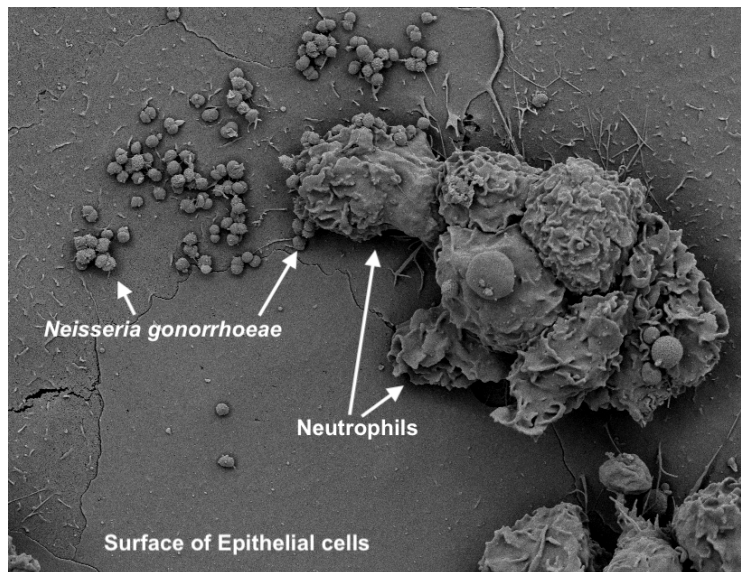


MicroRogue: Neigo (*Neisseria gonorrhoeae*)

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Scanning electron micrograph of epithelial cells infected with *N. gonorrhoeae*, showing neutrophils that have migrated across the epithelium in response to the bacteria. Image captured by Evan R. Lamb.

Claim to fame: a sexually-transmitted pathogen and master of disguises

The rising incidence of gonorrhea, a classic sexually transmitted infection (STI). Infectious agents that are sexually transmitted have a notorious place in human history. One of these is the bacterium Neigo which causes the disease gonorrhea. Diseases with symptoms like gonorrhea are mentioned in ancient Greek and Roman texts, the Old Testament of the Bible, and even in ancient Egyptian writings. However, it wasn't until 1879 that a German physician, Albert Ludwig Sigmund Neisser, identified *Neisseria gonorrhoeae* as the culprit. Neigo is a diplococcus, meaning it appears under the microscope as two attached round cells.

Despite condoms being effective at reducing transmission of Neigo, gonorrhea is a major and increasing problem throughout the world today, with about 90 million new cases globally every year. The rising number of cases is accompanied by an increase in antibiotic resistance. According to the World Health Organization, *N. gonorrhoeae* is a "superbug" because some isolates are resistant to all recommended antibiotics. For these reasons, researchers are actively seeking new therapies for gonorrhea, including vaccines.

Transmission. Neigo can only infect humans and no other animals, and only survives inside people, not on surfaces like toilet seats. It must be transmitted directly from person-to-person to cause disease.

The disease. Neigo typically targets the genital tracts of men and women, but also causes infections of the throat, rectum, and eyes. While gonorrhea's best-known symptom is pain when urinating, many infections, especially in women, don't cause noticeable symptoms. Sometimes

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the bacteria get into the bloodstream and can also infect other body sites, including joints like the knees.

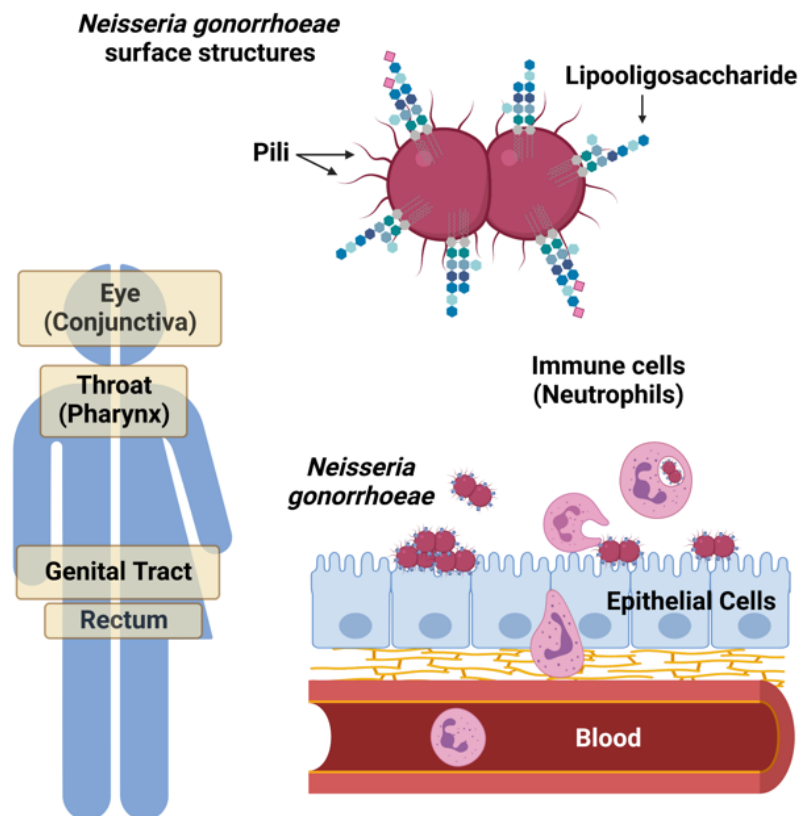
Undiagnosed infections, and diagnosed and treated infections that persist because they do not respond to antibiotic treatment, cause damage to tissues that can result in infertility and may even be life-threatening. Without antibiotics, infections can last for weeks to months. This makes it especially important to promptly diagnose and treat infections by Neigo.

