Pharmacology 439

MED439

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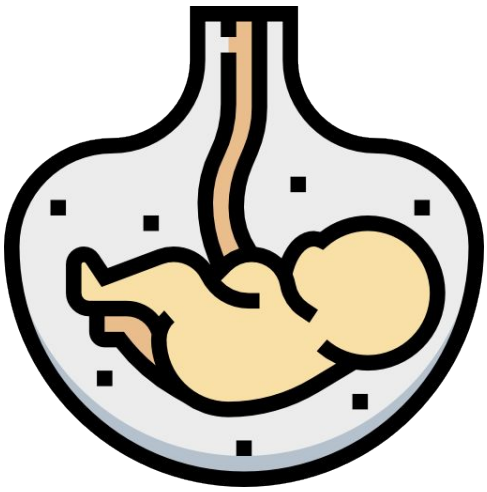

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Pharmacology team 439

Drugs Used in Treatment of Syphilis & Gonorrhea

Objectives:

By the end of the lecture , you should know:

- List the drugs used in the treatment of syphilis & gonorrhea
- Describe the mechanism of action and adverse effects of each drug
- Describe the contraindications of drugs used
- Describe the recommended regimens used for the treatment of syphilis & gonorrhea
- Know the alternative treatments in allergic patients

Color index:

Black : Main content
Red : Important
Blue: Males' slides only

Pink : Females' slides only
Grey: Extra info or explanation
Yellow: Dr. notes (439)

Green: Dr. notes (438)

Syphilis

- Is a sexually transmitted disease caused by **bacterium Treponema Pallidum** [a spiral -shaped, Gram-negative highly mobile bacterium].
- T. pallidum enters the body via skin and mucous membranes through abrasions during sexual contact or blood transfusion or placental transfer from a pregnant woman to her fetus.
    - **Congenital Syphilis:** If a woman is pregnant and has symptomatic or asymptomatic early syphilis, disseminating organisms may pass through the placenta to infect the fetus.
    - **Manifestation:** Perforation of Palate. →

- May become chronic without treatment.

Stages of Syphilis

Disease progresses in stages (primary, secondary, latent and tertiary), signs and symptoms vary depending upon stage of disease.

01

Primary stage :

- Painless skin ulceration (a chancre).

02

Secondary stage :

- Diffuse skin rash & mucous membranes lesions. (Condylomata lata)
- Palmar/plantar rash

03

Latent stage :

- In latent syphilis there are little to no symptoms which can last for years.
- 70% may have no symptoms (Asymptomatic)

04

Tertiary stage : (Spread to other organs)

- Approximately 30% of untreated patients progress to the tertiary stage within 1 to 20 years.
- Rare because of the widespread use of antibiotics.
- Manifestations as cardiovascular syphilis (syphilitic aortitis and an aortic aneurysm). And CNS syphilis

Drugs used in the treatment of Syphilis [1]

Penicillins
- Penicillin G
- Procaine Penicillin G
- Benzathine Penicillin G

First Choice

Tetracycline
- Doxycycline

Macrolides
- Azithromycin

Cephalosporins [1]
- Ceftriaxone
- Cefixime

Used in case the patient is allergic to penicillins

β-Lactam Antibiotics [2]:

1) Natural Penicillins

Drug	Benzylpenicillin (penicillin G)	Procaine penicillin G	Benzathine penicillin G
MOA	★ Inhibits bacterial cell wall synthesis through inhibition of transpeptidase enzyme required for crosslinks (cell wall synthesis) • Bactericidal. • Drug of choice for the treatment of syphilis.		
P.K	• Given I.V • Short duration of action (not more than 4h)	• Given I.M. • delayed absorption. • Long acting (24 hrs)	• Given I.M. • Delayed absorption. • Long acting (days), 2.4 million units is given once (will not be asked about the dose).
	All these penicillin preparations are: • β lactam ring is Acid unstable so it decomposes in acidic medium. [2] ★ **Penicillinase (β-lactamase)sensitive (an enzyme which can inactivate penicillin , produced by certain bacteria)** • Not metabolized. • Excreted unchanged in urine through acid tubular secretion. • Renal failure prolong duration of action [3]		
ADR	★ **Hypersensitivity** [4] (**number one** adverse effect) • Convulsions with high doses or in renal failure (rare) • Super infections.		

2) 3rd generation cephalosporins

Drug	Ceftriaxone
MOA	• Inhibits bacterial cell wall synthesis. • Bactericidal.
P.K	• Given parenterally (i.v.) • Eliminated via biliary excretion (so in renal failure I have another route of excretion) • Long Half-life
ADR	• Hypersensitivity reactions • Thrombophlebitis • Superinfection • Diarrhea

1) Not allergic to penicillins? Prescribe Penicillin. Allergic and not pregnant? Tetracycline. Allergic and pregnant? Cephalosporins or Macrolides.
2) Thus never given orally.

