Gonococci attach to mucosal cells. They bind to the microvilli of non-ciliated columnar epithelium [no attachment to ciliated cells]. The microvilli draw the bacteria to the surface of the cell. Enter the cells by endocytosis. This means they get a host membrane bound vacuole that is inside the cell. They penetrate into them and multiply, the vacuole is transported to the base of the cell. Next they pass thru the mucosal cells into the sub-epithelia space and establish infection.

Pili [also known as fimbriae] needed for initial attachment. Non-piliated cells are avirulent [if pure and unchanging]. The infection is still viable as they can due without pili once in the sub-epithelial space. pilin a protein that mediates the initial attachment to human cells. Why turn off? Pili are antigenic, turning them off or changing them is useful. As an aside, the pili are the strongest biological motors known, they can pull 100,000x its weight. They can pull a nanonewton.

The molecular mechanism for these changes is known. Here are several ways:
1. Turning off:
   a. phase variation--turn off pillin once infection established for binding to columnar epithelium. Promoters acted upon by pilA/B transcriptional activators for pilE1/2 and opaE1 these are attuned to environmental conditions.
      E is for expressed
   
   b. slip stranded synthesis—change of reading frame by errors in DNA replication in areas of repeats: pilC, opa--more ways not to get products

2. antigenic variation—
   a. change out the antigenic parts via cassettes of the pillin proteins [idea is to confuse, make immune system have to start over again.
   b. homologous recombination in the conserved regions between the microcassettes.
Mix of the two: $P^s$ soluble--pilin [decoy pili- phenotype], loci: S=silent, E=express, L=long

DIAGRAMS

Opa protein directs a tighter attachment after the initial attachment with the host cell surface and directs migration into the epithelial cells. N.g has the ability to make zero, 1 or several outer membrane proteins called Opa [PII]. As we have seen they can undergo phase variation. Each strain has 10 or more strains. The opa also binds to LOS on other Ng’s making a cluster—that constitutes a biofilm.

Por protein protects phagocytosed bacteria from intracellular killing by preventing phagolysosome fusion. Further gonococcal porins are involved in preventing phagocytic cells from mounting the respiratory (oxidative] burst that would generate free radicals and kill the bacteria. Porins also induce the local release of TNFalpha which leads to inflammation. PI [also called por—same thing!] is an invasion that mediates penetration of the cell. Each strain of Ng only expresses 1 por—however there are variations.

Rmp [PIII]--reduction modifiable protein. This is an outer membrane protein—it does not undergo antigenic variation. It complexes with LOS and por but antibody against Rmp blocks the antibodies to por and LOS [which would be bacterialcidal] so in fact annti-Rmp antibodies increase susceptibility to infection!. There is an E coli with a very similar molecule —so having seen that can heighten infection. --protects other surface antigens such as por and los from antibodies capsule- antiphagocytic
Also make IgAse [destroys IgA on mucosal surface]
Tbp1, Tbp2--transferrin binding proteins, mediate acquisition of iron [yes appears redundant with Lbp]
opa--opacity protein mediates the firm attachment to epithelial cells and invasion into cells
Lbp-lactoferrin binding protein--mediates acquisition of iron
LOS--lipooligosaccharide-has endotoxin activity [lipid A + core oligo induces TNF-a], this is responsible for the scarring.
beta-lactamase--more and more have this, acquiring the ability to hydrolyze penicillin.