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Decline in hepatitis B infection observed after 11 years of regional vaccination among Danish drug users

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Running title: Decline of chronic hepatitis B in drug users

Abstract:

The aims of this study were to determine the current prevalence of viral hepatitis and HIV among drug users, and to compare this prevalence with previous findings in the same geographical region. Cross-sectional surveys of drug users attending treatment centers on the island of Funen with approximately 500,000 inhabitants were administered in 1996 and 2007. The 2007 prevalence estimates were: anti-HBc 50.2%, HBsAg 1.1%, anti-HCV 66.8%, HCV-RNA 40%, and anti-HIV 1.1%. The corresponding 1996 prevalence values were: anti-HBc 70% ($P < 0.0001$), HBsAg 9.8% ($P < 0.0001$), anti-HCV 82.8% ($P < 0.0001$), HCV-RNA 56.3% ($P = 0.002$), and anti-HIV 1% ($P = 1$). The 2007 prevalence of viral hepatitis decreased due to the increasing proportion of non-injectors. Among injectors, the prevalence remained unchanged except for a significant decrease in HBsAg. The 2007 prevalence of ongoing HBV infection among infected (HBsAg/anti-HBc proportion) was the lowest that to our knowledge has been reported among drug-users. Vaccination coverage among susceptible persons tested in 2007 was 24%, compared to 0.7% in 1996. Therefore, despite an unchanged prevalence of anti-HBc among injecting drug users, a highly-significant drop in HBsAg prevalence was seen during the last decade. This observation may be linked causally to an increase in hepatitis B vaccination of the susceptible population. Our findings suggest that even incomplete vaccination, without persistent protective anti-HBs levels, may induce an immune memory sufficient to prevent chronic infection upon transmission.

Keywords: Hepatitis C; HIV; Prevalence.

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Chronic hepatitis B and C are among the leading causes of hepatocellular cancer and end-stage liver disease worldwide. Denmark is considered a low-prevalence country for both infections. The estimated prevalence of chronic hepatitis B is 0.3% in the general population [Susan Cowan, personal communication], but higher in certain risk groups, such as immigrants from endemic areas and intravenous drug users. Among drug users, prevalence values between 8.4% and 9.3% were reported in the 1990s, but current estimates are unavailable [Christensen et al., 2000; Fuglsang et al., 2000]. However, a study of drug-related deaths in Denmark in 2004 suggests a significant decline in the risk of contracting chronic hepatitis B infection [Christensen et al., 2006a]. For hepatitis C, it is estimated that <1% of the general population is antibody positive, whereas the prevalence among drug users has been reported to be between 70% and 87% [Christensen PB, 1999; Fuglsang et al., 2000; Westh et al., 1993]. The human immunodeficiency virus (HIV) prevalence in the general population of Denmark has been estimated at 0.07% [Lohse et al., 2005], but the corresponding value for drug users is 0-4% [Christensen et al., 2000; Christensen et al., 2006a; Fuglsang et al., 2000].

Vaccination of drug users against hepatitis B virus (HBV) has been recommended since the 1980s, and since 2005 this vaccination has been offered free of charge. In the early 1990s, an outbreak of hepatitis B took place among drug users in southern Denmark [Christensen et al., 2001].

Accordingly, a hepatitis B vaccination campaign was launched in the region in 1996, and this campaign has been in operation to this day. As part of the initial campaign, drug users in treatment centers were screened for bloodborne viral infections [Christensen PB, 1999].

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4 The primary aim of this study was to estimate the 2007 prevalences of viral hepatitis and HIV, and
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7 to compare these estimates with previous findings in the same geographical region. The HBV
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10 vaccination status among drug users was also determined.
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Methods:

A survey investigating the prevalence of chronic hepatitis and HIV infection was performed among drug users attending treatment centers in the county of Funen in 2007. Clients present during these visits were eligible to participate in the survey, after written informed consent was obtained. A standardized questionnaire about hepatitis and vaccination status was answered by the participant. Afterwards, blood samples for serologic analysis were drawn and separated within eight hours. The samples were either analyzed immediately or kept frozen at -80 °C until analyzed. All samples were analyzed with the AxSYM™ assays (Abbott Laboratories, North Chicago, IL, USA) according to the manufacturer's instructions. Samples were tested for hepatitis B surface antigen (HBsAg), antibodies to hepatitis B surface antigen (anti-HBs), antibodies to hepatitis B core antigen (anti-HBc), antibodies to hepatitis C virus (anti-HCV), and antibodies to human immunodeficiency virus (anti-HIV). If HBsAg was present, samples were tested for hepatitis E envelope antigen (HBeAg), antibodies to hepatitis E envelope antigen (anti-HBe) and antibodies type IgM to hepatitis B core antigen (anti-HBc IgM). Quantitative anti-HBs analysis was performed with AxSYM AUSAB™, that is calibrated according to the WHO standard. Samples with anti-HBs ≥ 10 IU/L were classified as reactive.

