Programme for preventing perinatal hepatitis B infection through screening of pregnant women and immunisation of infants of infected mothers in the Netherlands, 1989-92

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See p 1197 and editorial

Abstract

***Objectives*—To launch a programme for the prevention of perinatal infection with hepatitis B in the Netherlands.**

***Design*—Routine antenatal screening and intervention programme.**

***Setting*—Community antenatal programme, the Netherlands.**

***Subjects*—Infants of mothers who were carriers of hepatitis B detected by routine screening.**

***Interventions*—Infants of infected mothers received hepatitis B immunoglobulin at birth and four doses of hepatitis B vaccine in conjunction with routine immunisation at 3, 4, 5, and 11 months of age.**

***Main outcome measures*—Results of screening and immunisation from 1989-92.**

***Results*—The coverage of screening increased from 46% in 1989 to 84% in 1992. Hepatitis B surface antigen was detected in 2145 women (0·44%). The coverage of postnatal immunoprophylaxis in 1645 neonates born to mothers who were carriers of hepatitis B was 85% (1391); in 3% (42) there was a delay in administration of immunoglobulin of over 24 hours. In 1991, 96% (537), 95% (532), 94% (525), and 87% (489) of the infants received the first, second, third, and fourth dose of vaccine, respectively. There was considerable variation in the timing of vaccination; 17% (258) of the infants received their first dose more than two weeks late. Of the 59% (583) of infants who received the fourth dose more than two weeks beyond target age, 14% (141) also received their first dose too late.**

***Conclusions*—A prevention programme for perinatal hepatitis B in an area of low prevalence, when incorporated into existing health care, is feasible and achieves satisfactory coverage rates. Intensive follow up is needed to improve adherence to the immunisation schedule.**

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Introduction

In the Netherlands the prevention of hepatitis B infection focuses on individuals at risk, and neonates born to carriers of hepatitis B constitute an important target group. A multicentre study showed a prevalence of hepatitis B of 0·7% among the pregnant population screened.[1] With an annual number of births of around 200 000 about 1400 infants will be at risk of infection each year.

Passive-active immunisation of neonates has been shown to be safe and highly efficacious in preventing perinatal infection with hepatitis B virus.[2-4] If women who are positive for hepatitis B surface antigen can be identified through antenatal testing immunoprophylaxis can be offered to their infants. Hepatitis B immunoglobulin given directly after birth followed by hepatitis B vaccination at the ages of 3, 4, 5, and 11 months, concomitant with the diphtheria-tetanus-pertussis-polio injections, can prevent more than 90% of hepatitis B infection and is associated with high antibody responses.[5-7] With a high dose of hepatitis B immunoglobulin at birth the timing of the start of vaccination seems less important, so for reasons of compliance and low cost delayed active immunisation in conjunction with visits for routine immunisation was considered an attractive alternative to early active immunisation as recommended by the manufacturers of the vaccine.[5,6] On 1 October 1989 a nationwide programme was launched to detect women positive for hepatitis B surface antigen by routine screening in the first trimester of pregnancy. Passive-active immunisation against hepatitis B was advised for their infants. This paper describes the programme logistics and coverage rates between 1 October 1989 and 31 December 1992.

Methods

NATIONAL GUIDELINES

The screening for hepatitis B surface antigen has been added to the routine testing for ABO, rhesus blood groups, and syphilis in the first trimester of pregnancy. Laboratory facilities have been enhanced in the existing 16 regional public health laboratories already responsible for this "prenatal panel." All samples positive for hepatitis B surface antigen are confirmed and tested for other hepatitis B virus markers—that is, hepatitis B e antigen and antibodies to hepatitis B core antigen. Positive test results are forwarded to the person taking care of the pregnant woman together with a protocol defining how an infant is to receive hepatitis B immunisation. Screening at delivery should be performed if the results of the test for hepatitis B surface antigen during pregnancy are not available.

The provincial immunisation administration, which provides vaccine and maintains a computerised database of births and immunisation records for every infant in the province until the age of 13 years, receives a copy of each positive test result together with the expected date of delivery. The administration sends a registration card for passive immunisation to the professional who takes care of the delivery. As the proportion of home deliveries is high the professional prescribes hepatitis B immunoglobulin. Infants receive 1 ml hepatitis B immunoglobulin containing 300 IU/ml intramuscularly as soon as possible after delivery. The registration card is returned to the provincial immunisation administration, and the mother is given a prescription for hepatitis B vaccine.

The administration is notified of all births by the local registry and thereupon checks the files for infants of mothers with hepatitis B. If no hepatitis B immunoglobulin card is returned two weeks after the expected delivery date, the administration contacts whoever is taking care of the woman to ascertain the outcome of pregnancy and administration of hepatitis B immunoglobulin.

