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SIGN of the times: Officials meet to assess global efforts against dangerous injections

(Cairo) — If you were in Cairo in late October and you had walked through the lobby of the Sheraton Guezirah, you might have noticed some studious-looking people having animated discussions in English, Arabic, French — maybe even Romanian. You might have seen some curious photographs — pictures of dirty needles and syringes sitting in a cooking pot in Africa, of young children handling bloody needles and syringes behind a clinic in rural Asia, of an injection being prepared at a blood-contaminated table in Eastern Europe. This was the annual meeting of the Safe Injection Global Network (SIGN). The group, about 80 health officials and researchers from around the world, had come together to assess their progress in the global battle against infectious diseases transmitted by dirty injection equipment.

When Americans receive medical injections, they generally take the sterility of the equipment for granted. Few Americans can imagine the enormous disease burden caused by unsafe needles in the developing world. According to an analysis by Adam Kane, risky injections cause annually 8-16 million cases of hepatitis B infection, 2.3-4.7 million cases of hepatitis C infection, and 80,000-160,000 cases of HIV infection. Every year, 26 million years of life are lost, and direct medical costs reach $535 million. A more recent analysis by Hauri and colleagues, presented at the Cairo conference, suggests that the disease burden may be even higher (see www.injectionsafety.org).

In some countries, a huge proportion of bloodborne illnesses is attributed to unsafe injections. In 1994, when CDC epidemiologists studied hepatitis B cases in Moldova, they were shocked to find that 52% were caused by unsafe injections (Hutin Y, et al. *Int J Epidemiol* 1999;28:782-86). In a similar study in Egypt in 1996, more than 40% of new hepatitis C cases were caused by unsafe injections (Frank C, et al. Abstract presented at the International Conference on Emerging Infectious Diseases, March 8-11, 1999, Atlanta). Other studies in Romania, Ukraine, India, Pakistan, and Taiwan have yielded similar results (for an excellent review, see Simonsen L, et al. *Bull. WHO* 1999;77:798-800).

A major contributor to the problem is the sheer volume of injections given in countries around the world — estimated at 12 billion per year. Surprisingly, 95% of these are given for therapeutic purposes, not for vaccinations, and most are medically unnecessary. In many developing countries, patients attribute near-magical qualities to injections, and providers prefer to administer vitamins, antibiotics, analgesics, and other medications parenterally. In most cases, these medications can be administered orally, and the injections are an unnecessary risk.

According to SIGN, the popular demand for injections in many countries is driven by a variety of different beliefs. In Pakistan, patients believe that injections are stronger

medications. In other countries, they believe that "injections work faster (Romania), that the pain of the injection is a marker of efficacy (some African countries), that a drug is more efficient when entering the body directly (Colombia, Thailand), and that injections represent a more advanced technology."

Health care providers in these countries are driven to overuse injections by patient demand, but also by their own beliefs that injected drugs have better efficacy and provide better compliance. In some countries, providers have strong economic incentives to give medications by injection. In Pakistan, for example, practitioners are able to charge a higher fee for injected medications than for oral drugs, and this leads to a massive overuse of injections. In a survey published this year, Khan and colleagues found that 81% of patients leaving clinics in Darsano Channo, a subdistrict 20 kilometers northeast of Karachi, got at least one injection (*Bull. WHO* 2000;78:956-63).

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"It took me a long time to understand the important role of frequency of exposure in this," said Dr. Yvan Hutin in an interview. Hutin leads the SIGN secretariat, which is housed at WHO in Geneva. "If you think about it, people in developing countries get a number of potential exposures to bloodborne pathogens, such as circumcisions, tattooing, blood transfusions, but these are really infrequent when compared to needle injections. In the Indian subcontinent, the rate of therapeutic needle injections is 5-7 per capita per year. In countries of the former Soviet Union, it is about 10 per capita. When you factor in the efficiency of viral transmission through parenteral exposure, you understand the pressure of exposure and the risk these injections present."

In some regions of the developing world, 50%–90% of injections are administered using equipment that is re-used without sterilization.

