SEXUALLY TRANSMITTED INFECTIONS

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- The sexually transmitted infections (STIs) are a group of communicable diseases which are transmitted by sexual contact.

SEXUALLY TRANSMITTED INFECTIONS (Cont..)

1. **Agents causing local manifestations**—called genital tract infections

- Lesions common to both sexes: Such as genital ulcers, urethritis, and anorectal lesions
- Female genital tract infections: Such as vulvovaginitis, cervicitis and others
- Male genital tract infections: Such as prostatitis, epididymitis, and orchitis.

SEXUALLY TRANSMITTED INFECTIONS (Cont..)

- 2. **Agents causing systemic manifestations** without producing local manifestations (e.g. HIV, hepatitis B and C).

Causative agents of sexually transmitted infections

Agents causing local manifestations (genital tract infections)
In both sexes:
Genito-ulcerative disease: ➢ **Syphilis:** Caused by *Treponema pallidum* ➢ **Chancroid:** Caused by *Haemophilus ducreyi* ➢ **Genital herpes**: Caused by herpes simplex viruses ➢ **Lymphogranuloma venereum:** Caused by *Chlamydia trachomatis* ➢ **Donovanosis:** Caused by *Klebsiella granulomatis* **Urethritis:** ➢ **Gonococcal urethritis:** Caused by *Neisseria gonorrhoeae* ➢ **Non-gonococcal urethritis (NGU)**: Caused by ❖ *Chlamydia trachomatis* (D-K) ❖ Genital mycoplasmas: *Ureaplasma urealyticum, Mycoplasma genitalium, M. hominis* ❖ Herpes simplex virus ❖ *Candida albicans* ❖ *Trichomonas vaginalis*

Causative agents of sexually transmitted infections (Cont..)

Agents causing local manifestations (genital tract infections)
In both sexes:
Other genital tract infections common to both sexes ➢ Genital tuberculosis: Caused by *M. tuberculosis* ➢ Anorectal lesions: ❖ Proctitis: Caused by HSV, gonococcus, *C. trachomatis* ❖ Anogenital warts: Caused by human papilloma virus

Causative agents of sexually transmitted infections (Cont..)

Agents causing local manifestations (genital tract infections)
In females only:
➢ **Vulvovaginitis:** Bacterial vaginosis, trichomoniasis and candidiasis ➢ **Mucopurulent cervicitis** caused by gonococcus, *C. trachomatis* ➢ **Pelvic inflammatory disease:** Presents as— ❖ Endometritis, salpingitis, oophoritis, tubo-ovarian abscess ❖ Extension to peritoneum can lead to peritonitis, pelvic abscess and perihepatitis ➢ Infections after gynecologic surgery ➢ Infections in pregnancy/postpartum
In males only:
Prostatitis, epididymitis, and orchitis
Agents causing systemic manifestations, no local lesions
HIV, Hepatitis B virus (HBV), Hepatitis C virus (HCV)

GENITO-ULCERATIVE DISEASE

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- Genito-ulcerative disease comprises of five important STIs— syphilis, chancroid, genital herpes, lymphogranuloma venereum and donovanosis.

Comparison of manifestations of genito-ulcerative diseases

Features	Syphilis	Genital Herpes	Chancroid	LGV	Donovanosis
Incubation period	9–90 days	2–7 days	1–14 days	3 days–6 weeks	1–4 weeks (up to 6 months)
Genital ulcer	Painless, single, indurated	Painful, multiple, bilateral, tiny vesicular ulcers	Painful, soft, usually multiple, purulent, bleeds easily	Painless, firm single lesion	Painless, single/multiple, beefy-red ulcer, bleeds readily
Lymphadenopathy	Painless, non-indurated (firm), bilateral	Painful, firm, often bilateral with initial episode	Painful, soft, marked swelling leads to bubo formation, unilateral	Painful and soft, unilateral	Absent (pseudobubo may be present due to subcutaneous swelling)
Treatment	Penicillin (single dose)	Acyclovir (7–14 days)	Azithromycin (single dose)	Doxycycline (21 days)	Azithromycin (7 days)

SYPHILIS (TREPONEMA PALLIDUM)

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- *Treponema pallidum* - causative agent of an ancient sexually transmitted infection (STI) 'syphilis'.
- The name *pallidum* refers to its pale-staining property.
- Discovered by Schaudinn and Hoffmann in 1905.

Genus Description

- Thin, flexible, elongated spirally coiled helical bacilli.
- Include *Treponema*, *Borrelia* and *Leptospira*
- Treponemes are slender spirochetes with fine spirals having pointed ends (*trepos*, meaning 'turn' and *nema*, meaning 'thread').
- Most of them are commensals in mouth and genitalia

Genus Description (Cont..)

- Only a few species are pathogenic to men, divided into two groups.
  - 1. **Sexually-transmitted:** *Treponema pallidum*—causes syphilis
  - 2. **Nonvenereal treponematosis:** *T. pertenue*, *T. endemicum* and *T. carateum*

Pathogenesis of Syphilis

- **Mode of transmission:**
  - Venereal
  - Non-venereal - direct contact, blood transfusion or transplacental
- **Spread:** *T. pallidum* penetrates through mucosa or abraded skin - Enter lymphatics and blood - systemic - primary lesion
- **Incubation period** - Variable (10–90 days)
  - Inversely proportional to the number of organisms inoculated

Clinical Manifestations of Syphilis

- Approximately, 30% of persons who have sexual exposure with an infected partner develop syphilis
- Clinically, patients suffering from syphilis pass through four stages if left untreated: primary, secondary, latent and tertiary (or late) stages.
- If transmitted vertically, the newborn babies develop a congenital form of syphilis.

Primary Syphilis

- **Primary (or hard) chancre:**
  - Single painless papule - ulcerated & indurated
  - Covered by thick exudate rich in spirochetes
  - Common sites – penis, cervix or labia
  - Heals within 4–6 weeks

Primary Syphilis *(Cont..)*

- **Regional (usually inguinal) lymphadenopathy**
  - Painless firm, non-suppurative, and often bilateral
  - May persist for months
- If acquired by non-venereal mode - primary syphilis is presented as:
  - Direct contact ⟶ extragenital, usually on the fingers
  - Blood transfusion ⟶ primary chancre does not occur

Secondary Syphilis

- Develops 6-12 weeks after healing of primary lesion
- Skin and mucous membranes - commonly affected and
  - **Skin rashes**

Secondary Syphilis *(Cont..)*

- **Condylomata lata -** Mucocutaneous papules coalesce to form large pink to grey lesion in warm moist intertriginous areas (such as perianal region, vulva, and scrotum)
- **Mucous patches** (superficial mucosal erosions)

Latent Syphilis

- Absence of clinical manifestations, positive serological tests, normal CSF findings.
- Patients still infectious – transmitting the infection - bloodstream or *in utero*
- May have one of the following fates:
  - Persistent lifelong infection (common)
  - Development of late syphilis (rare)
  - Spontaneous cure

Late or Tertiary Syphilis

- **Gumma (late benign syphilis):** Locally destructive granulomatous lesions - bone and skin
- **Neurosyphilis:** Chronic meningitis, vasculitis, general paresis of insane and tabes dorsalis
- **Cardiovascular syphilis:** Aneurysm of ascending aorta and aortic regurgitation

