

DRUGS USED FOR THE TREATMENT OF SYPHILIS & GONORRHEA

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(Slides are adopted and modified from
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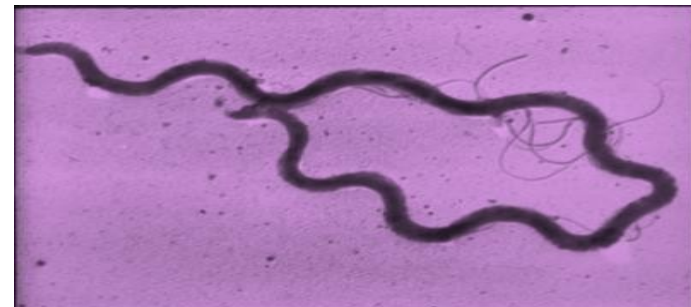
ILOS

At the end of lectures, the students should

- List the drugs used in the treatment of syphilis & gonorrhoea.
- 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 & gonorrhoea
- Know the alternative treatments in allergic patients.

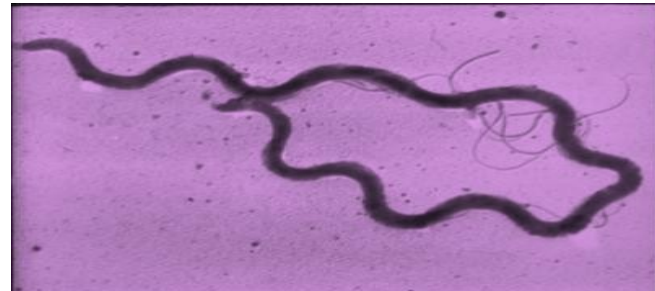
WHAT IS SYPHILIS?

- Sexually transmitted disease
- Caused by *Treponema pallidum*
- a spiral-shaped, *Gram-negative* high 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.



SIGNS AND SYMPTOMS

- The signs and symptoms of syphilis vary depending upon stage of disease.
- **Disease progresses in stages (primary, secondary, latent, and tertiary).**
- **May become chronic without treatment**



STAGES OF SYPHILIS

PRIMARY STAGE

- Painless skin ulceration (a chancre)



SECONDARY STAGE

- Diffuse skin rash & mucous membranes lesions



SECONDARY SYPHILIS: PALMAR/PLANTAR RASH



Source: Seattle STD/HIV Prevention Training Center at the University of Washington, UW HSCER Slide Bank

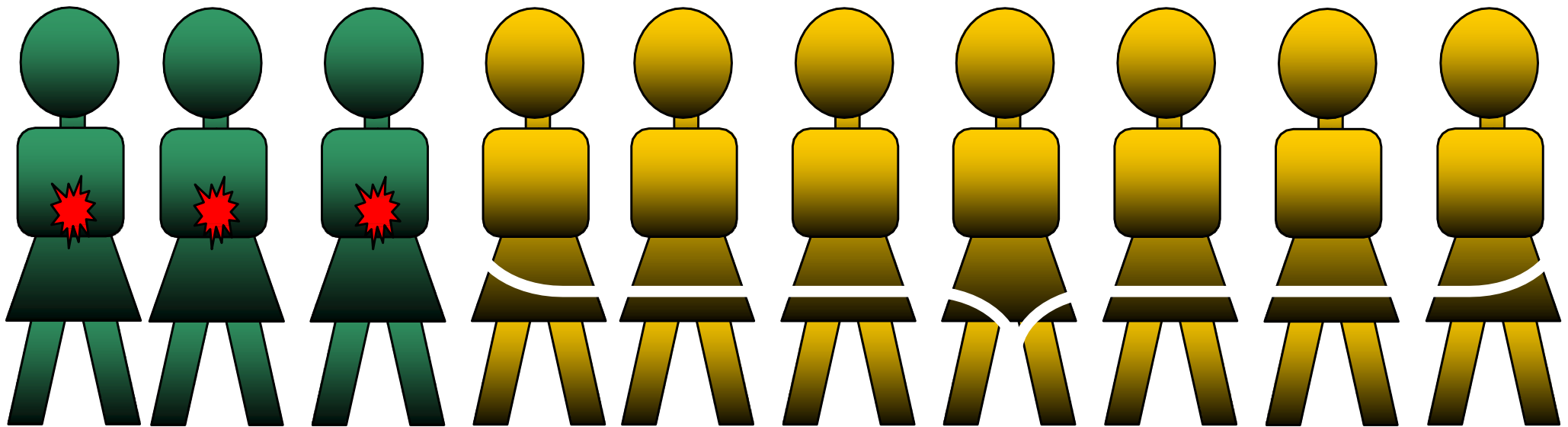


Source: CDC/NCHSTP/Division of STD Prevention, STD Clinical Slides

LATENT STAGE

In latent syphilis there are little to no symptoms which can last for years.