HBsAg reactive samples were confirmed by the AxSYM HBsAg Microparticle Enzyme Immuno Assay (MEIA). Anti-HIV and anti-HCV reactive samples were confirmed with Line Immuno Assay (LIA) tests. Quantitative HCV-RNA and HBV-DNA tests were performed with in-house real-time PCR assays at the Department of Clinical Immunology, Aalborg Hospital. The sensitivities of these assays were 29 IU/mL for HCV-RNA and 30 IU/mL for HBV DNA [Krarup et al., 1998; Krarup et al., 2008]. If serology results were not obtained during the survey, results from routine serology tests within one year of the survey date were used. All previous positive HIV tests were included.

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7 The treatment centers' vaccination program for hepatitis B consisted of 20 μ g HBsAg (Engerix
8 B®)(GlaxoSmithKline Biologicals, Rixensart, Belgium) administered in the deltoid muscle at days
9 0, 7, 21, and at 3 months to anti-HBc-negative susceptible clients. The treatment was supplemented
10 with a hepatitis A vaccination consisting of inactivated hepatitis A virus (Havrix®)
11 (GlaxoSmithKline Biologicals, Rixensart, Belgium) given as a two-dose schedule if the client was
12 anti-HAV negative. Anti-HBs tests were performed one month after the last dose of vaccine, and
13 titers ≥ 10 IU/L were considered protective. Additional vaccines were offered if protection was not
14 achieved. Vaccination status was ascertained by interview and extracted from client records.
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28 Data was entered into an Access (Microsoft office 2003, Seattle, WA, USA) database and proofread
29 for clerical errors. Statistical analysis was performed with STATA version 10 (Statacorp LP,
30 College Station, TX, USA); nonparametric tests (Fischer's exact test and Wilcoxon rank sum test)
31 were used as appropriate. This study was approved by the research ethics committee of Region
32 Southern Denmark (Project-ID VF-20060078), and by the Danish Data Protection Agency.
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Results:**Client demographics**

Of the 759 clients who attended the treatment centers in 2007, 374 (49%) were included in the present study. The most frequent reason for exclusion was client absence at the time of the study visit. Additionally, 54 clients who participated in both surveys were excluded from the 2007 survey. Based on the treatment center register of all clients non-participants did not differ significantly by age or gender. In 2007, 235 (73%) of the clients were male, with a median age of 40 years (interquartile range (IQR) 34-47). The prevalence of injecting drug users (IDUs) was 75%; median time since first injection was 12 years (IQR 7-19 years). 137 clients with known IDU status (62% of available clients) from 1996 were included in the present study.

Overall prevalence

The prevalence of hepatitis B and C infection fell significantly during the time between the two surveys for the entire surveyed population (Table I). Anti-HBc decreased from 70% to 50.2% ($P < 0.0001$), and anti-HCV decreased from 82.8% to 66.8% ($P < 0.0001$). The HIV prevalence remained low and unchanged (1.1%). The overall change in prevalences was primarily due to an increase (7% to 25%) in the proportion of non-injectors, as this group displayed a much lower prevalence of bloodborne viral infections.

Prevalence changes among IDUs

The prevalence of HBsAg among IDUs decreased from 7% in 1996 to 1.3% in 2007 ($P = 0.005$), and the prevalence of anti-HBc IgM antibody fell from 29% to 1.4% ($P < 0.0001$). The total anti-HBc prevalence remained stable (Table II). The 1996 survey was performed in the late part of an HBV outbreak with many recent infections. The exclusion of anti-HBc IgM positives still resulted

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4 in a significant HBsAg decline between the two surveys, from 6% to 1.3% ($P = 0.024$).

