النادي الطبي MC راضي

Done By :
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لا تنسونا من دعائكم بالتوفيق

الدكتور حكا مهم نميز شو المرض يلي self limiting و المرض اللي بحتاج antibiotic

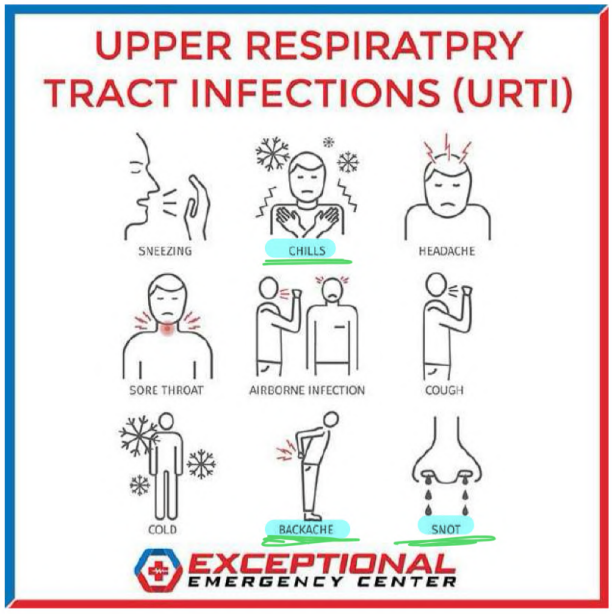
Viral infection is usually self-limited , however it doesn't always decay You must give antibiotics in bacterial infections

بهمنا نعرف الsymptoms عشان نعرف نتعامل مع ال case scenario بالامتحان

Upper respiratory tract infection (URTI)

- Cough
- Sore throat
- Runny nose
- Nasal congestion
- Headache
- Low-grade fever
- Facial pressure
- Sneezing

ph.5



- The onset of symptoms usually begins one to three days after exposure and lasts 7–10 days, and can persist up to 3 weeks. → which is Fine بس انه مش أشهر

↳ In viral

If it happens Once a year , it is fine
antibiotics غير treatment و صار بدو chronic infection ل اكتر من مرة بالسنة اتحوّل

URTI pharmacological management if its viral = self limited (only supporting medicines (pain killers) but we should not take antibiotics لانه رح يضرني اكثر ما انه رح يفيدني

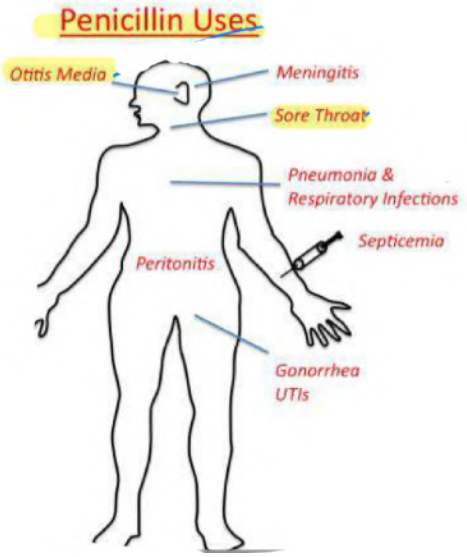
Penicillin → 3 Groups

- **Penicillin G**: Gram-positive and –negative cocci, gram-positive rods and anaerobes.
-
- **Broad-spectrum penicillins (gram-negative bacilli)**: second generation (ampicillin, amoxicillin), third generation (carbenicillin) and fourth generation (piperacillin)

لازم نعرف الاسماء

2nd gen → is widely used , 3rd, 4th are less used

- All penicillins have relatively short half-lives and require frequent administration.

