During an outbreak of hepatitis A predominantly among men who have sex with men (MSM) in Copenhagen, Denmark, in 2004, we did a case-control study to determine risk factors for infection. A case was an MSM >17 years, with men (MSM) in Copenhagen, Denmark, in 2004, we did a case-control study to determine risk factors for hepatitis A infection among MSM in Copenhagen. The results are in accordance with findings in other European outbreaks. As the general immunity to hepatitis A increases and the outbreak potential increases, we recommend health education and hepatitis A vaccination to all MSM not living in monogamous relationships, especially if they visit gay saunas or other places with frequent partner change. To stop spread of hepatitis A among MSM in Europe, a European consensus on prevention and control measures may be required.

**Key words:** Case-control study, hepatitis A, homosexuality, male; sexual behaviour

**Introduction**

In Denmark, anti-HAV IgM positive hepatitis A virus (HAV) infection is notifiable by clinicians. HAV is not regarded as endemic in Denmark and susceptibility in the population is high. The majority of infections are imported by children of foreign origin returning from visits to friends and relatives in endemic countries [1]. Subsequent secondary spread in childcare institutions is a common cause of small outbreaks. Outbreaks of hepatitis A among men who have sex with men (MSM) have been reported from several cities in Europe and worldwide. In Copenhagen, outbreaks among MSM occurred in 1977 [2] and in 1991 [3]; with 21 and 17 reported cases of hepatitis A respectively. Studies have shown that hepatitis A is a sexually transmitted infection (STI) in MSM. The main risk factors identified are oral-anal sex (rimming) or digital-anal sex [4,5], visiting certain bars or saunas [6,7,8], having sex with anonymous partners or group sex [4,5], sexual contact of a non-sexual nature and contaminated food [7] also contribute to infection.

From January 2004 an outbreak of hepatitis A affecting predominantly among men who have sex with men (MSM) in the city of Copenhagen, Denmark, was investigated. A case-control study was conducted to determine risk factors for hepatitis A infection in this outbreak in order to inform targeted preventive measures.
Outbreak report

Methods

A case was defined as an MSM > 17 years, living in Copenhagen, in whom hepatitis A infection with positive anti-HAV IgM was diagnosed between 1 June and 14 August 2004, and who did not have contact to a hepatitis A case in his household in the six weeks before onset of illness. Cases were selected from the notifications received.

Controls, frequency matched to the cases date of onset of illness, were selected at the annual Copenhagen Gay Pride Festival on 14 August 2004 from MSM resident in Copenhagen. Based on the result of a saliva antibody test (Methods: see [10]) only persons susceptible to hepatitis A were included as controls. Data on exposure was collected for a six week period before illness onset and for the same period in controls using piloted self-administered questionnaires. To protect privacy, patients were contacted by their physician who obtained informed consent before posting a questionnaire to them. Information collected included: eating in restaurants/cafes/bars, shellfish consumption, whirlpool use, travel abroad, contact with hepatitis A cases, number of regular and casual sexual partners, venues for sexual contact, sexual contacts abroad or arranged via internet, oral-anal and digital-anal sex practices, history of STIs. Additionally, controls were asked about their attitude towards vaccination.

Data analysis was performed in STATA 8.0. Matched odds ratios and 95% confidence intervals were calculated for each exposure factor. Adjusted odds ratios were calculated using conditional logistic regression analysis. Exposure factors with P values < 0.20 and confounding variables such as age were included. The final model was build by backward elimination of variables above the threshold of P = 0.10.

Results

In 2004, 163 cases of hepatitis A in men > 17 years were notified to the Department of Epidemiology, SSI. In the past five years the median number of annually reported cases of hepatitis A among men of this age group was 13 (range 7-25). Of the 163 cases, 107 were from Copenhagen, 56 from the rest of Denmark. The incidence rate in Copenhagen was 23 per 100 000 and declined with increasing distance from the capital [FIGURE 1].

The following results are restricted to cases in Copenhagen. Of the 107 patients, 68 (64%) were reported to be MSM and five to be heterosexuals. For 34 patients, the sexual orientation was not known [FIGURE 2].

Patient ages ranged between 19 and 73 years with a median of 41. Ninety seven (91%) patients were residents in Denmark. Thirty seven (35%) patients were admitted to hospital.. Forty nine (46%) cases were reported by general practitioners and 58 from hospital in-or outpatient departments.

Case-control study

The case-control study conducted among MSM included 18 cases and 64 controls. Physicians of 36 notified cases were asked to recruit their patients for the study; 30 patients agreed to participate and 24 of these (80%) returned questionnaires. Six patients did not fulfil the case definition (four self-identified as heterosexual, one was infected by a household contact and one did not live in Denmark during the exposure period). Saliva samples were taken from 105 MSM visiting the Copenhagen Pride Festival: 86 (82%) had no detectable antibodies against HAV; 15 (14%) were IgG positive, two of these were also IgM positive; four samples were inconclusive. Of the 86 without detectable antibodies, 17 reported having been vaccinated against hepatitis A, three were not in Copenhagen during the period required and two refused to participate. Therefore, 64 (61%) of the participants were included as controls.

