Successful hepatitis A vaccine debuts

Each year, some 30,000 cases of hepatitis A surface in the United States. Though this viral infection tends to be fairly benign, the liver inflammation it causes cannot be taken lightly: It claims roughly 100 lives annually.

The virus typically spreads by contaminated food and water. Public health officials combat it with water chlorination, sewage treatment, educational campaigns for good hygiene (such as hand washing), and the administration of immune globulin (antibodies harvested from survivors of the disease). Researchers now announce the development of a far more potent weapon: a safe and highly effective vaccine.

Though hepatitis A tends to crop up in sporadic outbreaks, one community of Hasidic Jews in Brooklyn has been plagued for years with a small, seemingly intractable annual recurrence of infection, especially among families with toddlers. So when David Nalin and his coworkers at Merck Sharp & Dohme Research Laboratories in West Point, Pa., were ready to test the efficacy of their new hepatitis A vaccine, they decided to focus on children in Kiryas Joel, a Hasidic community in Monroe, N.Y. Many residents of the hepatitis-plagued Brooklyn community regularly spend their summers at this resort in the lower Catskill Mountains.

"It was virtually certain that the start of summer vacation in late June would bring the virus up [to Monroe] with children from that community in Brooklyn," explains Nalin. Working with Kiryas Joel pediatrician Alan Werzberger, Nalin's team identified 1,037 Hasidic children who were full-time residents of the Monroe community and who had no previous exposure to hepatitis A. Beginning in June 1991, Werzberger's staff gave each child an intramuscular injection; half the children received the new vaccine, while half received a placebo.

Because the disease has a latency period of two to three months, the researchers could judge vaccine efficacy only by cases of clinical disease that appeared 50 or more days after the inoculations. In "one of the shortest vaccine efficacy trials in history," Nalin says, the investigators broke the codes identifying the vaccine and placebo groups after a little more than five months. The data showed that all 25 cases of hepatitis A occurring 50 or more days after treatment occurred in children who received the placebo, the team reports in the Aug. 13 New England Journal of Medicine.

Seven cases of hepatitis did appear among vaccinated children, but only within 18 days after inoculation. Nalin interprets the trial to mean that "at least as early as day 21 — and probably before that — the vaccine was 100 percent protective."

The data also suggest that this or related chemically inactivated (killed-virus) vaccines now under development may reduce or eliminate clinical symptoms in many persons who receive their inoculations shortly *after* becoming infected with the hepatitis A virus, says Leslye D. Johnson, chief of the enteric diseases branch of the National Institute of Allergy and Infectious Diseases in Bethesda, Md.

Moreover, she notes, "because you don't have [asymptomatic] carriers of this disease as you do with hepatitis B and C, the only real reservoir [of the virus] is going to be people in the acute phase of infection." The result? Johnson says it is now possible to envision eradicating hepatitis A — as smallpox was once eliminated — through a program of worldwide immunization.

Data from this trial and unpublished results from an ongoing study conducted by SmithKline Beecham with children in Thailand suggest "it is likely that the levels of antibody developing after a complete series of three immunizations will lead to protection for at least five to 10 years," asserts Stanley M. Lemon of the University of North Carolina School of Medicine in Chapel Hill, in an editorial in the June Hepatology. That's much longer than the four to six months of protection afforded by immune globulin, Johnson notes.

Nalin adds that controlled studies performed for Merck in Israel "showed that [injections of] immune globulin caused more pain and local irritation than did the vaccine." Moreover, unlike immune globulin, the vaccine is not derived from blood, so the new immunizations pose no risk of transmitting pathogenic viruses that may have contaminated a donor's blood.

Indeed, Johnson concludes, the new vaccine represents "the first major advance" in hepatitis A prevention in more than 50 years.

Merck plans to submit its vaccine data to the Food and Drug Administration this year. Nalin predicts the vaccine will become commercially available "certainly by 1994." — *J. Raloff*

Targeting hospital screening for HIV

An estimated 1 million persons living in the United States today have already been infected with the AIDS-causing human immunodeficiency virus (HIV). Though an estimated one-fifth of them entered a hospital in 1990, most of those patients probably did not know about their HIV infection, suggests a new study by the Centers for Disease Control (CDC) in Atlanta.

If U.S. hospitals in the most AIDS-prone communities were to offer voluntary and confidential HIV screening and counseling to all patients age 15 to 54, in just one year they might identify up to 110,000 persons who unknowingly harbor HIV, the CDC study indicates. Indeed, the investigators conclude, this approach might steer many newly infected and still asymptomatic people into treatment, prolonging their lives and helping to limit the spread of the virus.

Though many researchers have recommended that hospitals test or offer HIV testing to all patients, such screening is expensive and money for testing and counseling remains tight, notes Robert S. Janssen, who led the new study. He and his co-workers sought a cost-effective way to identify people with HIV infection.

In their study, they conducted HIV assays on 196,000 anonymous but systematically collected blood samples — essentially leftovers of samples obtained for other purposes. Participating hospitals identified each sample only by the unsuspecting donor's age, sex, ethnic background, medical condition, and inpatient or outpatient status.

"Two-thirds of the HIV-positive patients in the 20 hospitals studied [entered] with conditions other than symptomatic HIV infection or AIDS," Janssen and his co-workers report in the Aug. 13 New England Journal of Medicine. Though HIV showed up in every medical category from psychiatry and violent assault to obstetrics and gynecology, age proved a strong discriminator. Patients 15 to 54 years old constituted half of those hospitalized, but represented 82 percent of HIV-infected individuals entering with conditions other than those characteristic of AIDS or HIV infection.

Most important, Janssen believes, was the study's "identification that the AIDS diagnosis rate for a hospital can serve as a surrogate marker" for HIV-infection rates, which vary widely by region. Hospitals don't compile AIDS diagnosis rates today, he says. But doing so would cost nothing — and would "probably take only 5 minutes" using hospitals' own annual tallies of discharged patients and local health departments' tallies of AIDS diagnoses attributed to each institution, Janssen contends.

The study indicates that hospitals with one or more newly diagnosed cases of AIDS per 1,000 discharges probably have enough patients with undiagnosed HIV infection to warrant screening.

Thomas C. Quinn of the Johns Hopkins University School of Medicine in Baltimore says the CDC report makes a persuasive argument for targeted, voluntary HIV screening. However, he asks, "Who's going to pay for it?" — *J. Raloff*