

## A LOCAL OUTBREAK OF QUINOLONE-RESISTANT GONORRHOEA IN NORWAY, JANUARY 2008

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Since 1994, the incidence of gonorrhoea in Østfold county, Norway, has remained within the range of 1-8 cases per year, with 40% of cases being imported from abroad. On 20 January 2008, a general practitioner in the county diagnosed two seemingly unrelated domestic cases of gonorrhoea in three days and started contact tracing.

A case was defined as a person with clinical symptoms of gonorrhoea who was a part of the sexual network. Available isolates from the samples taken were tested for resistance.

Among 13 contacts identified in the sexual network, eight were classified as cases on the basis of symptoms, four of whom had laboratory-confirmed gonorrhoea. The index case acquired the infection abroad. The three isolated strains were resistant to ciprofloxacin, but sensitive to ceftriaxone which was used for treatment.

In the outbreak described, most cases were diagnosed only after contact tracing although they had had symptoms. A quinolone-resistant strain was imported from abroad and introduced into the population. The Norwegian national treatment guidelines, which still recommend quinolones for empirical treatment, should be updated.

### Introduction

#### Background

Gonorrhoea is a sexually transmitted disease with a high transmission rate and a short incubation period of two to seven days [1]. The risk of male to female transmission is assumed to be as high as 50-70% per sexual intercourse and the risk of female to male transmission is estimated to be 20-30% [2].

The disease most frequently manifests as purulent discharge and dysuria, but up to 50% of women and 2-5% of heterosexual men can be asymptomatic. Rectal and pharyngeal infections are frequently asymptomatic. Untreated patients can be carriers for several months with late complications such as pelvic inflammatory disease, fistula formation and urethral strictures [2].

Culturing of *Neisseria gonorrhoeae* has lower sensitivity than some newer methods [3,4], but obtaining a culture is important for determining antimicrobial resistance [2]. Laboratories and clinicians are obliged to report data on gonorrhoea patients anonymously to the Norwegian surveillance system of communicable diseases (Meldingssystem for smittsomme sykdommer – MSIS) (5). Since 1993, over 90% of the samples from the patients reported to MSIS have been cultured.

With a mean incidence of 5.4 per 100,000 between 2002 and 2007, gonorrhoea is currently a rare disease in Norway. The imported cases represented 30-40% of all cases reported in the same period. In the Østfold county, where the outbreak occurred, a yearly incidence of 1-8 cases has been registered since 1994, with about 40% of cases imported from abroad.

In Norway, the doctor who treats a patient with a sexually transmitted disease is in charge of contact tracing. Patients can opt to notify their contacts themselves or the contacts are notified by the doctor [6]. Treatment is recommended to all sexual contacts of a patient diagnosed with gonorrhoea [6], regardless of symptoms or test results. Control samples should be taken from the patients at least a week after the completed treatment to check whether the treatment was successful and no re-infection from the sexual partners occurred during this time.

#### The outbreak

On 17 January 2008, a male patient was diagnosed with gonorrhoea by his general practitioner. On 20 January, another man presented to the same general practitioner with symptoms of gonorrhoea. The two patients had no sexual contact with each other and had not travelled abroad recently. Both had a positive culture of *N. gonorrhoeae*. The general practitioner started contact tracing. We describe the results of the investigation.

#### Methods

##### Epidemiological investigation

A confirmed case was defined as a person with a positive culture for *N. gonorrhoeae* or a person who was the only possible source of the infection for a culture-positive case.

A probable case was defined as a person who experienced symptoms such as purulent discharge, dysuria or pelvic pain and was sexually linked to a confirmed case.

Every new contact was asked about all his/her sexual contacts. All available sexual contacts were tested for gonorrhoea, hepatitis B virus (HBV), hepatitis C virus (HCV), HIV, chlamydia and syphilis. All cases and contacts were asked about recent sexual exposure and symptoms according to the standard MSIS reporting form for clinicians [5].

## Microbiological investigation

All hospitals and general practitioners in the county routinely send their microbiological samples to the same public laboratory at Østfold hospital. Here, swabs from different anatomical locations were cultured on modified Thayer Martin (MTM) agar. Morphologically distinctive cultures were stained by Gram and tested for oxydase. Further identification of *N. gonorrhoeae* was done using commercial identification kit API NH [7] and agglutination in antiserum using the Phadebact Monoclonal GC test [7].

For resistance testing, the isolates were then cultured on Mueller Hinton agar with 1% Isovitalex and 1% haemoglobin supplements. The determination of the minimum inhibitory concentration (MIC) was done by Etest [8].

