

• pharmacology

* Antifungal

- 1 polyene (fungicidal)** → **tergosterol**
- **Amphotericin B** :: systemic infection, slow IV infusion, ↓ penetrate BBB, long t_{1/2}, Renal toxic. Liposomal penetration (↓ toxicity).
 - **Nystatin** :: toxic in systemic use, Tx for superficial candidiasis of mouth, esophagus & GIT (P).
 - **Natamycin** :: not absorbed P_o, Fungal Keratitis (eye).

2 flucytosine :: fungistatic, ↓ DNA, effect in meningitis + AIDS, synergistic with Amphotericin B.



- 3 Azoles (fungistatic)** → **↓ P₄₅₀ demethylase** → **tergosterol** → **↓ growth**
- **Ketoconazole** :: good in P_o, ↓ adrenal & gonadal steroidogenesis (tx chushing & prostate ca), ↓ tergosterol → ↓ Action of Amphotericin B. ↓ Bioavailability with (H₂ blockers, PPI).
 - **Fluconazole** :: good in P_o (plasma in P_o = IV), not altered by acidity, Itraconazole is better in same dose, ↓ drug interaction, doc (cryptococcal meningitis & coccidiomycosis), AIDS.
 - **Itraconazole** :: poor IV, food → ↑ absorption, Loading doses, ↑ Lipid soluble
 - **Voriconazole** :: ↑ potent, Reversible visual disturbances.
 - **posaconazole** :: Broad-spectrum, SI: GIT symptoms, Mucor species & zygomycetes.
- Triazoles

 - penetrate CNS
 - ↓ endocrine disturbance
- Azole Family**

Imidazoles	Triazoles
Ketoconazole Miconazole Clotrimazole	Fluconazole Itraconazole Voriconazole

4 Echinocandias → **capofungin** :: ↓ β-D glycan synthesis, ↓ metabolized (N-acetylglucosamine, fungicidal).

5 cutaneous mycotic infection

- **polyenes** :: Amphotecrin B, Nystatin, Natamycin (Topical)
- **Tolnaftate** :: Tinea pedis (80%), pedis (Athlet foot).
- **Topical Azoles** :: + warfarin → Bleeding, edema, vulvar disease.
- **Griseofulvin** :: ↓ mitosis, ↑ toxicity, insoluble in H₂O, fatty meal → ↑ absorbed, nail dermatophyte (Keratin, ↑ time).
↳ SE: peripheral neuritis, syncope.
- **Allylamine** → **Terbinafine** :: prolonged tx, azotemia, ↓ squalene epoxidase → ↓ tergosterol. doc: Dermatophytes.
↳ ↑ dose → Human squalene epoxidase (cholesterol)

• All antifungal cause hepatotoxicity.

* Diuretics (saluretics).

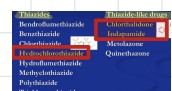
1 Osmotic (mannitol) :: Osmotic pressure in kidney → withdraw H₂O → ↑ excretion, Bronchiectasis (mucus), PCT, tx of ↑ intracranial pressure, SI: Extracellular volume expansion.

2 CA inhibitors · PCT & aqueous Humor

- **Acetazolamide** :: PC, Tx of glaucoma & Acute mountain sickness & seizures.
- **Dorzolamide & Brinzolamide** :: ophthalmic drops, SE (metabolic acidosis & Renal stones).

3 Thiazides :: Tx of hypercalciurea, HTN & edema (HE), most used, DCT, All or none, inactive in RF (GFR < 20) & ↓ ADH (DI)

- **indapamide** :: vasodilator
- SE: ↓ K & Mg (MI or digoxin tx), goat, ↑ dose → ↓ uric acid Reabsorption.



- 4 **Loop diuretics** - ceiling & efficacy, potent & short action, thick ascending, (Na/K/2Cl), dose → effect. most effective with RF (GFR < 10), Tx: Acute pulmonary edema & +CSH. SI: ↓K, ↓Mg, ototoxicity.
- **furosemide**: 3rd potent, Tx: hypercalcemia & TADH.
 - **Bumetanide**: most potent.
 - **Ethacrynic acid**: prodrug,
 - **Torsemide**: active metabo, 2nd potent.