70% may have NO SYMPTOMS



TERTIARY SYPHILIS

- 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).

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.

Perforation of Palate



DRUGS USED IN THE TREATMENT OF SYPHILIS

□ **Penicillins*****

- Penicillin G
- Procaine Penicillin G
- Benzathine Penicillin G

□ **Tetracyclines e.g. doxycycline**

□ **Macrolides e.g. azithromycin**

□ **Cephalosporins**

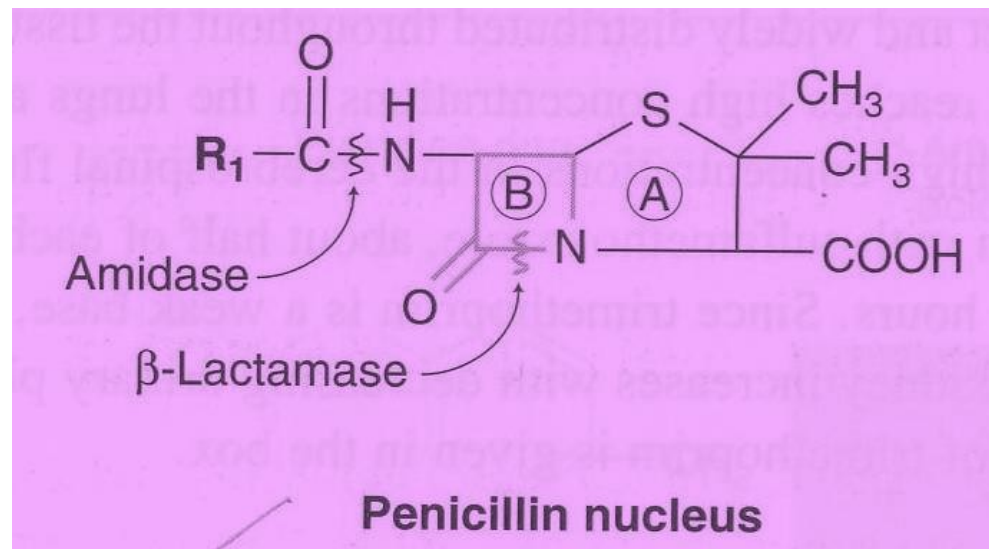
- Ceftriaxone
- Cefixime

β -Lactam Antibiotics

PENICILLINS

Mechanism of action

- Inhibits bacterial cell wall synthesis through inhibition of transpeptidase enzyme required for crosslinks .



NATURAL PENICILLINS

- Benzylpenicillin (penicillin G)
- Procaine penicillin G
- benzathine penicillin G

PENICILLINS USED FOR TREATMENT OF SYPHILIS

□ Penicillin G

✓ Short duration of action, given i.v.

□ Procaine penicillin G

✓ Given i.m. - delayed absorption.

✓ Long acting

□ Benzathine penicillin G

✓ Given i.m. - Delayed absorption.

✓ Long acting, 2.4 million units is given once.

PENICILLINS USED FOR TREATMENT OF SYPHILIS

All these penicillin preparations are:

- Acid unstable
- Penicillinase sensitive (β -lactamase sensitive)
- Not metabolized
- Excreted unchanged in urine through acid tubular secretion.
- Renal failure prolong duration of action.

ADVERSE EFFECTS OF PENICILLINS

- **Hypersensitivity**
- **Convulsions with high doses or in renal failure**
- **Super infections**

TETRACYCLINES

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

TETRACYCLINES

Doxycycline

- **Given orally**
- **Long acting**
- **100 mg BID daily for 14 days.**

SIDE EFFECTS

- **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.**

CONTRAINDICATIONS

- **Pregnancy**
- **Breast feeding**
- **Children (below 10 yrs)**

MACROLIDES

AZITHROMYCIN

MECHANISM OF ACTION

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

PHARMACOKINETICS

- **Acid stable**
- **Penetrates into most tissues except CSF**
- **Half life : 2-4 days**
- **Once daily oral dose**
- **Should be given 1hour before or 2 hrs after meals**
- **No effect on cytochrome P450**

