Sexually transmitted diseases (STD)

- **Also known as verenereal diseases (VD) or sexually transmitted infections (STI)**
- Transmission – sexual contact, including vaginal intercourse, oral sex, and anal sex
- Have been well known fro hundreds years
- **Classification**: **bacterial, viral, fungal, parasitic**

Spirochetes

- **Slender**, motile, flexible, **undulating**, gram-negative bacteria
- Characteristic **corkscrew (helical) shape**
- Can be aerobic, anaerobic or facultative anaerobic
- Pathogenic spirochetes are included in

3 genera: Treponema, Borrelia and Leptospira

Syphilis - aetiology and transmission

- spirochaete ***Treponema pallidum*** (thin, helical (0.1 to 0.5 × 5 to 20 µm), **gram-negative bacteria**
- 3 periplasmic **flagellae** are inserted at each end. These spirochetes **do not grow in cell-free cultures**
- too thin to be seen with light microscope ba Gram or Giemsa staining, but **dark-field microscopy** or **fluorescent microscopy** is suitable

Note: related to *T. pallidum* subspecies *endemicum* causes endemic syphilis (bejel); *T. pallidum* subspecies *pertenue* causes yaws; and *T. carateum* causes pinta. Bejel, yaws, and pinta are nonvenereal diseases

Virulence factors

- **Generally classical virulence factors are not known**
- **Outer membrane proteins** promote **adherence to host cells**
- **Hyaluronidase** may facilitate **perivascular infiltration**
- **Coating of fibronectin** protects against phagocytosis
- **Tissue destruction** primarily results **from host's immune response** to infection

Syphilis - pathogenesis

- the organism **enters** the body through **minute abrasions** (skin, mucous memranes)
- **local slow multiplication** – infiltration the lesion with plasma cells and macrophages (endarteritis)
- **incubation period – 3 weeks**
- **<u>stages</u>**
- 1. **primary (skin lesion – chancre)**

  2. **secondary (skin lesions disperse over the body – rash, pailoma-like lesions in anogenital or oral area - condylomata lata)**

  3. **tertiary – late phase** (all tissues may be involved , local multiplication and destruction of the tissue - arteritis, dementia, blindness, granulomatous lesions (gummas) may be found in bone, skin)

Note: not all patients go through all the stages, after 1. and 2. stages patients usually remains free of the disease)

Syphilis – congenital syphilis

- **In utero infections** can lead to serious **fetal disease**, resulting in **latent infections**, **multiorgan malformations**, or **death of the fetus**.
- Most infected infants are **born without clinical evidence** of the disease, but **rhinitis** then develops and is followed by a widespread desquamating **maculopapular rash**.

Teeth and bone malformation, blindness, deafness, and cardiovascular syphilis are common in untreated infants who survive the initial phase of disease.

Syphilis – primary stage

Syphilis – secondary stage

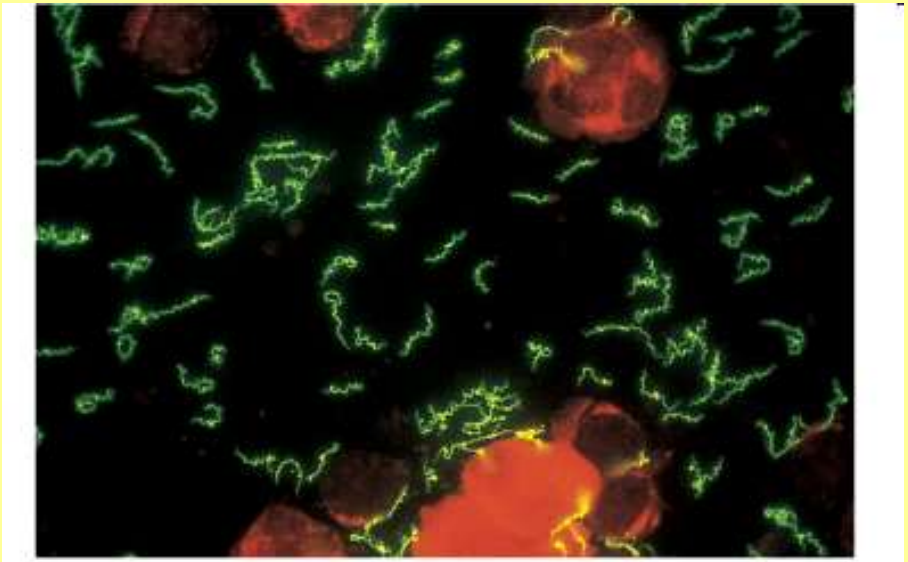
Syphilis – tertiary stage

Laboratory dg - microscopy

- the diagnosis of **primary**, **secondary**, or **congenital syphilis** can be made **rapidly** by **dark-field examination** of the exudate from skin lesions

Laboratory dg – fluorescent microscopy

• spirochetes **do not survive transport to the laboratory**, and **tissue debris can be mistaken for spirochetes**. Material collected **from oral and rectal lesions should not be examined because nonpathogenic spirochetes can contaminate the specimen**. A more useful test for detecting *T. pallidum* is the **direct fluorescent antibody test**



Laboratory dg – serology, nontreponemal tests

•**Nontreponemal tests** measure immunoglobulin (Ig)G and IgM antibodies (also called **reaginic antibodies**). The antigen used for the nontreponemal tests is **cardiolipin,** which is derived from beef heart. The two tests used most commonly are the **Venereal Disease Research Laboratory (VDRL) test** and the **Rapid Plasma Reagin (RPR) test.**

