Epidemiology of hepatitis B and C in Europe

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Keywords : hepatitis B, hepatitis C, epidemiology, review.

Introduction

Six distinct viruses causing viral hepatitis have been identified, each differing in the severity of disease they cause, epidemiological characteristics, modes of transmission and recommendations for control. These six viruses are hepatitis A, B, C, D, E and G.

Hepatitis A virus (HAV) is characterised by low mortality, no chronic carrier state and lifelong immunity following infection. Modes of transmission include faecal-oral, person-to-person, and contaminated water and food.

Historically, infection with HAV was a common in young children and not considered a public health problem. With improved hygiene and socio-economic conditions however, the virus now often strikes at a later age and with more severe consequences.

The outcome of hepatitis B virus (HBV) infection is often severe, with acute HBV infection leading to chronic carrier state, cirrhosis, liver cancer and death. Six to 10 percent of infected adults will become chronic carriers ; infection during infancy and early childhood frequently progresses to the chronic carrier state, with 70-90 percent of neonates becoming chronic carriers. Hepatitis B is transmitted through infected blood and body fluids, perinatal transmission, horizontal transmission, sexual transmission and intravenous drug use. Both plasma derived and recombinant vaccines are approved for use in most parts of the world ; even so, worldwide one million deaths per year are directly related to HBV infection. To control the disease, the World Health Assembly recommends that "the most effective strategy is incorporation of universal hepatitis B vaccination into the routine infant or adolescent immunisation schedules".

Discovered in 1889, the hepatitis C virus (HCV) is a small, single-stranded RNA virus. It is estimated that approximately 3% of the world's population has HCV. The virus is blood-borne, and the majority of those infected with HCV show no symptoms initially. Approximately 50% of people infected with HCV become chronic carriers : of these, half develop cirrhosis or liver cancer.

The hepatitis Delta virus (HDV) is associated with hepatitis B. Too small to replicate itself, the Delta virus lives as a parasite on the hepatitis B virus, using the s antigen of HBV to multiply. The Delta virus is relatively rare and is not present with every case of HBV infection. The progression to chronicity is not common. If HBV infection does become chronic, however, the Delta virus speeds the progression to chronic liver disease. Vaccination against HBV protects against Delta infection as well.

Formally known as enterically transmitted NANB hepatitis, hepatitis E virus (HEV) has no chronic carrier state and does not cause chronic liver disease. Hepatitis E infection is highly dangerous however, for pregnant women, causing up to 20% mortality in women in their third trimester of pregnancy. Largely transmitted through faecal-oral transmission, hepatitis E epidemics are usually waterborne epidemics. The disease can be controlled through the provision of safe water and food. There is no vaccine as yet, though prototype vaccines are in the pipeline.

The hepatitis G virus (HGV) was identified in 1995. It is an RNA virus with a worldwide distribution. Hepatitis G is transmitted parenterally through blood and blood products, and through intravenous drug use. HGV appears to cause both self-limited and chronic disease. Presently, it is not known if a normal carrier state exists and the potential role of HGV in cirrhosis and hepatocellular carcinoma has still to be investigated. The current view is that HGV causes infection but little liver damage.

In this paper the epidemiology of viral hepatitis B and C are further dealt with.

Hepatitis B

Prevalence of HBV in the world

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

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 (1,2). This represents an enormous reservoir of the virus.

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April 9, 1998.

According to the figures of the World Health Organisation, 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 (3). Hepatitis B may account for most of the 1 to 2 million deaths estimated to occur each year from hepatitis (4).

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 I).

Table I. — **Distribution of hepatitis B endemicity worldwide (based on ref. 2, 3, 5)**

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

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 Arctic Rim, parts of the Middle East and some countries of Eastern Europe such as Albania, Moldavia and Romania (2). Approximately 70 to 90 % of the population show serological evidence of past or current HBV infection. Countries included in this high endemicity category have carrier prevalences varying between 8 and 20%. 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 7% are carriers (2,5). 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 large proportions of HBV infections occur in adolescents and adults, who are more likely to develop acute clinical disease. 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 carrier (5). 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.

Prevalence of HBV 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 (6). Owing to underreporting and the fact that at least 50% of hepatitis B virus infections are asymptomatic, the World Health Organisation 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 (6).

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 Moldavia), hepatitis B is a serious threat to community health, with an estimated annual incidence of 520 hepatitis B virus infections per 100,000 (6). 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, Moldavia, Poland and Romania 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 (Greece, Italy, Spain and Portugal) 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 (7).

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 (7).