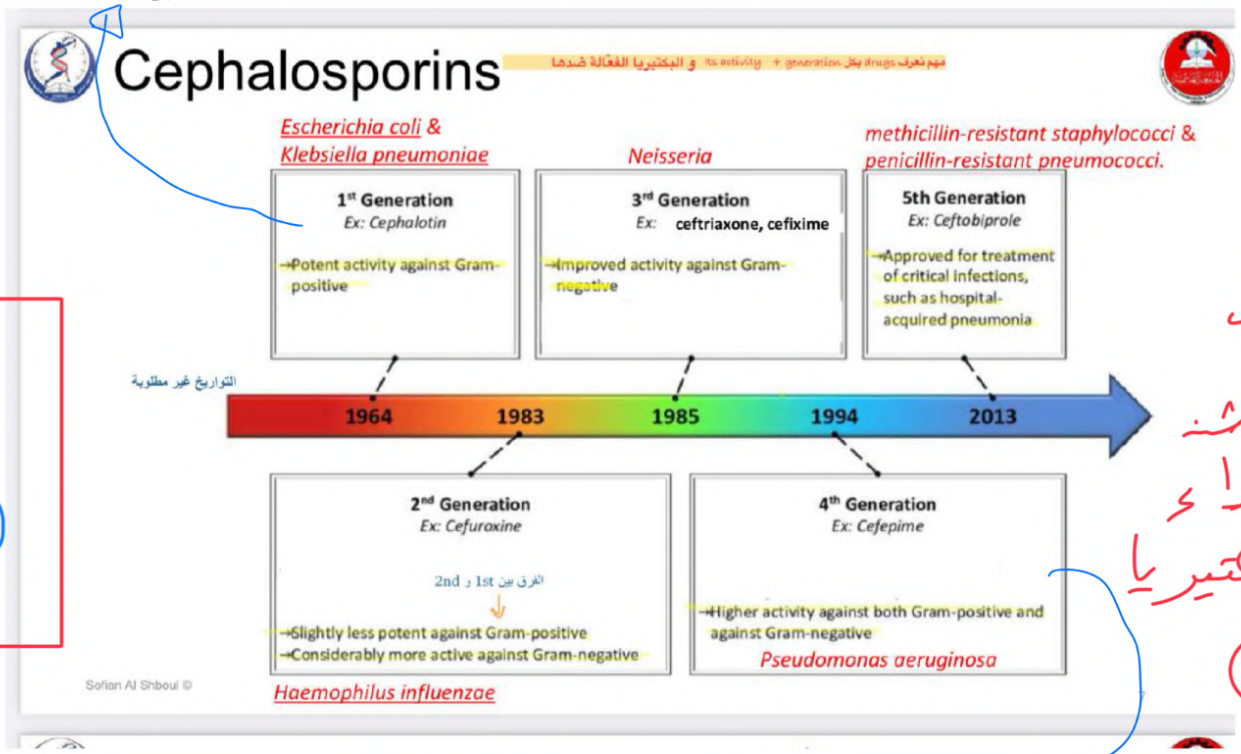


Ph. 5

اقوى ضد ال G-ve

Cephalosporins

فيهم نعرف drugs بكل its activity + generation و البكتيريا الفعّالة ضدها



Ph. 5

مهم تعرف الجينيراشن مع الدواء مع البكتيريا

Very wide spectrum

Macrolide

حسب الجمله لدهاتوضيح :

(معناها انه كويسات against G+ve وال G-ve مش كثير)

- Gram-positive bacteria and limited Gram-negative bacteria
- Antimicrobial spectrum is slightly wider than that of penicillin >> common substitute for patients with a penicillin allergy.

الفروقات بينه وبين ال Penicillins

- Unlike penicillin, they are **effective against** Legionella pneumophila, mycoplasma, mycobacteria, and chlamydia.
- **Azithromycin, Clarithromycin and Erythromycin** → كثير مستعملين

Ph.5

Upper respiratory tract infection: **Acute epiglottitis**

Patients need airway management before treatment

This figure shows how it is serious

- direct inspection using a laryngoscope.

- Do not use tongue depressor or attempt throat swab → can cause laryngeospasm

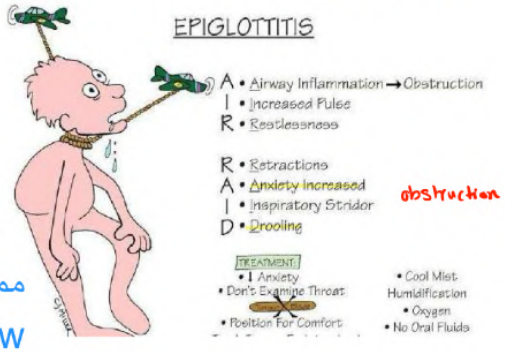
tongue depressor لل داعي قاما في ، laryngeoscopy طريق عن يكون والتشخيص

Airways management then I give the treatment

- requires immediate airway management (tracheal intubation). → ممنوع اكيله روح عالدار

ممكن نضطر لل tracheal intubation لانه

we need to open the air flow



Upper respiratory tract infection:

Disease	Symptoms	Pathogens (common)	Pharmacotherapy
Rhinitis	Cough, headache, fever*, sore throat and rhinorrhea	Viruses	Supportive: Dextromethorphan, Anti-histamines, Pain-killers, Decongestants.
Pharyngitis	Sore throat, difficulty speech and swallowing, swollen tonsils and bad breath	Strep. Pyogens: Penicillin/Amoxicillin (Oral)^^ > Cephalosporin (Cephalexin) ^^ > Macrolide (Azithromycin) Viral: self-limiting: conservative + oral CS (1-2 for pain on swallowing) + lidocaine wash + NSAIDs Candida albicans: clotrimazole	
Sinusitis	Nasal congestion, facial swelling, tenderness, discharge (colour?) Yellow & Green	Strep. Pneumonia and H. Influenza.	❖Amoxicillin/clavulanic acid ^^ > doxycycline or cephalosporins3rd (cefixime) ^^ > fluoroquinolone (levofloxacin or moxifloxacin) ❖Chronic: Intranasal saline, Intranasal corticosteroids, Oral corticosteroids and antibiotics (limited evidence, after culture)
Acute Otitis Media	Ear pain (otalgia), fever, sensation of fullness	Strep. Pneumonia, H. Influenza and Staph. aureus	Amoxicillin-clavulanate^^ > cephalosporin (Cefuroxime)^^ > doxycycline or macrolide (Azithromycin)
Diphtheria	Sore throat, lack of appetite, low-grade fever and grey or white patch develops in the throat	Corynebacterium diphtheriae	Diphtheria antitoxin (horses) + erythromycin ^^ > penicillin
epiglottitis	Trouble swallowing, drooling, fever, aphonia and an increased breathing rate	Streptococcus pneumoniae and haemophilus influenzae	requires immediate airway management (tracheal intubation). Cephalosporin3rd (ceftriaxone) + vancomycin
Croup and laryngitis	"barking/brassy" cough, inspiratory stridor, hoarseness, difficult breathing, fever and runny nose Starts or get worse at night	Mainly viral (parainfluenza and influenza) Rarely bacterial	Corticosteroids and nebulized epinephrin Used in very specific cases: Cephalosporin3rd (ceftriaxone) + vancomycin

Acute epiglottitis
ممنوع نقعد للمريض
روح لأنها حالة طارئة
وقد نضطر نعمل (tracheal intubation) عشان يتنفس وما يموت
Croup
ملاحظة: بالعادة ممنوع نستخدم (Anti biotic) ممكن تستخدم ويفيد المريض، بس مش هذا الـ (AB) المرض لسا موجود ومع زيادة عمر المريض والمقاومة الـ (AB) بصير عنده (Resistant) لكثير أنواع
مد جواز المناعة

Lower respiratory tract infection:

Disease	Symptoms	Pathogens (common)	Pharmacotherapy
bronchitis	**Acute:** cough (≤3 weeks (Sputum?), wheezing, shortness of breath, chest pain. **Chronic**: productive cough that lasts for three months or more per year for at least two years**. (remember COPD)**	primarily viral (parainfluenza and influenza), could be bacterial infection (Mycoplasma)	**Acute:** Paracetamol and nonsteroidal anti-inflammatory drugs (NSAIDs) Antibiotics should generally not be used **Chronic:** Quit smoking, vaccinations, rehabilitation, and inhaled bronchodilators and steroids
bronchiolitis	Fever, cough, runny nose, wheezing, and breathing problems. Complications: dehydration and aspiration pneumonia	Mainly viral (RSV)	No diagnostic test are required No specific treatment, home care is sufficient Hospital admission for oxygen, support with feeding, or intravenous fluids No clear evidence for antibiotics, antivirals, bronchodilators, or nebulized epinephrine?!

