

Burden of hepatitis B virus infection in Belgium

André Meheus, Carine Dochez

Incidence of hepatitis B virus (HBV) infection

Different types of data are available to describe the epidemiology of HBV infection. Most industrialised countries have systems in place to register/notify cases of hepatitis B (acute hepatitis B disease: symptomatic/clinical cases only; all cases: symptomatic plus asymptomatic cases) to a centralised health authority. These surveillance systems allow the estimation of the incidence of hepatitis B, which provides the best estimate for the risk for this condition.

As there is considerable underreporting, reported figures for hepatitis B must be corrected by a factor 2 to 10, depending on the country considered. Furthermore, symptomatic cases of hepatitis B comprise only 33-50% of all HBV infections, which means that the number of reported cases of hepatitis B disease must be multiplied further by a factor 2 to 3 to obtain an estimate of the true incidence of HBV infection. In summary, figures of reported clinical hepatitis B must be adjusted by a factor between 4 and 30 to estimate the true incidence of HBV infection.¹

Flanders (the northern, Dutch-speaking part of Belgium) updated in December 2000 its compulsory notification system, categorising infectious diseases in Group 1 (immediate telephonic reporting) and Group 2 (reporting by a laboratory or health worker within 48 hours of diagnosis). The different types of viral hepatitis are reportable in Group 2 (Table 1).²

Sentinel surveillance system in Belgium

The universal reporting system for infectious diseases, which includes also viral hepatitis, was shown in the 1970s to perform very poorly³ with most healthcare workers not reporting at all. Therefore, Belgium developed already in 1979 an additional surveillance system through a network of sentinel general practitioners (GPs).^{4,5} This sentinel GP system registered new cases of symptomatic viral hepatitis in the period 1982-1984 and 1991-1992. Aetiology of acute hepatitis was established through laboratory testing and estimates of annual incidence of the different types of viral hepatitis for the Belgian population were made.^{6,7}

Based on registrations through the GP sentinel surveillance system in 1991-1992, annual incidence of acute clinical hepatitis B in Belgium was estimated at six cases per 100,000 total population (95% CI = 4-10).⁸ All patients were between 20 and 49 years old. Incidence was 14 per 100,000 in 20-29 year olds, seven per 100,000 in the 30-39 year group, and five per 100,000 in the 40-49 years age group; 77% of cases were males. Major risk factors were sexual contact (31%), injecting drug use (23%), travel to endemic countries (23%), potential iatrogenic exposure (23%), and professional exposure (8%). None of the registered hepatitis B cases had received hepatitis B vaccine; 45% of cases were absent from work with a mean period of absenteeism of 81 days.

Table 1: Overview of the diseases to be reported in the Flemish Community²

Group 1	Group 2	
Botulism	Brucellosis	Anthrax
Febris recurrens	Cholera	Leptospirosis
Haemorrhagic fever	Diphtheria	Listeriosis
Legionellosis	Gastro-enteritis (> 2 cases)	Protozoan infections
Malaria	Gonorrhoea	Psittacosis
Meningococcosis	<i>H. influenzae</i> type b meningitis	Rickettsiosis
Plague	Hantaviriosis	Scabies
Poliomyelitis	Hepatitis A	Shigellosis
Rabies	Hepatitis B	Syphilis
Typhus	Hepatitis C	Tetanus
Any serious infectious disease	Pertussis	Trichinosis
Getting epidemic characteristics	Typhoid fever	Tuberculosis
	Yellow fever	
To be reported immediately by phone by physician and laboratory, to be confirmed in writing within 24 hours	Report within 48 hours after diagnosis by physician and laboratory	

A Meheus, C Dochez, Network for Education and Support in Immunisation (NESI), University of Antwerpen, Antwerpen, Belgium
Correspondence to: A Meheus, Network for Education and Support in Immunisation, University of Antwerpen, Campus Drie Eiken, Universiteitsplein 1, B-2610 Antwerpen, Belgium.
E-mail: carine.dochez@ua.ac.be

