

### Consent From Parents

"Our method of obtaining informed consent has changed progressively since 1956," Dr. Krugman said.

Now, he said, the parents of the children accepted for admission to Willowbrook are invited to discuss in a group session the studies that the doctors do in a special area of the school.

Another scientist at the lecture, Dr. Alfred M. Prince of the New York Blood Center, paid tribute to Dr. Krugman's "courage and imagination" in doing the research and said that the N.Y.U. pediatrician had been "unjustly criticized."

Such hepatitis studies at Willowbrook and at other institutions need to be enlarged, Dr. Prince said.

Dr. Krugman said that the "crucial" factor involved in his group's studies was a protein called Australia antigen.

Dr. Baruch Blumberg and his associates at the Institute for Cancer Research in Philadelphia, discovered the protein in 1963 in an aborigine as part of genetic studies that they conducted in Australia.

Hence, Dr. Blumberg named the protein the Australia antigen. Subsequently, Dr. Blumberg's group linked the Australia antigen with hepatitis.

That discovery, a committee of the World Health Organization said recently, "has been the most spectacular advance in the seemingly insoluble problem of human hepatitis."

### 'Explosion of Knowledge'

About the same time, Dr. Prince detected at the blood center what he called serum hepatitis antigen in the blood of patients with the disease. Further testing showed that Dr. Prince's serum hepatitis and Dr. Blumberg's Australian antigens were identical.

"An explosion of knowledge" about hepatitis then resulted, Dr. Krugman said.

"The studies that the research reported yesterday were done on a total of 68 children, 3 to 10 years old. The children were admitted to Willowbrook in eight groups during the five-year period from 1965 to 1970.

Dr. Krugman said his group had tested two types of immunizations, both involving the Australia antigen, on these children.

One type was active immunization. By exposing the children to a heat-treated serum called MS-2, the doctors purposefully stimulated the youngsters' bodies to produce over a several-week period immunologic defense substances called antibodies.

The principle is the same as when doctors inject a killed virus vaccine against diseases such as influenza.

The other type was passive immunization, which protects through transfer of preformed antibodies such as those derived from a person who has recovered naturally from the disease.

This is the principle involved when doctors inject gamma globulin to protect individuals exposed to infectious hepatitis.

Supplies of gamma globulin are derived from blood donated by large numbers of individuals. The antibodies that people form after an attack of infectious hepatitis thus is pooled, or mixed, and used to modify the illness in persons exposed to the disease.

Gamma globulin generally has not proved effective in preventing serum hepatitis.

In the active immunization studies, Dr. Krugman used a boiled preparation of serum containing Australia antigen. After adding a small amount of water to prevent heated serum

from clotting, members of his team boiled the mixture for one minute.

This was just long enough to destroy its ability to cause disease. Yet this technique preserved the serum's ability to stimulate production of antibodies against Australia antigen in some children.

"Two inoculations were more effective than one," Dr. Krugman told the doctors, and "one inoculation gave enough protection to prevent some cases and to modify others."

Further, he said, "the individuals who received two injections of the boiled serum were not only protected against hepatitis but they also developed antibodies against the disease."

### Serum Administered

The doctors said that they had given the boiled serum to 14 children at Willowbrook. Of the 10 children who received just one injection, four

were protected against serum hepatitis, Dr. Krugman said, whereas it modified "the hepatitis infection of the [other] six children."

"All four children" who received two injections of the boiled serum of four-month intervals, he said, "had significant protection against hepatitis during the 70-day period of observation."

Three children had no evidence of hepatitis. The doctors said they found laboratory evidence of hepatitis in the fourth child "on only one day."

The passive immunization studies, Dr. Krugman said, could not have occurred without the cooperation of Dr. Prince of the blood center at 310 E. 67th Street here. Researchers at that center, Dr. Prince said, are also conducting similar studies.

The World Health Organization noted that serum containing antibody to Australia antigen "has been extremely scarce." When it has been detected, the patient usually has been a hemophiliac, suffering from the genetic disease that prevents his blood from clotting normally after a cut or bruise.

Doctors suspect that hemophiliacs develop the antibodies from repeated exposures to the hepatitis virus from the hundreds of transfusions they have received to stay alive. Persons receiving scores of transfusions for other medical reasons could also develop such antibodies.

### Hemophiliac Donor

From one hemophiliac who had an extraordinary high level of antibody to Australia antigen and who voluntarily donated the plasma portion of his blood during the last three years, Dr. Prince said he had prepared a small quantity of gamma globulin. The special gamma globulin has about 100,000 times the antibody found in the commercial supply of gamma globulin.

What the group did was to expose 15 children to serum containing Australia antigen, which from past experience they knew would have caused infection in almost every susceptible child.

The serum that the doctors used had been obtained from a child who got the identical type of hepatitis at Willowbrook.

But four hours after such exposure, the doctors gave the regular commercial gamma globulin to five children and the

hemophiliac's gamma globulin to the 10 others.

Dr. Krugman's team said that the hemophiliac's gamma globulin had proved "extraordinarily effective in preventing serum hepatitis" in the Willowbrook children.

"All 10 who received the special" globulin prepared from the hemophiliac were protected against hepatitis, Dr. Krugman said, but "the standard gamma globulin did not protect three of the five children who received it."

Dr. Prince cautioned his colleagues about the scarcity of the serum-hepatitis-antibody-rich gamma globulin. The entire supply has been allocated for the necessary research studies, he said, and "none is available for clinical use."

If the immunizations are licensed in the future on the basis of further evaluation, Dr. Krugman said they could be used to protect persons with a high risk of getting hepatitis.

Among such people would be patients knowing weeks in advance that they needed surgery and blood transfusions, such as for open heart operations.