Carbonic Anhydrase inhibitor 1- CAI   A+I = M

glucoma   metabolic acidosis   Di(C)hlorphimide   Acetazolmide   methazolamide

CIA have eye on epileptic patients because ISIS how are sleeping (living) on the mountins have NaCl bomb due to problem in their brain

sleep apnea

high altitude "Acute mountin sickness"   tolearance   NaCl ↑ resobtion   ↳ ↑CSF

increase NH_3 in blood

SO CAI buy Cl^- gas + Ca^+ stones by NH_4^+ + k^+ + citrate

↳ hyperchloramtic   ↳ Decrease Ca^+ solubld

and use Cl^- gas to attack ISIS, which cause to them hypersentivity + hepatic enecphalopathy

bone marrow suppressant
interstetial nephritis

Rare as diurtecs

↳ due to NH_3 ↑↑

↓ HCO_3^-/Na

↳ used for metabolic alkalosis

---

highly celeling

Loop Diuretics

ototoxicity "The mixer of milk and energy drink"

treat

A Deaf guy called Fares came to your clinic → fursomide

with acute renal fauilre   Hyperglycemia   → Hyperurecmia

partially metabolized

He has DM + gout, ~~the symptoms~~

He had rash / Allergy + pulmonary congestion + → treat

PG

torsamide   ← torsade depointis in the last year. you asked for

Farest ethan = pulmonary congestion

Blood test and the results showed that Fares

Fares + Bum Bum - against CIA

had hypo Mg^+, Na^+, k^+, Cl^-, H^+, you asked him "

phenoxy acetic dervatives

what did he drink in this morning", he said that

1- ethancrynic acid

he mix a milk with "Bum Bum" drink energy,

loop

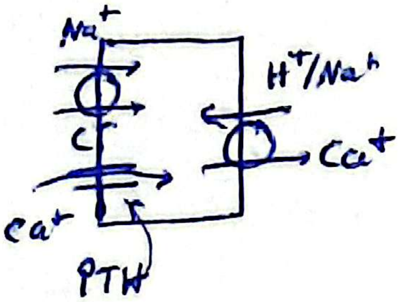
Fur(o)smide   resorbed from distal tubule Ca^+ → normal   Bumetnide

(t)orsmide   increase renal out flow

↳ $t_{1/2}$↑ "active metabolite

You Dignosed him with acute renal fauilre due to toxicity → forced diuresis

thiazide



Indapamine, Metolazone

① enhance Ca^+ resobtion "in distal + proximal"
* ① CIA inhibitor ② PG release ③ reduce response to vasoconstrictor
* tolerance after 3-5 days: due to NaCl resobtion
* first line therapy for HTN by 1+2+3
* orally, except chlorothiazide IV
* Chlorothalidone → long t1/2
* Indapamine → excreted by biliary duct
* All → compete with uric acid "hyperurecmia"

Adverse effects: Hyper "urea, glucose, lipidemia"
Hypo K^+, H^+, Na^+ → due to ADH release
weakness & impotence → due to volume deple
paresthesia → due to CIA
↳ ↑ thirst, reduce renal capacity to dilute urine

* Allergy "anemia, thrombocytopenia, pancreatitis, necrotizing alveolitis"
* photosensitivity

treat: HTN, edema → mild congestive pulmonary "Loop Diuretics"
↳ hepatic renal insuffic. "not loop diuretics" working blood
↳ ex: Ascites

Nephrolithiasis "hypercalciuria", Nephrogenic DI
↳ restriction of Na^+, NaCl water loss in distal → cause increase resobtion in the proximal tube

K^+-sparing Diuretics:
Aldosterone → excrete K^+, H^+ → from intercalated cell → act on it
→ Cl^- → move in collecting duct in paracellular pathways

Aldosterone antagonist: spironolactone, Eplerenone
* extensive enterohepatic cycling, extensive binding to plasma "as loop Diuretics"
low Bioavailability ← * Canrenone → active metabolite

Adverse: Hyper K^+, metabolic acidosis, Gynecomastia + BPH "not in eplerenone"
GIT upset: Reduce dose in hepatic disease
↳ keto + itraconazole → increase blood level of eplerenone by inhibition of CYP3A4

Spiro → spiral between hepatic enter.

K+ sparing: (2) Na+-channels blockers: Amiloride, urine
↳ Depend on PG, inhibit K+/H+ secretion

trimetrine → 2 m
↳ excreted by liver / active metabolite have shorter t1/2 than trimetrine.

