# Short versus standard schedule Hepatitis B vaccination to injecting drug users in prisons and drug treatment centres

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ABSTRACT

IDUs constitute a high risk group for HBV infection, both in prison and in society in general. Infection rates amongst this group are 100 times higher than amongst the general population. The recognition of this high risk factor of HBV amongst IDUs is generally accepted, and the Danish authorities recommend preventive vaccination for IDUs against HBV [56]. Unfortunately, new IDUs are infrequently in contact with health services and consequently are rarely offered the opportunity to receive vaccination. Several Danish drug treatment centres have offered vaccination to high risk adult IDUs for some time, whereas in prisons this service has only recently been made available. An added difficulty is that IDUs are not often willing to embark on and maintain a vaccination program. This may be one of the reasons why only 2% of Danish IDUs are vaccinated against HBV[1].

However, studies carried out amongst IDUs have found that between 21 and 65% of them have spent time in prison [31], although many IDUs did not spend sufficient time as inmates to receive the three vaccinal doses according to the standard program. This meant that treatment according to the accepted standard program was infrequently completed. It is commonly believed that a possible alternative is a "high-speed" program of three doses applied in a period of three weeks. This leads to the possibility of raising program completion to over 80%, However, this type of treatment may be less effective for seroprotection.

This study does not set out to validate the effectiveness of different vaccination programs. The vaccines used in these cases have been fully evaluated and results taken from vaccination programs amongst young healthy adults are comparable. The aim of this paper is to study compliance with different vaccination HBV programs that are offered to IDUs in prison. The use of data taken from studies of healthy individuals offers little in the way of useful information for this paper.

Consequently, this paper puts forward the question as to which program should be offered to IDU inmates.

In this study, we have included information provided by drug treatment centres about seroprotection so as to establish better estimates. Obviously this can not provide answers to vaccination compliance in prison. But the individuals receiving assistance in treatment centres have similar problems as regards the percentage of response to vaccination and frequency of infection.

Key Words: Hepatitis B, Vaccination, Prison

## INTRODUCTION

Hepatitis B (HBV) constitutes a major health problem to injecting drug users (IDUs) in Scandinavia as in the rest of the world. As vaccines against hepatitis B are available these infections are potential preventable even when transmission cannot be avoided. In a newly concluded survey of Danish prisoners only 2% of identified IDU prisoners were vaccinated against HBV.[1]

There are three major problems with vaccination of IDUs. 1) Many IDUs become infected with HBV early in their injecting career before they are offered vaccination. 2) A low compliance to standard vaccination schedule among IDUs, and 3) A low efficacy among IDUs compared to healthy young adults.

## HEPATITIS B AMONG IDUS

### Prevalence:

In a review by Levine, the worldwide HBV prevalence among 9566 IDUs was 74% (range 38-99.2) with 9% HBsAg positive.[2] The prevalence of HBV has probably decreased since the middle eighties and seems to follow the tendency in the general population, only at a much higher level.[3-4] Cyclic outbreaks of HBV have been repeatedly reported, supposed to reflect the gradual accumulation of new susceptible IDUs.[2, 5- 6]

Three Danish studies of hepatitis among IDUs have recently been concluded.[1, 7-8] Results are in agreement and give an average prevalence for Danish IDUs of 66.0% [95% confidence 62-70%] for HBV. The prevalence of hepatitis B markers (and markers of other bloodborne infections) increases with duration of drug use. [1, 9]

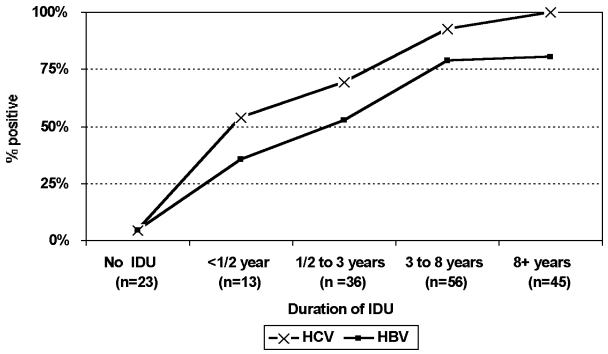


Figure I: Prevalence of hepatitis among Danish IDUs according to duration of druguse.[1]

