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Hepatitis B: A public health problem

by

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1. Abstract

Hepatitis B is a major public health problem and remains an important infection in the community despite the availability of safe and effective vaccines since more than 15 years.

Because hepatitis B infection is largely asymptomatic, with possible longterm complications occuring after many years, it has not received the attention it deserves. The failure of the high risk immunization strategy and a better understanding of the burden of disease of hepatitis B, have caused a profound re-evaluation of the current vaccination strategies (1, 2).

Government delegates to the World Health Assembly agreed in May 1992 that all countries should integrate hepatitis B vaccination into their national immunization programmes by 1997 (3).

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In western Europe, some countries still remain unconvinced that the burden of disease warrants the expense of universal vaccination. However, epidemiological data emphasize the necessity for action. In addition, economic evaluations showing that universal hepatitis B vaccination is cost-effective in low-endemic countries, indicate that control of hepatitis B by universal immunization is attainable.

Key words

Belgium, Epidemiology, Hepatitis B, Prevention, Public health.

2. The clinical consequences of hepatitis B

2.1. The virus

The hepatitis B virus (HBV) belongs to a group of viruses known as the hepadnaviridae (4). Forty-two nanometers (nm) in diameter, it consists of a DNA viral core and an outer protein coat (nucleocapsid). The viral core contains partially double stranded DNA, a DNA polymerase, a core antigen (HBcAg) and an „e" antigen (HBeAg). The HBeAg is a cleavage product of the HBcAg (5).

The nucleocapsid carries the major antigenic determinant of the virus, i.e. the hepatitis B surface antigen (HBsAg)[a]. Excess HBsAg exists in serum in spherical and tubular forms, and highly purified preparations of the spherical forms are the basic component of HB vaccines.

When HBV infects an individual, the viral DNA completely reproduces itself within the liver cells of its host.

The HBV has no direct cytopathic effect; its presence evokes an immune response which leads to immune lysis of the infected hepatocytes[b] and subsequent cell death; this may result in serious pathological consequences. The incubation period for hepatitis B infection (=time between infection and onset of symptoms) varies between 50 and 180 days.

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[a] HBsAg was formerly called Australia antigen. It is immunogenic but not infectious, and forms the basis of hepatitis B vaccines.

[b] After infection, the virus introduces into a hepatocyte; this infected hepatocyte shows viral antigens on its surface. These represent a target for cyototoxic T cell lysis (5).

2.2. Course of the HBV infection

2.2.1. Acute versus chronic infection

Hepatitis B infection produces a wide variety of acute and chronic manifestations, ranging from asymptomatic disease without jaundice to a fulminating disease resulting in death.

There are three major outcomes of hepatitis B infection: after infection one may present a symptomatic or asymptomatic acute infection and subsequently develop lifelong immunity, one may become a chronic carrier, and be at risk of serious longterm complications, or one may die of fulminant hepatitis within days after onset. Approximately 25% of chronic carriers will die from cirrhosis or primary hepatocellular carcinoma (6).

These serious complications are usually preceded by chronic active hepatitis (with active replication of the virus), causing a significant number of years of morbidity and considerable loss of working time.

The reasons why some patients are capable of clearing the virus whilst others cannot do so and remain carriers, are not yet completely understood (5,7,8).

Several factors have been suggested as influencing the risk of a person becoming a longterm carrier of the virus; male gender (9,10), young age at infection (5,7,8-11) and a compromised immune system have been reported to increase the risk of carriership after HBV infection (12). A severe course of acute hepatitis B seems to be related to an enhanced immune response, while the development of the carrier state and chronic liver disease might be the result of a defective or immature immune system (12).

In neonates, specific suppression of the cell-mediated immune response may be involved (5,7). The high carrier rate in babies born to a HBeAg positive carrier mother suggests that one function of the HBeAg may be the induction of immunotolerance in the baby, favouring the persistence of HBV in infancy and childhood (7).

In adults several mechanisms underlying the development of chronic carrier state have been postulated. In general, viral persistence may be related to a specific failure of T cells to recognize HBV antigens. Individuals with a relative deficit in T-cell function (the aged, the immunosuppressed, the young) have been shown to be more likely to develop chronic HBV infection.

2.2.2. Outcome of HBV infection

The outcome of HBV infection is mainly determined by the age at which infection occurs, most probably due to the underlying immune situation at that age.

The probability of developing symptoms subsequent to an acute HBV infection is directly related to age (10, 13). The development of chronic HBV infection is inversely related to age (10, 13).

Table 1 shows the outcome of HBV infection according to age and reveals that HBV is a mainly asymptomatic disease, in children as well as in adults.

