

# ***Neisseria***

***Gram negative coccus***

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# ***Important Human Pathogens***

***Neisseria gonorrhoeae***

***Neisseria meningitidis***

# ***General Characteristics of Neisseria spp.***

- **Aerobic**
- **Gram-negative** cocci often arranged in pairs (**diplococci**) with **adjacent sides flattened** (like coffee beans)
- **Oxidase positive**
- Most **catalase positive**
- Nonmotile
- Acid from oxidation of carbohydrates, not from fermentation

# *Neisseria* Associated Diseases

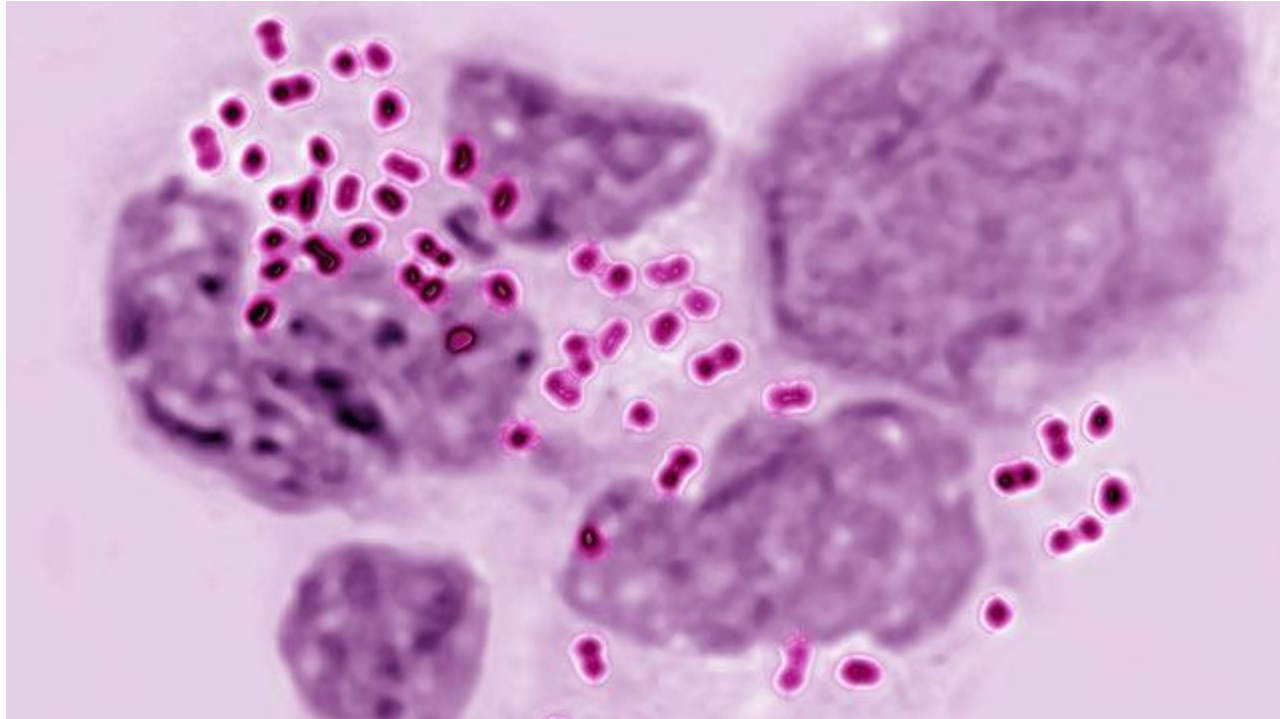
Organism	Diseases
<i>N. gonorrhoeae</i>  (ophthalmia neonatorum)	Urethritis, cervicitis, salpingitis, pelvic inflammatory disease, proctitis, bacteremia, arthritis, conjunctivitis, pharyngitis
<i>N. meningitidis</i>	Meningitis, meningococcal meningitis, bacteremia, pneumonia, arthritis, urethritis
Other <i>Neisseria</i> species	Opportunistic infections

***Neisseria gonorrhoeae***  
***(gonococcus)***

# *Neisseria gonorrhoeae*

- **Transmitted by sexual contact**
- **Gram-negative diplococci flattened along the adjoining side**
  - Requires complex media
- **Fastidious, Capnophilic and susceptible to cool temperatures, drying and fatty acids**
- **Produce acid from glucose, but not from other sugars**

