A Program to Provide Hepatitis B Immunoprophylaxis to Infants Born to HBsAg-Positive Asian and Pacific Island Women

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Between January 1, 1984, and December 31, 1985, there were 545 women from Asia and the Pacific Islands who gave birth to a total of 572 infants at Highland General Hospital in Oakland, California (accounting for 20% of all deliveries at that hospital). For countries having more than ten women giving birth during the study period, the percentage of women screened prenatally for HBs antigen (Ag) ranged from a high of 100% (Laos) to a low of 54% (Philippines). HBsAg-positivity rates ranged from a high of 21% (Tonga) to a low of 0% (India). A total of 52 infants was born to 49 HBsAg-positive mothers, and 40 (77%) of the infants received hepatitis B immune globulin (HBIG) within 12 hours of birth. While 80% of the infants received HBIG and at least one dose of hepatitis B vaccine, only 35% received the recommended schedule of HBIG and three doses of vaccine.

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Mother-to-infant transmission of hepatitis B virus (HBV) plays a major role in maintaining high infection rates of hepatitis B within many Asian populations. For example, in Taiwan, 5% to 20% of the population are HBs antigen (Ag) carriers,[1] and it is estimated that as many as 35% to 50% of these carriers are infected perinatally by their mothers.[2]

Studies have shown that the rate of development of the HBV carrier state in infants born to mothers positive for HBsAg may be reduced by as much as 80% to 90% with the timely use of hepatitis B immune globulin (HBIG) and hepatitis B vaccine.[3-5] Such efficacy is notable in light of the fact that HBsAg carriers have significantly higher rates of cirrhosis and hepatocellular carcinoma than noncarriers.[6]

Since 1981, the Immunization Practices Advisory Committee (ACIP) has issued a series of revised recommendations aimed at preventing mother-to-infant transmission of hepatitis B.[7-10] Current ACIP guidelines recommend (1) that mothers belonging to groups at high risk of acquiring or transmitting hepatitis B infection (including women of Asian or Pacific Island descent) be tested routinely for HBsAg during the prenatal period; (2) that all infants born to HBsAg-positive women receive hepatitis B immune globulin (0.5 ml intramuscularly) after physiologic stabilization and preferably within 12 hours of birth and hepatitis B vaccine (0.5 ml [10 μg] intramuscularly) at birth and 1 and 6 months of age, and (3) that all infants receiving hepatitis B immunoprophylaxis be tested for HBsAg and anti-HBs at 12 to 15 months of age to monitor the success or failure of therapy.

Since 1975 more than 750,000 Southeast Asian refugees have entered the United States; nearly 40% of these new refugees have settled in California.[11] About 45% of Southeast Asian refugees are younger than 18 years, and 40% are female.[11]

The purpose of this study was twofold: to determine the extent to which Asian and Pacific Island women delivering at a county hospital in Alameda County were screened prenatally for HBsAg during the time period 1984-1985, and to ascertain the timing of HBIG and hepatitis B vaccine administration to those infants born to HBsAg-positive mothers.

Patients and Methods

The study cohort was selected by using birth certificates filed at the Office of Vital Registration, Alameda County Health Care Services Agency. Birth certificates were reviewed for all infants born at Highland General Hospital (Oakland, California) in the two-year period, January 1, 1984, through December 31, 1985. The following information was obtained from the birth certificates: country of birth and name of the mother and name and date of birth for each infant.

Information gained from the birth certificates was used to compile a list of the names of all mothers born in Asia or the Pacific Islands who were delivered of an infant at Highland General Hospital in 1984-1985. Medical records were reviewed for the results of prenatal HBsAg screening. Medical records were then reviewed for those infants born to HBsAg-positive Asian or Pacific Island mothers to determine if and when HBIG and hepatitis B vaccine were administered.

Highland General Hospital is a county-operated 260-bed acute care hospital. The hospital serves as the site of delivery

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ABBREVIATIONS USED IN TEXT

ACIP = Immunization Practices Advisory Committee
Ag = antigen
HBIG = hepatitis B immune globulin
HBV = hepatitis B virus

for the women who receive their prenatal care at the hospital itself and for many women who are seen prenatally at one of the various county and community clinics. The infants in this study who were born at Highland General Hospital received postnatal care at either the hospital pediatrics clinic or at one of the other county or community clinics.

