



Drugs used for the treatment of syphilis & gonorrhea

Objectives:

- **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 treatment of syphilis & gonorrhea
- **Know** the alternative treatments in allergic patients.

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Drug's name | Doctors' notes | Important | Extra

« قل سيروا في الأرض فانظروا كيف بدأ الخلق »

أخيراً وليس آخراً! XD

قال رسول الله صلى الله عليه وسلم: "خير الناس؛ أنفعهم للناس"

كل الشكر والتقدير للأعضاء المبدعين، للذين عملوا واجتهدوا..

بكم ارتقينا بفضل الله ومنته!

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هديل الفرير

نخص بالشكر الجزيل للأعضاء المستثمرين معنا من بداية السنة الثانية وحتى نهايتها.. ما قصرتموا!! ^^

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Drugs used in the treatment of Syphilis

Penicillins

Procaine P.
Penicillin G
Benzathin P

Inhibits bacterial cell wall synthesis through inhibition of transpeptidase enzyme required for crosslinks
▪ **Bactericidal**

3RD GENERATION CEPHALOSPORINS

Cefixime
Ceftriaxone

Inhibit bacterial cell wall synthesis
▪ **Bactericidal**

TETRACYCLINES

Doxycycline

Inhibit bacterial protein synthesis by reversibly binding to 30 S bacterial ribosomal subunits.
▪ **Bacteriostatic**

MACROLIDES

azithromycin

Inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits.

Penicillins are the 1st choice, if there is allergy, then use other suitable drugs shown here.

To Understand Better

Syphilis

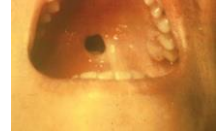
- It is a sexually transmitted disease, caused by bacterium **Treponema pallidum**. **Gram -ve bacteria**, a spiral-shaped, highly mobile bacterium
- T. pallidum enters the body via skin and mucous membranes through abrasions during sexual contact
- Disease progresses in stages, may become chronic without treatment.

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.

Either during pregnancy or during birth.

Pic: fetus effected with syphilis.



Congenital Syphilis - Perforation of Palate

Four Stages of Syphilis

Primary stage

painless skin ulceration (a chancre).



Secondary Stage

Diffuse skin rash & mucous membranes lesions.



Secondary Syphilis: Palmar/Plantar Rash

Most common characteristic of 2ry syphilis



Latent stage

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. **Occurrence of this disease can affect other organs mainly neurological syphilis and CVS syphilis.**
- Rare because of the widespread use of antibiotics.
- Manifestations as **cardiovascular syphilis (syphilitic aortitis, which may result in aneurysm formation).**

β-Lactam Antibiotics

Drug	1 - Penicillins (First line treatment)		
Mech. of action	<ul style="list-style-type: none"> Inhibits bacterial cell wall synthesis through inhibition of transpeptidase enzyme required for crosslinks. (Bactericidal). Kills bacteria bc it's work on transpeptidase enzyme which is s part of wall synthesis, this enzyme required for formation of the cross-link between glycan units. (Cell wall of bacteria consist of glycan units.) Natural Penicillins: classified as antistaphylococcal <ul style="list-style-type: none"> Narrow spectrum of activity Active against gram positive organisms, gram negative cocci, and non β-lactamase producing anaerobes. (bc β-lactamase producing bacteria causes resistance (penicillin will not destroy them) β-lactamase sensitive. = easily gets degradation by B-lactamase produced by bacteria 		
P.K (preparation)	Penicillin G "crystalline penicillin" 1 st discovered (Benzylpenicillin)	Procaine penicillin G	Benzathine penicillin G (1 st line treatment)
	Short duration of action ~ 30 min, I.V. If syphilis affect CNS , we use Penicillin G or Procaine penicillin G + when they give procaine penicillin, they give it in combination with Probenecid* .	Long acting, every 24-48hrs. Has local anesthetic.	Longest acting, every 3-4 weeks. 2.4 million units is given once → the dose is changing depending upon the stage of infection. Used as prophylactic in rheumatic fever. غير مطالبين بالجرعات
	Given I.M. - Delayed absorption. (Pro-drug) They are Penicillin G + Procaine/Benzathine, the combination is to prolong t1/2 , they produce "Depot forms" , They are <u>slowly absorbed</u> into the circulation and persist at low levels over a long time period.		
All of these penicillin preparations are: <ul style="list-style-type: none"> Acid unstable that's why they are given by injection, not orally. Penicillinase sensitive bc it's β-lactamase sensitive Not metabolized Excreted unchanged in urine through <u>acid tubular secretion (active secretion)</u> → adjust the dose in renal failure. Renal failure prolong duration of action. 			<div style="border: 1px dashed gray; padding: 5px; font-size: small;"> *Probenecid inhibits the secretion of penicillins by competing for active tubular secretion via the organic acid transporter and, thus, can increase blood levels → increase duration of action of penicillins. </div>
ADRs	<ul style="list-style-type: none"> Hypersensitivity Convulsions > very rare, only in high dose or renal failure Super/secondary infections 		

