With the Willowbrook project brought into public controversy as an example of a medical investigation whose mere description sounds damning, MEDICAL NEWS essayed to find out more precisely what the program is doing and where it might stand in regard to the ethical tenets of human experimentation.

The Willowbrook study has been going on for 11 years. For two years before that, a survey was conducted at Willowbrook to establish definitely what had become a distinct clinical impression to some of the institution's medical staff – that infectious hepatitis was endemic there.

The director of the hepatitis project since its inception has been Dr. Saul Krugman, Professor of Pediatrics and department chairman at New York University School of Medicine. He describes Willowbrook, a sprawling facility at the edge of a woodland belt on Staten Island, as "probably unique" for an investigation of this kind.

"Willowbrook was not chosen because its population was mentally retarded," Dr. Krugman said, "but because it had endemic infectious hepatitis and a sufficiently open population so that the disease could never be quieted by exhausting the supply of susceptibles." The patient population is nearly 5,500, a total that Dr. Krugman believes is the biggest in any one facility for the mentally retarded in the U.S.

Most Patients Are Children

In addition, he said, Willowbrook's patients are predominantly children; a few years ago the median age was 12, today it is slightly lower because the only general admissions have been to the infant facilities–the only buildings not overcrowded.

"It was well recognized," Dr. Krugman said, "that infectious hepatitis was a mild and relatively benign disease in children as compared with adults. Experience at Willowbrook indicated that the disease observed there was especially mild. Consequently only the Willowbrook strains of infectious hepatitis would be used for the study."

With the preliminary survey pointing to Willowbrook as a feasible place to investigate hepatitis immunity, Dr. Krugman organized his study plans and presented them to the N.Y.U. Committee on Human Experimentation, to the state Department of Mental Hygiene (which operates Willowbrook), and to the Armed Forces Epidemiological Board (whose sanction was needed if the project was to get supporting funds from the military).

DR. KRUGMAN

All three bodies approved the study, and financial support came in what would be the first of a series of contracts from the Army's Research and Development Command.

According to plan, a 16-bed isolation unit was set up at Willowbrook, complete with its own kitchen and ward attendants. The idea was to protect the study subjects from Willowbrook's other endemic diseases–such as shigellosis, measles, rubella, and respiratory and parasitic infections–while exposing them to hepatitis.

Aside from the obvious emotionally inflammatory aspects of the study, the principal ones being that the subjects are children and mentally retarded, the factor in the Willowbrook investigation that has drawn the most fire for a number of years is that subjects are deliberately induced to acquire a disease.

"That sounds bad when you say it that way," Dr. Krugman acknowledged. "But it's just as important to mention that at Willowbrook it has been inevitable that most newly admitted children will become infected [with hepatitis] in the first six to 12 months after entering the institution."

This intense exposure of Willowbrook patients to infectious hepatitis meant that study subjects had to be drawn from outside the institution's population to provide a reasonable chance they would be susceptible to the disease.

The investigators took the obvious course: they proposed the study to parents of retarded children who had been accepted but not yet admitted to the school. The first contact was made by a psychiatric social worker in the course of processing applicants. "If the parents were interested, then they talked to a member of the investigation's medical staff," Dr. Krugman said.

What Are Parents Told?

This usually was Dr. Joan Giles, Research Associate Professor of Pediatrics at N.Y.U., who has been on duty full-time at Willowbrook since the hepatitis study began. What does Dr. Giles tell parents?

"I give as full an explanation as I can," she said. "And there are a lot more positive things to tell them now than there were 11 years ago. I explain that there is no vaccine against infectious hepatitis, that the disease is always present here, and that their child is quite likely to come in contact with it by the intestinal-oral route common to a close-quartered group of this type.

"I also tell them that we can modify the disease with gamma globulin but we can't provide lasting immunity without letting them get the disease. I explain that we use blood serum taken from Willowbrook patients who had hepatitis and that experience has shown a minimum dosage that can induce the disease in a form even less severe than occurs naturally in patients outside the hepatitis unit."

Concerning the risks, Dr. Giles said she explains what hepatitis can do when it progresses to a severe stage. And she may also explain what jaundice is. But, in addition, she mentions that there is no evidence that the artificially induced disease has ever caused permanent damage to any of the study subjects, that the incidence of jaundice has been well controlled with gamma globulin, and that most of the hepatitis cases in the unit "are hard to tell from the sniffles unless you know what you're looking for."

At the end of her briefing and after any questions have been answered, Dr. Giles said she advises the parents to ask their family physician for his opinion on the program. "Some doctors have called me with a few more questions," she said, "but usually the parents are willing to sign the consent form after they talk with me."

With few exceptions, according to Dr. Krugman, this has been the procedure for obtaining parental consent in the hepatitis program since it began. Written permission has been secured for every child enrolled in the study. On the average, a new study group is begun every three months. The number of children in each group ranges from six to 14; their ages have run between three and 10 years.

All serum used in the study has been taken from Willowbrook patients early in their hepatitis episode. It is inoculated into suckling mice and four different tissue cultures to rule out the possibility of other viral or mycotic agents, Dr. Krugman said. Then it is injected as straight serum, not concentrated, into the study subjects. Dosage volumes have ranged from 0.25 ml. down to 0.025 ml. The result of the injection is that the susceptible children get infectious hepatitis. In most of them, said Dr. Giles, the only way to be certain they have it is to run serum transaminase tests. Jaundice occurs in about 8 per cent of the subjects. Dr. Krugman said the jaundice was "very transitory . . . very slight, and frequently only Dr. Giles can recognize that the child is jaundiced." In the general patient population at Willowbrook, the incidence of jaundice with hepatitis is 15 per cent.

Children remain in the isolated hepatitis unit for about two months, which more than covers the incubation period for the common type A strain (30-40 days). When all liver chemistry tests have returned to normal, the subjects are moved to an observation ward for another month or so, partly to guard against the possibility that they might be harboring an infrequent type B strain whose incubation period ranges as high as 80 days or more.

What has the Willowbrook study provided in the way of research benefits?

According to Drs. Krugman and Giles, there has been much time spent on evaluating dosages–both of the minimal amount of virus-containing serum needed to cause a mild form of the disease and of the optimum amount of gamma globulin that would allow the development of a passive-active immunity.

As a result, the investigators felt they knew enough about it to begin–last September–a routine program of GG administration to every new patient at Willowbrook. One injection is given on admission, and a second four months later. The best dosage range appears to be 0.01 or 0.02 ml. per pound. The program has cut the