Many — or most — of these unnecessary injections are given using dirty equipment. According to a review by Simonsen (see above), in several regions of the developing world, 50%-90% of therapeutic injections are administered using equipment that is re-used without sterilization. In these regions, needles are used routinely on 3-10 patients before they are discarded or sterilized, and it is common to see needles destined for re-use soaking in a pot full of tepid water. The use of multi-dose vials compounds the risk. Additionally, needles are often discarded without being destroyed and are then scavenged for re-sale and re-use.

SIGN's strategy is three-pronged. First, provide sterile injection equipment, preferably equipment that is cheap and cannot be re-used, such as auto-disable syringes. Second, manage the disposal of medical waste. Third, change the behavior of providers away from the use of reusable equipment and away from unnecessary therapeutic injections.

Hutin said SIGN members had found it easier than expected to address the problem of needle re-use. "Every intervention that has been tried has been effective," he said. Hutin related a recent success in Burkina Faso, where needle re-use dropped dramatically — from about 80% to 4% — in just five years. Hutin said the cause of the drop was probably a move by the Burkina Faso government to decentralize the distribution of pharmaceuticals and injection equipment in rural areas of the country.

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Early findings indicate that it may be possible to reduce injections simply by increasing the amount of talking between providers and patients during medical visits.

Reducing the huge number of unnecessary injections in developing countries will be more difficult, Hutin said. Early findings indicate that it may be possible to reduce injections simply by increasing the amount of talking between providers and patients during medical visits. Along these lines, participants at the Cairo meeting agreed that SIGN must follow "a holistic approach to safe and appropriate use of injections that goes beyond the simple provision of supplies to also include behavior change activities…."

At the Cairo meeting, researchers unveiled some new tools for the global effort. SIGN, in collaboration with a Seattle non-profit, the Program for Appropriate Technology in Health (PATH), is advancing the use of auto-disable syringes. The Bill and Melinda Gates Children's Vaccine Program recently made a $278,000 grant to SIGN for the development and testing of a "safe injection behavior change toolkit" that countries can use to change providers' injection practices. The Global Alliance for Vaccines and Immunization (GAVI) said recently that injection safety is one of the most important indicators of the quality of immunization programs (for a description of GAVI, see the *Hepatitis Control Report*, Spring 2000 issue).

SIGN was organized in 1999 when infection control and immunization officials from CDC and WHO decided to formally combine their efforts against unsafe injections. The mission of SIGN is "to achieve safe and appropriate use of injections worldwide by concerted action under a common strategic framework." SIGN is made up of individuals, public and private organizations, and national public health officials. ■

As rates plunge, response to hepatitis A vaccination recommendations varies among states

(Atlanta) — A little more than a year after the Advisory Committee on Immunization Practices (ACIP) published new recommendations for routinely vaccinating children against hepatitis A in 11 high-rate states, only a few states have begun implementing the new recommendations. In some key states, the impetus to begin routine vaccination has been blunted by dramatic declines in the reported rate of hepatitis A. This is a national trend — for the first six months of 2000, the U.S. rate (as reported to CDC) stood at less than half the historical national rate of 10 per 100,000 person-years.

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ACIP published the recommendations in October 1999 after CDC experts became convinced that, "to achieve a sustained reduction in hepatitis A rates, a shift is needed from the present immunization strategy to one that achieves widespread routine vaccination of children…" (MMWR, October 1, 1999;48:RR-12). Under the recommendations, "children living in areas where rates of hepatitis A are at least twice the national average should be routinely vaccinated."

ACIP specifically recommended that, in states where the average annual hepatitis A rate during 1987-1997 was ≥ 20 per 100,000 (i.e., approximately twice the national average), children should be routinely vaccinated statewide. The states that fell within the ACIP criterion were Arizona (average rate for 1987-1997 of 48 per 100,000), Alaska (45), Oregon (40), New Mexico (40), Utah (33), Washington (30), Oklahoma (24), South Dakota (24), Idaho (21), Nevada (21), and California (20). During 1987-1997, these states accounted for approximately 50% of the cases of hepatitis A reported in the United States, although they made up only 22% of the U.S. population.