Drugs used in Allergic Patients To Penicillins:

Allergic or can't tolerate, Start as following;

- ① Macrolides e.g. **Azithromycin**
- ② Tetracyclines e.g. **Doxycycline**
- ③ Cephalosprins (3rd generation); **Ceftriaxone** "I.V.", **Cefixime** "PO"

Penicillin V has a spectrum similar to that of *penicillin G*, but it is not used for treatment of bacteremia because of its poor absorption. *Penicillin V* is more **acid-stable** than *penicillin G* and is often employed orally in the treatment of infections.

β-Lactam Antibiotics

Drug	2- Cephalosporines (3 rd generation)	
MOA	<ul style="list-style-type: none"> Inhibit bacterial cell wall synthesis Bactericidal 	
P.K	Cefixime (orally)	Ceftriaxone (injection)
	<ul style="list-style-type: none"> More effective against gram negative bacteria. Given orally Excreted Mostly unchanged in the <u>urine</u> <div style="background-color: #e0f2f1; padding: 5px; margin-top: 10px;"> <p>لازم نعرف كمعلومة عامة إنه أغلب الـ beta-lactam Abiotics تعتمد على Renal excretion هذي المعلومة لازم تبقى ثابتة عندنا!! عشان لو عندنا مريض مصاب بالفشل الكلوي لازم آخذ بالي!!</p> </div>	<ul style="list-style-type: none"> Given parenterally (i.v.) Eliminated via <u>biliary excretion</u> (here is an exception, ceftriaxone is excreted via biliary, not renal excretion, so we can use it in renal failure pts 😊) Long Half-life.
ADRs	<ul style="list-style-type: none"> Hypersensitivity reactions Thrombophlebitis → if given by injection e.g. ceftriaxone. Superinfections Diarrhea <p style="text-align: right;">تشبه البنسلين تقريباً</p>	

Tetracyclines

Drug	Doxycycline
MOA	<ul style="list-style-type: none"> Inhibit bacterial protein synthesis by reversibly binding to 30S bacterial ribosomal subunits. Bacteriostatic.
P.K	<ul style="list-style-type: none"> Given orally → Well absorbed orally Long acting 100 mg twice daily for 14 days → The interval of taking this drug depends upon the stage of the disease, e.g. 2ry & 3ry → 29 dys.
ADRs	<ul style="list-style-type: none"> Nausea, vomiting, diarrhea (NVD) & epigastric pain. Not characteristic, NVD in most of drugs. Brown discoloration of teeth in children. Deformity or growth inhibition of bones in children as they bind to tissues undergoing calcification for example, <u>teeth</u> and <u>bones</u>. Hepatic toxicity (prolonged therapy with high dose). Vertigo Superinfections. Photosensitivity → have to protect yourself from sunlight.
C.I	<ul style="list-style-type: none"> Pregnancy & Breast feeding Children (below <u>10 yrs</u>)

Mind Map | Gonorrhoea

Drugs used in the treatment of Gonorrhoea

Uncomplicated gonorrhoeal infections

- 3rd generation Cephalosporins

- Fluoroquinolones

Ciprofloxacin Ofloxacin

Inhibit DNA synthesis by inhibiting DNA gyrase enzyme

- **bactericidal**

- Spectinomycin

Inhibits protein synthesis by binding to 30 S ribosomal subunits.

complicated gonorrhoeal infections

- Silver nitrate

precipitation of bacterial proteins by liberated silver ions

- Erythromycin

Gonorrhoea

Gonorrhoea

Caused by, *Neisseria gonorrhoea*, Pus producing bacteria, Gram –ve cocci



Recommended regimens: (1st line treatment)



❖ Uncomplicated gonorrhoeal infections

- **1st choice:** 3rd generation cephalosporins, 500mg **ceftriaxone**, I.M. or 400 mg of **cefixime**, po. Typically given **with** a single dose of **azithromycin** (1gm, po) or **doxycycline** (100 mg BD, p.o.).

