
- Depolarizing drugs, only a small percentage reaches the NMJ, while the rest is metabolized.

❖ Slide 11,12,13,14:

- Succinylcholine functions as acetylcholine does, but with a prolonged depolarization and duration of action.
- The doctor said the table is only for making things clearer and is not that important.

- Non-depolarizing drugs, in high doses: enter the pore of the ion channel and hence occupy the receptor, inhibiting Ach binding, therefore there is no AP and there is no contraction.
- Tubocurarine is a standard muscle relaxant, functions as a competitive inhibitor of acetylcholine, results in no more contraction of the muscle upon an action potential. Potency of other drugs is measured relative to it. It is extracted from plants and is used by red Indians for hunting, Curare is not absorbed from the intestinal tracts so it is safe to eat the hunted animals.

- Tubocurarine is given IM → relaxes muscles, mainly respiratory.
- Its **antidote** is an acetyl cholinesterase inhibitor, which results in increased amounts of acetylcholine that can compete with tubocurarine on its receptor, thus, restoring the normal status of the muscle –responsive to action potentials by contracting-.

❖ Slide 26:

- Regurgitation is when the gastric juices go back into the larynx and the pharynx; this is due to the paralysis of the sphincters and may cause aspiration pneumonia.
- Muscle pain is only caused by depolarizing agents.

❖ Slide 28:

- Diazepam (Valium) is an anti-anxiety (anxiolytic) drug in small doses since it helps relax the muscles and is a sedative drug in high doses. Its receptors are found in the CNS.

❖ Slide 29:

- Baclofen is more useful than Diazepam since it is less sedative.

❖ Slide 31:

- Diplopia: double vision.
- Dysphagia: swallowing difficulties.
- Dysarthria: speaking difficulties.
- Dyspnea: breathing difficulties.
- The most common use of Botulinium toxin is for cosmetic purposes.
- Cerebral palsy: is a disease of the newborns, resulting from cerebral injury during birth by severe uterine contractions (شلل الدماغ).

❖ Slide 33:

- Malignant in this case doesn’t refer to cancer, it means 'difficult'.

◆ Slides #3

❖ Slide 1,2:

- Pain is a very important symptom as it is the main reason that drives people to seek healthcare.
- Different types of pain indicate different diseases.

❖ Slide 3:

- Narcotic Analgesics: specific receptors are opioid receptors in the brain and spinal card. Relieve both visceral and musculoskeletal pain. There is a great risk of addiction.

❖ Slide 5:

- COX1is essential and is produced all over the body.
- COX2 is produced in certain amounts and locally in response to a stimulus. (localized effect if blocked and drugs that target the receptor of the COX2 pathway are hence more selective)

❖ Slide 6:

- Arachidonic acid can undergo two pathways, LOX (lipooxegenase) and COX (cyclooxegenase); as you inhibit the COx pathway by NSAIDs you might stimulate the LOx pathway, leading to bronchospasm, congestion and bronchial asthma.

❖ Slide 7:

- Antipyretic: reduces fever, it is the original indication for these drugs (old). The prototype is aspirin.
- They used to believe that pain was only due to a central effect until the discovery of prostaglandins.
- Anticoagulant: This is fairly recent. Primary use of Aspirin: prevents platelet coagulation, especially people with ischemic heart diseases.
- Anti-inflammatory: Aspirin was used for treating rheumatoid arthritis in high doses and hence was toxic. This is no longer done.

❖ Slide 8:

- Allergenic: Some people are very sensitive to this and may develop asthma even when taking small doses.

❖ Slide 9:

- PG work as a homeostatic mechanism to preserve the integrity of the intestinal and gastric mucous membranes.

❖ Slide 10:

- Hepatic dysfunction is rare. Acetaminophen is paracetamol.
- Low doses inhibit uric acid secretion; this may lead to uric acid retention and hyperuricemia.
- Uterine relaxation: especially in late pregnancy (last few weeks) since the uterus will be sensitive to PG activity, this will delay labor for a few days.

❖ Slide 11,12:

- Salicylates are the prototype for NSAIDs; they are derived from salicylic acid. Replace an acetyl group → Aspirin, which is acetyl salicylic acid.
- They are weak acids, at their pka they are 50% ionized 50% unionized, the unionized form is the absorbed form. Their pka is almost the same as the stomach's pH (fasting). They are mostly absorbed in the small intestine.
- They are highly protein bound; therefore, can displace other drugs that have a lesser affinity to plasma proteins and hence enhance their toxicity. Protein binding functions as a reservoir for the drug.
- First order: depends on normal decay, follows the half life principle. This applies to most drugs, although aspirin follows zero order kinetics when used in high doses. Zero order: doesn't depend on the half life.
- Salfasalazine: anti inflammatory, used for inflammatory bowel diseases such as ulcerative colitis, not used orally, usually given through rectal administration.

