**TOPICAL AGENTS AND ANTISEPTIC AGENTS**

**To be able to classify topical drugs, their MOA and indications under below sub topics;**

1. Ophthalmic drugs; mydriatics, antibacterial, antivirals,anaesthetics, anti-allergic
2. Dermatological preparation, antibacterial antifungals, antiseptic, antipruritis, anti-ectoparasites preparation.
3. keratolytic, topical steroids, antibiotics
4. **Ophthalmic drugs;**

**Introduction**

The bioavailability of intra-ocular administered drugs depends on pH and other pharmaceutical properties of the vehicle. Mostly delivered as drops in aqueous solution.

Formulations which prolong the time in contact with the eye surface are gels, ointments, solid inserts, soft contact lenses and collagen shields.

Drug penetration into the eye itself is approximately linearly related to the concentration of drug applied.

Nasolachrymal drainage plays a key role in the systemic absorption of drugs administered to the eye which undergoes hepatic first-pass metabolism. Thus ocular drugs such as β-adrenergic antagonists can cause wheezing in asthmatic patients.

**Classification**

mydriatics, antibacterial ,antiviral, anaesthetics, mycotics, anti-allergic, antiseptic, antipruritis,

**i)Mydriasis** (**pupillary dilatation)**

Pupillary dilatation is often required for detailed examination of the retina.

Two groups of drugs dilate pupils ;-muscarinic antagonists (anticholinergics) and sympathomimetics.

Short-acting relatively weak mydriatics, such as **tropicamide**, facilitate retinal examination. **Cyclopentolate** and **atropine** are preferred for producing cycloplegia (paralysis of the ciliary muscle) for refraction in young children. **Atropine** is also used for the treatment of iridocyclitis (inflammation of the iris) mainly to prevent posterior synechiae( adhessions of the iris), when it is often combined with **phenylephrine**.

**1. Anticholinergics mydriatics eye drops**

**Tropicamide;** Single drop of 0.5% solution, Photosensitivity and blurred vision and maximum onset of effect is systemic absorption can occur in 20–40 min and lasts 3–6 h

**Cyclopentolate;** Single drops of 0.5 or 1.0%

adverse effect as above. All anticholinergics are antagonists at the solution, maximum onset of M3 receptor on the effect is in 30–60 min and ciliary muscle lasts 24 h

**Atropine;** Single drop of 0.5 or 1.0%, maximum onset of effect is 30–40 min and lasts 7–10 days adverse effect as above

**2. Sympathomimetics** /**Sympathetic stimulation: α1-agonists**

**Phenylephrine;** One of two drops of 10% Systemic absorption can occur (avoid in solution, lasts up to 12hr patients with coronary artery disease or hypertension)

**ii) Antibiotics/drugs used to treat eye infections**

Appropriate selection of an antibacterial agent and the route of administration depend on the clinical findings and culture and sensitivity results. Acute bacterial conjunctivitis is usually due to *Staphylococcus aureus* or *Streptococcus*.

Chloramphenicol, gentamicin, fusidic acid or one of the fluoroquinolones (e.g. ciprofloxacin, ofloxacin), all of which are available as eye drops, may be appropriate. neonatal eye infection apply **TEO** once in both eys

**Eye drops**

**Broad-spectrum** **antibacterials -> {**Chloramphenicol, Fluoroquinolones (e.g. norfloxacin, ofloxacin, ciprofloxacin) Framycetin sulphate , Aminoglycosides (e.g. gentamicin sulphate, neomycin sulphate), Ciprofloxacin hydrochloride **}**

**Specific antibiotics**

Chlortetracycline 🡪Chlamydial infections

Gentamicin sulphate and Tobramycin-**-->** Pseudomonas aeruginosa infections

Sodium fusidate- **-->**Staphylococcal infections Hypersensitivity reactions

**Side effects**.

* All the eye drops causes local burning and itching and hypersensitivity reactions
* **Cipr**ofloxacin drops causes corneal ulceration; best avoided in children Local irritation and hypersensitivity reactions.

