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Gonorrhoea – current threat? Epidemiological analysis of gonococcal infections

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Abstract:

Sexually Transmitted Diseases (STD's) are diseases transmitted via sexual contacts by reproductive system as well as urinary system. Many patients have encountered easily treatable STDs which pose no relative threat to the patient's health, however increasing numbers of people struggle against infections resistant to treatment, which may lead to death. Both immunocompetent patients and those with a compromised immune system may develop bacterial infections. STDs include diseases such as bacterial vaginosis, cytomegalia, candidiasis, trichomoniasis, syphilis, chlamydia and gonorrhoea. The aim of the following article is to present the most important information on *Neisseria gonorrhoeae* and data regarding gonorrhoea morbidity over the 2008-2018 period. The article discusses the

epidemiology, symptomatology, diagnostic procedures and treatment of gonorrhoea infections in closer detail. Data used in the article comes from research studies, most recent recommendations, guidelines and bulletins from the National Public Health Institute (PZH).

Key words: gonorrhoea, venereal diseases, epidemiology, *Neisseria gonorrhoeae*, prevention, Crede's procedure

Introduction:

In recent times behaviours such as migration, early sexual initiation and frequent changes of sexual partners are becoming increasingly common. The prophylaxis of bacterial infection amongst sexually active women and their partners may prevent the spread of STDs in both genders and counteract the unfavourable course of a possible pregnancy. Bacterial infections during pregnancy pose a significant threat to the health of a mother and her baby. Majority of bacterial infections are asymptomatic which leads to their late detection. (1) Annually, the World Health Organisation (WHO) analyses data gathered on 4 particular STDs, which include: chlamydia, trichomoniasis, syphilis and gonorrhoea. The estimates regarding morbidity and prevalence of gonorrhoea differ depending on regions and sex, remaining high. STDs may influence national economy and the financial fluidity of individuals. The following analysis looks at both global and regional data, discusses prophylactic measures to be taken, programme of intervention and identifies the resources needed for limiting the spread of gonorrhoea. There exists an urgent need for the public health community to increase the availability of screening, diagnostic procedures, prophylactic measures and treatment for STDs. (2) Sexually transmitted infections (STIs) are one of the most common diseases influencing the quality of life worldwide. STIs cause patients to feel stigmatised, lower self-esteem, cause the formation of stereotypes and can be linked to sexual violence. (3) STIs have a direct impact on the reproductive health of children, they may cause pregnancy complications, carcinogenesis and facilitate the transmission of Human Immunodeficiency Virus (HIV).

Gonorrhoea is caused by a Gram-negative, diplococci, obligate aerobe, capsule-less bacteria *Neisseria gonorrhoeae*. *N. gonorrhoeae* is usually isolated on Thayer-Martin agar and requires a CO₂ environment enriched to grow which distinguishes it from other species of *Neisseria*. Most species of *Neisseria* grow in humid areas in a range of temperatures 35-37°C. Gonococci are pathogenic exclusively for humans, they have an affinity for columnar epithelium, rarely for transitional epithelium of the urinary and reproductive systems. The infection is usually localised in the mucous membrane of the urethra, cervical canal, anus, pharynx and conjunctiva. (4,5) Infections by gonococci are usually asymptomatic in women. The lack of noticeable symptoms causes the development of an undetected and untreated infection which may in turn lead to serious complications. (6) Globally, gonorrhoea is a significant threat to human health. In recent years, the increasing resistance of gonorrhoea to wide spectrum cephalosporin's has become particularly worrying.