TABLE 1
Outcome of HBV infection by age (adapted from ref. 13)

	Symptomatic infection	Chronic carrier state
neonates-infants	< 5%	15-95%*
children (1-5 y)	5-15%	20-50%
older children, adolescents, adults	30-35%	6-10%

* Depending on the HBeAg-status of the mother.

Acute illness will develop in about 35% of infected adults (10). The symptoms may range from mild to severe hepatitis. Rarely, fulminant liver failure may occur (0.5%), which results in a case-fatality rate of 80% (8). About 60 to 65% of infected adults will experience an asymptomatic or subclinical infection. Most adults will clear the virus after an acute hepatitis B infection and develop lifelong immunity. Six to ten percent of infected adults fail to clear the virus after infection and will become chronic carriers of the virus (10, 13). Those who have had an asymptomatic infection are more likely to become a chronic carrier[a] than those with an icteric, symptomatic disease (4, 10).

These carriers have up to a 50% probability of developing chronic liver disease, of whom approximately 50% will develop chronic active

[a] The high carrier rate of HBV in those who do not remember an acute hepatitis B illness suggests that among carriers, asymptomatic or subclinical infection must be extremely frequent (4).

hepatitis, which often progresses to cirrhosis and primary hepatocellular carcinoma (14, 15).

Of the global population of chronic HBV carriers about 10 to 15% are expected to die of cirrhosis, and 4% of primary hepatocellular carcinoma[a] at some time in the future (4, 14-17).

Among infected neonates or young children only a very small percentage show an acute clinical hepatitis (< 5%) (13, 18, 19). A much smaller number of infected newborns will develop a fulminant hepatitis (0.1%), of whom 90% will die within 10 days after onset of the disease (18, 19). Most of the infected neonates will have a completely asymptomatic course of infection.

The younger the age at infection, the more likely carriership will occur. Of infected neonates up to 95% will become carriers (95%, if their mother is HBeAg positive). Approximately 20 to 50% of children infected before the age of 5 will become carriers.

For infected infants and neonates, complications and subsequent death will usually occur during the peak years of adult productivity, when familial, social and financial responsibilities are particularly heavy. Furthermore, these carriers will be infectious throughout their childhood, adolescence and adulthood and therefore able to spread the infection to others by the different modes of transmission.

According to these epidemiological findings, it is obvious that a vaccination programme targeted at adolescents and adults would fail to prevent early childhood infections and subsequently many chronic infections.

3. Epidemiology of hepatitis B

3.1. In the world

Hepatitis B is one of the world's most common and serious infectious diseases.

[a] One large prospective study in Taiwan has shown that the relative risk of HBsAg-postive persons for developing primary hepatocellular carcinoma is 223 times greater than for persons without HBsAg (17).

It is estimated that about two billion people who are alive today have at some time been infected with HBV; about 350 million are chronic carriers of HBV, i.e. over 5% of the world's population (6). This represents an enormous reservoir of the virus.

According to the figures of the World Health Organization, the number of carriers worldwide increases by approximately 10 million per year. These carriers are potentially susceptible to the debilitating or fatal consequences of HBV infection, in terms of fulminant hepatitis, chronic liver disease, liver cirrhosis or primary hepatocellular carcinoma (20).

Hepatitis B may account for most of the 1 to 2 million deaths estimated to occur each year from hepatitis (21).

The prevalence of HBV infection varies considerably in different geographic parts of the world. The world can be divided into three zones of endemicity of HBV, based on the overall prevalence of HBV markers and HBV carriers, and on the primary modes of HBV transmission (table 2).

Areas of *high endemicity* include South-East Asia, the Pacific Basin, the Amazon Basin, Africa, China, the Asian Republics of the Commonwealth of Independent States (CIS), the Artic Rim, parts of the Middle East and some countries of Eastern Europe such as Albania, Moldova, and Romania (6). Approximately 70 to 90% of the population shows serological evidence of past or current HBV infection. Countries included in this high endemicity category have a carrier prevalence varying between 8 and 20% (table 2). In these regions the primary mode of transmission is through perinatal or horizontal transmission, which both account for the persistence of high rates of chronic HBV infections.

More than 70% of the world's population and more than 80% of the world's chronic HBV carriers live in these areas.

The Middle East, Central and South America, Central Asia and some parts of eastern and southern Europe are considered regions of *intermediate endemicity*. In these areas, 20 to 55% of the population has HBV markers and 2 to 8% are carriers (6, 23). In these areas both horizontal and sexual transmission are the most important modes of HBV transmission.

Acute viral hepatitis is a primary cause of morbidity, because a large proportion of HBV infections occur in adolescents and adults, who are more likely to develop acute clinical disease.