Already in the period 1982-1984, a first registration of clinical viral hepatitis was done through the GP sentinel system, with an attempt to distinguish between the different types of acute viral hepatitis.^{6,9} Estimated incidence of clinical hepatitis B was 25 (95% CI = 21-28) per 100,000

total population. Age distribution of cases was much more widely spread over the age groups than in 1991-1992, when 62% of cases were found in the 20-29 year age group. In 1982-1984, peak incidences were in the age groups 10-19 years, 40-49 years, and 60 and more years; risk factors were also very different, with 44% of cases indicating hospitalisation/medical intervention and 30% with no risk factor mentioned.

The decrease of the estimated incidence of clinical hepatitis B between 1982-1984 and 1991-1992 from 25 to six per 100,000 total population (i.e. with a factor 4.2) is spectacular. But a greatly decreasing incidence was also found for all clinical viral hepatitis (from 178 to 76 per 100,000, i.e. 2.3 times), for hepatitis A (from 72 to 23 per 100,000, i.e. 3.1 times), and for hepatitis C (from 15 to three per 100,000, i.e. 5.0 times).

The spectrum of risk factors also changed considerably. While in 1982-1984 iatrogenic hepatitis B transmission seemed still significant, in 1991-1992 hepatitis B clearly became a lifestyle disease, largely related to homo- and heterosexual activity, travel, and injecting drug use.¹ A change in sexual patterns of behaviour in the 1980s in relation to fear of HIV/AIDS might also have played a role in the decreasing incidence of clinical hepatitis B.

When interpreting the above figures derived from the GP sentinel surveillance system, two issues should again be stressed: 1) true cases might be underestimated as the system is limited to GPs, so some hepatitis B cases seen by paediatricians or in internal medicine might not be reported; 2) only acute clinical hepatitis is reported, so incidence of HBV infection should be estimated to be two to three times higher.¹

Mandatory notification versus GP sentinel surveillance

As shown in Table 2, there is considerable underreporting through the universal compulsory notification system. Only 11% of all cases of acute viral hepatitis are notified, while this proportion is 24% in the case of acute hepatitis B.

Incidence of clinical viral hepatitis B based on compulsory notification is 1.5 per 100,000 population (estimated incidence based on GP sentinel surveillance being six per 100,000).

If we want to estimate the incidence of HBV infection from the compulsory universal system for clinical hepatitis B we must multiply notified incidence by a factor 4 for underreporting and by 2 to 3 for asymptomatic infections. This means that annual true incidence of HBV infection in Belgium should be approximately 18 per 100,000 total population, meaning a total annual number of new infections of around 1800 (Belgium has approximately 10,000,000 inhabitants).

A supplementary problem with the compulsory notification system is that instead of notifying only clinical hepatitis B, healthcare workers have started to notify infections found during active case finding, while cases reported through the laboratory system have been added to reporting by clinicians. This happened for instance in the province of Antwerpen: notified cases of hepatitis B were 27 in 1998, 68 in 2000, and 270 in 2002, i.e. a four-fold increase. This could be explained

by notification of infections found through case-finding, adding laboratory hepatitis B notification and the occurrence of a few clusters of iatrogenic transmission due to capillary blood devices used in homes for the elderly.¹⁰ Adding asymptomatic cases to the reporting of acute hepatitis B cases complicates comparability and interpretation of the data. It was therefore recently recommended not to do so or at least to keep both categories separately.¹¹

Hepatitis B seroprevalence data

Global epidemiology of HBV infection is based on prevalence of HBV surface antigen (HBsAg) in the population. Countries are classified into three categories of hepatitis B virus endemicity: low (<2%), intermediate (2-7%), and high (=8%) prevalence of HBsAg. Both Flanders and Belgium as a whole are low-endemic areas (<2% HBsAg), historically classified in the subcategory 'very low-endemic' (i.e. <0.8% HBsAg and <20% overall HBV markers).¹²

