Urinary tract infections

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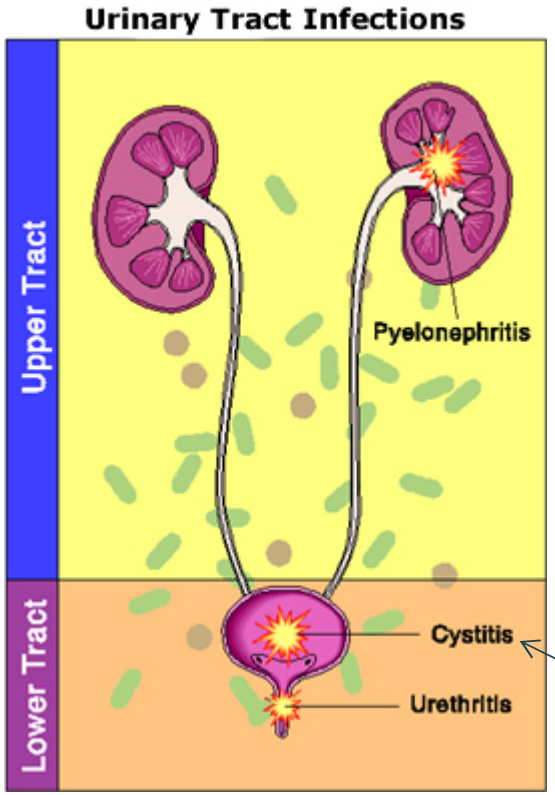
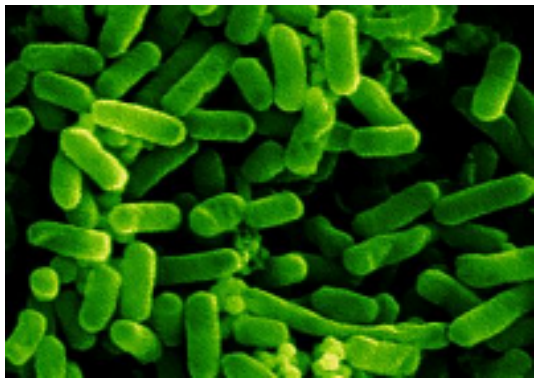
The second most common infectious disease in the body