(tri)metrine adverse effect
↳ 2m → leg cramp

liver → Glucose intolerance & not by hypo K+ - induced insulin secretion
eye → photosensitivity
renal ×3 → Nephrolithiasis
→ Acute renal failure if given with Indomethacin!
→ Interstitial Nephritis + Azotemia

used in: (1) excess mineralocorticoids
(2) conjunction with other diuretic to reduce K+ loss
(3) Hypo K+

Osmotic diuretics - filtered not resorbed, e.g. "Mannitol, urea, isosorbide"
↳ water loss is higher than Na+ loss

* mannitol - Diuresis + PG release → ↑ tubular flow "decrease Na+ resorption"
↳ used in acute renal failure
↳ not orally, Not metabolized

(Man)(itol) → red eye → hemo..
↳ ICP, IOP ↑
red eye + brain

used in: (1) Reduce: (1) Intracranial (2) occular pressure
(2) increase urine volume in acute renal failure from hemolysis or rhabdomyolysis

Adverse effects Hyper K+ Na+, Headache, (EC V expansion + Hypo Na+ prior to diuresis)

ADH antagonist: AQP2 → apical
AQP 3,4 → basolateral
↳ Democlocyclin + Lithium, Coni, tali vaptan

ADH - vape △ cone, tall

Conivaptan → IV "not in chronic"
if orally need to be monitored
↳ t1/2 - (5-10) hr

Effect: Nephrogenic DI

Antifungal (1) superficial - tricho-, Epidermo- → phyton, microsporum
↳ Candidia

(2) Systemic: -
Caused by Advances in surgery

* Amphotericin B: - Binds ergosterol → make pore
Act against fungi + Leishmania

poor oral absorption, only used orally :- in fungal GIT infection

* complexed with deoxycholate for infusion

Liposomal amphotericin, High protein Bind, Poorly cross BBB except in meningitis

- $t_{1/2}$ = 15 days
- → decrease toxicity

Adverse effects - ① infusion related toxicity reduced by reducing the infus '

② slower cumulative toxicity - ① Nephrotoxicity (80%)
- → Reversible "prerenal failure"
- → irreversible "prolonged administration"
- impaired renal concentration, tubular acidosis
- ↓ Mg^+, Na^+, K^+
- → ↑ urea, creatinine

③ Anemia → leukopenia
④ Hepatic dysfunction, thrombocytopenia, Anaphylaxis
⑤ Seizure "intrathecal therapy" + chemical arachnoiditis

activity - fungicidal / yeast - Candida albicans, Cryptococcus Neoformans
Endemic Histoplasmosis, Coccidioides, blastomycosis
mold - mucor, Aspergillus

---

* Nystatin - similar as Amphotericin but toxic ↑ — topical or suppositories '

---

* Flucytosine - pyrimidine analog "narrow spectrum", synergistic with
  - → Amphotericin B
  - → for cryptococcal meningitis

IV, orally "

cytosin permease — FdUMP → DNA, FUTP → RNA

"resistance happened in monotherapy"

* Human can't convert it to active metabolite

* well absorbed (90%), widely distributed CNS, excreted by kidney by GFR

$t_{1/2}$ = 3-4 hr, Dose reduction in renal

* Flucytosine - Adverse effects - narrow therapeutic window

① GIT → (enterocolitis) ② Alopecia ③ Bone marrow Depress, anemia, neutropenia, thrombocytopenia

| Flucytosine → cancer patient have chemotherapy | mnemonic

Azoles — Imidazole → Clotrimazole, keto; triazoles → Itra, Flu, voric

[Itraconazole, flu+VZV]

fungistatic

Spectrum - yeast / Endemic / dermatophyte

Voric, itra → Aspergillus + amphotericin-resistant Pseudallescheria boydii

Azoles Mechanism :- inhibition of cytochrome 450 → for synthesis of ergosterol which alter membrane fluidity. **Fungistatic** → reduce amphotericin B binding sites

* **Fluconazole** :- PO, IV , Reach high concentration in CSF + ocular fluid
  * Effective in most fungal meningitis + Candidemia + mucocutaneous Candida "cryptococcal, coccidioidal"
  * Fungicidal in high concentration: vagina, saliva, skin, nails
  * prophylactic in Bone marrow transplant + AIDS
  * excreted unchanged in urine
  * Adverse effects: ① widest therapeutic index ② Nausea, headache, abdominal pain + Stevens Johnson Syndrome in AIDS ③ Hepatitis ④ Doesn't inhibit Drug metabolism + steroidogenesis

Flu conazole → high (index, Hepato), Flow → No Drug interaction

* **Itraconazole** :- Fatty, first pass, lipid soluble, low bioavailability with rifampicin, low BBB penetration, excreted in urine
  ① Dimorphic fungi "Drug of choice" ② aspergillosis ③ dermatophytosis mycosis
  Adverse :- Hypo K⁺