Since 1981 Highland General Hospital has participated as one of several San Francisco Bay Area hospitals in an ongoing New York Blood Center study of an experimental recombinant hepatitis B vaccine. As part of the New York Blood Center study, women born in Asia or the Pacific Islands who gave birth at Highland General Hospital have been screened prenatally for HBsAg and HBeAg. To be included in the New York Blood Center trial, an infant delivered at Highland General Hospital had to be born to a mother who was positive for both HBsAg and HBeAg. These infants have been given the experimental vaccine by health care workers who visited the infants at their homes (Hooi Yeap, RN, San Francisco General Hospital, oral communication, October 1985).

Infants born to HBsAg-positive, HBeAg-negative mothers were not included in the New York Blood Center trial. Instead, these infants were treated in a program sponsored by the Alameda County Health Care Services Agency. In this program, the infants received the currently licensed plasma-derived hepatitis B vaccine (0.5 ml [10 μg] given intramuscularly at birth and at 1 and 6 months) in hospital or at one of the county or community clinics. All infants born to HBsAg-positive mothers, regardless of whether they were in the New York Blood Center trial or in the Alameda County Health Care Services Agency program, were supposed to have HBIG (0.5 ml intramuscularly) administered to them at birth by hospital personnel.

Because the intent of the study reported here was to determine the effectiveness of the perinatal hepatitis B-prevention program administered by the Alameda County Health Care Services Agency, the analysis of hepatitis B vaccine use in this study excludes those infants enrolled in the New York Blood Center trial.

Medical records of all infants born to HBsAg-positive mothers were reviewed at Highland General Hospital to determine how many doses of vaccine were administered; if fewer than three vaccine doses were noted in the hospital medical record, a check was made to determine whether the infant received any vaccine at the clinic where the mother received her prenatal care. More than six months was allowed to elapse following the birth of an infant before that infant was classified as having had a given number of doses of vaccine.

Results

Between January 1, 1984, and December 31, 1985, a total of 545 women from Asia or the Pacific Islands were delivered at Highland General Hospital of 572 infants (5 mothers gave birth to twins, whereas 22 mothers were delivered of single infants on two different occasions during the study period). The 572 infants accounted for 20.0% of all infants born at the hospital during the two calendar years (572/2,866).

For the 545 women who gave birth at Highland General Hospital in 1984-1985, Table 1 shows, by country of birth, the results of the hepatitis B screening.

A total of 52 infants was born to the 49 HBsAg-positive mothers in this study. Figure 1 shows the time schedule when the 52 infants received hepatitis B immune globulin: 25 of the infants (48%) received HBIG within 2 hours of delivery, 40 infants (77%) had HBIG administered within 12 hours of birth, 7 infants (14%) received HBIG more than 12 hours after birth, while 5 infants (10%) received no HBIG.

Figure 2 summarizes the vaccine schedule for the infants born to HBsAg-positive mothers. In all, 12 infants were excluded from the analysis because of their participation in the New York Blood Center trial. Thus, of the 40 infants remaining in the Alameda County Health Care Services Agency program, 14 (35%) received three doses of vaccine, 10 (25%) received two doses, 10 (25%) received one dose and 6 (15%) received no vaccine.

Of the 40 infants, 6 were born to mothers who were positive for both HBsAg and HBeAg; the mothers of these 6

TABLE 1.—*Results of Hepatitis B Screening of Asian and Pacific Island Women Giving Birth at Highland General Hospital, 1984-1985*

Country	Women Giving Birth, No.	Screened, No. (%)	HBsAg Pos No. (%)	HBeAg Pos No. (%)
Cambodia . . .	137	135 (99)	11 (8)	3 (2)
Vietnam	101	96 (95)	7 (7)	3 (3)
Laos	100	100 (100)	13 (13)	4 (4)
Philippines . .	59	32 (54)	1 (3)	0 (0)
China	55	53 (96)	10 (19)	3 (6)
Tonga	38	29 (76)	6 (21)	5 (17)
Korea	17	15 (88)	1 (7)	0 (0)
India	11	8 (73)	0 (0)	0 (0)
Others*	27	16 (59)	0 (0)	0 (0)
Totals	545	484 (89)	49 (10)	18 (4)