Urinary Tract Infection



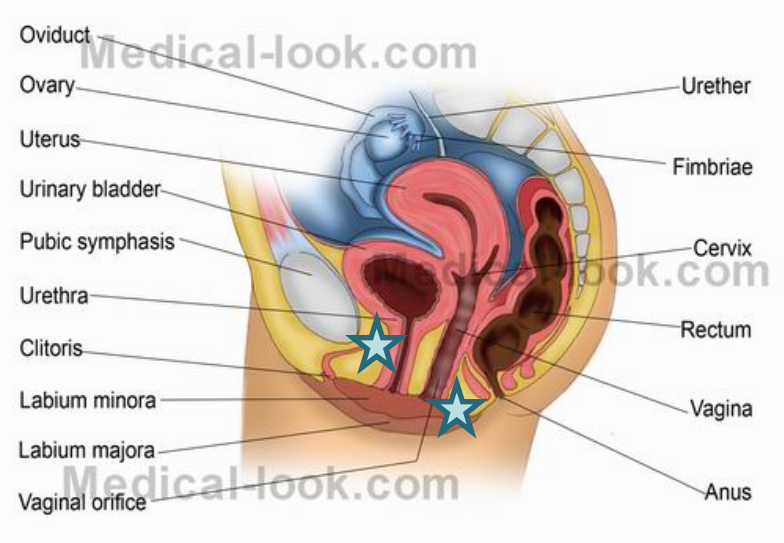
Most common site

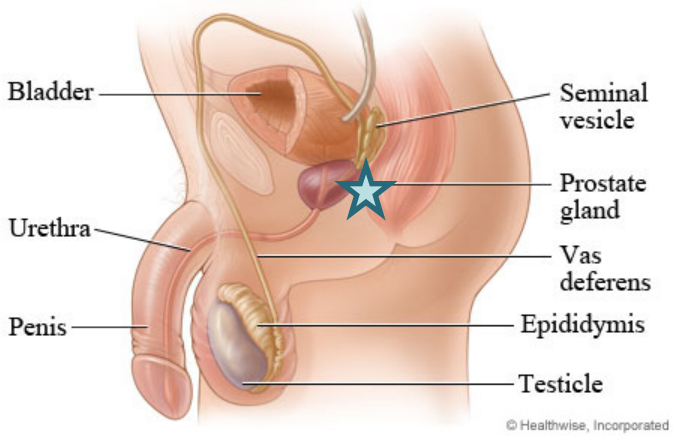


Escherichia coli

Most common cause

Higher occurence in women

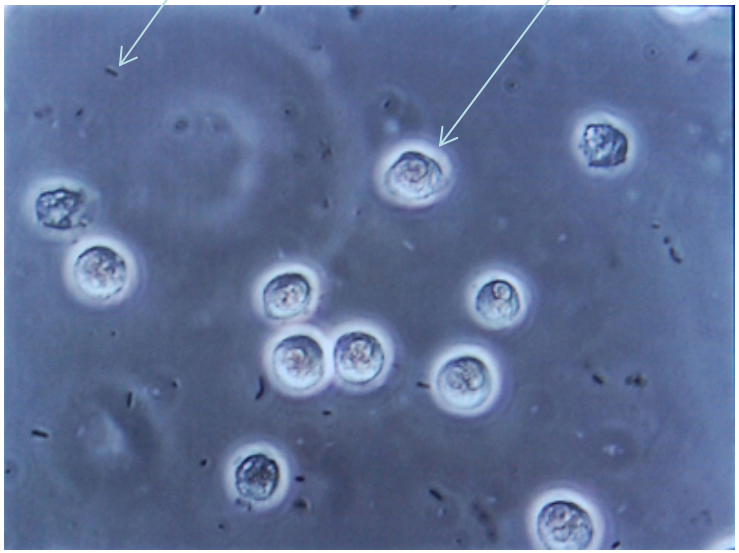




Anamnesis & symptoms

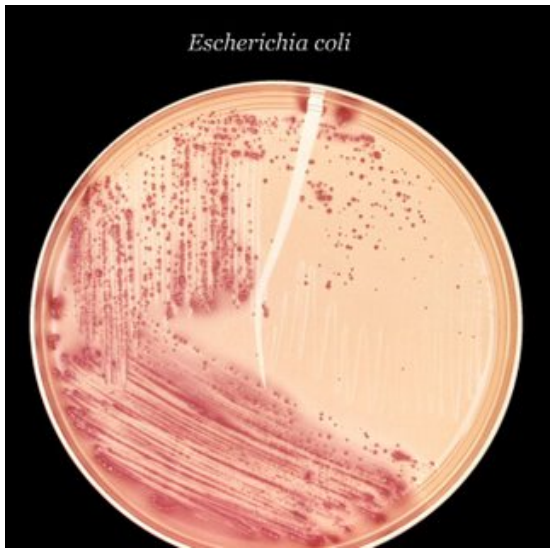
- Pain or burning feeling during urination (dysuria- refers to painful urination).
- Feeling of urgency (of need to urinate frequently), although the actual amount is very small
- Altered appearance of urine
  - red (bloody)
  - cloudy (containing pus)

Laboratory diagnosis

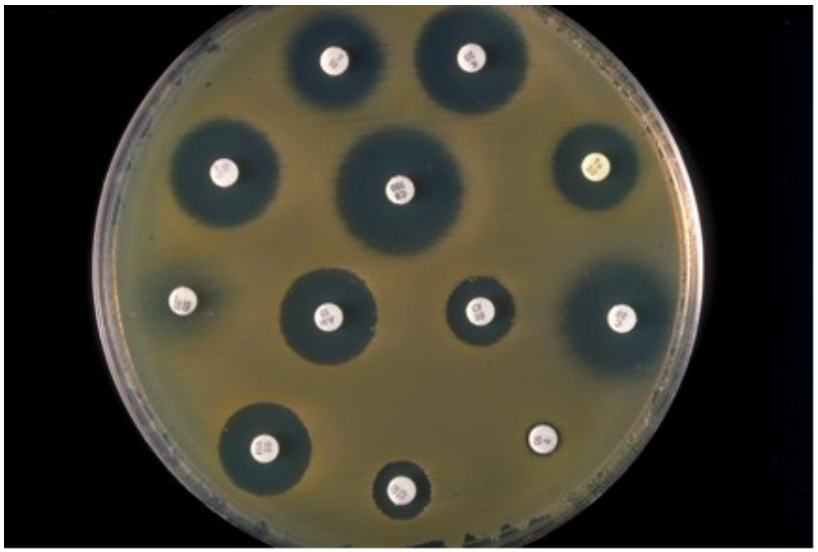


Diagnosis is based on a test of the urine. Here we look for bacteria in the urine TOGETHER WITH white or red blood cells.

