

# Acute Hepatitis B in Western Sweden – Genotypes and Transmission Routes

M. Lindh, P. Horal, G. Norkrans

## Summary

A retrospective study of acute hepatitis B (AHB) during 1995–1996 in Göteborg, Sweden, was carried out to investigate whether the increasing number of hepatitis B virus (HBV) carriers due to immigration in northwestern Europe has influenced the incidence or genotype heterogeneity. 24 cases of AHB were identified, the probable transmission route of which was intravenous drug use (IVDU) in 11 (46%), heterosexual in six (25%), homosexual in one, hemodialysis in two and unknown in four cases. In no case was the source an immigrant with chronic HBV infection. Genotype D was seen in 12 patients, seven being anti-HCV-positive IVD users, two probably infected heterosexually and three with an unknown source. Genotype A was found in six patients: three IVD users, a sexual partner of an IVD user and two dialysis patients. Genotype B was found in one patient infected during travel to Vietnam, and genotype C in one patient, probably infected sexually from a previously identified chronic carrier. In conclusion, genotype D is the main genotype and IVDU still the major risk factor for AHB in Göteborg, while transmission from immigrants appears to be of minor importance despite the fact that this group comprises over 90% of the young, highly infectious carriers.

## Key Words

HBV · Epidemiology · Genotyping

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## Introduction

Formerly, acute hepatitis B (AHB) was mainly a problem in certain risk groups, such as health care workers, recipients of blood products, dialysis patients and homosexuals. In the last few decades, the incidence of AHB has decreased in northwestern Europe [1–3], in particular in these risk groups, probably as a result of preventive measures. Instead, intravenous drug use (IVDU) and heterosexual transmission have gained in importance [4, 5]. During the same period the number of chronic hepatitis B virus (HBV) carriers has increased dramatically, due to immigration from endemic regions [2]. This could result in secondary cases and the appearance of foreign

genotypes in patients with AHB. For example, genotypes B and C would be observed in case of transmission from East Asian carriers who are often highly viremic. In the present study, we analyzed the epidemiological situation with focus on genotypes and transmission routes, studying all identified cases of AHB during 1995 and 1996 in Göteborg, a city on the west coast of Sweden with a large immigrant population.

## Patients and Methods

### Patients

Residents in Göteborg with verified AHB during 1995–1996 were included. The patients were identified at the Department of Infectious Disease, the Department of Clinical Virology or through reports to the Department of Communicable Disease Control and Prevention. Göteborg has 450,000 inhabitants, 20% of whom are immigrants, the majority from areas with high or medium to high prevalence of HBV infection. Essentially all adult patients with acute hepatitis and a verified or suspected viral etiology are admitted to the Department of Infectious Diseases. Reporting new cases of acute viral hepatitis to the Department of Communicable Disease Control and Prevention has been mandatory for many years. The diagnosis was confirmed by anti-HBc IgM or (in three patients, including two dialysis patients) a shift from negative to positive HBsAg. Except for the two patients infected at a dialysis unit, all patients had been admitted to the Department of Infectious Diseases, Östra Hospital, which is the only infectious diseases clinic in the area. Data were registered from patient files.

### Serology

HBsAg and anti-HBc IgM were analyzed by AxSym CoreM (Abbott, Abbott Park, IL). Anti-HCV was analyzed by Murex anti-HCV (Murex Diagnostics Ltd, Kent, UK).

### Genotyping

Restriction fragment length polymorphism (RFLP) of amplicons from the S or pre-S [6, 7] regions was used for genotyping. As described previously, most genotype D strains produce either of two

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pre-S RFLP patterns (arbitrarily designated D1 and D2, Figure 1) due to a single nucleotide difference (at nt 2847). These terms (D1 and D2) are also used in this paper.

## Results

24 patients with AHB were identified, 21 males and three females. The mean age was 34 years (range 21–59 years). 18 patients were native Swedes and six were immigrants; four from the Middle East, one from Argentina and one from Vietnam. As shown in table 1, the probable transmission route was IVDU in 11, heterosexual in six, homosexual in one, dialysis in two and unknown in four cases. Out of the six heterosexually transmitted cases, two (both females) were infected from IVD users, and two (both immigrants from the Middle East) acquired the infection during travels to eastern Europe and the Middle East, respectively. In two cases, classified as acquired by IVDU, heterosexual transmission was possible, but considered less probable than IVDU. Ten of the 24 patients were anti-HCV positive; all but one of them admitted IVDU.

Genotype A was found in six patients, B in one, C in one and D in 12 and could not be established in four cases because PCR was negative (Table 1). In seven of the 12 cases with genotype D the probable infection route was IVDU, in two cases it was heterosexual contact and in three the source was unknown. The seven IVD users with genotype D presented a pre-S genotyping pattern D1, as did one anti-HCV-positive patient who denied IVDU. One patient infected sexually in the Middle East and two with unidentified source of infection showed pre-S RFLP pattern D2. Genotype A was found in three patients probably infected by IVDU, in one patient infected sexually from an IVD user, and in two patients infected at a dialysis ward. Sequencing (not shown) revealed that the strains from the two dialysis patients were phylogenetically close to a database sequence of Philippine origin (M57663), identifying the source as a fellow dialysis pa-

