

10-Year Action Plan Set for Liver Disease Research

BY JEFF EVANS
Senior Writer

The focus of liver and biliary disease research in the United States through 2015 has been set with the release of the National Institutes of Health's Action Plan for Liver Disease Research.

The decade-long initiative is the result of coordinated effort between federal health agencies and the 18 institutes, centers, and offices in the NIH that support liver and biliary disease research. The plan is geared toward the rapid translation of findings from basic research to clinical practice, and vice versa.

Employees of NIH and federal agencies developed the plan with help from extramural researchers, physicians, and representatives of professional and patient advocacy groups.

The action plan includes 214 research goals, but 10 major goals cut across multiple disciplines in liver and biliary disease research:

- Improve the success rate of therapy for chronic hepatitis C.
- Develop effective antiviral therapy regimens for the long-term management of chronic hepatitis B.
- Develop effective therapies for the treatment of nonalcoholic and alcoholic fatty liver disease.
- Detect hepatic fibrosis with tests that

are sensitive, specific, and noninvasive.

- Detect hepatocellular carcinoma at earlier stages in high-risk patients with new screening tests.
- Develop ways to prevent gallstones.
- Understand further the etiology of biliary atresia.
- Improve the safety, and determine the best use, of living donor liver transplantation.
- Develop standardized and objective diagnostic criteria of major liver diseases and their grading and staging.
- Reduce the overall mortality from chronic liver disease and cirrhosis.

In the plan, each research goal is rated according to whether it is a short- (1-3 years), medium- (4-6 years), or long-term (7-10 years) goal and whether the degree of difficulty of reaching the goal involves high, intermediate, or low risk.

The Liver Disease Subcommittee of the statutory Digestive Diseases Interagency Coordinating Committee will assess the plan through announcements and periodic meetings, including open meetings after 5 and 10 years.

NIH's investment in liver and biliary disease research has increased from about \$125 million in 1993 to \$388 million in 2003.

To review the full action plan, go to www.niddk.nih.gov/fund/divisions/ddn/lldr/lldr_action_plan.htm.

H. pylori Eradication Does Not Prevent NSAID-Related Ulcers

BY TIMOTHY F. KIRN
Sacramento Bureau

SAN ANTONIO — Treating *Helicobacter pylori* infection in patients who take NSAIDs does not help prevent the development of peptic ulcer disease, Willem F. Lems, M.D., said at the annual meeting of the American College of Rheumatology.

In his study, 347 patients with culture-confirmed, *H. pylori* infection and a history of long-term NSAID use were randomized to receive *H. pylori* eradication treatment or a placebo.

Three months after treatment, peptic ulcers were diagnosed by endoscopy in 6 of 172 patients who had been actively treated, compared with 8 of 175 patients in the placebo group. One patient in the treated group and two patients in the placebo group developed endoscopic duodenal ulcers.

There was no significant difference between the groups in terms of the prevalence of gastroduodenal erosions (41 treated versus 51 placebo). Nor was there any difference in the rate of dyspepsia.

No patient in either group developed a symptomatic ulcer, an ulcer bleed, or ul-

cer perforation at any time during a full 12-month follow-up.

At the 3-month endoscopic examination, 87% of the treated patients and 21% of the placebo-treated patients were free of *H. pylori*.

The study adds to a body of literature on *H. pylori* and NSAID-associated ulcer that has been a bit confusing, said Dr. Lems of VU University Medical Center, Amsterdam.

While *H. pylori* eradication has been shown definitively to reduce ulcer recurrence in patients not taking NSAIDs, reports on what eradication does for patients on NSAIDs have been conflicting.

Although his study has the scientific strength of being a prospective trial, Dr.

Lems said, it also could have been confounded by the fact that patients had to have been on long-term NSAID therapy already. His patients could have been a select group who were already able to tolerate NSAID treatment, and the results of treatment could be different for individuals just starting treatment.

A fairly large percentage of the patients (53%) were either on gastroprotective therapy with a proton-pump inhibitor or were taking a selective cyclooxygenase-2 inhibitor.

