

Verity Bevan investigates the second most common sexually transmitted bacterial infection

# Gonorrhoea: An unlikely love affair

**S**INCE THE discovery of gonorrhoea in 1879 by Albert Neisser, this disease has become the second most common sexually transmitted bacterial infection.

Neisser learned and adopted the techniques of his peers to visualise bacteria using the newest microscopic methods. By staining smears with methylene blue and using oil-immersion techniques, he could observe bacteria using x1000 magnification. Originally, the organisms he saw were given the name micrococcus; however it was a colleague, Paul Ehrlich, who first coined the name gonococcus. Since then, the *Neisseria* group of organisms, so named after Neisser himself, has been added to and comprehensively characterised. The group also contains *Neisseria meningitidis*, well known for causing meningitis. Other members are largely commensals of the oropharynx and gastrointestinal tract. All the Neisseriaceae are Gram negative diplococci, producing oxidase positive colonies. The pathogenic *Neisseria* are distinguishable by detection of pre-formed enzymes, for which commercial tests are available. Both organisms are able to ferment glucose, but *N. meningitidis* is also able to ferment maltose. Gonorrhoea is responsible for infecting millions of people worldwide each year.

Trends in the prevalence of gonococcal infection are apparent. Rises in infection have been noted following wartime, as soldiers returning home passed infections onto their wives as a result of promiscuity whilst away from home. During the 1950s, the advent of penicillin saw a

decrease in infections; however, the rapid emergence of resistant strains in the 1960s and 1970s, saw the infection rate increase once again. The 1980s brought the new danger of HIV. A powerful campaign promoting the use of condoms and practicing 'safe sex' also drove down the rate of gonococcal infection, as well as other sexually transmitted diseases, (STIs). Nowadays, complacency is seeing infections on the rise once more. Treatments for HIV have been developed so intensively, patients are living longer and healthier lives. The classical 'it will never happen to me' attitude is proving a dangerous one, especially among the 18 to 25 year old age group where the increase is most noticeable. Other contributing factors are a decrease in the age at which individuals become sexually active, the number of sexual partners that they have and the advent of going abroad with the intention of having sexual relationships.

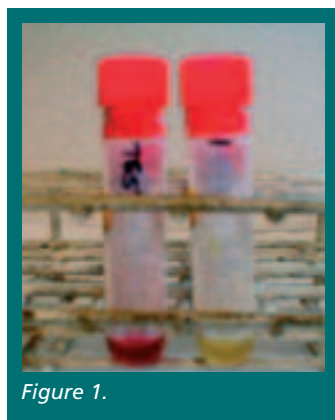


Figure 1.

The infection is only transmissible via direct contact with an infected sexual partner. It can affect males and females equally. Pathogenicity is influenced by the presence of pili, hair-like structures that help the organism attach to the

columnar epithelia of the urethra wall in males and the cervix of females. The vaginal wall is not able to be colonised as this is made up of squamous epithelia. An acute inflammatory response follows with the engulfment of the bacteria in to polymorphonuclear cells. It is thought that gonococcus is able to survive this hostile environment due to various mechanisms that protect it from the lysozymes and reactive oxygen species that are produced during inflammation. Migration of the organism in to the subepithelial space induces a purulent discharge, leading to the clinical signs of gonorrhoea infection. Despite an initial IgA response, the bacteria are able to switch the pili genes on and off, (phase variation), as well as rearranging the genes coding for pili and other surface markers. In this way it is capable of evading the immune system and eliciting the symptoms associated with gonorrhoea.

Symptoms are often very apparent. Approximately 90% of males experience a purulent discharge from the urethra. Females are more likely to be asymptomatic, with up to 50% presenting with no abnormal physiology. Other symptoms can include lower abdominal pain and dysuria. Pharyngeal infections are largely asymptomatic. Rectal infection may be accompanied by tenderness and a discharge, though this is relatively uncommon. It is advised that anyone suspecting that they are infected, should seek medical attention. The general practitioner is able to refer those most at risk to the Genito-urinary medicine, (GUM) clinic, where a comprehensive physical

examination may take place. A full sexual history will be taken to determine the level of risk for the individual. This will also indicate the primary sites that might be investigated. For example, homosexual males may require a rectal sample to be taken.

Samples are taken from the urethra in males as routine. Additional samples from the rectum and pharynx are taken in accordance with sexual history. Female samples are taken from the cervix, urethra and vagina. As with males, the rectum and pharynx may also be sampled. Typically all these specimens are screened for various other STIs to avoid repeating the procedure, which can be an uncomfortable experience.

Diagnosis of gonorrhoeal infection is subject to the isolation of the bacterium. Bacterial culture is both sensitive and cheap to perform. It has the added advantage that further tests can be carried out to determine antimicrobial susceptibility. In the GUM setting, the direct culture of genital specimens is the most effective method of isolation. Selective agars are now widely available for the culture of gonorrhoea. These often contain an antimicrobial cocktail to suppress the growth of normal genital flora, and prevent overgrowth with *Candida*. Common formulations such as Vancomycin, Colistin, Nistatin and Trimethoprim, (VCNT) or Lincomycin, Colistin, Amphotericin and Trimethoprim, (LCAT), are available from leading manufacturers. Confirmatory laboratory tests are performed on positive cultures. These include an oxidase test, a Beta-lactamase production test

and a Gonocheck, (EY Laboratories Inc.), to detect prolyliminopeptidase, a preformed enzyme produced almost exclusively to gonorrhoea (figure 1).