Cultivation & susceptibility to ATB



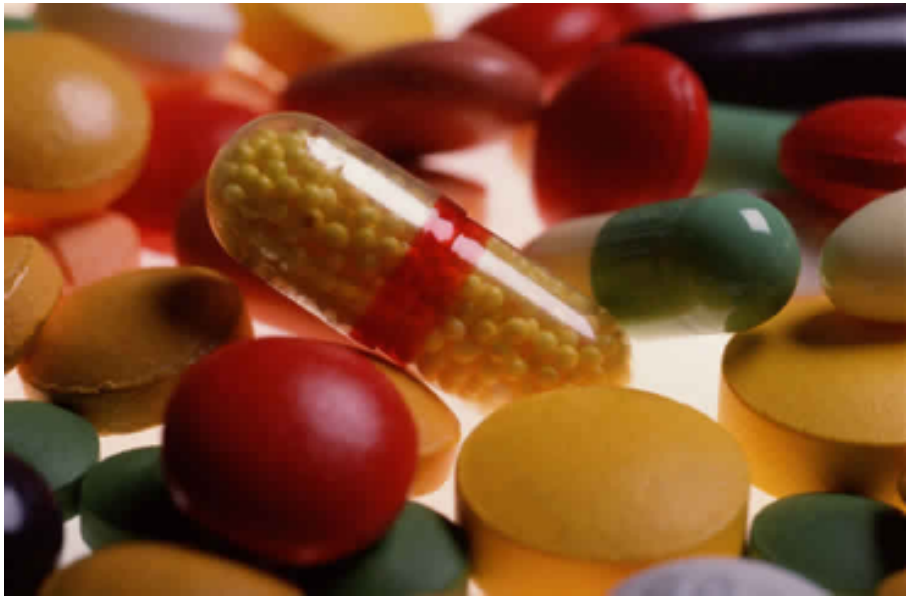
Cultivation will give us a proper diagnosis.



A sensitivity test will show which antibiotics that should be used for proper treatment.

Only E-coli can be cultivated like this. If the cultivation is negative, try other means of cultivation. The cause of disease might be *Chlamydia trachomatis* or *Neisseria gonorrheae*

Treatment



After selection of proper antibiotics, start the treatment. A grown-up needs approximately seven days to get rid of the infection, while a child need about three days.

Other most frequent bacterial agents of UTI

- *Proteus mirabilis* – associated with urinary stonesprobaly because of production of urease which acts on urea to produce ammonia, rendering the urine alkaline (E.coli, Proteus – usually community UTI)

- other enterobacteria (Klebsiella, Enterobacter, Serratia) and *Pseudomonas aeruginosa* (all the agents ussually hospital UTI)

- Gram-positive species – *Staphylococcus saprophyticus* (young sexually active women), *Staphylococcus epidermidis* and enterococci (in hospitalized patients)