# ***Neisseria gonorrhoeae* in Urethral Exudates**



# *Epidemiology of Gonorrhea*

- Sexually-transmitted disease
- **Found only in humans**
- Asymptomatic carriage is major reservoir
- Lack of protective immunity and therefore **reinfection**, partly due to **antigenic diversity** of strains
- Higher risk of disseminated disease in patients with complement deficiencies



# ***Differences Between Men & Women with Gonorrhea***

## **In MEN**

- **Urethritis; Epididymitis**
- Most infections among men are **acute and symptomatic** with **purulent discharge & dysuria** (painful urination) after 2-5 day incubation period
- The two bacterial agents primarily responsible for **urethritis** among men are ***N. gonorrhoeae*** and ***Chlamydia trachomatis***

# ***Differences Between Men & Women with Gonorrhea***

## **In WOMEN**

- **Cervicitis; Vaginitis; Pelvic Inflammatory Disease (PID); Disseminated Gonococcal Infection (DGI)**
- Women often **asymptomatic** or have atypical indications; Often untreated until PID complications develop
- **Pelvic Inflammatory Disease (PID)**
  - May also be asymptomatic, but difficult diagnosis accounts for many false negatives
  - Can cause scarring of fallopian tubes leading to infertility or ectopic pregnancy

## ➤ **Disseminated Gonococcal Infection (DGI):**

- Result of gonococcal bacteremia
- Often skin lesions
- Petechiae (small, purplish, hemorrhagic spots)
- Pustules on extremities
- Arthralgias (pain in joints)
- Tenosynovitis (inflammation of tendon sheath)
- Septic arthritis
- Occasional complications: Hepatitis; Rarely endocarditis or meningitis

# Gonorrhoea

<u>Females</u>	<u>Males</u>
50% risk of infection after single exposure	20% risk of infection after single exposure
Asymptomatic infections frequently not diagnosed	Most initially symptomatic (95% acute)
Major reservoir is asymptomatic carriage in females	Major reservoir is asymptomatic carriage in females
Genital infection include cervix (cervicitis), but vagina, urethra, rectum can be colonized	Genital infection generally restricted to urethra (urethritis) with purulent discharge and dysuria
Ascending infections in 10-20% including salpingitis, tubo-ovarian abscesses, pelvic inflammatory disease (PID) , can lead to sterility	Rare complications may include epididymitis, prostatitis, and periurethral abscesses
Disseminated infections more common, including septicemia, infection of skin and joints (1-3%)	Disseminated infections are very rare
Can infect infant at delivery (conjunctivitis, ophthalmia neonatorum)	More common in homosexual men

# ***Pathogenesis of Neisseria gonorrhoeae***

- **Fimbriated cells** attach to intact mucus membrane epithelium
- **Capacity to invade intact mucus membranes or skin with abrasions**
  - Adherence to mucosal epithelium
  - Penetration into and multiplication before passing through mucosal epithelial cells
  - Establish infection in the sub-epithelial layer
- **Most common sites of inoculation:**
  - **Cervix (cervicitis)** or vagina in the female
  - **Urethra (urethritis)** or penis in the male

# Virulence Factors Associated with *Neisseria gonorrhoeae*

Virulence Factor	Biologic Effect
Pilin	Protein that mediates initial attachment to nonciliated human cells (e.g., epithelium of vagina, fallopian tube, and buccal cavity); interferes with neutrophil killing
Por protein (protein I)	Porin protein—promotes intracellular survival by preventing phagolysosome fusion in neutrophils
Opa protein (protein II)	Opacity protein—mediates firm attachment to eukaryotic cells
Rmp protein (protein III)	Reduction-modifiable protein—protects other surface antigens (Por protein, LOS) from bactericidal antibodies
Transferrin-binding proteins	Mediate acquisition of iron for bacterial metabolism
Lactoferrin-binding proteins	Mediate acquisition of iron for bacterial metabolism
Hemoglobin-binding proteins	Mediate acquisition of iron for bacterial metabolism
LOS	Lipooligosaccharide—has endotoxin activity
IgA <sub>1</sub> protease	Destroys immunoglobulin A <sub>1</sub> (role in virulence is unknown)
$\beta$ -lactamase	Hydrolyzes $\beta$ -lactam ring in penicillin

