

A Synopsis of Developing Diagnosis and Treatment for Gonorrhoea: Takeaways

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ABSTRACT

The progressive decline in sensitivity of *Neisseria gonorrhoeae* to the medicines indicated for treatment has prompted worries about the public health hazard of antibiotic-resistant gonorrhoea. This is not a novel mechanism, as the organism has consistently evolved resistance to all current antibiotics used in therapy since the beginning of the antibiotic era. However, the history of modifying gonorrhoea therapy recommendations is complex, with diagnostic test techniques and surveillance influencing the process. Understanding the impact of these variables may shed light on current attempts to address this reemerging public health concern. We looked at the existing techniques for diagnosing gonorrhoea and the public health recommendations for treating it. Qualitative interviews with top investigators whose research have helped create gonorrhoea management techniques over the last 50 years supplemented the literature study. The process of building antimicrobial resistance to antibiotics extensively used for treatment appears to be irreversible. Many of the present worries are similar to previous ones. The public health risk of growing antibiotic resistance by *N. gonorrhoeae* has grown as a result of a reduced pipeline releasing new gonorrhoea treatments. Improved methods for diagnosing gonorrhoea have also significantly impacted the understanding of the disease burden produced by *N. gonorrhoeae*. The leadership of the US Public Health Service has also moulded and enhanced the management of this critical public health issue.

Keywords: gonococcal antimicrobial resistance, gonorrhoea diagnosis, diagnostic testing, and gonorrhoea therapy.

I. INTRODUCTION

Gonorrhoea is spread through sexual contact with an infected person or from a mother to a child during birth. Infected males may experience

pain or burning with urination, discharge from the penis, or testicular pain. Infected females may experience burning with urination, vaginal discharge, vaginal bleeding between periods, or pelvic pain. Complications in females include pelvic inflammatory disease and in males include inflammation of the epididymis. Many of those infected, however, have no symptoms. If untreated, gonorrhoea can spread to joints or heart valves. Gonorrhoea affects about 0.8% of women and 0.6% of men. An estimated 33 to 106 million new cases occur each year. In 2015, it caused about 700 deaths. Diagnosis is by testing the urine, urethra in males, vagina or cervix in females. It can be diagnosed by testing a sample collected from the throat or rectum of individuals who have had oral or anal sex, respectively. Testing all women who are sexually active and less than 25 years of age each year as well as those with new sexual partners is recommended; the same recommendation applies to men who have sex with men (MSM). Gonorrhoea can be prevented with the use of condoms, having sex with only one uninfected person, and not having sex. Treatment is usually with ceftriaxone by injection and azithromycin by mouth. Resistance has developed to many previously used antibiotics and higher doses of ceftriaxone are occasionally required.

Signs and symptoms

Gonorrhoea infections of mucosal membranes can cause swelling, itching, pain, and pus formation. The time from exposure to symptoms is usually between two and 14 days, with most symptoms appearing between four and six days after infection, if they appear at all. Both men and women with infections of the throat may experience a sore throat, though such infection does not produce symptoms in 90% of cases. Other symptoms may include swollen lymph nodes around the neck. Either sex can become infected in the eyes or rectum if these tissues are exposed to

the bacterium, which can lead to pain with bowel movements, rectal discharge, or constipation.

Women

Half of women with gonorrhoea are asymptomatic but the other half experience vaginal discharge, lower abdominal pain, or pain with sexual intercourse associated with inflammation of the uterine cervix. Common medical complications of untreated gonorrhoea in women include pelvic inflammatory disease which can cause scars to the fallopian tubes and result in later ectopic pregnancy among those women who become pregnant.

Men

Most infected men with symptoms have inflammation of the penile urethra associated with a burning sensation during urination and discharge from the penis. In men, discharge with or without burning occurs in half of all cases and is the most common symptom of the infection. A narrowing and stiffening of the urethral lumen causes this pain. The most common medical complication of gonorrhoea in men is inflammation of the epididymis. Gonorrhoea is also associated with an increased risk of prostate cancer.

Infants



An infant with gonorrhoea of the eyes

If not treated, gonococcal ophthalmia neonatorum will develop in 28% of infants born to women with gonorrhoea.