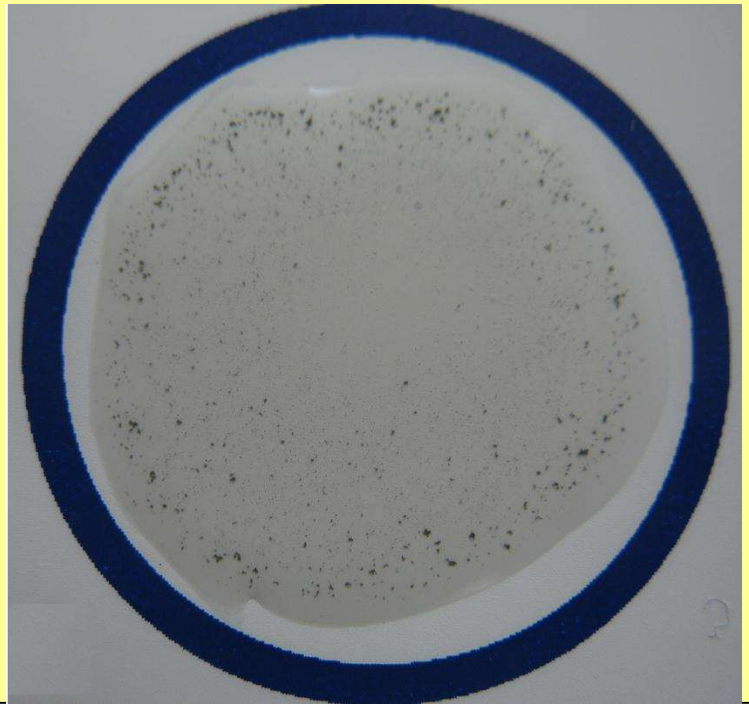


Fig. Positive agglutination in reagin test

Laboratory dg – serology, treponemal tests

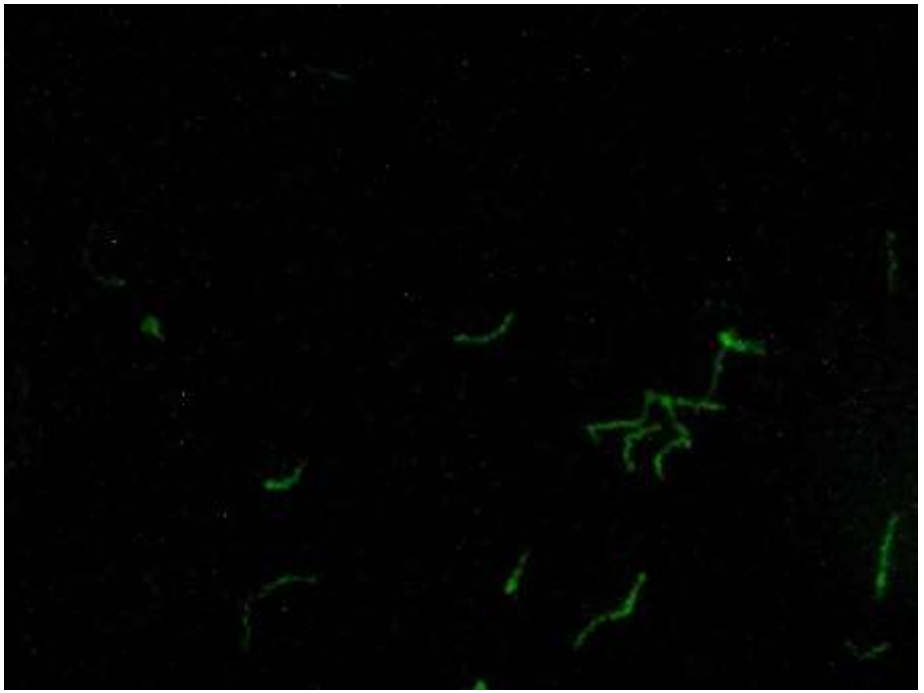
- The tests **most commonly used** are the fluorescent **treponemal antibody-absorption** (FTA-ABS) **test** is an **indirect fluorescent antibody test.** *T. pallidum* immobilized on glass slides is used as the antigen. The slide is overlayed with the patient's serum, which has been mixed with an extract of nonpathogenic treponemes. The fluorescein-labeled antihuman antibodies are then added to detect the presence of specific antibodies in the patient's serum.

- Treponema pallidum particle **agglutination** (TP-PA) test. The TP-PA test is a **microtiter agglutination test.** Gelatin particles sensitized with T. pallidum antigens are mixed with dilutions of the patient's serum. If antibodies are present, the particles agglutinate. A variety of specific **enzyme immunoassays** (EIAs) have been developed recently and appear to have sensitivities and specificities similar to the FTA-ABS and TP-PA tests.