Congenital Syphilis

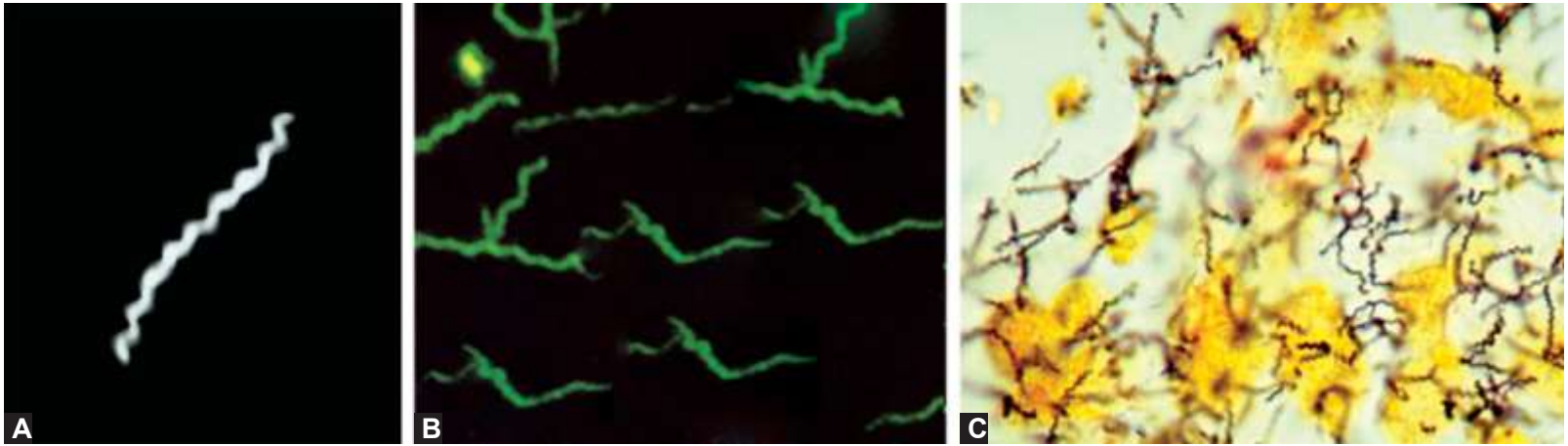
- Mother-to-fetus transmission can lead to development of various congenital manifestations

Laboratory diagnosis of Syphilis

Microscopy

- Dark ground microscopy
- Direct IF staining for *T. pallidum* (DFA-TP)
- Silver impregnation method
  - Levaditi stain (for tissue section)
  - Fontana stain (smear)

Laboratory diagnosis of Syphilis (Cont..)



Direct microscopy of *T. pallidum:* **A.** Dark ground microscope; **B.** Direct fluorescent antibody staining for *T. pallidum* (DFA-TP); **C.** Silver impregnation method

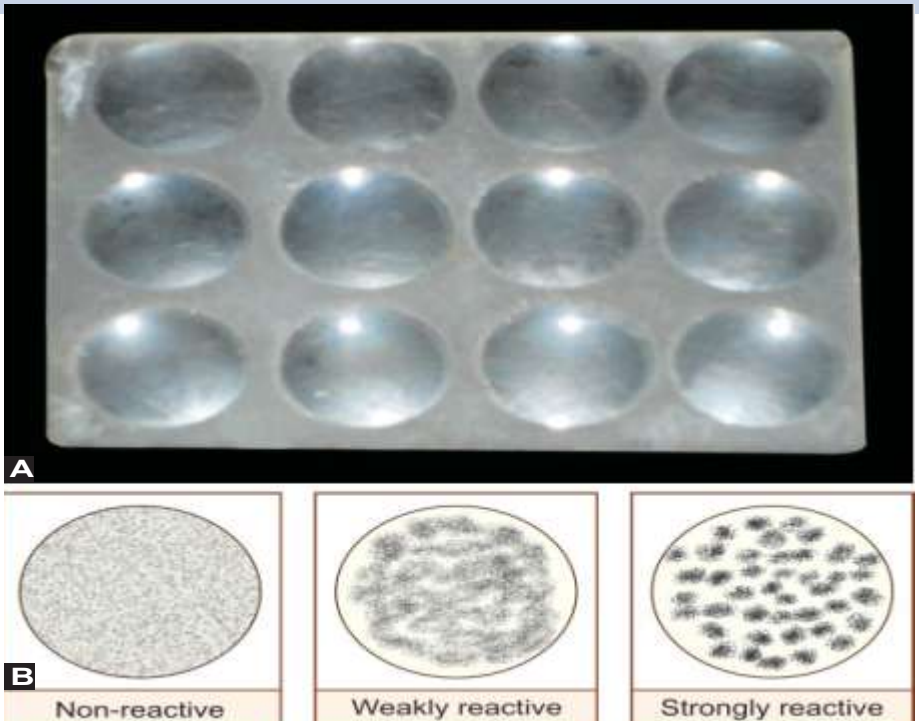
Laboratory diagnosis of Syphilis (Cont..)

- **Culture:** Not cultivable, maintained in rabbit testes
- **Serology** (antibody detection):
  - ***Non-treponemal or STS (standard tests for syphilis):*** (Reagin antibodies are detected by using cardiolipin antigen)
  - ***Specific/Treponemal test:*** Specific antibodies are detected by using *T. pallidum* antigens

Laboratory diagnosis of Syphilis (Cont..)

- ***Non-treponemal or STS (standard tests for syphilis):*** (Reagin antibodies are detected by using cardiolipin antigen)
  - VDRL (Venereal disease research laboratory) test
  - RPR (Rapid plasma reagin)
  - TRUST (toluidine red unheated serum test)
  - USR (Unheated serum reagin test).

Laboratory diagnosis of Syphilis (Cont..)



A. VDRL slide; **B.** VDRL test results

Laboratory diagnosis of Syphilis (Cont..)

- ***Specific/Treponemal test:*** Specific antibodies are detected by using *T. pallidum* antigens:
  - TPI (*Treponema pallidum* immobilization test)
  - FTA-ABS (Fluorescent treponemal antibody absorption test)
  - TPA (*T. pallidum* agglutination test)
  - TPHA (*T. pallidum* hemagglutination test)
  - TPPA (*T. pallidum* particle agglutination test).

Testing Algorithm

- CDC recommends to use a **testing algorithm** comprising of non-treponemal test (as screening test), followed by treponemal test (for confirmation) for serodiagnosis of syphilis.
- In area with high-prevalence for syphilis, **reverse algorithm** - cost-effective where a treponemal test is performed first, followed by non-treponemal test.

Testing Algorithm *(Cont..)*

Testing for syphilis in pregnancy:

- Every pregnant woman - undergo a non-treponemal screening test at her first antenatal visit and, if there is high-risk of exposure, again retested at the third trimester and at delivery.

Syphilis and HIV

Both syphilis and HIV affect each other's pathogenesis.

- Genital syphilis facilitates transmission of HIV through the abraded mucosa (2 to 5 fold increased risk)
- Patient with HIV, if develops syphilis later → rapid progression to late stages of syphilis and neurological involvement

Syphilis and HIV (Cont..)

- **Problems in the diagnosis of syphilis in HIV infected people are:**
  - Confusing clinical picture, Lack of serologic response
  - Unusually high titers in non-treponemal tests
  - Failure of non-treponemal test titers to decline even after treatment
  - Disappearance of treponemal test reactivity over time

Treatment of Syphilis

- **Penicillin** - drug of choice for all the stages of syphilis:
  - Primary, secondary, or early latent syphilis: single dose of Penicillin G
  - Late latent CVS or benign tertiary stage: penicillin G is given single dose weekly for 3 weeks
  - Neurosyphilis -aqueous crystalline or procaine penicillin G is given for 10–14 days.

Treatment of Syphilis (Cont..)

- **Alternative drug is used in patients with penicillin allergy:**
  - Primary, secondary, latent, CVS or benign tertiary syphilis - tetracycline
  - Neurosyphilis or pregnancy or associated HIV - desensitization to penicillin

Evaluation after Treatment

- Non-treponemal tests
- **For primary and secondary syphilis:** At least fourfold decline in the titer by the third or fourth month and an eightfold decline in the titer by sixth to eighth month
- **Latent or late syphilis, or patients with multiple episodes of syphilis:** Gradual decline in titer, low titers may persist for years

CHANCROID (HAEMOPHILUS DUCREYI)

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- **Chancroid (or soft chancre) - sexually transmitted infection**
  - Painful genital ulceration that bleeds easily
  - No inflammation of surrounding skin
  - Enlarged, tender inguinal lymph nodes (bubo)

Epidemiology

- Common cause of genital ulcers in developing countries.
- Transmission predominantly heterosexual
- Males to females ratio - 3:1 to 25:1
- Chancroid and HIV: Chancroid increases both the efficiency of transmission and the degree of susceptibility to HIV infection.

