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Short Abstracts

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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

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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.
Hepatitis associated with transfusion and substitution therapy.
Roundtable discussion
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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
vigorously 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 (or glycerol removal) is
not yet clear.

Inactivation of the infective agent has also been proved to be success-
ful. 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.