Epidemiology:

Globally, over a million new cases of curable, STD infections are reported every day. According to the WHO in 2012, 78 million cases of gonorrhoea have been reported. Developing countries have the highest rates of STIs in the world. In 2010, treatable STDs have accounted for over 11 million years of life spent in impaired health by infected patients. (7) Factors such as: urbanisation, traveling, globalisation, decrease in the efficiency of treatment, low detectability have an influence on high morbidity due to STDs. (8) The most common STD is chlamydia, caused by the bacteria *Chlamydia trachomatis*. The next most common STD is gonorrhoea (1,9) Estimates show that due to frequent asymptomatic

infections, the number of cases of gonorrhoea might be four times greater. 80% of symptoms may be overlooked. Gonorrhoea may relapse. Data from the Centres for Disease Control (CDC) show that over 25% women in Florida, after being successfully treated for gonorrhoea, have been reinfected. Mentioned data justifies screening previously infected women and their sexual partners. (10)

Europe:

Over the 2008-2017 period, 558 155 new cases of gonorrhoea have been confirmed in 29 European countries. In Europe, a general rise of incidence to gonorrhoea can be identified over the years. (fig. 1) In 22 European countries with comprehensive surveillance systems for STDs, the incidence indicators for gonorrhoea have risen from 8,2 infected/100 000 citizens to 23 infected/100 000 citizens over the 2008-2017 period. The incidence has doubled for both sexes. Since 2008, the greatest rises of incidence indicators for gonorrhoea have been recorded in Portugal and France. The rising numbers of infected individuals increase the possibility of developing gonococci resistant to currently available treatment.

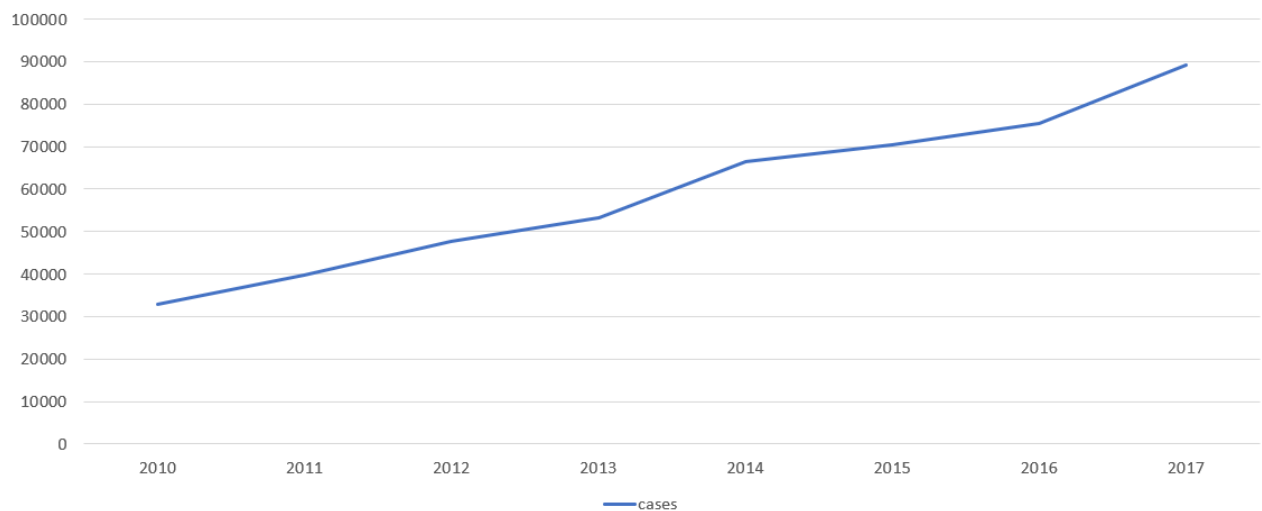


Figure 1. Rate of confirmed gonorrhoea cases by year, EU/EEA countries reporting consistently, 2008–2017