Laboratory Diagnosis

- **Specimens:** Exudate or swab from the edge of the ulcer and lymph node aspirate
- **Direct microscopy:**
  - Pleomorphic gram-negative coccobacillus; occurs in groups or in parallel chains
  - Bipolar staining
  - **School of fish or rail road track appearance.**

Laboratory Diagnosis (Cont..)

- **Culture:**
  - Requires factor X (hemin), but not factor V
  - Rabbit blood agar/chocolate agar enriched with 1% isovitalex and made selective by adding vancomycin
  - Chorioallantoic membrane of the chick embryo
- **Optimum conditions -** 10% CO2, high humidity & incubation at 35°C for 2–8 days
- **Biochemical reactions:** *biochemically* inert

Laboratory Diagnosis (Cont..)

- **Slide agglutination test:** specific antiserum confirmative
- **Multiplex PCR assay**

Treatment of Chancroid

- Drug of choice: Azithromycin (1g oral; single dose)
- Alternative drugs: Ceftriaxone, ciprofloxacin or erythromycin
- Treatment of all the sexual partners is essential

HERPES GENITALIS

HERPES GENITALIS

- Genital herpes is caused by herpes simplex viruses (HSV- 1 and 2).
- Produce widespread disease - cutaneous, mucocutaneous and systemic diseases.
- **Genital ulcers:** Characterized by multiple, painful, bilateral (widely spaced), tiny vesicular ulcers
- **Inguinal lymphadenopathy**: Enlarged, tender, firm, often bilateral

HERPES GENITALIS (Cont..)

- **Recurrent episodes** - milder and recover faster than primary genital herpes.
- **Associated symptoms** - fever, headache, malaise, myalgia, itching, dysuria, vaginal and urethral discharge
- **Other genital infections** : Urethritis, vulvovaginitis, cervicitis, endometritis and salpingitis, rectal (HSV proctitis) and perianal infections following rectal intercourse

HERPES GENITALIS (Cont..)

Laboratory diagnosis:

- **Staining of scrapings** from the base of the lesions with Giemsa's (Tzanck preparation), or Papanicolaou's stain - giant cells or intranuclear inclusions of HSV infection
- **Viral antigen** (by direct IF) **or viral DNA** (by PCR) - detected in scrapings from lesions

HERPES GENITALIS (Cont..)

Laboratory diagnosis (Cont..):

- **Multiplex platforms** of PCR and real-time PCR
- **Isolation** of the virus in scrapings from lesions.

Treatment of Genital herpes

- Effective drugs in genital herpes - acyclovir, valacyclovir, or famciclovir.
- **First episode:** Oral acyclovir is given for 7-14 days.
- IV acyclovir - severe disease or associated neurologic complications
- **Recurrent genital herpes:** Short-course (1 to 3 day) regimens.

LYMPHOGRANULOMA VENEREUM (LGV)

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- Lymphogranuloma venereum (LGV) is an invasive systemic sexually transmitted infection, caused by *Chlamydia trachomatis* serovars L1, L2, and L3

LYMPHOGRANULOMA VENEREUM (LGV)
(Cont..)

- Clinical course passes in three stages:
- **First stage:** Painless papule, ulcer or vesicle on penis or vulva
- **Second stage:**
  - **Bubo -** Enlarged, tender & soft Inguinal lymph nodes
  - **Fistulae** - Buboes breakdown -discharge - spread - chronic fistulae
  - **Systemic symptoms** - fever, headache and myalgia

LYMPHOGRANULOMA VENEREUM (LGV)
(Cont..)

- **Third stage:** in untreated cases
  - Rectal stricture or rectovaginal and rectal fistulae
  - Esthiomene - edematous granulomatous hypertrophy of vulva, scrotum or penis
  - Elephantiasis of the vulva or scrotum

LYMPHOGRANULOMA VENEREUM (LGV)
(Cont..)

- **Diagnosis** - based on serology; biopsy is contraindicated - risk of sinus tract formation
  - **NAAT:** *C. trachomatis* will be positive
  - **Antibody detection** by ELISA or microimmunofluorescence (MIF)
  - Direct detection of **inclusion bodies** by direct IF or for culture confirmation

LYMPHOGRANULOMA VENEREUM (LGV)
(Cont..)

- **Frei test:** Skin test, used in the past - demonstrate type IV hypersensitivity
- **Treatment:** Longer treatment course – necessary.
  - Doxycycline for 21 days - drug of choice.
  - Azithromycin (weekly once for 3 weeks) - alternatively

DONOVANOSIS

DONOVANOSIS

- Also called *granuloma inguinale*, an **STD**
- *Klebsiella granulomatis (*old name - *Calymmatobacterium granulomatis)*
- **1882 – McLeod** - first described disease in Kolkata (Calcutta)
- **1905 - Charles Donovan** in Chennai (Madras) demonstrated **"Donovan bodies"** in the genital lesion

DONOVANOSIS (Cont..)

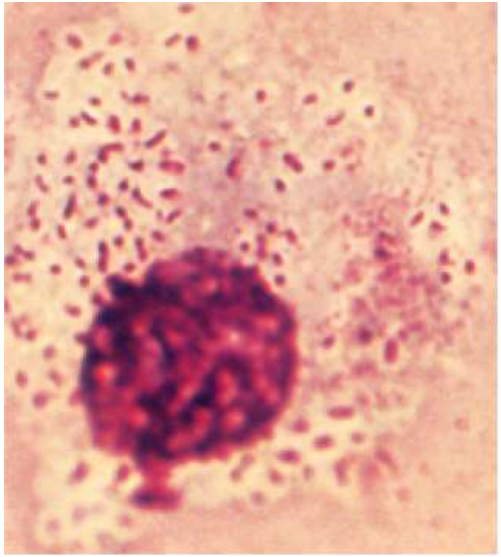
- Donovanosis is prevalent in India, Brazil, Papua New Guinea and parts of South Africa
- **Risk factors** - poor hygiene, lower socioeconomic status and multiple sex partners

Clinical Features

- **Incubation period** :1–4 weeks
- **Lesion:** Starts as a painless papule - beefy red ulcer that bleeds readily when touched
- **Sites:** Genitals (90%) - prepuce, frenum & glans in men and labia minora in women
- **Pseudobubos** in inguinal region (10%) – due to subcutaneous abscess

Laboratory Diagnosis

- **Specimen collection:** Swab, piece of granulation tissue
- **Direct microscopy:**
  - Rapid Giemsa or Wright's stain
  - **Donovan bodies** - Large cyst like macrophages filled with deeply stained capsulated bacilli - *safety-pin (bipolar) appearance*
  - Non-motile, capsulated and gram-negative



Laboratory Diagnosis

- **Culture:** egg yolk medium and on HEp-2 cell lines
- **Molecular Method: PCR** -to differentiate *Klebsiella granulomatis* from other *Klebsiella species - phoE gene*

Treatment of Donovanosis

- Azithromycin 1g orally once per week or 500 mg daily for at least 3 weeks, until all lesions have completely healed
- Alternatively, doxycycline or co-trimoxazole - for 14 days.

URETHRITIS

GONOCOCCAL URETHRITIS

GONOCOCCAL URETHRITIS

- *Neisseria gonorrhoeae* is noncapsulated, gram-negative kidney-shaped diplococcus.
- Causes ‘gonorrhea’, a sexually transmitted infection (STI) - commonly manifests as cervicitis, urethritis and conjunctivitis.

