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Drugs used in treatment of gonorrhea and syphilis

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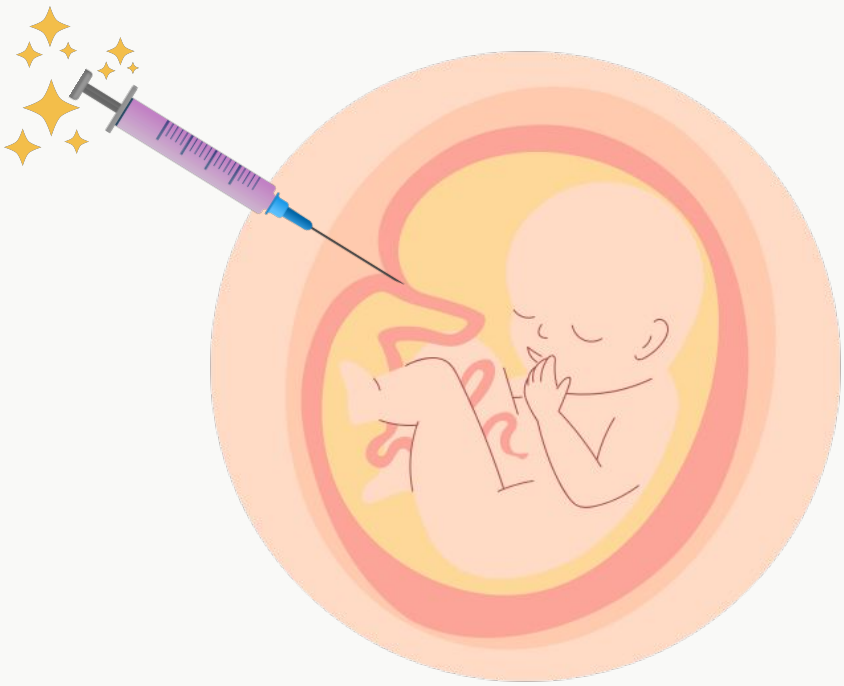


- Main text
- Male slide
- Female slide
- Important
- Dr, notes
- Extra info

EDITING FILE

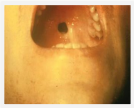
Objective

- 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.

Syphilis

Introduction

- It is a sexually transmitted disease caused by 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, organisms may pass through the placenta to infect the fetus.
  - Manifestation: **Perforation of Palate.**
- May become chronic if left untreated.



Stages of Syphilis

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

Primary stage:
- Painless skin ulceration (a chancre).

Secondary stage:
- Diffuse skin rash & mucous membranes lesions.
- Palmar/plantar rash.

Latent stage:
- In latent syphilis there are little to no symptoms which can last for years.
- 70% may have no symptoms.

Tertiary stage:
- 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).

Drugs used in the treatment of Syphilis

Penicillins are the first choice 2.3.4 are used in case the patient is allergic to penicillins

1. Penicillins	2. Tetracyclines	3. Macrolides	4. Cephalosporins 3rd generation
• Penicillin G • Procaine Penicillin G • Benzathine Penicillin G	• Doxycycline	• Azithromycin	• Ceftriaxone • Cefixime

Drugs used in treatment of syphilis
(β-Lactam Antibiotics)

1) Natural Penicillins

drug	Penicillin G (Benzyl penicillin)	Procaine Penicillin G	Benzathine Penicillin G
MOA	• Inhibits bacterial **cell wall** synthesis through inhibition of transpeptidase enzyme required for crosslinks of peptidoglycans. • **Bactericidal.**		
P.K.	- Given I.V - Short duration of action	- Given I.M (delayed absorption). - Long acting.	- Given I.M (delayed absorption). - Long acting, 2.4 million units is given once.
	All these penicillin preparations are: ○ Acid unstable "not given orally, given parenterally" ○ Penicillinase sensitive (β-lactamase sensitive). ○ Not metabolized. ○ Excreted unchanged in urine through acid tubular secretion. ○ Renal failure prolongs their duration of action."So you need to decrease the dose" ○ procaine & benzathine make the combination long acting		
ADRs	• Hypersensitivity. • Convulsions with high doses or in renal failure. • Super infections.		

2) 3rd generation cephalosporins

Ceftriaxone

MOA	• Inhibit bacterial **cell wall** synthesis. • **Bactericidal**
P.K.	• Given parenterally (I.V). • Eliminated via biliary excretion "used for renal failure (other B-lactams are eliminated by the kidney" • Long Half-life.
ADRS	• Hypersensitivity reactions. • Thrombophlebitis. • Superinfection. • GIT upset: Diarrhea.