Case patients and controls were similar with regards to residence within Copenhagen, but patients were older than controls [TABLE 1]. The proportion of HIV-infected people was higher among patients than controls. Neither patients nor controls reported a previous syphilis infection.
The study suggests that sexual activity was the major mode of transmission in this hepatitis A outbreak among MSM. Sex with casual partners and sex in gay saunas contributed to the spread of hepatitis A among MSM.

However, as the study period encompassed only part of the outbreak, we must be cautious about extrapolating results to the whole period of the outbreak. The study may be further limited by a small sample size. Controls selected at the festival may not be representative of the total MSM population in Copenhagen. However, since it is impossible to select controls directly from the study population, we consider our approach the best possible way to represent a broad spectrum of the cases.

After adjusting for confounding, sex with casual partners (adjusted odds ratio [aOR] 8.7; 95% CI 1.6-48.9) and sex in private homes (aOR 0.1; 95% CI 0.0-0.5) seem to respectively increase and decrease the risk of infection. Because of the time dependency, sex in gay saunas did not prevail as an independent risk factor in the multivariate analysis.

Two thirds of controls disclosed their sexual orientation to their general practitioner. Of 36 controls, who had had casual sex, 11 had been recommended hepatitis A vaccination (gay campaigns [5], an STI clinic [4], and general practitioners [2]). Among controls, 53 (83%) were willing to be vaccinated against hepatitis A. However, only 14 (26%) were willing to pay for the vaccination.

**Discussion**

The study suggests that sexual activity was the major mode of transmission in this hepatitis A outbreak among MSM. Sex with casual partners and sex in gay saunas contributed to the spread of hepatitis A among MSM.

Matched univariate analysis of exposure factors [TABLE 2] suggests that HAV infection was not associated with consumption of seafood or eating outside home. There was no evidence of a cluster of cases linked specific food outlets or restaurants. Travelling abroad was less frequent for case patients than controls. Patients had a median of three sexual partners in the six weeks before illness and controls, a median of two.

Patients were more likely to have had sex with casual partners than controls. One third of both patients and controls had sex with partners they met via the internet. HAV infection was associated with sex in gay saunas. This association was very strong in May and June, when 9 of 10 patients were exposed (OR_{MH} 129.2, 95% CI 7.6-2197.5), but not in the later part of the study. No single sauna was implicated. Sex at cruising grounds and toilets was not associated with infection.

Sex at private homes appeared protective. Participation in group sex was reported by 17% of the patients and 5% of controls. High risk practices such as oral-anal and digital-anal sex were common among both cases and controls, and were not associated with increased risk of HAV infection.

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**Discussion**

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partners within a short period of time. In Copenhagen, gay saunas are popular places for both Danes and visitors from abroad to have casual sex. There are at least seven saunas in Copenhagen. However, one third of cases were admitted to hospital. Costs associated with hospital admission and days off work could be avoided by vaccination. In HIV-infected individuals, HAV infection has been associated with prolonged HAV viraemia, which might lead to longer infectivity and increased risk of spread in this population [15]. Inactivated HAV vaccine is safe in HIV-infected individuals [16].

The prevalence of anti-HAV antibodies among MSM tested at the Copenhagen Pride Festival was 14%. This is low compared with a serological study in two gay saunas in Copenhagen conducted in 1984, where 36% of sauna attendees were immune to HAV – a figure three times higher than in the general Danish population at that time [17]. It is uncertain whether this reflects an overall decline of hepatitis A infections among MSM over the last 20 years, because sauna attendees may not be representative of the population of MSM attending the festival. However, it suggests that the population of MSM in Copenhagen is susceptible to hepatitis A infection and therefore need to be alerted of the risks of infection and how to prevent it.

Based on the results of the investigation we suggest recommending hepatitis A vaccination to all MSM who are not in a monogamous relationship, especially if they visit gay saunas or other places with frequent partner change.

Opportunities for vaccination could be visits to general practitioners (although not all MSM disclose their sexual orientation to their doctor), sexual health clinics or outreach campaigns at saunas or mobile clinics. Willingness to be vaccinated was high among MSM, but a considerable number were reluctant to pay for the vaccination. This attitude may be influenced by information about the importance of vaccination. As free hepatitis B vaccination is available for MSM in Copenhagen, exchanging the monovalent vaccine for the combined hepatitis A and B vaccine would make protection against hepatitis A available at little extra costs.

We further suggest that adequate hygiene should be ensured in saunas. An information campaign on risks and prevention of hepatitis A transmission should be targeted at sauna visitors (both Danish and international guests). To stop spread of hepatitis A among MSM in Europe, a European consensus on prevention and control measures may be required.

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