Virulence Factors

- **Pili or fimbriae -** Adhesion to host cells & prevent phagocytosis
- **Outer membrane proteins –**
  - **Porin (protein I)** - >50% of OMP
    - PorB.1A strains - local and disseminated gonococcal infections
    - PorB.1B strains- local genital infections only

Virulence Factors (Cont..)

- **Opacity-associated protein (Protein II) -** adhesion to neutrophils & other gonococci
- Transferrin-binding and lactoferrin-binding proteins
- IgA1 protease - protection from mucosal IgA
- Lipo-oligosaccharide (LOS)

Clinical Manifestations

Gonorrhea: Produces various infections in males, females

- **Males:**
  - **Acute urethritis** – Most common manifestation
  - Purulent urethral discharge ('gonorrhea'- flow of seed)
  - Incubation period is 2–7 days
  - Complications - epididymitis, prostatitis, balanitis & water-can perineum

Clinical Manifestations (Cont..)

- **Females**
  - **Infection is less severe** – More asymptomatic carriage than males
  - **Mucopurulent cervicitis** – Most common presentation
  - **Vulvovaginitis** – in prepubertal girls & postmenopausal women- vagina mucosa thinned out & higher pH

Clinical Manifestations (Cont..)

- **Spread -** Bartholin's gland, endometrium and fallopian tube. Salpingitis and pelvic inflammatory disease - sterility
- **Fitz–Hugh–Curtis syndrome** – Rare - peritonitis & perihepatic inflammation.
- **Both the sexes**
  - Anorectal gonorrhea
  - Pharyngeal gonorrhea
  - Ocular gonorrhea

Clinical Manifestations (Cont..)

- **Pregnant women**
  - Prolonged rupture of the membranes, premature delivery, chorioamnionitis, and sepsis in the infant
- **Neonates (Ophthalmia neonatorum)**
  - Purulent eye discharge within 2–5 days of birth

Clinical Manifestations (Cont..)

- **Disseminated gonococcal infection (DGI)**
  - Rarely following gonococcal bacteremia
  - Polyarthritis and rarely dermatitis & endocarditis
- **In HIV-infected persons**
  - Nonulcerative gonorrhea

Epidemiology

- Incidence decreased in developed countries
- Under reporting due to stigma
- **Host** - exclusively human disease
- **Source** - asymptomatic female carriers or less often patient
- **Transmission :** sexual contact (venereal) and mother to baby during birth.

Laboratory Diagnosis - *Specimen Collection*

- Urethral swab in men and cervical swab in women
- Dacron or rayon swabs
- In chronic urethritis - secretion after prostatic massage or morning drop of secretion

Laboratory Diagnosis - *Transport Media*

- Charcoal-coated swabs kept in Stuart's transport medium ,
- Amies medium,
- JEMBEC or Gono-Pak system

Laboratory Diagnosis - *Microscopy*

- Gram-negative intracellular kidney-shaped diplococci

Laboratory Diagnosis - *Culture*

- Endocervical culture has a sensitivity of 80–90%
- Cervical swabs contain normal flora - selective media preferred (Inhibit commensal Neisseria)
- **Thayer Martin medium** - Chocolate agar with antibiotics

Laboratory Diagnosis - *Identification*

- Gonococci - catalase and oxidase positive
- Ferment only glucose, but not maltose and sucrose
- Automated systems - MALDI-TOF can be used.

Laboratory Diagnosis - *Molecular Method*

- Nucleic acid amplification tests (NAATs) - PCR - detection of *N. gonorrhoeae* from the clinical specimens targeting 16s or 23s rRNA gene.

Treatment of Gonorrhea

- **Third generation cephalosporins** – DOC for uncomplicated gonococcal infection - both the sexual partners should be treated
  - Ceftriaxone (250 mg given IM, single dose)
  - Cefixime (400 mg given orally, single dose)
- If coexisting chlamydial infection – azithromycin or doxycycline added.

Prophylaxis

- No vaccination available for gonococci.
- Early detection of cases
- Treatment of both partners
- Tracing of contacts
- Health education about safe sex practices - use of condoms.

NON-GONOCOCCAL URETHRITIS

NON-GONOCOCCAL URETHRITIS

- Chronic urethritis where gonococci cannot be demonstrated
- NGU is more common than gonococcal urethritis.
- **Bacteria:**
  - *Chlamydia trachomatis: Most common agent*
  - Urogenital *Mycoplasma: Ureaplasma urealyticum* and *Mycoplasma hominis*

NON-GONOCOCCAL URETHRITIS

- **Viruses:** Herpes simplex virus
- **Fungi -** *Candida albicans*
- **Parasites -** *Trichomonas vaginalis*

Differences between gonococcal and non-gonococcal urethritis

Features	Gonococcal urethritis	Non-gonococcal urethritis
Onset	48 hours	Longer (>1 week)
Urethral discharge	Purulent (flow of seed-resembling semen)	Mucous to mucopurulent
Complication	DGI (polyarthritis and endocarditis) Water-can perineum	**Reiter's syndrome:** Characterized by conjunctivitis, urethritis, arthritis and mucosal lesions
Diagnosis	➢ Gram stain ➢ Culture on Thayer Martin media	➢ For *Chlamydia*—culture on McCoy and HeLa cell lines ➢ For *Trichomonas*—detection of trophozoite ➢ For *Candida*—detection of budding yeast cells in discharge ➢ For PCR—can be done for HSV or *Chlamydia*
Treatment	Ceftriaxone	➢ For *Chlamydia*—Doxycycline ➢ For *Trichomonas*—Metronidazole ➢ For *Candida*—Clotrimazole (as vaginal cream or tablet)

CHLAMYDIA TRACHOMATIS INFECTIONS

Genus Description

- Chlamydiae are obligate intracellular bacteria
- Cause a spectrum of diseases - trachoma, lymphogranuloma venereum (LGV), conjunctivitis, pneumonia and psittacosis

Classification

- Based on genetic characteristics
  - *Chlamydia: C.trachomatis.*
  - *Chlamydophila: C.psittaci and C.pneumoniae*

Chlamydiae are Bacteria, Not Viruses

Chlamydiae resemble viruses

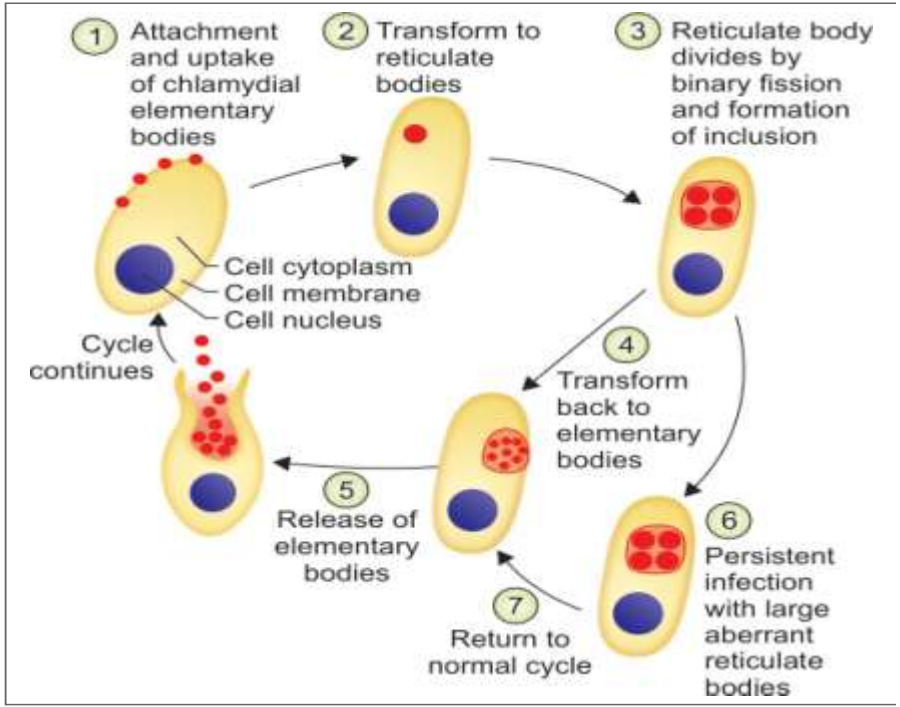
- Obligate intracellular
- Can not grow in artificial media, grow in cell lines, embryonated egg or animals
- Filterable– pass through bacterial filters
- Produce intracytoplasmic inclusions.

