EPIDEMIOLOGY SECTION

Connecticut Epidemiologist

STATE OF CONNECTICUT DEPARTMENT OF HEALTH SERVICES
Douglas S. Lloyd, M.D., M.P.H., Commissioner

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HEPATITIS B VACCINE

Hepatitis B is a potentially serious infection which may have severe sequelae. Although the disease occurs worldwide, there is large variation in the prevalence of hepatitis B virus (HBV) markers in different geographic areas. Serosurveys utilizing three HBV markers (HBsAg, anti-HBs, and anti-HBc) provide the best estimates of cumulative rates of infection in various populations. The United States is a low prevalence country, with prevalence rates of 7-10%. However, even in low prevalence countries, there can be significant variations within subgroups of the population (Table 1).

TABLE 1
PREVALENCE OF ALL HBV MARKERS AND ESTIMATED ANNUAL INCIDENCE RATES IN VARIOUS U.S. POPULATION GROUPS (1,2)

Level of Risk	Population Group	Prevalence All Markers (%)	Annual Incidence
HIGH	Immigrants/Refugees from areas of high endemicity	70-85	--
	Institutionalized Mentally Retarded	35-90	1-10
	Users of Illicit Parenteral Drugs	50-80	4-33
	Homosexually Active Males	35-80	12-19
	Household Contacts of HBsAg Carriers	26-61	2-5*
	Hemodialysis Patients	20-80	3-14
	Pts. Receiving Factor VIII or IX for Clotting Disorders	76-96	1-10**
INTERMEDIATE	Prisoners (Male)	10-80	5-10*
	Staff of Institutions for Mentally Retarded	10-33	13-20
	Health Care Workers with Frequent Blood Exposure	15-30	1-10
	Promiscuous Heterosexuals	15-31	2-5*
LOW	General U.S. Population	5-10	0.1
	Health Care Workers - No or Infrequent Exposure to Blood	3-10	1

*Data are not available. These estimated incidence rates are based upon prevalence, modes of transmission of Hepatitis B in the group, and extrapolation from groups with known incidence rates and a comparable prevalence and mode of transmission.

**Published annual attack rates are 13-20%. However, these seem to be too high for the prevalence listed and may reflect outbreaks rather than endemic levels.

The Centers for Disease Control estimate that in the United States there are approximately 200,000 cases per year. The annual cost of nearly $750 million includes physician and hospital costs, as well as time missed from work during acute illness and convalescence. In Connecticut, about 3,000 new cases occur each year. Approximately 10% of these new cases will become part of the pool of HBsAg carriers. Incidence rates in Connecticut are significantly higher than the national rates (Table 2).

TABLE 2
REPORTED INCIDENCE* OF HEPATITIS B
CONNECTICUT AND THE NATION, 1977-1981

Year	Connecticut	United States
1977	9.8	7.7
1978	6.7	6.9
1979	6.9	7.0
1980	12.3	8.3
1981	16.6	9.1

*Cases per 100,000 population.

We believe that this is due primarily to rigorous follow-up of hepatitis reports, application of strict criteria for classifying cases as hepatitis A, B, or Non A-Non B, and extensive use of available laboratory technology by the medical community. Furthermore, we believe that our figures more accurately reflect the true incidence of hepatitis B.

The Vaccine

Hepatitis B vaccine is the first vaccine to be produced entirely from human blood plasma of HBsAg positive individuals. It is a suspension of inactivated surface antigen particles.

Only healthy individuals, who are HBsAg positive are selected as donors. Each donor receives a complete physical examination, which includes a history and suitable laboratory tests. They are further monitored at each donation. The donor's hemoglobin, hematocrit, and serum protein levels must be within normal limits. Levels of serum aminotranferase activity are permitted to exceed those limits set for otherwise healthy donors, but they must be stable. Blood donor centers are licensed and inspected by the FDA.

Production of the vaccine takes 65 weeks. The manufacturing process includes 1) precipitation of the protein from the plasma, 2) purification and concentration of HBsAg, 3) biophysical treatment to eliminate infectious virus and extraneous components, 4) sterilization by filtration, 5) inactivation of any residual virus with formalin, 6) pooling of the antigen, and 7) adsorption to assure maximum antigenicity. The processes inactivate all groups of animal viruses. Safety tests are conducted in chimpanzees after the inactivation process (step 5).