According to data gathered by ECDC, 89 239 new confirmed cases of gonorrhoea have been reported in 2017 in 27 European countries, which accounts for a 17% increase since 2016. The general incidence index was 22,2 cases/100 000 citizens. The number of reported cases of gonorrhoea in Europe differs across countries, where the more new cases have been reported in northern Europe. The overall ratio of cases reported in men to cases reported in women was 3,2:1. Men engaging in sexual acts with other men accounted for 47% of cases in 2017. Ratio of infected men to infected women <2 have been reported in Latvia (1,7), Denmark (1,6) and Estonia (0,6). While the highest ratios were recorded in Poland (14), Croatia (14) and Romania (12). The highest number of reported cases in 2017 was found in citizens in the age groups 25-34 (37% of cases) and 15-24 (36%). (11) (fig.2)

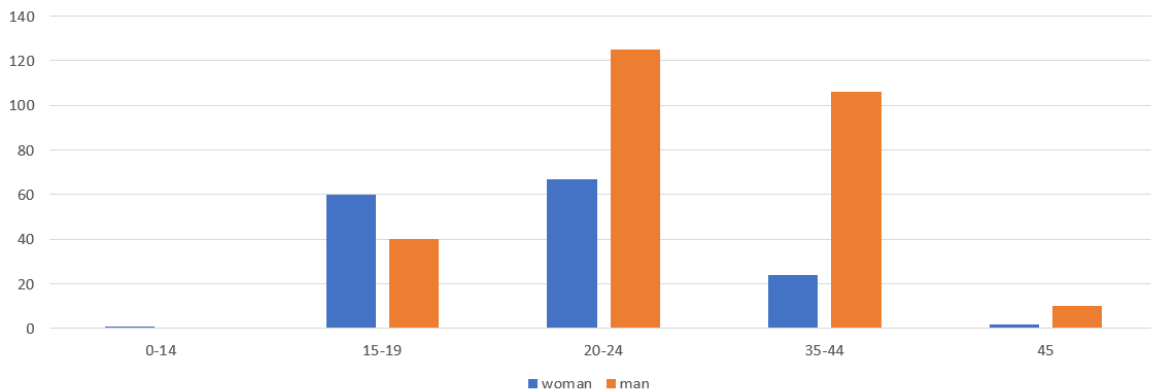


Figure 2. Distribution of confirmed gonorrhoea cases per 100 000 population by age and gender, EU/EEA, 2017 (11)
Poland:

Over the 2010-2018 period, there is a small decrease in annually new reported cases of gonorrhoea in Poland. Currently, the average number of new cases is 466 cases/year. (fig.3) After analysing data from the National Institute of Public Health, a noticeable increase of incidence to gonorrhoea is reported where the number of new cases rose from 298 in 2011, to 733 in 2012. Mazowieckie was the voivodship with the highest incidence index. An unexpected rise in new cases was recorded in pomorskie voivodship in 2012. (12)

