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matic. One case cited by Dr. Dogo involved a 3-year-old boy with nevus pigmentosus. The cryoprobe was applied at  $-196^{\circ}\text{C}$  for four minutes; the therapy was repeated three times after scattered pigmented elements had reappeared. A year later the patient's face showed marked clearing.

Another patient, a 42-year-old man, with spinocellular epithelioma had been treated with diathermal coagulation without appreciable results. The lesion had first appeared about three years earlier and was manifested by moderate ulceration of the lower lip. Liquid nitrogen spray was applied for six minutes on both sides of the lip. Some im-

provement was noticeable 5 days later, and 40 days later spontaneous healing occurred.

Histological control examinations months later resulted in negative findings as far as neoplastic cells were concerned. "... Secondary damage from the destruction of the tissues with liquid nitrogen is clearly inferior to that which would have been caused by surgical removal," commented Dr. Dogo.

"We have some grounds to hope that—once the methodology and application techniques [of cryosurgery] have been improved—low temperatures can become a weapon in association with those already being used in the fight against the most dangerous menace to man's survival."

### Hepatitis vaccination may be possible

*continued from page 27*

rate in such studies is often about 70%, Dr. Krugman said.

"In the ten children who received the special gamma globulin—up to day 78, nothing. As of day 78 (the day of the lecture) there is one who has antigen," said Dr. Krugman. "What will happen next week, or next month, I just don't know. But I think the findings are significant enough to tell us that this is an extraordinary preparation. It deserves intensive study."

The gamma globulin developed by Dr. Prince

and associates was derived by standard fractionation techniques, using the pooled plasma of a single hemophilic donor, Dr. Prince told the assembly. He pointed out that hemophilia patients are repeatedly exposed to serum hepatitis and frequently have extraordinarily high antibody levels.

The gamma globulin in under study at three institutions for retarded children to determine if it will prevent spontaneous contact infections.

"We have also carried out studies on the induction of passive immunity in these children—the antibody levels that can be induced, and how they persist," Dr. Prince said.

"Our preliminary findings indicate that children who receive 0.01 cc/pound of body weight will develop measurable antibody titers. These can be detected with the hemagglutination assay for two to three months."

Two months after administration of this gamma globulin, the children have on the order of  $10^{11}$  antibody molecules per milliliter of blood, he said, adding "this is a considerable degree of potential passive immunity."

This degree of passive immunity might be effective against contact infections involving small numbers of virus particles, Dr. Prince suggested. It might also be effective against some infections acquired from contaminated needles.

"I would question very seriously whether such levels would ever be sufficient to neutralize the quantity of virus present in transfusion. One unit of blood from a carrier of hepatitis virus contains on the order of  $10^{15}$  to  $10^{16}$  virus-like particles."

"The past 25 years have been a frustrating and difficult era for investigators involved in hepatitis research," concluded Dr. Krugman. "The important key which enabled us to open the door with these findings was the discovery of the Australia antigen by Dr. Baruch Blumberg and his associates, and the subsequent contributions by other investigators who devised sensitive tests for the determination of susceptibility and immunity to serum hepatitis."

Alfred Prince, MD, has a warning about the new high-titer gamma globulin developed by his group:

"There is likely to be a demand by clinicians for this product. However, none of this product is available. The (New York) Blood Center has applied for a license to make more of this product and distribute it, but this is a matter before the Division of Biological Standards. We have none available in physical terms; it has all been allocated to the research studies.

"One must keep in mind also the theoretical possibility that antibody conferred passively may inhibit the primary immune response of the host. Therefore, even though clinical disease may be modified, it is possible that the actual primary of the host may also be modified. The chronic carrier state may be increased in frequency.

"I think, therefore, that these studies must be pursued actively and energetically, but cautiously. The time is certainly not yet present when this material can be recommended for clinical use. But I think it is evident that the eventual goal in all of these studies is the prevention of serum hepatitis. It is now approaching."



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