TABLE 2
Distribution of hepatitis B endemicity worldwide (based on ref. 6, 20, 22 and 23).

Endemicity area	Carrier rate %	Prevalence of HBV markers %	Primary mode of transmission
High	8-20	70-90	perinatal horizontal
Intermediate	2-7	20-55	horizontal sexual
Low	0-2	< 20	sexual parenteral

Low endemicity areas include North America, western and northern Europe, Australia and parts of South America.

In these regions, the prevalence of HBV markers is less than 20%, while 0 to 2% of the people are carriers (23). Most infections occur in adults through parenteral (needle sharing, occupational exposure) or sexual transmission. In these areas, acute disease is a significant cause of morbidity.

3.2. In Europe

In most of the European countries, the notification of acute hepatitis B infections is mandatory but not well established. Consequently, the number of cases notified each year is far below the true overall incidence of hepatitis B virus infections, causing an underestimation of the real burden of disease. Approximately 160,000 cases of acute hepatitis B infections are reported each year in the WHO European Region (24).

Owing to underreporting and the fact that at least 50% of hepatitis B virus infections are asymptomatic, the World Health Organization Regional Office for Europe estimates that 1 million people are infected in the WHO European Region every year. Of these, approximately 90,000 will become chronically infected and about 22,000 will possibly die from cirrhosis and liver cancer (24).

Unexpectedly high prevalence rates of hepatitis B carriage have been found in many parts of eastern and central Europe and the former Soviet Union. In countries of the Central Asian Republics of the former Soviet Union and in some countries of Eastern Europe (Romania, Albania and Moldova), hepatitis B is a serious threat to community health with an esti-

mated annual incidence of 520 hepatitis B virus infections per 100,000 (24). The remaining countries of Eastern Europe have an estimated annual incidence rate of approximately 130 hepatitis B virus infections per 100,000. The need for universal hepatitis B vaccination is unquestioned in most of Eastern and Central Europe and the Central Asian Republics of the Newly Independent States. Although Albania, Bulgaria, Moldova, Poland, Romania and Slovenia have been able to obtain hepatitis B vaccines, so far, financial resources to make these vaccines available have not been found for most countries in the former Soviet Union.

In Southern Europe[a] the prevalence of HBV carriers varies between 1 and 5%. The overall prevalence of HBV has been estimated at 10 to 20%. The annual incidence rate of HBV infections is approximately 36 per 100,000 (25).

Most carriers result from infections acquired early in life. As prevalence of HBeAg among carrier mothers is rather low, horizontal transmission rather than perinatal transmission plays a major role in the epidemiology of HBV in these countries (25).

In Western Europe the HBsAg carrier rate ranges from 0.1 to 1.0% and the overall HBV markers prevalence rate varies between 5 and 10%. Acute hepatitis B is more frequent in young adults, with a peak incidence of 20 to 30 acute cases per 100,000 in the 20-30 age groups (25).

As far as risk factors could be traced, sexual transmission prevails and accounts for at least 40% of cases. Intraveneous drug use (IVDU) would account for 10 to 25% of hepatitis B cases of identified origin (25).

Northern Europe[b] shows the lowest rates of hepatitis B infections: the HBsAg carrier rate and the overall prevalence of HBV have been estimated at less than 0.5% and less than 5%, respectively (25). The annual incidence of HBV infections is approximately 9 per 100,000.

In the light of the implementation of new vaccination programmes in different parts of Europe, the follow-up of the epidemiological situation of HBV in Europe will be very important and will reveal the importance of the impact of vaccination on the dynamics of HBV infection.

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[a] Greece, Italy, Spain and Portugal.

[b] United Kingdom, Sweden, Norway, Ireland, Iceland, Finland and Denmark.

4. Transmission

Because HBV produces persistent carriership, chronically infected people serve as the primary virus reservoir. Acutely infected persons serve as temporary reservoir.

HBV is present in different body fluids in carriers as well as in people suffering from the acute infection.

Hepatitis B is spread through contact with infected blood [a] and body fluids such as semen, saliva and vaginal secretion. The virus has also been identified in other body fluids such as sweat, tears, breast milk, urine and faeces[b]; however, only the infectious property of blood, semen, vaginal secretion and saliva has been clearly demonstrated (26).

As defined epidemiologically, there are currently four recognised modes of transmission: transmission from mother to child at birth (perinatally/vertically) (27), transmission through contact with saliva, small wounds or abrasions from an infected person (28, 29) (horizontally[c]), sexual transmission (30) and transmission through parenteral exposure to blood or other infective fluids (31, 32).

