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Review Article

A dive into gonorrhoea's past

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ABSTRACT

Gonorrhoea has a long-standing presence in human history, being recognized as one of the earliest sexually transmitted infections (STIs). While its exact origins are debated, there are references to a disease resembling gonorrhoea in ancient texts. The Chinese emperor Huang Ti mentioned a condition similar to gonorrhoea in his medical writings around 2600 BC. Additionally, some interpret passages in the book of Leviticus in the Old Testament as descriptions and precautions for gonorrhoea. Gonorrhoea, one of the oldest known STIs, has undergone significant changes in diagnosis and management over the centuries. Despite periods of decline, there has been a resurgence of the infection in recent decades. The emergence of drug-resistant strains and risky sexual behaviour may have contributed to this resurgence. To combat the spread of gonorrhoea, it's crucial to promote safe sex practices and provide comprehensive sex education, especially among teenagers. Timely adjustments to treatment regimens to address drug-resistant strains are also essential. By taking these steps, we can work towards reducing the prevalence and impact of gonorrhoea globally.

Keywords: Gonorrhoea, Nucleic acid amplification test, The clap

INTRODUCTION

Gonorrhoea has a long-standing presence in human history, being recognized as one of the earliest STIs. While its exact origins are debated, there are references to a disease resembling gonorrhoea in ancient texts. The Chinese emperor Huang Ti mentioned a condition similar to gonorrhoea in his medical writings around 2600 BC. Additionally, some interpret passages in the Book of Leviticus in the Old Testament as descriptions and precautions for gonorrhoea.[1,2]

Historically, terms like "strangury" were used to describe gonorrhoea by figures such as Hippocrates, attributing it to the "pleasures of venus." Celsus, a Roman encyclopaedist, was familiar with the disease and its complications, even performing catheterizations on patients with urethral strictures.[3,4] The term "gonorrhoea" was coined by the Greek physician Galen, describing it as an "unwanted discharge of semen."

The term "the clap" has also been associated with gonorrhoea, with theories suggesting it comes from the sensation experienced during urination or from an ancient practice of "clapping" an infected penis with a book to remove pus. Some link it to French brothels known as "Les Clapiers," translating to "rabbit huts," where the disease was prevalent.[5] During these times, men were often viewed as victims while women were erroneously blamed for harbouring diseases due to misconceptions about female reproductive biology.

Historically, STIs like gonorrhoea have been linked to wartime, with Roman soldiers during Julius Caesar's campaigns believed to have suffered from it.[6,7] STIs, including gonorrhoea, also caused significant mortality during the Crimean War in the mid-19th century. In an attempt to curb its spread, laws were enacted, with English parliament passing a law around 1161 AD to address what was referred to as "the perilous infirmity of

burning." Similarly, the French king Louis IX implemented a law in 1256 AD.[8]

Confusion between gonorrhoea and syphilis emerged with the introduction of syphilis in Europe in the late 15th century. Notable surgeons like Ambroise Paré and John Hunter initially considered both gonorrhoea and syphilis as manifestations of the same disease, adding to the historical complexities of understanding these STIs.[9,10]

In 1879, Albert Ludwig Sigesmund Neisser (Figure 1) identified the causative organism of gonorrhoea, which was later named Neisseria gonorrhoeae. His ground-breaking discovery was published in 1882.[11] Following this, Leistikow in 1882 and Bumm in 1885 successfully cultured the organism. Bumm even managed to induce the characteristic symptoms of gonorrhoea by inoculating the organism into the male urethra. Another significant development was the gonococcal complement fixation test introduced by Muller and Oppenheim in 1906.[12]

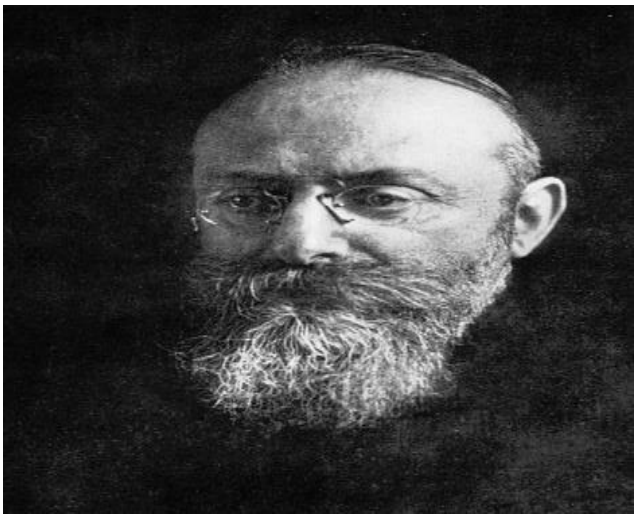

Figure 1: Albert Ludwig Sigesmund Neisser.

In terms of public health measures, ophthalmia neonatorum became a notifiable disease in England and Wales in 1914.[13,14] Crede's method, a procedure to prevent this condition, is still practiced in some regions with success. Stuart's medium, designed for transporting gonococci, was developed in 1946 by Stuart and colleagues. Later, in the late 1960s, Chacko and Nair formulated the Chacko Nair medium specifically for culturing gonococci.

