

# Hepatitis Control Report

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## Report from Richmond: After celebrating a record high HB vaccination rate, hepatitis workers find miles to go

*Editor's note: The National Hepatitis Coordinators' Conference is the largest regular meeting in the United States devoted to the control of viral hepatitis. Every year, hepatitis control specialists from around the country gather with experts from CDC, advocacy groups, and vaccine manufacturers to discuss the latest strategies for controlling viral hepatitis. Here is where leaders in the field present new epidemiological information, plans for control, and changes in budgets and strategies. This year's meeting was held in Richmond, Virginia on July 29 through August 2. Over 320 people attended, a new record. As always, the Hepatitis Control Report was there to bring you the highlights.*

### Sweet success: National hepatitis B immunization rate hits a record high

For the first time since 1991, when CDC recommended that all American children be vaccinated against hepatitis B soon after birth, the rate of immunization among two-year-olds has reached over 90%. The surprise announcement came on August 1 at the National Hepatitis Coordinators' Conference in Richmond, Virginia.

Dr. Lance E. Rodewald, Director of the Immunization Services Division at CDC's National Immunization Program, told the conference that the 2000 three-dose completion rate for hepatitis B vaccination in the U.S. had reached a stunning 90.3%. As he announced the news, the audience erupted in applause. "The mainstreaming of hepatitis B vaccination has worked!" he said.

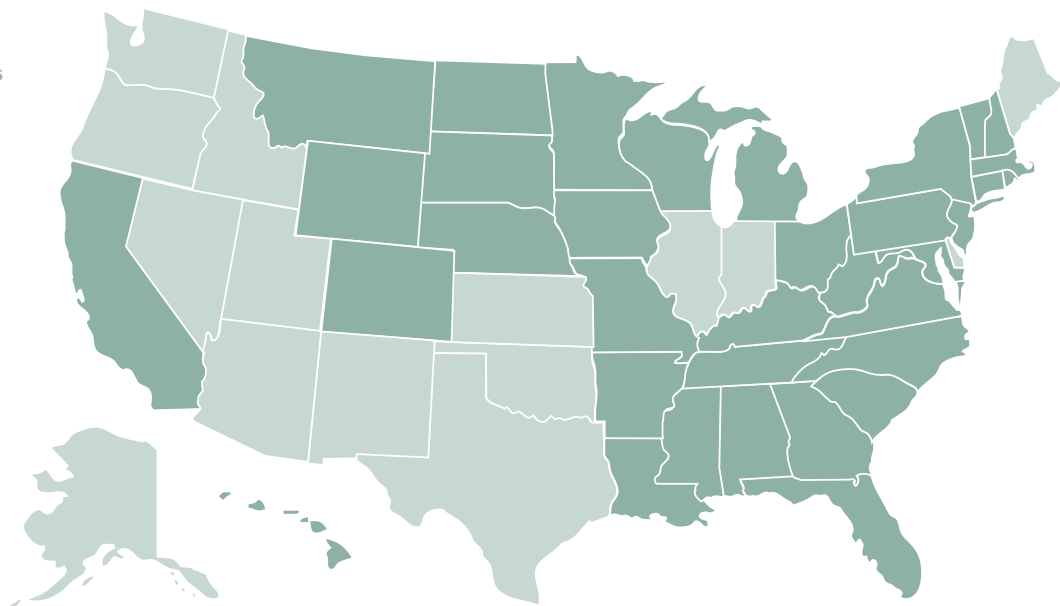
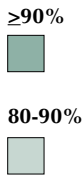
The U.S. hepatitis B vaccination rate now exceeds the rate for some long-established vaccines, including four-dose diphtheria-tetanus-pertussis (DTP) and three-dose polio. The three-dose hepatitis B vaccination rate is now essentially tied with the one-dose measles-mumps-rubella (MMR) vaccination rate.

The hepatitis B vaccination rate rocketed from zero in 1992 to over 80% in 1996 and has continued to climb. In 2000, 36 states had rates of over 90% (see figure on page 2). Topping the list were Rhode Island (96.4±1.9%), Iowa (96.1±2.6%), and North Dakota (96.7±2.5%). At the bottom were Texas (84.5±3.1%), Alaska (82.7±4.8%), and Utah (81.1±5.0%).

