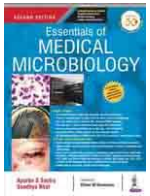
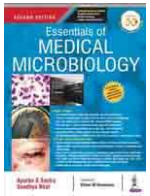


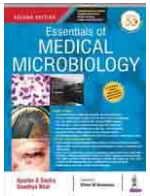
NEISSERIA & MORAXELLA



Learning objectives

At the end of the session, the students will be able to

- Describe morphology and antigens
- Describe Pathogenesis & Clinical features
- Choose appropriate lab diagnosis and interpret the results
- Describe prevention and treatment

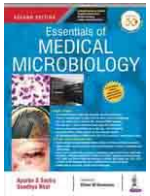


General features

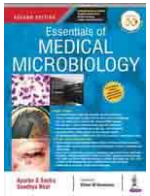
- Gram-negative diplococci, Catalase and oxidase positive
- Non-motile, aerobic

- **Pathogens**
- *Neisseria gonorrhoeae*
- *Neisseria meningitidis*

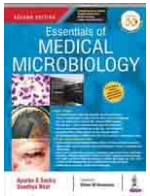
- **Commensals** - *N. lactamica, N.flavescens, N. mucosa, N. sicca, N. subflava,*



NEISSERIA MENINGITIDIS (MENINGOCOCCUS)



- capsulated gram-negative diplococci
- with adjacent sides flattened (lens-shaped/half moon-shaped)



- **Capsular Polysaccharide**

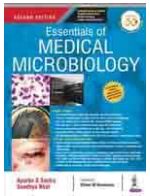
- 13 serogroups - **A, B, C, X, Y** & **W135**—account for the majority of cases of invasive disease

- Non-capsulated – Non-pathogenic

- Outer membrane proteins
- LPS and endotoxin
- IgA proteases
- Transferrin binding proteins

- **Disease patterns**

- Group A – Epidemic Subsaharan Africa, Sporadic globally
- Group B – MC in USA, Hyperendemic cases (>5/lakh)
- Group C – Outbreaks & Sporadic cases
- Group X & Y- Small outbreaks & Sporadic cases
- Group W135- Sporadic cases, epidemics in Subsahara



EPIDEMIOLOGY

- High prevalence areas – Sub-Saharan Africa
- India – Sporadic cases, occasional outbreaks in North India
- Season – Winter & spring
- Age – 2 peaks – 3m-5yrs, 15-25 yrs

EPIDEMIOLOGY

- **Risk factors that promote colonization include:**

- Overcrowding & semiclosed communities - schools, military and refugee camps, Travelers (Hajj pilgrims)

- Smoking

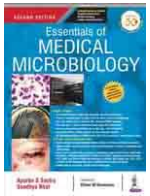
- Viral and *Mycoplasma infection of respiratory tract*

- **Risk factors that promote disease :**

- Deficiency of terminal complement components (C5–C9)

- Hypogammaglobulinemia

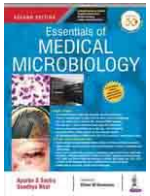
- hyposplenism.



Pathogenesis

- **Source** – Only Humans, nasopharyngeal carriers (mainly children) - MC
- **Mode of transmission- droplet inhalation**
- portal of entry - nasopharynx
- **Spread of infection from nasopharynx to meninges**

1. Hematogenous route causing septicemia (most common)
2. Direct spread along olfactory nerve through cribriform plate
3. Through conjunctiva - rare



Clinical Manifestations

- **Asymptomatic** colonization -most common
- **Rashes:** A non-blanching rash (petechial or purpuric) – 80%
- **Septicemia** - endotoxin induced endothelial injury →increased vascular permeability and intravascular thrombosis
- **Waterhouse–Friderichsen syndrome -** fulminant meningococcemia - large purpuric rashes, shock, DIC, bilateral adrenal hemorrhage and multiorgan failure

Clinical Manifestations

- **Pyogenic meningitis**

- 3–5 years of age - fever, vomiting, headache, neck

- **Chronic meningococcemia** – rare - repeated episodes of petechial rash, fever, arthritis, and splenomegaly

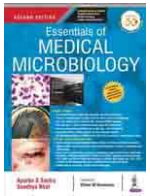
- **Postmeningococcal reactive disease** - Immune complexes develop 4–10 days later →arthritis, rash, iritis, pericarditis, polyserositis, and fever

- **Mortality** - >10%, up to 50% when untreated and high frequency (>10%) of severe sequelae.