5. Regional patterns of transmission

The predominant modes of transmission of HBV vary throughout the world, with percutaneous and sexual transmission predominating in developed countries and horizontal and vertical transmission predominating in developing countries (table 2).

In North America and western Europe infection is usually acquired in adult or adolescent life, when susceptibility to infection still exists. HBV infection is most often acquired through parenteral (percutaneous) or sexual contact[d], and is common in – but not limited to – individuals or

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[a] HBV has been shown to circulate at levels > 10^8 virions per ml in HBeAg-positive persons. Concentrations in semen and saliva are 10^3 times lower than in the serum of the same individuals.

[b] The lower concentrations of virus in these fluids suggest a proportionally lower likelihood of transmission of infection, unless they are clearly contaminated with blood or there is repeated exposure (26).

[c] Mostly affecting infants and children.

[d] In the US, parenteral drug users, heterosexuals and homosexuals with multiple sexual partners represent the 3 largest groups at high risk, collectively accounting for 59% of reported cases (33).

groups with a high-risk behaviour defined by lifestyle or occupation (e.g. intravenous drug use, sexual activity with multiple partners and occupational exposure).

In the low endemicity countries perinatal transmission accounts for 10 to 20% of new HBV carriers, occurring primarily in minority groups (26). Apparently, even in these regions perinatal transmission remains important. HBV transmission among adolescents and adults accounts for approximately 95% of acute HBV cases, and 70 to 75% of new chronic HBV cases annually. Because most infections occur in adults and older adolescents, who are more likely to present with clinical disease, hepatitis B forms a significant cause of morbidity in these low endemicity regions.

In the intermediate endemicity areas, HBV transmission occurs at all ages and patterns of HBV transmission generally represent a combination of perinatal, childhood and adult transmission. A small proportion (10 to 20%) of HBV carriers has been estimated to result from perinatal transmission; early childhood infection is responsible for maintenance of a substantial carrier population (26). The highest rates of infection are probably among older children, adolescents, and younger adults. Racial and socio-economic differences contribute to variations in disease prevalence within these regions.

In high endemicity countries most adults show evidence of previous HBV infection. In these high endemicity regions infection is often acquired at or near the time of birth, or – even more often – in early childhood by horizontal transmission, leaving almost no possibility for HBV infection through other modes of transmission later in life.

Depending on distribution of hepatitis B e antigen (HBeAg) among carriers in high endemic regions, horizontal or perinatal transmission will be more likely to occur.

In Asia, 8 to 15% of parturient women are HBsAg carriers, and 35 to 50%[a] of these are HBeAg positive (34). Hence, perinatal transmission will occur very efficiently, infecting a considerable number of neonates at birth.

[a] Why Asian women are more likely to remain HBeAg positive compared to African women is not fully understood. Possible explanations include genetic predisposition to remain HBeAg positive (26), or perinatal infection itself, that might predispose to retention of HBeAg positivity, in contrast to early childhood infection (11).

It is estimated that 3 to 5% of all infants become HBV carriers and between 30 and 50% of all HBV carriers in these countries result from perinatal HBV transmission (26). Perinatal transmission is not the sole determinant of the high rate of HBV infections in these regions. Horizontal transmission is also frequent and accounts for most of the remaining chronic carriers and for the majority of HBV infections.

Due to these two modes of transmission, only a small proportion of the adult population remains susceptible for HBV (5 to 20%) (26).

In other areas of high endemicity where the rate of HBeAg positivity is low, such as Africa and the Middle East, perinatal transmission contributes less to the HBV carrier pool than does horizontal transmission. In Africa and the Middle East, 10% to 15% of parturient women are HBV carriers, but less than 20%[a] are HBeAg positive (35,36). It is assumed that in these areas 10 to 20% of chronic HBV infections result from perinatal transmission. HBV infection is acquired rapidly among young children (horizontally) within families, primarily from chronically infected mothers and siblings (37), so that 80 to 90% become infected by the age of 10 years (26). Of course, changes in hygiene, lifestyle and socio-economic factors may influence the relative contribution of the four different modes of transmission.

6. Epidemiology of hepatitis B and prevention policy in Belgium

Belgium belongs to the low endemicity countries for hepatitis B (25).

In general, infection is likely to occur after adoption of a specific lifestyle (drug addiction, multiple sex partners) or occupation. As far as specific risk factors could be traced in the notification from low endemic countries, sexual transmission appeared to account for at least 40% of cases, and intraveneous drug use for 15 to 20% (25).

There are wide variations in both the reporting and the accurate diagnosis of hepatitis B in many countries. This is also the case in Belgium, where prevalence data for viral hepatitis are scarce and incidence data non-existent.

