

to use the recombinant genes because I believed that they would increase the possibility of introducing beta-globin genes that would be functionally effective, and would impose no additional risk to the patient” The patients thus far have shown neither any benefit nor harm from the treatment.

Cline resigned as chief of the UCLA Division of Hematology-Oncology when charges of misconduct were made earlier (SN: 11/1/80, p. 278), but he maintains his faculty position. Although no NIH funds were used for Cline's travel to Israel and Italy or his clinical experiments there, NIH money had been used at UCLA in the preparation of the genetic material.

The NIH action represents the first case in which an individual investigator has been required to get prior NIH approval for recombinant DNA experiments when such approval is not generally required, and also the first case in which an investigator at an institution with a “general assurance” approved by the NIH needs to get prior approval for each protocol using human subjects. In addition, it is the first time the institutes of NIH have been asked to reconsider existing grants in light of a conduct report. □

Rapid diagnosis of legionellosis

Although legionellosis (also known as Legionnaires' disease) affects 125,000 persons in the United States annually, early diagnosis of this life-threatening pneumonia is not possible unless physicians take biopsy specimens, which they are often reluctant to do, and unless labs have the equipment to analyze the specimens for *Legionella*, the bacteria that cause the disease. Thus, scientists are looking for less invasive, easier methods of diagnosing the disease early, such as identifying antigenic material from *Legionella* in patients' body fluids (see p. 361).

Now such a diagnostic technique may have been found by Richard B. Kohler, assistant professor of medicine at Indiana University School of Medicine in Indianapolis. As he reported at the Third International Symposium on Rapid Methods and Automation in Microbiology in Washington last week, the technique consists of using radioimmunoassay to identify *Legionella* antigen in the urine of legionellosis victims. When the method was performed on a handful of legionellosis patients, it detected the bacterial antigen as often during the first three days of illness as later on. And once the patients got antibiotics for the disease, the antigen disappeared from their urine.

A limitation to this diagnostic approach, however, is that it can detect antigen in urine from only one species of *Legionella*—*Legionella pneumophila*—not from others that can also cause legionellosis. □

Drug therapy for gallstones

Gallstones (crystallized bits of cholesterol in the gallbladder) are no small problem. Ten percent of all Americans, and one-fifth of those over 40 years of age, have them. Gallstones in turn often lead to upper abdominal discomfort, bloating, belching and food intolerance and sometimes to more serious problems such as acute or chronic inflammation of the gallbladder or cancer of the gallbladder. The only treatment available has been surgical removal of the gallbladder.

Now a relatively safe and often effective drug therapy for gallstones has been found—a natural bile acid present in the gallbladder called chenodeoxycholic acid. The news was reported in New York at the recent meeting of the American Gastroenterological Association.

Ten years ago Leslie J. Schoenfield, director of gastroenterology at Cedars-Sinai Medical Center in Los Angeles (then at the Mayo Clinic in Rochester, Minn.), and several of his colleagues found that chenodeoxycholic acid could dissolve gallstones. Because of this discovery's potential value, the National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases decided, in 1973, to fund a \$10 million, multicenter trial to determine how safe and effective chenodeoxycholic acid might be as a gallstone drug. First Schoenfield and other scientists participating in the trial performed research to learn more about how gallstones are formed and dissolved. Then they demonstrated the safety of chenodeoxycholic acid in experimental animals. In 1976 they enrolled 916 gallstone patients in the clinical trial. One group of patients got 750 mg of chenodeoxycholic acid daily, another group got 375 mg daily and a third group got a placebo daily. All the patients were then followed for two years, with the last patients completing two years of follow up in August 1980.

The results of the clinical trial suggest

that chenodeoxycholic acid is safe for humans. For instance, loose bowel movements occurred in 41 percent of patients getting the 750 mg dose, but the diarrhea was mild. And while the drug was able to mildly raise blood levels of cholesterol (a heart disease risk factor), it did so in only 10 percent of patients who took 750 mg of it daily. Chenodeoxycholic acid totally dissolved gallstones in 14 percent of patients who took the 750 mg dose, and partially dissolved gallstones in 27 percent of patients who took that dose. There was somewhat less efficacy among patients who took 375 mg of the drug daily—a total gallstone dissolution in 5.2 percent of patients and a partial gallstone dissolution in 23.6 percent of patients. In contrast, very little gallstone dissolution took place among placebo patients—a total dissolution in only 0.8 percent of patients and a partial dissolution in only 10.2 percent of patients. Thus, Schoenfield and his colleagues conclude that chenodeoxycholic acid at 750 mg daily “has a role in treating appropriately selected patients with cholesterol gallstones,” provided those patients understand the potential benefits and risks of the drug as compared with those of surgery or of physician observation without treatment.

The FDA will now evaluate the results of this trial as well as pending applications from drug companies eager to market chenodeoxycholic acid in the United States. Meanwhile, Schoenfield and his colleagues are undertaking yet another trial—to see whether chenodeoxycholic acid can prevent the recurrence of gallstones among patients for whom the drug has already dissolved gallstones. And further down the road, another natural bile acid found in the gallbladder—ursodeoxycholic acid—may turn out to be just as effective as chenodeoxycholic acid in dissolving gallstones but with fewer side effects. Preliminary clinical results indicating that this might be the case were reported at an American Chemical Society meeting in Atlanta in April by Ashok Kumar Batta of the New Jersey Medical School in Newark. □

Beta-endorphin as arthritis culprit

Of all the peptides in the brain that produce psychological or behavioral effects, beta-endorphin is one of the most intriguing—and controversial. It may or may not relieve depression and schizophrenia, depending on which studies one cites; it may relieve pain; it may be involved in the body's regulation of heat and maybe even in the body's preparation for a food shortage. Now beta-endorphin has been implicated in rheumatoid arthritis and other arthritis diseases, Charles W. Denko of the Fairview General Hospital in Cleveland reported last week in Boston at the annual meeting of the Arthritis Foundation.

Denko and his colleagues have found

that levels of beta-endorphin were significantly lower in both blood and joint fluids from patients with rheumatoid arthritis, osteoarthritis, gout and other rheumatic diseases than in blood and joint fluids from healthy persons, and especially low in the blood and joint fluids of patients with chronic and extremely painful arthritis, notably rheumatoid arthritis.

Denko foresees these findings benefiting patients with arthritis diseases. For instance, beta-endorphin might eventually help ease arthritis sufferers' disease processes and pain once the price of producing the substance is lowered and it has been approved for clinical use by the Food and