In Western Europe the HBsAg carrier rate ranges from 0.1 to 0.5% 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 (7).

As far as risk factors could be traced, sexual transmission prevails and accounts for at least 40% of

cases. Intravenous drug use (IVDU) would account for 10 to 25% of hepatitis B cases of identified origin (7).

Northern Europe (United Kingdom, Sweden, Norway, Ireland, Iceland, Finland and Denmark) 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 (7). 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.

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 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 ; however, only the infectious property of blood, semen. vaginal secretion and saliva has been clearly demonstrated (8).

As defined epidemiologically, there are currently four recognised modes of transmission : transmission from mother to child at birth (perinatally/vertically) (9), transmission through contact with saliva, small wounds or abrasions from an infected person (10, 11) (horizontally), sexual transmission (12) and transmission through parenteral exposure to blood or other infective fluids (13, 14).

In the low endemicity countries perinatal transmission accounts for 10 to 20% of new HBV carriers, occurring primarily in minority groups. 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.

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, 15) : 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 (16, 17). With few exceptions, the effect of the "high risk" strategy has been the immunisation 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 immunise these persons, this strategy will not control hepatitis B on a population basis.

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

In 1991 the Global Advisory Group on Viral Hepatitis set targets for the introduction of HB vaccine into national immunisation programs. These targets were approved and endorsed by the World Health Assembly in March 1992 (1,2).

By early 1998, more than 95 countries have a national policy of including hepatitis B vaccine as a routine part of their infant and/or adolescent immunisation programme. These countries represent approximately 40% of the world's 145 million new-borns 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 long-term 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 Centre for Disease Control (CDC, 1993) estimated the number of deaths that resulted from different infectious diseases before vaccines were available. 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. World Health Organisation experts use these recent findings to demonstrate that HBV is, in the long-term, 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 immunisation has been implemented in the U.S., New Zealand and Canada. In Western Europe, France, Germany, Italy, Luxembourg, Portugal, Spain and Switzerland have national policies to immunise adolescents or infants or both with hepatitis B vaccine. Decision for implementation has been supported by the results of several cost-effectiveness and cost-benefit analyses. Belgium, Greece, the Netherlands and Turkey are seriously studying the issues or are financially planning the introduction of universal vaccination programmes (2).

Conclusion

The currently emerging data on the long-term 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 immunisation is attainable (2).

The choice of whether infant and/or adolescent immunisation 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 Organisation goal and to control hepatitis B in the community. Any attempt at eradicating the hepatitis B virus will require international co-operation 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.

Hepatitis C

History

Even though since the 1970s blood was systematically screened for hepatitis B, still post transfusion hepatitis occurred. This form of hepatitis was called non A-non B. The virus that caused most of these forms of hepatitis was isolated in 1989 and named the hepatitis C virus (HCV) (18). Since then, our knowledge of the biology, epidemiology and pathophysiology of HCV has increased exponentially. HCV is the most common cause of post-transfusion and community acquired non-A, non-B hepatitis and cryptogenic cirrhosis worldwide.

Virology

The HCV is a small (50 nm), single-stranded enveloped RNA virus of the flavivirus family. On the basis of nucleic acid sequences, six different genotypes of the HCV have been identified, each with one or more subtypes (a, b, c, ...), and each associated with specific geographic areas and transmission routes. In addition, nucleotide variability may be present in viruses circulating within an individual. These are referred to as quasispecies and may reflect the consequences of ongoing immune surveillance and viral mutation. Some genotypes such as 1a, 1b and 4 seem to be less responsive to interferon therapy, but no clear association with disease outcome or severity has been demonstrated despite initial suggestions that infection with genotype 1b is more likely to lead to cirrhosis or hepatocellular carcinoma (19).

Epidemiology

Transmission

The primary route of transmission is through infected blood, but in up to 50% of the cases no obvious transmission factor could be found. The findings of HCV in sperm, saliva, vaginal secretions and other bodily fluids were more likely to be due to the presence of minor blood quantities, since recent studies confirm total absence of the virus in these fluids. So, only blood-blood contact can pass on the virus (19). Risk factors for HCV infection include intravenous drug use, transfusion of blood products, hemodialysis, tattooing, high-risk sexual behaviour, exposure to health care and organ transplants from HCV-positive donors (20). Recently, cocaine snorting has been suggested a significant risk factor for HCV infection when it involves sharing of blood contaminated straws (21). However, 40-50% of patients with HCV infection have no identifiable risk factor and the mode of viral transmission in these cases remains unknown.