Laboratory dg – serology, treponemal tests

- The tests **most commonly used** are the fluorescent **treponemal antibody-absorption** (FTA-ABS) **test**

Procedure:
1.Dilution of patients´sera (Ab) and inoculation on slide where Ag is fixed
2. Add antihuman Ab labeled by fluorochrom
3. Observew using fluorescent microscope

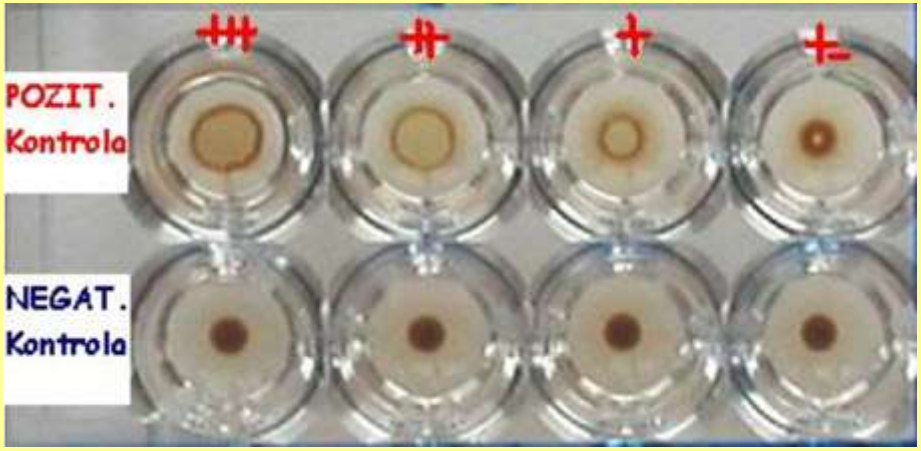


Positive result

http://www.medmicro.info

Laboratory dg – serology, treponemal tests

• Treponema pallidum particle **agglutination** (TP-PA) test. The TP-PA test is a microtiter agglutination test. Gelatin particles (or erytrocytes TPHA) sensitized with **T. pallidum antigens** are mixed with dilutions of the patient's serum. If antibodies are present, the particles agglutinate. A variety of specific **enzyme immunoassays** (EIAs) have been developed recently and appear to have sensitivities and specificities similar to the FTA-ABS and TP-PA tests.



TPHA test

http://www.medmicro.info

Treatment, prevention, control

- **penicillin** is the **drug of choice**
- long-acting **benzathine penicillin** is used for the **early stages**
- **penicillin G** is recommended for **congenital and late syphilis.**
- **tetracycline** and **doxycycline** can be used as alternative antibiotics for patients allergic to penicillin. Only penicillin can be used for the treatment of neurosyphilis; thus, penicillin-allergic patients must undergo **desensitization**. This is also true for pregnant women, who should not be treated with the tetracyclines. Because protective vaccines are not available, syphilis can be **controlled** only through the practice of **safe-sex techniques** and adequate contact and treatment of the sex partners of patients who have been documented with infection.

Gonorrhea

- **agent – Neisseria gonorrheae** attack mucous membranes of genitourinary tract, eye, rectum, throat
- **symptoms**
- acute suppuration, tissue invasion (chronic inflammation, fibrosis)
- men – urethritis, yelow, creamy pus and painful urination (also could extend to epidymidis), can be asymptomatic
- women – primary infections – endocervix extend to uretra, vagina rising mucopurulent discharge and progress to uterine tubes (salpingitis) firosis and obliteration of the tubes (20% infertility)
- **Gonococcal bacteremia** lead to **skin lesions** (hemorragic paules and pustules) and **suppurative arthritis, endocarditis is rare but severe**
- **Sometimes meningitis and eye infections in adults**
- **Ophtalmia neonaturum – conjunctivitis progress, if untreted results in blindless**

Antigenic structure

- **antigenically heterogeneous** - frequently switching one antigenic form (pilin, Opa, lipopolysacharide – surface exposed Ag) to another **to avoid host defenses**
- this switching takes place in every 10^3 gonococci
- **from multiple genes** for pilin **only one gene** is **inserted into the expresion site – expression of many antigenically different pilin molecules over time**
- surface structures and their role:
  pili (fimbriae) - adhesion
  POR protein – nutrients enter the cell,
  OPA proteins - adhesion
  RMP protein – antigenically conserved
  lipooligosaccharide (LOS) – does not long O antigen like LPS, **express simultaneously more than one**, **endotoxic effects, structurally resemble human cell membranes (mimicry) – evading immune system**
  other proteins

*** Physiology and structure**

-growth best at 35° to 37°C in a humid atmosphere supplemented with CO2 (**chocolate agar** or selective media e.g. Thayer-Martin medium)

- **oxidase** and **catalase** positive; acid produced from **glucose** oxidatively

-**virulence factors** (outer surface with multiple antigens): e.g. pili protein; Por proteins

*** Diagnosis**

- **Gram stain** of urethral specimens is accurate for symptomatic males only

-**culture** is sensitive and specific but has been replaced with **nucleic acid amplification** assays in most laboratories

*** Epidemiology**

- **humans are the only natural hosts**, **transmission is primarily by sexual contact**

-disease most common at ages 15 to 24 years, people who have multiple sexual encounters carriage can be asymptomatic, particularly in women

*** Treatment, Prevention, and Control**

- **ceftriaxone** - uncomplicated cases; **fluoroquinolone** - in susceptible population; penicillin should be avoided because resistance is common

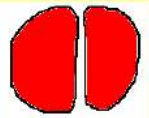
- **doxycycline** or **azithromycin** should be - for infections complicated by Chlamydia

- for neonates, prophylaxis with 1% silver nitrate; ophthalmia neonatorum - ceftriaxone