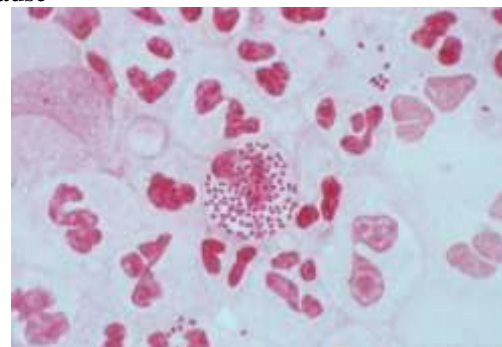
Spread

Sexual intercourse with an infected individual can transmit gonorrhoea, as can a mother's transmission of the disease to her newborn child. Males infected with the infection may have testicular discomfort, penile discharge, or pain or

burning when urinating. Vaginal discharge, vaginal bleeding between periods, pelvic discomfort, and burning when urinating are all possible symptoms for female infected individuals. Male complications include inflammation of the epididymis, whereas female complications include pelvic inflammatory disease. However, many sick people do not show any symptoms. If left untreated, gonorrhoea can spread to the heart valves or joints. Between 0.8% and 0.6% of women and men, respectively, suffer from gonorrhoea. Between 33 and 106 million new instances are thought to arise annually. It led to over 700 fatalities in 2015.

If left untreated, gonorrhoea can spread from the original site of infection and infect and damage the joints, skin, and other organs. Indications of this can include fever, skin rashes, sores, and joint pain and swelling. In advanced cases, gonorrhoea may cause a general feeling of tiredness similar to other infections. It is also possible for an individual to have an allergic reaction to the bacteria, in which case any appearing symptoms will be greatly intensified. Very rarely it may settle in the heart, causing endocarditis, or in the spinal column, causing meningitis. Both are more likely among individuals with suppressed immune systems, however.

Cause



Neisseria gonorrhoeae in pus from a case of gonorrhoea in a man (Gram stain)

Gram-negative, intracellular diplococci were seen in Gram-stained pus from a urethral discharge. *Neisseria gonorrhoeae* is the bacteria that causes gonorrhoea. A person who has once contracted an infection can get it again by coming into contact with an infected individual; prior infection does not offer immunity. Without exhibiting any symptoms or indicators of their own, infected individuals may be able to continually infect others.

Spread

The most common ways for the illness to transmit between people are through anal, oral, or vaginal intercourse. One vaginal contact with an infected woman can increase a man's chance of contracting the illness by 20%. Men who have sex with men (MSM) are at a greater risk. While receptive MSM may get anorectal gonorrhoea, insertional MSM may experience a penile infection following anal intercourse. A single act of vaginal contact with an infected male can expose women to the virus 60–80% of the time.

During childbirth, a woman may pass on gonorrhoea to her newborn; this condition is known as ophthalmia neonatorum when it affects the infant's eyes. It could be able to spread via items tainted with bodily fluids from an affected individual. Usually dying within minutes to hours, the germs do not live long outside the body.

Risk factors

Research has shown that males who have sex with men and sexually active women under 25 are more likely to get gonorrhoea.

Other risk factors include:

- Having a new sex partner.
- Having a sex partner who has other partners.
- Having more than one sex partner.
- Having had gonorrhoea or another sexually transmitted infection.

Complications

Untreated gonorrhoea can lead to major complications, such as:

- **Infertility in women.** Gonorrhoea can cause pelvic inflammatory disease (PID) by spreading into the fallopian tubes and uterus. PID can be lethal, especially in immunocompromised individuals, and can cause scarring of the tubes, infertility, and an increased risk of pregnancy problems. PID must be treated right away.

- **Infertility in men.** Gonorrhoea can result in inflammation of the epididymis, a tiny, coiled tube in the back of the testicles that houses the sperm ducts. Epididymitis can cause infertility if left untreated.
- **Infection that spreads to the joints and other areas of the body.** The bacteria that cause gonorrhoea may infect the joints and other regions of the body by spreading through the circulation. Possible side effects include fever, rash, skin sores, joint discomfort, oedema, and stiffness.
- **Increased risk of HIV/AIDS.** The human immunodeficiency virus (HIV), which causes AIDS, is more likely to infect people who have gonorrhoea. Individuals with HIV and gonorrhoea who are not receiving antiretroviral medication may be more likely to infect their partners with both illnesses.
- **Complications in babies.** Babies that are born with gonorrhoea from their mothers may experience infections, lesions on their scalps, and blindness.