Now, a little more than a year after the recommendations were published, only one state, Alaska, has responded to them by adopting routine vaccination of all

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schoolchildren. In two other states, Oklahoma and Texas, requirements for routine vaccination had already been initiated before ACIP made its recommendations (indeed, these states' policies probably helped inspire the ACIP action). Oklahoma began discussing a statewide vaccination mandate as early as 1996, in the midst of a giant statewide epidemic involving over 5,000 reported cases. Two years later, Oklahoma became the first U.S. state to adopt a statewide school entry mandate for hepatitis A vaccination. The Texas school entry mandate was initiated in 1998 and adopted in 1999. It applies to children living in 32 high-rate counties along the U.S.-Mexico border.

The newest requirement, in Alaska, was approved on September 8, 2000 by the Alaska State Board of Education as part of a general revamp of the state's immunization rules (the state simultaneously adopted its first school entry and daycare requirement for hepatitis B vaccination). For the 2001-2002 school year, hepatitis A vaccination will be required for all Alaskan children in kindergarten through 12th grade or in licensed daycare.

In Arizona, hepatitis A vaccination is required only in Maricopa County (Phoenix), and only for children aged 2-5 in out-of-home care, including Head Start and daycare programs. The state passed this requirement in January 1999 in response to a large communitywide outbreak in the county.

Arizona had the nation's highest hepatitis A incidence rate during 1987-1997 (although the rate has fallen in the past two years) and it tops the list of states covered by the 1999 ACIP recommendation. Currently, hepatitis A vaccination is required only in Maricopa County (Phoenix), and only for children aged 2-5 in out-of-home care, including Head Start and daycare programs. The state passed this requirement in January 1999 in response to a large communitywide outbreak in the county. A case-control study linked the outbreak to attendance at daycare centers. The Arizona Department of Health Services has no current plans for a statewide hepatitis A vaccination requirement, but it does recommend vaccination for all Arizona children aged 2-5, and it has supported wide-scale vaccination on American Indian reservations.

California reported approximately 11% of all U.S. hepatitis A cases during the period 1987-1997, the greatest percentage of any state, meaning that routine vaccination there could substantially reduce the total number of cases reported in the U.S. Earlier this year, the California legislature passed a bill adding a school entry requirement for hepatitis A vaccination effective in 2003, but the measure was vetoed by Governor Gray Davis. In his veto message, Davis said, "Widespread community acceptance is needed for school/childcare entry requirements to be effective. For hepatitis A vaccine, such acceptance needs more time to develop, and 2003 may be too soon for this to happen."

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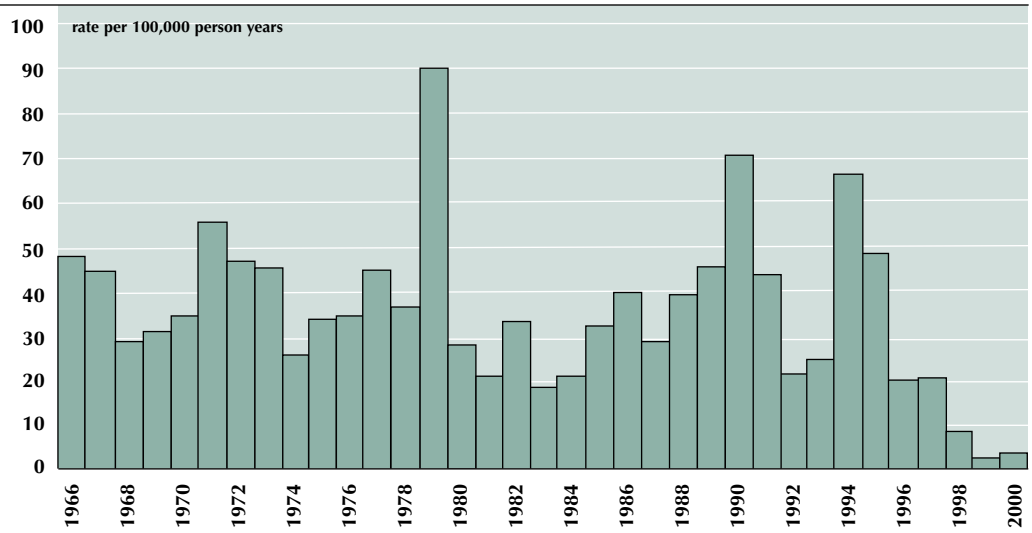
The California legislation was sponsored by SmithKline Beecham, one of the manufacturers of hepatitis A vaccine (and a sponsor of this publication) and supported by the California Nurses Association, the California Medical Association, and other state groups. But, according to sources close to the process, the California Department of Health Services was worried that the state's immunization system could not absorb the addition of another school entry requirement on the heels of one adopted just last year for varicella vaccination. Additionally, some pediatricians balked at the cost of hepatitis A vaccine, which, for many, would have come out of their existing managed care capitation payments. When added to the cost of other recently added vaccines, such as varicella and 7-valent pneumococcal conjugate vaccine, this became a serious liability for the legislation. The bill also suffered from a general perception among California providers that hepatitis A is not a critical public health problem, sources said (see story on the hepatitis A disease burden in Los Angeles in this issue of the *Hepatitis Control Report*).