iii) **Antiviral agents for eye infections drugs**

**Drug Route --------------🡪Indication for use**

* Idoxuridine Topical**-->** Herpes simplex keratitis
* Aciclovir Topical (3%) **-->**Herpes simplex keratitis.
* Foscarnet Intravenous/intravitreal- **-->**Cytomegalovirus retinitis
* Ganciclovir Intravenous/intravitreal**-->** Cytomegalovirus retinitis

**Toxicity;** Punctate keratopathy (death of the cells on the surface of iris and pupil) and hypersensitivity

**iv) Anti-allergy drugs used to treat inflammatory disorders in the eye**

**a) NSAIDs** are used to reduce post-operative inflammation.

Several ophthalmic preparations are diclofenac, flurbiprofen and ketorolac.

**b)Sodium cromoglicate** or **nedocromil** drops are used in long term treatment of allergic conjunctivitis.

its very safe and only causes local stinging as a S.E

**c) Glucocorticosteroids**

Example preparations; **hydrocortisone** or **betametasone;**

**available** as drops or ointment).

Topical ocular glucocorticosteroids should only be used under specialist supervision to treat uveitis and scleritis, and sometimes in the post-operative setting.

**Side effects/ contraindications**

Exacerbate glaucoma in genetically predisposed individuals

Thinning of the cornea or perforation of the sclera may occur in susceptible patients.

They should **never** be used to treat the **undiagnosed ‘red-eye’** which could be due to a herpes infection, may progress to loss of the eye.

**d) Antihistamines and mast cell stabilizers**

Examples; antazolineand **azelastine**.

use; to treat allergic or seasonal conjunctivitis.

side effects

Ocular irritation, oedema of the eyelids orblurred vision can occur

systemic effects (e.g. drowsiness).

**v) Local anaesthetics and the eye**

* **Oxybuprocaine** and **tetracaine** -> topical local anaesthetics.
* **Proxymetacaine** causes less initial stinging ->useful in paediatric patients.
* **Tetracaine** -> minor surgical procedures. **Oxybuprocaine** or a combination of **lidocaine** and **fluorescein** ->used in tonometry (test procedure detecting intraocular pressure).
* **Lidocaine** +OR - **adrenaline** is often injected into the eyelids –for minor surgery.
* **Lidocaine** inj--**>** surgical procedures on the globe of the eye.

**vi) Drugs used to constrict the pupil and to treat glaucoma**

Principles of therapy for glaucoma

Acute glaucoma is a medical emergency.

**Mannitol** can reduce the intra-ocular pressure acutely by its osmotic effect.

In addition, therapy with a carbonic anhydrase inhibitor (iv acetazolamide or topical dorzolamide) may be required.

This is then supplemented with either a topical β-adrenergic antagonist (e.g. timolol) or a cholinergic agonist (e.g. pilocarpine), or both

**Topical agents for glaucoma**

* **Dorzolamide 2% solution**

It’s a topically applied carbonic anhydrase inhibitor, which may be used either alone or as an adjunct to a β-blocker**. MOA;** works by reducing amount of fluid produced by the eye. Systemic absorption does occur and systemic side effects (e.g. rashes, urolithiasis) may require drug withdrawal.

**Adverse effects**; local irritation of the eye and eyelid with burning, stinging and visual blurring, drooping of the eyelid, dry eyelids , sore throat and a bitter taste.

* **Prostaglandin analogues**

**Latanoprost 0.005% ;** prostaglandin F2α analogue.

It is used in those intolerant of β-blockers or as add-on therapy when the response to the first drug has been inadequate.

it is inactive prodrug which readily penetrates the cornea and is hydrolyzed to the free acid which diffuses out of the cornea into the aqueous humour and lowers the intra-ocular pressure by increasing uveoscleral outflow.