The 2000 rates were high in all racial and ethnic groups, Rodewald said. The highest rate, 92%, occurred in Alaska Native/Native Americans and Asian/Pacific Islanders. A slightly lower rate, 88%, occurred in African-Americans. Rates were high in urban, suburban, and rural areas (91%, 91%, and 89%), and in families above and below the federal poverty level (91% and 89%).

Rodewald estimated that, since the CDC recommendation in 1991, 1,800 gallons of

Percent of children 19-35 months of age with 3 doses of hepatitis B vaccine, by state, National Immunization Survey, 1999-2000



hepatitis B vaccine per year had been administered to children in the U.S. birth cohort. In 2000 alone, the federal and state governments purchased over 13 million doses of the vaccine. Of those, 9.3 million were purchased with federal Vaccines for Children funds, 2.7 million were purchased with 317 funds (direct CDC immunization grants to the states), and 2.0 million were purchased with state funds.

“The payoff for this investment has been tremendous,” Rodewald said. Citing unpublished research by Zhou et al., Rodewald estimated that, in the 1999 U.S. birth cohort, 194,000 hepatitis B infections had been prevented by routine infant vaccination, including 56,000 symptomatic infections and 14,000 chronic infections.

Amid the happiness over a record hepatitis B vaccination rate, Rodewald sounded a note of caution. The 2000 rate, he said, does not reflect any effects from the 1999 controversy over thimerosal, a mercury-based preservative used in some childhood vaccines. The controversy caused most hospitals and pediatricians to stop administering the recommended birth dose of hepatitis B vaccine (for a discussion of the thimerosal controversy and its effect on the birth dose, see the *HCR*, Summer 1999, Fall 1999, Summer 2000, and Spring 2001 issues, all available on our website, [www.hepatitiscontrolreport.com](http://www.hepatitiscontrolreport.com)). Manufacturers removed thimerosal from all hepatitis B vaccines within a year after the controversy and health officials have repeatedly recommended that the birth dose be resumed. Despite these recommendations, the birth dose has not fully recovered. Because children who begin the hepatitis B vaccine series at birth are more likely to complete the series than children who begin the series later in life, future measurements of the national hepatitis B vaccination rate will probably be lower than the rate in 2000. Rodewald said restoring and promoting the birth dose is one of the keys to maintaining a high rate of hepatitis B vaccination.

Rodewald said the high 2000 hepatitis B vaccination rate does not reflect any effects from the 1999 thimerosal controversy, which caused many hospitals and pediatricians to stop giving the recommended birth dose.

<p>The <i>Hepatitis Control Report</i> is an editorially independent newsletter devoted to news on the control of viral hepatitis. The <i>Report</i> is not affiliated with its sponsors or any other public or private entity.</p>	<p><b>Editorial advisors</b>          Fernando A. Guerra, MD          Director, San Antonio, Texas          Metropolitan Health District           William Schaffner, II, MD          Chairman, Department          of Preventive Medicine,          Vanderbilt University</p>	<p><b>Writer-editor</b>          Frederic E. Shaw, MD, JD          Assistant Commissioner          for Policy and Planning,          Texas Department of Health</p>	<p><b>Publisher</b>          Vasil J. Pappas, Jr.          Precision Media Works          29 Bala Avenue, Suite 106          Bala Cynwyd, PA 19004          Tel: 610 664 2793           ©2001 Precision Media Works          ISSN: 1091-8930</p>
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Rodewald said another key to maintaining a high hepatitis B vaccination rate is school and daycare vaccination requirements. As of June 2001, twenty-four states had laws requiring hepatitis B vaccination in kindergarten, first grade, and middle school. Only four states had no requirement for hepatitis B vaccination: Montana, South Dakota, Alabama, and Maine.

## Some states make big strides in tracking infants of HBsAg-seropositive moms

*Editor's note: CDC estimates that 20,000 infants are born annually to mothers who are seropositive for hepatitis B surface antigen (HBsAg). These children have a 10% to 80% chance of becoming infected themselves, depending on the mother's hepatitis B e antigen status. Of those infants who do become infected, 90% will develop chronic hepatitis B virus infection. Part of the agency's strategy for reducing perinatal hepatitis B transmission is screening all pregnant women for HBsAg during each pregnancy, with the goal of ensuring that all babies born to HBsAg-seropositive mothers receive prompt immunoprophylaxis and completion of the three-dose hepatitis B vaccine series by six months of age, that all treated babies receive post-vaccination serologic testing, and that all susceptible household and sexual contacts of HBsAg-seropositive mothers are identified and vaccinated.*

In 1999, the most recent year for which data are available, the states detected only about 50% of infants born to HBsAg-seropositive mothers. In the last two years, however, some states have reported major successes in raising their rates of detection, according to Tasneem Malik, a public health advisor at CDC's National Immunization Program who spoke at the conference in Richmond.