* **Voriconazole** :- PO, IV , eliminated by hepatic metabolism
  Adverse :- visual Disturbance "resolve in 30 min"
  Activity: ① Candidiasis ② Fluconazole resistant Candida ③ Cryptococcus + dimorphic fungi ④ As or more than Amphotericin B against Aspergillosis
  Metabolized by CYP

* topical :- Mic, clotrim, ECO → vulvovaginal candidiasis "topical", oral thrush "clotrimazole"
  → Dermatophytic infection :- tinea "creams"
  shampoo of ketoconazole → pityriasis versicolor / seborrheic dermatitis

* **Terbinafine** :- allylamine , PO → skin, nails, Adipose
  topical → lipophilic + keratinophilic
  Fungicidal for many skin fungi "dermatophytes"
  inhibit squalene epoxidase used in onychomycosis + tinea
* **Naftifine** :- same thing but act only against tinea → cruris, corporis
  Adverse → joint + muscle pain

* **Echinocandins** :- cyclic A.A + long F.A → Caspo + Mica + Anidula "fungin"
  inhibit (1-3 B) glucan

Echinocandins: broad, poor oral, ↑ IV due to ↑ protein solubility

t1/2 → caspo → 10 hr, mica → 13 hr, anidula → 36 hr
↳ loading dose required

Dose adjustment need in hepatic insufficiency

Used in: ① Candidiasis ② Esophageal candidiasis ③ Empiric therapy for febrile neutropenia !!!
④ salvage therapy for invasive aspergillosis refractory to amphotericin B

Adverse: ① elevation of liver enzyme ② Micafungin → increase level of nifedipine, cyclosporine, sirolimus
④ Anidulafungin → releas histamine ⑤ phlebitis / thrombophlebitis

---

Genital infection: nitroimidazole: ① Metronidazole (t1/2 = 7.5) ② tinidazole (t1/2 = 12-14)

nitro group reduced by target cells

both: orally, high permeability "simple diffusion"
Extracellular = Intracellular rapidly

metronidazole PO / IV / topical / parenteral

metabolized by liver "decrease in hepatic dysfunction"

Used in: ① Bacterial vaginosis: Gardenella, prevotella, Mobiluncus, Mycoplasma
② trichomoniasis ③ amebiasis → hepatic + intestine, gut X, cyst X "Entamoeba histolytica"
④ Giardiasis ⑤ G- → Clostridium, Bacteroides + streptococcus
mefalic, Neutropenic, intraabdominal infection, Antibiotic Associated enterococcal or brain abcess,

METRONIDAZOLE

- M → mefalic
- N → Neutropenic
- T → IV → GIT → seizure
- R → Rush
- D → Dysuria + Dark urin
- A → Alcholism
- ZOLE → pancreatitis

CNS, contraindicated in pregnancy + lactation

Drug interaction: warfarin, phenytoin, phenobarbiturate → increase elimination
increase Li⁺ toxicity
cimetidine → decrease elimination

Clindamycin: inhibit microbial protein synthesis by binding to 50S
identical to erythromycin

resistance: ① enzymatic degradation ② receptor mutation ③ receptor modification "methylase"
④ G+ resistant because poor permeability

Resistance to clindamycin cause resistance to macrolide

Activity against:- ~~Aerobic~~ Anerobic G+ve, Bacterial vaginosis, Some G(+) coccave

resistant against:-
↳ Aerobic G(-), Some Anerobic G(-) "B. fragilis", GBS

Enetro cocuss, G(+) areobic

kinetic: (1) widley distriputed Bone, Placenta, Breast

(2) ~~taken by phagocitic cells~~ (3) peneter well absess except Brain

metabolized in liver, t1/2 2.5 hr, 6 hr → anuria, no dose adjustment

used in:- lung absess, aspiration pnumonia
" with aminoglycosides + cephalosporins
| osetamylets
| Infect of femal Genit
Infect of from fecal spelage

Adverse:- thrombophelebitis, Superinfection ∴ psedamonus colitis + thrombocytopenia.

Antiherpetic: Acyclovir:- 3 phosphoralation / inhibit DNA synthesis
Compete with (d)-GTP
Chain termination

✓ low Bioavalblity, oral topical, IV

cleared by glomerular filtration + tubular secretion

t1/2 = 3 hr anuria = 20 hr, Diffuse readily on all body fluids

Adverse:- IV → reversible crystlinne nephropathy, interstial nephritis

neurologic toxocity. uncommon with adequate hydration and avoidance of rapid infusion

Probenecid + cemtidine → decrease clearance