- 5 **K sparing**: ↓ efficacy
 ↳ tx of Resistance
 ↳ ↓ Na intake
 ↳ change dose & time
 ↳ combination
- **Aldosterone antagonist**: Po, collecting duct, Tx: Hirsutism (antiandrogenic), HTN
 - ↳ **Spironolactone**: SE: Gynecomastia & Breast tenderness } ↑K → Arrhythmic
 - ↳ **Eplerenone**: more potent
 - **non steroidal**: Po, DCT & collecting duct, ↓ Na channels.
 - ↳ **Amiloride**
 - ↳ **Triamterene**: SE: +hydrochlorothiazide → Renal tubular damage.

• All diuretics cause erectile dysfunction.

* UTI pharmacology

• most effective drugs: Trimethoprim-sulfamethoxazole, cephalosporin, Quinolones, Nitrofurantoin, Fosfomycin.

- 1 **Quinolones & Fluoroquinolones**: ↓ gyrase enzyme → ↓ DNA synthesis, cidal, affected with food (Ca & Fe), Po
- Resistance: efflux pumps, protection, mutation → ↓ binding affinity.
 - SE: cardiac toxicity (QT), GIT, ↓ cartilage development, carcinogenic
 - 1st: **Nalidixic acid**: G⁺
 - 2nd: **Ciprofloxacin, ofloxacin**: G⁻ ← complicated UTI
 - 3rd: **Levofloxacin**
 - 4th: **Moxifloxacin** } pseudomonas & anaerobic

- 2 **Nitrofurantoin**: cidal, ↑ use in cystitis, many MoA → ↓ Resistance, SE: pulmonary fibrosis, CI: G6PD.
- ↳ G⁺ & G⁻ (E. coli)

- 3 **Fosfomycin**: ↓ peptidoglycans, Rapid Resistance → single dose, SE: metallic taste, stuffy nose, vaginal discharge
- ↳ G⁺ & G⁻ (including many antibiotic-resistant organisms).

* posterior pituitary hormones. (Neurohormones)



- 1 **ADH**
- Receptors: V_{1a} (vc & ↑ platelet aggregation), V₂ (↑ H₂O Reab & ↑ factor VIII), V_{1b} & V_{III} (↑ ACTH Release).
 - ↑ ADH → Dilutional hyponatremia, Tx: furosemide, water restriction, fludrocortisone → ↑ Na, saline
 - ↳ **conivaptan**: non selective, IV
 - ↳ **Tolvaptan**: selective V₂, Po } uses: ↑ ADH, CHF, Liver cirrhosis.
 - ↓ ADH (DI) (-pressin)
 - ↳ **Natural (pitressin)**: ↓ + 1/2 (15 min)
 - ↳ **Lypressin (porcine)**: ↓ DoA (4 hr)
 - ↳ **Desmopressin**: widely used, ↑ DoA (12hr), ↓ gangrene SI.
 - ↳ **Pelypressin**: strongly vc, dentistry uses
 - ↳ uses: DI, nocturnal enuresis, Hemophilia, Bleeding esophageal varices
 - ↳ SI: Anginal & Abdominal pain, H₂O intoxication.

2 Uterine Stimulant

- Oxytocin: - IV, induction of Labor (\uparrow sensitivity $> 20w$), SE: - Rupture of uterus & ADH-Like
 - ↳ antagonist: Atosiban: - \downarrow contraction (tocolytic) in premature delivery
- prostaglandins (- prost)
 - Dinoprostone (PGE₂)
 - Dinoprost (PGF_{2 α})
 - carboprost (PGF_{2 α})
 - Gemeprost (PGE₁)→ drug of choice in abortion. orally, parentally & sublingual.
- Ergot alkaloids: - postpartum hemorrhage, (\uparrow Risk of fetal death)
 - ↳ (-gonovine): - Ergonovine & Methylergonovine.

3 Uterine Relaxant (tocolytics): - premature delivery (20-36w) \rightarrow \uparrow newborn survival

- β -agonist: - Ritodrine (mc, \uparrow effect), Terbutaline, SE: - chest pain
- Mg-sulfate: - \uparrow adenylate cyclase & Ca dependent ATPase. Tx: - convulsions of pre-eclampsia
- progesterone: - Dydrogesterone
- oxytocin competitive antagonist: - Atosiban
- \downarrow prostaglandin synthesis (NSAID): - Indomethacin & meloxicam
- Nifedipine: - major CI to tocolytics: - fetal distress.