The rate of detection for each state is estimated annually by CDC. Using data from national serologic surveys such as the National Health and Nutrition Examination Survey (NHANES) and vital records statistics, the agency makes demographic adjustments to estimate the "expected" number of births to HBsAg-seropositive mothers in each state. Since 1993, CDC has assessed each state's performance by calculating the ratio of reported births to HBsAg-seropositive mothers to the expected number in the state (to make the estimates as conservative as possible, the agency uses the lower 95% confidence interval as the denominator).

Some states have done very well. In 1999, Arkansas identified 95 births to infected women, which was 186% of the expected number calculated by CDC. Rhode Island (143%), Minnesota (125%), and North Dakota (113%) all detected more than the expected number of births. At the other end of the spectrum were Vermont (20%), Virginia (10%), and Iowa (8%).

Not surprisingly, some states that have done poorly against the CDC estimates have complained that the estimates are too high. But CDC officials have defended the accuracy of their calculations. Dr. Harold Margolis, Acting Director of the CDC Division of Viral Hepatitis, entitled his presentation on the subject in Richmond, "The CDC Estimates are Correct, End of Discussion."

Malik said some poorly-performing states have dramatically increased the number of births detected in the past two years to levels higher than they had dreamed possible. Ohio, for example, increased the number of detected births from 110 in 1998 to over 300 in 2000 after it did a systematic overhaul of its entire perinatal hepatitis B program. "Initially, we looked at the CDC estimate of 251 cases and said, 'No way!'" said Ann Richardson, public health nurse consultant at the Ohio Perinatal Hepatitis B Program. But the program made several improvements to its detection system, including adding maternal HBsAg status to the newborn metabolic screening card

Some states have done very well at identifying births to HBsAg-seropositive women, such as Rhode Island, Minnesota, and North Dakota.

Ohio increased the number of detected births from 110 in 1998 to over 300 in 2000 after it did a systematic overhaul of its entire perinatal hepatitis B program.

used for all Ohio children. The program also worked closely with the state epidemiologist to insure that all HBsAg-seropositive women of childbearing age, whether known to be pregnant or not, were reported to the program for follow-up.

Alabama increased its detection rate by routinely searching the state's immunization registry, which automatically receives identifying data on all Alabama births. Brian Wheeler, the Alabama Perinatal Hepatitis B Manager, said, "By taking the first name and date of birth for known HBsAg-seropositive women and periodically searching the registry for additional unreported births, we discovered over 150 infants that would not have been otherwise reported."

Florida has also dramatically improved its rate of detection of infants to infected mothers. By implementing a new reporting law and revamping the procedure used for reporting cases to health departments, Florida increased the reported number of exposed infants from 425 to 658 in just one year, 1999 to 2000. The state is using a new web-based disease reporting system called MERLIN to collect all disease reports, including HBsAg seropositives, into a single database. Tony Richardson, Hepatitis Prevention Program Coordinator at the Florida Department of Health, said, "MERLIN ends our paper reporting system. With it, we can confirm that cases meet case definitions, communicate better with the county health departments, and export data to the CDC NETSS file. It gives us real-time reporting, quicker turnaround for reviewable cases, and more complete and accurate reporting."

Richardson also touted the effect of a new law in Florida that mandates reporting of all HBsAg seropositives to local and county health departments. "The new law caused a big increase in reporting," Richardson said. Almost all reported HBsAg cases come from laboratories -- very few come from MDs or hospitals, he said.

CDC has emphasized the value of laws that mandate HBsAg screening of pregnant women and require both laboratories and providers to report HBsAg seropositives. States with such laws have higher rates of detection and follow-up of births to HBsAg-seropositive mothers. In 1999-2000, 28 states had screening or reporting laws in place. Nine states had reporting laws only, and 19 states had both screening and reporting laws.

## Hepatitis B vaccine coverage of Asian American children is rising

For more than 20 years, epidemiologists have recognized that Asian and Pacific Islander (API) immigrants and their children are at increased risk for hepatitis B infection. In 1995, the CDC Advisory Committee on Immunization Practices recommended that all API children under age 11 who were born to first generation immigrants be vaccinated. In 1999, the committee said that special efforts should be made to vaccinate API children who were born, or whose parents were born, in countries with hepatitis B virus infection rates of 2% or higher. CDC has set a goal for the year 2004 that 90% of API children under the age of 19 will have received the hepatitis B vaccine series.