Diagnosis

Gram stain and culture were used to identify gonorrhoea in the past, but more recent diagnostic techniques based on the polymerase chain reaction (PCR) are becoming popular. It is necessary to do a culture to ascertain the bacteria's antibiotic susceptibility in the event that the first therapy is unsuccessful.

For the screening and diagnosis of gonorrhoea infection, tests that detect genes specific to *N. gonorrhoeae* using PCR (also known as nucleic acid amplification) are advised. These PCR-based diagnostics need cervical/vaginal swabs, urethral swabs, or urine samples. It is also possible to detect the presence of *N. gonorrhoeae* in all specimen types, except urine, using culture (growing colonies of bacteria to isolate and identify them) and Gram-stain (staining bacterial cell walls to show morphology). Research on gonorrhoea infections using swab samples has not revealed significant differences in the number of patients treated between home and clinic collection. It is uncertain how this will affect safety, partner management, reinfection rates, and the number of patients treated.

No additional testing is required to confirm the diagnosis of a gonorrhoea infection if a direct Gram stain of urethral pus (a male genital infection) shows the presence of Gram-negative and oxidase-positive diplococci. However, because

the *N. gonorrhoeae* organisms are less abundant in cervical swabs, direct Gram staining is useless. A cervical swab also has a higher risk of producing a false-positive result because it is unable to differentiate *N. gonorrhoeae* from Gram-negative diplococci that are part of the normal vaginal flora. Cervical swabs must thus be cultured in the above-mentioned conditions. The diagnosis is established if oxidase-positive, Gram-negative diplococci are recovered from a cervical/vaginal swab specimen culture. For the identification of infections of the mouth, rectum, eyes, blood, or joints—areas where PCR-based diagnostics are not readily available in all labs—culture is particularly helpful. Additionally, culture is helpful for epidemiological (outbreaks, surveillance), treatment failure analysis, and antibiotic sensitivity testing.

Every potential mucosal location, including the throat, cervix, urethra, and rectum, should be cultured in individuals who may have a disseminated gonococcal infection (DGI). It is also necessary to get three sets of blood cultures. It is necessary to gather synovial fluid when septic arthritis is present.

It is recommended that all individuals who test positive for gonorrhoea also be tested for syphilis, chlamydia, and the human immunodeficiency virus. Research has indicated that between 46 and 54 per cent of young individuals with gonorrhoea also have co-infection with chlamydia. 46% of Americans between the ages of 14 and 39 who have a gonorrheal infection also have a chlamydial infection. Gonorrhoea and chlamydia tests are therefore frequently combined. The risk of HIV transmission is five times higher for those with a gonorrhoea infection diagnosis. Furthermore, during a gonorrhoea episode, infected individuals who are HIV positive have a higher risk of shedding and spreading HIV to uninfected partners.

Screening

For all sexually active women under 25, the United States Preventive Services Task Force (USPSTF) advises screening for gonorrhoea in women who are at higher risk of infection. The prevalence of chlamydia and extragenital gonorrhoea is higher among males who have sex with men (MSM). The USPSTF also advises regular screening for those who have had several sexual partners, have tested positive for gonorrhoea in the past, use condoms inconsistently, perform sexual favours for pay, or have sex while under the influence of drugs or alcohol.

Prenatal care in the United States includes screening for gonorrhoea in women who are (or want to become) pregnant and who are determined to be at high risk for STDs.

Prevention

Safe sex

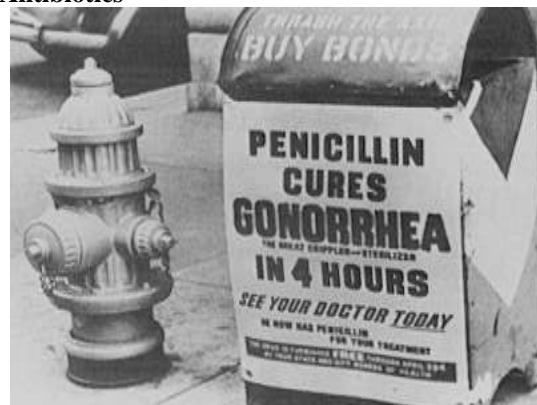
Using condoms correctly, abstaining from sexual activity, or limiting sexual activity to a mutually monogamous relationship with an uninfected individual can all dramatically lower the chance of infection, as is the case with most STDs.

To ensure that the virus has been eradicated, those who have already been affected are urged to return for follow-up care. It has been discovered that email and text messaging, in addition to phone communication, enhance infection retesting.