❖ Slide 13:

- Salicylate is excreted in all these forms in the kidneys as well as free salicylate.

❖ Slide 14:

- ADR = adverse drug reactions, this is an extension of the pharmacologic activity of salicylate.
- Hyperventilation: causes respiratory alkalosis with high doses of aspirin/salicylate.

- Salicylism: noticed a long time ago when the willow tree (الصفصاف) was used by red Indians, they used to cook the plant and treat fever with it, the leaves caused some toxicity.
- Symptoms of Salicylism include: delirium, hyperventilation, severe tinnitis and severe headache.

- Reye's syndrome: hepatoencephalopathy. For this reason salicylate is no longer used to treat children. (There is baby aspirin: the dose is baby (smaller dose), it is not for babies!)
- Ulcerogenic: most important problem when it comes to NSAIDs occurs even with lower doses.

❖ Slide 15:

- Acetaminophen: in America. Paracetamol: in Europe, Jordan.
- Weak PG synthesis inhibitor compared to salicyalte, which leads irreversible inhibition that lasts for the whole life of the enzyme and hence new enzymes must be synthesized, it takes a week to regenerate them. We conclude that Acetaminophen is not a good anti-inflammatory agent
- It crosses the blood-brain barrier. It is a good analgesic since it works also on CNS levels. May be a better analgesic than salycilate since it doesn't inhibit PG synthesis profoundly, and it doesn't cause severe GI irritation.

❖ Slide 17:

- Severe hepatotoxicity with high **suicidal** doses (intentional overdose, not accidental). It is still the safest drug.
- N- acetylcysteine is the antidote, it replenishes glutathione stores when given in the first 24 hours, but it is difficult to detect a suicidal dose in the that time period.

❖ Slide 18:

- First day: Emesis (vomiting) diaphoresis (excessive sweating)... etc are all non-specific symptoms. In the next day, signs of hepatic necrosis…etc + lab signs → progression of disease. If the condition is not treated/reversed by the 3rd stage → comma. By the 4th stage (5-21 days), the patient will die if untreated.

❖ Slide 19:

- Nomogram: a type of graphs. This one predicts prognosis. Above blue line → probable hepatotoxicity.

❖ Slide 21:

- Can be given parenterally for renal colic (spasm of smooth muscles, severe pain). Can also be given through IV administration. Its commercial name is Voltaren.

❖ Slide 22:

- Mild activity on the stomach. Intermediate between the two previously mentioned drugs in potency. Very safe. Teratogenic whereas paracetmol can be used by pregnant women.

❖ Slide 23:

- Old, no longer used due to toxicity.
- Pancytopenia**:** Elimination of bone marrow elements (WBC) → bone marrow suppression.

❖ Slide 24:

- COx II: the induced form of COx at the sites of inflammation. They are more effective in treating inflammatory processes. They are selective for COx2 whereas the rest have a wide-spread action.
- Selective: relative, variable, lost with higher doses. Specific: Exact/definite.

❖ **Slide 27:**

- Takes weeks to months, whereas the rest work immediately.
- Hydroxychloroquine: Antimalarial. Thalidomide: phocolemia (loss of limbs). Gold salts: rheumatoid arthritis.

❖ **Slide 29:**

- Biologic: immunologic, affect various regions of IgG.

❖ **Slide 32:**

- Gout: A chronic inflammation due to uric acid crystals accumulating in joints → inflammation process activated → mono/polynuclear phagocytes are recruited. We need anti inflammatory drugs as well as drugs that help excrete uric acid or inhibit its synthesis.

❖ **Slide 34**:

- Colchine: Not a NSAIDs. Anti-inflammatory, very effective/potent for treatment of acute gout (usually due to hypercalcemia) since it is rapidly absorbed.

❖ **Slide 37:**

- Probenecid: prevents urinary elimination of Penicillin and enhances uric acid excretion in urine.
- Sulfinpyrazone: anti-inflammatory.

❖ **Slide 38:**

- Allupurinol: prevents the formation of uric acid by inhibiting Xanthine Oxidase. Also used in the case of hyperuricemia.
- Zyloric (not written in the slides!): inhibits uric acid formation.