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6 Correspondingly, the HBsAg prevalence among antiHBc positives fell from 8% (7/90) in 1996 to
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8 1% (1/151) in 2007 ($P = 0.002$). During the interim between the two surveys, the time until half of
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10 the population became infected after initiating injecting drug use rose from three to 13 years for
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12 HBV, but the HCV time lag remained stable at 1-2 years (Fig. 1).
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18 **Prevalence changes in non-IDUs**

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20 Among the non-IDU population, no significant changes in prevalence were observed; however,
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22 only 9 non-IDUs were included in the 1996 survey (Table II).
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28 **Hepatitis B vaccination**

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30 Among the participants in the 2007 survey, 24% (76/320) had been vaccinated against hepatitis B in
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32 the treatment centers prior to the survey. Among those vaccinated, 47% (34) displayed protective
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34 levels of anti-HBs, 24% (18) were negative for all hepatitis B serologic markers, and 28% (21) were
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36 anti-HBc positive (with/ without anti-HBs), indicating previous HBV-infection.
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40 Among participants not registered as vaccinated, 39% (90/232) tested negative for all hepatitis B
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42 serologic markers, and hepatitis B vaccination was indicated for these participants. 32% (75/232)
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44 were “anti-HBc only” (anti-HBc positive and anti-HBs negative).
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47 In the 1996 survey only 0.7% (1/137) was vaccinated. ($P < 0.001$).
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51 **HIV and hepatitis C**

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53 Three of the IDUs were identified as anti-HIV positive (1.3%) during the 2007 survey.

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55 Additionally, 1.1% (5/439) of the non-participants had previously tested positive for anti-HIV, and
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57 thus the overall prevalence of anti-HIV was 1.1%. This rate was unchanged compared to 1.0%
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(2/203) in 1996. The hepatitis C prevalence remained high and unchanged among IDUs, with 85% exposed (anti-HCV positive) and 53% currently infected (HCV-RNA positives) (Table II).

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Discussion:

Analysis of two surveys performed 11 years apart revealed that IDUs continued to be at high risk for viral hepatitis, and at a much higher risk than non-injectors. The most important difference between the two surveys was a significant decline in HBsAg among IDUs without a corresponding decline in anti-HBc (table II). This decline in the current infection proportion (HBsAg/anti-HBc, the sAg/core proportion) from 7.7% (7/90) in 1996 to 0.7% (1/151) in 2007 has to our knowledge not been reported previously.

The SAg/core proportion represents an unknown mixture of chronic and acute infection. However, the SAg/core proportion has been reported as rather stable across HBV surveys in low endemic countries and among IDUs. An international review of 20 studies of 7,626 IDUs in 1994 (prior to routine vaccinations among drug users) reported an overall 9.3% prevalence of HBsAg, with an average SAg/core proportion of 13% [Levine et al., 1994]. A 1997 survey in Copenhagen, where no HBV epidemic was observed among drug users, reported a SAg/core proportion of 8.4%, and in a Danish prison survey in 1996, 14% was recorded [Christensen et al., 2000; Fuglsang et al., 2000]. This study's 1996 SAg/core proportion was therefore in accordance with previous reports, but the 2007 SAg/core proportion was significantly lower (table I and II).

There are several possible explanations for this observation. The difference could reflect a high proportion of recent infection in 1996, when an outbreak of hepatitis B had taken place in the years just prior to sampling. This hypothesis is supported by the high proportion of anti-HBc IgM positives found in 1996. The low SAg/core proportion in 2007 could reflect a situation in which the 1996 acute infections had been cleared, leaving the patients only anti-HBc positive. However, the prevalence found in 1996 was not higher than reported elsewhere, and when clients participating in

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4 both surveys were excluded, similar results were obtained (table II). The cross-sectional study
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6 design hindered assessment of whether the low 2007 SAg/core proportion was due to a decrease in
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8 the number of chronically-infected individuals, or whether the acute infections had a shorter
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10 HBsAg-positive phase. As there were only 3 HBsAg positives in the 2007 survey, both scenarios
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12 must have diminished, consequently lowering the risk of further transmission. These results are
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14 supported by the observation that the time from exposure (drug injection) needed to infect half of
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16 the population with hepatitis B increased from 3 to 13 years between the two surveys (Fig. 1). A
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18 lower overall prevalence of anti-HBc in 2007 among IDUs was also found, although this figure was
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20 not statistically significant (table II).
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28 The HBsAg decline coincided with an increase in HBV vaccination coverage from 0.7% to 24% in
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30 the period between the two surveys. The vaccination coverage reported between the surveys was
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32 probably a conservative estimate, as some drug users may have been vaccinated outside the
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34 treatment centers included in this study. In addition to treatment center vaccination, all drug users
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36 admitted to Danish prisons have been offered hepatitis B vaccination since 2000. Depending on the
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38 uptake among prisoners, this initiative could have covered more than half of the drug-using
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40 population within a six-year period [Christensen et al., 2006b]. The protective levels of anti-HBs
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42 (without detectable anti-HBc) among 4% of the 2007 clients who claimed unvaccinated status
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44 support the underreporting hypothesis. Documentation on the rate of full vaccination course
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46 completion was unavailable. However, even persons who are vaccinated without developing a
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48 durable anti-HBs response may have enough immune memory to protect against the development of
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50 chronic infection upon transmission. This scenario was reported in follow-up studies of childhood
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52 HBV vaccination in which anti-HBc sero-conversion was observed in a number of cases without
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4 development of chronic hepatitis B [Bialek et al., 2008; But et al., 2008; Dentinger et al., 2005;
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6 Harpaz et al., 2000; McMahon et al., 2005; van der Sande et al., 2006].
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9 Decreasing the carrier pool by implementing vaccination programs leads to an increased immunized
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11 population proportion. Individuals who have cleared their infections may also contribute to some
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13 degree of herd immunity among the individuals who were not previously infected or vaccinated.
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18 In conclusion, for the first time, a decline in hepatitis B infection among drug users in Denmark has
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20 been demonstrated, and this decline coincides with an increase in HBV vaccination coverage. Due
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22 to the cross-sectional design of this study, a definitive causal relationship between vaccination
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24 coverage and declining prevalence of HBV infection could not be established. Nonetheless, the
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26 results of the present study suggest that every effort should be taken to enhance vaccination
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28 coverage among drug users in the future.
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33 34 35 Acknowledgements:

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43 of interest are associated with this publication and there has been no significant financial support for
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45 this work that could have influenced its outcome.
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Reference List

Bialek SR, Bower WA, Novak R, Helgenberger L, Auerbach SB, Williams IT, Bell BP. 2008.

Persistence of protection against hepatitis B virus infection among adolescents vaccinated with recombinant hepatitis B vaccine beginning at birth: a 15-year follow-up study. *Pediatr. Infect. Dis. J.* 27:881-885.

But DY, Lai CL, Lim WL, Fung J, Wong DK, Yuen MF. 2008. Twenty-two years follow-up of a prospective randomized trial of hepatitis B vaccines without booster dose in children: Final report. *Vaccine.*

Christensen PB. 1999. Bloodborne viral infections in Funen – a seroepidemiologic study. In: University of Southern Denmark. p 1-142.

Christensen PB, Krarup HB, Niesters HG, Norder H, Georgsen J. 2000. Prevalence and incidence of bloodborne viral infections among Danish prisoners. *Eur. J. Epidemiol.* 16:1043-1049.

Christensen PB, Krarup HB, Niesters HG, Norder H, Schaffalitzky de Muckadell OB, Jeune B, Georgsen J. 2001. Outbreak of Hepatitis B among injecting drug users in Denmark. *J. Clin. Virol.* 22:133-141.

Christensen PB, Kringsholm B, Banner J, Thomsen JL, Cowan S, Stein GF, Jurgensen GW, Grasaasen K, Georgsen J, Pedersen C. 2006a. Surveillance of HIV and viral hepatitis by analysis of samples from drug related deaths. *Eur. J. Epidemiol.* 21:383-387.

Christensen PB, Hammerby E, Smith E, Bird SM. 2006b. Mortality among Danish drug users released from prison. *International Journal of Prisoner Health* 2:13-19.

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2
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4
5 Dentinger CM, McMahon BJ, Butler JC, Dunaway CE, Zanis CL, Bulkow LR, Bruden DL, Nainan
6
7 OV, Khristova ML, Hennessy TW, Parkinson AJ. 2005. Persistence of antibody to hepatitis
8
9 B and protection from disease among Alaska natives immunized at birth. *Pediatr. Infect.*
10
11 *Dis. J.* 24:786-792.
12
13
14
15 Fuglsang T, Fouchard JR, Ege PP. 2000. [Prevalence of HIV and hepatitis B and C among drug
16
17 addicts in the city of Copenhagen]. *Ugeskr. Laeger* 162:3860-3864.
18
19
20
21 Harpaz R, McMahon BJ, Margolis HS, Shapiro CN, Havron D, Carpenter G, Bulkow LR,
22
23 Wainwright RB. 2000. Elimination of new chronic hepatitis B virus infections: results of the
24
25 Alaska immunization program. *J. Infect. Dis.* 181:413-418.
26
27
28
29 Krarup HB, Andersen S, Madsen PH, Okkels H, Hvingel BH, Laurberg P. 2008. Benign course of
30
31 long-standing hepatitis B virus infection among Greenland Inuit? *Scand. J. Gastroenterol.*
32
33 43:334-343.
34
35
36
37 Krarup HB, Drewes AM, Madsen PH. 1998. A quantitative HCV-PCR test for routine diagnostics.
38
39 *Scand. J. Clin. Lab Invest* 58:415-422.
40
41
42
43 Levine OS, Vlahov D, Nelson KE. 1994. Epidemiology of hepatitis B virus infections among
44
45 injecting drug users: seroprevalence, risk factors, and viral interactions. *Epidemiol. Rev.*
46
47 16:418-436.
48
49
50
51 Lohse N, Hansen AB, Jensen-Fangel S, Kronborg G, Kvinesdal B, Pedersen C, Larsen CS, Moller
52
53 A, Willumsen L, Obel N. 2005. Demographics of HIV-1 infection in Denmark: results from
54
55 the Danish HIV Cohort Study. *Scand. J. Infect. Dis.* 37:338-343.
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McMahon BJ, Bruden DL, Petersen KM, Bulkow LR, Parkinson AJ, Nainan O, Khristova M, Zanis C, Peters H, Margolis HS. 2005. Antibody levels and protection after hepatitis B vaccination: results of a 15-year follow-up. *Ann. Intern. Med.* 142:333-341.