Pos = positive

*Samoa, Fiji, Guam, Japan, Malaysia, Indonesia, Thailand, Singapore, Burma

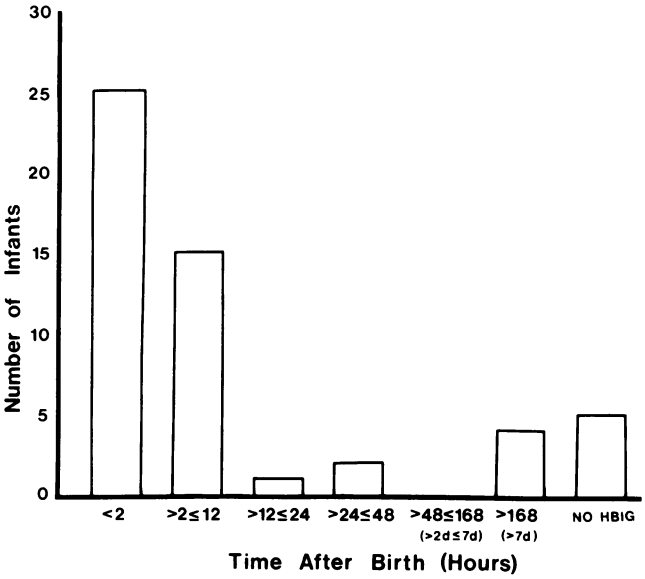

Figure 1.—Schedule of administration of hepatitis B immune globulin (0.5 ml intramuscularly) given to infants born to Asian or Pacific Island HBsAg-positive women, Alameda County, 1984-1985.

infants were inadvertently excluded from the New York Blood Center trial. The average number of doses of vaccine given to infants born to HBeAg-positive carrier mothers (average 2.0 doses) did not differ significantly from the average number of doses given to infants born to HBeAg-negative carrier mothers (average 1.8 doses).

Table 2 summarizes the hepatitis B prophylaxis administered to the 40 infants born to HBsAg-positive mothers. While 32 infants (80%) received HBIG and at least one dose of hepatitis B vaccine, only 14 (35%) of the infants received the recommended schedule of HBIG plus three doses of vaccine. There were no significant differences in the extent of treatment administered to those infants born in 1984 compared with the group of infants born in 1985.

Discussion

Mother-to-infant transmission of hepatitis B virus among Asians and Pacific Islanders is an important issue in many areas of the United States for two reasons. First, these two population groups have high HBsAg carrier rates and are therefore at risk of infecting their infants during the birth process. Second, a significant number of Asian refugees has arrived in the United States since 1975, thereby directly adding to the population cohort at highest risk for mother-to-infant transmission of HBV. As of September 30, 1984, there were eight states that had more than 20,000 Southeast Asian refugees in residence (Table 3).

Highland General Hospital cannot be considered a typical county hospital with respect to its perinatal hepatitis B program, as the hospital has been a participant during the past five years in an ongoing trial of an experimental hepatitis B vaccine. As a result, health care personnel are likely to have been much more aware of the need for prenatal screening of women from Asia or the Pacific Islands.

There are several factors, however, that make Highland General Hospital similar to other county hospitals. For example, the hospital serves a predominantly uninsured population, representing numerous different races and nationalities.

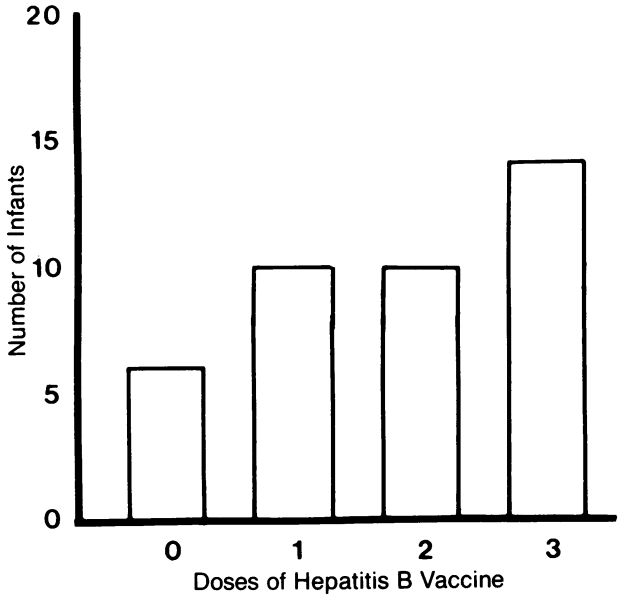

Figure 2.—Number of doses of hepatitis B vaccine (0.5 ml [10 μg] intramuscularly) administered to infants born to Asian or Pacific Island HBsAg-positive women, Alameda County, 1984-1985.

Many of the women who present to the hospital do so with late or no prenatal care. A significant proportion of the women who give birth at Highland General Hospital are subsequently lost to follow-up, and it is often difficult to monitor the health of the infants born to such women.

Four areas are discussed concerning Alameda County's perinatal hepatitis B prevention program: screening of women, treatment of infants born to HBsAg-positive mothers, costs of administering the program and recommendations for increased program effectiveness.