## Results

### Epidemiological investigation

In total, 13 contacts were identified forming a sexual network. Among these, six fulfilled the case definition criteria for confirmed case and two were considered probable cases (Figure). The age range of the cases was 19 to 30 years and five out of eight cases were women. Seven out of eight cases were immigrants from different continents, mostly residing in Norway for more than 10 years.

After the initial two cases had been diagnosed on 17 and 20 January, a third one was discovered through contact tracing on 24 January (Figure, contact nr 3). She was symptomatic but tested negative for gonorrhoea. However, it was established that she was the only link between cases 1 and 2 and therefore classified as confirmed case and treated.

Another case (contact nr 4) was identified on 24 January. He was notified by the second case and consulted a doctor. He revealed that he had visited his country of origin in Asia in September 2007, experienced symptoms there and was treated by a local doctor. His

symptoms continued in Norway and his general practitioner treated him for urinary tract infection with trimetoprim. The symptoms persisted for several months, yet he did not consult a doctor again. We concluded this case had initiated the outbreak.

The fifth case (contact nr 5) was identified on 25 January through contact tracing. She had visited a doctor due to symptoms on 16 January but was treated for urinary tract infection. Later, the woman developed a clinical picture of pelvic inflammatory disease and tested negative for chlamydia, but gonorrhoea was not suspected. She underwent laparoscopic appendectomy. From the start, she was treated with several antibiotics. Her sample for gonorrhoea was taken only after she had been identified as a contact of a confirmed case.

Two more cases (contacts nr 6 and 7) were found through contact tracing. Both were symptomatic, one had already visited a doctor and although she wanted to be tested for all STDs, a sample for gonorrhoea was taken only after she was traced as a contact. The other had previously received a symptomatic treatment with azitromycin and penicillin, which did not completely improve her symptoms.

The two women (contacts nr 6 and 7) and two men (contacts nr 2 and nr 4 – the index case) met on a single occasion to have sex. Our findings suggest that this was when the infection was transmitted from the index case to three people.

The last case was identified in the wife of the index case (contact nr 8). She was notified by a general practitioner after the index case had resisted informing her. Her mild symptoms started months ago and persisted.

The specific symptoms, experienced by the eight cases are shown in the Table. In addition, five asymptomatic contacts were identified in the sexual network (contacts nr 9 to 13). All cases and most of the asymptomatic sexual contacts were treated and educated about safe sex.

We failed to deliver the treatment to an asymptomatic prison inmate (contact nr 12), whose sample was negative for gonorrhoea, and an asymptomatic woman (contact nr 13), whose partner, belonging to the sexual network, was also asymptomatic and tested negative.

The cases were tested for gonorrhoea again at least a week after the completed treatment and all were negative. Available contacts (1-11) were also tested for other sexually transmitted infections (STI). All were negative except two men who had a past HBV infection.

At the time of writing this article, no other cases have been linked to this outbreak.

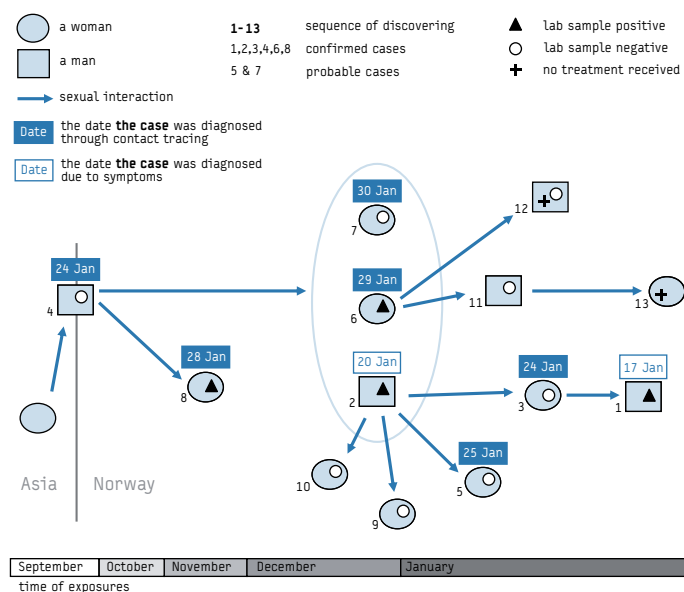
### Microbiological data

Samples for culturing were obtained from all the cases and were positive in four cases (Figure). Among the swabs that tested positive, two were from cervix, two from urethra, one from the anus and one from the pharynx (Table).

