Success of a program of routine prenatal screening for hepatitis B surface antigen: the first 2 years

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Prenatal screening for hepatitis B surface antigen (HBsAg) restricted to women with defined risk factors for chronic hepatitis B virus (HBV) infection fails to identify many carriers. A centralized program of routine HBsAg screening for all pregnant women in Alberta was introduced in 1985. We collected and analysed data for the first 2 years of the program in Edmonton to determine the frequency of risk factors for HBsAg positivity, the proportion of multiparous HBsAg-positive women not identified in previous pregnancies, the efficiency and cost-effectiveness of providing immunoprophylaxis to infants at risk of HBV infection and the degree of success in inducing adequate protection. A total of 149 women (158 pregnancies) were found to be HBsAg positive. Risk factors were readily ascertainable for 85% of the women; the remaining 15% would not have been identified through risk-selective screening. The most common risk factors were Oriental ethnic origin, history of hepatitis, jaundice or multiple transfusions of blood or blood products, and occupational exposure to blood. Although 86% of the multiparous HBsAg-positive women had risk factors, only 7% had been identified in previous pregnancies. The Alberta program appears to be cost-effective. We conclude that only routine prenatal screening will identify all infants at risk of perinatal HBV infection and that a comprehensive public health program involving central laboratories, private physicians and public health staff can be highly effective and efficient in protecting infants against hepatitis B.

Le dépistage prénatal de l'antigène de surface de l'hépatite B (AgHBs) limité aux femmes qui présentent un risque précis d'infection par le virus de l'hépatite B (VHB) chronique ne réussit pas à dépister de nombreuses porteuses. On a lancé, en 1985, un programme centralisé de dépistage de routine de l'AgHBs chez toutes les femmes enceintes de l'Alberta. Nous avons recueilli et analysé des données sur les 2 premières années du programme à Edmonton afin d'établir la fréquence de facteurs de risque au sujet de la présence de l'AgHBs, la proportion de femmes multipares qui ont réagi positivement et n'ont pas été identifiées au cours de grossesses antérieures, l'efficience et la rentabilité d'une immunoprophylaxie aux nouveaux-nés qui risquent une infection à HBV et la mesure dans laquelle on a réussi à assurer une protection suffisante. Au total, 149 femmes (158 grossesses) ont réagi positivement au test de dépistage de l'AgHBs. Les facteurs de risque ont été faciles à établir dans 85 % des cas. Le dépistage sélectif selon le risque n'aurait pas réussi à identifier les 15 % restants. Les facteurs de risque les plus fréquents étaient l'origine ethnique orientale, des antécédents d'hépatite, d'ictère ou de transfusions multiples de sang ou de produits du sang, et l'exposition professionnelle au sang. Même si 86 % des femmes multipares qui ont réagi positivement présentaient des facteurs de risque, 7 % seulement avaient été identifiées au cours de grossesses antérieures. Le programme albertain semble rentable. Nous en concluons que seul un dépistage prénatal de routine permettra d'identifier tous les nouveaux-nés qui risquent une infection périnatale par le VHB, et qu'un programme complet d'hygiène publique auquel participeront des laboratoires centraux, des médecins du secteur privé et des services d'hygiène publique peut réussir à protéger efficacement les nouveaux-nés contre l'hépatite B.

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The potentially serious clinical consequences of mother-infant transmission of hepatitis B virus (HBV) have been well documented. As many as 70% of infants born to women who are chronic carriers of hepatitis B surface antigen (HBsAg) become infected with HBV.[1] The virus carrier state develops in up to 90% of infected infants, with a lifetime risk of 25% of death from chronic liver disease or hepatocellular carcinoma.[1] The administration of hepatitis B immune globulin (HBIG) soon after delivery, followed by three doses of hepatitis B vaccine, has proved successful in preventing perinatal HBV transmission in about 85% to 95% of cases.[2-4] Since immunoprophylaxis is most effective if started as soon as possible after delivery, prenatal identification of pregnant women who are carrying HBV (HBsAg positive) is desirable.