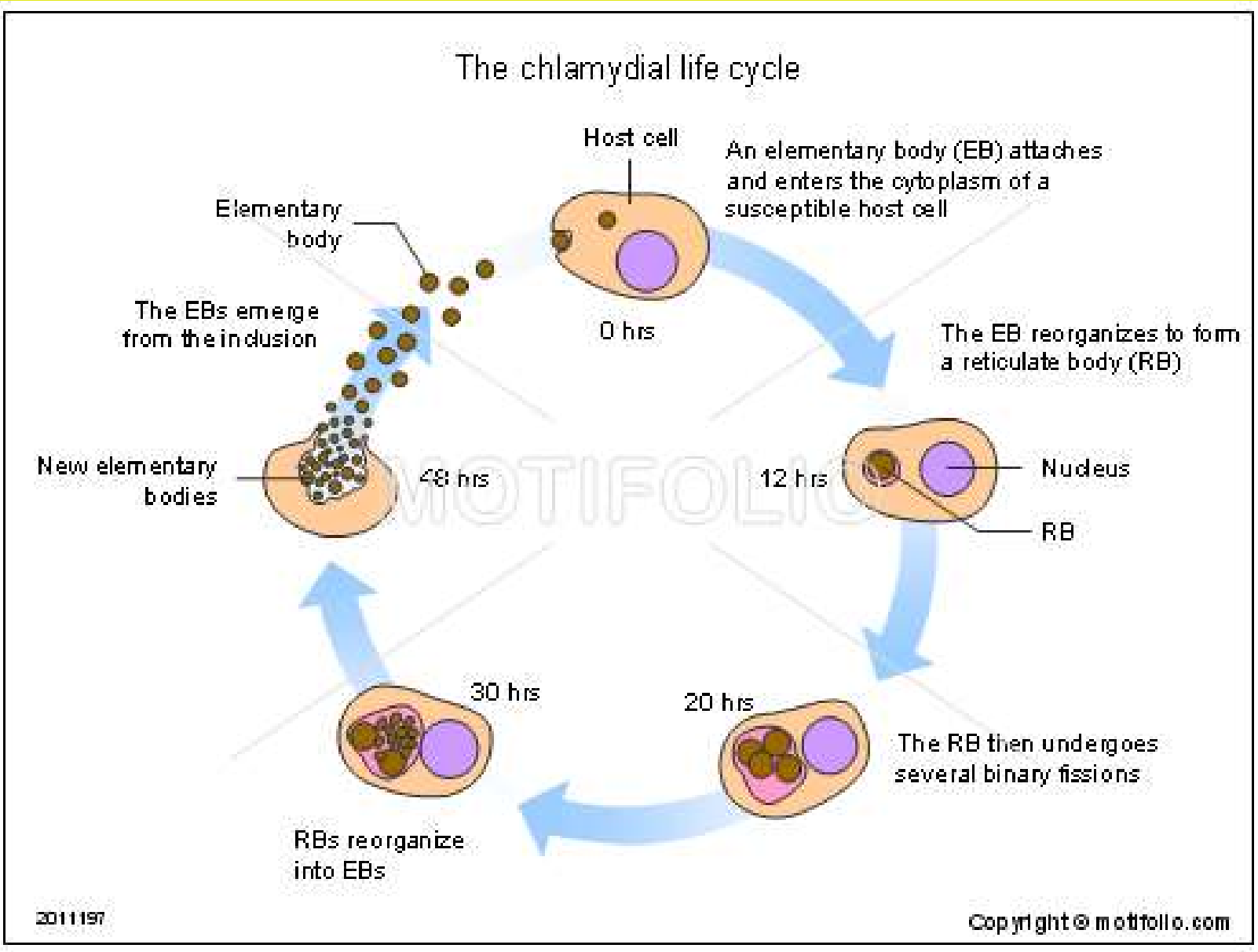
- **prevention** consists of **patient education** (e.g. condoms) and aggressive follow-up of sexual partners of infected patients

- effective vaccines are not available

Fig. Schematically gram-negative cocci in resembling in coffee beans arragements



Chlamydia – intracellular cycle



Chlamydia

Defect metabolism – intracellular bacteria

genera – Chlamydia (*C. trachomatis*), Chlamydophila (*C. pneumoniae, C. psittaci*)

C. trachomatis – different serotypes – different diseases

trachoma: developing countries, transmission – directly and undirectly, chron. inflamation of cornea, blindness, transmission – contaminated water

Oculogenital chlamydiosis: most frequently STD (asymptomatic, uretritis, cervicitis, newborns – conjunctivitis, if spread – salpingitis, sterilitis)

Lymfogranuloma venereum – STD, inguinal lymphfadenitis, hemorragic ulcerative proctitis

Chlamydia

Diagnosis – ***C. trachomatis*:** direct detection PCR, antigen (swab uretra, cervix, urine), **dif.dg** – other STD,