[a] Why Asian women are more likely to remain HBeAg positive compared to African women is not fully understood. Possible explanations include genetic predisposition to remain HBeAg positive (26), or perinatal infection itself, that might predispose to retention of HBeAg positivity, in contrast to early childhood infection (11).

Extrapolation and assumptions based on data from sentinel practices are the only way to have an idea about hepatitis B incidence in Belgium. A recent survey in Flanders shed more light on hepatitis B prevalence data among the general population.

To situate the epidemiology of hepatitis B in Belgium, the limited data sources will be gone through systematically.

Subsequently, current prevention policy in Belgium is presented, highlighting the legislation governing the conduct of hepatitis B prevention.

6.1. Registration system

6.1.1. Compulsory notification

In Belgium, hepatitis B is a compulsory notifiable disease; it is usually reported by the doctor who makes the diagnosis to the provincial health inspectorate. 'Compulsory notification' in Belgium is, as in many other countries, very inadequate. Instead of achieving the stated objectives, the figures based on compulsory notification give a totally misleading picture of the real situation.

The notification in Flanders (population = 5,180,000) varies over a 10 year period (1984-1993) between 28 and 113 hepatitis B cases per year. The average number of cases per year over this 10 year period is 70 hepatitis B cases per year (95% C.I.: 48-91). Data from the general practitioners sentinel system demonstrate that this is a serious underestimation of the real incidence figures.

The *effect of the hepatitis B vaccination campaign* in our country, directed mainly at health care workers and newborns of HBsAg positive mothers, will have little measurable influence on the total number of hepatitis B cases notified. It has been suggested that these two above-mentioned groups make up only 5 to 10% of the total group of infected people in low endemicity countries.

The results obtained through the general practitioners sentinel system revealed that the actual number of cases of all viral hepatitis was approximately 20 to 60 times higher than those shown by the official notification figures (38-41). This illustrates the enormous underreporting of viral hepatitis in general and hepatitis B in particular (table 3).

In addition, notification of acute hepatitis B cases will clearly underestimate the total number of new infections because: (1) asymptomatic

infections will not be included, and these make up a large part of the total number of infections; (2) symptomatic cases may occur in individuals who do not seek medical advice, and (3) symptomatic cases seen by a doctor are not always further investigated serologically and/or notified.

In short, the current compulsory notification data for Belgium can hardly be used; the above-mentioned remarks encourage us to interpret the results with the necessary caution.

6.1.2. Sentinel practices

Viral hepatitis was one of the health topics registered by the sentinel practices for the period 1979-80, 1982-84 and also, more recently, 1990-92.

The registration included every new case of hepatitis in the study period for which a clinical diagnosis was made in a person over the age of 5.

The annual incidence of acute hepatitis B in Belgium, registered through the sentinel practices was 25/100,000 for the period 1982-84 (42-46). The annual number of clinical hepatitis B cases in Belgium was estimated at 2,400. As at least 60% of infections are asymptomatic, it can be assumed that about 7,200 HBV infections occured annually in

TABLE 3
Outcome of the statutory notification in Belgium

Region	Disease/ Infection	Annual Number Notified	Estimation of real number	Multiplication Factor	System
Belgium	Viral hepatitis	770*	45,000	59	sentinel practices Flanders (1978): ref.40
			36,000	47	sentinel practices Belgium (1979-'80): ref.41
Belgium	Viral hepatitis	771**	14,700	20	sentinel practices Belgium (1982-'84): ref. 42
Flanders	Hepatitis B	70***	1,453	20	sentinel practices Belgium (1982-'84): ref. 42

* average for 1976-1980
** average for 1982-1983
*** average for 1984-1993

Belgium during that study period. For the more recent study (1991-1992) 618 cases of clinical hepatitis B were registered, i.e. an annual incidence of 6/100,000 (45). All reported cases were aged 20-49 year, and 55% of them were between 20 and 29 years of age. The most predominant way of transmission was sexual contact (36%), travel abroad to endemic regions (27%) and intravenous drug use (18%).

Compared to the previous registration period, data from 1991-1992 show a statistically significant decrease. A similar decline has also been observed in other European countries (45, 47). Iwarson and Devroey et al. attribute these findings mainly to changes in behaviour caused by Aids prevention programmes or anxiety about Aids, needle exchange programmes and a decreasing number of iatrogenic infections (45, 47).

6.2. Prevalence studies

In Belgium few prevalence data are available. Table 4 summarizes only more recent prevalence studies (48). Some data are based on screening results of persons which were included for a vaccination trial; this gives a false negative picture since people who have already had jaundice would not offer to take part in a hepatitis B vaccination trial.