Chlamydiae are Bacteria, Not Viruses
(Cont..)

Chlamydiae are confirmed to be bacteria:

- Possess both DNA and RNA
- Cell wall similar to that of gram-negative bacteria
- Multiply by binary fission
- Susceptible to a wide range of antibacterial agents

Life Cycle


1 Attachment and uptake of chlamydial elementary bodies
2 Transform to reticulate bodies
3 Reticulate body divides by binary fission and formation of inclusion
Cell cytoplasm
Cell membrane
Cell nucleus
Cycle continues
4 Transform back to elementary bodies
5 Release of elementary bodies
6 Persistent infection with large aberrant reticulate bodies
7 Return to normal cycle

Chlamydia trachomatis Infections

- *Chlamydia trachomatis* is primarily a human pathogen, causing ocular, urogenital and neonatal infections

Typing of Chlamydia

Biovars:

- Historically, based on the disease produced, *C. trachomatis* was subdivided into two strains or biovars.
- 1. TRIC (Trachoma-inclusion conjunctivitis)
- 2. Lymphogranuloma venereum (LGV) biovar

Features of Chlamydia infections

Species	Character	Biovar	Serotype(s)	Disease
C. trachomatis	➢ Forms compact inclusions mixed with glycogen matrix ➢ Sensitive to sulfonamide ➢ Natural human pathogen ➢ Leaves the host cell with a scar	TRIC	A, B, Ba, C	Trachoma
			D-K (D, Da, E, F, G, H, I, Ia, J, Ja, K)	➢ Genital chlamydiasis ➢ Inclusion conjunctivitis ➢ Infant pneumonia
		LGV	L1, L2, L3	Lymphogranuloma venereum

Features of Chlamydia infections *(Cont..)*

Species	Character	Biovar	Serotype(s)	Disease
C. *psittaci*	➢ Forms diffuse vacuolated inclusions without glycogen matrix ➢ Resistant to sulfonamide ➢ Natural pathogen of birds ➢ Leaves the host cell by lysis	NIL	Many serotypes	• Psittacosis (Atypical interstitial pneumonia) • Transmission is by inhalation route—pet birds (parrots) and poultry (turkeys and ducks) • No man-to-man transmission

Features of Chlamydia infections *(Cont..)*

Species	Character	Biovar	Serotype(s)	Disease
C. pneumoniae TWAR agent	➢ Exclusive human pathogen ➢ Forms inclusions without glycogen matrix ➢ Resistant to sulfonamide	NIL	Only 1 serotype	• Community-acquired atypical pneumonia • Associated with: atherosclerosis and asthma

Genital Infections (C. trachomatis Serovars D–K)

- **Nongonococcal urethritis (NGU):** Most common cause of nongonococcal urethritis (30–50%)
- Differs from gonococcal urethritis (GU) by:
  - Incubation period is 7–10 days, compared to 2–5 days for GU
  - Symptoms: Mucopurulent discharge is followed by dysuria and urethral irritation (GU has purulent discharge).

Genital Infections (C. trachomatis Serovars D–K) (Cont..)

- **Postgonococcal urethritis (PGU)**
- **Epididymitis and proctitis:** Commonest cause of epididymitis in males
- **Reactive arthritis (Reiter's syndrome):** Conjunctivitis, urethritis, arthritis & characteristic mucocutaneous lesions
  - Men : women =10:1

Genital Infections (C. trachomatis Serovars D–K) (Cont..)

- **In females:**
  - Mucopurulent cervicitis - endometritis, salpingitis, PID & pelvic peritonitis
  - Perihepatitis (Fitz–Hugh–Curtis syndrome)

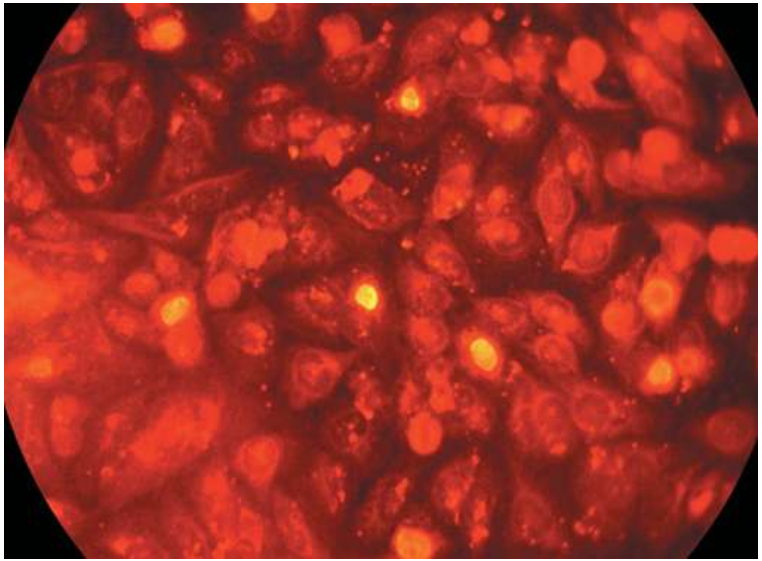
Laboratory diagnosis of Chlamydial infections

- **Specimen:** Depends on the type of lesions
- **Microscopy:** Detects chlamydial inclusion bodies
  - Gram staining, Lugol's iodine and other stains - Castaneda, Machiavello or Gimenez stains
  - Direct IF: Used for direct detection of inclusion bodies.

Laboratory diagnosis of Chlamydial infections (Cont..)

- **Antigen detection (LPS antigens):** By enzyme immunoassays
- **Culture:** It was the gold standard method in the past
  - Egg (yolk sac), mice inoculation and cell line culture
  - Cell lines of choice - McCoy, HeLa (for *C. trachomatis*), HEp2 (for *C. pneumoniae*).

Laboratory diagnosis of Chlamydial infections
(Cont..)



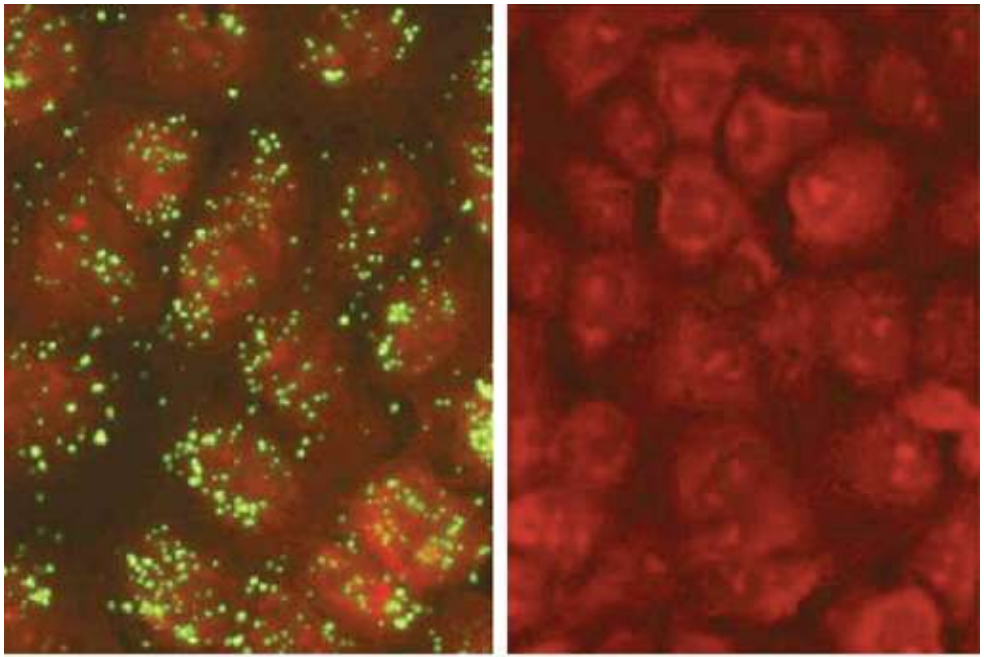
HeLa cells infected with *Chlamydia trachomatis*

Chlamydia trachomatis inclusion bodies (brown) in a McCoy cell culture

Laboratory diagnosis of Chlamydial infections (Cont..)