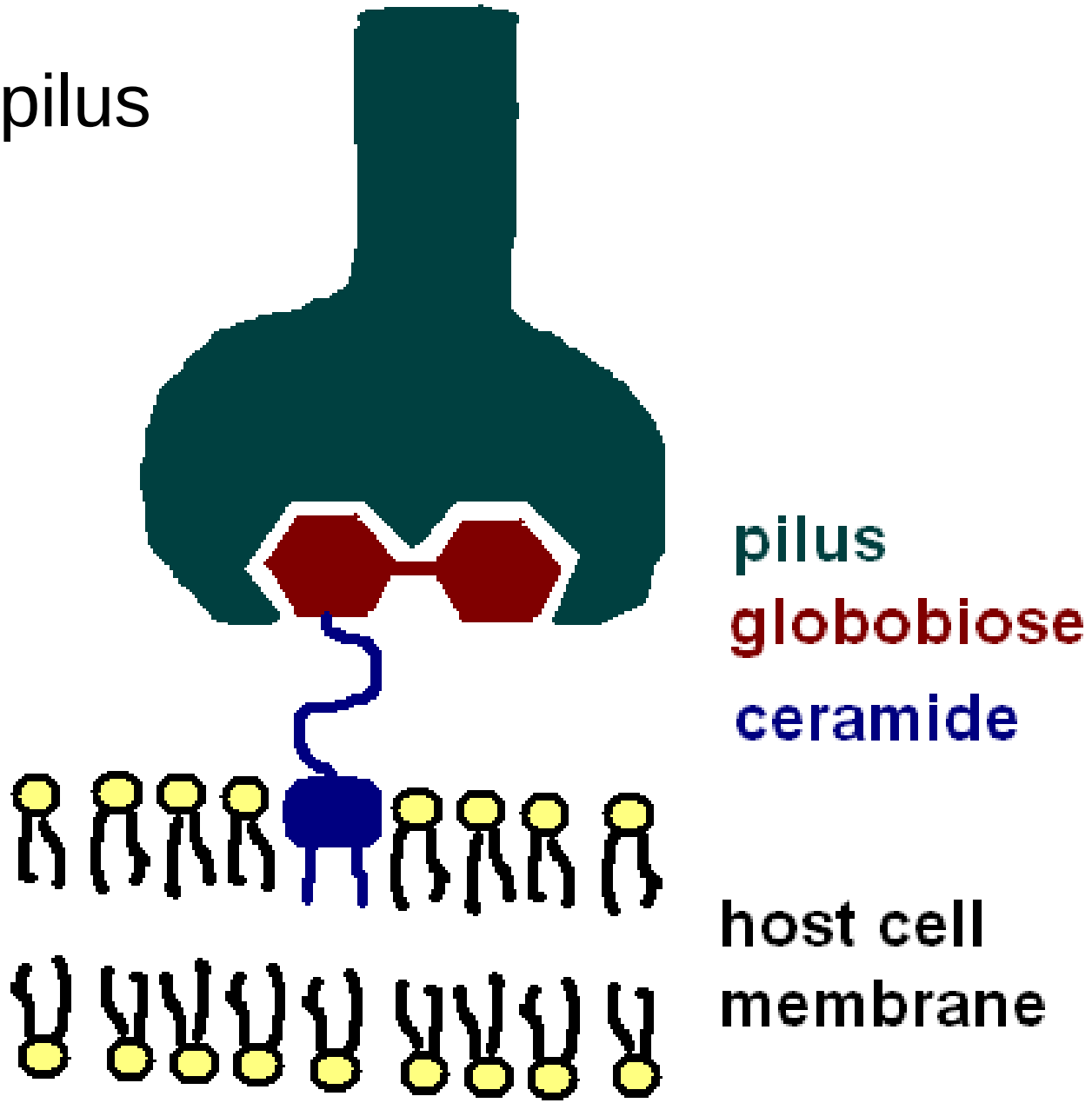
Factors predisposing the infection (host)

- normal host – pH, chemical content and flushing mechanism of urine helps dispose of bacteria
- man/woman anatomical differencies
- anatomical abnormalities/underlying diseases: obstruction of bladder (pregnancy, paraplegia, sclerosis multiplex, vesicoureteral reflux in children)
- colonization of the colon and vagina with uropathogenic *E. coli*
- urinary tract catheters – major predispozing factors (may inserted bacteria directly into bladder via lumen or by tracking between the outside of the catheter and uretrall wall, disruption of normal bladder function)

Bacterial virulence factors

- adhesins – key feature of uropathogens, close proximity to mucosal cells – better stimulation of inflammatory response
- type 1 pili (primarily colonization of vagina)
- P pili (in strains caused kidney infections, many different types, recognize receptor – globobioze), structural genes *pap (pyelonephritis associated pili)*
- some adhesins are afimbrial *(AFAi,AFAIII)*
- it is worth raising questions about the well-accepted dogma that adherence is essential trait of uropathogens

P pilus



Salyers, Bacterial pathogenesis

Bacterial virulence factors

• toxins – probably act inflammation by LPS (endotoxins) or exotoxins

• **LPS** act alone or synergistically with P pili to evoke inflammatory response – PMNs move through mucosa and cytokines into bladder lumen

• some uropathogens produce **hemolysins** (HlyA) belong to family RTX henolysisns (repeats in toxin) **creating pores into host cells** (could cause kidney damage), if levels of toxin too low also can have effects – cytokines releasing and superoxide production

• other virulence factors – siderophore based systems (iron aquisition from outside the bacterial cells), capsules – serum resistannce,

Organization and regulation of virulence genes

- regulation of P pili is environment dependent (temperature, glucose, aminoacids…) - bacteria adapt to mucosal surfaces and can evade host defenses
- uropathogenic *E.coli* – usually production of multiple adhesins, (switching on/off)
- structural genes clustered on bacterial chromosome

Sexually transmitted diseases (STD)

- also known as venereal disease (VD), (STInfections)
- transmission between humans by means of sexual contact, including vaginal intercourse, oral sex, and anal sex
- have been well known for hundreds of years
- **Classification** of the infections:

- **Bacterial**
- **Viral**
- **Fungal**
- **Parasitic**

Bacterial STD

- Syphilis
- Gonorrhoea
- Chlamydia infection
- Mycoplasma & Ureaplasma

Syphilis - aetiology and transmission

- spirochaete *Treponema pallidum* (thin, helical (0.1 to 0.5 × 5 to 20 μm), gram-negative bacteria
- 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
- 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-filed microscopy** or **fluorescent microscopy** is suitable

Virulence factors

- **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

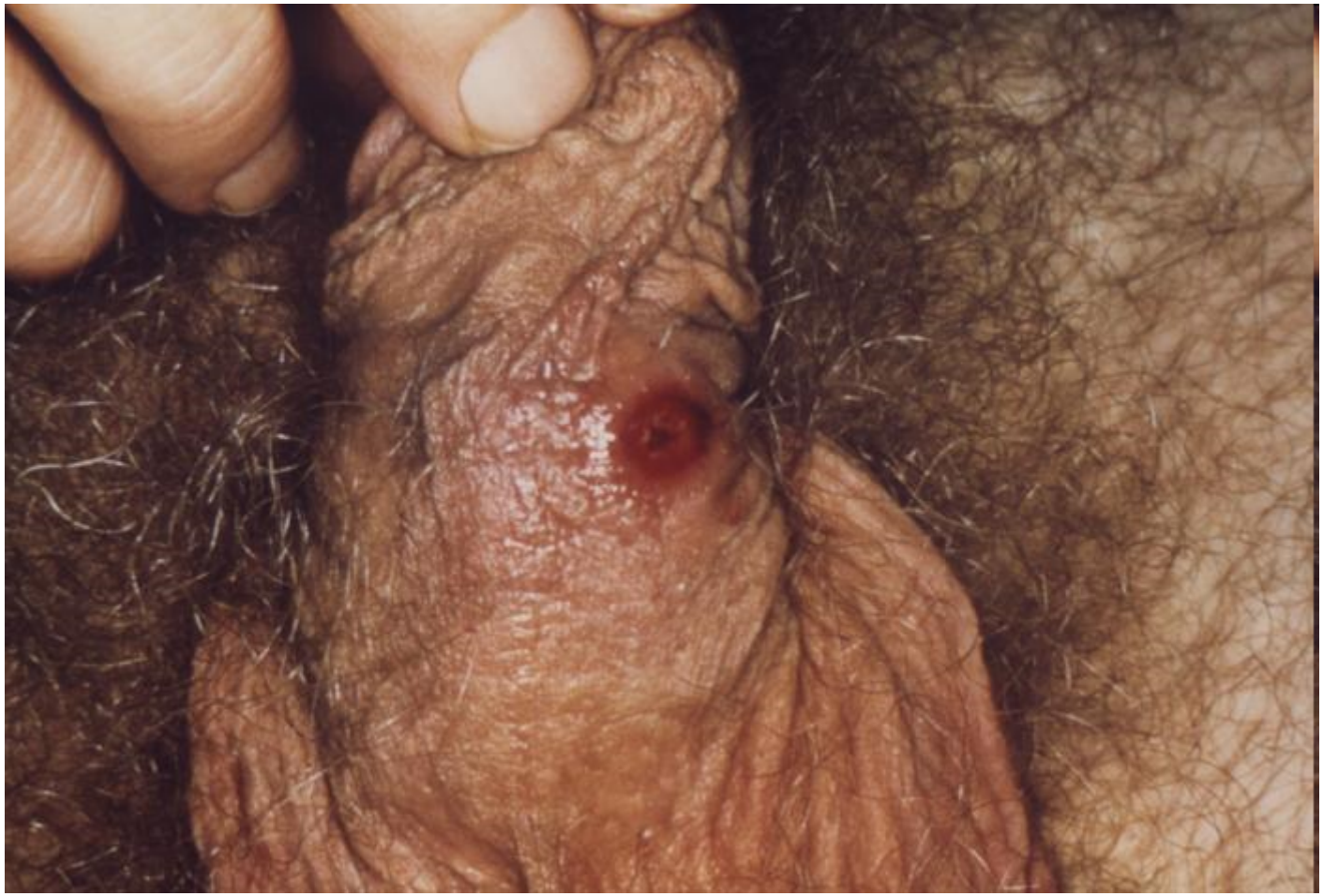
- the organisms enters the body through minute abrasions (skin, mucous memranes)
- local slow multiplication – infiltration the lesion with plasma cells and macrophages (endarteritis)
- **incubation period – 3 weeks**
- **stages – primary (skin lesion – chancre), secondary (skin lesions disperse over the body), 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,)
- not all patients go through all the stages, after 1. and 2. stages patients usually remains free of the disease)

