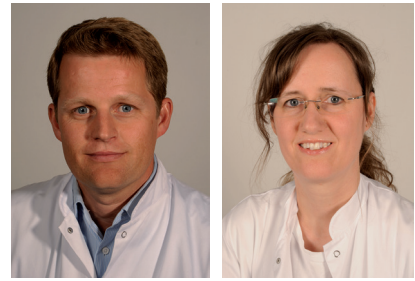


Controversies and Challenges in Venereology in Denmark

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In recent years several challenges and controversies have arisen in the field of venereology in Denmark. Some of these challenges appear to be unique for Denmark, while others have also arisen in the other Nordic countries. Of course, it is possible that the issues faced in Denmark today may arise in other Nordic countries in the future.

Human papilloma virus

In February 2016, the human papilloma virus (HPV) vaccine was changed in the Danish childhood immunization programme; Gardasil was replaced by the vaccine Cervarix. Cervarix protects against the two oncogenic HPV types 16 and 18 that are responsible for approximately 70% of all cervical cancers (1). The two vaccines are similar with regards to the level of protection against cervical cancer and reported side-effects. However, unlike Gardasil, Cervarix does not protect against genital warts. When Gardasil was originally introduced into the Danish childhood immunization programme there was a significant decline in genital warts among both young women and men (2). Following the change of vaccine to Cervarix, it is likely that the incidence of genital warts will increase once again. It is planned that all girls who have already received at least 1 dose of Gardasil are to be completed with this vaccine before the end of January 2017.

However, no matter which vaccine is included in the programme it will have no effect if the girls are not vaccinated. In Denmark the HPV vaccine is given at the age of 12 years. Statistics from Statens Serum Institute from April 2016 show that only 27% of girls born in 2003 received the HPV vaccine. Thus, due to the low level of vaccine uptake, an alarming number of deaths from cervical cancer will not be prevented.

Until April 2016, a total of 242 women filed claims for HPV vaccine side effects to the Danish Patient Compensation Association, which decides compensation claims for patients injured in connection with treatment by the Danish Health Service. For comparison, only 37 persons in Sweden and 8 in Norway have filed a claim until April 2016 (Danish Broadcasting Corporation, 23 April 2016).

In November 2015, the European Medicines Agency (EMA) released a new evaluation report on the safety of HPV vaccines. This reevaluation was done on a Danish initiative. The report concluded that the available evidence does not show that HPV vaccines are linked to the suspected serious side-effects postural orthostatic tachycardia syndrome (POTS) and complex regional pain syndrome (CRPS). In particular, the syndrome complex POTS was debated in Denmark in 2015. The conclusion drawn by the EMA was based on a thorough review of the published research articles, data from the companies' clinical trials, and suspected adverse reactions reported by patients and doctors, as well as additional data provided by member countries, including Denmark. The EMA also consulted with a group of leading experts in the field of vaccines, POTS and CRPS, and assessed the detailed information received from a variety of patient groups. In December 2015, the World Health Organization (WHO)'s Global Advisory Committee on Vaccine Safety (GACVS) pronounced on the safety of HPV vaccines. Like the EMA, GACVS concluded that, based on existing knowledge, there is no evidence of safety problems with the vaccines that would support changing the vaccines. Vaccine safety is monitored closely by both the EMA and the Danish Medicines Agency. Scandinavian doctors should therefore not be afraid to support national HPV immunization programmes.

Syphilis

Syphilis has been known in Europe for over 500 years. In 1530 the Italian physician Girolamo Fracastoro portrayed the disease symptoms in a poem about the shepherd Syphilus, who later became the eponym of the disease. The exact origin of syphilis is unknown; one hypothesis is that the disease was carried to Europe by returning crewmen on the Santa Maria from Christopher Columbus's voyage to the Americas. Syphilis, which also became known as the French disease, the Gallic disease and the Great Pox, spread rapidly as a deadly epidemic across Europe (3).

This, in brief, is the historical description of syphilis. In the 1990s syphilis appeared to be predominantly a disease of historical interest, since it was considered almost extinct in

the Nordic countries. In 1995, only 15 cases of syphilis were reported in Denmark. However, in the past 20 years, a 50-fold increase, to 777 cases in 2015, has been observed (4). The majority of those infected are men who have sex with men (5). However, in recent years there has been a considerable increase among heterosexual men and women, and it seems that syphilis is being reintroduced in both sexes. Approximately one-third of infected men are HIV-positive. HIV and syphilis are a bad combination, as each can facilitate infection by the other (5).

Penicillin remains the drug of choice to treat syphilis, and even though it has been used to treat the disease for many decades, we still have no issues with resistance to penicillin.

Gonorrhoea

In contrast to syphilis, gonorrhoea has progressively developed resistance to the antibiotics prescribed to treat it. Following the spread of gonococcal fluoroquinolone resistance, the cephalosporin antibiotics have been the foundation of recommended treatment for gonorrhoea. The emergence of cephalosporin-resistant gonorrhoea would significantly complicate the ability of providers to treat gonorrhoea successfully, since we have few antibiotic options left that are simple, well-studied, well-tolerated and highly effective. Thus, it is disturbing that treatment failure to third-generation cephalosporin has been confirmed in Norway and Sweden (6, 7). To our knowledge, so far, no cases have been reported in the other Nordic countries.

Since 2011 there has been an increase in Denmark in the number of cases of gonorrhoea, especially among heterosexuals. In 2015, 2,735 cases were reported, compared with only 492 in 2011 (8) (Fig. 1). Even though some of the increase may be due to change in the reporting system, the number is alarming. In 2015 the recommended treatment in Denmark was changed to intramuscular ceftriaxone, 500 mg, in combination with oral azithromycin, 2 g. Denmark never introduced cefixime as

a treatment option. It is worth mentioning that, among the cases of gonorrhoea from 2015, 26% of cases had a negative culture and were only detected by the nucleic acid amplification test (NAAT) (8).

To conclude, we need to focus on the venereology part of our specialty, as the demand for our expertise is growing rapidly!

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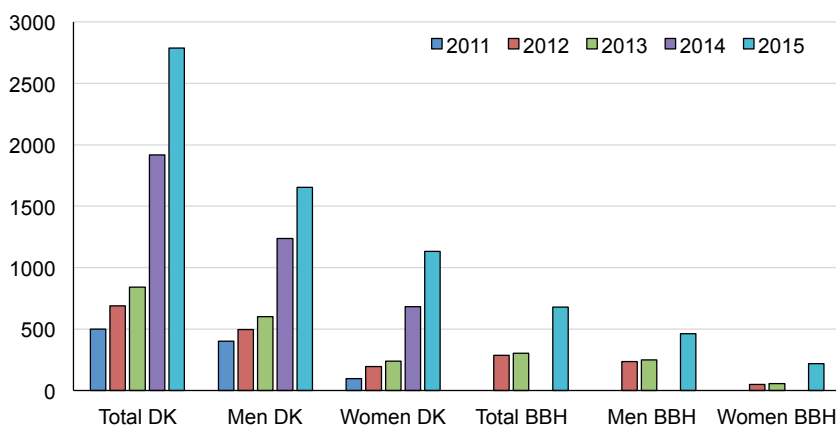


Fig. 1. Number of cases of gonorrhoea in Denmark (DK) and the Venereal Clinic Bispebjerg Hospital (BBH) 2011–2015 (missing data from 2011 and 2014 BBH) (8–12). Since 2014, data has been extracted from the Danish Microbiology Database (MiBa) (8).