Tetracycline

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.
ADRs	• Nausea, vomiting ,diarrhea & epigastric pain (given with food). • Brown discoloration of teeth in children. • Deformity or growth inhibition of bones in children. • Hepatic toxicity (prolonged therapy with high dose). • Vertigo. • Superinfections. • Phototoxicity
C.I	Anything related to children: • Pregnancy. • Breast feeding • Children (below 10 yrs)

Macrolides

Azithromycin

MOA	• Inhibits bacterial protein synthesis by binding to bacterial **50S** ribosomal subunits.
P.K	• Acid stable. • Penetrates into most tissues except CSF. • Half life: 2-4 days (very long duration of action). • Once daily oral dose • Should be given 1 hour before or 2 hours after meals. "to not affect its absorption" • No effect on cytochrome P450 (advantage, because other macrolides like Clarithromycin, erythromycin inhibit P450 enzymes)
ADRs	• **GIT upset:** Nausea, vomiting, abdominal pain and diarrhea. • **Allergic reactions:** Urticaria and mild skin rashes.

WHO Guidelines for the Treatment of Syphilis

1. Early Syphilis

Adults (Primary, secondary and early latent syphilis of not more than two years duration)	**Pregnant woman** Same as non-pregnant, but Doxycycline is #
"Benzathine penicillin G: "First choice .million units once I.M 2.4	
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, or • **Ceftriaxone**: 1 g IM once daily for 10–14 days, or • **Azithromycin**: 2 g once orally.	• **If penicillin is not allowed due to allergy, use:** • **Erythromycin**: 500 mg orally four times daily for 14 days • **Ceftriaxone**: 1 g IM once daily for 10–14 days, or • **Azithromycin**: 2 g once orally.

2. Late Syphilis

Adults *(infection of more than two years duration without evidence of treponemal infection)*	**Pregnant woman**
• **Benzathine penicillin G**: 2.4 million units 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**.	**If penicillin is not allowed due to allergy, use:** • **Penicillin desensitization**. • **Erythromycin:** 500 mg orally four times daily for 30 days • **Ceftriaxone**: 1 g IM once daily for 10–14 days, or • **Azithromycin**: 2 g once orally.

3. Congenital Syphilis

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

Only natural penicillins are used for infants:

- **Aqueous crystalline penicillin G**: 100,000–150,000 units/kg/day, administered as 50,000 units/kg/dose IV every 12 hours during the first 7 days of life and every 8 hours thereafter for a total of 10 days, or
- **Procaine penicillin G**: 50,000 units/kg/dose IM in a single daily dose for 10 days, or
- **Benzathine penicillin G**: 50,000 units/kg/dose IM in a single dose.

Gonorrhea

Introduction

- Caused by **Neisseria gonorrhoeae**: a pus producing bacteria (gram -ve diplococci)
- Transmitted during **sexual contact** with affected person.
- Many people have no symptoms.
- Men & women may have burning with urination
    a. **Men:** discharge from the penis | Testicular pain.
    b. **Women:** vaginal discharge | vaginal bleeding between periods | Pelvic pain

1) Treatment of *uncomplicated* Gonorrhea

CDC Recommended regimens at last slide

First line treatment:

3rd generation cephalosporins:

Ceftriaxone *(500 mg **I.M** single dose)* | **Cefixime** *(400 mg **orally** single dose)*

- **To cover chlamydia: typically given in combination with:**
    - A single dose of **Azithromycin** (1gm orally)
    - or **Doxycycline** (100 mg orally twice daily (BID) for 7 days)

Fluoroquinolones:

Ciprofloxacin *(500 mg)* | **Ofloxacin** *(400 mg)*

M.O.A	• **Single oral dose** • **All Bactericidal: Inhibit DNA synthesis by inhibiting DNA ★gyrase enzyme (required for DNA supercoiling)** & cell division resulting in bacterial cell death
ADRs	• GIT: Nausea ,vomiting & diarrhoea . • CNS: Headache & dizziness. • May damage growing cartilage & cause **Arthropathy** • **Phototoxicity**, avoid excessive sunlight
CIs	• **Pregnancy** & Nursing mothers • **Children (younger than 18 years)**

Alternative treatment:

- in patients that cannot tolerate or be treated with cephalosporins or quinolones

Spectinomycin

M.O.A	• **Inhibits protein synthesis by binding to 30S ribosomal subunits** • **Given 2g I.M, once**
ADRs	• Pain at the site of injection. • Fever • Nephrotoxicity (not common).