### Incidence:

Incidence studies among IDUs are difficult to perform due to problems with recruitment and compliance.[2] Most studies have been performed in drug treatment centres and are not necessary applicable to IDUs outside of treatment. Table I sum-

| Country (1. author) | Sample/ period | Population At risk | Time at risk in py[a] | Sero-conversions | Incidence /100 py | Prevalence at entry | Ref. |
|---|---|---|---|---|---|---|---|
| Holand (Ameijden) | DTC[b] (1985-88) | HBV : ? | 132 | 12 | 9.1 | 73% | 10 |
| USA (Levine) | Outreach program[c] (1988-92) | HBV : 240 | 74 | 78<br>0 | 1988: 24.4<br>1992: 0 | 73% | 11 |
| Australia (Crofts) | Outreach program (1990-95) | HBV: 286 | 276 | 5 | 1.8 | 45% | 12 |
| USA (Hagan) | DTC (1994-96) | HBV: 460 | 509 | 46 | 10.0 | 68% | 13 |
| Switzerland (Broers) | DTC (1988-95) | HBV : (88) | (238) | 5 | 2.1 | 1988: 61%<br>1995: 28% | 14 |
| Average incidence | All cited | HBV | (1680) | 203 | 12.1 [10.4-13.9][d] | | d |

a: Person years (al data in parentheses estimated by the author).
b: Drug Treatment Centres (most methadone maintenance clinics).
c: IDUs recruited both at treatment centres and at street level, to include IDUs not in contact with drug programs
d: Based on:[10-14]

Table I. Incidence studies of HBV among IDUs.

maries studies on transmission rates among IDUs. These incidence studies show elevated levels of viral transmission compared to the general population (where reported incidence is in the order of 100 times lower).

Studies mentioned in Table I and additionally studies with incidence rates gives a reported range of HBV incidence of 0-24/100 py, with a mean incidence of 12.1/100 py [95% C.I. 10.4-13.9].

The average incidence calculates might overestimate current transmission rates among IDUs because of the decreasing incidence over time.

## HEPATITIS B AMONG PRISONERS

### Prevalence:

The literature of serological studies from prison populations has produced a broad range or results. In general the prevalence increases with the proportion of IDUs in the survey and with the level of serological markers in the general population. With these reservations prevalence of HBV has been found among 10-73% of tested with 0-15% HBsAg positive.[15-19] Among non-IDU prisoners prevalence is much lower, 1-3 times the prevalence in the general population.[17, 26]

In Scandinavia variable results have been found. In Norway 0-8% of prisoners were HBsAg positive (13.1% among IDUs) and 20-30% had past HBV infection, compared to 4.1% in the general population.[17, 22] Likewise, in a recent survey, 9,3% among IDU prisoners in the Danish State prison of Nyborg were HBsAg positive and 55% had past infection compared to 0,5% and 13% respectively among non-IDU prisoners.[1] A survey among IDUs from Stockholm's remand prison performed in 1994 is shown in Table II.[9]

| Year of rist injection | < 1975 (n = 312) | 1975-1984 (n = 327) | 1985-1994 (n = 269) |
|---|---|---|---|
| HBV | 92.0% | 74.6% | 54.6% |
| HCV | 98.4% | 96.6% | 78.7% |
| VIH | 19.5% | 17.0% | 3,0% |

Table II. Prevalence of hepatitis among Swedish IDUs in remand prison[9].

### Incidence:

Reported incidence in prison studies (Table III) is significantly lover than among IDUs studied outside. The only exception is a study where the incidence is a mixture of transmission in and outside prison.[30] There may be several reasons for the lower incidence in prison: not all prisoners included are IDUs and several studies have an overrepresentation of long-term prisoners. These are believed to have less frequent risk behavior.[31] A third factor is that most studies of IDU outside prison are older than the prison studies and therefore must be anticipated to have higher incidence due a falling incidence during the last decade.[14]

It is a constant finding that IDU and young age is related to seroconversion. But interestingly Crofts found a "protective" effect of prison against hepatitis C seroconversion. This is supported by the lower incidence in prison, but it could also be due to a confounding effect of age or IDU in this study.[30] The inverse relation to age is the opposite of what has been found by most cross sectional studies. These findings are not in disagreement, but reflects that surveys investigate cumulated exposure.