في حالة القونوريا **يَا** أعطي ceftriaxone لحاله! لأن الباكثيريا ممكن تسوي مقاومة له، فعشان كذا لازم أعطي combination

- ^sometimes they give azithromycin or doxycycline not for the gonorrhoea but to avoid a complication with chlamydial infection
- Unlike syphilis gonorrhoea is **harder to treat**; it has limited choices because it's capable of developing resistance very fast/

Gonorrhoea treatment

- ✓ **1st choice:** 3rd generation Cephalosporins → e.g. **Ceftriaxone**, **Cefixime**
- ✓ **2nd choice:** Fluoroquinolones → **Ciprofloxacin**
- ✓ **3rd choice:** **Spectinomycin**

Drug	Fluoroquinolones	Spectinomycin
MOA	<ul style="list-style-type: none"> ○ All are bactericidal ○ Inhibit DNA synthesis by inhibiting DNA gyrase enzyme (required for DNA supercoiling). ○ Is given as single oral dose of : <ul style="list-style-type: none"> • Ciprofloxacin (500 mg) • Ofloxacin (400 mg) <p>خلونا نتفق إن كل BacteriCidal Abiotics تشتغل على cell wall & nucleic acids (باستثناء Aminoglycoside) مع إنهم يشتغلون على protein إلا أنهم bacteriCidal</p>	<ul style="list-style-type: none"> ○ Inhibits protein synthesis by binding to 30S ribosomal subunits. ○ Is given 2 g, I.M., once.
ADRs	<ul style="list-style-type: none"> ○ GIT: Nausea , vomiting & diarrhea ○ CNS: Headache & dizziness ○ May damage growing cartilage and cause arthropathy. ○ Phototoxicity, avoid excessive sunlight (this ADR is w\ fluoroquinolones & tetracyclins) 	<p>Not sever, can be tolerated.</p> <ul style="list-style-type: none"> ○ Pain at site of injection ○ Fever ○ Nephrotoxicity (not common).
C.I	<ul style="list-style-type: none"> ○ Pregnancy ○ Nursing mothers ○ Children under 18 years ○ Epilepsy and cardiovascular disorders 	

What is the Alternative treatment in pts that cannot tolerate or be treated with **cephalosporins** or **quinolones**? → **Spectinomycin**

Gonorrhea

Complicated gonorrheal infections

Spread through blood stream, **EYE**, Joints, Heart, valves, Brain

تحصل مع الحامل أثناء الولادة؛ المولود راح يتأثر غالباً في عينه

Harmful effects of gonorrhea

It can spread from a mother to a child during birth → Newborn **eye infections**, may lead to blindness

Treatment of Complicated infections With conjunctivitis

Silver nitrate

- It has **germicidal** effects due to **precipitation of bacterial proteins** by liberated silver ions.
- Put into conjunctival sac once **immediately** after birth (no later than 1h after birth)

Erythromycin

- 0.5% ointment for treatment & prevention of corneal & conjunctival infections.
- Put into conjunctival sac **immediately** after birth (no later than 1 hr after delivery)
- Can be used as alternative or additional to silver nitrate

* **Silver nitrate** and **erythromycin** are used in new born with complicated infection with conjunctivitis.

Summary-1

TREATMENT OF SYPHILIS

1- Penicillins (β -Lactam Antibiotics)			2- Cephalosporines			
Drug	Penicillin G	Procaine penicillin G	Benzathine penicillin G	Cefixime	Ceftriaxone	
	Short duration of action, given I.V	Given I.M - Delayed absorption. Long acting.		Third generation cephalosporins		
MOA	<ul style="list-style-type: none"> Inhibits bacterial cell wall synthesis through inhibition of transpeptidase enzyme required for crosslinks . Bactericidal 			<ul style="list-style-type: none"> Inhibit bacterial cell wall synthesis Bactericidal 		
P.K	<ul style="list-style-type: none"> Acid unstable. Penicillinase sensitive. Excreted in urine through acid tubular secretion. Renal failure prolonged the duration of action. Not metabolized 			<ul style="list-style-type: none"> Given orally Excreted unchanged in the urine 	<ul style="list-style-type: none"> Given I.V. Eliminated via biliary excretion Long Half-life 	
ADRs	<ul style="list-style-type: none"> Hypersensitivity. Convulsions. Super infections. 			<ul style="list-style-type: none"> Hypersensitivity reactions Thrombophlebitis. Superinfections. Diarrhea. 		
3- TETRACYCLINES			4- Macrolides			
Drug	Doxycycline			Azithromycin		
MOA	<ul style="list-style-type: none"> Inhibit bacterial protein synthesis by reversibly binding to 30S bacterial ribosomal subunits. Bacteriostatic 			<ul style="list-style-type: none"> Inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits. Bacteriostatic 		
P.K	<ul style="list-style-type: none"> Given orally. Well absorbed orally. Long acting Twice daily for 14 days. 			<ul style="list-style-type: none"> Acid stable Penetrates most tissues except CSF Half life : 2-4 days Once daily 2g oral dose Should be given 1 hour before or 2 hours after meals No effect on cytochrome P450 		
ADRs	<ul style="list-style-type: none"> Nausea, vomiting ,diarrhea, Vertigo & epigastric pain Brown discoloration of teeth in children. Deformity or growth inhibition of bones in children Hepatic toxicity (prolonged therapy with high dose). Superinfections. ❖ Contraindications : Pregnancy. Breast feeding. Children (below 10 yrs). 			<ul style="list-style-type: none"> GIT upset: Nausea, vomiting, abdominal pain & diarrhea. Allergic reactions: urticaria, mild skin rashes. 		

