HEPATITIS B VACCINE EFFICACY TRIAL

A new vaccine against hepatitis B has been developed. Szmuness, et. al. have reported the results in the New England Journal of Medicine (Oct. 9, 1980).

BACKGROUND:

Development of a vaccine against hepatitis B has been delayed because of the difficulty in culturing the hepatitis virus in vitro. However, in 1970-73 Krugman, et. al. laid some of the groundwork for active immunization against hepatitis B by determining that hepatitis B infective serum boiled to inactivate the virus prevented or modified the infection in 70% of subjects vaccinated with this material.

The new vaccine is a purified, concentrated preparation of formalin – inactivated HBsAg (hepatitis B surface antigen) particles derived from the plasma of chronic carriers of HBsAg. The trial of its efficacy is summarized below.

STUDY METHODS:

This study was a placebo-controlled, randomized, double-blind clinical trial of the vaccine in 1083 homosexual men in New York City. Previous baseline studies on the same population (more than 10,000 men included) showed that its members are at high risk of infection by hepatitis B virus (HBV). The prevalence of HBV markers (HBsAg, anti-HBs, or anti-HBc) in this population was 68% or ten times that found in male volunteer blood donors.

Criteria for enrollment in this study included evidence of freedom from past and present hepatitis B infection. All subjects had to be negative for the above HBV markers and had to have alanine aminotransferase levels (ALT, also called SGPT) below 50 IU.

Each subject was assigned at random either to the vaccine or to the placebo groups for the duration of the study. Each 1.0 mL dose of vaccine contained 40 micrograms of formalin-activated, purified HBsAg. The vaccine, or placebo, was administered as 3 injections: the first dose as soon as the lab results were available, the second dose one month later, and the third dose six months after the first.

Follow-up visits were scheduled for two years after the last injection: one per month for three months, then one each three months thereafter. The subjects were tested for all HBV markers at each visit.

The vaccine group had 549 subjects, of whom 473 completed their injection (86%). The placebo group had 534 subjects, of whom 455 completed their injections (85%). Ninety-one percent of the scheduled follow-up visits were completed.

ANTIBODY RESPONSE TO THE VACCINE:

All of the subjects were anti-HBs negative at the beginning of the study. Ninety-six percent of the vaccine group developed anti-HBs antibodies whereas, only 5% of the placebo group developed anti-HBs.

CLINICAL RESULTS:

For the first 18 months of follow-up, clinical hepatitis B (symptoms of hepatitis, ALT > 90 IU and serological evidence of hepatitis B) developed in only 1.4% of the vaccine recipients as compared to 18.1% of the placebo group, a significant difference (p < 0.0001). If all cases of hepatitis B infection (clinical hepatitis B, mild cases with ALT > 45 IU., and cases with HBsAg or anti-HBc) are included, the vaccine group had an infection rate of 7.6% and the placebo group had a rate of 35%. If one only counts those clinical hepatitis B cases which occurred after the 3 vaccine or placebo injections were complete, the rate in vaccine recipients was 0.42% (2 of 473) and that in placebo recipients was 7.03% (32 of 455).

EDITORIAL COMMENT:

The development of hepatitis B vaccine and the demonstration that such a vaccine prevents HBV infection represent major advances in the control of this serious, widespread disease. The number of cases of acute hepatitis B in the United States has been estimated to be at least 80,000 to 100,000 per year with a fatality rate of 1 to 2%. It is estimated that the total number of HBV carriers is close to 0.8 million in this country. A substantial number of these carriers do eventually develop chronic active hepatitis and cirrhosis. In Asia and Africa there is evidence that HBV is the single most important causative factor of hepatocellular carcinoma; an extremely widespread cancer among middle-aged men. Thus, future immunization programs against HBV infection may ultimately affect not only the incidence of acute hepatitis B and the pool of chronic carriers but may also reduce morbidity and mortality from related diseases.

It is projected that the hepatitis B vaccine will be available in 1982.
TOXOCARA LARVA MIGRANS—SURVEILLANCE

The larvae of *Toxocara* species, the common roundworms of dogs (*T. canis*) and cats (*T. cati*), are capable of infecting human beings who ingest fertile infective eggs. Between one-third and one-half of households in the United States have one or more dogs and essentially 100% of puppies under three months of age are infected with and shed *T. canis*. Because eggs are not immediately infective and require at least 10 days of soil incubation, humans are infected by ingesting embryonated eggs in soil where puppies have defecated (dooyparks, public parks).