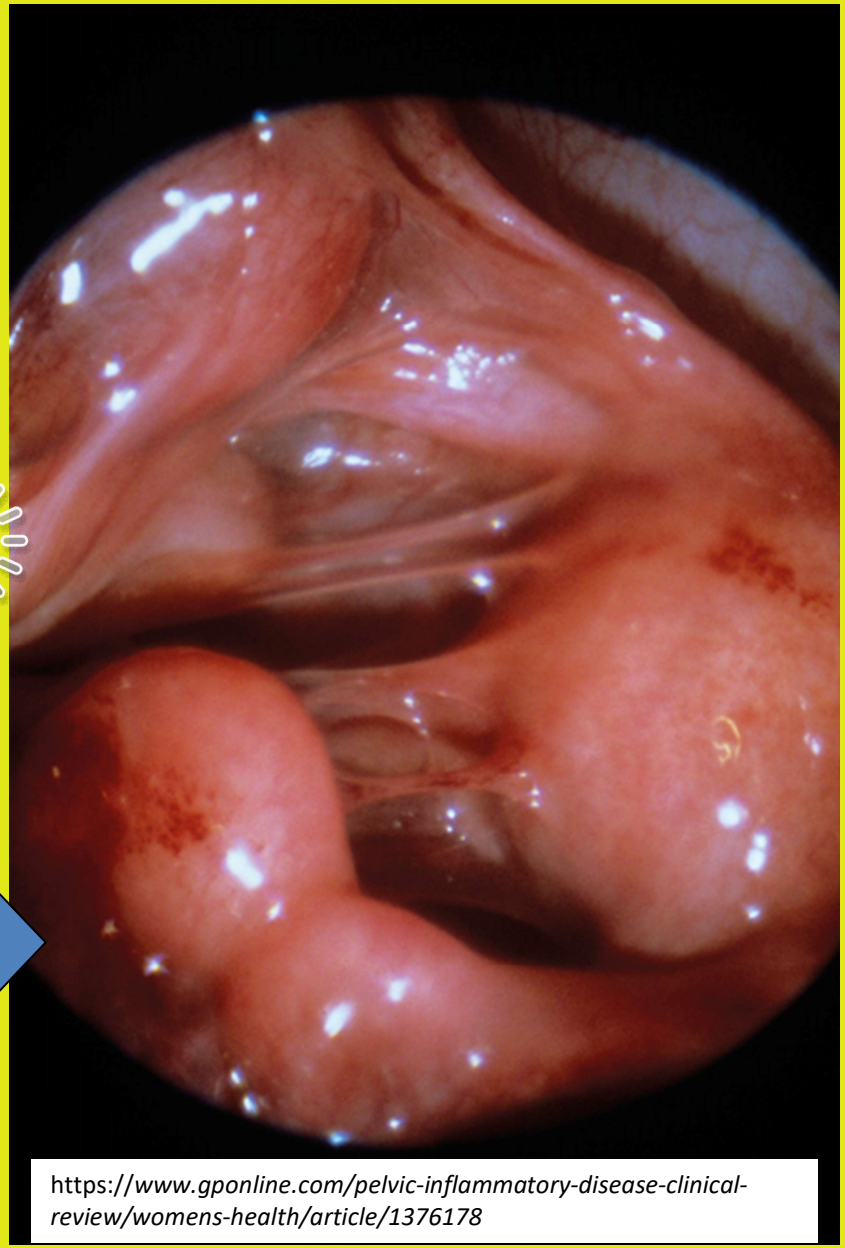
Therapy – **macrolides, tetracyclines**

Chlamydial cervicitis

https://teachmeobgyn.com/sexual-health/sexually-transmitted-infections/chlamydia/

Chlamydial pelvic inflamatory disease (PID)

infekce a zánět horních pohlavních cest; to může zahrnovat **endometrium, vejcovody a/nebo vaječníky, stejně jako okolní peritoneum**.



https://*www.gponline.com/pelvic-inflammatory-disease-clinical-review/womens-health/article/1376178*

Mycoplasma

genera – Mycoplasma and Ureoplasma

Small organisms (up to 250 nm), smallest genome – fastidious, cultivation is not relevant for dg

Cell wall free organisms – inactive cell wall active antibiotics

Epidemiology – ***M. pneumoniae*** – most frequent – children and young adults, spread- secretion of upper resp.tract, ***M. hominis, Ureoplasma genitalium, U. urealyticum*** – urogenital infections

Patogenesis – host cell is essential, adherence and using nutrients, peroxides and superoxides – harm affected tissue

Mycoplasma

Symptoms *M. pneumoniae* infections – incubation period around 21d, usually mild, infection of upper resp.tract, cca 10% pneumonia – without alteration of total status (polymorbid patients – serious course), complication – peri- a myocarditis, meningoencefalitis

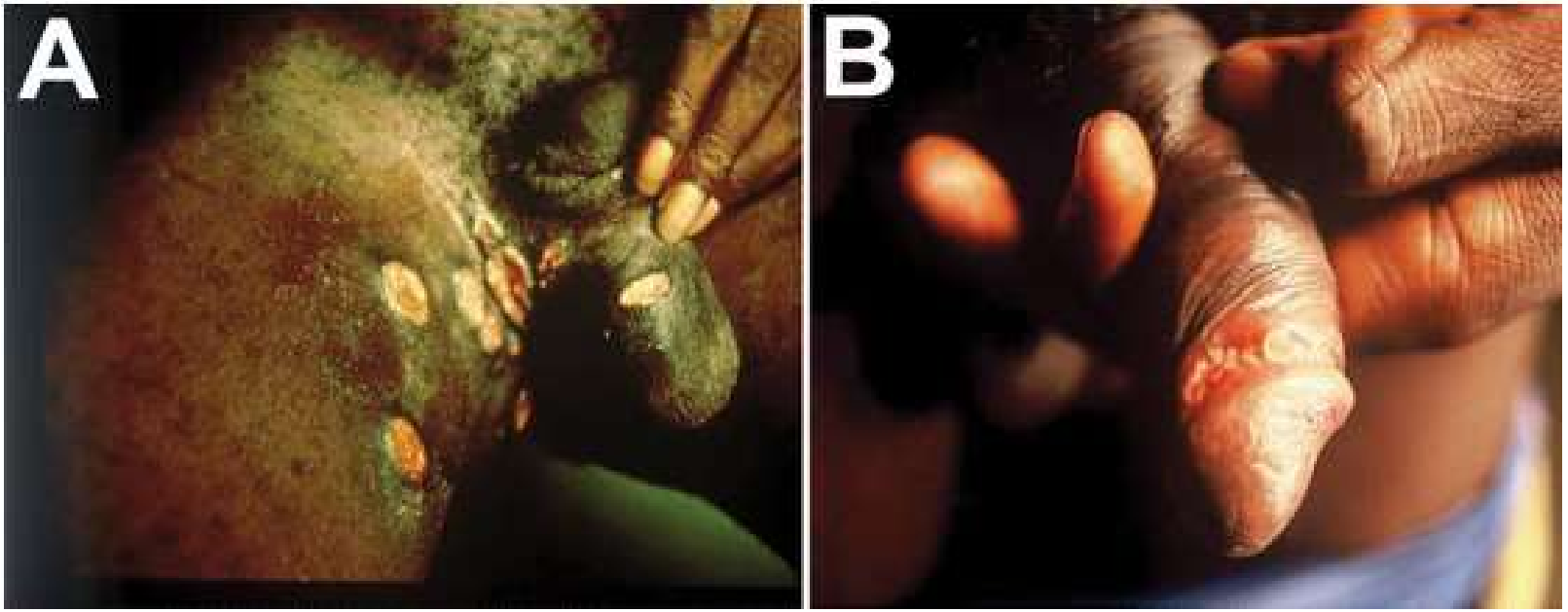
M. hominis, M. genitalium and ***Ureoplasma ureolyticum*** infections – uretritis, cervicitis apod.