Systemic absorption does occur via conjunctival and mucous membranes. Latanoprost is cleared by hepatic metabolism.

**Side effects**; local irritation with stinging, burning and blurred vision.

Punctate keratopathy, and it increases the amount of brown pigment in the iris in patients with mixed-coloured eyes, which may be a cosmetic problem.

T**ravoprost** and **bimatoprost** are related prostaglandin analogues.

* **α2-AGONISTS**

**Brimonidine/alphagan 0.1% or 0.15%**

is a selective α2-agonist, used for chronic open angle glaucoma when other drugs are unsatisfactory.

Used alone or as an adjunct to β-blocker therapy in chronic glaucoma.

It decreases aqueous humour production and increases uveoscleral flow.

Trace amounts do get into the circulation and undergo hepatic metabolism.

**Toxicities;** local ocular irritation and occasional corneal staining

**Systemic adverse effects;** dry mouth, headache, fatigue, drowsiness and allergic reactions.

contraindicated; patients taking monoamine oxidase inhibitors (MAOIs)

Precaution;severe coronary artery disease or taking tricyclic antidepressants**.**

**Apraclonidine ;** selective α2-agonist which is formulated for ophthalmic use**.**

1. **DERMATOLOGICAL PREPARATION, ANTIFUNGALS**

**INTRODUCTION**

Skin conditions account for up to 2% of consultations in general practice.

Adverse reactions to topical or systemic drugs produce a wide variety of skin lesions.

Drugs applied topically to the skin may act locally and/or enter the systemic circulation and produce either a harmful or beneficial systemic pharmacological effect. “If it’s wet, dry it; if its dry, wet it.

**Percutaneous absorption**

The rate of diffusion of a chemical across the skin is related to the features below:

• Its concentration when applied

• The surface area to which it is applied

• Its movement through the epidermis (the *diffusion constant*) decreasing the barrier to its mobility through the layers hydrate the skin

• The relative tenacity with which it binds to its vehicle compared with epidermis (the *partition* *coefficient*) by increasing its hydrophobic component

• The thickness of the stratum corneum (barrier) absorption is also greater in regions in which the skin is thinner.

**What to consider**

* Treatment of skin disorders depends on accurate diagnosis; steroids are not useful for all rashes and may cause harm if used inappropriately.
* Acne is treated first line with keratolytics; and if systemic antibiotics are indicated, use oral oxytetracycline or erythromycin (but do not use tetracyclines in children under 12 years). Vitamin A analogues should only be used in refractory cases.
* In eczema, identify the causal agent and minimize/eradicate exposure if possible.
* For dry, scaly eczema, use **emollients** plus a keratolytic; for wet eczema use drying lotions or zinc-medicated bandages.
* Topical **glucocorticosteroids** are required, but dont use high-potency glucocorticosteroids on the face. Use the lowest potency steroid for the shortest time possible required producing clinical benefit.
* In psoriasis, simple emollients should be used to treat mild cases. Keratolytics may be used in moderate cases.
* Additional therapies for more severe cases of psoriasis include topical vitamin D analogues, PUVA, oral **acitretin** and cytotoxic drugs. Although glucocorticosteroids are effective, tachyphylaxis occurs, and on withdrawal pustular psoriasis may appear.

1. **Topical antibacterial skin prep.**

Topical treatment is often employed using **topical antibacterials**, **zinc sulfate, lime sulfur, and iodine** containing compounds

Antibacterials incorporated into topical preparations include: chlortetracycline; oxytetracycline, neomycin,which may be effective against superficial infections caused by bacteria including: Bacillus; Actinomyces; Clostridium; Streptococci and Staphylococci.

**Fusidic acid**

effective against infections caused by Staphylococci; Actinomyces; Neisseria and some Clostridium species.