- **Nucleic acid amplification tests (NAAT)**, e.g. PCR
  - The most sensitive and specific method
  - Currently the diagnostic assay of choice.
- **Serology (antibody detection):**
  - CFT or ELISA using group specific LPS antigen
  - Micro-IF test detects antibody against species and serovar specific MOMP antigen.

Anti-Chlamydia microimmunofluorescence test (MIF)



Positive reaction

Negative reaction

Treatment of C. trachomatis infections

For uncomplicated genital infection or trachoma or adult conjunctivitis:

- Azithromycin - drug of choice - single dose of 1 gram tablet, per oral
- Alternatively doxycycline, tetracycline, erythromycin or ofloxacin - 7 days
- Ceftriaxone - added to the regimen as co-infection with gonococcus may be present in most of the cases.

Treatment of C. trachomatis infections (Cont..)

For complicated genital infection:

- Doxycycline (100 mg twice daily), or erythromycin (500 mg four times daily) - given for:
  - 2 weeks for pelvic inflammatory disease and epididymitis
  - 3 weeks for LGV.

Prevention

- Periodic screening of high-risk groups, such as young women having multiple sex partners
- Treatment of both the sex partners
- Use of barrier methods of contraception - condoms
- Abstain from sex till 7 days after starting the treatment.

UROGENITAL MYCOPLASMA INFECTIONS

UROGENITAL MYCOPLASMA INFECTIONS

- *Mycoplasma (M. hominis, M. genitalium)* and *Ureaplasma (U. urealyticum* and *U. parvum)* - associated with urogenital tract disease.
- Frequently colonize female lower urogenital tract - vagina, periurethral area and cervix
- Transmission: Sexual contact or mother to fetus during birth.

Clinical Manifestations

- Non-gonococcal urethritis and epididymitis (mainly due to *Ureaplasma* and *M. genitalium*)
- Pyelonephritis (*M. hominis*), and urinary calculi (*Ureaplasma*)
- Pelvic inflammatory disease (mainly due to *M. hominis*)
- Postpartum and postabortal infection
- Non-urogenital infections (rare, due to *M. hominis*): Brain abscess, wound infections or neonatal meningitis.

Laboratory Diagnosis

- Culture and PCR - appropriate methods for diagnosis of urogenital mycoplasmas.
- *Ureaplasma* forms very tiny colonies of 15–50 µm size - previously named as T-form *Mycoplasma*.

Treatment of Urogenital Mycoplasma infections

- Macrolides (azithormycin) - drug of choice for *Ureaplasma* and *M. genitalium* infections
- Doxycycline - drug of choice for *M. hominis*

OTHER GENITAL TRACT INFECTIONS COMMON TO BOTH SEXES

GENITAL TUBERCULOSIS

GENITAL TUBERCULOSIS

- **In female patients** - affects the fallopian tubes and the endometrium - cause infertility, pelvic pain, menstrual abnormalities and adnexal swelling.
- **In male patients,** genital TB preferentially affects the epididymis, producing a slightly tender mass - drain externally through a fistulous tract. Other manifestations - orchitis and prostatitis.

ANORECTAL LESIONS

ANORECTAL LESIONS

- Frequently seen in—
  - (1) women and men who practice of anal-genital intercourse;
  - (2) HIV-infected and other immunocompromised patients.
- Common anorectal lesions - proctitis causing rectal ulcers, anal abscess and anogential warts

ANORECTAL LESIONS (Cont..)

- **Anogenital warts**: Also called as condyloma acuminata - caused by human papilloma virus (HPV)
- **Site:** Genital area - the penile shaft, scrotum, or labia majora of the vagina or in the anal area

ANORECTAL LESIONS (Cont..)

- **In HIV-infected patients**, anorectal lesions tend to last longer, more severe, and are more difficult to treat compared with infections in the immunocompetent individuals

FEMALE GENITAL TRACT DISEASE

FEMALE GENITAL TRACT DISEASE

Common infections of female genital tract - vulvovaginitis, mucopurulent cervicitis, pelvic inflammatory disease, infections after gynecologic surgery and infections associated with pregnancy.

VULVOVAGINITIS

VULVOVAGINITIS

- Vulvovaginitis refers to inflammation of the vaginal mucosa (called vaginitis) and the external genitalia vulva (called vulvitis).
- Most common genital tract infection in females.
- Women present with vaginal symptoms - abnormal discharge with/without offensive odor or itching

Differential diagnosis of vulvovaginitis

Feature	Vulvovaginal Candidiasis	Trichomonal Vaginitis	Bacterial Vaginosis
Etiology	*Candida albicans*	*Trichomonas vaginalis*	*Gardnerella vaginalis*, various anaerobic bacteria
Typical symptoms	Vulvar itching and/or irritation	Profuse purulent discharge; vulvar itching	Malodorous, slightly increased discharge
Discharge	Scanty, white, thick and cheesy	Profuse, white or yellow	Moderate, thin, white to gray
pH of vaginal fluid	Usually ≤ 4.5	Usually ≥ 5	Usually >4.5
Fishy odor with 10% KOH	None	May be present	Present
Vaginal inflammation (erythema)	May be present	Colpitis macularis (strawberry appearance)	None

Differential diagnosis of vulvovaginitis (Cont..)

Feature	Vulvovaginal Candidiasis	Trichomonal Vaginitis	Bacterial Vaginosis
Microscopy of vaginal discharge	- Leukocytes, epithelial cells; budding yeast cell with pseudohyphae	- Leukocytes; trophozoites seen in 80–90% of symptomatic patients	Clue cells, few leukocytes, no/few lactobacilli (Nugent's score ≥7)
Other laboratory findings	Isolation of *Candida* spp.	Antigen detection or PCR	Culture, broad-range PCR
Treatment of the patient	Azole cream, tablet	Metronidazole or tinidazole	Metronidazole (tablet) and clindamycin cream
Treatment of sexual partner	None; topical treatment needed in case of *Candida* dermatitis of penis	Usually treatment needed	None

Trichomoniasis

- Most common parasitic sexually transmitted infection (STI), caused by a flagellated parasite *Trichomonas vaginalis*.
- Has only trophozoite stage; there is no cyst stage.

Trichomoniasis

- Trophozoite has two forms:
  - Flagellated trophozoite: Infective as well as the diagnostic form
  - Amoeboid trophozoite: Actively replicating form, found in the tissue feeding stage of the life cycle.

Life Cycle

- Asymptomatic females - reservoir of infection.
- Humans acquire infection by sexual route.
- Flagellated trophozoites after entry - amoeboid forms - multiply in the genital tract and cause infection - again transform back to flagellated trophozoites - discharged in vaginal/urethral secretions.