Soon after hepatitis B vaccine became available in North America, in 1982, screening for HBsAg was strongly advocated for pregnant women considered to be at increased risk for HBV infection.[1,5-7] Despite the ready access to immunoprophylaxis at no direct cost to patients, the infrequent requests for HBIG and the small amount of hepatitis B vaccine requisitioned for newborns during the first 30 months after its licensure in Canada suggested that few physicians in Alberta were actually testing pregnant women for HBsAg. Similar observations elsewhere have since led to recommendations for routine prenatal hepatitis B screening rather than selective screening on the basis of recognized risk factors.[8-15]

In 1985 Alberta introduced a province-wide program of routine prenatal HBsAg screening. We analysed data collected during the first 2 years of the program in Edmonton to determine (a) the most common risk factors for HBV infection among HBsAg-positive women, (b) the number of HBsAg-positive women with no identifiable risk factors, who would not have been identified through selective screening, (c) the number of multiparous HBsAg-positive women not identified in previous pregnancies (which would suggest failure to identify these women without routine screening), (d) the efficiency and cost-effectiveness of identifying and providing immunoprophylaxis to infants at risk of perinatal HBV infection and (e) the level of protection against hepatitis B produced in infants.

Methods

Beginning in August 1985 all routine prenatal blood samples submitted from all regions of Alberta to the Canadian Red Cross Society Blood Transfusion Service (CRCSBTS) in Calgary and Edmonton were assayed for HBsAg with a highly sensitive and specific enzyme immunoassay (Auszyme II, Abbott Laboratories, North Chicago, Ill.).[16] The CRCSBTS is responsible for blood typing and antierythrocyte antibody screening of all prenatal patients; therefore, no extra blood samples or requisitions from physicians were needed to carry out the initial HBsAg screening. Women who were found to be positive for HBsAg had a second assay; if the result was positive a confirmatory neutralizing antibody test was done at the CRCS National Reference Laboratory, Toronto (moved to Ottawa in June 1987). Women confirmed to be HBsAg positive at the first prenatal visit were retested at 36 weeks' gestation to ensure that the result reflected a true chronic-carrier state rather than an acute, clinically inapparent infection that subsequently resolved. The few women who presented for delivery without a record of prenatal screening were tested for HBsAg as soon as possible after admission to hospital.

The attending physician was informed by letter and telephone of the initial result for each HBsAg-positive patient. In Edmonton the telephone interviewer routinely recorded specific information on risk factors for HBV infection, including ethnic origin, occupational exposure to blood, history of hepatitis, jaundice or multiple transfusions of blood or blood products, use of injection drugs by the woman or her sexual partner(s), history of close contact with HBV carriers and any record of previous identification of HBsAg-positive status. The physician was informed that arrangements would be made for HBIG to be sent to the appropriate hospital 2 weeks before the patient's expected date of delivery. The medical officer of health of the local health unit was notified of HBsAg-positive women by letters from provincial health department staff.

Arrangements were made to administer HBIG and the first dose of hepatitis B vaccine in the hospital, as soon as possible after delivery. Two additional doses of vaccine were given at the health unit, about 1 to 2 months and 6 months after birth, usually in conjunction with visits for routine immunization. It was advised that children be tested at 1 year of age for HBsAg and antibody to HBsAg (anti-HBs). Vaccine was also offered to other household contacts of HBsAg-positive women. Compliance with recommendations was monitored by provincial health department staff through regular reminders just before the expected date of delivery, after HBIG should have been administered, after the infant was 6 months of age and at 1 year of age.

Data were obtained from the initial telephone interview with the attending physician and a review of the hospital chart, including the prenatal record, standardized for all pregnant women in the province. We reviewed the data for all confirmed HBsAg carriers whose first prenatal blood sample was positive between Aug. 1, 1985, and July 31, 1987, and who were scheduled to give birth in Edmonton.

Results

Over the study period 122 233 prenatal blood samples were screened for HBsAg in the Alberta program, 76 608 being tested by the CRCSBTS in Edmonton. A total of 403 women were confirmed to be HBsAg positive, for a province-wide rate of 0.3%. In Edmonton we identified 149 HBsAg-positive women, 9 of whom had two pregnancies, for a total of 158 pregnancies carried to term. The number of live births in Edmonton during the study period was 28 028, for an HBsAg positivity rate of about 1 per 180 live births (0.6%).

The ethnic origin of the 149 women was as follows: Oriental, 109 women (73%); white, 21 (14%); Arabic, 4 (3%); East Indian, 3 (2%); African, 3 (2%); Haitian, 1 (1%); Jamaican, 1 (1%); and native Indian, 1 (1%). In six cases (4%) the ethnic origin was unknown. Being of Oriental extraction was by far the most common risk factor: 82 (75%) of the 109 Oriental women had no other identifiable risk factors for HBV infection. The next most commonly identified risk factors were history of hepatitis, jaundice or multiple transfusions of blood or blood products (15 women [10%]) and occupational exposure to blood (12 women [8%]). Only two women (1%) acknowledged a history of injection drug use, and one (1%) was aware of exposure to a family member with chronic hepatitis B. In 22 cases (15%) there was no identifiable risk factor.