SIDE EFFECTS

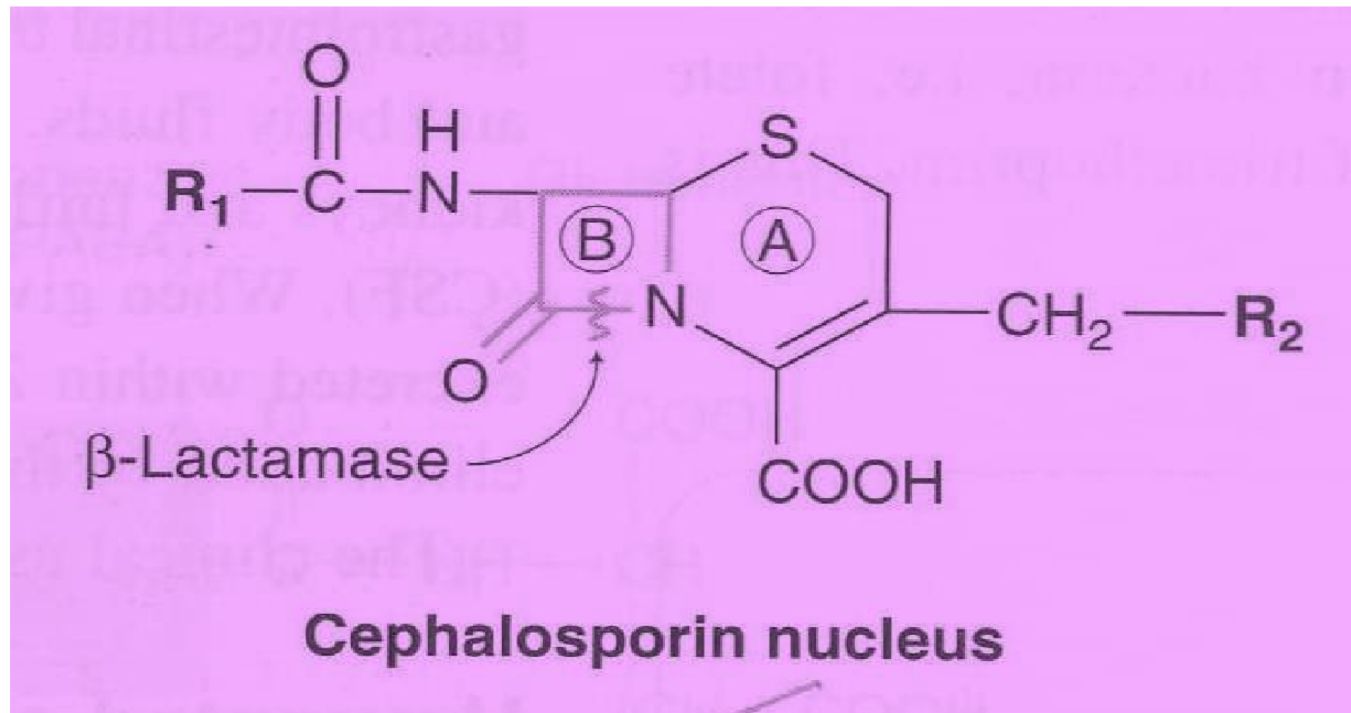
- **GIT upset:** Nausea, vomiting, abdominal pain & diarrhea.
- **Allergic reactions:** urticaria, mild skin rashes.



CEPHALOSPORINES

□ Inhibit bacterial cell wall synthesis

□



GENERATION CEPHALOSPORINS

Ceftriaxone

- **Third generation cephalosporins**
- **Given parenterally (i.v.)**
- **Eliminated via biliary excretion**
- **Long Half-life**

ADVERSE EFFECTS OF CEPHALOSPORINS

- Hypersensitivity reactions
- Thrombophlebitis
- Superinfections
- Diarrhea

Early syphilis

WHO GUIDELINES FOR THE Treatment of *Treponema pallidum* (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.

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.

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 four times daily for 14 days
Ceftriaxone 1 g IM once daily for 10-14 days or,
Azithromycin 2 g once orally.

Late syphilis WHO GUIDELINES FOR THE Treatment of *Treponema pallidum* (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

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.

Congenital syphilis

WHO GUIDELINES FOR THE Treatment of *Treponema pallidum* (syphilis)