Clinical Feature

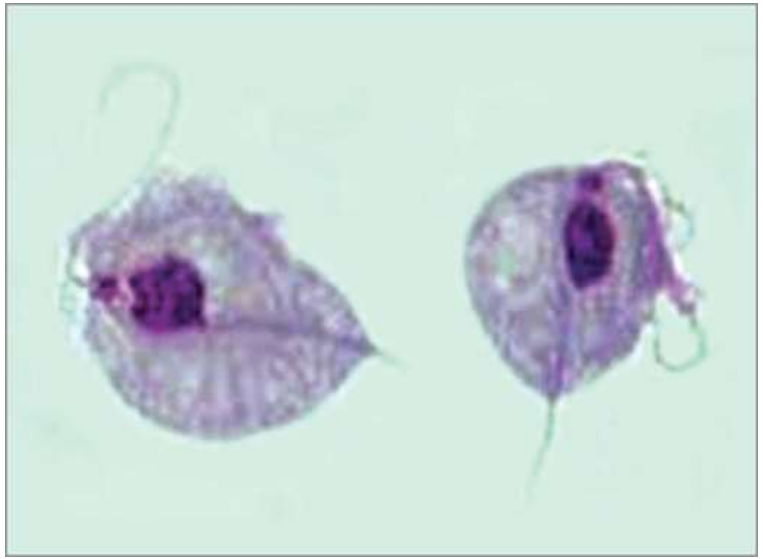
- **Asymptomatic infection: 25-30%**
- **Acute infection (vulvovaginitis)**
  - Females - commonly affected and are presented as vulvovaginitis (thin profuse foul smelling purulent discharge)

Clinical Feature (Cont..)

- Strawberry appearance of vaginal mucosa **(Colpitis macularis)** -in 2% of patients. Characterized by small punctate hemorrhagic spots on vaginal and cervical mucosa
- Other features - dysuria and lower abdominal pain
- In males, the common features are nongonococcal urethritis and rarely epididymitis, prostatitis and penile ulcerations

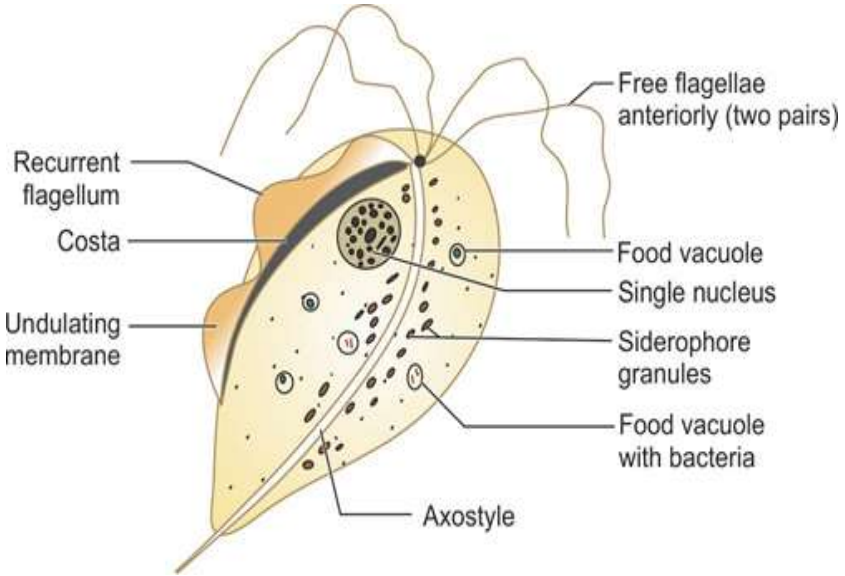
Laboratory Diagnosis

- Vaginal, urethral discharge, urine sediment and prostatic secretions - examined.
- **Wet (saline) mount** of fresh samples (within 10–20 minutes of collection) - jerky motile trophozoites and pus cells.



Laboratory Diagnosis *(Cont..)*

- **Other staining methods** - permanent stains (e.g. Giemsa and Papanicolaou stain), acridine orange fluorescent stain and direct fluorescent antibody test (DFA).



Laboratory Diagnosis *(Cont..)*

Culture:

- Culture is the gold standard method for diagnosis.
- Specimen - processed immediately into media - Lash's cysteine hydrolysate serum media.

Laboratory Diagnosis *(Cont..)*

Antigen Detection in Vaginal Secretion:

- More sensitive than microscopy, easy to perform and indicates recent infection.
- Both rapid ICT and ELISA are available using monoclonal antibodies.

Laboratory Diagnosis *(Cont..)*

Antibody Detection:

- ELISA - whole cell antigen preparation and aqueous antigenic extract to detect anti-trichomonal antibodies in serum and vaginal secretion of the patients.

Laboratory Diagnosis *(Cont..)*

Molecular Methods:

- Highly sensitive, replaced the culture techniques; target *T. vaginalis* specific genes - beta-tubulin gene.

Laboratory Diagnosis *(Cont..)*

Other Supportive Tests:

- Raised vaginal pH (>4.5)
- Positive whiff test
- Increased pus cells

Treatment of Trichomoniasis

- Metronidazole or tinidazole - drug of choice.
- Standard therapy: 2 g, single dose is usually effective
- Both the sexual partners - treated simultaneously to prevent reinfection, especially asymptomatic males .

Bacterial Vaginosis

- Affects women of reproductive age
- Associated with an alteration of the normal vaginal flora.

Bacterial Vaginosis (Cont..)

- **Increase in the concentrations of**:
  - *Gardnerella vaginalis,*
  - *Mobiluncus (motile, curved, gram-variable or gramnegative,* anaerobic rods),
  - Several other anaerobes [*Prevotella and some Peptostreptococcus],*
  - *Mycoplasma hominis*

Bacterial Vaginosis (Cont..)

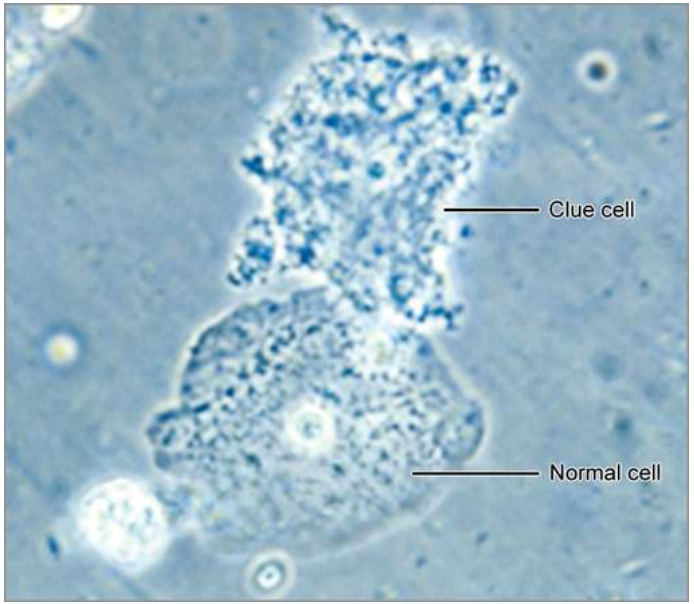
- **Decrease in the concentrations** of lactobacilli (which maintain normal vaginal pH acidic, thereby inhibiting the growth of pathogenic organisms).

Risk Factors

- Coexisting other infections - HIV, *Chlamydia trachomatis & Neisseria gonorrhoeae*
- Recent unprotected vaginal intercourse
- Vaginal douching
- Premature rupture of membranes and preterm labor

Amsel's Criteria

- Any 3 of the following 4 must be present:
- 1. Profuse thin white homogeneous **vaginal discharge** uniformly coated on vaginal wall
- 2. **pH** of vaginal discharge > 4.5
- 3. Accentuation of distinct fishy odor after vaginal secretions are mixed with 10% solution of KOH (***Whiff test***)
- 4. **Clue cells**



Laboratory Diagnosis

Nugent's score :

- Scoring system followed for the diagnosis of bacterial vaginosis
- Done by counting the number of *Gardnerella vaginalis, Mobiluncus and* lactobacilli present in the Gram-stained smear of vaginaldischarge
- A score of more than or equal to 7 is diagnostic

Laboratory Diagnosis (Cont..)