Hepatitis A incidence
New Mexico, 1966-2000

Note:
Rate for 2000 is estimated.

Source:
CDC and New Mexico
Department of Health.



In New Mexico, the state Department of Health proposed a regulation earlier this year that would have required hepatitis A vaccination for all children in kindergarten through 12th grade. The proposal was backed by SmithKline Beecham and supported by the American Liver Foundation at a public hearing in September. But two prominent pediatricians spoke against the measure, and other state experts testified that New Mexico's policy of voluntary, targeted vaccination, directed at children in the highest-rate counties, was successfully addressing the problem (see the *Hepatitis Control Report*, Fall 1999 issue). The final regulation "recommended" vaccination for children but did not require it. The state plans to propose another regulation that will mandate vaccination for schoolchildren in counties that have 3-year running average rates of ≥ 20 per 100,000 or are subject to epidemics.

In New Mexico, the state Department of Health proposed a regulation earlier this year that would have required hepatitis A vaccination for all children in kindergarten through 12th grade. But, the final regulation "recommended" vaccination for children but did not require it.

The impetus for a school entry requirement in New Mexico was weakened by a recent downswing in the state's rate of hepatitis A. The state's historically high rate has plunged since 1997 (see chart).

In Utah, the state's Scientific Vaccine Advisory Committee has drafted a bill to go before the legislature in January 2001. It proposes a progressive school entry requirement for hepatitis A vaccination beginning in July 2002. The state health department is optimistic that the legislation will pass, although funding issues must still be worked out.

Oregon has no current plans for routine vaccination, but the state health department hopes to start a working group soon to begin discussing the issue of mandatory vaccination requirements. Hepatitis A in Oregon has occurred historically in large sweeping epidemics in adults. The last outbreak occurred in 1994-97 and the state's rate has now fallen to a new low. Three other states, Idaho, South Dakota, and Washington, have no plans for routine hepatitis A vaccination, but all three states currently provide the vaccine to high-risk groups. In all three states, hepatitis A rates are at their lowest since the 1960s.

Editor's note: This article was written in part by Casey C. Wisecarver, MPH, editor of Hepatitis A Alert, *a biannual review of hepatitis A incidence in the U.S. (casey_wisecarver@compuserve.com).* ■

Vaccine wars: House chairman assails ACIP ethics

(Washington) — The House Government Reform Committee, chaired by Congressman Dan Burton, has issued a report highly critical of ethical practices at the CDC's Advisory Committee on Immunization Practices (ACIP) and a vaccine-related advisory

committee at FDA. Last year, Burton requested detailed personnel and financial records for all Department of Health and Human Services employees, plus members of ACIP and other advisory committees, who were involved in vaccination "at any level" (see story in the *Hepatitis Control Report*, Fall 1999 issue).