Other prevalence data were obtained during screening programmes in the framework of a health information and education project or were collected on the basis of routine screening.

As HBV prevalence is a cumulative value, increasing with age[a], age-standardized prevalence figures would allow a comparison between the various groups at risk. Unfortunately, for the majority of 'prevalence studies' no ages were given.

Overall, these serological surveys demonstrate that, although hepatitis B is uncommon among adults in the general population in low endemicity countries, it is highly prevalent in certain groups (table 4).

6.3. Prevalence in the general population

A sero-epidemiological study was undertaken in 1993-1994 in a sample of the general population in Flanders. The purpose of this study

[a] As long as no generation or cohort effect, occurs.

TABLE 4

Prevalence of serologic markers of HBV in different population groups in Belgium (48)

Population groups in Belgium	Mean age (years)	N° tested	Prevalence of serologic Markers of HBV						Year of study
			HBsAg			Any marker			
			N	%	95% c.i.	N	%	95% c.i.	
Political refugees from high endemicity countries	ND[d]	774	86	11.1	8.9-13.3	601	77.6	74.7-80.6	1987-89
Mentally retarded in institutions	19.5	770	79	10.3	8.1-12.4	399	51.8	48.3-55.3	1985-86
IV-drug users	24.0	131	10	7.6	3.1-12.2	72	54.9	46.4-63.5	1990
Sexually active homosexuals	ND	520	18	3.5	2.1-5.4	189	36.3	32.2-40.5	1985-86
Sexually active homosexuals (a)	28.0	195	8	4.1	1.8-7.9	67	34.4	27.7-41.0	1981-82
Homosexual and bisexual men	33.8	370	7	1.9	0.5-3.3	128	34.6	29.7-39.4	1990
Household contacts of institutionalized mentally retarded:									
— HBV positive cases	53.1	111	12	11.0	5.0-16.6	31	28.0	19.6-36.3	1990-91
— HBV negative cases	49.7	166	0	0.0	0.0-2.2	8	4.8	2.1-9.3	
Health care workers – frequent blood contact	ND	1129	ND	ND	ND	113	10.0	8.3-11.8	1982-83
Health care workers-no or infrequent blood contact	ND	1289	ND	ND	ND	53	4.1	3.1-5.3	1982-83
Personnel in institutions for the mentally handicapped 1982-83	ND	1290	ND	ND	ND		94	7.3	5.9-8.8
female prostitutes	ND	197	2	10	0.1-3.6	69	35.1	28.4-41.7	1987-92
female prostitutes (b)	34.5	123	0	0.0	0.0-1.4	19	15.4	9.1-21.8	1990-91
blood donors	ND	5.344	16	0.3	0.1-0.4	ND	ND	ND	1987
pregnant women	ND	8.641	68	0.78	0.60-0.97	ND	ND	ND	1982-87
prisoners (c)	ND	791	35	4.4	3.1-6.1	167	21.1	18.3-24.0	1992-93
adoptees (international)	2.8	148	10	6.8		ND	ND	ND	1993

a An incidence study carried out in the same Antwerp homosexual community revealed an annual HBV-incidence rate of 12 %.

b Only one (0.8 %) women admitted IV drug use compared to 14 (7 %) in the previous study. This could explain the difference in HBV-prevalence.

c HBsAg-prevalence was 12 % among IVDU-prisoners, compared to 3.6 % among non-users; prevalence of HBV-markers was 38.5 % in IVDU prisoners versus 24.7 % in non-users.

d no data available.

was to obtain a clear picture of the prevalence of hepatitis A, B and C. Between April 1993 and February 1994, 4,058 blood samples were drawn and collected. The study group obtained was similar in composition to the Flemish population regarding age and gender. For hepatitis B, 9.9% of the study group showed serological evidence of hepatitis B markers: 6.9% of the participants was positive for anti-HBs/anti-HBc, 0.7% was HBsAg positive and 3.5% was solely anti-HBs positive. The prevalence of HBV markers in Belgians was 6.9%, significantly lower compared to 13.4% among non-Belgians (49).

6.4. Current prevention policy in belgium

The present strategy for hepatitis B prevention in Belgium, consists of vaccination of certain categories of individuals at higher risk of HBV infection (because of medical history, age groups or occupational exposure) and screening of blood, blood products and donor material. There exists legislation governing the conduct of this prevention measures.