To determine the number of HBsAg-positive women not identified through previous selective screening we further examined the records of multiparous HBsAg-positive women. Of the 103 pregnancies of multiparous women 89 (86%) of the women had at least one risk factor for HBV infection. Only 7 women (7%) had been identified as HBsAg positive during a previous pregnancy, and another 20 (19%) had been identified on other occasions (Table 1).

Of the 158 pregnancies identified as being at risk for perinatal transmission of HBV infection 3 did not result in a live birth, and four women moved out of the province before delivery. Of the 151 infants born in Edmonton 3 (2%) were lost to all follow-up, and one mother refused hepatitis immunization for her infant. Table 2 shows the immunization status and anti-HBs test results among the 148 infants offered immunoprophylaxis.

Serum samples were obtained from 67 infants about 6 months after the third dose of hepatitis B vaccine had been given. All were negative for HBsAg, and 66 (98%) were reported to have levels of anti-HBs indicative of immunity. The parents of most of the remaining 71 children who completed the immunization program refused or neglected to have anti-HBs testing done; a few reported that their children had been tested, but the results were unavailable.

Discussion

Several recent studies involving a hospital or community-based obstetric population have shown that routine screening of pregnant women for HBsAg is warranted.[8-12] Our study demonstrates the success of a province-wide routine prenatal screening program that began in August 1985.

Several factors made it difficult to determine accurate rates of HBsAg positivity among pregnant women in Alberta. Owing to changes in name through marriage and the likelihood that duplicate blood samples were submitted during the same pregnancy in some cases (in addition to the samples obtained at 36 weeks' gestation) the number of women represented by the 122 233 blood samples screened could not be determined. Migration of women out of the province as well as termination of an unknown number of pregnancies through spontaneous or therapeutic abortion precluded accurate calculation of the proportion of pregnant women

Table 1: Distribution by parity of 149 women (158 pregnancies) found to be positive for HBsAg* through routine prenatal screening program in Edmonton between August 1985 and July 1987, as well as proportions identified previously

Parity on entry	No. of pregnancies	No. (and %) of women	
		Identified before screening program	Identified during previous pregnancy
0 (n = 55)	55	4 (7)	–
1 (n = 52)	56	9 (16)	3 (5)
2 (n = 31)	34	4 (12)	2 (6)
3 (n = 8)	10	2 (20)	2 (20)
4 (n = 3)	3	1 (33)	0 (0)
1–4 (n = 94)	103	20 (19)	7 (7)

*HBsAg = hepatitis B surface antigen.

screened for HBsAg who actually gave birth in Alberta. The data for the Edmonton study population were derived from the provincial screening program. As a result, the exact number of Edmonton residents who were included in prenatal screening and subsequently gave birth at one of five city hospitals could not be extracted as a subpopulation from the total. Our estimates of HBsAg positivity rates among pregnant women in the province (0.3%) and in Edmonton (0.6%) are comparable to the rate of 0.6% determined in a pilot study conducted in Manitoba during 1987–88.[17]

In our study risk factors could readily be determined for 85% of the HBsAg-positive women. This proportion is much higher than the rate of about 50% reported by other investigators[8–12] and is almost certainly due to the method of data collection. One of four interviewers contacted the attending physician in each case of HBsAg positivity, which likely increased our identification of salient risk factors that the physician might otherwise have overlooked. Despite the large proportion of high-risk pregnancies in our study, 15% of the HBsAg-positive women would not have been identified even if risk-selective screening were completely effective. Thus, 22 infants would have remained unprotected against HBV infection.