Parenteral transmission

Up to 50% of the HCV infections occur through parenteral routes. Since the implementation of mandatory screening of blood and blood products, this way of transmission is becoming scarce in the western world. The risk of acquiring HCV infection from transfusion of screened blood or plasma is currently extremely small. In a recent study (22) in the US, the risk of receiving blood from a donor in the window period of infectivity was estimated at 1 in 100,000. Three such cases have been reported in Europe from 1995 to 1996

(23-25). For patients on maintenance hemodialysis the risk for infection is associated with the frequency of dialysis and also to increasing years on dialysis, which suggests probably poor infection control practices allowing patient-to-patient transmission (26,27). A study in Sweden, comparing two dialysis units, revealed in one institution no risk of spread of the infection, while in the other unit 36% of the patients became infected during a three year period, including patients who had not received blood (28). Transplantation related transmission is also very common even though this is also decreasing with the increased safety of blood supply. Nosocomial transmission is likely if disinfecting procedures are inadequate and contaminated equipment is shared between patients. Previous hospitalisation is an epidemiological risk factor in patients with HCV infection and this may account for a substantial proportion of HCV infections among patients lacking a history of transfusion or other obvious parenteral exposures (29). A case-report in 1996 (30) reports of surgeon-to-patient transmission of HCV during cardiac surgery, although the frequency of this route of transmission remains to be established.

Intravenous drug use is, as mentioned above, an extremely high risk of HCV infection.

Worldwide 70-90% of intravenous drug users are anti-HCV positive (31).

Vertical transmission of HCV

In 3 to 5% of new-borns of HCV carrier mothers, perinatal transmission occurs. This risk is associated with the HCV RNA levels of the mother or with concomitant human immunodeficiency virus (HIV) infection (20). Because a higher proportion of the infections from mother to child happen after vaginal delivery as opposed to caesarean, transmission probably happens perinatally (32). No evidence has been given of infection through breast-feeding (33).

Sexual and household transmission

Hepatitis C is not a sexually transmitted disease since sexual transmission is exceptional. However, sexual risk behaviour that increases the risk of trauma might enhance the transmission of the HCV (34). The prevalence of HCV antibodies in homosexual men is not significantly higher than in the general population, irrespective of the number of sexual partners, HIV status or receptive anal intercourse (35). Household (nonsexual) spread of HCV cannot be considered a risk factor since non-blood body fluids do not even show detectable HCV RNA by PCR (36). Intrafamilial clustering of HCV infection has been reported however, especially in areas of intermediate or high endemicity (29). Common to all such reports is the higher prevalence of infection in the older contacts and in those who had lived longer with the index case (usually spouses, but often parents of the index case).

Diagnostic tests

Unlike antibodies to hepatitis A and B viruses, antibodies to HCV are not protective and, in most cases, are markers for disease (20). So, to advise a patient whether their infection is acute, chronic or resolved and to give a meaningful long-term prognosis, knowledge of the vireamic state of the patient is necessary (37). Since 1990 two categories of techniques to detect the HCV became available (38). Serological tests are based on the detection of antibodies directed to genotype specific HCV epitopes. These tests are easy to use and relatively low in cost. The disadvantages are the indirect determination of HCV genotype without genome analysis, lack of sensitivity compared to molecular genotyping techniques and subtyping is still not possible with the existing assays. Genotyping techniques are based on detection of genotype specific nucleotide sequences in the HCV genome. This is a labourintensive and expensive method that cannot be used in routine clinical settings. Because they are based on PCR amplification, a high specificity and the possibility of subtyping are the main advantages. Two unique problems in diagnosing HCV remain, even with the third generation tests. The serological tests are unable to differentiate between acute, chronic or past infection ; more advanced (and expensive) techniques are necessary for this. The other problem is the window period between the infection and the first detectable marker, which normally takes 6 to 10 weeks, but occasionally up to 9 months. Specific markers of past infection and recovery and of immunity remain to be identified (39). Next to diagnosing HCV through serum tests, another important tool in the assessment is liver biopsy. It permits determination of the degree of inflammation (grade of hepatitis) and the amount of fibrosis present (stage of hepatitis). Biopsy spaced several years apart may be useful in determining progression of liver disease (19).