Blood donor data are readily available, but in general grossly underestimate true prevalence of HBsAg in the population. A seroprevalence study based on a representative (age, sex, nationality/ethnicity) sample of the Flemish population was conducted in 1993-1994.¹³

Serum samples were analysed from 3,866 patients (traumatology, orthopaedics, otolaryngology, general surgery and intensive care departments in 10 hospitals). Prevalence of the different HBV markers is given in Table 3; 0.7% appeared to be HBV carriers and overall, 9.9% had an HBV marker. The category 'anti-HBs alone' could indicate previous infection with loss of anti-HBc or hepatitis B vaccination; it was estimated that two thirds of this category (prevalence 2.3%) was due to previous vaccination. This allows to estimate prevalence of previous exposure to/infection with HBV at 7.6% (0.7% HBsAg + 5.1% anti-HBs/anti-HBc + 0.6% anti-HBc alone + 1/3 x 3.5% anti-HBs alone). Related to the population of Flanders (5,825,000 inhabitants), this means that 40,000 are HBV carriers and 443,000 have been exposed to the virus. If we compare HBV markers for the Belgian and non-Belgian population in the sample, non-Belgians are at higher risk for HBV infection and are less often vaccinated (Table 4). Prevalence of HBV markers by age shows a very low prevalence (0.4%) in under 15-year olds with clear increases in 15-24-year olds (3%) and 25-34-year olds (7%), pointing to HBV transmission mainly in young adults (mainly sexual transmission and, to a lesser degree, injecting drug use). In a seroprevalence study in Wallonia (the southern, French-speaking part of Belgium), prevalence of exposure to HBV was 3.9% in 18-29-year olds, a rate similar to the one found in Flanders; among 5- to 9-year olds, 1.9% showed HBV exposure, of which 1.2% were HBV carriers.¹⁴

In Flanders, a prevalence study of the different types of viral hepatitis was conducted in 2003, 10 years after the initial one.¹⁵ Instead of a hospital-based sample, the study population was now selected from the general public, and hepatitis tests were done on saliva specimens. Only HBsAg was determined in 1,830 swabs suitable for testing. Prevalence of HBsAg was 0.66% (95% CI=0.51-0.84), a rate very similar to the one found in the 1993 study (0.7% HBsAg prevalence; 95% CI=0.5-1.0%).¹³

Table 2: Comparison of data on acute viral hepatitis and hepatitis B from compulsory notification with sentinel GP surveillance in 1991-1992 (data adapted from reference 8)

	Compulsory notification (n)	Estimates based on sentinel GPs (n)	Percentage notified (%)
Hepatitis B	280	1150	24
All viral hepatitis	719	6308	11

Table 3: Prevalence of hepatitis B virus markers in the Flemish population in 1993-1994 (n = 3866)¹³

Hepatitis B marker	Prevalence (%)	Prevalence (95% CI)
HBsAg	0.7	0.5 - 1.0
Anti-HBs / anti-HBc	5.1	4.5 - 5.9
Anti-HBc alone	0.6	0.4 - 0.9
Anti-HBs alone	3.5	2.9 - 4.1
Any HBV marker	9.9	9.0 - 10.9

Table 4: Prevalence of hepatitis B virus infection (%) in the Flemish population in 1993-1994, according to nationality¹³

	Belgians (n = 3190)	Non-Belgians (n = 247)
HBsAg positive	0.7	1.2
HBV exposed	6.9	13.4
Vaccinated (estimation)	2.3	0.8