## VACCINATION AGAINST HEPATITIS B

Vaccine against HBV has been available since 1982 were the first plasma-derived vaccines were licensed. These vaccines were formalin-inactivated extracts of HBsAg particles from healthy hepatitis B carriers. This vaccine was extensively evaluated in clinical trials and found to be both immunogenic and protective.[36] The efficacy trials of this vaccine established the seroprotective level of immunity to be 10 IU/l of anti-HBs. Above this level no clinical illness or chronic carriers were found, although subclinical infection did occur.[37-39] The next generation vaccine was genetically engineered by expressing the entire S-gene in a bacterial or yeast vector, thereby avoiding possible viral contamination.

| Country/ (1. author) | Sample/ (period) | Population at risk | Seroconversions/ Time at risk in PY[1] | Incidence /100 PY | Prevalence | IDU% | Ref. |
|---|---|---|---|---|---|---|---|
| USA/ (Kelley) | Military prison (1982-85) | HBV : ? | 25/(1250) | 2 | ? | ? | 32 |
| USA/ (Decker) | State-prisons (1983-84) | HBV : 275 | 4/290 | 1,38 | 28,8% | 51% | 33 |
| USA/ (Hull) | State-prison (1982-83) | HBV : 122 | 1/(125) | 0,8 | 46,8% | 41% | 33 |
| Australia/ (Crofts)[2] | State-prison (1991-92) | HBV : 180 | IDU: 9/(47)<br>non-IDU: 1/(32) | 19,3<br>3,1 | 52%<br>16% | 46% | |
| Germany/ (Keppler) | Prison for women[3] (1992-94) | HBV : 91 | IDU: 9/(?)<br>non-IDU: 2/(?) | | 63%<br>28% | 50% | 35 |
| | | HBV : 101 | IDU: 23/(?)<br>non-IDU: 1/(?) | | 66%<br>29% | | |
| Denmark/ (Christensen) | State prison 1996-97 | HBV : 90 | IDU: 2/12,5<br>non-IDU: 1/30,7 | 15,6<br>3,3 | 64,3<br>13,5 | 43% | 1 |
| Average incidence[5] | All cited | HBV: ? | 43/1787,2 | 2,4[1.8-3.2] | | | |

1 Person years (all data in parentheses estimated by the author, ~ indicates only approximate data available).
2 Test at entry and re-entry median time in prison 44 days, outside 153 days.
3 Data from medical records over two years. No time at risk stated. 49% (20/41) of transmissions occurred in prison.
4 IDUs tested at entry and re-entry, time in prison not stated.
5 Based on [1, 30, 32-34]

Table III. Incidence studies of HBV among prisoners.

It proved to have the same high efficacy (95% of young healthy adults seroprotected by the 0,1,6 month regime) as the plasma-derived vaccines, but has for ethical reasons not been evaluated against placebo.[40-41]

Table IV compares resent studies of the anti-HBs response among healthy adults after three doses of vaccine. The four first rows are with the standard schedule that has been shown to induce seroprotection among 95% of young healthy adults. A possible reason for the lower response rates in the two US studies was that serology test were performed later than one month after last dose. Lower vaccine response in healthy populations has been found among males, smokers, obese and a decreasing immune response is seen with increasing age.[36]

The rest of Table IV shows the effect of accelerated regimes with data of seroprotection after the third dose. Most of the studies incorporated a booster after one year because of lower antibody titers achieved by the accelerated schedule. As anti-HBs >10 IU/l at month 7 after the standard regime has been proven to protect against clinical hepatitis B, this table indicates that a booster dose may not be necessary.

Table V summaries recent IDU vaccination trials. In some but not all IDUs have a lower compliance and seroprotection rate after a standard regime. The picture for the accelerated regimes is not clear: some found the same seroprotection level, while others found a markedly lower responsrate. This may partly be due to anti-HBs test performed already at month 3

or only after 9-10 month when the anti-HBs titer might be increasing respectively decreasing as compared to month 7. Also if anti-HBc positives are included in vaccination trials this could overestimate vaccine response rates.[1] Although a poorer vaccination response cannot be excluded with an accelerated regimen, this could be compensated by a higher compliance with short schedules.