Clinical manifestations

Clinical symptoms in patients with acute hepatitis C tend to be milder than those seen in patients infected with the other hepatitis viruses. Most cases are asymptomatic and only 25% of patients with post transfusion hepatitis develop jaundice (40). The hepatitis C infection is considered to be chronic when the viraemia remains for longer than 6 months. Typical for HCV is that most infections will become chronic. Of the HCV infected 60-80% will become carrier of whom 30% will develop cirrhosis and 20% of these will evoluate to hepatocellular carcinoma (41-43). The average time to clinically significant hepatitis is 10 years, the average time to cirrhosis is 21.2 years and the average time to hepatocellular carcinoma is 29 years (44). The natural history of chronic hepatitis C is best documented in transfusion-associated cases, but the long-term prognosis is difficult to predict because the morbidity is

affected by many interactive factors (45). The clinical presentation of chronic hepatitis C may vary depending on the host immune system and the source and duration of infection. Most commonly patients have fluctuating aminotransferase levels but are asymptomatic or have mild fatigue.

Prevalence of HCV in the world

Based on the prevalence in different countries, the World Health Organisation (WHO) estimates that 3% of the world population is infected with the HCV. Roughly 200 million chronic carriers risk liver cirrhosis and/or liver cancer (46). The prevalence of hepatitis C in blood donors has now been ascertained in many countries (29). In most western countries, the prevalence ranges from 0.3% to 0.7%. Japan and southern Europe have higher rates, 0.9 to 1.2%. By extrapolation from studies on seropositivity among blood donors in different European countries, approximately 1.2 million individuals in Europe are HCV positive, 70% of them will develop some degree of chronic liver disease. Nevertheless, these figures will give an underestimate of the true prevalence in the general population since blood donors undergo strict pre-screening and are excluded in case of risk behaviour. In general can be said that blood donors seem to have overall prevalences 25-50% lower than the corresponding general population. A study in the US showed that the prevalence of HCV among healthy blood donors was 0.1 to 0.7% and in the general population 1.4%. In India, China, Cuba and Ethiopia prevalence ranges from 1 to 1.5% were reported among blood donors. High prevalences (1.6-3.5%) were found in some parts of Japan, Indonesia, Turkey, the Middle East, Brazil, and some parts of Russia. Extremely high prevalences have been found in Africans ; for example, in South Africa up to 4.2% of men are anti-HCV positive and in Egypt, up to 15% of persons in community surveys have tested positive (in Cairo even up to 26%) (29). A high prevalence of HCV is found in many risk groups exposed to blood or blood components (20). High prevalences are found in haemophiliacs, 50-90% of whom are anti-HCV positive, depending upon age, duration of infection, factor VIII requirement and the source of factor VIII. The prevalence among intravenous drug users is extremely high (70-92%), because of repeated exposure to carriers of HCV through shared, contaminated material. Several other groups have been shown to be at risk. These include hemodialysed patients, particularly in endemic areas such as Japan and the Middle East (45). Anti-HCV is also common in transplant patients requiring frequent blood transfusions, including renal, liver and bone-marrow transplant recipients. Multiple transfused patients with thallasaemia major also have very high prevalences. Nosocomial or occupational exposure is being evaluated. Health care workers appear to be at relatively low risk. The current distribution of HCV variants has been mapped (33,47). Within Japan, Taiwan and parts of China, genotypes 1b, 2a and 2b are most frequently found. Infection with type 1a in Japan appears to be confined to haemophiliacs who have received commercial (US produced) blood products. However, this genotype accounts for the majority of infections in Thailand, Singapore and possibly Bangladesh and Eastern India. In North and Central Africa genotype 4 is highly prevalent, while in South Africa infections are mainly of the 5a subtype. Type 6 is only found in Hong Kong. In South and North America 1a and 1b are most common. North America has next to this also a lower prevalence of 2a, 2b, 3a and 4. In Europe the subtypes 1a, 1b, 2c and 3a are most common.

The situation in Europe

The prevalence of HCV among blood donors in Europe ranges from very low (0.04-0.09%) in the UK and Scandinavia, to low (0.15-0.5%) in the rest of western Europe and moderate (0.61%) in southern Europe (29). In general, a high level of consistency has been found between the prevalence, risk factors and disease pattern of hepatitis C infection throughout a number of European countries. This may lead to a pan-European approach to the prevention and treatment of HCV infection. Overall the prevalence in the general population is between 0.5 and 2%. Table II gives an overview of the HCV prevalence patterns in Europe (48). As shown above, risk groups include dialysis patients and intravenous drug users, but also groups reluctant to practise safe sex (no condom use, high number of sexual partners and sex involving trauma). Another group at high risk is the immigrant population. In Italy the immigrants from Africa had a prevalence of 6% compared to 0.8-1.5% in the general population. In Belgium the prevalence of HCV among immigrants was 2.1% (general population 0.87%) (49). Still, the far most important risk group for hepatitis C infection in