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

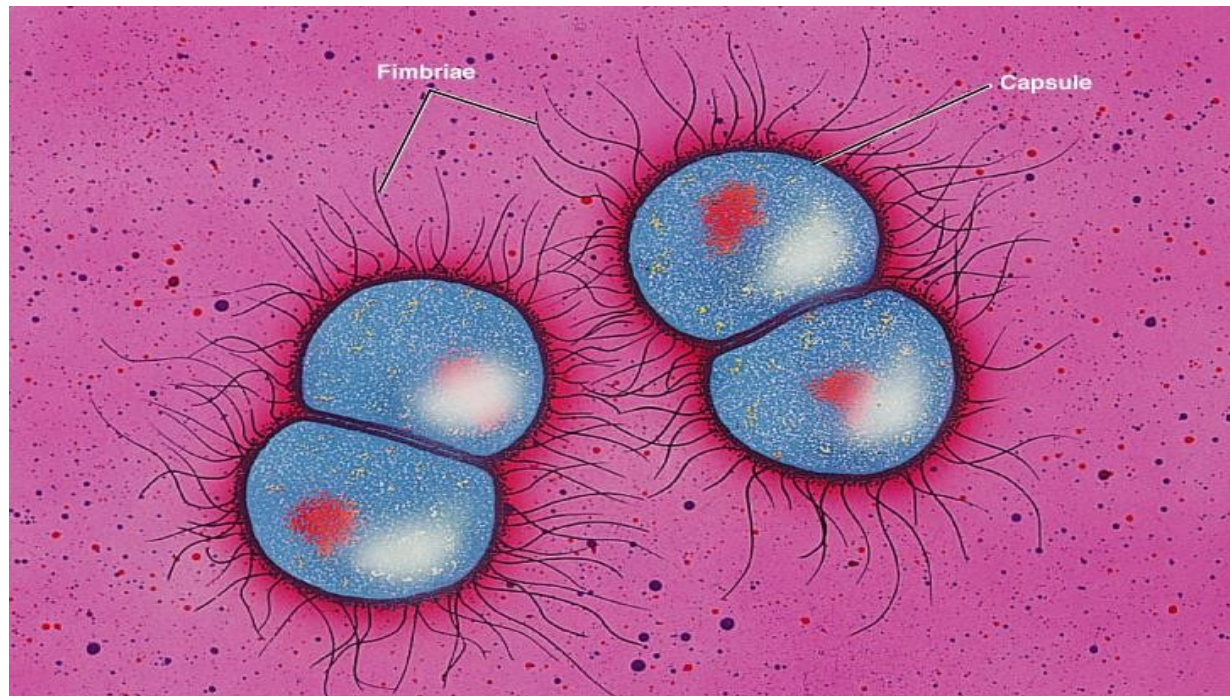
Aqueous benzyl penicillin (I.V.)
100 000-150 000 U/kg/day for 10-15 days

or

Procaine penicillin (I.M.)
50 000 U/kg/day single dose for 10-15 days

GONORRHEA

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



GONORRHEA

- 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.

DRUGS USED IN THE TREATMENT OF GONORRHEA

- **3rd generation Cephalosporins*****

 - e.g. Ceftriaxone, Cefixime

- **Fluoroquinolones****

 - e.g. Ciprofloxacin

- **Spectinomycin**

RECOMMENDED REGIMENS (1ST LINE TREATMENT)

Uncomplicated gonorrheal infections

3rd generation cephalosporins

500mg ceftriaxone, I.M.

or 400 mg of cefixime, po

Typically given in combination with

a single dose of azithromycin(1gm, po)

or doxycycline(100 mg BID, p.O.) for 7

days.

FLUOROQUINOLONES

Single oral dose of :

Ciprofloxacin(500 mg)

Ofloxacin(400 mg)

MECHANISM OF ACTION OF FLUOROQUINOLONES

- All are bactericidal
- Inhibit DNA synthesis by inhibiting DNA gyrase enzyme (required for DNA supercoiling).

SIDE EFFECTS

- **GIT:** Nausea , vomiting & diarrhea
- **CNS:** Headache & dizziness
- May damage growing cartilage and cause arthropathy.
- **Phototoxicity**, avoid excessive sunlight

CONTRAINDICATIONS

- **Pregnancy**
- **Nursing mothers**
- **Children under 18 years**

SPECTINOMYCIN

- **Inhibits protein synthesis by binding to 30 S ribosomal subunits.**
- **Is given 2 g, i.m, once.**

SIDE EFFECTS

- **Pain at site of injection**
- **Fever**
- **Nephrotoxicity (not common).**

COMPLICATED GONORRHEAL INFECTIONS

If left untreated, it can spread through blood stream into:

- EYE
- Joints
- Heart valves
- Brain

HARMFUL EFFECTS OF GONORRHEA

It can also spread from a mother to a child during birth.

Newborn eye infections **conjunctivitis**, may lead to blindness



OCULAR PROPHYLAXIS IN NEWBORNS

- **WHO guidelines** suggest one of the following options for topical application to both eyes immediately after birth:
- Silver nitrate 1% solution or
- Erythromycin 0.5% eye ointment or
- Tetracycline hydrochloride 1% eye ointment or
- Povidone iodine 2.5% solution (water-based) or
- Chloramphenicol 1% eye ointment

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 1 h 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)**