In the early 1990s, Romania had a high incidence of hepatitis B, with over 30 cases per 100,000 population annually. The disease represented a serious public health problem, especially for children. As a result, public health measures were introduced during the 1990s such as the enforcement of the use of single-use needles and a routine vaccination programme for children and health workers. This paper describes the change in incidence of HBV infection in Romania from the late 1980s until 2005, and demonstrates the impact of those measures. They have lead to a dramatic decrease in hepatitis B incidence across the country: overall, the incidence has decreased from 43 per 100,000 in 1989 to 8.5 per 100,000 in 2004. The decrease has been most prominent in children under 15, dropping from 81 to 11 per 100,000 population and year during that period.

Introduction

Despite the availability of safe and effective vaccines, hepatitis B virus (HBV) infection remains a serious global public health problem, with an estimated two billion people infected and more than 350 million chronic carriers [1].

HBV infection can be either self-limiting or chronic. People with acute, self-limiting infection clear the infection spontaneously and develop protective immunity to the virus. Children are less likely than adults to clear the infection. The risk of developing a chronic infection is inversely related to the age at infection and ranges from over 90% in those infected as newborns to under 5% in immunocompetent adults [2]. Around 15 to 25% of chronic carriers develop cirrhosis or hepatocellular carcinoma [3].

HBV surface antigen (HBsAg) is the first detectable viral antigen to appear during infection, and the one most frequently used to screen for the presence of HBV infection. HBsAg disappears with clearance of the infection. Instead, IgG antibodies against the surface and core antigens (anti-HBs and anti-HBc) become detectable. A sample negative for HBsAg but positive for anti-HBs indicates either a past infection or vaccination. Chronic HBV infections are characterised by persistence of HBV surface antigen (HBsAg) in the serum for at least six months [2].

Romania has a history of high incidence of hepatitis B, especially in children. Between 1990 and 2002, it reported a yearly incidence of 10-50 HBV infections per 100,000 population [4]. According to two comparative studies on morbidity rates conducted in 1990 in several European countries, hepatitis B was endemic in Romania [5,6]. In a study conducted in Bucharest (April-July 1990), the prevalence was high in all age groups, with 47% of adults and 40% of children aged 0-16 years positive for at least one HBV marker (HBsAg and/or anti-HBc). Among infants (children under three years of age) living in orphanages, the prevalence of at least one HBV marker (HBsAg and/or anti-HBc) was 55%. In the same study, almost 8% of pregnant women were found to be HBsAg-positive [5].

A different study performed in 1990 reported a prevalence of current HBV infection (determined as HBsAg positivity) of 3.8% among pregnant women in northwestern Romania [7]. The most effective route of infection is transmission from infected mothers to newborns, both perinatal and during early childhood [7]. Other possible forms of transmission include contaminated blood products and tissues, child-to-child transmission, re-use of contaminated needles and syringes, and unprotected sexual contact [1].

Another study from 1995 showed that 32% of pregnant women admitted to give birth in southern Romania had evidence of past or current HBV infection (determined by presence of either anti-HBc or HBsAg) [8].

The following preventive measures have since been taken in Romania to control the high incidence and prevalence of HBV infection:

1991 After reports on HIV infections associated with the possible re-use of syringes and needles among children in Romanian orphanages, single-use syringes were introduced for immunisation programmes and in all healthcare settings in Romania. By the late 1990s, single-use syringes and needles were reported to be the standard for all injections [9].

1992 The generalised use of modern immunoenzymatic assays (ELISA for HBsAg and anti-HBc) was introduced for blood donations and viral hepatitis diagnostics.

1995 The HBV vaccine was introduced into the routine immunisation schedule for newborns (first dose at birth) and health care workers.

1999 HBV vaccination was expanded to include nine-year-old children (born before vaccine introduction in the Extended Programme of Immunisation (EPI)) and medical students.

2004 HBV vaccination was expanded to include 18-year-olds (born before vaccine introduction in the EPI).

Since 1995, Romania has used the following hepatitis B vaccination schedules:

• For newborns, the first dose of HBV vaccine is given 24 hours after birth, with second and third doses at two and six months of age (0-2-6). Since 2002, a combined vaccine against HBV and diphtheria, tetanus, and pertussis (DTP-HBV) has been used for the second and third doses.

This paper describes the change in incidence of HBV infection in Romania, 1989-2005, marker (HBsAg and/or anti-HBc). Among infants (children under
For schoolchildren, teenagers and health care workers, a standard vaccination schedule of three doses, with the first after birth, and the other two at one and six months of age (0-1-6), has been used.

This study was conducted in order to assess the impact of these public health measures and to describe the incidence of HBV infection in Romania over a period of over 15 years, from 1989 until 2005.

**Methods**

Surveillance data on hepatitis B incidence in Romania was obtained from the following two reporting systems and used to describe the change in hepatitis B epidemiology from 1989 to 2005:

1. The mandatory reporting of acute viral hepatitis (in place since 1978). The reports are sent on a monthly basis. Data for acute hepatitis A, B, and C are collected in an aggregated format by type of hepatitis, district, age groups, and type of residence (urban or rural). The primary data are reported by infectious diseases hospitals and general practitioners to the local (district) public health authorities, and from there to the National Health Statistics Centre.