Syphilis – congenital syphilis

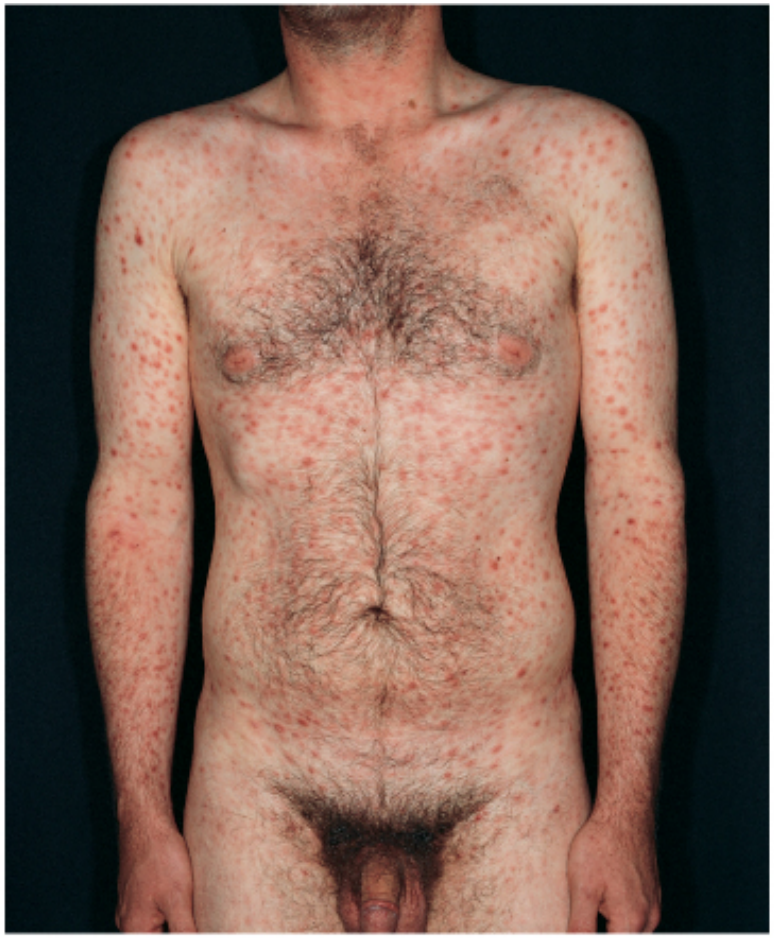
•**In utero infections** can lead to serious **fetal disease**, resulting in **latent infections**, **multiorgan malformations**, or **death of the fetus**.

• 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.