Diagnosis – ***M. pneumoniae*** – **undirect detection** – most frequently – IgA after 1 weak, since 10d IgM, also CFR, **direct detection** – nasopharyngeal swab, sputum, BAL – PCR, or CRP, **dif.dg** – chlamydiosis, Q fever, legionelosis, ***M. hominis, M. genitalium a Ureoplasma*** – **direct detection** – uretral swab, cervix, dif. dg – *Neisseria gonorrhoeae, Trichomonas vaginalis*

Therapy – betalactam antibiotics not effective, **macrolides, tertracyclines** (fluorochinolony)

Other STD

Bacterial - *Haemophilus ducreyi* – a fastidious gram-negative bacterium, is the causative agent of **chancroid**, a genital ulcer disease (GUD). The organism is usually spread during sexual intercourse through microabrasions, and the disease usually manifests as multiple painful superficial ulcers associated with inguinal lymphadenitis, dg – usually clinical, treatment – azithromycin, ceftriaxone



Ulcers caused by infection with *Haemophilus ducreyi*. A, B) **Genital ulcers** in adult patients from Ghana https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4696685/)

Other STD

Viral (see also virology lecture)

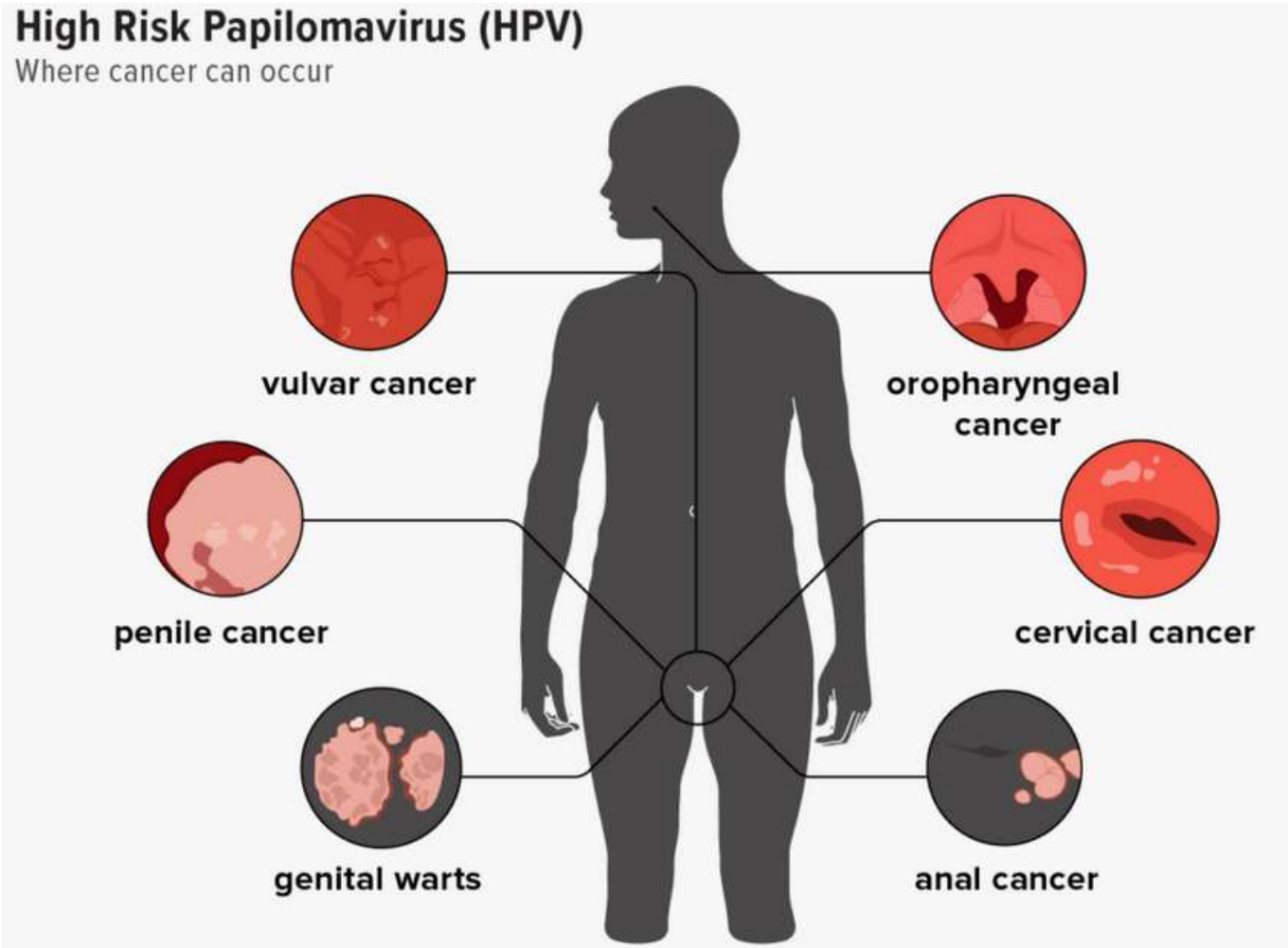
* human papilomavirus infection (HPV)