There were no significant difference, between groups in terms of the prevalence of gastroduodenal erosions or the rate of dyspepsia.

Liver Markers Tied to Psoriasis Flares

BY BETSY BATES
Los Angeles Bureau

PARIS — At least one abnormal biologic liver parameter was found in 20 of 22 patients with generalized pustular psoriasis, highlighting a previously underestimated connection between liver involvement and the disease, French researchers reported at the European Congress on Psoriasis 2004.

Extracutaneous manifestations of generalized pustular psoriasis are well recognized, and include arthritis and mucosal involvement.

Although liver abnormalities have been noted in isolated cases, the full extent of liver involvement has not been fully explored, noted Manuelle A. Viguier, M.D., of the department of dermatology at Saint-Louis Hospital in Paris.

Liver tests were performed on 22 consecutive patients admitted to the hospital for a flare of their generalized pustular psoriasis; tests were

done at the time of the flare and several weeks later.

Patients with abnormal biologic tests (bilirubin, γ -glutamyl transferase, alkaline phosphatase, aspartate aminotransferase, or alanine aminotransferase serum counts) underwent a more extensive liver work-up, which included a drug intake analysis, serologic detection of hepatitis B virus and hepatitis C virus infections, abdominal ultrasound examination, liver histology, and endoscopic retrograde cholan-

giopancreatography or magnetic resonance cholangiopancreatography.

Abnormal biologic liver tests were a very common finding at the time of a psoriasis flare, occurring in nearly all patients.

Half of the 22 patients studied had pronounced abnormalities: jaundice in 4, γ -glutamyl transferase higher than four times the normal value in 10, alkaline phosphatase higher than twice the normal value in 7, and transaminases higher than three times the normal value in 7.

"These abnormalities returned to [the] normal range at the time of remission of pustular psoriasis and relapsed when new cutaneous attacks occurred," Dr. Viguier and associates noted in their poster presentation.

Liver biopsies revealed neutrophilic cholangitis. Magnetic resonance studies showed features characteristic of sclerosing cholangitis in three of four patients who underwent such examinations.

"Biliary involvement related to neutrophilic cholangitis should be added to the spectrum of extracutaneous manifestations of this disease, and physicians should be aware of such complications in order to avoid both invasive liver investigations [that aren't useful] and withdrawal of drugs with potentially deleterious consequences on the course of the disease," Dr. Viguier said.

Drug-induced liver toxicity was explored but ruled out as a cause of the sclerosing cholangitis-like changes that the investigators observed. Rather, the disease itself appears to be responsible.

The team is planning a study to test whether a sclerosing evolution of biliary involvement is present in patients with recurrent flares of generalized pustular psoriasis.

The abnormalities returned to the normal range at the time of remission of pustular psoriasis and relapsed when new attacks occurred.

Consider Early Colorectal Ca Screening in African Americans and Hispanics

ORLANDO, FLA. — Colorectal cancer occurs at a high enough rate in African Americans and Hispanics under 50 years of age to warrant screening starting at age 40, according to Jaydutt Vadgama, Ph.D., of the Charles R. Drew University of Medicine and Science, Los Angeles.

In a retrospective study, Dr. Vadgama found that of 148 patients who had been diagnosed with colorectal cancer at the Martin Luther King/Drew Medical Center during 1996-2004, 38 (26%) were younger than 50 years of age. At diagnosis, the 38 patients had a median age of 42 years at diagnosis. Half of the patients under age 50 had a family history of colorectal cancer.

During 1993-1997, 46% of the 11,615 cases of colorectal cancer in African Americans and Hispanics

in California occurred in patients younger than 50 years.

"Colorectal cancer screening should be considered in African Americans and Hispanics beginning at age 40 regardless of family history," the researchers suggested in a presentation at the annual meeting of the American College of Gastroenterology.

The college's guidelines on colorectal cancer screening, published in 2000, recommend that patients at higher than average risk for colorectal cancer (because of family history among two or more first-degree relatives) should be screened by colonoscopy at an age of 40 years or 10 years younger than the age of the youngest affected relative at diagnosis, whichever is earlier.

—Jeff Evans