Infection in man may be one of two distinct forms of illness, visceral and ocular. Visceral larva migrans (V.L.M.) is typically a disease of toddlers (1–5 years) with a history of pica and is characterized by fever, hepatomegaly, leukocytosis, persistent eosinophilia, hypergamaglobulinemia and elevated isoeastrogglutinins. Other symptoms include cough, wheezing, diarrhea, malaise, irritability, weight loss, skin lesions and seizures. Mild pulmonary involvement is common and is accompanied by transient pulmonary infiltrates in approximately half the cases. Ova and parasites are not formed in man and, therefore, stool exams are not helpful in the diagnosis of V.L.M. Ocular larva migrans (O.L.M.) tends to occur in older children and adults without a history of pica and requires a much smaller infective dose. The retinal lesion is a granuloma, usually solitary, situated posteriorly near the optic disk and macula. Common complaints at presentation include visual loss, strabismus and, more rarely, eye pain. Less than 1% of patients have a history of concurrent or antecedent V.L.M.; however, the association with recent exposure to puppies is significant. Eosinophilia is not prominent and anti-*Toxocara* titers are rarely as high as those in children with V.L.M. It is felt that O.L.M. results from ingestion of a small number of eggs and a subsequently prolonged incubation period as the larva migrate toward the eye, unrestrained in the tissues by the host’s immune defense. Clinically, O.L.M. is difficult to differentiate from retinoblastoma, the most common eye tumor in children. The recent serologic test for *Toxocara* antibodies (found in high titer in the vitreous humor of O.L.M. patients) has improved diagnostic capabilities.

The relatively new ELISA (Enzyme-linked immuno-sorbent assay) for *Toxocara* larval antibody now used routinely by C.D.C. has a sensitivity of 78% and a specificity of 92% and can, therefore, differentiate toxocaralisis from other helminthiases. The predictive value of the ELISA using a titer of greater than or equal to 1:32 is higher than 85%. Previous serologic tests lack such sensitivity and specificity. As toxocarasis is not a reportable disease and the diagnosis prior to development of the ELISA was difficult, the true magnitude of T.L.M. (*Toxocara* larva migrans, both V.L.M. and O.L.M.) is unknown. Of 2500 sera submitted to CDC in 1978 for ELISA testing, most positive results were from southern states. In an 18 month period, a pediatric ophthalmologist in Atlanta diagnosed 41 cases of seropositive O.L.M. representing 37% of the retinal disease in his referral population. Retrospective seroprevalence surveys using the ELISA method in the United States yield a prevalence among the general population of 3.5%; the rate is higher in younger age groups, males and blacks (up to 25% in young black males). An estimated 3.5 million people in the United States are infected with *T. canis*. It is not known what proportion of these develop clinical disease. Prospective studies must be conducted to determine the incidence of infection, to assess pathogenicity and to distinguish simple associations from actual cause.

To document incidence and morbidity associated with toxocarial infections and to elucidate more clearly the epidemiologic risk factors, the Louisiana Division of Disease Control (DHH), with the cooperation of the Centers for Disease Control, has begun a toxocarial surveillance project. We encourage all physicians to consider the diagnosis of *Toxocara* larva migrans (either V.L.M. or O.L.M.) in children with a comparable systemic or ocular illness, particularly if such a patient has a history of pica and/or lives in a household with a dog. We invite you to submit serum specimens from these individuals to the State Health Laboratory for toxocarial antibody testing by the ELISA method. We will be pleased to discuss cases or answer questions you may have. Our number is 504-568-5005.