* herpes (HSV1 or HSV2)

* human immunodeficiency virus/acquired immune deficiency syndrome (HIV/AIDS) (see virology lecture)

* hepatitis B (see virology lecture)

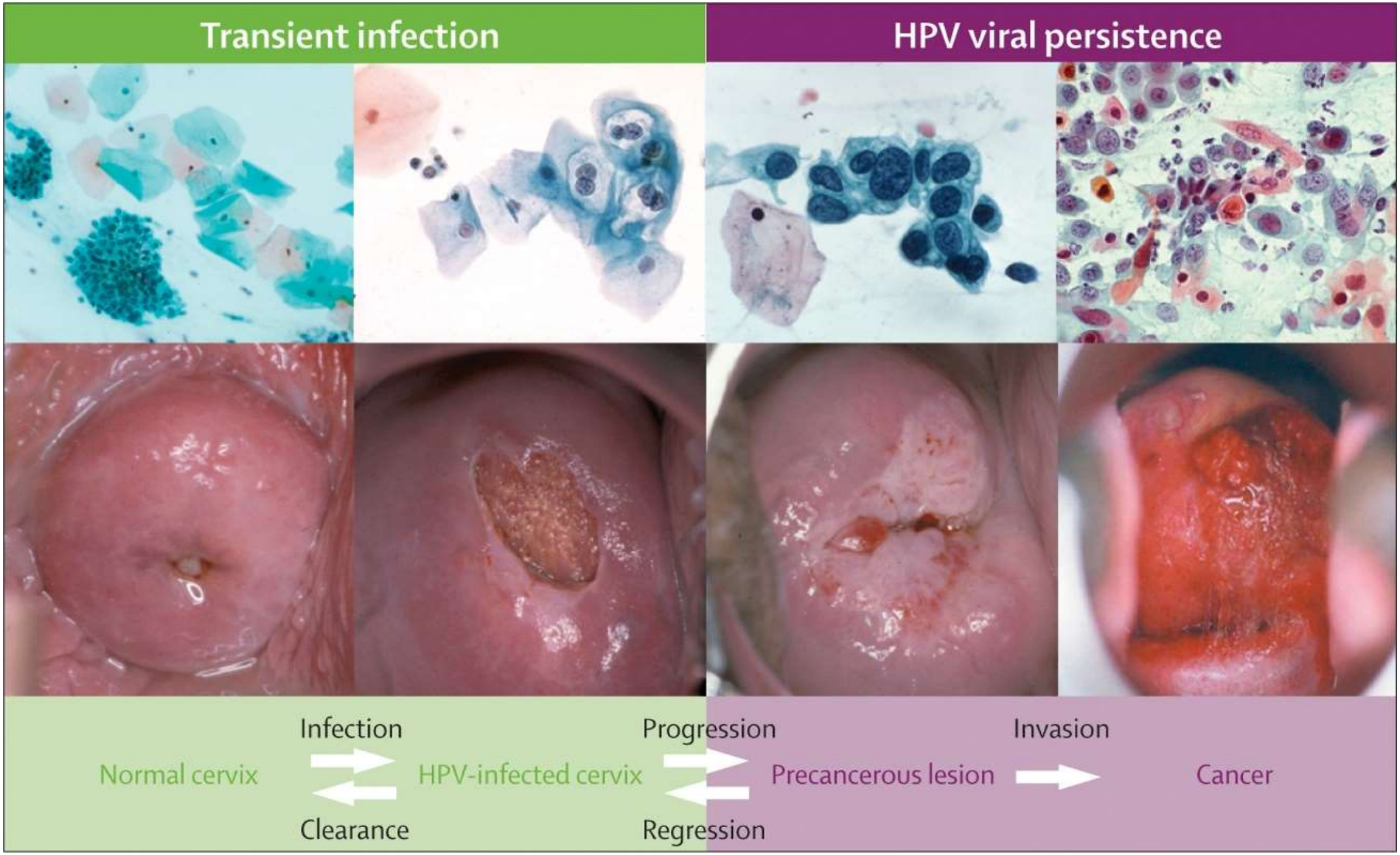
Other STD



Human papillomavirus (HPV) is the most common sexually transmitted virus, with doctors diagnosing roughly 13 million new cases every year. The virus can pass on through skin-to-skin vaginal, anal, or oral sex. A person may not realize that they have the infection because it sometimes causes no symptoms (https://www.medicalnewstoday.com/articles/high-risk-hpv).