Laboratory Diagnosis

- **Specimen Collection** - cerebrospinal fluid (CSF), blood and skin scrapings from petechial rashes
- **CSF** processed immediately. **Never be refrigerated** meningococci may die on refrigeration
- **Blood culture** in BHI broth
- Nasopharyngeal swabs, pus or scrapings from rashes carried in transport media (such as Stuart's medium) → **selective media**

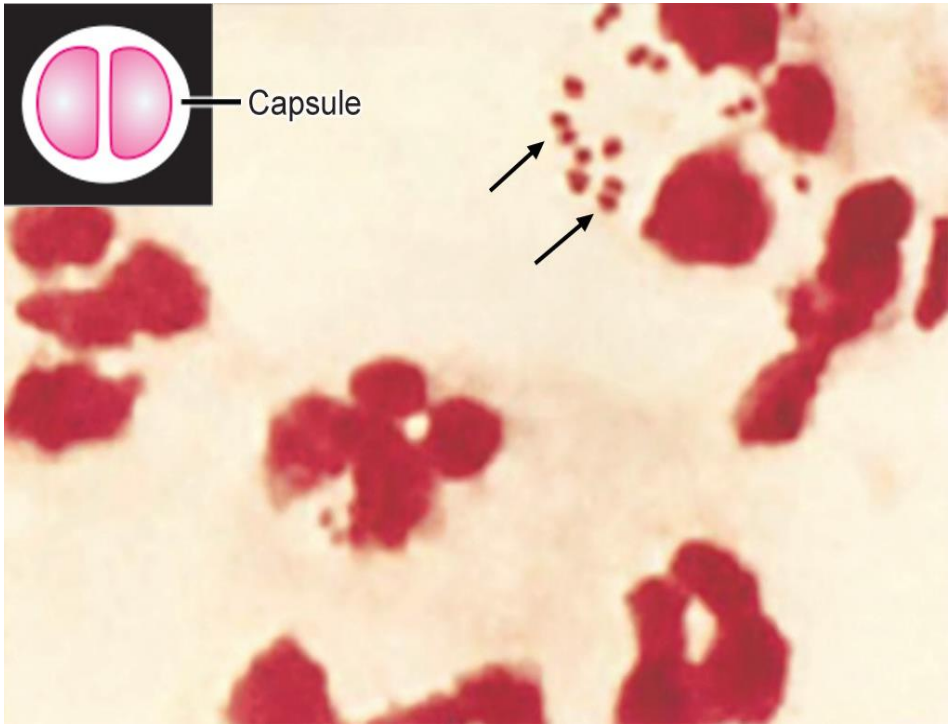
- Thayer Martin medium, New York City medium

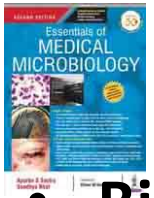


CSF Examination

1st portion	2nd Portion	3rd Portion
Supernatant – -Biochemical analysis -Capsular Ag Deposit – Gram stain	Inoculated on enriched media under 5–10% CO2– Blood agar, chocolate agar	Inoculated into enriched broth - BHI broth

- Gram-negative diplococci with adjacent sides flattened (lens or half-moon-shaped)
- Present inside the polymorphs and often extracellular also





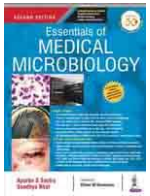
- **Biochemical Tests**

- Catalase and oxidase positive
- Ferment glucose and maltose but not sucrose.

