**Neisseria gonorrhoeae** ("gonococcus" or "GC")

- **strict human pathogen**
- **Gram-negative**
- **no flagella**
- **diplococcus**

Fastidious, requires complex growth medium, CO₂ (e.g. "chocolate" agar - contains lysed blood)

- **Aerobic**
- **oxidation of glucose only to acid**
- **Oxidase-positive**
- **Mostly catalase positive**

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**N. gonorrhoeae virulence determinants:**

- **Pili** (extend from cytoplasm through the outer membrane):
  - Mediate attachment to nonciliated cells
  - Increase resistance to killing by neutrophils
  - Provide "twitching" motility on surfaces
  - Antigenic variation due to intrabacterial DNA rearrangements between the pilin expression locus and numerous nontranscribed (silent) genes
  - Phase variation in pilin expression (on/off) during infection, through slipped-strand mispairing mechanism

[Image of bacteria]
Opa (opacity) proteins — if grown on agar, have "opacity" to them — write, etc. growth color.

Multiple alleles (~14) may be expressed by individual bacteria — separate gene w/ its own promoter & no known recombination.

Each Opa has unique characteristics

Some bind extracellular matrix components — attach to surface

Facilitate binding to self and/or certain cell types — microcolonies/clumping

Some may facilitate invasion of host cells — starts w/ epithelium & goes through.

Independent, phase variation in expression of each Opa during infection, through slipped-strand mispairing mechanism

LOS (lipooligosaccharide)

Highly branched, no O-antigens (different from LPS)

Endotoxin activity

Stimulates inflammatory response and TNF-α release

Undergoes antigenic variation during infection — new LOS forms w/in infection & evades host immune response

Undergoes sialic acid modification — binds factor H + cells & helps degrade C3b so that cells don't die.

May bind host complement regulator factor H, which protects against alternative pathway of complement

Porin proteins — very antigenic.

Serotype specific

May facilitate invasion of host cells — binding att.

May bind host complement regulator factor H, which protects against alternative pathway of complement (associated with disseminated disease)

Disseminated disease binds factor H, has sialic acid, etc.
IgA; protease

Cleaves secretory IgA - protects against antibody?

Transferrin-, lactoferrin- and hemoglobin-binding proteins

Acquisition of iron for bacterial metabolism

Natural competence

Bacteria easily acquire extracellular DNA

Facilitates rapid spread of beneficial genes

* mixed infxn or variation w/in infxn \( \rightarrow \) gets spread to others by spontaneous lysing

Resistance to antibiotics

Associated with acquired plasmid- and chromosome-encoded genes

* plasmid is more problematic bc plasmids more

High percentages of isolates resistant to \( \beta \)-lactams, tetracycline or both

Increasing number of fluoroquinolone resistant isolates

* \( \beta \)le constant exposure \( \rightarrow \) resistance dev. & is passed on
Pattogenesis
1. Anchoring u/fili
2. Tight adherence of Opa pry to epithelial microvillenues
3. Start twitching & moving → spread
4. Invade cell, move to opposite side of mucous memb. → systemic infxn
   (most resist All. complement)

Clinical Manifestations

Symptoms of gonorrhea are very similar to those of chlamydia
   You must confirm diagnosis

Also, consider possible co-infections with other STDs
   especially chlamydia

Incubation 2-5 days

Purulent, cream-colored discharge → pus, full of lact
   (compare with more mucoid discharge of chlamydia)

Men:
   Restricted to urethra
   (90-95% are symptomatic) → fairly strong, so will seek help
   * 5-10% are not symptomatic

Urethral discharge ("The Drip")

Dysuria (painful urination)
   consider gonorrhea in differential diagnosis of dysuria

Rare complications in males:

Epididymitis → swollen testicle
   Prostatitis
   Periurethral abscesses

Women:
   Cervix is primary site of infection

Vaginal discharge → not as noticeable & location

Dysuria
   consider gonorrhea in differential diagnosis of dysuria
   * unfortunately, MD's think cystitis & etc. wrong Tx.

Abdominal pain → ascending genital infxn, into fallopian tubes, etc.
**Laboratory Diagnosis**

Swab exudate or collect synovial fluids, blood during acute disease (<1 week)

Gram stain for diplococci: but freq. negative
confirmatory if urethral or endocervical specimen
look for commensals
only suggestive if oral specimen → not diagnostic
(commensal *Neisseria* species common in nasopharynx)

Follow inconclusive or negative results with culture

Culture is:
sensitive
specific
can assess antibiotic resistance (determines therapy)

Plated on selective (modified Thayer-Martin, Vanc+) and non-selective (chocolate blood agar, Vanc-) media
Positive identification: oxidase-positive, Gram-negative diplococci growing on selective media, acid produced oxidatively from glucose only → only utilize glu.

**Nucleic Acid Amplification Tests (NAAT):** PCR → prone to errors

**Treatment and Prevention**

Uncomplicated cases: ceftriaxone, ciprofloxacin, ofloxacin

Unresponsive cases: culture for in vitro susceptibility testing, as antibiotic resistances on the rise

Neonates: prophylaxis at birth with 1% silver nitrate, 1% tetracycline, or 0.5% erythromycin,
treatment of disease with ceftriaxone

Always consider coinfection with other STDs, esp. chlamydia

Aggressive follow-up of sexual partners of infected patients

Patient education

There is no effective vaccine for gonorrhea