6.4.1. Specific categories of individuals at higher risk

The repayment of hepatitis B vaccination by Health and Invalidity Insurance[a] is foreseen for the following categories of patients:

A. haemophilia patients,
B. haemodialysis patients and candidate dialysis patients,
C. patients with chronic renal insufficiency awaiting a kidney transplant,
D. patients awaiting organ transplantation, especially candidates for liver transplantation,
E. patients having cardiac surgery requiring the administration of large quantities of blood,
F. patients suffering from thalassaemia,
G. newborns and children under the age of 3 years of HBsAg positive mothers (whatever the HBeAg status) (this category is now included in J.),
H. the mentally handicapped,
I. households of HBV carriers positive for HBeAg or HBV-DNA positive,
J. all children under the age of 13 years.

In practice this means that people are only considered for reimbursement for hepatitis B vaccines if they are included in the above men-

[a] In Dutch: Rijksinstituut voor Ziekte- en Invaliditeitsverzekering (RIZIV).

tioned list, are entitled to claim, have their vaccines prescribed by their treating physician and the advising physician has given his approval. These are all stages to be gone through before the vaccine can actually be administered. It is clear that all these steps do not facilitate the implementation of vaccination; in addition, this prevention strategy can hardly be called universal vaccination programme.

In May 1996, there was an official agreement (9 Belgian Ministers involved; BS: 22 april 1997) to make hepatitis B vaccination available free of charge through the collective prevention systems (Mother and Child Care and Medical School Services) to neonates and 11 years old adolescents. In addition, pediatricians and general practicioners could offer the vaccine for free as well. Unfortunately, this prevention programme has not yet been implemented.

6.4.2. Screening of blood, blood products and donor material

The Royal Decree of 10 November 1971 (BS: 5 May 1972) forbids the taking of blood from potential blood donors who are not Australia antigen or Australia antibody negative. In addition the law foresees systematic screening for Australia antigen and antibody.

The aforementioned law was altered following the discovery of the Human Immunodeficiency Virus (HIV). This new law (Royal Decree of 18 July 1985; BS: 31 July 1985) forbids the taking of blood from potential donors whose case history shows that they belong to or could belong to a high risk group for HIV. The 'discouragement campaign' as a result of this Royal Decree, would indirectly have an additional effect on HBV-prevention in blood transfusion.

In practice this means that Belgium has access to a safe blood bank at an early stage.

From the epidemiological point of view these measures are the most radical means of keeping parenteral transmission of hepatitis B (at least through the administration of blood or blood products) to the absolute minimum.

In Belgium approximately 700,000 units of blood are screened annually for HBsAg (L.Muylle, pers. comm.). Screening donors for HBsAg will detect 4 to 6 HBsAg positive carriers per 1,000 donors tested and prevent overall about 30 HBsAg positive transfusions per year,

which would result in approximately 10 cases of clinical hepatitis B and 2 to 3 carriers.

Whether every organ, sperm or egg-cell donation is systematically screened for HBsAg (and since 1.8.1985 for HIV as well) is difficult to monitor; it remains a personal decision of the treating physician and is his responsibility.

6.4.3. Regulation within the framework of the fund for occupational diseases

The Royal Decree of 2 February 1988 (BS: 10.2.1988) refers to the specific regulations regarding reimbursement for hepatitis B vaccine in certain circumstances and for certain categories of employees. According to the law the employer must take the steps necessary to offer these employees the possibility of vaccination against hepatitis B; at the same time the employees cannot be forced to accept vaccination.

The Fund for Occupational Diseases estimates that the total group entitled to repayment of vaccination costs amounts to approximately 240,000 employees and annually about 10,000 students.

The Fund for Occupational Diseases plaid a major role in the tremendous decrease of the number of hepatitis B cases in Health Care Workers in Belgium: from 1983 to 1991 repayment of vaccination costs was made to 142, 370 employees and students (50). This represents a sum of 452 million BEF over the years. Over and against this are the figures for compensation for work related to hepatitis B infections: in 1980, 173 requests for compensation were retained. In 1990, there were only 10 requests. Based on an economic analysis it was shown that the vaccination costs were largely counterbalanced by the benefits of avoided hepatitis B cases (51).

Globally it can be said that hepatitis B is at present only rarely seen as an occupational disease. Hepatitis B has possibly become less frequent in the health sector than in the general population.