- **Molecular Diagnosis**

- **Serology**

- Antibodies to capsular Ags - ELISA.
- Retrospective diagnosis of disease
- To know response to vaccination
- Diagnosis of chronic meningococcemia.



- **Third-generation cephalosporins – DOC**
- **Penicillin** can also be given; however, reduced sensitivity reported from few countries
- **Symptomatic treatment**, such as aggressive fluid resuscitation (for shock) and measures to decrease intracranial pressure.

Prevention

- **Chemoprophylaxis -** To eradicating colonization of close contacts

- **Ceftriaxone** -DOC, Alternatives – Rifampicin, Ciprofloxacin

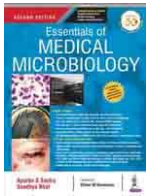
- **Immunoprophylaxis** - Polysaccharide vaccine

- Bivalent (A & C) or Quadrivalent (A,C,Y, & W135)

- **Two doses -** children of 3–18 months **Single dose** to > 2 yrs

- **Efficacy >95%** Duration of protection - 3–5 years

- **No vaccine for serogroup B – capsule** less immunogenic & encephalitogenic

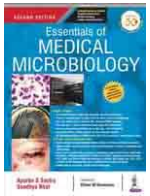


Prevention

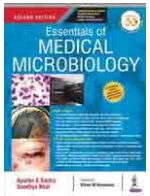
- **Conjugated vaccine**

- Can be given to children < 3yr
- **Indication** - high-risk people

1. contacts of patients during outbreaks
2. Splenic dysfunction
3. Terminal complement component deficiency
4. Taking eculizumab therapy
5. Laboratory staff at risk.



NEISSERIA GONORRHOEAE (GONOCOCCUS)



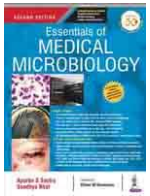
Virulence Factors

- **Pili or fimbriae -** Adhesion to host cells & prevent phagocytosis
- **Outer membrane proteins –**

- Porin (protein I) - >50% of OMP

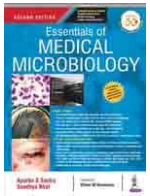
- PorB.1A strains - local and disseminated gonococcal infections

- PorB.1B strains- local genital infections only



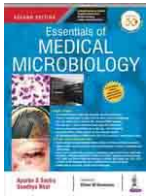
Virulence Factors

- **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) -** endotoxic activity.



Clinical Manifestations

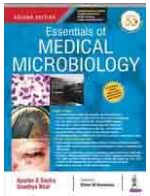
- **Gonorrhea**
- **Males:**
- **Acute urethritis** MC manifestation
- Purulent urethral discharge (‘gonorrhea’- flow of seed)
- Incubation period is 2–7 days
- Complications - epididymitis, prostatitis, balanitis & water-can perineum



Clinical Manifestations

- **Females**

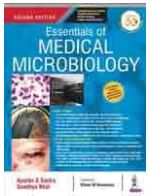
- **Infection is less severe** – More asymptomatic carriage than males
- **Mucopurulent cervicitis** - MC presentation
- **Vulvovaginitis** – in prepubertal girls & postmenopausal women- vagina mucosa thinned out & higher pH
- Not in adult females - resistant to gonococcal infection (low pH and thick stratified squamous epithelium)



Clinical Manifestations

- **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

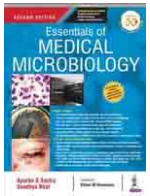
- **Pregnant women**

- prolonged rupture of the membranes, premature delivery, chorioamnionitis, and sepsis in the infant

- **Neonates (Ophthalmia neonatorum)**

- colonized maternal genital flora

- Purulent eye discharge within 2–5 days of birth



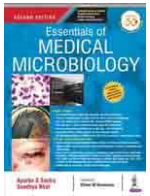
Clinical Manifestations

- **Disseminated gonococcal infection (DGI)**

- Rarely following gonococcal bacteremia
- Polyarthritis and rarely dermatitis & endocarditis

- **In HIV-infected persons**

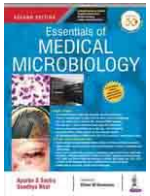
- Nonulcerative gonorrhea



Epidemiology

- Incidence decreased indeveloped countries
- Under reporting due to stigma
- **Host** - exclusively human disease
- **Source** - asymptomatic female carriers or less often patient
- **Transmission**

1. sexual contact (venereal)
2. Mother to baby during birth.