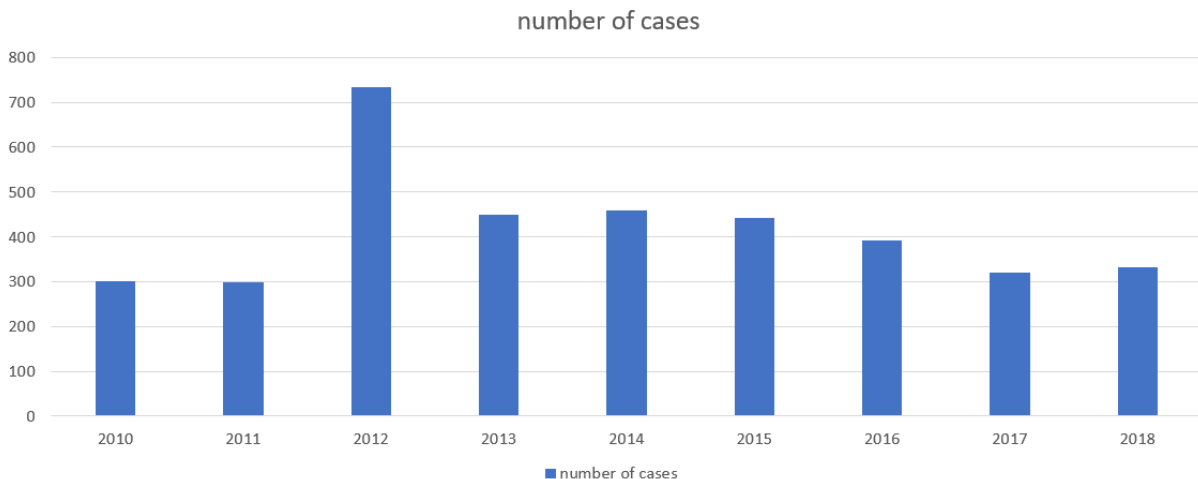


Figure 3. The number of new cases on gonorrhoea

The number of new cases per capita in Poland (1,3 cases/100 000) may appear modest relatively to the numbers found in the rest of European countries (20 cases/100 000), however the marginal number found in Poland may be correlated with the subpar efficiency of detecting new cases. Due to low detectability and reportability, the numbers of new cases and general morbidity found in Poland may be understated, the presented number may not reflect the real spread and intensity of incidence in Poland. In most European countries, the systems for reporting new cases as well as healthcare and its availability for infected individuals varies from the ones available in Poland. (13)

Transmission of gonorrhoea:

Transmission of gonorrhoea: *Neisseria gonorrhoeae* infections are transmitted via sexual contact (oral, vaginal and anal). Vertical transmission (mother to child) is also possible, mainly during birth if the mother is infected.

In 2017, men engaging in sexual acts with other men (MSM – men who have sex with men), made up the largest part of the infected population (47%). (fig.4) In MSM, the infection is localised in 3 areas: the pharynx, anus and urethra. Up to 96% of infections localised in the urethra gave symptoms, however the majority of infections localised in the pharynx and the anus were asymptomatic. Areas of symptomless infections, especially the pharynx, are the factors responsible for the widespread of infections among MSM. (14,15) Studies investigating sexual acts amongst MSM report that most of this populations members engage in oral intercourse (77%). (16) Nevertheless, due to frequent cases of gonorrhoeal pharyngitis in young, homosexual men renouncing their engagement in any sexual acts (“kissing-only partners”), kissing has been suggested as a ways of transmission of gonorrhoea infection. (1)

The main localisation of gonorrhoea infection in heterosexual population tends to be the urethra and the cervix. Most heterosexual men with a urethral infection, quickly notice alarming symptoms and seek medical assistance (usually within a couple days of symptoms). Around half of the infected heterosexual women are asymptomatic, which often leads to the infection being overlooked and left untreated. (15)