***Neisseria meningitidis***  
***(meningococcus)***

# *Neisseria meningitidis*

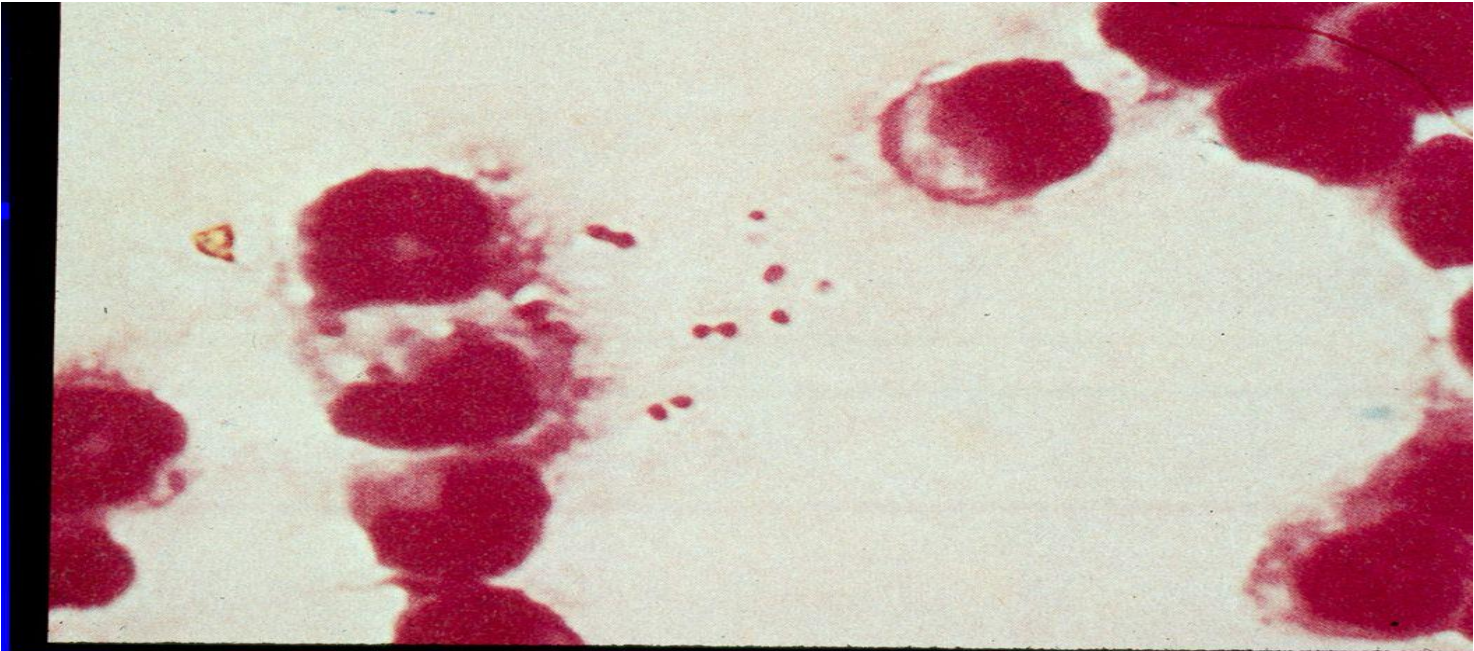
- Encapsulated small, gram-negative diplococci
- Second most common cause (behind *S. pneumoniae*) of **community-acquired meningitis** in previously healthy adults
- **Pathogenicity:**
  - **Pili-mediated**
  - **Antiphagocytic polysaccharide capsule** allows systemic spread
  - Toxic effects mediated by **lipooligosaccharide**
- Serogroups **A, B, C, Y, W135** account for about 90% of all infections



# ***Diseases Associated with Neisseria meningitidis***

- **Following dissemination of virulent organisms from the **nasopharynx**:**
  - ✓ **Meningitis**
  - ✓ **Septicemia**
  - ✓ **Meningoencephalitis**
  - ✓ **Pneumonia**
  - ✓ **Arthritis**