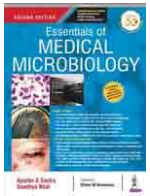


Laboratory Diagnosis

- **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

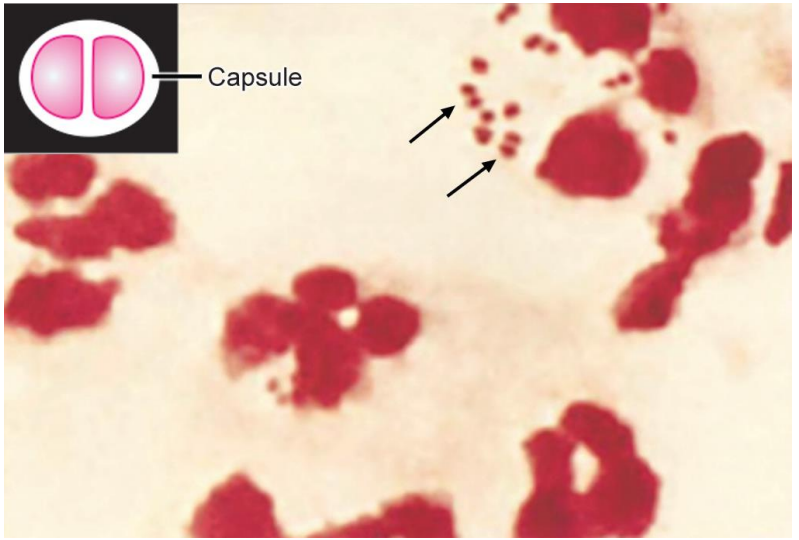
- **Transport Media** - Charcoal-coated swabs kept in Stuart's transport medium , Amies medium, JEMBEC or Gono-Pak system

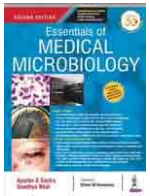


- **Microscopy**

- Gram-negative intracellular kidney-shaped diplococci

- 50% sensitive





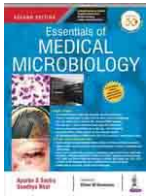
Laboratory Diagnosis

- **Culture**

- Endocervical culture has a sensitivity of 80–90%

- Cervical swabs contain normal flora - selective media preferred (Inhibit commensal Neisseria)

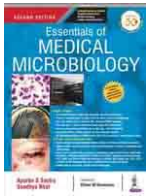
- **Thayer Martin medium** - Chocolate agar with vancomycin, colistin and nystatin
- **Modified New York City medium** - Lysed blood agar and lincomycin, colistin, trimethoprim and amphotericin B
- **Martin–Lewis medium.**



Laboratory Diagnosis

- **Biochemical Tests**

- To differentiate gonococci from other commensal *Neisseria species*
- Gonococci are catalase and oxidase positive
- Ferment only glucose, but not maltose and sucrose.

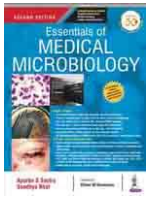


TREATMENT

- **Third generation cephalosporins** – DOC foruncomplicated 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.