Gonorrhea

2) Treatment of complicated Gonorrhea

complicated Gonorrhea

- 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:
  - **Silver nitrate** 1% solution
  - **Erythromycin** 0.5% eye ointment
  - **Tetracycline hydrochloride** 1% eye ointment
  - **Povidone iodine** 2.5% solution (water-based)
  - **Chloramphenicol** 1% eye ointment

a. Silver nitrate	b. Erythromycin
It has **germicidal effects** due to **precipitation of bacterial proteins** by liberated **silver** ions (NOT nitrate).	0.5% ointment For treatment & prevention of corneal and conjunctival infections

Put into conjunctival sac **immediately after birth** (no later than 1 hr after delivery) to avoid the risk of blindness

CDC recommended regimens for *uncomplicated* gonococcal infections

Regimen for uncomplicated gonococcal infections of the cervix, urethra, or rectum:

- **Ceftriaxone**
  - 500 mg IM as a single dose for persons weighing <150 kg
  - For persons weighing ≥150 kg, 1 g of IM
- if ceftriaxone not available:
- **Cefixime** 800 mg orally as a single dose
- **Gentamicin** 240 mg IM as a single dose + **Azithromycin** 2 g orally as a single dose (gentamicin is not preferred due to its side effects)
- **If chlamydial infection has not been excluded when treating with cephalosporins**
  - Add doxycycline 100 mg orally twice daily for 7 days.
  - **During pregnancy**, azithromycin 1 g as a single dose is recommended to treat

Summary L9 Treatment of Syphilis

B- lactams

1-Natural Penicillins | Penicillin G			2- 3rd gen Cephalosporins	
Benzyl penicillin Penicillin G (short acting) I.V	**Procaine Penicillin G (long acting) I.M**	**Benzathine Penicillin G (long acting) I.M**	**Ceftriaxone I.V**	**Cefixime**
MOA & P.k	• Inhibits bacterial **cell wall** synthesis (through inhibition of **transpeptidase** enzyme required for crosslinking) → **Bactericidal** • **Penicillinase-sensitive (b- lactamase sensitive)** • **Renal excretion**		• Inhibits bacterial **cell wall** synthesis → **Bactericidal** • Penicillinase-resistant • **Biliary excretion**	
Uses	**Drug of Choice**		**Patients allergic to penicillins**	
ADRs	• **Hypersensitivity** • Convulsions with high doses or in renal failure • Superinfection		• Hypersensitivity • Thrombophlebitis • Superinfection • Diarrhea	

Tetracyclines

Doxycycline (Orally)

MOA	• Inhibit bacterial **protein** synthesis : (by **reversibly** binding to **30S** bacterial ribosomal subunits) → **Bacteriostatic**
ADRs	• **Brown discoloration of teeth in children** • **Deformity or growth inhibition of bones in children** • NVD & epigastric pain (given with food) • Hepatic toxicity, phototoxicity • Vertigo • Superinfections
# *Contraindications*	• **Pregnancy** • Breastfeeding • Children < 10 yrs

Macrolides

Azithromycin

MOA	• Inhibit bacterial **protein** synthesis (by **reversibly** binding to **50S** bacterial ribosomal subunits)→ **Bacteriostatic** • No effect on CYP450 (unlike erythromycin or clarithromycin)
ADRs	• GIT upset: NVD & abdominal pain • Allergic reactions: urticaria & skin rashes

Summary L9 Treatment of Gonorrhea

Uncomplicated

1- First line treatment

a) 3rd generation cephalosporins:

Ceftriaxone IM | Cefixime Orally

- **Typically given in combination with:**
  - A single dose of **Azithromycin**
  - or **Doxycycline** (contraindicated in pregnancy)

b) Fluoroquinolones:

Ciprofloxacin | Ofloxacin

M.O.A	**All Bactericidal:** Inhibit DNA synthesis by inhibiting DNA gyrase enzyme *(required for DNA supercoiling)*
ADRs	• GIT: Nausea ,vomiting & diarrhoea . • CNS: Headache & dizziness. • May damage growing cartilage & cause **Arthropathy** • **Phototoxicity**, avoid excessive sunlight
CIs	• **Pregnancy** & Nursing mothers • Children under 18 years

2- Alternative treatment:

in patients that cannot tolerate or be treated with cephalosporins or quinolones

Spectinomycin

M.O.A	• **Inhibits protein synthesis by binding to 30S ribosomal subunits**
ADRs	• Pain at the site of injection. • Fever. • Nephrotoxicity (not common).

Complicated

Prophylaxis of neonatal conjunctivitis

Topical: a.Silver nitrate b.Erythromycin c.Tetracycline hydrochloride d.Povidone iodine e. Chloramphenicol

	a. Silver nitrate 1% solution	**b. Erythromycin** 0.5% ointment
M.O.A	• **Precipitation of bacterial proteins** by liberated **silver ions** → **Germicidal** effects	• for treatment & prevention of corneal & conjunctival infections
Use	**Put into conjunctival sac immediately after birth (no later than 1 hr after delivery)**	

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