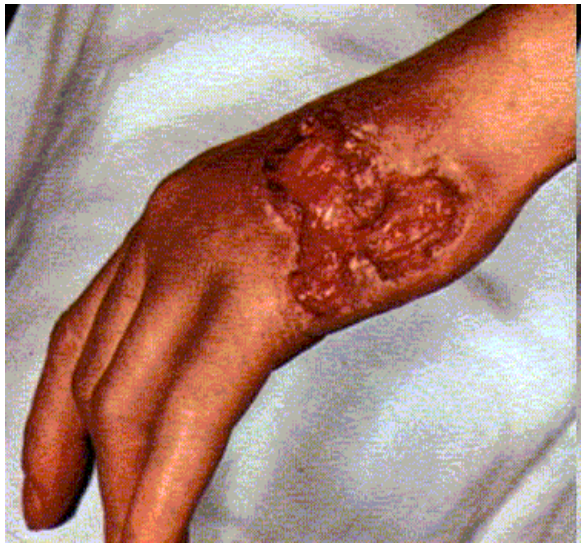
Syphilis – primary stage

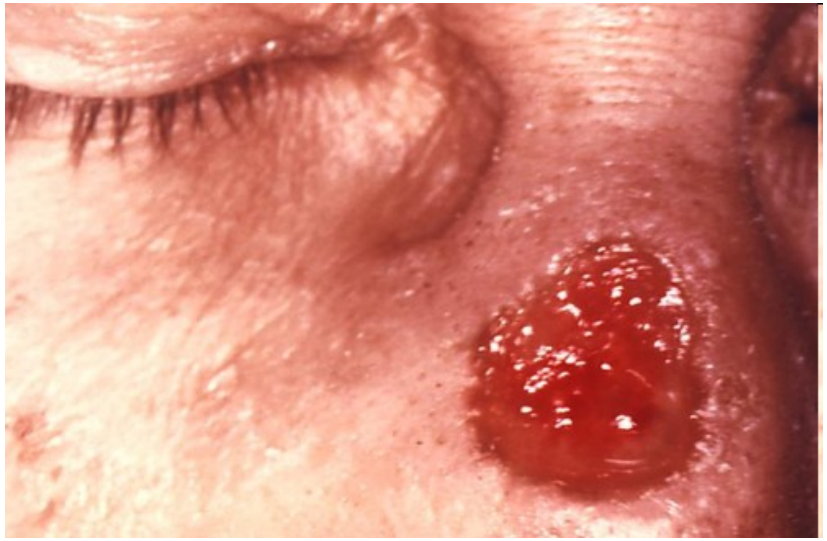


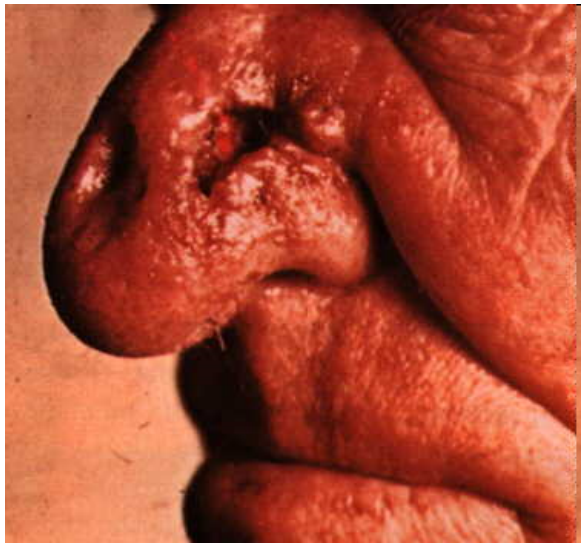
Syphilis – secondary stage

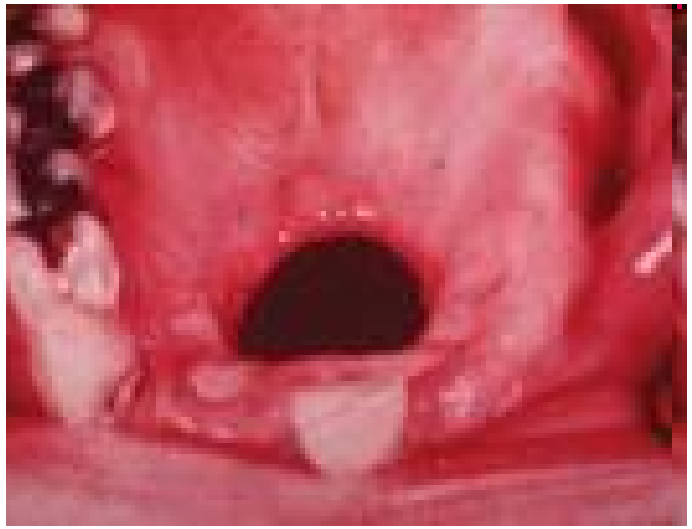


Syphilis – tertiary stage



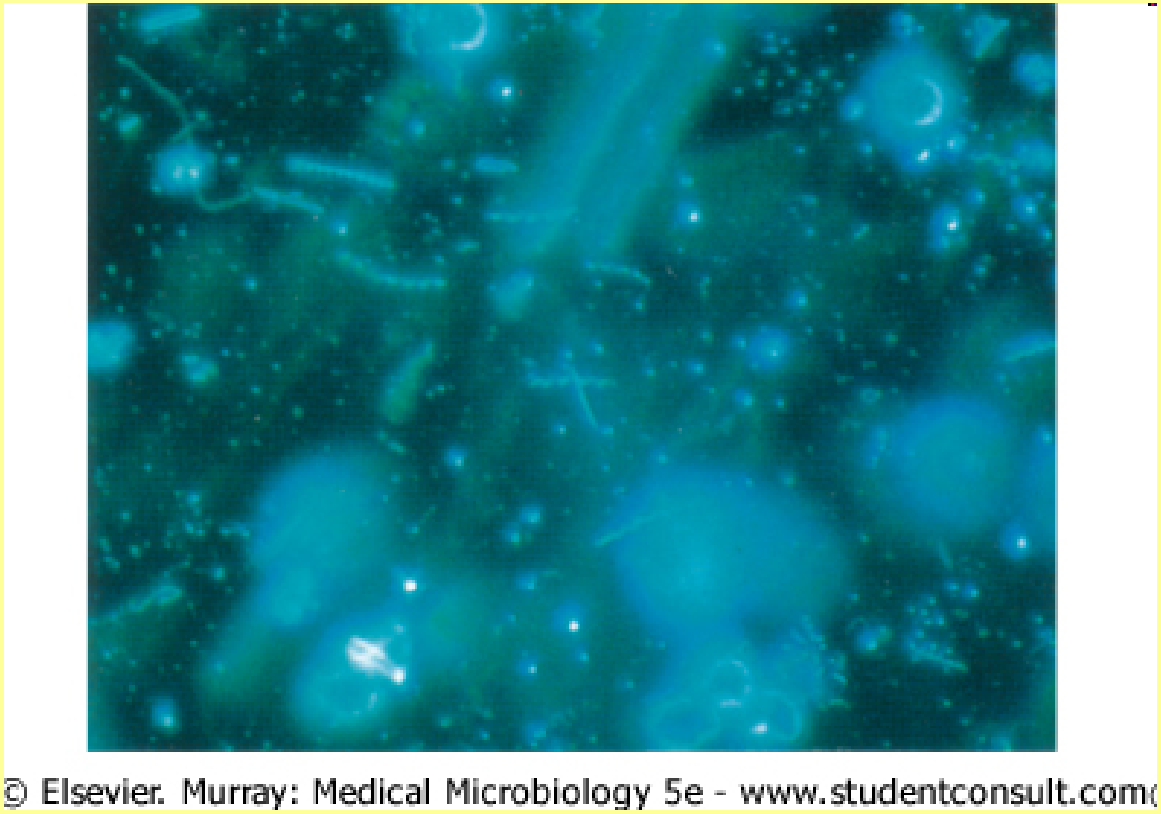






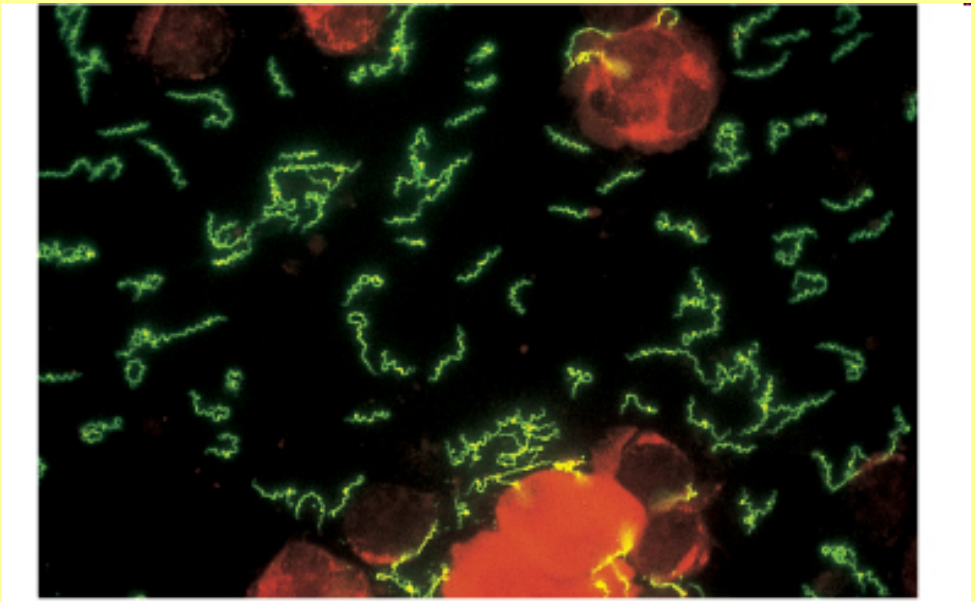
Laboratory dg - microscopy

•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**



Syphilis

Laboratory dg – serology, nontreponemal tests

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•**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.**

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.

Treatment, prevention, control

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Laboratory dg – serology, treponemal tests

- **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**

Neisseria gonorhoeae

*** 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

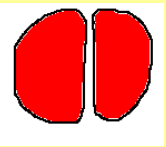
- **doxycycline** or **azithromycin** should be - for infections complicated by Chlamydia

- 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



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

References

- Murray et al. Medical Microbiology, 2007
- Jawetz, Melnick and Adelbergs Medical Microbiology, 2007
- web references