1. Even though Sometimes a patient who is allergic to penicillin is also allergic to cephalosporins
2. Procaine penicillin G and benzathine penicillin G are formulations to prolong the duration of penicillin G action.
3. so we should be careful when prescribing it to a renal failure patient.
4. (ask patient if they have experienced sensitivity to any β lactam antibiotics)

Tetracyclines [1]

Drug	Doxycycline
MOA	• Inhibit bacterial protein synthesis by reversibly binding to **30S** bacterial ribosomal subunits. • Bacteriostatic.
P.K	• Given orally. • Well absorbed orally. • Long acting. • 100 mg twice daily for 14 days.(we will not ask about the dose, just be familiar with the frequency of administration and duration of therapy)
ADR	• Nausea, vomiting ,diarrhea & epigastric pain (given with food). ★ Brown discoloration of teeth in children [2]. ★ Deformity or growth inhibition of bones in children. Avoid dairy products. • Hepatic toxicity in prolonged therapy with high dose. • Vertigo. • Superinfections. • Phototoxicity.
C.I	• Pregnancy. • Breast feeding. • Children (below 10 yrs).

Macrolides

Drug	Azithromycin
M.O.A	• Inhibits bacterial protein synthesis by binding to bacterial **50S** ribosomal subunits. • Bacteriostatic
P.K	• Acid stable → orally once daily • Penetrates into most tissues except CSF. • T1/2 2-4 days . • Should be given 1 hour before or 2 hours after meals [3]. ★ No effect on cytochrome P450 [4].
ADR	• **GIT upset:** Nausea, vomiting, abdominal pain and diarrhea. • **Allergic reactions** (rare & mild)**:** urticaria and mild skin rashes.

1. All antibiotics that **inhibit bacterial protein synthesis** are bacteriostatic except for aminoglycosides.Aminoglycoside effect depends on its concentration. only the antibiotics that **inhibit cell wall or DNA or RNA synthesis** are bactericidal.The rest are bacteriostatic.
2. it binds to calcium so deposited in teeth and bones.
3. because of food interactions
4. Neither inducer or inhibitor, that's why we prefer azithromycin over other drugs of its group e.g. clarithromycin & erythromycin (also preferred because the frequency of administration of erythromycin is high)

WHO Guideline for Treatment of Syphilis [1]

Prof Hanan: Doses aren't important, just know the drugs and that in late stage the duration will increase

Early syphilis

Adults
(primary, secondary and early latent syphilis of not more than two years duration)

- **benzathine penicillin G** 2.4 million units once I.M per week.
- **procaine penicillin G** 1.2 million units I.M. for 10–14 days .

If penicillin is not allowed due to allergy, use :

- **Doxycycline** 100 mg twice daily orally for 14 days
- **Ceftriaxone** 1 g IM once daily for 10–14 days
- **Azithromycin** 2 g once orally.

Pregnant woman

- **benzathine penicillin G .** 2.4 million units once I.M.
- **procaine penicillin G** . 1.2 million units I.M. for 10–14 days

If penicillin is not allowed due to allergy, use :

- **Erythromycin** 500 mg orally 4 times daily for 14 days
- **Ceftriaxone** 1 g I.M once daily for 10–14 days
- **Azithromycin** 2 g once orally.

Late syphilis

Adults
(infection of more than two years duration without evidence of treponemal infection)

- **benzathine penicillin G .** 2.4 million units nits I.M. once weekly for three consecutive weeks.
- **procaine penicillin G .** 1.2 million units I.M. for 20 days .

If penicillin is not allowed due to allergy, use :

- **Doxycycline** 100 mg twice daily orally for 30 days

Pregnant woman

- **benzathine penicillin G** . 2.4 million units nits I.M. once weekly for three consecutive weeks.
- **procaine penicillin G .** 1.2 million units I.M. for 20 days

If penicillin is not allowed due to allergy, use :

- **Erythromycin** 500 mg orally 4 times daily for 30 days
- **Ceftriaxone** 1 g IM once daily for 10–14 days
- **Azithromycin** 2 g once orally.

Congenital Syphilis

In infants with confirmed congenital syphilis or infants **who are or clinically normal, but whose mothers had untreated syphilis**

- **Aqueous crystalline penicillin G** (I.V.) 100 000–150 000 U/kg/day for 10 days, administered as 50,000 units/kg/dose every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days
- **Procaine penicillin G** (I.M.) 50 000 U/kg/day single dose for 10 days
- **Benzathine penicillin G** (I.M.) 50,000 U/kg/dose single dose

1. Erythromycin can also be used in non pregnant but azithromycin is preferred.

Gonorrhea [1]

- Caused by **Neisseria gonorrhoeae** [a gram -ve cocci], a pus producing bacteria .
- Transmitted during sexual contact with affected person.
- Many people have no symptoms
- Men may have burning with urination, discharge from the penis or testicular pain.
- Women may have burning with urination, vaginal discharge, vaginal bleeding between periods or pelvic pain.