Primary adult vaccination consists of three intramuscular doses of 1 ml. of vaccine (20 ug/1.0 ml.). The second dose is given at one month following initial vaccination, and the third at six months. Immunosuppressed patients, including hemodialysis patients, should receive three 2 ml. doses (40 ug). Children below the age of 10 should receive three doses of 0.5 ml. (10 ug). Field trials of the U.S. manufactured vaccine (Merck, Sharp and Dohme) have shown 80-95% efficacy in preventing infection or disease among susceptible individuals (2). In individuals who developed antibodies after vaccination and before exposure, protection was complete.

Studies by Szmuness suggest that the vaccine is at least partially effective even after the recipient has been exposed to the virus (3). Rabies vaccine is the only other vaccine known to be effective after exposure to a virus. This phenomenon may be related to the long incubation period of hepatitis B.

Between October 1975 and September 1982, 19,000 individuals have been vaccinated. The vaccine has been shown to be safe and effective. Follow-up of vaccine recipients ranges from a few months to more than seven years. To date, no long-term reactions have been reported. No known cases of hepatitis B or Non-A/Non-B hepatitis have been transmitted by the vaccine. No known occurrences of acquired immune deficiency syndrome (AIDS) have been associated with it (4).

Side effects of the vaccination have been limited to soreness and redness at the injection site. The ACIP lists no contraindications for the vaccine.

Screening

The issue of serological screening to identify potential vaccine recipients is primarily an economic issue. Immunization of individuals with previous hepatitis immunity carries no known risks. Various strategies have been examined for cost effectiveness. Four variables must be considered: 1) the cost of the vaccine and its administration, 2) the cost of testing for susceptibility, 3) the prevalence of immune individuals in the group, and 4) the likelihood of acquiring the infection if not immune. If the expected prevalence of serologic markers for HBV is greater than 20%, screening is cost effective if the costs of screening are no greater than $30 per person. If the expected prevalence is less than 8% and if the costs of screening are greater than $10 per person, vaccination without screening is cost effective.

In the institutional setting, the cost of screening may be reduced by testing a large number of specimens at the same time. However, for the individual patient, the cost of screening may add a further expense to an expensive vaccine.

Only one antibody test, either anti-HBc or anti-HBs, is needed for routine screening. Anti-HBs will identify persons previously infected except for carriers. Anti-HBc will identify all previously infected persons including carriers. For testing groups with higher carrier rates, anti-HBc may be preferred to avoid unnecessary vaccination of carriers. The test results are often reported out in terms of presence or absence of antibodies. It is now appreciated that quantitative levels of antibody

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may be important in terms of immunity. For radioimmune assay tests (RIA) these quantitative levels are referred to as the S/N ratio (5).

Vaccine Candidates

National recommendations for initial use of the vaccine focus on groups known to be at high risk of acquiring HBV. Prevalence rates for all HBV markers and estimated annual incidence rates are summarized in Table 1.

The Advisory Committee on Immunization Practices (ACIP) feels that high-risk patient groups should be defined locally since communities may have different high-risk groups. The committee believes that high-risk groups generally include illicit drug users, homosexually active males, institutionalized mentally retarded children, refugees from countries with high rates of hepatitis B, and dialysis patients. These high-risk groups were developed based upon prevalence of hepatitis markers. The State of Connecticut Department of Health Services is presently evaluating factors in terms of guidelines for vaccine use. These will be reviewed in a future issue.

Future Considerations

Guidelines for the use of HBIG following exposure have been previously published (6). The way in which post-exposure prophylaxis should be interfaced with the use of vaccine is still under consideration.

Because of the slow immune response to the new vaccine, it has been suggested that combining passive with active immunization might be the best way to protect individuals already exposed or with a high risk of continuous exposure. Preliminary studies showed that the passively-acquired antibody did not interfere with an active immune response to the vaccine whether administered simultaneously with the vaccine or one month later (7). Such treatment might be used in cases of needlestick and for sexual contacts of patients with acute Hepatitis B or of infectious carriers. However, additonal work is ongoing and at this time, these suggestions are merely proposals. No recommendations for combining passive and active immunization will be made by ACIP until further research can support this strategy.