Burton's report said, "conflict of interest rules employed by the FDA and the CDC have been weak, enforcement has been lax, and committee members with substantial ties to pharmaceutical companies have been given waivers to participate in committee proceedings." But, an expert close to the issue said, "ACIP has always been particularly attentive to avoid even an appearance of conflict of interest."

The Burton report, entitled "Conflicts in Vaccine Policy Making: Majority Staff Report," was published in August (www.house.gov/reform/staff_report1.doc). It said "conflict of interest rules employed by the FDA and the CDC have been weak, enforcement has been lax, and committee members with substantial ties to pharmaceutical companies have been given waivers to participate in committee proceedings." Specifically, the report complained that ACIP members who are not allowed to vote on certain recommendations due to financial conflicts of interest are allowed to participate in committee deliberations and advocate specific positions; that ACIP members do not fully disclose conflicts of interest; and that some members have either real or apparent conflicts of interest because of financial ties to vaccine manufacturers.

CDC has not responded to the report publicly. But an expert close to the issue said "ACIP has always been particularly attentive to avoid even an appearance of conflict of interest. There is nothing to be gained from reacting to this." The agency had been reviewing ACIP's ethics practices for several months preceding the Burton report and officials are now studying whether it should make changes based on the report.

A major dilemma for CDC is that most vaccine research in the U.S. is funded by pharmaceutical companies, and it is very difficult to recruit knowledgeable vaccine experts for ACIP membership who are not involved in manufacturer-funded research. At a June 15 congressional hearing on the ethics issue before Burton's committee, Dr. Dixie Snider, Associate Director for Science at CDC, said,

A major dilemma for CDC is that most vaccine research in the U.S. is funded by pharmaceutical companies, and it is very difficult to recruit knowledgeable vaccine experts for ACIP membership who are not involved in manufacturer-funded research.

> Federal advisory committees inherently have members who may have potential financial conflicts of interest because … the members are chosen for service based on their expertise in the areas in which advice is sought by the government. Experts in the vaccine field frequently have affiliations with, or may be engaged in research conducted by, academic institutions or other institutions which may receive funding from vaccine manufacturers. … This professional experience which contributes toward the development of their immunization expertise also may result in potential conflicts of interest.

Snider pointed out that Congress has "recognized the need for service on federal advisory committees by these experts and has provided for waivers of the conflict of interest prohibitions … when the need for the individual's services outweighs the potential for a conflict of interest created by the financial interest involved." Waivers are granted annually to every ACIP member on condition that the member "publicly discloses relevant interests at the beginning of each ACIP meeting and that the member abstains on votes involving entities with which the member has a current direct financial interest, when that vote could potentially result in a significant financial impact on the entities," Snider said.

Burton has been a harsh and persistent critic of the federal government's process for approving and recommending childhood vaccines. He has held a series of committee hearings focused on postulated ties between vaccines and diseases such as autism (see the *Hepatitis Control Report*, Spring 1999 issue). Burton has said he believes his own grandson's autism is related to vaccination. Vaccine experts from university, government, and professional groups have testified repeatedly that there is no current scientific evidence for any association between vaccination and autism. ■

Top hepatitis control abstracts from IDSA 2000

The 38th annual meeting of the Infectious Diseases Society of America was held in New Orleans on September 7-10. Here are the top hepatitis control abstracts:

Diabetic supplies transmitted HBV in a nursing facility

An outbreak of hepatitis B in a skilled nursing facility was apparently transmitted through diabetic supplies, according to researchers at CDC and in California. The outbreak came to light in November 1999 when a resident of the facility developed acute hepatitis B. A serosurvey of 158 residents showed that 5 (3%) of the residents had acute hepatitis B infection. All the infected residents were diabetic and resided on the same unit of the facility. Infection was strongly associated with diabetes mellitus, and acutely infected residents had received significantly more insulin, more insulin doses, and more finger sticks on Wednesdays, the day when the number of finger sticks performed on the unit was the greatest. The investigators said ongoing hepatitis B virus transmission was probably caused by contamination of diabetic supplies. They recommended regular cleaning of glucometers, avoiding transport of diabetes care supplies between patients during blood glucose monitoring, and separating blood testing procedures from insulin administration (Khan AJ, Cotter SM, Schulz B, Mosher K, Rosenberg J, Fiore AE, Bell BP. Nosocomial transmission of hepatitis B virus infection at a skilled-nursing facility).

