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State of Connecticut, Department of Public Health
Stephen A. Harriman, Commissioner

New Haven County Liver Study (NHCLS)

The New Haven County Liver Study (NHCLS) is part of the Connecticut Emerging Infections Program. This study is being conducted jointly by the Yale University School of Medicine Department of Epidemiology and Public Health and the Section of Digestive Diseases, the Connecticut Department of Public Health, and the Hepatitis Branch of the Centers for Disease Control and Prevention (CDC).

The purpose of this study is to conduct population-based, prospective surveillance for newly diagnosed and existing cases of chronic liver disease (CLD) among residents of New Haven County. Epidemiological and clinical data are used to better characterize CLD of all causes, with emphasis on infectious causes.

Patients who present with liver-related disorders to gastroenterologists participating in the New Haven County study are enrolled as potential cases. A case of CLD is defined as a patient with the persistence of liver test abnormalities for more than 6 months; or biopsy, radiographic, or clinical evidence of long standing hepatic injury. Incident cases are defined as patients fulfilling the CLD definition in the 12 months before their initial consultation. Patients meeting the case definition more than 12 months before their initial presentation are considered prevalent cases.

The protocols for the NHCLS were developed in collaboration with the Hepatitis Branch of the CDC. Final approval for the protocols was granted by the Yale University Human Investigations Committee on June 6, 1998, following interim approval, which was granted in November 1997. The following summarizes the current status of this project.

In This Issue

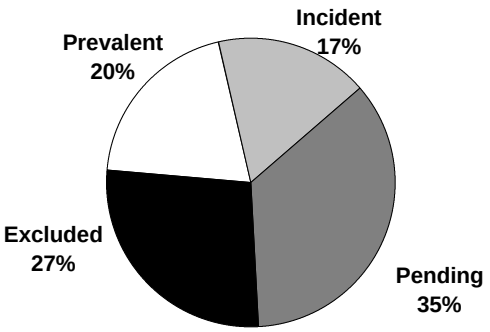
All 57 New Haven County gastroenterologists were asked to participate in active surveillance. Of those, 51 (89%) agreed to participate representing 18 (72%) of 25 practices in the county. Those who declined tended not to see patients with liver disease and/or referred these patients to gastroenterologists who agreed to participate.

Screening for cases of CLD began February 1, 1998 and will continue for a minimum of 3 years. The NHCLS Nurse Coordinator works with each practice to identify patients who may fulfill the case definition. As of January 31, 1999, 691 patients were screened (Figure 1). Of those, 138 were prevalent cases and 120 were incident cases. Of the 120 incident cases, more than 50% appear to have underlying hepatitis C infection. Of the remaining 433 screened patients, 245 potential cases are pending further follow-up and 188 were excluded based on residency or alternate diagnosis.

Longitudinal follow-up of patients enrolled in the study will be done by reviewing medical charts on a periodic basis. The current method of case finding is limited to gastroenterology practices. Therefore, there is likely to be underreporting of CLD as primary care physicians may not routinely refer patients to gastroenterologists for further management. To assess the degree of underreporting and the completeness of incident case finding, a mailed survey of county primary care practitioners and office-based retrospective

surveillance for cases of CLD will take place. In addition, a review of diagnoses obtained by liver biopsy on county residents will be conducted as another means to assess the completeness of case finding.

Figure 1. Screening for cases of CLD by case status (n=691), New Haven County, Connecticut, February 1, 1998 - January 31, 1999.



Editorial Note: Chronic liver disease, including chronic viral hepatitis and cirrhosis, is an important cause of morbidity and mortality in the United States (U.S.). The age adjusted death rate, based on death certificate data from 1989, was 10.4 per 100,000 persons, making CLD the ninth most frequent cause of death (1).

Chronic hepatitis B virus (HBV) and chronic hepatitis C virus (HCV) infection are important causes of CLD. Approximately 5000 of the 1-1.25 million HBV carriers in the U.S. die from CLD each year, and some investigators have calculated that as many as 50% of male carriers may develop primary hepatocellular carcinoma (HCC) during their lifetime. An estimated 8-10,000 of the 3.9 million persons in the U.S. chronically infected with HCV die each year from chronic hepatitis and cirrhosis (2,3). The HCV infection is also associated with HCC: this complication was found in 11-19% of HCV infected individuals among four studies with mean follow-up periods of 4 to 11 years (4).

Chronic infection with HCV or HBV is likely to underlie a substantial proportion of cases of CLD. In an unpublished CDC population-based study conducted in the U.S., Neal, and olleagues. carried out active surveillance for clinical CLD in Jefferson County, Alabama over 1 year and found a cumulative incidence rate of 12 cases per 100,000 persons (personal communication, B. Bell, CDC). Of 140 incident and prevalent cases in which the etiology could be examined, 62 (44.2%) cases had chronic HCV infection alone or with coinfection with HBV or concurrent alcohol use, and 20 (14.2%) had HBV infection alone or with coinfection with HCV or concurrent alcohol use.