Neigo's adaptation to the human host. Neigo has many features that make it especially good at living in people.

- First, using its long hair-like structures known as pili, it tightly binds to human epithelial cells that line sites of infection. Pili can lengthen and retract, which allows Neigo to crawl along human cell surfaces and join with other bacteria to form clusters that are hard to dislodge.

Neigo also uses its pili to take up DNA, which helps the bacterium share genes with others living on the infected body surfaces – including genes that make the bacteria antibiotic resistant.

- Second, Neigo's surface is made of sugars attached to lipids, known as lipooligosaccharide. These sugars mimic structures that are normally found on human cells, so the immune system doesn't recognize them as foreign, and therefore something it should attack.



Schematic of Neigo, the cells it infects, and the body sites where it causes disease. Created with BioRender.

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- Third, Neigo is constantly changing its surface components, including lipooligosaccharide and pili. This leads to lots of variation of the bacterial surface, which is thought to help the bacteria avoid detection by the immune system. This is one reason why people can get gonorrhea again and again.

Our defenses and Neigo's ways of resisting them.

- The first line. When Neigo attacks our epithelial cells, white blood cells known as neutrophils move from the bloodstream to the site of infection to fight the bacterium. Neutrophils are the body's first responders to infection and injury – they are what cause pus at an infected cut, for example. Neutrophil influx is one reason why infection with Neigo causes local pain and swelling.

Neutrophils attempt to kill Neigo cells by swallowing them and releasing onto them many toxic components, like bleach and hydrogen peroxide. However, this doesn't seem to affect Neigo very much, since some bacteria are found alive inside the neutrophils. Part of the reason it survives in neutrophils is its ability to resist the toxic oxidants that neutrophils make. Another reason is that the bacteria have pumps that pump out of the cell some of the toxic materials made by neutrophils. Neigo also sneaks inside neutrophils in such a way that doesn't induce the neutrophils to release all their toxic components, so the bacteria may avoid these defenses entirely.

- The second line. Infections leads to activation of immune response proteins known as the complement system that can target and lyse (dissolve) the bacteria. Neigo withstands this too, by coating itself in proteins and sugars that block lysis.

These strategies make Neigo especially good at staying alive during infection. Because our bodies cannot clear the infection and the bacteria persist, increasing amounts of immune proteins and cells arrive to fight the bacteria. The resulting inflammation is thought to cause the tissue damage that leads to infertility and other consequences of gonorrhea.

Neigo also steals metal nutrients from us! Both we and microbes need trace amounts of various metals for many of our enzymes to work. One of our mechanisms to resist infections is to hold on to these metals very tightly, using specific metal-binding proteins, so that pathogens are starved of them and cannot grow. For instance, metals like iron and zinc are bound tightly by proteins that are released in mucus and by immune cells, so bacteria can't use them.

This doesn't affect Neigo though! These sneaky bacteria have receptors on their surface that lock onto human metal-binding proteins and steal the metals out of them, which are then brought into the bacterial cell.

Neigo grows on waste materials produced by our cells. Neigo also needs sugars as building blocks and to make energy, but so do human cells. But rather than compete with human cells for the same nutrients, Neigo uses the waste products from human cells to grow and thrive.

Neigo is a super clever MicroRogue!

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The importance of Neigo. The increase in cases around the world, the rise in resistance to antibiotics, and the harmful effects on human health make gonorrhea a high priority for global health. It is therefore important to study Neigo, a true master of disguises, to identify its vulnerabilities. We keep uncovering new ways that Neigo establishes infection when it is constantly challenged by the environment in the human body. Understanding what enables Neigo thrive in humans can help the field develop new treatment options against this scourge of global health.