Screening

Of the eight countries having more than ten women giving birth at Highland General Hospital in 1984-1985, prenatal screening exceeded 80% for six; pregnant women born in the Philippines and Tonga were screened less frequently.

Two explanations may partially account for the relatively infrequent screening of women from the Philippines. First, because Filipinos generally speak English well, it may be that some health care workers assume such women to be from the United States. Second, the Hispanic surnames of many Filipinos may incorrectly suggest to some that these women are from Latin-American nations. Nevertheless, it is important to test this population group prenatally for HBsAg status; in their study of the prevalence of HBsAg in pregnant Asian-American women by country of birth, Stevens and co-

TABLE 2.—*Hepatitis B Prophylaxis Administered to Infants Born to Asian and Pacific Island HBsAg-Positive Mothers, Alameda County, 1984-1985 (N=40)*

Treatment	Infants, No.		Percent of Total Infants Born to HBsAg-Pos Mothers	
HBIG and vaccine		32		80
HBIG + 1 dose vaccine	9		23	
HBIG + 2 doses vaccine	9		23	
HBIG + 3 doses vaccine	14		35	
HBIG only		3		8
Vaccine only		2		5
1 dose	1		3	
2 doses	1		3	
3 doses	0		0	
Nothing		3		8
Totals		40		101

HBIG = hepatitis B immune globulin, HBsAg-Pos = positive for HBs antigen

TABLE 3.—*Estimated Southeast Asian Refugee Population By State—September 30, 1984**

State	Southeast Asian Refugees, No.
California	285,100
Texas	51,300
Washington	32,600
New York	24,800
Illinois	23,400
Pennsylvania	23,900
Minnesota	22,600
Virginia	21,000
Total 8 states	484,700
Total United States	711,000

*From Report to the Congress, January 31, 1985: Refugee Resettlement Program, Office of Refugee Resettlement, US Department of Health and Human Services.

workers found 5% of women from the Philippines to be positive for HBsAg.[5]

The observation that only 77% of the women from Tonga in this study were screened prenatally for HBsAg is important given their significant carrier rate of both HBsAg and HBeAg.

In general, in most of the instances where prenatal screening for HBsAg failed to occur, the women involved came to Highland General Hospital with either little or no prenatal care. This observation is based on the date in a woman's medical chart that states when prenatal care was begun. All women, however, regardless of how much prenatal care they had received, were tested for rubella titer and hematocrit before delivery. Thus, even though blood was drawn on all women prenatally, it appears that the HBsAg assay was omitted in some instances because of failure to recognize the women involved as being at high risk for transmitting HBV.

Treatment

The efficacy of a perinatal hepatitis B treatment program depends on administering HBIG on the same day an infant is born, and preferably within 12 hours of birth.[10]

In this study, while 32 of 40 infants (80%) received HBIG at birth and at least one dose of vaccine, only 14 infants (35%) were given the full recommended course of three doses of vaccine. Of the 26 infants who received less than the recommended course of vaccine, 1 was reported to have left the area; the remaining 25 infants are presumed to have either left the area without the knowledge of their primary care provider or simply to have been lost to follow-up despite still residing in the area. It is also possible that some of the infants received doses of hepatitis B vaccine at clinics or physicians' offices outside of the county health care system (this is not likely to have occurred frequently, given that the mothers in this study relied on county medical resources for much of their health care needs).

Of the 25 infants who received less than the recommended regimen of immunoprophylaxis, 21 were born to HBeAg-negative women, while the remaining 4 had HBeAg-positive carrier mothers. Though no serologic follow-up results are available, there is a high probability that few if any of the infants born to HBeAg-negative carrier mothers became HBsAg-positive because HBeAg-negative mothers rarely transmit HBV to their infants in the perinatal period.[10] The four infants born to the HBsAg-HBeAg-carrier mothers, however, had a greater risk of becoming infected, based on the observation that 70% to 90% of untreated infants born to HBsAg-HBeAg-positive mothers are infected perinatally.[10] One of these four infants received only HBIG at birth and no vaccine.

Costs

The costs incurred in a program of preventing mother-to-infant transmission of hepatitis B include the cost of screening women prenatally for HBsAg, the cost of administering HBIG and vaccine to those infants born to HBsAg-positive mothers and the cost of testing the treated infants for HBsAg and anti-HBs at 12 to 15 months of age.