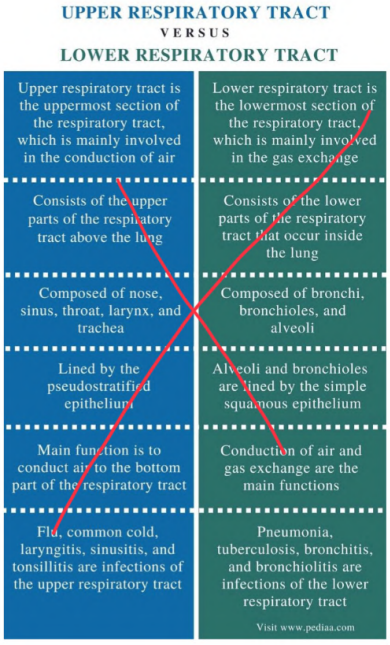
Lower respiratory tract infection (LRTI)

- A group of disease effect the respiratory system below the throat
- Pneumonia, lung abscess, bronchiolitis and bronchitis.
- Symptoms include shortness of breath, weakness, fever, coughing and fatigue

Antibiotics: bronchiolitis ولا bronchitis بالعاده ما بستعملها في

- the first line treatment for pneumonia
- NOT effective and NOT indicated for parasitic or viral infections.
- Acute bronchitis typically resolves on its own with time.
- Vaccines available for many pathogens

Ph. 6



Ph.6

مهم لسؤال (case)

Community-acquired pneumonia (CAP)

- Patients >65, شخص عندو مشاكل و امراض تانيه و صابتو ال pneumonia او عمره فوق 65 سنةً
- Patients with **comorbidities** such as chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; asplenia; immunosuppression; prior antibiotics within 90 days: او انو الو بياخد 3 من antibiotic اشهر

يعني لما يكون المريض comorbidities بجيب ال first line اللي بالسلايد القبل و بدمجهم بحيث بعطي كبسولة amoclan و كبسوله تانيه اما بتكون لل macrolide او لل doxycycline وحده منهم و بعطيهم للمريض و orally

First: amoxicillin/clavulanate + macrolide or doxycycline

Alternative: Cefpodoxime OR cefuroxime + macrolide OR doxycycline

Alternative: Fluoroquinolone (Levofloxacin or Moxifloxacin)

Duration of therapy:

هون قصدو انو لو بدي اوقف الدواء عن المريض بعد الخمس ايام لازم اشيك انو الو يومين ما عندو و لا اجت عليه حراره فلو حكالك انو فعلاً ما علي حراره من يومين خلص بوقف العلاج

minimum of 5 days, should be afebrile for at least 48 hours, clinically improving (based on symptoms and vital signs).

لازم برضو كمان نتأكد انو ما ضل عليه اعراض يعني مش بس قصة راحة الحراره لاء اعمل تشيك ع وضعه قبل ما اوقف العلاج

Patients with documented MRSA or Pseudomonas aeruginosa should receive a **minimum of 7** days treatment.

dangerous

اذا رجع المريض بعد ٣-٥ ايام ولسا ما تحسن فعال AB غير فعال فبعطيه antibiotic معناته هذا ال

* مع انو نادرًا انهم يكونوا بالسبب CAP

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Lower respiratory tract infection (LRTI) Ph. 6

treatment جدول بلخص ال

CAP	❖ Patients without comorbidities: Amoxicillin **OR** A macrolide (azithromycin or clarithromycin) **OR** Doxycycline ❖ Patients with comorbidities: amoxicillin/clavulanate + macrolide or doxycycline ^^> **Alternative**: Cefpodoxime OR cefuroxime + macrolide OR or doxycycline ^^> **Alternative**: Fluoroquinolone (Levofloxacin or Moxifloxacin) ❖ <u>hospitalized patient (non-ICU):</u> Ampicillin/sulbactam **OR** ceftriaxone + azithromycin or doxycycline **Alternative:** Fluoroquinolone (Levofloxacin or Moxifloxacin) ❖ <u>hospitalized patient (ICU)</u> levofloxacin + aztreonam + an aminoglycoside (gentamicin, tobramycin)
HAP	• < 5 days since admission and **NO MDR**: Ampicillin-sulbactam or Ceftriaxone • > 5 days since admission **+ MDR**: Cefepime + Vancomycin + Levofloxacin
Atypical	➢ Mycoplasma : doxycycline or macrolide ➢ Chlamydophila : doxycycline, macrolide, fluoroquinolones. ➢ Legionella: macrolide (azitromycine preferred) +/– rifampicin.
Aspiration	Depends on the setting in which aspiration occurred: CAP: ampicillin-sulbactam or fluroquinolone (high risk: add clindamycin) HAP: : vancomycin + piperacillin-tazobactam
Viral	No specific antiviral medications are recommended Influenza A: rimantadine or amantadine Influenza A or B may be treated with oseltamivir, zanamivir or peramivir.