Table II. — **Prevalence of hepatitis C in different groups (based on ref. 33)**

Country	*Blood donors*	*General population*	*Health care workers*	*Dialysis patients*	*IV drug users*
Germany	0.1%	0.4%	0.6%	20%	> 50%
Switzerland					61%
Spain	0.38%			30%	
Belgium		0.87%	0.11%	12%	57%
France		1.15%		33%	75-85%
Italy	0.68-0.73%	2.2%	0.98%	18-45%	70%

Europe are those that were (are) intravenous drug users at some stage in their lives. A study in the UK showed that most HCV positive drug users had seroconverted within three years of starting to use drugs (48).

Therapy

Current treatment consists of antiviral agents and immunomodulatory agents aimed at altering viral replication and modifying the immune response of the host. At present alpha interferon is the most widely accepted form of therapy for chronic hepatitis C. In many cases though. when interferon is stopped, aminotransferases and HCV RNA promptly return to pretreatment levels. Only 15-20% of the patients treated with interferon for six months will have a sustained response, i.e. normal levels of aminotransferase and the absence of HCV RNA for at least six months (41). Prolonged therapy, up to 18 months, will yield a sustained response in 25-30% of the patients. Next to the duration of the therapy, other factors are associated with a better chance of responding to interferon, such as absence of cirrhosis, lower pre-treatment HCV RNA levels and infection with HCV genotypes other than type 1 (20,41). Although the use of interferon may be associated with many side effects, most patients are able to continue their normal daily activities (19). These side effects include fatigue, leukopenia, thrombocytopenia and neuropsychiatric effects such as depression. According to the US National Institutes of Health, patients with chronic HCV infection, persistently raised serum aminotransferase concentrations and histologic evidence of progression to cirrhosis, should be treated with interferon. They recommend against treatment in case of normal aminotransferase levels and decompensated cirrhosis (19). Because of the side effects, small proportion of patients responding and high cost, new approaches are being developed. The most promising of these is the adjunctive therapy of ribavirin, an orally administrated nucleoside. Preliminary studies suggest that when ribavirin is used together with interferon, there is a significantly higher rate of sustained response (from 18% to 36%) compared to interferon alone (19). For patients with advanced liver disease, liver transplantation is sometimes the only therapeutic option (20). The outcome after transplantation for hepatitis C is good, with patient and graft survival of about 85% to 90% at 1 year. However, virtually all patients become reinfected and about one half develop histological evidence of chronic hepatitis after a few months.

Control and prevention of hepatitis C

Given the limited effectiveness of current treatments, major efforts should go to the prevention of HCV infection. The principal components of a control strategy are (48) :

— Measures to establish adequate public health and information systems addressing occurrence, distribution and cost of infection, and trends in these over time
— Measures to interrupt transmission
— Measures to counsel and control disease in those already infected
— Further research

Public health and clinical information systems should be evaluated and/or set up to monitor trends, occurrence and effectiveness of intervention programs. These systems should also be designed in such a way that coverage of interventions and targeting of new interventions can also be monitored.

To interrupt transmission the universal screening of blood donors has been very effective and almost eliminated parenteral transmission through the transfusion of blood and blood products. However, the tests available for commercial use are unaffordable for some developing countries and special efforts should be made to develop cheap screening tests.

Public health policies on HIV transmission, such as safe sex campaigns and needle exchange programs, are likely to have their influence on HCV transmission as well. Information on HCV could therefor be integrated in HIV prevention programmes building upon their experience. For healthcare workers, the general recommendations on hygiene and precaution, developed to prevent other blood-borne diseases can be implied. Raising awareness through appropriate staff training and institutionalisation of infection control procedures should be standard implementations.

The prevention of vertical, sexual and other modes of transmission requires measures focused both on HCV-infected individuals and on the general population. Counselling should be offered to fully inform HCV-positive individuals to reduce the risk of transmitting HCV to others. Precautions in terms of not sharing toothbrushes, razors and avoiding contact with bleeding wounds should be encouraged. The need for further research is clear from this review. The priorities include development of cheaper screening tests, information on geography, social, demographic and behavioural features of HCV infection in the wider community, natural history of HCV infections, mechanisms and effciency of transmission routes, economical evaluations, etc. Next to this, major efforts are being made to develop a vaccine against HCV. However, the presence of multiple genomic subtypes and mutants and the transient efficacy of neutralising antibodies encumber this research.

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