2. A case-based passive surveillance system for acute viral hepatitis, in place since 1997 in order to provide additional data regarding risk factors, vaccination status and laboratory results. The case classification is based on standard case definitions (European Union case definitions since 2004), a standard investigation form is filled in by the epidemiologist from the local public authorities and sent quarterly to the four regional public health institutes. The data are analysed on the regional level and transferred to the National Centre of Communicable Diseases Prevention and Control.

**Results**

**Overall trend in HBV incidence**

Based on the mandatory reporting of acute infections, the trend in hepatitis B incidence in Romania was followed over a period of almost 20 years, from 1986 to 2004. Since 1989, the incidence has decreased significantly, from 43 per 100,000 population in 1989 to 25 per 100,000 in 1995 and 8.5 per 100,000 in 2004 (Figure 1) [10]. The numbers show a steady decrease, with the exception of a slight increase around 1995.

**Trend according to age group**

Two main age groups, 0-14 year-olds and over 14 year-olds, were analysed separately in order to assess the effect of the new vaccination policy. The data clearly show that the trend in hepatitis B incidence is decreasing for both age groups (Figure 2).

Both curves show a relapse around 1993-1995. This temporary increase is stronger for the group of 0-14-year-olds, but is followed by a sharp decline in the number of acute infections. As of 2005, there were almost no reports of hepatitis B in this age group.

**Impact of immunisation programmes**

Since 1995, Romania’s vaccination policy has focused primarily on children. By the end of the period between 1995 and 2004, over 95% of the 0-18-year-olds had been immunised, according to data from the Centre for Prevention and Surveillance of Communicable Diseases at the Institute of Public Health in Bucharest. Routine immunisation coverage of children is estimated based on the WHO methodology (EPI cluster) [11] at 18-24 month of age.
The vaccine coverage for health care workers was 63% (data from the Centre for Prevention and Surveillance of Communicable Diseases). In addition, other people can be vaccinated on a voluntary basis as a result of health promotion campaigns between 2001 and 2004, but the cost of the vaccine has to be paid by the vaccinees themselves.

In order to assess in a comprehensive manner the impact of the vaccination programme on the hepatitis B incidence in children, data for children at different ages were compared. Figure 3 shows the numbers reported in the years 1990 (before the introduction of routine HBV vaccination), 1998 (three years after the introduction of routine HBV vaccination of newborns) and 2005 (10 years after the introduction of routine HBV vaccination).

Three years after the introduction of routine vaccination of newborn children, a dramatic reduction in HBV infections was observed in all children under the age of 14. By 1998, the danger of infection had almost disappeared in children under the age of four years who had received the vaccine at birth. But even in the group of 5-14 year-olds, a dramatic effect was already apparent in 1998. There was a further reduction in incidence in these age groups by 2005, when routine immunisation covered children up to the age of 10 years.

Geographical differences

To assess possible geographical differences within Romania, we compared the hepatitis B incidence in 1995 and 2004 based on districts. As shown in Figure 4, there was significant heterogeneity throughout the country in 1995, with some districts reporting an incidence of under 11.7 per 100,000 population, compared to over 36.7 per 100,000 in others. In 2004, all districts had reduced their HBV incidence to be under 11.7 per 100,000.

Discussion

According to HBV serology data published in the final report of the European Sero-Epidemiology Network 2 (ESEN2) [12], 28% of serum samples from Romania in 2002 were positive for anti-HBc and 8% for HBsAg. The number of new cases has further decreased since then, especially in children, indicating the overall success of the public health measures adopted during the 1990s that is due to the introduction of single-use syringes, blood testing and more general precautions.

Since 2003, Romania has had a hepatitis B incidence in the range of 0-10 cases per 100,000 [4]. It is currently an intermediate prevalence country for chronic HBV infection with 2 to 7% of the population HBsAg-positive [3].

When HBV vaccination was introduced, it aimed at reaching a high coverage for different age groups of children and teenagers in a reasonable period of time through a programme compatible with human and financial resources. By 2005, a vaccination coverage of over 95% had been reached and was reflected in an almost complete disappearance of new hepatitis B cases registered in children. However, it needs to be noted that hepatitis B infection in children is often asymptomatic and therefore may be underreported.

Already by 1998, three years after the introduction of routine vaccination, almost no new hepatitis B infections were reported from the age group of 0-4-year-olds, and the incidence was dramatically reduced even in older children. This is probably due to the fact that vaccination of their younger siblings has reduced the risk of child-to-child transmission, while immunisation of health workers has reduced the risk of infection of children in health care institutions.

Analysis of the development by district indicates that the immunisation programme has been implemented effectively in all parts of Romania, with all districts having reduced the hepatitis B incidence to below 11.7 per 100,000 population by 2004. Despite this encouraging development regarding HBV infection control in Romania, many actions should still be taken, in particular a more efficient approach to increase the vaccination coverage in hard-to-reach groups of population (e.g. Roma) who often suffer from new hepatitis B cases [13]. A study performed in Bucharest in 2001 suggested that the transmission of acute viral hepatitis B and also C was more frequently associated with individuals’ behaviour (in 19% of hepatitis B and 20% of hepatitis C cases) than with iatrogenic transmission. In the case of hepatitis B, sexual contacts with more than one partner are the most common route of transmission (16%) [14].
References

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This article was published on 10 January 2008.