See also the **video**:https://www.sierracounty.ca.gov/692/Human-Papillomavirus-HPV

Other STD



https://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2807%2961416-0/fulltext?_eventId%3Dlogin=&code=lancet-site

Other STD

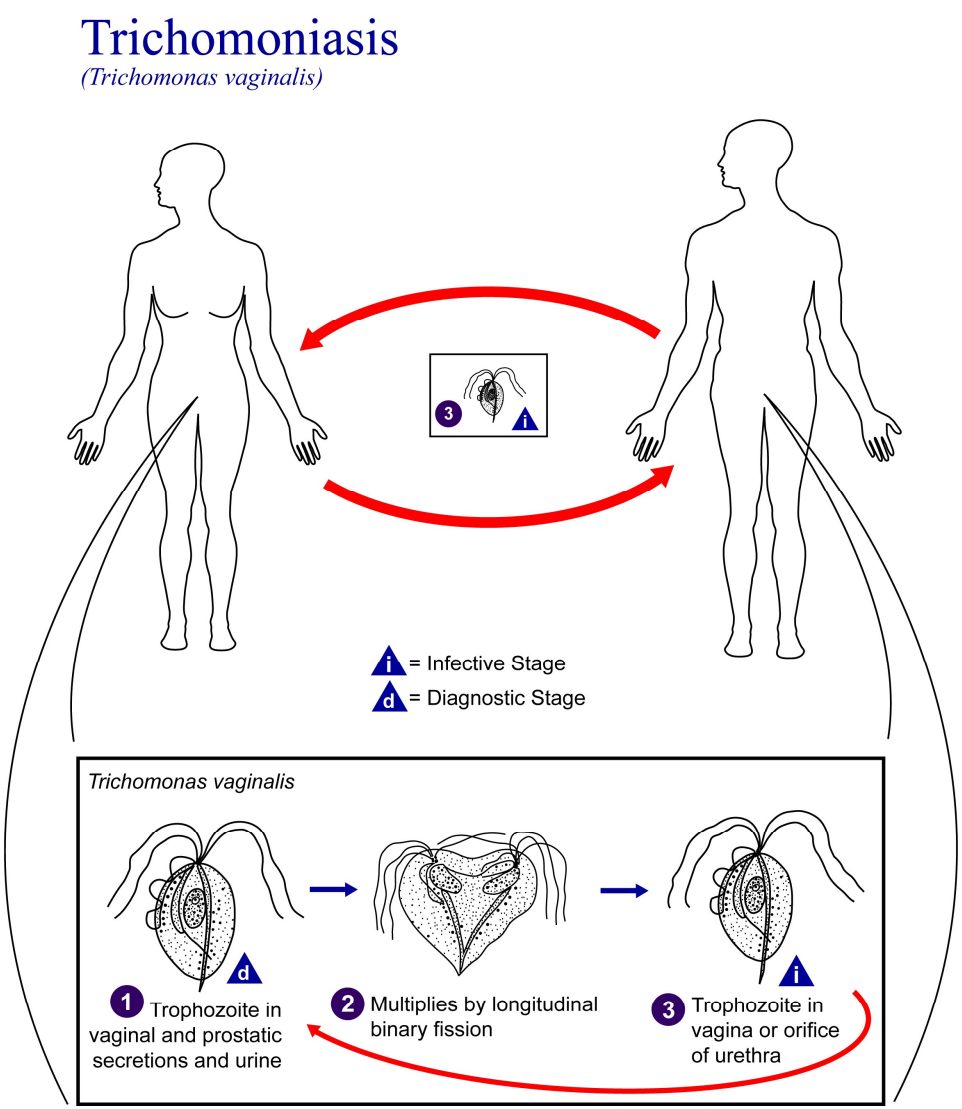
Genital herpes (HSV1 or HSV2)

https://teachmeobgyn.com/sexual-health/sexually-transmitted-infections/genital-herpes/

symptoms: https://www.youtube.com/watch?v=j2_vdpPuivE

treatment: *https://www.youtube.com/watch?app=desktop&v=PJtY9ixUdzs*

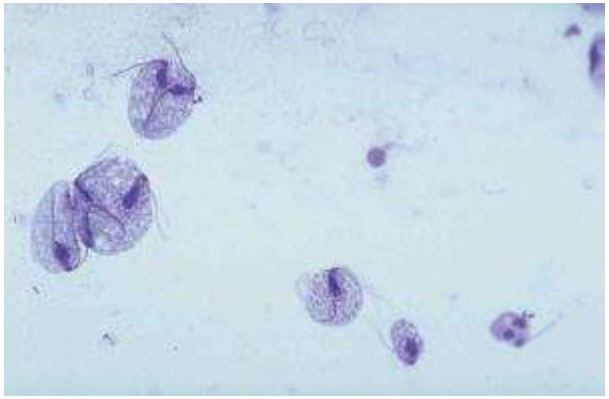
Other STD parasitic agents



Trichomoniasis is the most common parasitic STD, though **scabies**, **lice**, and **giardia** are also common parasitic STIs.

Trichomonas vaginalis **(see also lecture Protozoa)**

- flagellated protozoan
- uretritis, vaginitis
- Dg – microscopy (vaginal discharge – Giemsa staining, see the fig. below), culture, PCR (first portion – urine)
- Treatment – metronidazole



https://us.vwr.com/store/product/8891018/i-trichomonas-vaginalis-i-trophozoites-slide