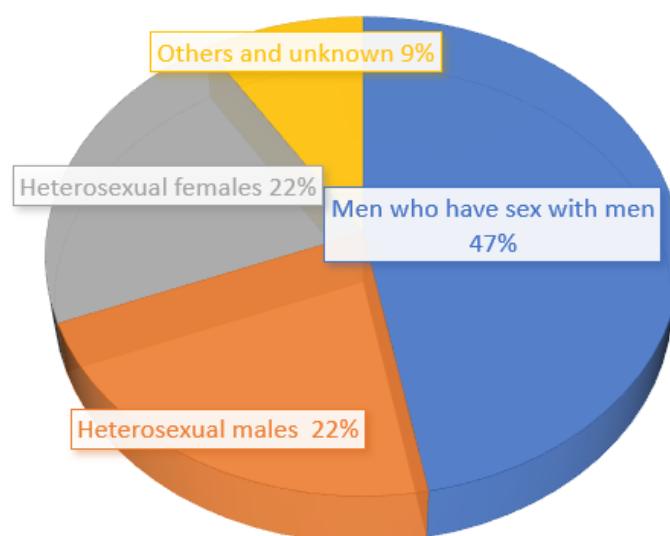
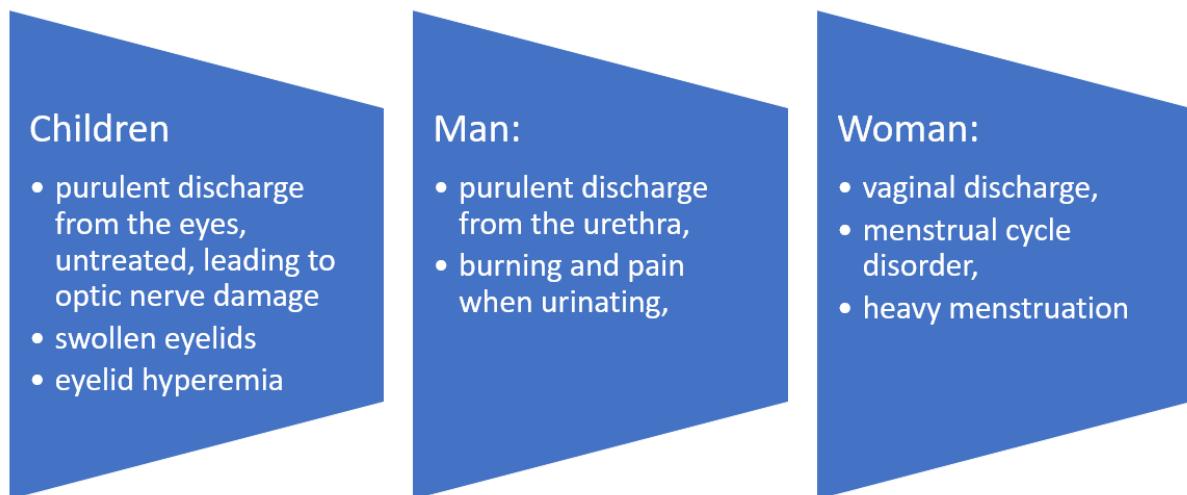


Figure 4. Percentage of gonorrhoea by transmission category and gender EU/EEA, 2017 (11)

Clinical manifestation:



Gonococcal ophthalmia neonatorum- is the most common manifestation of gonorrhoea infection in infants born by an infected mother. The presence of a gonorrhoeal infection during gestation poses a risk for both the mother and her baby. Due to the risk of perinatal complications, every pregnant woman is screened for gonorrhoea. Caesarean section does not eliminate the possibility of vertical infection. (1,17) The probability of the infant acquiring gonococcal neonatal conjunctivitis during birth by an infected mother is estimated at 30-47%. (18) However, if prophylactic measures are undertaken, mentioned likelihood is decreased by up to 10%. (5) The risk of IUGR (Intrauterine Growth Restriction) increases if a gonorrhoeal infection is detected before birth (before amniorrhexis). In the presence of perinatal infection, there is a risk of septic miscarriage (13%), premature amniorrhexia (29%) and chorioamnionitis. (1,17)

The symptoms of gonorrhoeal infection appear 2-5 days after birth. Gonococci may infiltrate the cornea which leads to inflammation, congestion/hyperaemia and profuse purulent discharge. The inflammation develops rapidly, where in later stages it may lead to corneal ulceration, endophthalmitis and loss of sight. (5,18)

Other, less common complications due to *Neisseria gonorrhoeae* infection include: dispersed gonococcal infection, septic arthritis, sepsis, sycosis and meningitis. (5,17)

Credé procedure has been introduced in 1880 by Carl Credé. The procedure involves the addition of 1% silver nitrate solution into the conjunctive sac of a newborn within 2 hours after birth. The procedure is associated with protection from the etiological agent of gonorrhoea. After the Credé procedure, it is recommended not to rinse the newborns eyes with physiological water solution. The Credé procedure is a standard procedure applied in Poland. In the United States, according to the American Academy of Pediatrics (AAP) it is recommended to apply 0,5% erythromycin containing ointment, in a similar fashion to the Credé procedure, 2 hours after birth. The current prophylactic procedures do not prevent infections caused by *Chlamydia trachomatis*. (18)