| Country/ Population/ (1. author) | Number | Vaccination schedule | Vaccination compilance | Time after 1. Vaccination | % seroprotected[a] | Ref. |
|---|---|---|---|---|---|---|
| USA/ HCW (Wood) | 595 | Recombivax HB /Engerix B 20µg 0,1,6 month | ND | 7-12 month | 89% | 42 |
| USA/safety pers. (Room) | 528 | -do- | ND | -do- | 88% | 43 |
| Denmark/ HCW (Jepsen) | 830 | Engerix B 20µg 0,1,6 month | 37% of total 86% of started | 7 month | 95% | 44 |
| Germany/ HCW (Hess) | 143 | Engerix B 20µg 0,1,6 month | 99% | 7 month | 96% | 45 |
| | 141 | -do- 0,1,2,12 month | 91% (3.dose) | 7 month | 90% | |
| France/ Mixed pop. (Marchou) | 270 | Genhevac B 0,1,2,12 month | | 12 month (Before 4.dose) | 95% | 46 |
| | | -do- 0,10,21 days,12. month | | 12 month (Before 4.dose) | 93% | |
| Germany/ HCW (Bock) | 101 | Engerix B 20µg 0,1,2 month | 57% of 498 available 93% of started | 7 month | 94%[c] | 47 |
| | 109 | -do- 0,14,21 days | | 7 month | 94%[c] | |
| | 96 | -do- 0,7,21 days | | 7 month | 94%[c] | |
| Sweden HCW (Wahl) | 27 | Hb vacine 10µg (MSD) 0,14,42 days | 98% | 7 month | 100% | 48 |
| | 26 | 0,1,6 months | 98% | 7 month | 100% | |

a: anti-HBs >10IU/L (percent of tested).
b: Health Care Workers.
c: No significant difference between groups. Response rate reported for the three groups combined.

Table IV. Hepatitis B vaccination response among healthy adults according to schedule.

| Country/ 1. author | Number at risk | Vaccination regime | Vaccination compliance | Time after 1. Vaccination | % seroprotected[a] | Ref. |
|---|---|---|---|---|---|---|
| Spain (Rodrigo) | 197 | Engerix B 20µg 0,1,2 month | 70% | 3 month | 57% | 49 |
| Italy (Mezalani) | 53 | Engerix B 20µg 0,1,6 month | 85% | 7 month | 94% (seroconversion) | 50 |
| Italy (Rumi) | 17 | -do- | ND | 7 month | 76% | 51 |
| | 15 anti-HBc only | -do- | ND | 7 month | 6% | |
| Italy (Salassa) | 63 (healthy controls) | Hevac B Pasteur 5mcg 0,1,6 month | 100% | 7 month | 100% | 52 |
| | 63 | -do- 0,1,6 month | 94% | 7 month | 85% | |
| | 56 | Engerix B 20µg | 100% | 3 month | 87% | |
| | 0[b],1,2,12 month | (3 dose) | | | | |
| | 106 | -do- | 98% | 3 month | 86% | |
| | 0,1,2,12 month | (3 dose) | | | | |
| France/ Prisioners (Rotily) | 292 (17% IDU) | Engerix B 20µg 0,1,2 month | 60% | ND | | 53 |
| Spain/ Prisioners (Bayas) | 191 (51% IDU) | Engerix B 20µg 0,1,6 month | 36% | 7-8 month | | 54 |
| Denmark (Christensen) | 32 0,1,2 month | Engerix B 20µg | 74% | 9-10 month | 50% | 1 |

a: anti-HBs >10IU/L (percent of tested).
b: 40µg at day 0.

Table V. Vaccination studies among injecting drug users.

## GUIDELINES FROM PRISON HEALTH CARE AUTHORITIES FOR IDU HEPATITIS VACCINATION

Swedish and Danish IDUs prisoners are offered Hepatitis B vaccine according to accepted guidelines (month 0, 1, and 6).

## OTHER ACCEPTED GUIDELINES

Engerix B®, the most commonly used Hepatitis B vaccine in Denmark is authorized in Denmark according to normal guidelines with 3 doses given a month 0, 1 and 6 and an accelerated treatment with 4 doses for newly exposed individuals. (month 0, 1, 2, and 12). The vaccine could also be applied by means of 3 doses during days 0, 7, and 21 on certain occasions. In this case one memory dose per year is recommended[55].

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