Erythromycin ointment is applied to the eyes of newborns entering the birth canal to avoid infection-related blindness. A favorable prognosis is typically the result of treating the underlying gonorrhoea.

Treatment

Antibiotics



Penicillin went into industrial manufacture in 1944, revolutionizing the treatment of various venereal infections.

Antibiotics are prescribed to treat gonorrhoea infections. As of 2016, both ceftriaxone injection and azithromycin orally were the most effective. However, due to rising rates of antibiotic resistance, local susceptibility patterns must be considered while determining therapy. Ertapenem might be a viable alternate therapy for ceftriaxone-resistant gonorrhoea.

Adults with gonorrhoea-infected eyes may require good personal hygiene and treatments. In the treatment of eye-infected gonorrhoea, adding

topical antibiotics did not enhance cure rates when compared to oral antibiotics alone. Erythromycin ointment is indicated for neonates to prevent gonococcal infant conjunctivitis.

Infections of the throat can be especially tough because drugs struggle to get concentrated enough to kill the germs. This is exacerbated by the fact that pharyngeal gonorrhoea is typically asymptomatic, and gonococci and commensal *Neisseria* species can coexist in the pharynx for extended periods while sharing antimicrobial resistance genes. As a result, an increased emphasis on early identification (i.e., screening of high-risk individuals, such as men who have sex with men; PCR testing should be investigated) and adequate treatment of pharyngeal gonorrhoea is required.

Sexual partners

It is advised that sexual partners be tested and maybe treated. Patient-delivered partner therapy (PDPT) is one approach for treating infected people's sexual partners, which entails giving the individual prescriptions or drugs to give to his or her partner without first having the health care physician examine him or her.

To prevent the transmission of the bacteria, the US Centers for Disease Control and Prevention (CDC) recommends that people who have been diagnosed and treated for gonorrhoea avoid sexual contact with others for at least one week after the last day of therapy.

Antibiotic resistance

Antibiotic resistance in gonorrhoea

Many previously useful antibiotics, including penicillin, tetracycline, and

fluoroquinolones, are no longer advised due to high resistance rates. Cefixime resistance has reached a point that it is no longer recommended as a first-line antibiotic in the United States, and if it is administered, the patient should be tested again in a week to see if the infection continues. Public health professionals are afraid that a growing pattern of resistance might herald a global pandemic. In 2016, the WHO issued updated treatment guidelines, indicating that "there is an urgent need to update treatment recommendations for gonococcal infections to respond to shifting antimicrobial resistance (AMR) patterns of *N. gonorrhoea*." High levels of resistance to previously recommended quinolones are common, and reduced susceptibility to extended-spectrum (third-generation) cephalosporins, another recommended first-line therapy in the 2003 recommendations, is growing, with some nations reporting treatment failures."

In 2021 and 2022, the SSI received gonococcal isolates from 1,405 and 1,843 distinct instances of gonorrhoea identified by culture in Danish DCMs. This represents 39% and 35% of all gonorrhoea cases registered in MiBa for the two years in question. In contrast, 37% of isolates were submitted in 2020, and 34% in 2019. In Denmark, the first-line treatment is monotherapy with ceftriaxone 500 mg delivered intramuscularly in a single dosage. If susceptibility has been demonstrated, ciprofloxacin 500 mg taken orally may be utilized. The isolates were evaluated for ceftriaxone, azithromycin, and ciprofloxacin resistance by measuring the minimum inhibitory concentration (MIC), mg/l, and penicillinase production, indicating a strong penicillin resistance. The results hereof are presented in Figure(a).