DRUG RESISTANCE

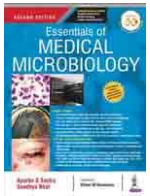
PPNG	**Penicillinase producing Neisseria gonorrhoeae** **-Plasmids coding for β-lactamases are transferred by conjugation**
CMRNG	**Chromosomally mediated resistant N. gonorrhoeae** **- Resistance to penicillin and tetracycline** **- Mutations at multiple sites, which decreases the permeability of the cell to antibiotics**
TRNG	**Tetracycline-resistant N. gonorrhoeae, plasmid-borne**
QRNG	**Quinolone-resistant N. gonorrhoeae**

Nongonococcal (Nonspecific) urethritis

- Chronic urethritis where gonococci cannot be demonstrated
- NGU is more common than gonococcal urethritis.
- **Bacteria:**

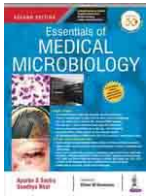
- *Chlamydia trachomatis: Most common agent*
- *Ureaplasma urealyticum, Mycoplasma hominis*
- Gonococcal infection, cocci in L forms

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



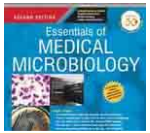
Gonococcal v/s Non-gonococcal urethritis

Features	Gonococcal urethritis (GU)	Non gonococcal urethritis (NGU)
Onset	48hrs	Longer (>1week)
Urethral discharge	Purulent	Mucous to mucopurulent
Complication	Polyarthritis and endocarditis Water-can perineum	Reiter's syndrome- conjunctivitis, urethritis, arthritis and mucosal lesions
	Other complications are common to both GU and NGU such as- • Males- epididymitis, prostatitis, seminal vesiculitis and balanitis • Females- Salpingits and pelvic inflammatory disease and Fitz-Hugh-Curtis syndrome	



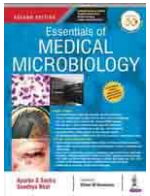
Gonococcal v/s Non-gonococcal urethritis

Features	Gonococcal urethritis (GU)	Non gonococcal urethritis (NGU)
Diagnosis	• Gram stain, • Culture on Thayer Martin media	• For Chlamydia-culture on McCoy and HeLa cell lines • Trichomonas- detection of trophozoite • Candida- detection of budding yeast cells in discharge • PCR- can be done for HSV or Chlamydia

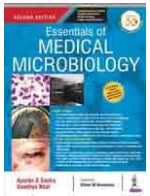


Meningococcus v/s Gonococcus

N.meningitidis	N.gonorrhoeae
Capsulated	Non- Capsulated
Diplococci adjacent sides flattened	Diplococci adjacent sides concave
Ferment glucose and maltose	Ferment only glucose
Rarely have plasmids	Usually possess plasmids, coding for drug resistance genes
Both intra and extracellular	Predominantly intracellular
Colony- circular	Colony- vary in size with irregular margin
Habitat- Nasopharynx	Habitat- genital tract (urethra, cérvix), rarely pharynx.



MORAXELLA



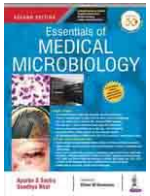
Moraxella catarrhalis

- **Morphology:** Gram-negative diplococci with flattened adjacent sides
- **Culture: Basal medium like nutrient agar**
- **Biochemical reactions: Catalase & oxidase positive**
- Differs from pathogenic *Neisseria as:*

- Does not ferment any carbohydrate

- Tributyrin hydrolysis test - Positive

- DNase test - positive.



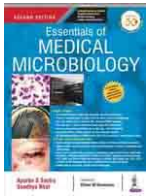
Moraxella catarrhalis

- **Pathogenesis**

- Opportunistic lower respiratory tract infections in adults with COPD

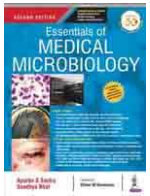
- Can rarely cause - otitis media, meningitis, endocarditis & sinusitis

- Some strains of *M. catarrhalis* secrete **beta-lactamases** which destroy penicillin that makes β-lactam antibiotics ineffective to meningococci and other penicillin-sensitive bacteria of the respiratory tract.



Moraxella lacunata

- Also called Morax-Axenfeld bacillus
- Non-fermenting gram-negative rod-shaped and generally present as pairs
- Causes catarrhal conjunctivitis, and angular conjunctivitis



THANK YOU..!