Pneumonia
Pathogens & Risk factors

ال pneumonia بشكل عام تشخص clinically
ال chest x ray, ... هي يتمل confirm
وال culture لتحديد antibodie المناسب
بس غالبًا بتحسن ال patient قبل ما تطلع نتيجة ال culture

- Bacteria or viruses and less commonly by fungi and parasites.
- The causative agent may not be isolated in about half of cases despite careful testing

صعب اني اقدر اعمل isolation للمسبب لهاي ال infection لانو بكون موجود بال lower R بالتالي مش دايماً بقدر اعرف شو ال causative ف بالعاده بعتمدو بالعلاج على تصنيف العدوى مثلاً لو كان CAP بعطيه ادويه معينه او HAP برضو ادويه معينه و هكذا (empirical therapy) لكن اول ما اشوف انو ما في استجابه مع المريض هون بكون حاسب حسابي و عامله culture

- Predisposing factors: smoking, immunodeficiency, alcoholism, chronic obstructive pulmonary disease, sickle cell disease (SCD), asthma, chronic kidney disease, liver disease, and biological aging.
- The use of acid-suppressing medications (PPI or H2 blockers) is associated with an increased risk of pneumonia.

طيب سؤال شو دخل مشاكل ال liver و ال kidney بالرئه ؟
مبدئياً اي انعكاس على sys من سيستمات الجسم ممكن يأثر على باقي السيستيمات فمثلاً ممكن مشاكل الكبد و الكلى تأثر على ال CVS لانو مربوطين بالدم كتير و اي تأثير فيه اكيد حيأثر على الRS و هاد بشكل غير مباشر
اما بشكل مباشر فهو ممكن انو انزيمات تصنع بالkidney و ال liver خاصة للlung و لانهم خربو بطلو يقدرو يزودو الرئه بهاي الانزيمات المهمه بالتالي ضعفت ال lung و صارت اكثر عرضه لل infection

Pneumonia
Signs and symptoms

- **Pulmonary:**

Cough (with or without sputum production), dyspnea, and pleuritic chest pain

tachypnea, increased work of breathing, and adventitious breath sounds, including rales/crackles and rhonchi.

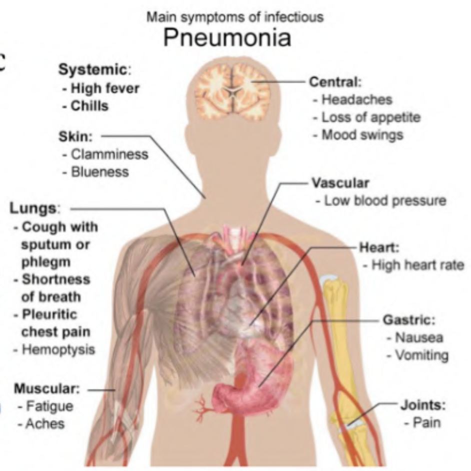
- **Systemic:**

دايماً بال LRT infection كل اعراض ال sys بتكون باعلى مراحلها و اقوى من اللي بتكون بال URT infection

Fever, chills, fatigue, malaise, chest pain (which may be pleuritic), and anorexia.

Tachycardia, leukocytosis with a leftward shift, or leukopenia are also findings that are mediated by the systemic inflammatory response.

Inflammatory markers, such as the erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and procalcitonin may rise, though the latter is largely specific to bacterial infections.



اكيد بسبب التعب و الارهاق و الحراره و خصوصاً زيادة التوتر كل هدول بأثرو على نبض القلب بحيث يعمل tachycardia و برضو

ال calcitonin بعمل على تحفيز ال T cells لمواجهة البكتيريا فهو قلنا احكي حيزيد procalcitonin يعني حيزيد ال precursor تاع ال calcitonin

Treatment of tuberculosis (TB)

must be treated with several drugs.