Today, nucleic acid amplification tests (NAATs) have become the gold standard for diagnosing gonorrhoea.[15]

TREATMENT HISTORY

The history of treating gonorrhoea spans several centuries, with early treatments being quite invasive and sometimes harmful. In the 16th century, mercury injections into the urethra were used as a treatment. By the 18th century, the severity of symptoms and the amount of pus from the urethra guided treatment choices. Mild cases were treated with bland fluids, while more extreme measures like bloodletting and urethral lavage were used for severe cases.[16,17]

Urethral lavage involved inserting a catheter into the urethra and flushing it with hot water (46-50°C).[18,19] The amount of water used was as much as the patient could tolerate, and the discomfort experienced during the procedure was believed to correlate with treatment success. This procedure was repeated over 2-3 days.

By the 19th century, alternative treatments emerged. Indonesian pepper known as cubebs and balsam from a South American tree called copaiba were used, albeit with varying success rates.[20,18]

Heat therapy was introduced as a treatment for gonorrhoea in 1913.[21] Initially used for gonococcal arthritis, it later expanded to include genital infections. In 1932, researchers at the university of Rochester discovered that exposing gonococcal cultures to temperatures of 41.5-42°C for 2 hours could kill 99% of the bacteria in vitro. This led to the use of a fever cabinet, which enclosed the patient's body, leaving only the head outside. The patient's body temperature was maintained at 41°C for 4-6 hours, with 5-6 sessions spaced 3 days apart.[22,23] Mayo clinic experimented with intravenous mercurochrome in hypertonic glucose, followed by hyperthermia. Some researchers even proposed pelvic heating by inserting heating elements into the vagina and rectum, maintaining a temperature of around 44°C for 2 hours. However, with advent of sulphonamides, heat therapy fell out of favour.

Silver nitrate, a popular 19th-century treatment, was replaced by protargol (silver proteinate), invented by Arthur Eichengrun and marketed by Bayer from 1897. This silver-based treatment persisted until the arrival of the first antibiotics in the 1940s.[24]

The first vaccine against gonorrhoea was derived from killed gonococci from Neisser's laboratory in 1890 and was introduced in 1909. However, its efficacy was low, and it didn't gain widespread use.[25,26]

In 1937, Dees and Colston introduced sulphonamides for treating gonorrhoea. According to the John Hopkins university clinic protocol, patients were initially given 4.8 grams of sulphonamides, which was tapered to 1.2 grams/day over 4 weeks. The treatment was found to be most effective when started during the second week of symptoms rather than the first, a phenomenon explained by the "Ehrlich hypothesis." This hypothesis posits that bacteriostatic agents like sulphanilamide require immune mechanisms for effective action. While symptoms typically cleared within a week, about 80% of patients achieved a cure after 3 weeks of treatment.

Sulphapyridine and sulfathiazole became available in the 1940-1941 as further additions to the treatment arsenal.[27]

Since the 1940s, penicillin has been the primary treatment for gonorrhoea. However, by 1946, the first cases of penicillin-resistant gonorrhoea had already been reported. In 1963, ampicillin was introduced by Willcox and showed a cure rate of 98%. Yet, resistance due to beta-lactamase and chromosomal mutations was identified in 1976 and 1980, respectively. Mutations in penicillin-binding proteins and alterations in efflux-influx systems are also attributed to penicillin resistance.[28,29]

Csonka and Knight introduced cotrimoxazole for gonorrhoea treatment in 1967. However, cross-resistance between penicillin and cotrimoxazole was reported in 1972, making it less effective in areas with high penicillin-resistant strains.[30]

Spectinomycin, introduced in 1967, replaced tetracycline as an alternative to penicillin. While effective for uncomplicated anorectal and urogenital gonorrhea, its efficacy against pharyngeal infections is limited.[31] It remains effective but is considered inferior to cephalosporins.[32]

Erythromycin was introduced in 1977, primarily for pregnant women with penicillin allergies. However, due to the development of resistant strains, its use is now mostly limited to treating ophthalmia neonatorum.[33]

Ceftriaxone became the recommended first-line treatment in 1989. Other cephalosporins, including cefixime, cefazolin, cefuroxime, and cephalexin, have also shown excellent cure rates. Despite this, cephalosporin-resistant strains have emerged in recent decades.

Aminoglycosides like kanamycin and gentamicin have proven highly effective against gonococci. They don't mask syphilis, allowing for the detection of coexisting Treponema pallidum infections.[34]

During the 1980s and 90s, norfloxacin and ciprofloxacin were used, but due to increasing resistance, the world health organization (WHO) and centres for disease control and prevention (CDC) no longer recommend fluoroquinolones for gonorrhoea treatment.[35]

The WHO introduced the syndromic approach to STI management in 1991, which was later adopted by the national AIDS control organisation in 1992.[36] Initially, the recommended drugs for treating gonorrhoea included a single dose of 400 mg cefixime, 500 mg ciprofloxacin, 125 mg ceftriaxone (intramuscular), or 500 mg erythromycin every 6 hours for 7 days. Additionally, a single dose of 1 g azithromycin was advised. Current recommendations have evolved to suggest a single dose of 1 g azithromycin paired with either 400 mg cefixime or 250 mg ceftriaxone.[37,38]

CONCLUSION

Gonorrhoea, one of the oldest known STIs, has undergone significant changes in diagnosis and management over the centuries. Despite periods of decline, there has been a resurgence of the infection in recent decades. The emergence of drug-resistant strains and risky sexual behaviour may have contributed to this resurgence.

To combat the spread of gonorrhoea, it's crucial to promote safe sex practices and provide comprehensive sex education, especially among teenagers. Timely adjustments to treatment regimens to address drug-resistant strains are also essential. By taking these steps, we can work towards reducing the prevalence and impact of gonorrhoea globally.

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