Another situation in which passive-active immunization should give good results is perinatally acquired HBV/ Anti-HBs given passively should protect the infant until active antibody is formed.

Researchers are also assessing the efficacy of hepatitis B vaccine for post-exposure use. Several other researchers are developing additional hepatitis B vaccines. Bacteria-produced antigens may be used for a commerical vaccine by the mid-1980s. The potential for synthetically produced vaccines is also being evaluated. Whether synthetic immunogen would produce antibodies which are protective and persistent remains to be determined. Clearly, alternative methods of production would provide both a cheaper and safer vaccine for future use.

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	AMEB ASIS	BOTULISM	BRUCELLOSIS	ENCEPHALITIS (TOTAL)	Primary	Pos	FOODBORNE OUTBREAKS	GONORRHEA	HEPATITIS A	HEPATITIS B	HEPATITIS NON A NON B	HEPATITIS UNSPECIFIED	LEGIONELLOSIS	LEPROSY	MALARIA	MEASLES	MENINGITIS (All Type	Aseptic	Hemophilus influenzae	Meningococcal	Other	MUMPS	PERTUSSIS	PSITTACOSIS	RABIES IN ANIMALS	REYE'S SYNDROME	ROCKY MT SPOTTED FEVER	RUBELLA	SALMONELLA	SHIGELLA	SYPHILIS	TUBERCULOSIS (TOTA	Pulmonary	Other	TYPHOID FEVER
TOTAL FOR SEPT.		0	0	2	2	0	5	880	5	45	1	4	2	0	4	0	26	14	6	2	4	1	3	6	1	•	0	0	148	170	25	17	11	6	0
CUMULATIVE 1982	27	1	3	20	16	4	19	7469	54	327	17	32	33	1	13	6	168	50	31	42	45	18	5	1	5	1	1	3	692	797	113	93	66	27	2
CUMULATIVE 1981	21	0	1	30	25	5	24	925	120	359	NR	49	60	1	16	10	213	70	42	59	42	41	2	1	6	4	3	12	600	239	105	127	106	21	10

SCOMBROID ASSOCIATED WITH BLUEFISH

During August, September, and October, six separate incidents of food poisoning, involving 22 individuals, all associated with bluefish, were reported to the State of Connecticut Department of Health Services. In five cases, the fish was prepared and served in restaurants. The fifth incident involved fish from a private catch which was prepared in a home.

All the cases demonstrated symptoms compatible with scombroid food poisoning (histamine intoxication). Comparison fish from the restaurants and from the private catch were found to contain high levels of histamine (range 124-210 mg/100 gm of fish). Levels of histamine above 20 mg/10 gm of fish are indicative of decomposition and levels above 50 mg/100 gm are potentially toxic.

Microbial decomposition, responsible for the breakdown of histidine to histamine, can be controlled by rapid icing of the fish after they are caught and use of appropriate storing temperature by the consumer. In Connecticut, the bluefish season peaks in August and runs until late November. All known or suspected occurrences should be reported to the local or state health department for appropriate follow-up.

CHILD AUTO SAFETY LAW TAKES EFFECT

Beginning October 1, 1982, children under four years old must be secured in a child restraint seat or seat belt depending on the child's age while riding in a car in Connecticut. There are presently 19 states that have passed some form of child auto safety legislation.

Children one to four years of age must be secured in either a child restraint that meets federal design requirements, or in a seat belt in the rear seat. For children less than twelve months of age, a special infant restraint that meets federal design requirements must be used.

The most readily available morbidity and mortality data in Connecticut are for children less than five years old. During 1978, 616 injuries were reported to the Connecticut Traffic Records System (for this age range), including one death. There were eight motor vehicle occupant deaths in this age group from 1977 to 1980.

We have the means to translate our concern for child auto safety into appropriate preventive measures. We in the public health and medical community should now promote their effective use.

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