7. Vaccination policy

Despite the availability of safe and effective hepatitis B vaccines for more than 15 years, the decision to use them on a broad scale has not been taken in many countries. Important is the lack of medical and public

awareness: the public does not perceive hepatitis B as a threat to the population at large; governments, expected to respond to public demand, have not considered hepatitis B prevention as a priority and have stressed selective prevention strategies. Experience has shown that targeting hepatitis B vaccine to 'high risk' groups and screening of pregnant women, strategies used in 'low endemicity' areas since 1982, have failed to control hepatitis B in any of those countries for a variety of reasons (1,33): most high-risk groups are difficult to access, there is a lack of perceived risk among those at risk, 30% or more persons with acute hepatitis B infection do not have identifiable risk factors, and some vaccination programmes are not fully implemented. As recently reported, in low-endemic countries universal antenatal screening for hepatitis B is not well or even not yet implemented, while selective antenatal screening failed to identify about half of the pregnant women whose neonates were at risk (52, 53). With few exceptions, the effect of the 'high risk' strategy has been the immunization of health care workers and some categories of patients. Approximately 85% of vaccine has gone to one group, the health care workers, which represents only 5 to 10% of reported hepatitis B cases in most European countries and in North America (1). While it is certainly desirable to immunize these persons, this strategy will not control hepatitis B on a population basis.

The failure of the high-risk immunization strategy and a better knowledge of the burden of disease have emphasized the necessity for action towards control of hepatitis B as a community acquired risk. Within this scope current vaccination programmes have been completely re-evaluated.

In 1991 the Global Advisory Group on Viral Hepatitis set targets for the introduction of HB vaccine into national immunization programs. These targets were approved and endorsed by the World Health Assembly in March 1992 (1, 6).

By beginning 1998, more than 95 countries have a national policy of including hepatitis B vaccine as a routine part of their infant and/or adolescent immunization programme. These countries represent approximately 40% of the world's 145 million newborns annually, but almost 60% of the world's 350 million carriers.

Although Europe and the United States can be considered to be regions of low endemicity for hepatitis B infection, the prevalence of carriers, the incidence of new cases and the burden of acute and chronic disease place HBV among one of the very important communicable diseases.

In terms of people affected and the gravity of its longterm consequences, HBV is more serious than most other infectious diseases. The estimated number of hepatitis B-related deaths in the United States is between 5,000 and 6,000 a year, i.e. five times the number of annual deaths estimated to have occurred from *Haemophilus influenzae type b* and ten times the number of deaths from measles before routine vaccination of children was introduced.

An analysis from the Centers for Disease Control (CDC, 1993) estimated the number of deaths that resulted from different infectious diseases before vaccines were available (Table 5). This illustrates the serious burden of disease posed by HBV, even for a low endemicity country.

Lifetime mortality from hepatitis B was 1,000 to 1,500 deaths per million population before vaccination, while deaths from *Haemophilus influenzae type b,* measles and mumps, for example, were less than half (table 5). World Health Organization experts use these recent findings to demonstrate that HBV is, in the longterm, the most important vaccine-preventable disease. This is a very powerful argument to convince health policy makers and doctors to use the vaccine.

Since 1992, in the low endemicity areas, universal hepatitis B immunization has been implemented in Australie, the U.S., New-Zealand and Canada. In Western Europe, France, Germany, Italy, Luxembourg, Portugal, Greece, Switzerland, Austria, Malta and Spain have national policies to immunize adolescents or infants or both with hepatitis B vac-

TABLE 5

Estimated life-time morbidity and mortality of vaccine-preventable diseases before the availability of vaccines in the U.S.

Disease	Clinical cases (per million)	Longterm sequelae (per million)	Deaths (per million)
Hepatitis B	25,000	7,000	1,000-1,500
Haemophilus influenzae b	5,000	1,500	300-600
Measles	900,000	300	200-400
Mumps	75,000	5	3-5
Polio	14,000	4,500	100-400
Pertussis	600,000	40	200-300
Rubella	300,000	750	10-15

Source: CDC, Atlanta, 1993

cine. Decision for implementation has been supported by the results of several cost-effectiveness and cost-benefit analyses. Belgium, the Netherlands and Turkey are seriously studying the issues or are making financial plannings for introduction of the universal vaccination programmes (6).

8. Conclusion

The currently emerging data on the longterm efficacy of hepatitis B vaccines, knowledge that infants, children and adolescents can be reached through already established vaccination delivery systems, and studies showing that these interventions are cost-effective, indicate that control and elimination of hepatitis B by universal immunization is attainable (6).

The choice of whether infant and/or adolescent immunization should be implemented depends on the country-specific epidemiology as well as on the organisation of the vaccine delivery systems.

In Europe, much work remains to be done to implement interventions that will bring us closer to the World Health Organization goal and to control hepatitis B in the community. Any attempt at eradicating the hepatitis B virus will require international cooperation and reconsideration of earlier vaccination strategies. A very exciting time in the history of preventive medicine is now in view, with the prospect of controlling and possibly eliminating one of the major health problems in humans, ranking in importance with the eradication of smallpox.

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