"This goal can be achieved," said Dr. Gary Euler at the Richmond conference. Euler is an epidemiologist at the CDC National Immunization Program. Targeting vaccinations at API children is made easier by the fact that, of the 220,000 Asian immigrants admitted to the U.S. every year, 80% settle in just 12 states, with California, New York, Hawaii, and Texas making up the largest proportion. Half of the immigrants live in just five U.S. cities.

Since the mid-1990s, CDC has funded catch-up vaccination projects for API

In 1999-2000, 31 states had screening or reporting laws for HBsAg-seropositive mothers.

CDC's goal is that 90% of Asian and Pacific Islander children under age 19 are vaccinated against hepatitis B by the year 2004.

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children in 15 states. Last year, the agency started projects in Honolulu, New Orleans, Philadelphia, and New York.

Euler said CDC now estimates that 64% of AAPI children have received the three-dose hepatitis B series. Between 1999 and 2001, the rate improved by 20% to 40%. The highest current rates are in children aged 0 to 7, a group that was subject to routine infant vaccination or state school entry requirements for hepatitis B vaccination. "What we know is that AAPIs under age nine are already vaccinated. AAPIs between 9 and 19 are poorly vaccinated, about 50%. Older teenagers are the least vaccinated, about 15%," he said.

In order to increase catch-up vaccinations in AAPI children, a variety of approaches must be used simultaneously, Euler said. State laws requiring vaccination for admission to middle school are very effective and ensure that 10% of the target birth cohort will be vaccinated every year. Because of language and cultural barriers, each AAPI ethnic group requires a unique and specific approach, he said.

The benefits of vaccinating AAPI children are substantial. In a target group of 500,000 AAPI children aged 9 to 19, vaccination will prevent 50,000 acute infections, 2,500 chronic infections, and 250 deaths from cirrhosis or liver cancer. For every dollar invested, at least \$4.44 is gained in medical and societal benefits, Euler said.

In a target group of 500,000 AAPI children aged 9 to 19, hepatitis B vaccination will prevent 50,000 acute infections, 2,500 chronic infections, and 250 deaths from cirrhosis or liver cancer.

## Big changes are coming for hepatitis C surveillance

CDC is proposing major changes in the way hepatitis C surveillance is conducted in the states. At the Richmond conference, Dr. Miriam Alter, chief of epidemiology at the CDC Division of Viral Hepatitis, said the agency believes that current hepatitis C surveillance methods are inadequate for today's needs. "Traditionally, we have collected only cases of acute hepatitis C, but we need to be in a different place now," Alter said.

The CDC effort is focusing on two main goals. First, the agency is revamping surveillance for acute hepatitis C by improving the case definition and laboratory reporting. Second, the agency is supporting the collection of all positive anti-HCV reports into databases at the state level.

Traditional surveillance for acute hepatitis C remains useful to detect rare outbreaks of hepatitis C (such as in health care settings), to roughly characterize groups at risk for infection in local areas, and to target and monitor prevention activities. But surveillance for acute hepatitis C is notoriously difficult and unreliable, in part because no serologic marker for acute hepatitis C exists. Historically, CDC has relied mainly on its sentinel county surveillance system for good epidemiologic information on acute hepatitis C. With the rising importance of hepatitis C nationally, however, it became clear that better data were needed to monitor acute hepatitis C at the regional and state levels. "The Sentinel County system does a good job of measuring national trends, but we recognized there was a need for more reliable state-specific data," said Dr. Annemarie Wasley, an epidemiologist at the CDC Hepatitis Division who works on hepatitis C surveillance.

Surveillance for acute hepatitis C is notoriously difficult and unreliable. Even so, it remains useful to detect rare outbreaks of hepatitis C, to characterize groups at risk, and to target prevention activities.

The states have been collecting cases of acute hepatitis C for many years, but the task is extraordinarily labor-intensive. Most reports of hepatitis C come in to health departments from laboratories as lone positive anti-HCV enzyme immunoassay (EIA) tests. Most are not accompanied by confirmatory supplementary tests, such as the recombinant immunoblot assay (RIBA), so departments cannot even tell if the anti-HCV tests are false positives. If the anti-HCV test is a true positive, the department still does not know if the test represents acute, chronic, or past infection. To determine that, a health department worker must call the patient or his physician to

learn whether the patient had elevated liver enzymes or clinical symptoms.