**Fungal skin infection**

**Antifungal Drug therapy**

**Dermatophytoses**

Ringworm infection can affect the scalp (tinea capitis), body (tinea corporis), groin (tinea cruris), hand (tinea manuum), foot (tinea pedis, athlete’s foot), or nail (tinea unguium). Scalp infection requires systemic treatment; additional application of a topical antifunga

**Candida infection of the skin->** Topical antifungal therapy with nystatin

Alternative topical agents are terbinafine vulvovaginitis or balanitis cream (100 000 units/g) or ketoconazole 2%, 1% or amorolfine 0.25% creams.

Systemic clotrimazole 1% or miconazole 2% cream therapy may be necessary in refractory cases. Consider underlying diabetes mellitus

**Fungal nail infections and onychomycosis dermatophytes -->**

Griseofulvin, 10 mg/kg daily for 6–12 months, or alternatively fluconazole200 mg daily, is applied daily for 6 months. If systemic therapy is not tolerated, tioconazole 28% for 6–12 months or amorolfine 5% is an alternative

**Pityriasis capitis, seborrhoeic dermatitis (dandruff) ->**Topical steroids clobetasol propionate severe cases may require additional 0.05%, or betamethasone valerate 0.1% with shampoo, topical ketoconazole 2% or clotrimazole 1%

**Pityriasis versicolor** /Pityriasis (tinea) versicolor ; treated with ketoconazole shampoo. Alternatively, selenium sulfide shampoo [unlicensed indication] can be used as a lotion.

**Tinea capitis ->**Systemic therapy with fluconazole, – itraconazole, miconazole or clotrimazole **Tinea corporis and Tinea pedis->** topical ketoconazole 2% or clotrimazole 1% applied for 2–3 weeks

**EXAMPLES OF antifungal preperations**

MOA;polyenes bind ergosterol; azoles inhibit 14-alpha demethylase;

allylamines inhibit squalene epoxidase.

**Butenafine\*** (Mentax) 1% cream 15, 30 g

**Ciclopirox** (Loprox) 1% cream, lotion 15, 30, 90 g

**Ciclopirox** (Penlac) 8% nail solution 6.6 ml

**Econazole\*** (Spectazole) 1% cream 15, 30, 85 g

**Ketoconazole\*** (Nizoral) 2% cream 15, 30, 60 g **Ketoconazole** (Nizoral) 2% shampoo

**Miconazole\*** (Micatin) 2% cream, powder, spray 15, 30, 90 g

**Naftifine\*** (Naftin) 1% gel, cream 15, 30, 60 g

**Oxiconazole** (Oxistat) 1% cream 15, 30, 60 g

**Clotrimazole** (Lotrimin, Mycelex)1% B cream, solution, lotion

**Ketoconazole** (Nizoral) 1% cream, shampoo

**Miconazole** (Zeasorb-AF Powder) 2% powder

**Terbinafine** (Lamisil) 1% cream, solution, spray

**Topical steroids**

Steroids or glucocorticoids are used in treating eczema, psoariasis and inflammatory skin conditions that cause pururitis

**Choice of formulation**

**Water-miscible steroid creams** are suitable for moist or weeping lesions whereas **ointments** are chosen for dry, lichenified or scaly lesions or where a more occlusive effect is required.

**Lotion**s; useful when minimal application to a large or hair-bearing area is required or for the treatment of exudative lesions.

**Occlusive polythene or hydrocolloid dressings** increase absorption, but also increase the risk of side effects; they are therefore used only under supervision on a short-term basis for areas of very thick skin (such as the palms and soles).

**MOA ;** prevents formation of mediators of inflammation forming cells.

They also affect collagen metabolism. Best absorbed from face, genitals and nappy areas.

Prolonged use in children may cause growth retardation.

C/I; perioral dermatitis, tb, viral,fungal, scabies dermatitis.