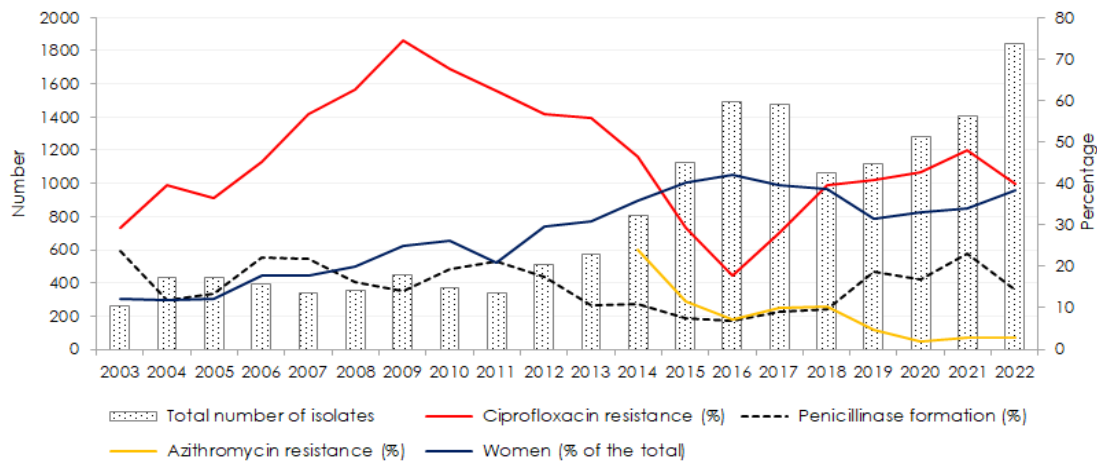


Figure (a): -Number of tested gonococcal isolates from men and women, and percentage occurrence of ciprofloxacin and azithromycin resistance and formation of penicillinase, 2003-2022

Ciprofloxacin resistance was found in 48% and 40% of the isolates in 2021 and 2022, respectively (compared to 43% and 41% in 2020 and 2019). In contrast, azithromycin resistance was found in 3% of isolates in both 2021 and 2022 (2% in 2020 and 5% in 2019).

As of January 1, 2019, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) proposes a new delimitation of resistance (MIC > 1 mg/L) and susceptibility (MIC ≤ 1 mg/L) for azithromycin. This drug should not be used as monotherapy in the treatment of gonorrhoea, but rather in conjunction with another effective antibiotic, primarily ceftriaxone.

Penicillinase formation was found in 23% of cases in 2021 and 14% in 2022 (17% in 2019 and 19% in 2020). In 2021, antimicrobial resistance was more common in male isolates than in female isolates. 56% of male isolates and 32% of female isolates were positive for ciprofloxacin. For azithromycin, the equivalent figures were 4% and 2%. In 2022, 48% of male isolates and 28% of female isolates tested positive for ciprofloxacin. 3% of male isolates and 2% of female isolates were

positive for azithromycin. Approximately 1% of female isolates and 2% of male isolates were resistant to azithromycin and ciprofloxacin.

Ciprofloxacin resistance has been developing since 2016, peaking at 48% in 2021 before falling to 40% in 2022, the lowest level since 2018. Azithromycin resistance decreased from 2018 to 2020, with the exception of a 0.9 percentage point increase in 2021, and the level of resistance maintained at 2.9% in 2021 and 2022. The percentage of isolates with penicillinase formation grew from 2020 to 2021, reaching 23%, the highest level reported since 2003, but then decreased to 14% in 2022, which is a lower level than the values seen in 2020 (17%) and 2019 (19%). Figure (a).

In 2021 and 2022, no ceftriaxone resistance was detected in any isolates. In 2021, the highest recorded MIC value was 0.064 mg/L, and 86% of all isolates had a MIC value <0.008 mg/L, Figure (b).

In 2022, the highest recorded MIC value was 0.032 mg/L, and 94% of all isolates had a MIC value <0.008 mg/L, Figure (b).