**SUGGESTED REFERENCES:**


INFLUENZA

As of the week ending January 24, 1981 influenza activity as measured by the Immunization Division’s active surveillance program was elevated above expected. The surveillance system consists of weekly reports from most Charity hospital emergency rooms, several schools and some nursing homes throughout the state regarding the incidence of both total illness and illness due to upper respiratory infection. Three of ten emergency rooms (Shreveport, Alexandria, Lake Charles) have documented an increase in total visits and visits for URI; schools in northeastern parishes and, more recently, in Orleans and Jefferson parishes have reported large increases in absenteeism. One nursing home in New Orleans experienced a small outbreak of influenza. Eight cases have been confirmed by laboratory methods including two by viral isolation (A/Bangkok/79) and six by seroconversion. Thus, Louisiana is presently experiencing an excess of influenza A, particularly in the northern parishes. As expected, the attack rate is highest among children and young adults and is characterized by fever, cough, sore throat, myalgias and headache lasting 3 to 5 days. We expect the “flu season” to continue through February and suspect that disease activity will increase in southern Louisiana.

On the national level, as of January 10, 1981, nine states have experienced widespread outbreaks of influenza and 17 states, primarily in the Northeast and Midwest, have reported regional outbreaks. At least 23 states have isolated A/Bangkok/79 (H3N2) virus; in addition, both Massachusetts and Texas have isolated H1N1 strains. No isolations of Influenza B have been reported. Deaths due to pneumonia and influenza (P and I), recorded in 121 cities, were elevated for the sixth consecutive week since December 13, 1980. Outbreaks of influenza produced by both H1N1 and H3N2 strains have occurred in several countries worldwide.

Fortunately, most individuals who contract influenza are not at risk of developing complications and only supportive care is indicated. This year’s vaccine provides protection against the currently prevalent strains (A/Bangkok/79 and A/Brazil/78) as well as B/Singapore/79 and is indicated for high-risk individuals (elderly and those with underlying disease as outlined in the August, 1980 edition of this publication). Nearly 50,000 vaccinations have been administered by parish health units. We continue to recommend that those individuals at risk of adverse consequences from infections of the lower respiratory tract receive influenza now. Amantadine hydrochloride (Symmetrel) is an effective chemoprophylactic agent for these high-risk individuals who are unvaccinated and exposed to influenza. Its administration should be considered concomitant with vaccination in these exposed patients until serum antibodies have time to develop (2 to 6 weeks). We encourage health care practitioners to submit throat cultures for viral isolation and paired serum samples for serology from suspected cases of influenza. Such specimens should be obtained during the febrile episode and sent to the State Health Laboratory. The Division of Disease Control will continue to recommend annual influenza vaccination for individuals at risk of complications. The documentation of current viral strains will guide the preparation of next year’s vaccine.
### SELECTED REPORTABLE DISEASES

(© Place of Residence)

<table>
<thead>
<tr>
<th>STATE AND PARISH</th>
<th>SUPPLEMENT</th>
<th>MEASLES</th>
<th>RUBELLA*</th>
<th>MUMPS</th>
<th>PERTUSSIS</th>
<th>TETANUS</th>
<th>ASPECTIC MENINGITIS</th>
<th>HEPATITIS A AND UNSPECIFIED</th>
<th>HEPATITIS B</th>
<th>LEGIONELLA DISEASE</th>
<th>MALARIA**</th>
<th>NEONATAL MIBLICOS</th>
<th>SHigelLOSIS, PULMONARY</th>
<th>TUBERCULOSIS, POLIOMYELITIS</th>
<th>TYPHOID</th>
<th>OTHER SALMONELLOSISe</th>
<th>UNDERNUTRITION</th>
<th>SEVERE</th>
<th>GONORRHEA</th>
<th>SYPHILIS, PRIMARY AND SECONDARY</th>
<th>RABIES IN ANIMALS</th>
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* Includes Rubella, Congenital Syndrome.
** Acquired outside United States unless otherwise stated.
From January 1, 1980, through December 31, 1980, the following cases were also reported: 7-Leptospirosis; 4-Brucellosis; 1-Staphylococcosis; 1-Cryptococcosis; 28-Trichinosis; 1-Poliomyelitis; non-paralytic; 4-Rocky Mountain Spotted Fever; 12-Encephalitis, Anthropod-Borne.
1-12-Encephalitis, Parasite-Borne.
3-12-Encephalitis, Neurotropic.
## SELECTED REPORTABLE DISEASES
(By Place of Residence)

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<th>Measles</th>
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<th>Mumps</th>
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<th>Malaria**</th>
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<th>Rabies in Parishes Cumulative, 1981</th>
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### Notes
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