Table 5: Prevalence of HBV infection in selected population groups in Belgium (in order of decreasing prevalence of any HBV marker)¹⁷

	n	HBsAg (%)	Any HBV marker (%)	Year of study
Political refugees	774	11.1	77.6	1987 - 1989
Injecting drug users	131	7.6	54.6	1990
Mentally handicapped in institutions	770	10.3	51.8	1985 - 1986
Adopted children	148	6.8	n.a.	1993
Male homosexuals	520	3.5	36.3	1985 - 1986
Prostitutes	197	1.0	35.1	1987 - 1992
Home contacts of HBV-positive mentally handicapped	111	11	28	1990 - 1991
Prisoners	971	4.4	21.1	1992 - 1993
Healthcare workers with blood exposure	1129	n.a.	10	1982 - 1983
Staff of institutions for mentally handicapped	1290	n.a.	7.3	1982 - 1983
Pregnant women	8641	0.8	n.a.	1982 - 1987

n.a.: not available

Many more data are available on prevalence of HBV infection in selected population groups, allowing the identification of so-called 'risk groups'. Table 5 summarises a number of those studies for the period 1982-1993.^{16,17} The problem with this type of data is that it is impossible to discern between increased prevalence due to at-risk behaviour and increased prevalence due to a highly different background prevalence of infection in individuals coming from diverse geographical areas. Nevertheless, these data are useful to target public health interventions.¹⁸ For instance, it was already clearly demonstrated in a study in Antwerpen, Belgium, in 1981-1982 that male homosexuals represent a high-risk group for hepatitis B virus infection: 4.1% were

HBsAg positive, 30.7% anti-HBs positive, and 34.4% positive for any HBV marker.¹⁹ Prevalence rates were very similar to those found in Amsterdam during that period. Sex workers are considered another high-risk group. In a study in Ghent, Belgium, among 123 prostitutes in 1988-1989, none was HBsAg positive, 16.2% were anti-HBc positive, and 19.5% were positive for any HBV marker;²⁰ in Brussels, Belgium, in 1995-1997, among 205 prostitutes 2.5% were HBsAg positive and 20.5% were positive for any HBV marker.²¹ In Antwerpen, Belgium, in 1999-2000, among 92 female prostitutes 2.2% were HBsAg positive and 20.7% were anti-HBc positive; among 20 male prostitutes, 10% were HBsAg positive and 40% were anti-HBc positive.²²

Among injecting drug users in a methadone maintenance programme, 62% were anti-HBc positive in Antwerpen (n=205) and 21% in Limburg (n=105).²³

Estimate of burden of disease

Based on the surveillance data discussed in the first part of this article, approximately 2,000 new HBV infections should occur in Belgium each year. In Figure 1, we use the Centers for Disease Control and Prevention (CDC) model on disease burden estimates for the United States of America (USA), which is largely applicable to other industrialised countries with HBV transmission mainly in older adolescents and young adults.^{12,24} The figure estimates the new annual HBV chronic carriers at 120 to 200, leading to approximately four deaths from liver cirrhosis and one death from primary liver cancer.

Belgium, as most of the countries of the WHO European Region, decided on universal hepatitis B vaccination by the end of the 1990s, based on burden of disease estimates for hepatitis B and on cost-effectiveness studies of different types of vaccination programmes.^{25,26} Only a few countries (i.e. the United Kingdom, the Netherlands, and the Scandinavian countries) kept a targeted vaccination programme (the so-called high-risk strategy).²⁷