Last year, Wasley worked with the Council of State and Territorial Epidemiologists (CSTE) to create a new case definition for acute hepatitis C. To meet the new definition, a patient's liver enzyme levels (alanine aminotransferase or ALT, indicating active liver damage) must be greater than seven times the upper limit of normal (ULN). This replaces the 2.5 times ULN required in the old definition. Wasley said 97% of patients with acute hepatitis C have ALTs greater than seven times ULN. Only 3% of chronically infected patients have such levels. The use of higher ALT levels makes the case definition more specific for acute disease, she said.

The new case definition for acute disease also uses a measure of the strength of the EIA reaction, the signal-to-cutoff ratio (S/CO), to reduce the need for health departments to track down RIBA supplementary tests. Under the new definition, if the EIA S/CO is equal to or greater than 3.8, the anti-HCV EIA is considered confirmed by itself, without resorting to RIBA confirmation. EIA tests with S/COs less than 3.8 must still be confirmed with a supplementary test. Alter presented data at the conference showing that the S/CO is highly correlated with seropositivity on RIBA. Blood samples with an S/CO greater than or equal to 3.8 have a 95% chance of being RIBA positive. Less than 15% of samples with an S/CO below 3.8 will be RIBA positive, she said.

Wasley said the new acute case definition will help health departments differentiate acute cases from chronic ones and allow them to concentrate their investigative resources on anti-HCV reports that are most likely to represent acute disease. The challenge now is getting laboratories to report ALTs and S/COs when they report anti-HCV results, Wasley said.

CDC is also rethinking surveillance for anti-HCV seropositivity. In the past five years, with hepatitis C exploding as a national health issue, many states have begun to wonder about their total disease burden from chronic hepatitis C. Both CDC and the states have recognized that anti-HCV seropositivity reports can be valuable for gauging the size of a state's hepatitis C problem and evaluating the effectiveness of prevention programs. The reports can also be used to contact infected persons to educate them about their infection and refer them for medical evaluation and treatment.

Approximately 30 states require positive anti-HCV tests to be reported to public health authorities. Many states have set up databases for these reports and have begun to use them for follow-up efforts (for a description of such programs in New Mexico and Florida, see the HCR, Summer 2000 and Winter 2000-2001 issues). But many such states have been overwhelmed with positive anti-HCV lab reports.

"Everyone in these health departments has boxes and boxes of these lab reports. But only a few health departments have the investigative resources to follow them up," Alter said.

Jeff Beckett, chief of the epidemiology section at the Maine Bureau of Health, agreed. "We've collected about 2,500 of these reports over a few years. Duplication is a big problem. Many patients get tested multiple times, and most of the reports are just anti-HCV positives, with no reports of supplemental tests," he said. Other states have had similar experiences.

At the Richmond conference, CDC unveiled a new proposed case definition that will be used to standardize surveillance for anti-HCV seropositivity nationwide. Under the new definition, a case will be defined as someone with a repeat anti-HCV positive test by EIA, verified by a more specific assay (such as RIBA or reverse transcriptase polymerase chain reaction for HCV RNA) or verified by an anti-HCV positive test

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About 30 states require anti-HCV tests to be reported to public health authorities. Many of these states have been overwhelmed with positive reports.

by EIA with an S/CO  $\geq 3.8$ . Like the new definition for acute cases, this one is expected to simplify the evaluation of positive anti-HCV case reports and reduce the amount of investigatory work that health departments must do.

Wasley said CDC is now pondering a number of issues around surveillance for anti-HCV seropositives, such as what demographic, clinical, and exposure information should be collected, and what information is needed to facilitate the tracing of contacts.

In Arizona, anti-HCV seropositivity became reportable in 1997, and the state established a database of HCV seropositives in 1998. To date, over 15,000 anti-HCV seropositive persons have been added to the database. Of those, 66% are male, 54% have symptoms related to HCV infection, 19% have cirrhosis, 9% have had or are waiting for a liver transplant, and only 15% have received antiviral therapy. Only 14% did not previously know of their infections.

In Arizona, anti-HCV positivity became reportable in 1997, and the state established a database in 1998. To date, over 15,000 anti-HCV seropositive persons have been added to the database, but the state has been able to investigate only 16% of them.