N/B not used as prophylaxis for a long period of time especially in children as it can cause adrenal suppression

ADR; Striae, folliculitis, skin atrophy, telengestiasis, hypersensitivity, pigmentation changes, acne formation and risk of secondary skin infections

**Drug examples**; betamethasone 15g cream 0.5%, hydrocortisone skin ointment.

combinations with antibiotics; quinocort/quinoderm has potassium hydroquinolone 0.5% and 1% hydrocortisone cream, extraderm contains betamethasone 0.1% and gentamycin 0.1% apply bd

1. **KERATOLYTIC, TOPICAL STEROIDS AND ANTIBIOTICS**

**Retinoids**

Are a family of naturally occurring and synthetic analogues of vitamin A.

The skin of subjects deficient in vitamin A becomes hyperplastic and keratotic

* E.g; keratolytic—Isotretinoin 30g 0.05% gel and po 10mg caps
* Topical tretinoin (*Retin-A,*
* acitretin (*Soriatane*)
* *Tazarotene*

**keratolytic—Isotretinoin 30g 0.05% gel and po 10mg caps**

MOA; Alters sebaceous glands and shrinks them🡺 reducing sebum excretion and comedogenesis

**uses;** for corns and calluses, warts, palmoplantar keratodermas, ichthyoses, and psoriasis

High doses of isotretinoin (2mg/kg/day) are effective as cancer chemoprevention agents to reduce the frequency of cutaneous malignancies in patients at increased risk

Indications

Primary keratinization dis-orders like **acne** vulgaris

Dosage for oral 0.5mg/kg daily for 4-8weeks or gel bd for same duration

**Side effects**

* Keratoconjuctivitis sicca (dry eyes due to inadequate moisture by tear)
* Joint and leg pain
* Mild elevation of serum alanine-aminotransferase, cholesterol and triglyceride concentrations
* erythema,hypopigmentation
* Inhibition of spermatogenesis
* extended teratogenic effect as a result of tissue storage for long periods.

**Warnings**: Monitor changes in haematology, blood chemistry, urine and tear production, teratogenic in humans

**tretinoin**

**Indications**

Primary keratinization disorders

**Side effects**

* Occasional allergic or irritant reaction.
* **Warning**: Gloves should be worn when applying the preparations; should not be applied by pregnant women.
* **Dose** apply daily until remission, then as necessary for maintenance. *Available preparations include:*

**POM Retin A (Janseen-Cilag) UK**

* *Cream,* tretinoin, 0.025%
* *Gel*, tretinoin 0.01%, 0.025%
* *Lotion,* tretinoin, 0.025%.

**Salicylic acid 16.7%**

* I**ndications**; acne, psoriasis and seborrhea, planter warts and dandruff.

Apply using applicator daily on only affected areas avoiding the facial and anogenital areas

**Selenium Sulfide**

Is a cytostatic and sporicidal agent

prepared in shampoos and lotions for scalp seborrheic dermatitis.

Higher concentrations are available by prescription for the treatment of pityriasis versicolor, which is caused by the yeast M. furfur, and tinea capitis.

**Others keratolytics**

**polytar liquid**( tar 0.3%,cade oil 0.3% coal tar 0.1% with arachis oil and alcohol 0.1%)

* Used on wet hairy areas. applied daily or thwice weekly until it clears
* Indications; acne,psoriasis and seborrhea,planter warts and dandruff

**For genital warts;**

**podophyllum** 20% ointment applies Pt leave on for 1–6 h then wash off 15 ml

**Imiquimod** (Aldara)**;** Apply to genital warts 3xweekly at night 5% cream 24 pks of 250 mg each

**Podofilox** (Condylox)**;**

Apply to genital warts bid 3 days/week consecutive 0.5% gel, soln 3.5 g

* Used for planter warts, applied two or three times weekly cover with plaster or occlude the area after application.
* contra indication ;pregnancy
* ADR; Inflammation of the surrounding skin. stop treatment if occurs

**Bleaching Agents/Depigmenting Agents**

All contain hydroquinone which inhibits enzymatic oxidation of tyrosine to 3-(3,4 dihydroxyphenyl-alanine [dopa]). Some agents also contain topical steroids, retinoids, sunscreen (SS); glycolic acid (G). **Hydroquinone\*** 4% cream

**Benoquin** 20% cream/ Monobenzone 20% 35.4 g. final depigmentation Apply bid until effect (2–4 months)

**Skin cleansers and Disinfectants**

Alcohol (70%) is commonly used for its solvent properties for the removal of superficial contamination.