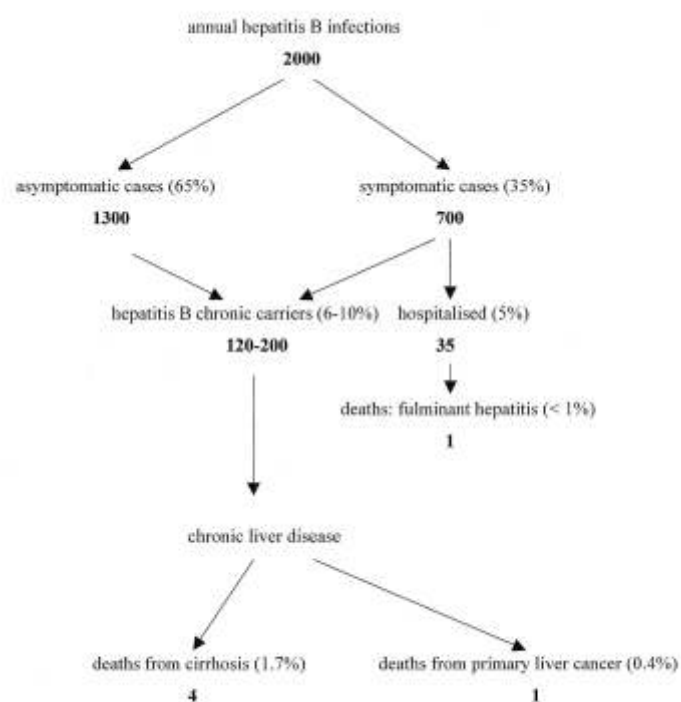


Figure 1: Estimated outcome of hepatitis B infection in Belgium (scheme adapted from reference 24)

Conclusion

HBV infection and the overall burden of disease caused by it is of importance in Belgium, but is by far not the priority health condition it is in the highly endemic regions of Africa, South-east Asia, and the Pacific islands. Belgium, as most of the European countries, introduced universal hepatitis B vaccination in 1999. A combined infant-adolescent

programme was implemented: a three-dose schedule in young adolescents (12-year olds cohort) and in 0-1 year olds integrated in the basic infant vaccination schedule. Since 2004, for hepatitis B vaccination of infants a combined, so-called hexavalent vaccine is used (IPV-DTPa-Hib-HBV). Twelve years after 1999, in 2011, the adolescent scheme can be stopped and in that year 24 birth cohorts will have been covered by universal hepatitis B vaccination.²⁸ The universal vaccination programme should have a considerable impact on incidence of hepatitis B virus infection in the country. The surveillance system in place should inform us timely about the real impact of hepatitis B vaccination, on condition that it is valid enough to do so.

