

## Protecting Future Generations through Immunization against Hepatitis B

Immunization with hepatitis B vaccine is our most effective weapon against hepatitis B virus (HBV) infection and its consequences. Among the estimated 1.25 million persons with chronic HBV infection in the United States, chronic liver disease and primary hepatocellular carcinoma cause an estimated 5000 deaths per year. Because the risk for chronic infection increases with decreasing age, persons infected in early childhood carry a disproportionately large burden of morbidity and mortality attributable to HBV. Adults who have had chronic HBV infection since childhood develop primary hepatocellular carcinoma at a rate of 5% per decade, which is 100 to 300 times the rate among uninfected persons.

The major objective of hepatitis B immunization is to prevent chronic infection, which will prevent sequelae such as primary hepatocellular carcinoma. In developing countries, where most infections are acquired in infancy and early childhood, routine childhood immunization against hepatitis B has been the primary strategy to accomplish this objective. The results of the study by Ni and colleagues (1) in this issue clearly show the success of this strategy in interrupting HBV transmission and preventing chronic infection. During the 15 years after routine childhood hepatitis B immunization was implemented in Taiwan, the prevalence of chronic HBV infection among children younger than 15 years of age declined from 10% to 0.7%, a decrease of 93%. Similarly, the overall prevalence of infection (as measured by antibody to hepatitis B core antigen) decreased almost 90%, whereas the prevalence of protective antibody (antibody to hepatitis B surface antigen) remained high. These results were obtained through a combination of routine infant immunization and catch-up immunization of older children and adolescents. The success of this strategy is further demonstrated by a 50% reduction in rates of primary hepatocellular carcinoma among Taiwanese children 6 to 14 years of age (2).

A second objective of hepatitis B immunization is to reduce the number of persons with chronic HBV infection who are highly infectious to others and, ultimately, to eliminate this source of HBV transmission. Chronically infected children are likely to be positive for hepatitis B e antigen (HBeAg), a marker of high infectivity.

However, as demonstrated in the study by McMahon and associates in this issue (3), two thirds of persons chronically infected with HBV clear HBeAg over time. Thus, elimination of perinatal and early childhood transmission could rapidly decrease the number of HBeAg-positive persons. Such a decrease has been demonstrated in Alaska (where the epidemiology of HBV infection is similar to that in Taiwan) after introduction of routine infant hepatitis B immunization and catch-up vaccination of children (4).

Even in the continental United States, where the overall rate of chronic infection is low, integration of hepatitis B vaccine into the existing childhood vaccination schedule has the greatest likelihood of successfully decreasing disease incidence (5). The established infrastructure for vaccine delivery to children ensures high coverage levels, and because the hepatitis B vaccine provides long-term protection against chronic HBV infection, these children will be protected as they move through adolescence and adulthood.

Our experience during the first decade after vaccine licensure demonstrated that targeting only adults and children at high risk for infection, including infants born to HBV-infected women, was not effective in preventing most cases of HBV infections (6). The adults at highest risk for infection were the ones who were most difficult to reach with vaccine, and a substantial proportion (30%) did not consider themselves as belonging to a risk group. Furthermore, many children remained at risk because their mothers were not screened for hepatitis B surface antigen and because up to 60% of childhood infections occurred in children born to HBsAg-negative women (7).

The extent to which children acquire HBV infection in the United States has not been appreciated, primarily because most infections in this age group are asymptomatic. Not including perinatal infections, recent estimates indicate that 16 000 children younger than 10 years of age were being infected annually in the United States before implementation of routine infant hepatitis B immunization in 1992 (8). However, by 2000, 90% of children 19 to 36 months of age had been fully immunized with three doses of hepatitis B vaccine

(9), and the incidence of acute hepatitis B among children younger than 15 years of age had decreased by 75% (Centers for Disease Control and Prevention. Unpublished data). Furthermore, in response to the 1995 recommendation for routine hepatitis B immunization of adolescents (10), a growing number of U.S. states are requiring vaccination for middle-school entry, and a number of programs provide hepatitis B vaccine to high-risk youth. Preliminary vaccine coverage data indicate that 48% of 13- to 15-year-olds have been vaccinated against hepatitis B (Centers for Disease Control and Prevention. Unpublished data).

Still, most HBV transmission and morbidity associated with acute hepatitis B occur among older adolescents and young adults, and most of these infections result from sexual transmission. Recommendations are long standing to vaccinate persons who report a history of multiple sex partners, those who receive treatment for a sexually transmitted disease, and men who have sex with men. However, vaccine is rarely offered in settings that provide health care to adults, and persons with high-risk sexual behaviors account for more than half of cases of newly acquired hepatitis B (Centers for Disease Control and Prevention. Unpublished data). Results of several studies indicate that health care practitioners do not routinely ascertain high-risk sex or drug histories from their patients and miss opportunities to inform and vaccinate persons at risk for hepatitis B (11, 12). Even in settings that provide services specifically targeted to high-risk adults (such as sexually transmitted disease treatment clinics, HIV counseling and testing sites, and drug treatment programs), hepatitis B vaccination is not offered routinely (13).

Expanding the cohorts of children immunized as infants and decreasing the number of HBeAg-positive persons will ensure that future generations are protected from HBV infection and its consequences. However, without a nationwide program to vaccinate adults at increased risk for this infection, acute disease will continue to occur and transmission of HBV will not be eliminated for decades.

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