Pelvic inflammatory disease (PID) is one of the complications caused by an untreated gonorrhoea infection. PID may lead to adhesions within oviducts and visceral adhesions, which may lead to infertility and greater probability of ectopic pregnancy. Spreading of the infection into the peritoneal cavity and the development of appendiceal or hepatic abscesses causes symptoms similar to the ones present in cholecystitis or acute appendicitis (Fitz-Hugh Curtis syndrome). (19)

In men, symptoms appear 3-5 days after infection, however sometimes the course of the disease may be asymptomatic.

Diagnostic procedure:

The fundamental diagnostic procedure is the isolation of gonococci on Thayer-Martin agar or PCR, nucleic acid amplification tests (NAAT). Swabs gathered from the patient should be immediately transferred to a containment suitable for transport and sent to the laboratory for Gram staining and isolation. The isolated gonococcus colony is a highly specific and highly sensitive method for determining a possible gonorrhoeal infection located in the conjunctiva, pharynx, cervical canal, urethra and anus. The isolated colony allows for the determining of drug-sensitiveness and the monitoring of antibiotic resistance of *Neisseria gonorrhoeae*, especially to cephalosporin's, penicillin, fluoroquinolones and tetracycline. Microscopic examination of the Gram stained colony has high clinical sensitivity and specificity for infected men only when the swab was taken from the urethra. (5,18,20)

Due to coinfections being common, possibly infected newborns of mothers with gonorrhoeal infections, should be screened for coinfection by syphilis, chlamydia, HIV and type B hepatitis. It is necessary to gather swabs from the newborn, mother and her sexual partners in order to screen the biological material for other possible STDs. (5,18)

Pregnant women in the risk group should be examined for gonorrhoeal infection during the 3rd trimester of gestation, in order to prevent vertical transmission. (21)

Based on the 10th of July 2013 ordinance from the Minister of Health, it is mandatory to report every case of gonorrhoea in Poland. (22)

Treatment:

Based on the guidelines, the fundamental empiric treatment of an uncomplicated gonorrhoeal infection of the urethra, cervical canal, anus or pharynx, involves administering 500mg of ceftriaxone i.m. and 2,0g of azithromycin per os. Alternatively, in Poland, a treatment with 1,5g azithromycin and 500mg ceftriaxone is available. Second-line treatment and treatment during pregnancy involves administering spectinomycin. Azithromycin in this case, is recommended only if the wellbeing of the mother exceeds the risk for the foetus. Azithromycin passes into breast milk. Fluoroquinolon is administered only if the etiological agent is susceptible. (20) According to the guidelines, an infected woman during pregnancy should be treated with a single 500mg dose of ceftriaxone i.m, alternatively with a single 2g dose of spectinomycin i.m. (1)

Neisseria gonorrhoeae has become resistant to almost all currently used medications, there is no effective vaccine to the bacteria either. Global Gonococcal Antimicrobial Surveillance Programme (GASP) initiated by the WHO indicates a significant problem in the increasing resistance of *Neisseria gonorrhoeae* to extended-spectrum cephalosporin's such as cefixime or ceftriaxone. Resistance to antimicrobial agents used to treat gonorrhoea severely impairs the ability to control gonorrhoeal infections. (8)

Summary:

In order to establish better global control over the spread of gonorrhoea, international cooperation is necessary. Actions to be taken include improvement of prophylaxis, early detection (developing quick and precise screening tests), diagnosing sexual partners for gonorrhoea and other STDs, improvement of surveillance and medication used in treatment. There is a requirement for quick, highly sensitive and specific diagnostic tests, effective and efficient medication and a vaccine against gonococci. Such actions could grant control over the spread of gonorrhoea.

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