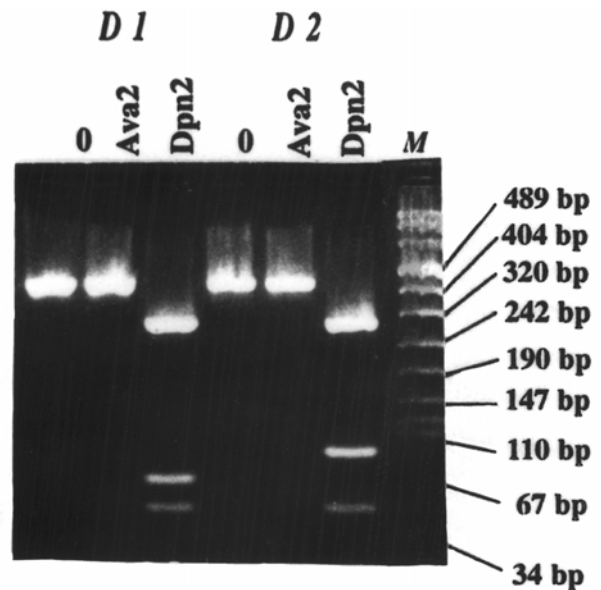


Figure 1  
Hepatitis B virus restriction fragment length polymorphism (RFLP) patterns representing genotype D. The first lane (0) shows untreated PCR product (nt 2823–80 in the pre-S region), and the second and third lanes show the same fragment incubated with Ava2 and Dpn2. Genotype D strains do not have any Ava2 site, but two (D2) or three (D1) Dpn2 sites.

tient who had contracted the infection in the Philippines. A genotype B strain was seen in one patient, a 36-year-old Vietnamese who had lived in Sweden since 1979, and who had probably been infected, via an unknown route, during travel to Vietnam. Genotype C was observed in the steady partner of a Swedish female chronic carrier, who also was found to be infected with genotype C, and who had probably contracted the infection 15 years earlier in Thailand.

Table 1

### Genotype and probable transmission route in 24 patients with acute hepatitis B.

Genotype	Transmission route					Unknown
	IVDU	Heterosexual, from IVDU	Heterosexual, other source	Homosexual	Dialysis	
A (n = 6)	3	1			2	
B (n = 1)						1
C (n = 1)			1			
D (n = 12)	6 <sup>a</sup>	2 <sup>b</sup>	1 (D2)			3 <sup>c</sup>
Not detectable (n = 4)		1		2	1	

D1 and D2 refers to genotyping patterns by pre-S RFLP (see Genotyping).

<sup>a</sup> all D1 and anti-HCV+; <sup>b</sup> both D1, 1 anti-HCV+; <sup>c</sup> 1 D1 and anti-HCV+, 2 D2

## Discussion

The present study indicates that the greatly increased prevalence of chronic HBV infection due to immigration has not influenced the incidence of AHB in Sweden, and that IVDU still is the major risk factor, being the probable transmission route in 46% of the cases (11/24). Heterosexual contact was the second most important transmission route, recorded in 25% (6/24); two of them were probably infected sexually from their IVD-using partner. In contrast, homosexual transmission appears to be rare (one case). It is possible that some infections considered as being transmitted through IVDU instead were sexually contracted. However, the fact that most of these patients also had HCV antibodies supports the view that they had indeed exposed themselves to blood

from fellow IVD users, as HCV is rarely transmitted sexually. Contact with female prostitutes may constitute a risk for acquiring HBV infection [8], but was not documented in any case.

Immigration has increased more than fivefold the number of chronic HBV carriers in Göteborg over the past 15 years and immigrants now constitute more than 90% of the HBV carriers in Göteborg, implicating a risk for an increasing incidence of AHB. However, transmission from immigrants with chronic HBV infection was not documented in any case, possibly indicating that the preventive measures directed towards this group (i.e. information and an offer of cost-free vaccination of steady sexual partners) are indeed effective. Thus, although asymptomatic cases of AHB were not identified in the present study, transmission from immigrant carriers to native Swedes seems to be rare. Instead, non-immune immigrants appear to be at risk for contracting HBV infection during visits to their area of origin: Three male immigrants who had been living in Sweden for several years acquired the infection traveling to endemic regions, at least two of them were probably infected by heterosexual route.

Genotype D dominated and was found in 12 cases, including seven IVD users and a sexual partner of an IVD user presenting a pre-S RFLP pattern D1. All but one of these eight patients with pattern D1 were anti-HCV-positive. We have previously observed that this pattern is typical for IVDU-related HBV infection while pattern D2 is mainly seen in carriers of Middle Eastern origin [7]. Genotype A, which originally prevailed in northern Europe and still predominates in Swedish chronic HBV carriers [6], was less important as the etiology of AHB, and was seen in known risk groups only (IVDU or dialysis). A reduced importance of genotype D was already observed in the 1970s, then described as a shift from serotype adw to ayw [9, 10].

In summary, the incidence of AHB has not increased despite the dramatic increase in the number of HBV carriers due to immigration. Instead, acute hepatitis is still strongly associated with IVDU. These results seem to indicate that further preventive efforts directed towards IVD users, mainly information and partner immunization, might be more cost-efficient than a general HBV vaccine campaign in low-prevalence countries like Sweden, at least in a shorter time perspective. The study also shows that genotyping is useful for analyzing the epidemiology of HBV infection and may be helpful in clinical work for tracing the source of infection in individual cases.

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