Summary-2

TREATMENT OF GONORRHEA

1- 3rd generation Cephalosporines (Cefixime, Ceftriaxone)

1st line treatment in Uncomplicated gonorrhoeal infections.

500mg ceftriaxone, I.M. or 400 mg of cefixime, po **in combination with** Typically given with a single dose of azithromycin(1gm, po) or doxycycline(100 mg BD, p.O.) .

2- Fluoroquinolones

3- Spectinomycin

Drug	Ciprofloxacin (500 mg)	Ofloxacin (400 mg)	Spectinomycin
MOA	<ul style="list-style-type: none"> Bactericidal. Inhibit DNA synthesis by inhibiting DNA gyrase enzyme (required for DNA supercoiling). 		Inhibits protein synthesis by binding to 30 S ribosomal subunits.
P.K.	Single oral dose		Is given 2 g, I.M. , once
ADRS	<ul style="list-style-type: none"> GIT: Nausea , vomiting & diarrhea. CNS: Headache & dizziness. May damage growing cartilage and cause arthropathy. Phototoxicity, avoid excessive sunlight. <p>❖ CONTRAINDICATIONS :</p> <ul style="list-style-type: none"> Pregnancy. Nursing mothers. Children under 18 years. 		<ul style="list-style-type: none"> Pain at site of injection. Fever. Nephrotoxicity (not common).

TREATMENT OF COMPLICATED GONORRHEAL INFECTIONS WITH CONJUNCTIVITIS

1- Silver nitrate

2- ERYTHROMYCIN

It has germicidal effects due to precipitation of bacterial proteins by liberated silver ions.

0.5% ointment for treatment & prevention of corneal & conjunctival infections.

P.K.	Put into conjunctival sac once immediately after birth (no later than 1 h after birth).
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MCQs

1- During which stages is syphilis contagious?

- A- Primary and late stages only
- B- Secondary and latent stages only
- C- Primary and secondary stages only
- D- Syphilis is contagious during all stages.

2- The term "chancre" is given to:

- A- the sores symptomatic of herpes
- B- the sore symptomatic of syphilis
- C- the growths symptomatic of genital warts
- D- all of the above

3- Which of the following statements is true regarding the properties of benzylpenicillin?

- A- It is a bacteriostatic agent.
- B- It is active over a wide range of bacterial species.
- C- It is resistant to β -lactamases.
- D- Certain individuals may have an allergic response to it.

4- Children younger than 8 years of age should not receive tetracyclines because these agents:

- A- Cause rupture of tendons.
- B- Do not cross into the cerebrospinal fluid.
- C- Are not bactericidal.
- D- Deposit in tissues undergoing calcification

5- A 25-year-old male returns home from a holiday in the Far East and complains of 3 days of dysuria and a purulent urethral discharge. You diagnose this to be a case of gonorrhoea. Which of the following is appropriate treatment?

- A- Ceftriaxone IM.
- B- Penicillin G IM.
- C- Gentamicin IM.
- D- Piperacillin/tazobactam IV.

6- 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 subunits

7- A 27-year-old man presents with complaints of a painless ulcer on his penis. He admits to having unprotected intercourse with a woman he met in a bar during a conference 2 weeks ago. A scraping of the lesion, visualized by dark field microscopy, demonstrates spirochetes, and a diagnosis of syphilis is made. Which of the following is the treatment of choice assuming the patient has no known allergies?

- A- Benzathine penicillin G
- B- Penicillin G
- C- Penicillin V
- D- Doxycycline

8- A drug that it has germicidal effects due to precipitation of bacterial proteins by liberated ions?

- A- Ciprofloxacin
- B- spectinomycin
- C- Silver Nitrate
- D- Erythromycin

9- A 39 female was taking a drug to treat her of gonorrhoea, later she developed nephrotoxicity; what is the name of the drug?

- A- Ciprofloxacin
- B- spectinomycin
- C- Silver Nitrate
- D- Erythromycin

10- One of the following is the mechanism of action of Ofloxacin?

- A- Inhibits protein synthesis by binding to 30 S ribosomal subunits
- B- Stimulate DNA supercoiling
- C- Stimulate protein synthesis required in phagocytosis
- D- Inhibits DNA gyrase enzyme

الحمد لله على التمام، آخر محاضرة فارما في سنوات العلوم الأساسية، لكنه بيلحقكم بعدين
أكيدا! p: .. لذلك ركزوا زين وأنتم تدرسون ولا تنسون تسيرون على التيم السنوات
الجاية بإذن الله!



Pharmacology 435

 @ pharmacology435

Sources:

1. 435's slides.