Information about the need for immunisation of her infant is given to the mother by a public health nurse. Access to primary health care is excellent: almost all

infants visit the child health clinics for routine check ups and childhood vaccinations, which are free of charge. A vaccination booklet containing four coupons for diphtheria-tetanus-pertussis-polio vaccine plus four coupons for hepatitis B vaccine is mailed by the provincial immunisation administration to the mother. Infants receive 1 ml of recombinant hepatitis B vaccine intramuscularly. The diphtheria-tetanus-pertussis-polio injection is given to the contralateral thigh at the same visit. The vaccination coupons are returned to the administration. If the appropriate coupon is not received within two weeks after the target age, the administration sends a reminder for vaccination to the parents.

EVALUATION OF COVERAGE AND COMPLIANCE

The coverage of screening was estimated by the number of screening tests divided by the number of notified births. The target ages for the general vaccination schedule in the Netherlands are 13, 17, 22, and 48 weeks. The data on the coverage of vaccination presented include the birth cohort of 1991, whose youngest member had reached the target age for the fourth dose of hepatitis B vaccine at 48 weeks of age. The infants studied for adherence to the vaccination schedule were those born between 1 October 1989 and 31 December 1992.

Results

Table I shows the coverage of screening. The overall prevalence for hepatitis B surface antigen was 0·44% (2145); 224 women were also positive for hepatitis B e antigen. The prevalence found in the urban centres of Amsterdam and Rotterdam was 0·79% (900/114 447) and 0·33% (1245/373 037) in the other regions. Screening at the time of delivery was performed in 174 cases; of these samples 3 (1·7%) were positive. A total of 1645 infants were born to mothers positive for hepatitis B surface antigen. Passive immunisation was given to 85% (1391) of the infants; 97% (1349) received hepatitis B immunoglobulin within 24 hours after birth and 99% (1377) within the first week of life. In the 254 remaining infants this injection was either not registered or not administered. Throughout the study the coverage rates of vaccination showed a rising trend, and in 1991 coverages of 96%, 95%, 94%, and 87% were registered for the four doses of vaccine, respectively (table I). It was reported that 18 infants left the country, seven infants died of causes not associated with vaccination, and five parents refused vaccination on religious grounds. Table II gives details of the number of vaccinees and timing of administration of the vaccine. Overall 17% (258) of infants received the first dose of vaccine more than two weeks later than planned. This percentage increased to 59% (583) for the fourth dose of vaccine; 14% (141) of these infants had already received the first dose of vaccine beyond the designated time.

TABLE I—*Coverage of screening and prevalence of hepatitis B surface antigen in pregnant women in the Netherlands per year, and coverage rates of passive-active immunisation in infants born to mothers positive for hepatitis B surface antigen, 1989-91. All figures are numbers (percentage)*

Detail	1989*	1990	1991	1992
Live births	46 351	197 198	199 057	195 730
Maternal samples tested	21 275† (46)	142 878 (73)	158 255 (80)	165 076 (84)
Maternal samples positive for HBsAg	97 (0·46)	639 (0·45)	732 (0·46)	677 (0·41)
Infants born to mothers positive for HBsAg‡	56	457	560	572
Infants given:				
HBIg	39 (70)	385 (84)	483 (86)	484 (85)
Vaccine 1	49 (88)	423 (93)	537 (96)	NA
Vaccine 2	48 (86)	414 (91)	532 (95)	NA
Vaccine 3	45 (80)	402 (88)	525 (94)	NA
Vaccine 4	38 (68)	327 (72)	489 (87)	NA

*Last quarter only.
†Data missing from three regional public health laboratories.
‡Data for Amsterdam excluded.
NA=not available.

TABLE II—*Time in weeks at which vaccine doses were administered in relation to target age and compliance with immunisation schedule projected as number of infants immunised more than two weeks after target age*

		Age at vaccination in weeks			No (%) with delayed vaccination	
Vaccine	No of infants	Target age	Median	5th and 95th Percentile	More than 2 weeks after target age	Dose 1 also >2 weeks late*
Dose 1	1509	13	14	9;20	258 (17)	
Dose 2	1461	17	18	15;26	371 (25)	219 (15)
Dose 3	1378	22	24	21;36	520 (38)	205 (15)
Dose 4	982	48	51	47;67	583 (59)	141 (14)

*When infant receives first dose of vaccine >2 weeks later than planned additional doses are probably also delayed.

Discussion

The results show that the integration of screening into routine antenatal care and the integration of hepatitis B vaccine into the existing childhood immunisation programme are effective because of excellent access to primary health care.