Ph.7

Treatment

Start for first line treatment

نظامان

عندي 2 regimens لل active Tb خاصه

ما بزبط اعطي بس دوا واحد لازم اعطي اكثر من دوا مع بعض

✓Two main regimens for pulmonary TB:

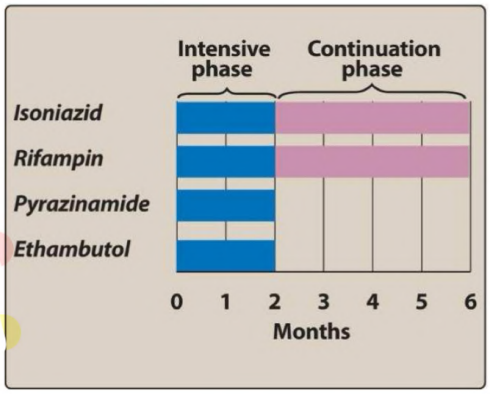
1) Traditional regimen (≥6 months): isoniazid, rifampin, pyrazinamide, and ethambutol

اقل اشي يعطيهم ل 6 اشهر

الي بالاصفر تخيرو

2) Shortened, four-month regimen: isoniazid, rifapentine, pyrazinamide and moxifloxacin

نظام



✓Both regimens have two treatment phases: 2 months then 4. and 8 weeks then 9 weeks

شرحها بالسلايد الجديد

الفرق بين ال regimen الاول و الثاني :
اول اشي المده بحيث واحد بس اربع اشهر يعني high compliance و واحد اقل اشي ست اشهر و تاع الاربع اشهر يعتبر cheaper مقارنة مع هداك و اخر فرق هما الادويه اللي بالاصفر بتختلف بكل واحد

بالتالي لو المريض ماشي مع كل الشروط تاع ال regimen الاربع اشهر ف خلص بخليه يمشي عليه لانو اغلب مواصفاته افضل

Treatment

For patient with multi drug resistant

Ph . 7

- **Second-line regimens for MDR-TB (TB resistant to at least isoniazid and rifampin):**

1) Fluoroquinolone (levofloxacin or moxifloxacin)
2) Bedaquiline ⊕ Linezolid
3) Add one or two: Clofazimine OR Cycloserine OR Pyrazinamide OR Ethambutol

Capreomycin, kanamycin, macrolides: no longer recommended for inclusion in MDR-TB regimens

Isoniazid (INH)

اسامي الانزيمات مهمه و ممكن يجي عليها سؤال

InhA & KasA are essential for the synthesis of mycolic acid

هدول انزيمات بساعدو بتصنيع ال mycolic acid اللي وظيفته انو يساعد ببناء ال cell wall تاع ال Mycobacterium tb

Ph.7

MOA:

Isoniazid (pro-drug) >> activated by a **mycobacterial catalase–peroxidase** (KatG) >> enzymes acyl carrier protein reductase (**InhA**) & β-ketoacyl-ACP synthase (KasA) >> Inhibits mycolic acid >> disruption in the bacterial cell wall.

(pro-drug)
ISONIAZID
↓ Kat G(catalase peroxidase in mycobacteria)
Active INH
↓ InhA & Kas (InhA (acyl carrier protein reductase, KasA (ß ketoAcyl Carrier protein synthetase))
Block Mycolic Acid Synthesis
↳ disruption in the bacterial cell wall

Resistance (follows chromosomal mutations):

1) mutation or deletion of **KatG** (producing mutants incapable of prodrug activation)
2) varying mutations of the **acyl carrier proteins** (InhA, KasA)
3) overexpression of the target enzyme InhA.

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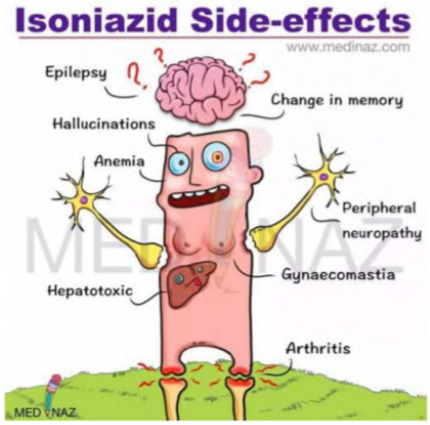
Isoniazid (INH)

The liver function test should be done on a weekly basis for patients with tb

Adverse effects

- **Hepatitis** (most serious adverse effect), If hepatitis goes unrecognized, and if isoniazid is continued >> fatal.



- **Peripheral neuropathy** (paresthesia of the hands and feet) >> relative pyridoxine deficiency caused by isoniazid (can be avoided by daily supplementation of pyridoxine (vitamin B6).
- **CNS** adverse effects: convulsions in patients prone to seizures.