Culture:

- *G. vaginalis* requires enriched media - chocolate agar, BHI broth with serum, etc.
- Gram-negative (appears gram-variable in smears), non-motile, small pleomorphic rod, which shows metachromatic granules

Treatment of Bacterial vaginosis

- Oral metronidazole, given twice daily for 7 days.

Vaginal Candidiasis

- *Candida albicans* - most common species to cause vaginal candidiasis (80% to 90% of cases), followed by *C. glabrata* and *C. tropicalis*.
- **Classical presentation:** Perivaginal pruritus (itching), erythema and vaginal discharge—typically thick and "cheesy" in appearance with pH <4.5

Vaginal Candidiasis (Cont..)

- **Risk factors** - pregnancy, hormone replacement therapy, steroid, diabetes or immunocompromised state
- **Laboratory diagnosis -** Culture of vaginal secretions on Sabouraud dextrose agar (pasty or dry white colonies), followed by identification by conventional (e.g. germ tube test) or automated methods (VITEK or MALDI-TOF)

Vaginal Candidiasis (Cont..)

Treatment:

- Primary treatment - oral fluconazole or itraconazole (for 1 day).
- Topical cream of clotrimazole may be given in milder cases

OTHER GENITAL TRACT INFECTIONS IN FEMALES

Mucopurulent Cervicitis

- Mucopurulent cervicitis (MPC) - inflammation of the columnar epithelium of the endocervix.
- **Agents:** Caused by agents of urethritis - *C. trachomatis, N. gonorrhoeae, Mycoplasma genitalium*

Mucopurulent Cervicitis (Cont..)

- **Clinical diagnosis:** The three cardinal signs of MPC are—
- (1) yellow mucopurulent discharge from cervix,
- (2) endocervical bleeding upon gentle swabbing, and
- (3) edematous cervical ectopy

Mucopurulent Cervicitis (Cont..)

- **Diagnosis:** Yellow cervical mucus on a white swab removed from the endocervix - pus cells
  - **Gram stain:** Presence of ≥20 pus cells/oil immersion field
  - Intracellular gram-negative diplococci
  - **PCR** specific for *N. gonorrhoeae*

Mucopurulent Cervicitis (Cont..)

Treatment:

- Ceftriaxone (single dose IM) followed by doxycycline (for 10 days).

Pelvic Inflammatory Disease (PID)

- Infection that ascends from the cervix or vagina - endometrium and/or fallopian tubes - reproductive tract to involve peritoneum.
- PID can be either primary or secondary.
  - 1. **Primary PID,** occurs spontaneously and usually sexually transmitted or
  - 2. **Secondary PID,** occurs following invasive intrauterine procedures

Etiology

- *N. gonorrhoeae* and *C. trachomatis.*
- Rare causes of PID include:
  - Genital mycoplasmas - *M. genitalium*
  - Anaerobic (peptostreptococci) and facultative organisms (*Prevotella* species)
  - *E. coli*, *Haemophilus influenzae*, and group B streptococci
  - Secondary to hematogenous dissemination (e.g. tuberculosis or staphylococcal bacteremia).

Clinical Manifestations

- **Endometritis**
- **Salpingitis** (inflammation of the fallopian tube)
- **Oophoritis** (inflammation of ovary) and tubo-ovarian abscess
- **Extension to peritoneum** can cause peritonitis, perihepatitis, perisplenitis, or pelvic abscess

Treatment of Pelvic inflammatory disease

- **Outpatient regimen:** Ceftriaxone (IM once) plus doxycycline (for 14 days) plus metronidazole (for 14 days).
- **Parenteral regimen:**
  - Cefotetan or cefoxitin plus doxycycline
  - Clindamycin plus gentamicin.

Bartholinitis

- Infection of bartholin gland and blockade of its duct.
- Mucus-producing gland present on each side of the vaginal orifice; opens through a duct on to the inner surface of the labia minora
- Anaerobic and polymicrobial infections originating from normal genital flora - common cause.

Infections in Pregnancy/Postpartum

Prenatal infections may be acquired from:

- **Hematogenous route** and then cross placenta to infect fetus or
- **Ascending genital** tract route from the vagina through ruptured membranes resulting in **chorioamnionitis**.

Infections in Pregnancy/Postpartum (Cont..)

Natal (during birth) infections: Infections transmitted through the infected birth canal during delivery include—

- **Bacteria:** Group B streptococci, *E. coli, Listeria monocytogenes, N. gonorrhoeae, C. trachomatis*
- **Viruses:** CMV, HSV, enteroviruses, hepatitis B virus, HIV.

Infections in Pregnancy/Postpartum (Cont..)

Postpartum infections:

- Puerperal sepsis - common in mother during postpartum period.
- All the organisms listed under natal infection - cause postpartum infection.
- These infections during birth or postpartum period - transmitted to the newborn to cause postnatal infections.

Group B Streptococcal Infection in Pregnancy

- *Streptococcus agalactiae* - commensal in maternal genital tract.
- Infection in pregnancy - peripartum fever, endometritis and puerperal sepsis
- Transmission of organism to the neonate during birth - neonatal sepsis and meningitis

Group B Streptococcal Infection in Pregnancy *(Cont..)*

- **Prevention:** Screening by rectal/vaginal swab culture is recommended at 35–37 weeks of pregnancy.
- **Chemoprophylaxis** - penicillin - carrier mothers during delivery

OTHER GENITAL TRACT INFECTIONS IN MALES

Prostatitis

- Prostatitis (inflammation of prostate gland) - caused by both infectious (bacterial agents) and noninfectious means.
- Bacterial prostatitis may present in acute or in chronic form.

Acute Bacterial Prostatitis

- Caused by *N. gonorrhoeae* and *C. trachomatis* in males of age <35 years.
- In males of >35 years - Enterobacteriaceae and *Enterococcus*.
- **Manifestations:** Fever, chills, malaise, myalgia, dysuria, pelvic/perineal pain and cloudy urine

Acute Bacterial Prostatitis (Cont..)

- **Complications:** Bacteremia, epididymitis, prostatic abscess, extension to joints, or rarely proceeds to chronic prostatitis
- **Treatment:** Ceftriaxone (IM, single dose), followed by doxycycline (for 10 days).

Chronic Prostatitis

- Enterobacteriaceae (80%) and *Enterococcus* (15%), occasionally by *Pseudomonas*.
- **Manifestations:** Low grade fever, urinary frequency, dysuria, urgency and perineal discomfort.
- **Treatment:** Ciprofloxacin or levofloxacin is given for 4 weeks.

Epididymitis

- Acute epididymitis - pain, swelling, and inflammation of the epididymis that lasts <6 weeks.
- **Young men:** *C. trachomatis* and less commonly by *N. gonorrhoeae*
- **In older men -** Seen following urinary tract instrumentation
- **In homosexual males:** Epididymitis following insertive rectal intercourse - Enterobacteriaceae.

Treatment of Epididymitis

- Ceftriaxone (single dose IM) followed by doxycycline (for 10 days) - epididymitis caused by *N. gonorrhoeae* or *C. trachomatis*.
- Oral levofloxacin - Enterobacteriaceae is suspected.

Orchitis

- Orchitis (inflammation of the testicles) is uncommon and generally acquired by the blood-borne dissemination of viruses.
- **Mumps** - etiological agent in most cases.
- Testicular pain and swelling following infection.
- Infertility following mumps orchitis is very rare.

Questions:

- Q1. Lugol's iodine is used to stain the inclusion body of:

a. *Chlamydia trachomatis*

b. *Chlamydophila psittaci*

c. *Chlamydophila pneumoniae*

d. *All of the above*

Questions:

- Q2. The most commonly used method for isolation of *Chlamydia*:

a. Culture on artificial media

b. Culture on Vero cell line

c. Inoculation into guinea pig

d. Culture on McCoy cell line