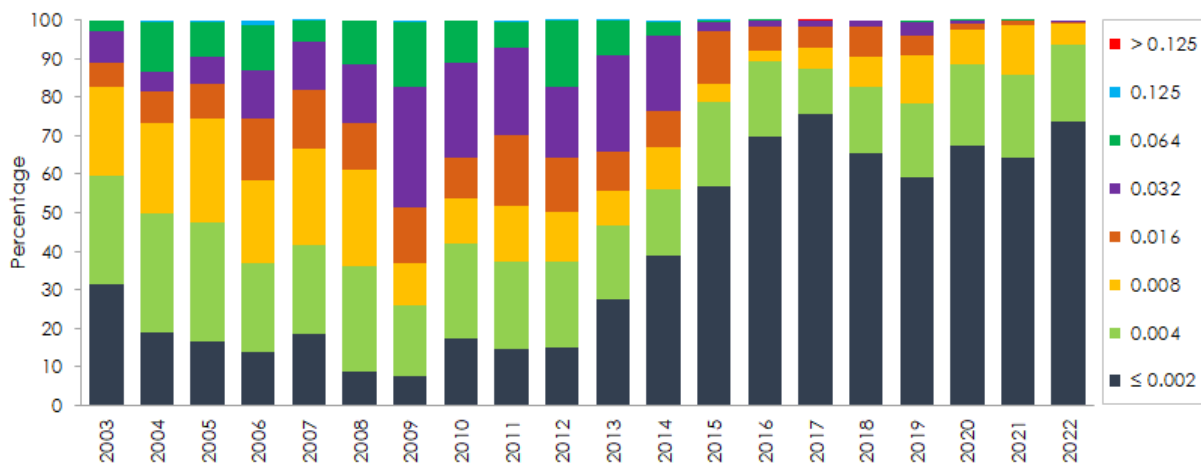


Figure (b): -Distribution of MIC values (mg/L) for ceftriaxone among gonococci, 2003-2022

Special antibiotics

As part of a collaborative EU effort, the Reference Laboratory examines somewhat more than 100 consecutively obtained isolates against a larger panel of antibiotics each year. In 2021 and 2022, none of the 121 and 135 isolates were resistant to cefixime (an oral cephalosporin that is not available in Denmark).

In 2021, 1,089 of 1,405 distinct isolates were associated with an NSID notice (notification received less than 30 days after the isolate sample date). The equivalent figures for 2022 were 1,456 out of 1,843 unique isolates. With this data, it is feasible to determine whether there is a link between antibiotic resistance, sexual orientation, and the patient's country of transmission.

	MSW		MSM		Women	
	Number	Percentage	Number	Percentage	Number	Percentage
Ciprofloxacin	154	41	218	70	111	29
Azithromycin	3	1	11	4	2	1
Ciprofloxacin + Azithromycin	3	1	8	3	3	1
Susceptible*	214	57	74	24	267	70

*Susceptible to ciprofloxacin and azithromycin

Table: - Antibiotic resistance and sexual orientation, 2021

	MSW		MSM		Women	
	Number	Percentage	Number	Percentage	Number	Percentage
Ciprofloxacin	199	36	209	75	168	28
Azithromycin	8	1	17	6	13	2
Ciprofloxacin + Azithromycin	3	1	12	4	4	1
Susceptible ^a	353	63	61	22	516	70

*Susceptible to ciprofloxacin and azithromycin

Table: - Antibiotic resistance and sexual orientation, 2022

In 2021, MSM isolates had the highest prevalence of ciprofloxacin and azithromycin resistance, whereas female isolates had the lowest frequency. MSM isolates had the lowest percentage of isolates sensitive to both azithromycin and ciprofloxacin, whereas female isolates had the greatest percentage. Ciprofloxacin levels in 2022 remained consistent with those in 2021. All three groups demonstrated a small increase in azithromycin resistance. Isolates from MSM had the greatest resistance rate of 6%, while isolates from MSW had the lowest at 2%. The proportion of isolates resistant to both azithromycin and ciprofloxacin was highest in the

MSM group (4%), and lowest in MSW and women (1%). The proportion of sensitive isolates was lowest among MSM (22%), and greatest among women (68%).

In Denmark, 1,003 isolates (92% of isolates related to an NSID notice) and 1,355 (93% of cases) contracted gonorrhoea in 2021 and 2022, respectively. A total of 59 (5%) and 83 (6%) of these cases were acquired overseas, and for 27 (2%) and 18 (1%) cases with a matching isolate, respectively, the place of transmission remained unknown. Tables A and B show the spread of antibiotic resistance.

	Denmark		Abroad		Not stated	
	Number	Percentage	Number	Percentage	Number	Percentage
Ciprofloxacin	445	44	30	51	17	63
Azithromycin	14	1	3	5	0	0
Ciprofloxacin + Azithromycin	11	1	3	5	0	0
Susceptible*	533	53	23	39	10	37