False positives can occur with organisms that are not Gram negative diplococci, therefore it is also important to check that the organism isolated has those characteristics. Together these elements constitute a positive identification of gonorrhoea. The culture may then have sensitivity testing performed using standard methods and according to laboratory protocol. Although the patient will already have been treated for the infection at the time of diagnosis, susceptibility testing remains necessary and has two main functions.

Firstly, it confirms that the infection was susceptible to the treatment given and that the infection would have been removed, secondly, to monitor the epidemiology of the organism, and any resistance trends that may appear.

Molecular methods are also available to detect gonorrhoea, although these have not yet been validated for genital specimens, however, urine samples can be used. Immediate diagnosis using Gram stained smears is also common practice in GUM clinics. This allows the patient to be counselled and treated on the day of assessment. Microscopic diagnosis is reliable for 90-95% of symptomatic males, versus 60-75% of asymptomatic patients. In females, the reliability is much lower, approximately 40%. This low figure is largely due to the presence of normal genital flora obscuring the presence of gonorrhoea in the smear. Male slides characteristically contain numerous pus cells, with obvious intracellular bacteria present. Gonococcus has a distinctive morphology to the trained eye, appearing as a

Gram negative 'bean-shaped' diplococcus. The use of neutral red over the more commonly used carbol fuchsin as a counter stain also enhances the appearance of the organisms (figure 2). Gram staining rectal and pharyngeal samples is not recommended as these sites contain commensal *Neisseria* that can be mistaken for gonorrhoea.

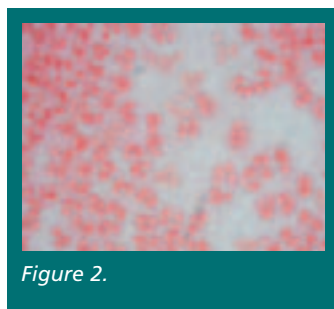


Figure 2.

All patients diagnosed with gonorrhoea are seen by a health adviser, who will explain the nature of the infection and the consequences it has on themselves and their partner. It is also stressed that compliance with the therapeutic regimen prescribed to them is crucial to a successful cure. The patient must also provide the names of previous sexual partners for follow up purposes. In symptomatic patients, all partners during the preceding fortnight are informed; however, if asymptomatic, all partners during the previous three months should be notified. The patient is also advised to abstain from further sexual encounters until after a follow up assessment.

Gonorrhoea infection is not always without complications. In males, transluminal spread of the organism can lead to infection of the epididymus and prostate. In females, pelvic inflammatory disease, endometriosis or salpingitis can lead to fertility problems. Disseminated infections such as arthritis, arthralgia,

tenosynovitis and skin lesions can also result from prolonged untreated gonorrhoea infection. These are extremely uncommon, occurring in less than 1% of cases. Gonorrhoea is also able to infect neonates on delivery. This is an infection of the eyes known as Ophthalmia neonatorum and is often apparent within the first two days of birth. Eye swabs can be taken to confirm diagnosis.

Treatment regimens are prescribed in accordance with national guidelines and will vary according to an individual's circumstance, for example, pregnant women, breast-feeding mothers and Beta-lactam sensitive patients must be suitably prescribed. Uncomplicated cases are treated using Ceftriaxone or Spectinomycin in the case of pregnant women. Previous regimens have used Penicillin as an effective treatment; however the emergence of resistant strains has led to this being withdrawn as a suitable treatment.

In recent years, resistance to Tetracycline and Ciprofloxacin has also been noted. If sensitivities are known it is possible to treat using Ciprofloxacin, Ofloxacin or Ampicillin. Ciprofloxacin and other Quinolones, as well as Tetracycline, should not be prescribed to pregnant women. Likewise, Ampicillin is unsuitable for patients known to be allergic to Beta-lactam antibiotics. Single dose therapies are highly recommended to increase patient compliance, and reduce the likelihood of re-infection.

Follow up appointments are arranged at the time of diagnosis, usually 2-3 weeks after original appointment. The purpose of this is to establish whether the infection has cleared, and to ensure the patient has not suffered any additional symptoms or side-effects following treatment. If

symptoms are apparent, retesting will be required. Asymptomatic patients largely do not require retesting as the efficacy of treatments usually deems this unnecessary. A second positive culture is usually attributed to reinfection or lack of patient compliance rather than drug failure.

On a national scale, the Gonococcal Resistance to Antimicrobials Surveillance Programme, (GRASP) also monitors the emergence of resistance. This study takes place during July and August each year. Isolates from a number of clinics and hospitals across England and Wales are sent to one of two reference laboratories. These laboratories perform susceptibility testing using agar dilution techniques. The data is then compiled and used to amend guidelines for the management of gonorrhoea as appropriate. Approximately half of all confirmed cases of gonorrhoea are diagnosed in the London area. Around a quarter are women, a quarter are homosexual males and half heterosexual males. Less than 10% of these can be attributed to unprotected sex whilst abroad; however, this proportion is increasing. An overall increase in infection of 7% was recorded between 2000 and 2001.

Gonorrhoea is likely to remain a prominent feature of future sexual health forums. The emergence of resistant strains is worrying, and should continue to be monitored. The need for new treatment regimens may be required in the near future. Until then the role of GUM clinics in the re-education of sexual behaviour is crucial for the control of these infections.

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