2nd INTERNATIONAL MAX v. PETTENKOFER SYMPOSIUM ON VIRAL HEPATITIS

München, Federal Republic of Germany
19 to 22 October, 1982

Short Abstracts

Max v. Pettenkofer Institute for Hygiene
and Medical Microbiology
of the Ludwig Maximilians University München,
Federal Republic of Germany

Scientific chairmen:
F. Deinhardt, M.D.
L.R. Overby, Ph.D.

REDUCTION OF INFECTIVITY OF HEPATITIS B VIRUS (HBV) AND A NON-A, NON-B HEPATITIS AGENT BY HEAT TREATMENT OF HUMAN ANTIHEMOPHILIC FACTOR (AHF) CONCENTRATES

F.B. Hollinger, G. Dolana, W. Thomas, F. Gyorkey, H. Kingdon

Department of Virology and Epidemiology, Baylor College of Medicine, Houston, Texas, and Hyland Therapeutics, Glendale, California

Non-A, non-B hepatitis is the major cause of posttransfusion hepatitis observed throughout the world. Patients requiring clotting factor concentrates are especially at risk. We have recently evaluated the effect of a heating process on the infectivity of HBV and a candidate non-A, non-B hepatitis agent incorporated into a human AHF concentrate. The AHF concentrate was manufactured from pooled human plasma and contained a non-A, non-B hepatitis agent. To this pool was added 300 or 30,000 chimpanzee infectious doses (CID) of HBV prior to heat treatment. The test and control material (heated and unheated AHF containing both non-A, non-B hepatitis virus and HBV) were inoculated into 6 chimpanzees. Non-A, non-B hepatitis developed in both chimpanzees receiving the unheated material as determined by enzyme alterations and ultrastructural changes. In one of these control animals, the transaminase level remained elevated signifying a persistent infection. No evidence of non-A, non-B hepatitis was detected in the four chimpanzees administered the heated preparations. Studies utilizing AHF containing 100-fold differences in HBV concentration showed that one of the factors influencing thermal inactivation is concentration of the virus. Both chimpanzees that received heated AHF containing 30,000 CID of HBV developed biochemical, histologic and serologic evidence of hepatitis B infection. The control animal, which had failed to resolve its non-A, non-B hepatitis infection, did not develop hepatitis B leading us to speculate that persistent non-A, non-B hepatitis infection can interfere with the subsequent replication of HBV. In the chimpanzee given unheated AHF containing 300 CID of HBV, HBsAg was detected 1½ months after biochemical/histologic resolution of the non-A, non-B hepatitis infection (4 months after the initial inoculation). Histological and biochemical changes occurred approximately 1 month later. In contrast, both chimpanzees receiving the heated material did not develop HBsAg until 7½ to 9 months postinoculation implying that heat-treatment significantly reduced the infectivity of HBV or altered its pathogenicity. Bioequivalency between heated and unheated preparations of the AHF concentrate remained the same. These preliminary studies indicate that a heating process may greatly reduce the risk of hepatitis transmission while retaining biological activity of the product.

$300 = 10^{2.48}$

$30\,000 = 10^{4.48}$

Hepatitis associated with transfusion and substitution therapy. Roundtable discussion

S. Seidl

Department of Immunohaematology, University Frankfurt am Main and Red Cross Donor Service Hessen

Post-transfusion hepatitis (PTH) continues to be one of the major complications of blood transfusion. PTH may be caused by hepatitis B virus or by the agents of hepatitis NANB. These hepatitis viruses are transmitted through blood transfusion or through administration of certain plasma derivatives. Among the different procedures for the prevention of PTH blood bank doctors have concentrated on the removal and on the inactivation of the infective agent.

Several attempts have been made to remove the hepatitis virus by vigorous washing procedures as they are used for frozen red cells. With the introduction of automated washing devices it seemed possible to eliminate the infective agent. In experimental trials blood was used which contained different concentration of HBsAg (as expressed by CPM). Low concentrations of HBsAg could be completely removed, however, in several units containing large amounts of HBsAg there was no reduction at all. At the present time none of the washing systems currently available is capable of eliminating the infectivity. Therefore, washed red cells cannot be considered to be hepatitis free, but may have a reduced risk of transmitting hepatitis.

Washing is also an important step in processing red cells which have been previously frozen and stored at -80 to -196°C. Earlier studies documented no case of hepatitis following administration of frozen washed red cells. Since most of these data base on retrospective studies, underreporting of anicteric PTH cases is likely. In an ongoing prospective study it was demonstrated that the frequency of PTH appears to be reduced when frozen deglycerolised red cells were transfused. Whether this is due to transmembrane washing(for glycerol removal) is not yet clear.

Inactivation of the infective agent has also been proved to be successful. After heating (10 hours at 60°C) certain plasma fractions (albumin, PPF) are considered to be hepatitis free whereas some of the most needed fractions (AHF and factor IX complex) are still associated with a high risk of PTH. During fractionation procedure the hepatitis viruses retained in those fraction from which clotting factors are manufactured. However, new developments have shown that heating (10 hours at 60°C) of glycine solutions of factor VIII eliminates the risk of transmitting hepatitis. Furthermore, with a special betaproprio-lactone treatment hepatitis free factor IX concentrates have been produced and a modification of this 'cold-sterilization'-procedure has been found to be also effective for the production of hepatitis safe factor VIII concentrates.