SCREENING

The coverage of screening is more complete than reported in Italy (51%) after three years of screening but similar to that reached in Taiwan (78%) after 15 months.[8,9]

Migration as well as termination of an unknown number of pregnancies preclude accurate calculation of the proportion of pregnant women screened for hepatitis B surface antigen who actually gave birth in the study period. It is not known how many pregnant women were not screened or were possibly tested in non-participating laboratories as 263 infants (16%) were reported to the provincial immunisation administration in the postnatal period. It is encouraging that the coverage of screening in the regional public health laboratories increased over the years.

The overall prevalence for hepatitis B surface antigen among the pregnant women was 0·4%. This prevalence is lower than the 0·7% described previously.[1] This may have several causes. Firstly, many professionals do not know about the screening programme, and women known to be carriers of hepatitis B are not always rescreened in subsequent pregnancies. Secondly, the pregnant women from whom screening data are missing could belong to a socially underprivileged group who do not seek routine antenatal care. Screening at delivery, usually outside office hours, was performed in a limited number of cases for financial and logistical reasons resulting in a four times higher prevalence. Thirdly, selection of populations previously studied may also play a part.

PASSIVE-ACTIVE IMMUNISATION

The provincial immunisation administration is responsible for the immunisation programme carried out in each province. The computerised data management and active role (information, cold chain, and reminders) of the administration result in very high rates of immunisation. Non-registration of passive immunisation in 15% of infants may not necessarily mean that hepatitis B immunoglobulin was not administered. Some candidates for immunoprophylaxis were apparently detected outside the appointed laboratories, and in large hospitals the registration was often incomplete. The suboptimal coverage needs full attention as active immunisation is delayed until the age of 3 months.

The administration of hepatitis B vaccine in combination with the national childhood vaccination programme resulted in a higher compliance than reported for the United States.[10-12] Still, the 87% of infants who completed hepatitis B vaccination is lower than the average of 93% of infants who complete the series of diphtheria-tetanus-pertussis-polio vaccine.[13] As most infants who require hepatitis B vaccine have

Key messages

- If women positive for hepatitis B surface antigen can be identified immunoprophylaxis can be offered to their infants
- From 1989 a nationwide programme in the Netherlands offered passive-active immunisation against hepatitis B for the infants of mothers detected positive for hepatitis B surface antigen during routine screening. After immunoglobin at birth four doses of vaccine were offered in conjunction with routine immunisations
- The coverage of screening increased from 46% of mothers in 1989 to 84% in 1992. Postnatal immunoprophylaxis was achieved in 85% of 1645 infants born to carrier mothers
- By 1991, 96%, 95%, 94%, and 87% of infants received, respectively, the first, second, third, and fourth doses of vaccine, but there was considerable variation in timing
- A prevention programme for perinatal hepatitis B in an area of low prevalence, incorporated into existing health care, is feasible and achieves satisfactory coverage

parents originating from Mediterranean or other immigrant countries, demographic variables and language barriers can be important reasons for incomplete immunisation.[14]

Although the coverage rates may not be fully reliable, the results over the years are encouraging. About 17% of infants, however, were not vaccinated according to schedule; mostly vaccinations were delayed. If an infant receives the first dose of vaccine later than the target age the second and third injections are probably also delayed as the recommended time interval between doses is four weeks. Off schedule immunisation remains a matter of concern, although some delay in the administration of vaccine does not seem to have an effect on the protective efficacy in Gambian infants, and protective antibodies still develop by using flexible schedules.[14,15]

CONCLUSIONS

The national programme for the prevention of perinatal hepatitis B infection was successfully implemented in the existing health care. Improvements, however, still have to be made. Routine antenatal screening for hepatitis B surface antigen should be enhanced, preferably in the selected laboratories. Vaccination should be improved through motivation of the parents concerned and education of health care workers. The registration procedures also need improvement.

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ONE HUNDRED YEARS AGO

CYCLE AMBULANCES.

The use of ambulances mounted on cycle wheels and driven by one or more cyclists appears likely to extend. The city of Birmingham was presented with a cycle ambulance some months ago. In this pattern a frame carrying a hooded detachable stretcher is supported on two bicycles, which could each be ridden by a cyclist. We now learn that a German surgeon, Dr. Hoenig, has designed an apparatus which he calls a cyclo-ambulance. It consists of a car covered in with canvas, which contains a folding litter, and rests on four side wheels, and a fifth wheel in front pedalled by a cyclist. A seat and pedals are also provided at the back for another cyclist. The top part of the car can be lifted off, a patient can then be placed on the litter, and the top replaced on the axles. The patient can be watched by the cyclist at the back through a glazed window; but the patient is also provided with means of attracting the attention of the cyclist by using the rubber ball of a cycle horn. An aperture in the side of the car affords access to the patient when he is in need of help. The ambulance is reported to be in experimental use in Berlin, and is easily steered and manipulated.

(*BMJ* 1895;ii:1181.)