For the two-year period encompassed in this study, the cost of the perinatal hepatitis B prevention program amounted to about $8,200. This figure is based on the following costs reported by the hospital pharmacy and contracting laboratory: $12 per HBsAg assay entailed in screening women prenatally, $16 per dose (0.5 ml) of HBIG and $23 per dose (0.5 ml) of hepatitis B vaccine administered to the infants born to HBsAg-positive women.

There are several reasons why the figure $8,200 understates the true costs that would have accrued had the prophylaxis program been more comprehensive. First, 61 women from Asia and the Pacific Islands were not screened prenatally for HBsAg. Second, only 35% of the infants born to HBsAg-positive women received the recommended regimen of HBIG and vaccine. Finally, no routine testing at 12 to 15 months for anti-HBs and HBsAg was done in those infants who received the recommended regimen of immunoprophylaxis.

Recommendations for Increasing Program Effectiveness

The goal of a perinatal hepatitis B prevention program is twofold: to identify HBsAg-positive women prenatally and to administer appropriate immunoprophylaxis to the infants born to carrier mothers.

The results of this study suggest several areas at the screening and treatment levels where program effectiveness might be enhanced.

Screening. The primary goals during the prenatal period should be determination of the HBsAg status of all Asian and Pacific Island women (both refugee/immigrant and US-born) and communication of these results to patients and appropriate health care workers. Specifically, the following recommendations are offered:

1. Health care workers involved in providing prenatal care to Asian and Pacific Island women should be informed about the high HBV carrier rates characteristic of these population groups and the need to routinely screen these women prenatally for HBsAg.

2. Every woman who tests positive for HBsAg during the prenatal course should be advised about the results. She should be informed about the potential for mother-to-infant transmission of virus and about the need for her infant to receive proper immunoprophylaxis. Because many Asian refugees may not understand English, appropriate interpreter resources should be available.

3. When a woman is identified as HBsAg-positive during the prenatal period, a system should be in place whereby the results of the positive test become known to the following health care providers: the hospital obstetric and pediatrics services, the hospital infection control nurse, the pediatrics clinic where the infant will receive posthospital care and the appropriate county public health personnel. To facilitate such a chain of communication, the following recommendations are offered:

- The woman's medical chart should be labeled in a manner that clearly notifies the hospital obstetric service of the HBsAg-positivity. Upon delivery, the infant's medical chart should be labeled to notify the pediatrics service that the baby was born to an HBsAg-positive mother.
- The infection control nurse at the hospital where delivery is planned should be notified of all HBsAg-positive women identified during the prenatal period. The infection control nurse could then ensure both that the obstetric service is aware of the HBsAg-positivity before delivery and, after delivery, that the infant receives proper immunoprophylaxis.
- Because a significant proportion of Asian and Pacific Island refugees take their infants to county-supported pediatrics clinics after being discharged from hospital, personnel in

the county communicable disease control office should also be notified of all prenatal HBsAg-positive results. Appropriate county public health personnel could then follow up on the infants to ensure that they receive the second and third doses of vaccine and the postimmunoprophylaxis serologic testing at 12 to 15 months.

Treatment. The primary goals of treatment are to ensure that all infants born to HBsAg-positive women receive the full recommended immunoprophylaxis and undergo serologic testing for HBsAg and anti-HBs at 12 to 15 months of age. Specifically, the following recommendations are offered:

1. The hospital obstetric service should have a protocol that clearly defines how an infant born to an HBsAg-positive mother is to receive HBIG and hepatitis B vaccine. Where pediatric and obstetric services overlap, the protocol should define which service has the responsibility for administering the immunoprophylaxis.

2. The hospital infection control nurse, notified during the prenatal course of a mother's positive HBsAg status, should ensure that each infant born to an HBsAg-positive mother receives HBIG and the initial hepatitis B vaccine before discharge from hospital.

3. The infection control nurse or the pediatrics service should notify the county public health personnel where follow-up pediatric care is planned for each infant born to an HBsAg-positive mother. This should be done at the time of discharge or shortly thereafter. County personnel (such as a public health nurse) could then follow up on each child to ensure that the second and third doses of vaccine are administered and that proper serologic testing is done on the infant at 12 to 15 months of age.

Conclusions

To determine the effectiveness of existing perinatal hepatitis B prevention programs, the health care community should continue to assess regularly the prenatal screening of pregnant women from Asia and the Pacific Islands and the appropriate use of hepatitis B immunoprophylaxis for the infants born to these women. This study has shown how such an assessment may reveal that a significant number of infants born to HBsAg-positive mothers in a given program are receiving less than the recommended treatment of hepatitis B prophylaxis.

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