With four disease investigators, Arizona has been able to investigate only 16% of anti-HCV seropositives reported to the database, and 931 have been offered education, counseling, and referral. Wasley said the Arizona program has provided a good minimum estimate of the amount of HCV infection in the state.

Wasley said CDC plans to integrate state-based HCV databases with the federal electronic disease surveillance systems, NETSS and NEDSS. The new case definition for acute hepatitis C is already published and in use. The new definition for anti-HCV seropositivity has been published in draft form and distributed to some state hepatitis coordinators and epidemiologists. Wasley said she anticipates it will become official later this year.

*Editor's note: CDC has recently published its national hepatitis C prevention strategy. It is available on the CDC hepatitis website: <http://www.cdc.gov/ncidod/diseases/hepatitis/>.*

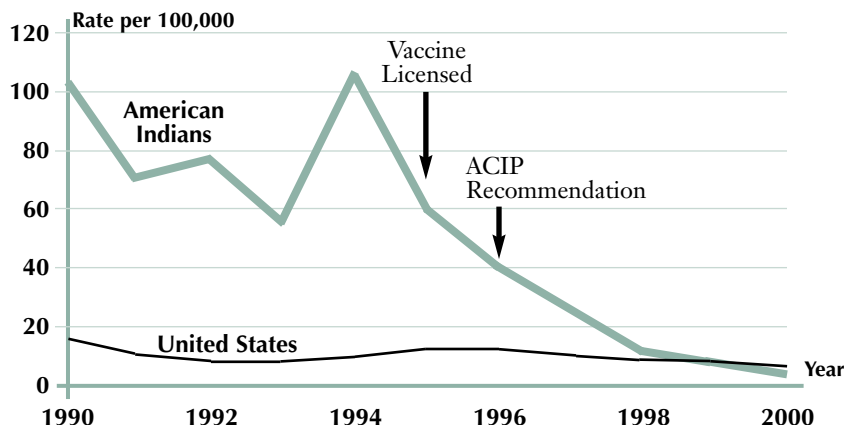
## Is hepatitis A going away?

Judging by the latest surveillance numbers for hepatitis A nationally and in several high-rate states, the disease appears to be going away in the U.S. But, at the Richmond meeting, Dr. Beth Bell, a hepatitis A expert at the CDC Hepatitis Division, said it is still too early to say goodbye to the disease (see stories on the falling incidence of hepatitis A in the *HCR*, Fall 2000 and Spring 2001 issues).

Bell said the disease has declined dramatically in some populations that have been widely vaccinated. In the American Indian population, for example, the rate of hepatitis A in 2000 was actually below the overall U.S. rate (see figure below). The

Annual hepatitis A incidence, American Indians & United States, 1990-2000

Source: CDC and Indian Health Service.  
Note: 2000 data are provisional.



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disease has nearly disappeared among American Indians who live on reservations. Bell said the 2000 rate of hepatitis A in 15 U.S. counties inside American Indian reservations was only about 1 per 100,000 for American Indians, compared to about 20 per 100,000 for all other races. Vaccination coverage rates on reservations now stand at 40% to 80%, she said.

“To sound a note of caution in all this good news, we don’t know how immune these populations need to be to obliterate infection, as opposed to just postponing outbreaks,” Bell said. “We need a few more years of surveillance data to put the current declines in context.”

In 1999, the Advisory Committee on Immunization Practices (ACIP) recommended that children living in 11 states with historical annual rates  $\geq 20$  per 100,000 be routinely vaccinated statewide. Three of those states, Oklahoma, Arizona, and Alaska, now have hepatitis A vaccination requirements for school entry (Arizona’s requirement applies only in Maricopa County).

ACIP also recommended that six states with historical annual rates of 10 to 20 per 100,000 consider routinely vaccinating all children in high-rate areas. One such state, Texas, enacted a school entry vaccination requirement in 1999 that applies to 32 border counties. Texas is now expanding its requirement to include non-border counties with high hepatitis A incidence rates.

Bell said the rate of hepatitis A in the 11 states that fall under the ACIP recommendation for routine vaccination fell to about 5 per 100,000 in 2000, the lowest rate recorded since national reporting began in 1952. The use of hepatitis A vaccine in those states has rocketed from less than 500,000 doses in 1998 to more than 2 million doses in 2000. Nationally, the hepatitis A rate has also continued to fall. The annualized rate for 2001 to date stands at about 4.7 per 100,000, even lower than the 2000 rate, Bell said.

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# Hepatitis Control Report

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