**Cetrimide**, **Chlorhexidine**, and **Povidone-iodine** are used for skin dis-infection. Contaminated wounds should be thoroughly washed with isotonic solutions such as sodium chloride 0.9% solution (Normal saline) or ringer’s solution.

If the wound is less than three hours old, antibacterials in the lavage solution will decrease the occurrence of wound infection. They work best if soaked within3 hours

**Antiparasitics**

**Parasiticidal preparations for the skin**

Scabies

**Permethrin or** **malathion** or **Benzyl benzoate**

Used; treatment of scabies (Sarcoptes scabiei);

malathion and permethrin should be applied twice, one week apart;

for benzyl benzoate in adults, up to 3 applications on consecutive days may be needed. It is important to warn users to reapply treatment to the hands if they are washed.

Patients with hyperkeratotic scabies may require 2 or 3 applications of acaricide on consecutive days to ensure that enough penetrates the skin crusts to kill all the mites.

**head lice (**Pediculus humanus capitis**).**

Should be treated using lotion or liquid formulations only if live lice are present.

use diluted shampoo

A contact time of 8–12 hours or overnight treatment is recommended for lotions and liquids; a 2-hour treatment is not sufficient to kill eggs.

In general, a course of treatment for head lice should be 2 applications of product 7 days apart to kill lice emerging from any eggs that survive the first application.

All affected household members should be treated simultaneously.

**Permethrin\*** (Elimite); scabies: 5% cream. Apply from neck to soles of feet, leave on overnight for 8–12 h, wash off in am; repeat in 1 week 60 g

**Permethrin\*** (Nix) For lice: 1% soln. Apply cream rinse to hair/scalp, leave on 10 min, shampoo hair. Repeat in 1 week. Use comb 60 ml

**Malathion** (Ovide) For lice 0.5% lotion; Apply to dry hair/scalp. Wash out after 8–12 h. Repeat in 1 week. Use nit comb. *(Best effi cacy among chemical pediculicides)*

**Ivermectin** (Stromectol); for scabies 6 mg

**SUNSCREENS**

Absorb ultraviolet radiation before it can be absorbed in the skin.

They are recommended to protect the skin from the major toxicities of sun exposure: sunburn and skin cancer.

Most available agents primarily absorb UVB, although newer preparations also provide protection against UVA.

**Physical sunscreens** (generally opaque, e.g **titanium dioxide** and **zinc oxide**) block all ultraviolet radiation.

The frequency of application of sunscreen is guided by the **SPF** (sun protection factor) of the preparation.

This derived value is the ratio of the time of ultraviolet exposure that causes erythema with the sunscreen to the time that causes erythema without the sunscreen. The higher the SPF, the less frequent the needed application of sunscreen.

ANTISEPTICS AND DISINFECTANTS /UNDECENOATES

**Undecenoic acid with zinc undecenoate** Treatment of athletes foot

to the skin Child: Apply twice daily, continue use for 7 days after lesions have healed

▶ Adult: Apply twice daily, continue use for 7 days after

lesions have healed

Prevention of athletes foot

**Chlorhexidine with nystatin**

Skin infections due to Candida spp.

TO THE SKIN Apply 2–3 times a day, continuing for 7 days

after lesions have

CAUTIONS Avoid contact with eyes and mucous membranes

Side effects Hypersensitivity . skin reactions

**BENZOATES/Benzoic acid with salicylic acid**

Ringworm (tinea) Apply twice daily

l CAUTIONS ; Avoid broken or inflamed skin . avoid contact with eyes . avoid contact with mucous membranes