*Susceptible to ciprofloxacin and azithromycin

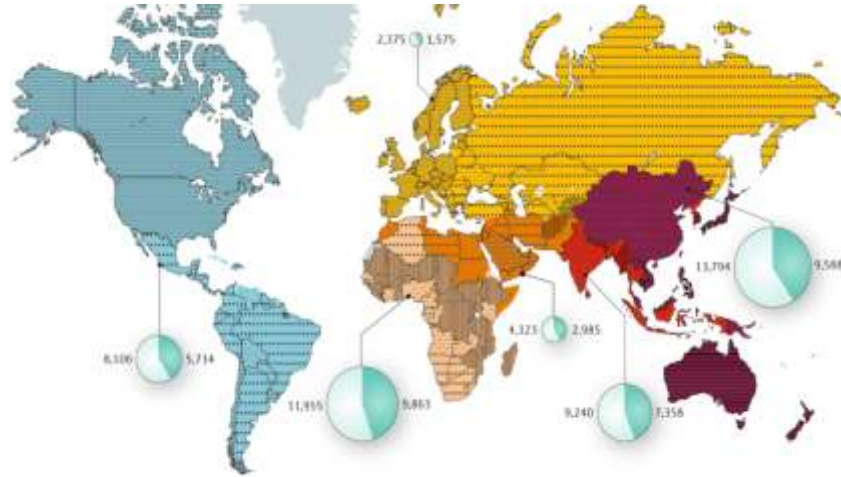
Table (a). Antibiotic resistance and country of infection, 2021

	Denmark		Abroad		Not stated	
	Number	Percentage	Number	Percentage	Number	Percentage
Ciprofloxacin	528	39	56	67	6	33
Azithromycin	33	2	5	6	0	0
Ciprofloxacin + Azithromycin	16	1	3	4	0	0
Susceptible ^a	810	60	25	30	12	67

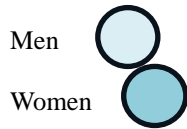
*Susceptible to ciprofloxacin and azithromycin

Table (b). Antibiotic resistance and country of infection, 2021

Prognosis



Cases of gonorrhoea



Gonorrhoea, if left untreated, can linger for weeks or months, with an increased risk of consequences. One of the consequences of gonorrhoea is systemic dissemination, which causes cutaneous pustules or petechiae, septic arthritis, meningitis, or endocarditis. This happens in 0.6–3% of infected women and 0.4–0.7% of infected males.

Untreated gonorrhoea can cause inflammation in men's epididymis, prostate gland, and urethra. Untreated gonorrhoea in women is

most commonly associated with pelvic inflammatory illness. Other complications include inflammation of the liver's surrounding tissue, a rare complication of Fitz-Hugh-Curtis syndrome; septic arthritis in the fingers, wrists, toes, and ankles; septic abortion; chorioamnionitis during pregnancy; neonatal or adult blindness due to conjunctivitis; and infertility. Men who have had gonorrhoea have a higher chance of developing prostate cancer.

Epidemiology

Epidemiology of gonorrhoea

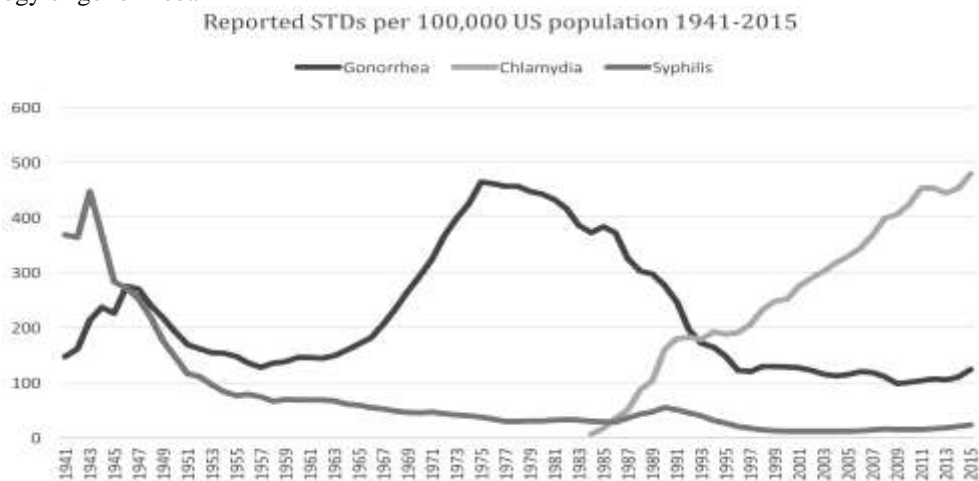


Table: - Gonorrhoea rates, United States, 1941–2015

Every year, around 88 million instances of gonorrhoea are reported, accounting for 448 million new cases of treatable STIs such as syphilis, chlamydia, and trichomoniasis. The incidence was highest in Africa, the Americas, and the Western Pacific, but lowest in Europe. In 2013, it killed around 3,200 people, up from 2,300 in 1990.