Although it is clear that a large number of persons in the U.S. are chronically infected with HBV or HCV and that many will develop CLD, the burden of disease needs to be better characterized. Other than the unpublished data cited above, there are few population-based data from which to determine the incidence and prevalence of CLD and the relative proportion of cases attributable to viral hepatitis and other etiologies (5). In addition, the manner in which the etiologic agent, combination of agents, or route of infection may affect important features of CLD, such as the rate of acquisition and progression, is poorly understood.

For further information on the New Haven County Liver Study, please contact the study's research staff at the Yale University School of Medicine, at (203) 764-4355.

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Availability of Lyme Disease Vaccine

On December 21, 1998, the Food and Drug Administration (FDA) licensed LYMErix™ (SmithKline Beecham Biologicals, Reixensart, Belgium),* a new vaccine against Lyme disease (LD). This report; which is adapted from the MMWR (1), summarizes information about this vaccine and provides epidemiologic information about LD relevant to vaccine use.

Each dose of LYMErix™ contains 30 mg of lipidated recombinant outer surface protein A (OspA) of *Borrelia burgdorferi* sensu stricto, the causative agent of LD in North America, adsorbed onto aluminum adjuvant (2). It is indicated for use in persons aged 15–70 years (2). Three doses of the vaccine are administered by intramuscular injection. The initial dose is followed by a second dose 1 month later and a third dose 12 months after the first. Vaccine administration should be timed so the second dose and the third dose are given several weeks before the beginning of the *B. burgdorferi* transmission season (2), which usually begins in April.

In a randomized, double-blind, multicenter trial involving 10,936 participants living in areas of the northeastern and upper north central United States (U.S.) where LD is endemic, the vaccine efficacy in preventing LD was 50% (95% confidence interval [CI=14%–71%) after the first two doses and 78% (95% CI=59%–88%) after three doses (2). Efficacy against asymptomatic seroconversion was 83% (95% CI=25%–96%) after two doses and 100% (95% CI=30%– 100%) after three doses (2). The duration of immunity following the three-dose vaccination series is unknown, and the need for booster doses has not been determined.

Local reactions at the site of injection were reported by significantly more vaccine recipients than placebo recipients (2). Unsolicited reports of myalgia, influenza-like illness, fever, and chills within 30 days after a dose were significantly more common among vaccine recipients than placebo recipients, but none of these were reported by >5% of either group (2). Reports of arthritis were not significantly different between vaccine and placebo recipients, but vaccine recipients reported significantly more transient arthralgia and myalgia following each dose of vaccine (2).

Lyme disease is the most commonly reported vectorborne disease in the U.S.. Since the implementation of a standardized surveillance case definition in 1991, >90% of cases have been reported from the northeast and north central states (3). Persons of all ages are susceptible to infection, but the highest reported rates of LD occur in children aged <15 years and adults aged 30–59 years. Transmission peaks from April through July, when the nymphal stages of the tick vectors of LD, *Ixodes scapularis* and *I. pacificus*, are actively seeking hosts. These ticks are found primarily in leaf litter and low-lying vegetation in wooded, brushy, or overgrown grassy areas and can transmit other diseases such as babesiosis and ehrlichiosis (4,5).

An estimated 85% of persons with symptomatic LD have the characteristic rash, erythema migrans (6). Untreated infection can cause arthritis or neurologic symptoms, such as radiculoneuropathy or encephalopathy. At any stage, the disease can usually be successfully treated with standard antibiotic regimens.

Strategies to prevent LD include avoiding tick habitats, wearing protective clothing, using repellents to avoid tick attachment, promptly removing attached ticks, and employing community measures to reduce tick abundance (7). Because the vaccine is <100% efficacious and does not provide protection against other tickborne illnesses, vaccination should not be considered a substitute for other preventive measures.

The LD vaccine should be targeted to persons at risk for exposure to infected vector ticks. This risk can be assessed by considering the focal geography of LD and the extent to which a person's activities place him or her in contact with ticks (3). Vaccination of persons with frequent or prolonged exposure to ticks in areas endemic for LD is likely to be an important preventive strategy (8). For persons with only brief or intermittent exposure to tick habitat in areas where LD is endemic, the public health

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benefits of vaccination, compared with early diagnosis and treatment of LD, are not clear (8). Recommendations for use of LD vaccine are being developed by the Advisory Committee for Immunization Practices.

For additional information about LYMErix™ please contact SmithKline Beecham at 1-800-596-3749, extension 800.

For general information about Lyme disease, including case rates for towns in Connecticut, please call the Department of Public Health (DPH), Epidemiology Section, at (860) 509-7994. Town and county Lyme disease statistics are also available from the DPH Web site at *http://www.state.ct.us/dph*.

*Use of trade names and commercial sources is for identification only and does not imply endorsement by the CDC, the U.S. Department of Health and Human Services, or the Connecticut Department of Public Health.

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