References

- Meheus A. Risk of hepatitis B in adolescence and young adulthood. *Vaccine* 1995; **13**(Suppl 1): 31-34
- De Schrijver K. Evaluatie van outbreakonderzoek en outbreaksurveillance in het kader van de verplichte melding van infectieziekten. PhD Thesis. Antwerpen: Universiteit Antwerpen, 2004: 215
- Meheus A, Eylenbosch W. Evaluation of the notification of venereal diseases as a basis for contact tracing in Belgium. *Tijdschr Soc Geneesk* 1976; **54**: 22-25
- Stroobant A, Van Casteren V, Thiers G. Surveillance systems from primary-care data: surveillance through a network of sentinel general practitioners. In: Eylenbosch W, Noah ND, eds. *Surveillance in Health and Disease*. Oxford: Oxford University Press, 1988: 62-74
- Lobet M, Stroobant A, Mertens R, et al. Tool of validation of the network of sentinel general practitioners in the Belgian health care system. *Int J Epidemiol* 1987; **16**: 612-618
- Walckiers D. Hepatitis in België 1982-1983. Registratienet van de huisartsenpraktijken. Scientific Institute of Public Health Division of Epidemiology, June 1987
- Vranckx R, Walckiers D, Stroobant A, Thiers G. Sero epidemiological characteristics of hepatitis C encountered in general practice in Belgium. *Eur J Clin Microbiol Infect Dis* 1992; **11**: 62-64
- Devroey D, Van Casteren V, Vranckx R. Evolutie van de incidentie van klinische acute virale hepatitis in de Belgische huisartsenpraktijk. Registratienet van de huisartsenpraktijken. Scientific Institute of Public Health, January 1997: 34
- Walckiers D, Vranckx R, Stroobant A, Thiers G. Quelques caractéristiques séro-épidémiologiques des hépatites virales en médecine générale: résultats d'une enquête-pilote réalisée en Belgique. *Rev Epidém Santé Publ* 1988; **36**: 429-435
- De Schrijver K, Maes I, Van Damme P, Tersago J, Moës E, Van Ranst M. An outbreak of nosocomial hepatitis B virus infection in a nursing home for the elderly in Antwerp (Belgium). *Acta Clin Belg* 2005; **60**: 63-69
- Recommendations for hepatitis A and B surveillance and prevention strategies: proposal from the EUROHEP.NET project to the European Commission. www.eurohep.net/files/reports/Recommendationsdec2005.pdf (Accessed February 2008)
- Margolis HS, Alter MJ, Hadler SC. Hepatitis B: evolving epidemiology and implications for control. *Semin Liver Dis* 1991; **11**: 84-92
- Beutels M, Van Damme P, Aelvoet W, et al. Prevalence of hepatitis A, B and C in the Flemish population. *Eur J Epidemiol* 1997; **13**: 275-280
- Van Loock F, Rubbens C. Enquête sur la prevalence de l'hépatite B en Communauté française de Belgique. Report Scientific Institute of Public Health, Brussels, November 1994
- Quoilin S, Hutse V, Vandenberghe H, et al. A population-based prevalence study of hepatitis A, B and C virus using oral fluid in Flanders, Belgium. *Eur J Epidemiol* 2007; **22**: 195-202
- Van Damme P. Hepatitis B: epidemiology and evaluation of vaccination. PhD Thesis. Antwerpen: Universiteit Antwerpen, 1994: 493
- Van Damme P, De Groote K, Deprettere A, Michiels P. Hepatitis A in België: epidemiologie en vaccinatiebeleid. *Tijdschr Geneesk* 1997; **53**: 1135-1145
- François G, Hallauer J, Van Damme P. Hepatitis B vaccination: how to reach risk groups. *Vaccine* 2002; **21**: 1-4
- Coester C-H, Avonts D, Colaert J, Desmyter J, Piot P. Syphilis, hepatitis A, hepatitis B, and cytomegalovirus infection in homosexual men in Antwerp. *Br J Vener Dis* 1984; **60**: 48-51
- Mak R, Plum J, Van Renterghem L. Human immunodeficiency virus (HIV) infection, sexually transmitted diseases and HIV-antibody testing practices in Belgian prostitutes. *Genitourin Med* 1990; **66**: 337-341

21. Prevost C, Cheront C, Bertrand F, Tonglet R. Relevance and feasibility of hepatitis B vaccine administration to prostitutes in Brussels, Belgium. *Arch Publ Health* 2000; **58**: 37-48
22. Wouters K, Van Damme P, Vercauteren A, Verheyen J, Castermans S, Meheus A. Sexually transmitted infections (STI) among prostitutes in Antwerp, Belgium. Importance and feasibility of a hepatitis B vaccination programme. *Arch Public Health* 2002; **60**: 27-38
23. Matheï C, Robaey G, Buntinx F, Van Damme P. Prevalence and determinants of hepatitis C in drug users in Flanders, Belgium: regional differences. *Arch Public Health* 2003; **61**(Suppl 1): 18
24. Shapiro C. Epidemiology of hepatitis B. *Pediatr Infect Dis J* 1993; **12**: 433-437
25. Beutels P, Tormans G, Van Damme P, Van Doorslaer E. Algemene vaccinatie tegen hepatitis B in Vlaanderen: kosten-effectief? *Tijdschr Soc Gezondheidsz* 1996; **74**: 272-281
26. Van Damme P, Kane M, Meheus A. Integration of hepatitis B vaccination into national immunisation programmes. *Br Med J* 1997; **314**: 1033-1037
27. Leuridan E, Vorsters A, Van Herck K, Van Damme P, for the Eurohep.net team. Hepatitis A and B surveillance and immunization programmes in Europe: EUROHEP.NET project. *Arch Public Health* 2005; **63**: 199-217
28. Van Kerschaver E. The Belgian Expanded Programme on Immunization (EPI) and hepatitis B vaccination. *South Afr J Epidemiol Infect*, this issue.