There are several difficulties with the use of risk criteria alone in screening pregnant women for HBsAg. First, physicians may not be familiar with these criteria. In a recent study 40% of obstetricians could name no more than two groups at high risk for HBV infection, and only 28% knew the recommended treatment for infants born to women who were HBV carriers.[14] Second, in a busy obstetric practice physicians may not take the time to elicit risk factors when taking the patient's history or may feel inhibited about asking for explicit details of the sexual or drug use history. Even if questioned the patient may not admit to a history of injection drug use or sexually transmitted disease.[8,14] Third, risk criteria vary from one authority to another. In addition to the standard recommendations[7] the inclusion of single marital status and low socioeconomic status as risk criteria has been found to increase the number of high-risk pregnancies identified.[18]

Table 2: Immunization status and results of test for antibody to HBsAg (anti-HBs) at 1-year follow-up among 148 infants offered hepatitis B immune globulin (HBIG) and vaccine

Variable	No. of infants
Date HBIG received	
Day 1	130
After day 1	2
Not recorded	15
HBIG refused by parent	1
Date first dose of hepatitis B vaccine received	
Within 1 wk after birth	133
After 1 wk	2
Not recorded	12
Vaccine refused by parent	1
Vaccination follow-up	
Lost before third dose	8
Died before third dose	1
Received third dose	138
Anti-HBs test result at 1 year	
Positive	66
Negative	1
Unknown or test not done	71

A persuasive argument for the use of routine prenatal HBsAg screening is found in our results for multiparous women. Despite the fact that 86% had at least one risk factor, only 7 of the 103 had been identified as HBsAg positive in a previous pregnancy. One could speculate that without routine screening most of the remaining 96 women would have completed the current pregnancy without being identified. Some of the women may previously have given birth in areas where HBsAg testing is not widely practised. However, of the nine women screened during two pregnancies in Edmonton over the study period, three consulted a different physician in their second pregnancy and were reidentified only through the routine screening program. Other women may have been identified elsewhere and did not volunteer this information or were not asked about it in their subsequent pregnancy. Some women may have been tested by their physicians independent of the provincial program. There is also a small chance that some women became HBsAg positive between pregnancies. It seems unlikely that any of these factors could account for the high number of women previously unrecognized as HBsAg positive.

The success of any perinatal hepatitis B prevention program is measured by its ability to ensure effective immunoprophylaxis among all infants identified through maternal HBsAg screening as being at risk.[8] Theoretically, the only infants not successfully treated in such a program would be the approximately 5% of at-risk infants who acquire HBV infection transplacentally.[7] The Alberta program achieved a much higher level of compliance in Edmonton than that reported by Jonas and associates[19] in Miami (94% v. 33% of the infants received the full three doses of vaccine). The levels of compliance with postimmunization testing for anti-HBs in Edmonton (49%) and in Miami (16%)[19] are disappointing but not particularly worrisome. Several reports have indicated that anti-HBs seroconversion occurs in about 90% of infants after immunization.[1–4] In our study only 1 (2%) of 67 children tested in Edmonton at about 1 year of age lacked protective levels of antibody.

Although there are limitations to calculating the cost-effectiveness of health care programs it appears that routine prenatal screening for HBsAg is worth while.[20,21] Arevalo and Washington[20] have suggested that a routine screening program could be cost-effective if a prevalence level of HBsAg among pregnant women of 0.06% were used as a cutoff point, assuming a perinatal transmission rate of 42.5% and an immunization efficacy rate of 90%. With the cost of the screening test plus that of the HBIG and vaccine required for infants of HBsAg-positive women, the cost of preventing one newborn in the United States from becoming a chronic HBV carrier is estimated at $12 700 to $20 700 (US).[14] In Alberta the cost of testing a serum sample for HBsAg was between $3 and $3.15, including reagents, laboratory supplies, and technician and clerical time. The cost per HBsAg-positive woman identified in the Alberta program has been estimated to be $800. Since each dose of the vaccine currently costs $27 per 0.5-ml vial, and HBIG is $30 per 1.0-ml vial, the cost of treating one newborn is $111. If administrative and community health staff expenses are included the total cost of preventing the chronic-carrier state per infant at risk is about $1275.[22] If one assumes that chronic HBV infection or its complications will not develop in all infants at risk the cost per case prevented is correspondingly higher.

Estimates for the Alberta program are lower than the estimate of $3702 per infant calculated in the Manitoba study;[17] this is due in part to the reduced costs for HBsAg test reagents supplied by the CRCSBTS. It is difficult to estimate the cost to the health care system of one HBV carrier infected from birth, but it would almost certainly be much higher than the cost per case prevented, even if the remaining uncertainties about perinatal transmission rates and the natural history of HBV infection in neonates are considered.[20]

We conclude that almost complete prevention of perinatally acquired chronic HBV infection is feasible through the province-wide routine HBsAg screening program, which includes centrally coordinated immunoprophylaxis and follow-up of infants who are at risk. The combination of relatively low laboratory costs, universal health care insurance and a strong public health immunization program makes routine prenatal HBsAg screening attractively cost-effective.

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