Of the positive cultures, one strain of *N. gonorrhoeae* died in the laboratory and was not available for further resistance testing. The rest of the isolates did not grow on Mueller Hinton agar, so MTM

## FIGURE

### Sexual network of an outbreak of gonorrhoea in Norway, January 2008



agar had to be used instead. The strains exhibited chromosomally mediated increases in minimal inhibitory concentration of penicillin (2) and additional intermediate resistance to erythromycin and azitromycin. They were resistant to ciprofloxacin, doxycyclin and trimethoprim and sulfamethoxazole and sensitive to ceftriaxone, which was used for treatment of the cases (Table). Phadebact Monoclonal GC test revealed the samples to be positive in the WI serogroup (serogroup WII/III negative).

### Discussion

We have described a localised outbreak of gonorrhoea in a very low incidence country. Although all of the eight cases experienced symptoms and most of them visited a doctor, six were diagnosed only after they had been linked to the outbreak through contact tracing.

Contact tracing in STI is particularly difficult as those infected may be reluctant to reveal the information about their sexual partners and/or may not wish their partners to be contacted by health officials. It is important that the contact tracing is done thoroughly to prevent the spread of the disease.

In the outbreak described here, we were not able to obtain a positive culture of *N. gonorrhoeae* from all the patients whom we regarded as cases due to their symptoms and epidemiological links. The reason some samples could not be cultured may be the lower sensitivity of culturing, partial sensitivity to the antimicrobials administered in the previous treatment or transportation problems. In the two probable cases, the symptoms might have had other etiological causes than gonorrhoea, such as Chlamydia infection. However, Chlamydia was also not proven, the onset of symptoms corresponded to the recent exposure to a gonorrhoea-positive case and the nature of the symptoms was more likely to arise from gonorrhoeal infection (Table, cases 5 and 7).

While the benefit from screening for gonorrhoea with culture might be low [6] in low prevalence countries, gonorrhoea should be an important differential diagnosis option in symptomatic patients.

Our investigation revealed that the delay in recognising the disease in several patients led to a further spread of infection, health complications and even one unnecessary surgical procedure.

With increased travelling and migration, a resistant strain from a country with different gonorrhoea epidemiology can be introduced into a low prevalence country. Some authors suggest to change the recommended first choice treatment if the infection originated from abroad [9,10]. As the links to a foreign country might not be recognised in sexual contacts of the index patient, it is important to obtain a culture of *N. gonorrhoeae* for sensitivity testing. Regardless of the previous travel history, immigrants are a high risk population for STI's and "being a person from Africa or Asia" has been previously recognised as a potential predictor of penicillinase-producing *N. gonorrhoeae* (PPNG) in Norway, [5,10].

Quinolone-resistant strains have become increasingly represented in several European countries [12,13] and a third generation cephalosporin is now recommended for empirical treatment in many countries [4,14]. Although the national treatment guidelines are currently under revision in Norway, the first drug of choice is still quinolone [11].

### Conclusion

This outbreak should serve as a reminder that effective contact tracing is crucial in preventing the spread of gonorrhoea. Gonorrhoea has become a rare disease, but should remain a differential diagnosis option, especially due to its high infectivity and the potential to spread. Clinicians should consider taking a sample from several anatomical sites, which is a simple, non-invasive procedure. Due to increasing antimicrobial resistance of *N. gonorrhoeae* and the potential of the infection being imported from abroad, national treatment guidelines should be followed cautiously. We recommend culturing, which enables routine antimicrobial resistance testing. We also believe that Norwegian national guidelines need to be updated promptly so that empirical treatment for gonorrhoea would be a third generation cephalosporin.

TABLE

Confirmed and probable cases in the outbreak of gonorrhoea in Norway, January 2008, by date of illness onset, anatomical location of positive sample and symptoms

Case	Case classification	Sex	Illness onset	Anatomical location of positive sample	Similar resistance pattern of <i>N. gonorrhoeae</i>	Phadebact serogroup	Experienced symptoms
1	confirmed	M	13 Jan 2008	urethra	yes	WI	dysuria, urethral discharge
2	confirmed	M	17 Jan 2008	urethra	yes	WI	dysuria, urethral discharge
3	confirmed	F	6 Jan 2008	no positive sample			pain, vaginal discharge
4	confirmed	M	Sept 2007	no positive sample			dysuria, urethral discharge
5	probable	F	17 Jan 2008	no positive sample			dysuria, vaginal discharge, salpingitis, abdominal pain
6	confirmed	F	Dec 2007	cervix, anus, pharynx	yes	WI	pharyngeal infection, fever, vaginal discharge, pelvic pain
7	probable	F	3 Jan 2008	no positive sample			pharyngeal infection, dysuria, fever
8	confirmed	F	Nov 2007	cervix	unknown		dysuria, vaginal discharge

Note: Case numbers correspond to numbers in Figure.

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