In 2005, there were 196 per 100,000 men aged 20 to 24 and 133 per 100,000 females aged 16 to 19. In 2013, the CDC reported that over 820,000 persons in the United States contracted gonorrhoea each year. The CDC receives reports for less than half of these illnesses. In 2011, the CDC received reports of 321,849 gonorrhoea cases. Between 1975 and 1997, the national gonorrhoea rate decreased with the adoption of a nationwide gonorrhoea control program in the mid-1970s. After a minor rise in 1998, the gonorrhoea prevalence has dropped marginally since 1999. In 2004, the reported gonorrhoea infection rate was 113.5 per 100,000 people.

In the United States, it is the second most prevalent bacterial sexually transmitted infection,

trailing only Chlamydia. According to the Centers for Disease Control and Prevention, African Americans are the most impacted by gonorrhoea, accounting for 69% of all cases in 2010.

The World Health Organization issued a warning in 2017 about the development of untreatable gonorrhoea strains after analyzing at least three instances in Japan, France, and Spain that resisted all antibiotic treatments.

In 2016, the WHO projected that there were 86.9 (95% uncertainty interval 58.6-123.4) million incident worldwide cases of gonorrhoea (global prevalence 0.9%) among individuals aged 15 to 49 (22). The epidemiological diversity of gonorrhoea manifests itself in the variability of the geographical distribution and prevalence among certain populations; determinants of such variability include sexuality and sexual orientation, socioeconomics, demographics, geographical and cultural ramifications (including stigma and taboos), and access to and quality of sex education, prevention, testing, and diagnostics, as well as political commitment in the provision of health.

History



During World War II, the U.S. government used posters to warn military personnel about the dangers of gonorrhoea and other sexually transmitted infections.

According to some academics, the biblical names zav (for a man) and zavah (for a female) refer to gonorrhoea.

Mercury has been suggested ^[by whom?] as a therapy for gonorrhoea. ^[when?] On board the rediscovered English vessel the Mary Rose, surgeons used a syringe to inject mercury into crewmen with gonorrhoea via the urinary meatus, according to some. The word "the clap" in connection to the disease dates back to the

sixteenth century when it referred to Les Clapiers, a medieval red-light district in Paris. Translating to "the rabbit holes," it was named after the little houses where prostitutes operated.

Silver nitrate was one of the most often utilized medications in the nineteenth century. However, Protargol eventually took its position. Arthur Eichengrün devised this form of colloidal silver, which Bayer began to commercialize in 1897. The silver-based therapy was utilized until the introduction of antibiotics in the 1940s.

The historical record does not provide a definite timing of the start of gonorrhoea as a prominent illness or epidemic. One of the oldest credible notations appears in the Acts of the English Parliament, which approved a statute in 1161 to prevent the spread of "the dreadful weakness of burning. The symptoms reported are similar to, but not indicative of, gonorrhoea. Louis IX of France issued a similar proclamation in 1256, substituting regulation with expulsion. Crusaders saw similar symptoms during their siege of Acre.

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Medieval public health physicians employed by their communities were responsible for treating prostitutes infected with the "burning," as well as lepers and other epidemic patients. Following Pope Boniface's total secularization of medicine, physicians were more ready to treat sexually transmitted infections.

Research

A vaccine for gonorrhoea has been developed that is effective in mice.^[86] It will not be available for human use until further studies have demonstrated that it is both safe and effective in the human population. The development of a vaccine has been complicated by the ongoing evolution of resistant strains and antigenic variation (the ability of *N. gonorrhoeae* to disguise itself with different surface markers to evade the immune system).

As *N. gonorrhoeae* is closely related to *N. meningitidis* and they have 80–90% homology in their genetic sequences some cross-protection by meningococcal vaccines is plausible. A study

published in 2017 showed that MeNZB group B meningococcal vaccine provided a partial protection against gonorrhoea. The vaccine efficiency was calculated to be 31%. In June 2023, GlaxoSmithKline won fast-track designation from the Food and Drug Administration for its vaccine candidate against gonorrhoea.

II. CONCLUSION

The bacterial and protozoal sexually transmitted diseases are widespread but treatable with widely available antimicrobials. However, threats of antimicrobial resistance are becoming more realized with the new emergence of gonococcal resistance isolates, which will significantly change the landscape of sexually transmitted diseases worldwide. One important tool in the battle against the increase in infections is the rapid diagnosis that molecular testing has allowed. Further advances in molecular diagnostics could lead to rapid typing of infectious strains and their resistance patterns.

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