van der Sande MA, Waight P, Mendy M, Rayco-Solon P, Hutt P, Fulford T, Doherty C, McConkey SJ, Jeffries D, Hall AJ, Whittle HC. 2006. Long-term protection against carriage of hepatitis B virus after infant vaccination. *J. Infect. Dis.* 193:1528-1535.

Westh H, Worm AM, Jensen BL, Kroon S, Kvinesdal B, Nielsen CM, Wantzin P. 1993. Hepatitis C virus antibodies in homosexual men and intravenous drug users in Denmark. *Infection* 21:115-117.

Table I. Antibody prevalences of Funen county drug users attending a treatment center by year

n pos/N total, %	2007 (n = 320)*		1996 (n= 221)		p-value
	n/N	%	n/N	%	
Anti-HAV total	91/316	28.8	36/157	22.9	0.188
Anti-HBs	121/312	38.8	77/191	40.3	0.778
HBsAg	3/318	0.9	20/205	9.8	<0.0001
Anti-HBc IgM	2/150	1.3	36/119	30.3	<0.0001
Anti-HBc	156/311	50.2	119/170	70	<0.0001
Anti-HBc only	79/156	50.6	43/118	36.4	0.02
HBeAg	1/3	33.3	8/33	24.2	1
Anti-Hbe	9/31	29	42/155	27.1	0.828
sAg/core proportion	3/156	2	20/119	16.8	<0.0001
Anti-HCV	209/313	66.8	164/198	82.8	<0.0001
HCV-RNA	116/290	40	76/136	56.3	0.002
Anti-HIV	3/318†	0.9	2/203	1	1

*Excluding 54 persons who participated in 1996.

†In addition, 1.1% (5/439) of the non-participants had previously tested positive for anti-HIV; the overall prevalence of anti-HIV was therefore 1.1%.

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Table II. Changes in serologic markers according to drug use in 1996 and 2007

	Non-IDU				p-value	IDU				p-value
	1996 n = 9 (7%)		2007 n = 79 (25%)			1996 n = 128 (93%)		2007 n = 241 (75%)		
n pos/N total, %	n/N	%	n/N	%	n/N	%	n/N	%		
Anti-HAV total	2/9	22	24/78	31	0.719	30/127	24	67/238	28	0.385
HBsAg	0/9	0	0/79	0	1	9/128	7	3/239	1.3	0.005
Anti-HBs	0/9	0	24/78	31	0.058	57/128	45	97/234	41	0.580
Anti-HBc IgM	0/1	0	0/5	0	1	26/90	29	2/145	1.4	<0.0001
Anti-HBc	1/9	11	5/78	6	0.491	90/126	71	151/233	65	0.239
Anti-HBc only	1/1	100	3/5	60	1	31/90	34.4	76/151	50.3	0.022
HBeAg	0/1	0	0/0	0	1	4/22	18	1/3	33	0.504
Anti-Hbe	0/9	0	1/2	50	0.182	34/126	27	8/29	28	1
sAg/core proportion*	0/1	0	0/5	0	1	9/90	10	3/151	2	<0.0001
Anti-HCV	1/9	11	9/79	11	1	115/128	90	200/234	85	0.257
HCV-RNA	1/9	11	4/77	5	0.433	70/119	59	112/213	53	0.301
Anti-HIV	0/8	0	0/79	0	1	0/127	0	3/239	1.3	0.554

*The sAg/core proportion is a calculated value (n HBsAg/n Anti-HBc)

Figure 1. Relationship between duration of intravenous drug use and sero-positivity.