* GnRH, LH, FSH

1 GnRH

- Agonist (-Reline): - pGlu-His-Trp (change \rightarrow antagonist), Gly 6 & 10 \rightarrow binding, ineffective Po
- uses
 - ↳ pulsatile: - Dx, \downarrow GnRH (Kallman's), infertility.
 - ↳ dose \rightarrow superagonists: - Ca of prostate & breast, contraceptive, IVF, polycystic ovarian syndrome
- SE: - osteoporosis & Resistance to tx
- antagonist (-Relix): - \downarrow Histamine Release.

2 LH & FSH

- MoA: - CAMP 2nd messenger
- Source: - Human menopausal gonadotropins (HMG, menotropin \rightarrow FSH & LH 1:1), rDNA preparations.

• HCG: - placenta, LH-Like, Recombinant preparations

• gonadotropins

- uses: - infertility, IVF, cryptorchidism (HCG)
- SI: - ovarian hyperstimulant syndrome (*), tumors, gynecomastia, failure of tx \rightarrow Abortion

• Estrogen antagonist

- clomiphene citrate, Tamoxifen
- uses: - M: - restoring fertility, F: - \uparrow ovulation, + HMG & HCG \rightarrow Regulate ovulation in IVF.
- SE: - menopausal manifestation, ovarian enlargement, cyst.

• if GnRH, LH, FSH, HCG & Estrogen antagonist fails: - Reproductive technology (IVF, IVM, ZIFT, GIFT).

- **Androgen**
 - DHT is x10 potent than testosterone.
 - uses
 - Danazol:- Endometriosis.
 - Testolactone (Laromatane):- Breast cancer.
 - Androgen:- anabolism (osteoporosis).
 - (-Testosterone) & Fluoxymestrone:- androgen Replacement.
 - SE:- acne, Jaundice, gall bladder stones (methyl-test), enlargement of prostate & Liver cancer.
- **Antiandrogens (-lutamide)**
 - uses
 - Finasteride^(5 α):- prostate Benign hyperplasia.
 - Cyproterone acetate (progestin):- acne & hirsutism, prostate ca.
 - Gossypol (σ^7 contraceptive):- antifertility agents.
 - Finasteride (cyotol):- baldness (topical).
 - SI:- \downarrow lipido, \downarrow ejaculate, \downarrow spermatogenesis.
- **Estrogen**
 - inactive Po, testosterone $\xrightarrow{\text{Aromatase}}$ Estrogen, Conjugation (enterohepatic circulation). → Estore Sulfonate
 - uses
 - Estrogen + progestone:- cancers (prostate, Breast, endometrial).
 - Estradiol (child), Estrone (menopause), Estriol (pregnancy).
 - Tamoxifen:- synthetic non-steroidal.
 - SE:- \uparrow Risk of thromboembolism & endometrial cancer.
- **Antiestrogens:- manage infertility (SERM), competitive antagonist.**
 - Tamoxifen:- antagonist on Bone, antagonist in Breast (cancer)
 - clomiphene citrate
 - SERM:- Raloxifene:- osteoporosis
 - Aromatase
 - Aminoglutethimide:- Selective.
 - Anastrozole, fadrozole:- non-selective.
- **progesterone**
 - maintain pregnancy, \uparrow Temp, aldosterone-Like effect.
 - Dydrogesterone:- IVF
 - (-gesterone) & Norethindrone
- **Antiprogestins:- mifepristone - cushing syndrome.**
- **Contraception**
 - M:- nonoxynol - spermicidal, (estrogen, GnRH, Androgens), surgical (vasectomy).
 - F:- Estrogens, Ethinylestradiol & mestranol.
 - progesterone \rightarrow minipills (continuous use):- norethisteron & medroxyprogesterone.
 - Estrogen + progesterone (sequential):- (mestranol/estradiol) + (Norgestrel/Norethisterone).
 - Ovulation, \uparrow viscosity, change motility of fallopian tube.
- **All Androgens, progestones, estrogen \rightarrow SI:- salt & water retention.**