

## Sexually Transmitted Infections

**Clinical Case Applicability:** pelvic inflammatory disease, infertility, chronic pelvic pain

### Learning Objectives:

1. Understand the pathophysiology of common STIs
2. Describe the long-term sequelae of STIs
3. Understand the mechanism of action for treatment of common STIs

**What is the pathophysiology of infectivity & treatment of these organisms?** (HPV: see CIN script)

#### HSV (herpes) (figure 1):

- Primary infection: entry through mucous membrane -> viral entry into sensory nerves -> retrograde axonal transport to dorsal root ganglion -> lifelong latency
- Reactivation: viral particles/proteins transported anterograde into skin/mucous membranes -> viral shedding and cell lysis -> vesicles/ulceration
- Treatment: Not curable; Nucleoside analogs (acyclovir) can ↓ frequency and severity of flares
  - **Acyclovir** -> converted to acyclovir triphosphate -> acyclovir triphosphate competitively inhibits and inactivates HSV DNA polymerases -> prevents further viral DNA synthesis

#### C trachomatis (chlamydia) (figure 2): Obligate intracellular organism that exists in 2 forms: extracellular infectious elementary bodies (EBs) and intracellular non-infectious reticulate bodies (RBs)

- EBs attach and invade vaginal epithelial cells through cell surface receptors -> EBs reorganize into a large RB inside a phagosome that migrates towards the cell nucleus -> RBs replicate via binary fission and forms an inclusion -> inclusion condenses into EBs -> cell lysis releases EBs that infect other cells
- Treatment: Curable with a single dose of **azithromycin** -> binds to 50S subunit of bacterial ribosome -> inhibits mRNA translation -> arrests RNA-dependent bacterial protein synthesis -> inhibits bacterial growth

#### N gonorrhoeae (gonorrhea): Gram-negative diplococci that are obligate intracellular bacterium

- Pili allows *N gonorrhoeae* to adhere to mucosal membrane -> bacteria penetrate mucosal membrane & invade cells
- Treatment: Curable with a single dose of **ceftriaxone** → binds to bacterial transpeptidases → disruption of bacterial cell wall cross-linking → damage to cell wall → cell lysis

#### T. pallidum (syphilis): Gram negative spirochetes

- Outer membrane promotes attachment to mucous membranes -> travels via lymphatic system to regional lymph nodes -> production of hyaluronidase which facilitate perivascular invasion -> disseminated disease
- Treatment: Curable in early stages with single dose of intramuscular **penicillin** → binds bacterial transpeptidases → disruption of bacterial cell wall cross-linking → damage to cell wall → cell lysis

#### T. vaginalis (trichomonas): Anaerobic flagellated protozoan

- Pathogenesis not well understood: postulated to involve contact-dependent and contact-independent mechanisms
- Treatment: Curable with a single dose of **metronidazole** → nitro group of metronidazole reduced by ferredoxin in anaerobic bacteria → nitro radical causes oxidative damage to bacterial DNA → cell death

### What are the long-term consequences of untreated STIs?

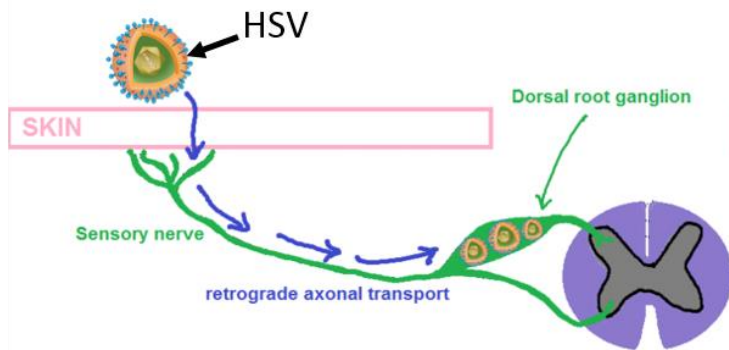
- Pelvic inflammatory disease (PID): ascending infection to the uterus & tubes → can cause infertility
- ↑ susceptibility to HIV: inflammation caused by trichomoniasis can ↑ risk of acquiring and spreading HIV
- Tertiary disease: untreated, disseminated syphilis can infect many organs including the CNS

### What is the pathophysiology underlying PID?

- Proliferative phase of the menstrual cycle → cervical mucosal barrier is thinner → allows bacteria to enter the uterus and subsequently the fallopian tubes
- Bacteria cause destruction of the epithelial cells, cilia and microvilli → localized inflammatory reaction → chronic inflammation with tissue remodeling and scarring

Figure 1

### Primary infection



### Reactivation

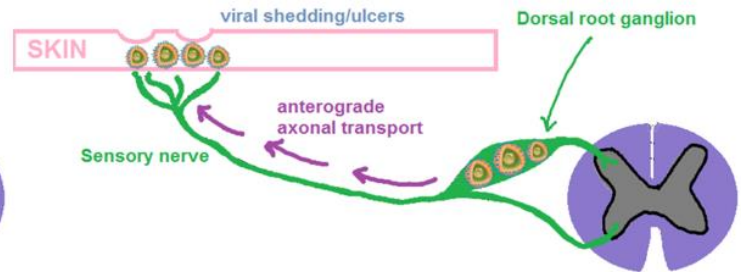
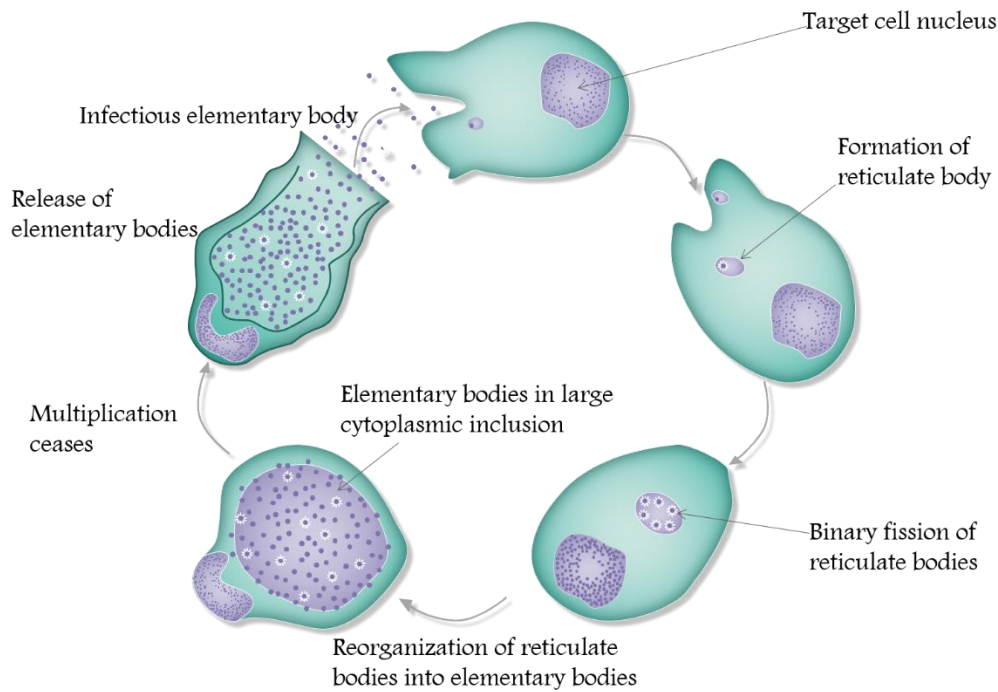


Figure 2

### Chlamydia Trachomatis



### References

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