Vietnam vets have higher prevalence of HCV infection

Researchers from the Veterans Health Administration (VHA) reported that veterans with HCV infection are younger ($P<0.0001$, Student's t test), more likely to be male ($p<0.0001$, c-square), and more likely to be from the Vietnam era of service ($p<0.0001$, c-square) than non-infected veterans. The study compared the demographic characteristics of veterans infected with HCV (determined through the VA's Emerging Pathogens Initiative surveillance system) with demographic data for all veteran patients served during federal fiscal years 1998 and 1999. For the two-year period, 54,682 veterans were reported as HCV infected. During the same period, the VHA served 4,1865,667 persons (Roselle GA, Danko LH, Kralovic SM, Simbartl LA. A two-year review of hepatitis C in the patient population of the Department of Veterans Affairs facilities).

Hepatitis A is a big problem in LA, say county officials

Epidemiologists from the Los Angeles County health department presented data on the disease burden in the county from hepatitis A. Using hospital discharge data, they calculated a multiplier that could be used to estimate the true number of hepatitis A cases in 1999. During that year, 1,060 cases were reported. According to the calculated multiplier of 5.2, they estimated the true number of cases in the county to be 5,512. Fifty-seven percent of reported cases were male and the median age was 39 years. The highest hospitalization rate, 5.7 per 100,000, occurred in the 5-14 year age group. Dehydration was a significant cause for hospitalization in children. There were no fatalities. The age-specific incidence rate was highest, 26.1 per 100,000, in the 5-14 year age group, and lowest, 0.9 per 100,000, in the >55 age group. The highest race-specific rate, 14.2 per 100,000, occurred in Hispanics. The authors said their study demonstrated the severity of underreporting of hepatitis A in the county and the importance of routine hepatitis A vaccination among 2-year-olds and special risk groups. "Recent recommendations for universal hepatitis A vaccination of 2-year-olds in some states provide hope for prevention…. Childhood health care providers need motivation to implement this recommendation before development of state law

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which will guarantee compliance," they said (see story in this issue of the *Hepatitis Control Report* on California's consideration of a school entry mandate for hepatitis A vaccination) (Mascola L, Veza M, Run G, Buchholz U, Peterson CL. Hepatitis A incidence in Los Angeles County (LAC), California: Prime profile for prevention). ■

Hepatitis control notes:

No link between hepatitis B vaccination and type 1 diabetes

At the September Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), researchers presented a study of the hypothetical association between hepatitis B and *Hemophilus influenzae* type b (Hib) vaccines and type 1 diabetes. They used diabetes registries from four large health maintenance organizations to identify 260 children with diabetes born since 1988, and matched three controls to each case according to HMO, sex, and birth date. They then reviewed the medical records of cases and controls. Using logistic regression, they estimated the relative risk of type 1 diabetes, adjusted for family history of diabetes in addition to the matching variables. The relative risk for the association of type 1 diabetes with Hib vaccine of 0.88 (95% CI 0.37-2.08). For hepatitis B vaccination, it was 0.81 (95% CI 0.45-1.36). They concluded that Hib and hepatitis B vaccinations are not associated with an increased risk of type 1 diabetes (Destefano F, Okoro CA, Mullooly JP, Hepatitis B and Hib vaccines are not associated with increased risk of type 1 diabetes).

VAQTA gets supplemental approval for extended use

FDA has approved a supplemental license for Merck's hepatitis A vaccine, VAQTA. The new approval extends the age range for the pediatric dose of VAQTA one additional year. VAQTA is now approved for use in ages 2-18 instead of ages 2-17. The new approval also extends the timing of the adult formulation booster dose from six months after the initial dose to six to twelve months. ■

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