Treatment of **uncomplicated** Gonorrhea

Drugs	3rd generation cephalosporins E.g Ceftriaxone | Cefixime	Fluoroquinolones E.g Ciprofloxacin
MOA	-	• Inhibit DNA synthesis by inhibiting **DNA gyrase enzyme** (required for DNA supercoiling (synthesis)) • Bactericidal
P.K	• Ceftriaxone (500 mg I.M) • Cefixime (400 mg orally) • Typically given in **combination** [2] with: ○ a single dose of azithromycin(1gm orally) ○ **or** doxycycline (if the patient suffers from CV disease)(100 mg orally twice daily) for 7 days	• Single oral dose of : ○ Ciprofloxacin (500 mg) ○ Ofloxacin (400 mg)
Uses	★ **1st line treatment** for uncomplicated gonorrheal infections	• 2nd choice of treatment
ADR	-	• GIT: Nausea ,vomiting & diarrhoea . • CNS: Headache & dizziness. ★ May damage growing cartilage & cause arthropathy. ★ Phototoxicity, avoid excessive sunlight
C.I	-	• Pregnancy • Nursing mothers • Children under 18 years. • Breastfeeding

Drug	Spectinomycin
MOA	• Inhibits protein synthesis by binding to **30S** ribosomal subunits
P.K	• Given 2g I.M, once
Uses	★ **Alternative treatment** in patient cannot tolerate or be treated with cephalosporins or quinolones
ADR	• Pain at the site of injection . • Fever and Nausea . ★ Nephrotoxicity (not common)

1. **According to WHO recommendations:**
   - First choice is 3rd generation cephalosporins.
   - Second choice is Fluoroquinolones.
   - Third choice is Spectinomycin.
2. because chlamydial infection could happen

Treatment of **complicated** Gonorrhea

- **Complicated gonorrheal infections :**
  If left untreated, Spread through bloodstream into:
  - Eye
  - Joints
  - Heart valves
  - Brain
- It can also spread from a mother to a fetus during birth
  - Newborn eye infection (conjunctivitis) may lead to blindness
- **Prophylaxis of neonatal conjunctivitis:**
  WHO guidelines suggest one of the following options for topical application to **both eyes immediately after birth: (only one of them)**
  - Silver nitrate 1% solution (mainly)
  - Erythromycin 0.5% eye ointment
  - Tetracycline hydrochloride 1% eye ointment
  - Povidone iodine 2.5% solution (water-based)
  - Chloramphenicol 1% eye ointment (mainly)

Drugs	Silver nitrate 1% solution	Erythromycin
Info	• **It has germicidal effects** due to precipitation of bacterial proteins by liberated **silver ions**.	• 0.5% ointment for treatment & prevention of corneal & conjunctival infections.
Use	• Put into conjunctival sac **immediately after birth** (no later than 1 hr after delivery) (after that it won't be so effective)	

Quiz

MCQ

Q1- A 22-year-old sexually active man presents to the Ambulatory care clinic with dysuria, penile discharge, and a swollen right knee. A joint aspirate of his right knee reveals many neutrophils as well as some gram negative diplococci. Which is the best choice to treat his condition?

A- Ceftriaxone B- Cephalexin C- Dexamethasone D - Meropenem

Q2-A 26-year-old sexually active HIV-negative man presents to his primary care physician with a nonpruritic maculopapular rash on his palms. He reports that about 6 weeks ago, he developed a non painful ulcer on his penis that healed spontaneously. He is injected with a single dose of benzathine penicillin G intramuscularly and sent home. What, if anything, should have been done differently for this patient's care?

A - A different antibiotic class should have been used
B - A different preparation of penicillin G (not benzathine) should have been used
C- Nothing—the course of action taken is entirely appropriate
D - Penicillin V should have been given instead of penicillin G

Q3-Which one of the following is the drug of choice for treatment of syphilis?

A.- ceftriaxone B - Benzylpenicillin penicillin G C. silver nitrate D - Ciprofloxacin

Q4- Which of the following is mechanism of action of Azithromycin?
A- Inhibit bacterial cell wall synthesis
B- Inhibit DNA synthesis by inhibiting DNA gyrase enzyme
C- Inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits.
D-Inhibit bacterial protein synthesis by reversibly binding to 30 S bacterial ribosomal subunit

Q5-Which of the following is a contraindication for Fluoroquinolones ?
A - Pregnancy B - Renal failure C- Hepatic failure D- Bleeding disorders

SAQ

A 24- year- old sexually active young man presents to the emergency department with dysuria, penile discharge, and a swollen right knee .A joint aspirate of his right knee reveals many neutrophils as well as some gram negative diplococci. Which is the best choice to treat his condition?
Q1-Which is the best choice to treat his condition?
Q2- Mention its MOA.
Q3- Enumerate 3 ADRS.

Answers:

MCQ

Q1	A
Q2	C
Q3	B
Q4	C
Q5	A

SAQ

Q1	Ceftriaxone
Q2	Inhibits bacterial cell wall synthesis.(Bactericidal)
Q3	Hypersensitivity reactions,Thrombophlebitis,Super infection Diarrhea

Thank you for all the love and support you gave the team in those two years!

Hope we made the context much easier to study.
God bless you, Future doctors.

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