# ***Neisseria meningitidis* in Cerebrospinal Fluid**



**CSF gram stain showing *Neisseria meningitidis***

# ***Epidemiology of Meningococcal Disease***

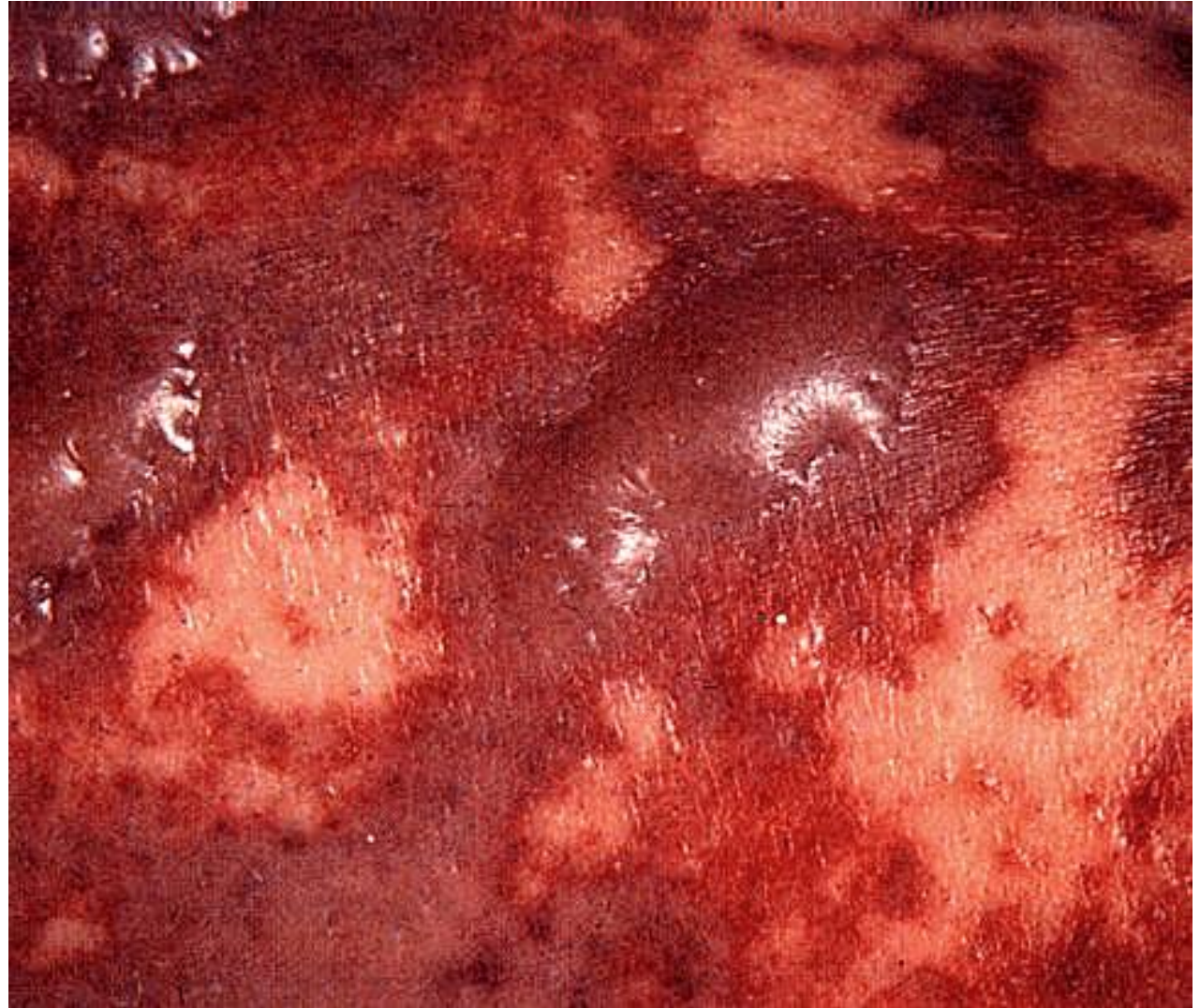
- **Humans only natural hosts**
- **Person-to-person transmission** by aerosolization of respiratory tract secretions in crowded conditions
- **Close contact** with infectious person (e.g., family members, day care centers, military units, prisons, and other institutional settings)
- Highest incidence in **children less than 1-5 years** as passive maternal antibody declines and as infants immune system matures
- Commonly **colonize nasopharynx** of healthy individuals; highest oral and nasopharyngeal carriage rates in school-age children, young adults and lower socioeconomic groups

# ***Pathogenesis of Meningococcal Disease***

- Specific receptors (GD1 ganglioside) for bacterial fimbriae on epithelial cells in **nasopharynx** of host
- Organisms are **internalized into phagocytic vacuoles, avoid intracellular killing**
- **Replicate intracellularly and migrate to subepithelial space**
- **production of endotoxin (lipid A of LOS)**

# ***Skin Lesions of Meningococccemia***

**Petechiae or  
hemorrhagic  
bullae.**



# ***Laboratory Characterization of Neisseria meningitidis***

- Large numbers (e.g.,  $>10^7$  cells/ml) of encapsulated, small, gram-negative diplococci and PMN's can be seen microscopically in **(CSF)**
- Transparent, non-pigmented nonhemolytic colonies on **chocolate blood agar** with **enhanced growth in moist atmosphere with 5% CO<sub>2</sub>**
- Oxidase-positive
- a new quadrivalent conjugate vaccine against serogroups A, C, W-135, and Y, is currently available