Regardless, what is the drug We never use monotherapy for TB

Ph. 7

Rifampin

يعني ممكن كمان يهاجم انواع بكتيريا تانيه و هاد الاشي بخليه اكثر عرضه انو يصيرله resistant بالتالي not specific against M.tb

- has broader antimicrobial activity **than isoniazid** and can be used as part of treatment for several different bacterial infections.
- **Never** given as a single agent in the treatment of active tuberculosis, why?

بسرعة بتجيلو resistant

Because resistant strains rapidly emerge during monotherapy

هو اصلاً هيك هيك بال active ما بنعطي monotherapy بس خصوصاً ال rifampin لانو

- Used prophylactically for individuals exposed to **meningitis caused by meningococci or H. influenzae**.

بالتالي ما في transcription و لا translation و بالتالي no protein synthesis و هيك بقضي عليها

MOA: blocks RNA transcription by interacting with the **β subunit** of mycobacterial DNA-dependent RNA polymerase.

Resistance: caused by mutations in the affinity of the bacterial DNA-dependent RNA polymerase gene for the drug.

Sofi 15

ركز أنه سوائل جسمه بتتحول للونه الأحمر زي البول والعرق والدموع وغيرهم

Rifampin

واعرف أنه بينتشر بردنه لكل الجسم بس انتشاره لل CNS قليل

وبتم امتصاصه عن طريق ال (Liver)

Adverse effects

(كل الادوية بتعمل هيك) GI upset

بسبب الحساسية

كمان شغله انو لازم المريض يكون بالمستشفى لانو عندو كل اسبوع blood workout

- Nausea, vomiting, and rash.
- **Hepatitis** and death due to liver failure are rare.

يعني اقل خطوره من اللي كان يعملها ال isoniazid

متقطع

- When rifampin is dosed intermittently, especially with higher doses, a **flu-like syndrome** can occur, with fever, chills, and myalgia, sometimes extending to **acute renal failure, hemolytic anemia, and shock**.

في اله مشتقات مثل (Rifabutin) بنعطى بداله بس بيكون مع المريض (HIV) راعاته الجانبيه نفسها بس زيد واعليها التهاب القزحية (Uveitis)

Pyrazinamide

One of the first line drugs

للآن كل الأدوية كانت oral

Good absorption

- Orally. short-course agent used in **combination** with isoniazid, rifampin, and ethambutol.
- MOA: **unclear!** اكتر كلمة ممكن تبسطني

Ph. 7

- Active against **tuberculosis bacilli**
- Penetrating the CSF. بالتالي بزبط بحالات ال extra pulmonary
- May contribute to **liver toxicity**. Because it is metabolized by the liver — بعمل hepatitis لكن بشكل اخف من الباقين

- Most of the clinical benefit from pyrazinamide **occurs early in treatment**. Therefore, this drug is usually **discontinued after 2 months of a 6-month** regimen.

ال action تاعو بيلش بسرعه و بنتهي بسرعه يؤخذ في بداية العلاج فقط

لو بتتذكرو احنا بفترة العلاج تاعت الاربع اشهر (بعد اول شهرين) استثنينا ال ethambutol و ال pyrazinamide و كملنا بس ب ال isoniazid and rifampin فأحد اسباب استثناء ال pyrazinamide هو انو بس بنستفيد منو ببداية العلاج بحيث الو short course agent

بعد الست اشهر بنرجع نعمل فحوصات و بنشوف ازا لازم نكمل كمان اربع اشهر او خلص

B) 2nd line treatment

(SE + MOA) : اكرف محلوفتين من كل دوى * (mechanism of Action, Side effect)

Cycloserine

1. Disrupts d-alanine incorporation into the bacterial cell wall.
   - Primarily excreted unchanged in urine. (accumulation in renal insufficiency)
2. Adverse effects: CNS disturbances (difficulty concentrating, anxiety, and suicidal tendency), and seizures may occur.

Bedaquiline

1. an ATP synthase inhibitor.
2. **Black box** warning for QT prolongation, and monitoring of the electrocardiogram is recommended.
   - Elevations in liver enzymes have also been reported and liver function should be monitored during therapy.

Thus cardiac patients (CVS events) + Arrhythmia should not receive Bedaquiline

Linezolid

1. inhibits bacterial protein synthesis by preventing the fusion of 30S and 50S ribosomal subunits
2. an alternative to vancomycin in inpatient settings, particularly MRSA.
3. AE: myelosuppression, neuropathy and hypoglycemia

Ph. 7