Blood Products Advisory Committee
Volume I - 10-6-83 Transcript
Summary

* see attached list of participants

Discussion first revolved around marker viruses. Points covered were

1) What transmissible agents are they talking about

2) what are the methods available to reduce virus contamination is plasma products

3) Constraints to the elimination of viruses & methods to establish the removal of transmissible agents. ie what is the test system?

It was stated that there are really only two agents known to be in plasma products - hepatitis B & non-A- which may or may not be plural.

Stated that only certain kinds of viruses & certain conditions will lead to contamination with an infectious load in the final product. FIRST one is a prolonged viremic state - shown by both the hepatitis viruses. Also an extremely high viral load - which the only one known is the hepatitis B which can go up to 10 to the 7th CID per ml in a hot lot.

It was stated that the active fractionation for AHF is mild.

Stated that the risk of a given lot of hepatis B to transmitting hepatitis B was very low at that time.

~~Stated that in last years & 1/2~~

It was stated that there are several newly indicated blood-born viruses. These included T cell leukemia virus, presumed to be an AHF & a parovirus.

Discussed unknown viruses- Marburg virus might get into the occasional pool. There's always a chance wrong stuff will get in a pool.

Hard data to say what viruses are there is very limited.

Discussion on effects of hepatitis on hemophilics.

Stated that there are a variety of methods that had been used for reduction of viruses: Fractionation

proposed - proposal that one could fractionate out the virus w/ polyethylene glycol & A filtration, immunofiltration method proposed - Both methods ultimately failed.

It was stated that fractionation does reduce infectivity.

~~Dis~~ mention of chemical inactivation; immunologic methods of the physical methods

~~Discussed the use of~~

of irradiation, heating & photodynamic actions - ~~Th~~ Discussed the big problem of killing the virus + Still ~~Without~~ keep most of the protein in its native state - Stated that AHF is a particularly unstable molecule.

Discussed that they did NOT

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want to develop new toxic products or create residues in the product. Another difficult question they faced was how to establish that reduction has been accomplished -

Discussed different types of viruses appropriate to use in ~~different~~ experiments using different methods -

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19-20 Dr. Hiatt: Discussed general principles affecting all METHODS of physical inactivation & some specific material related to the two methods.

He stated that it's easy to inactivate viruses since they are among the easiest of all living forms to kill. The problem is to inactivate them without doing excessive damage to the material, the rest of the material in the system.

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Discussion on 2 ~~the~~ Physical methods- ultraviolet irradiation & photodynamic action - on the basis of their differential action w/

ultraviolet irradiation - it is narrow. ~~the~~ Ultraviolet irradiation was seen as a promising way to sterilize plasma as long as 30 yrs prior. Discussion over the problems w/ this method. Advantages of ultraviolet inactivation are primarily that it has a long & usually successful history - The drawbacks are the REQUIREMENT for very thin layers; the fact you cannot use glass as a vessel to contain the liquid .. & the problem of any continuous flow method.

Discussion on photodynamic action as a possible method.

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with This Came 30 yrs prior in connection w/ hepatitis in plasma.

Discussion on experiments done in 1953 wherein reconstituted plasma was spiked with eastern equine encephalomyelitis virus. The contaminated plasma was pumped through a device at a flow rate of 12 liters an hour. After the treatment all detectable eastern equine encephalomyelitis virus were destroyed & the plasma itself was NOT grossly altered. Its electrophoretic composition was unchanged & upon recalcification, its clotting time was unchanged. At that juncture, photodynamic & certain other candidate methods

were taking the interest of the Nat'l Research Council Committee in charge of investigating sterilization of blood & blood plasma — however there were several human volunteers who died because of the failure of Candidate in activating processes to completely eliminate hepatitis in plasma — This upset all the attempts to Find methods to sterilize plasma & at that time synthetic plasma extenders & greater use of whole blood seemed like better alternatives.

The sterilization of plasma stopped as a subject for

intensive investigation, as far as the hepatitis virus was concerned in about 1955 AND only now is it being resumed-

Stated that the lists of chemical inactivators given today are similar to those given 25 years ago.

Historical Discussion on inactivating viruses. It was stated that generally inactivation can occur either by changes in the nucleic acid, or changes in the protein that prevent delivery of the nucleic acid into a functional region of the target cell.

Discussion on Classes of Chemical inactivators - & factors affecting chemical inactivation.

p. 43 mention of ineffective organic solvents.

It was stated that after searching numerous possibilities through the ~~[illegible]~~ ds of Clinical inactivating a good agent is found - You must be aware that the Clinical inactivator may NOT Be what it seems - also the ~~[illegible]~~ inactivating agent may have its own undesirable properties. Even if You can avoid the undesirable effects of the inactivating agent - it can still affect the product - It was also stated in certain situations the inactivator is under inappropriate conditions or in insufficient concentrations & it can react w/ nucleic acids & not achieve inactivation, it can be a

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[redacted]

P52 mutagen.

Discussion of a specific method of viral inactivation – lipid extraction.

Discussed experience w/ inactivation of hepatitis viruses in plasma

Lengthy discussions of current experiments concerning inactivation of hepatitis B virus, & non-A; non-B viruses

Discussion on chloroform experiments

P 7x Stated that with the best systems for non-A, non-B hepatitis, as many as 1,000 ~~infectious~~ infectious doses of hepatitis B virus can slip through the best detection systems.

~~Also~~ Stated that w/ present

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technology, there is no serologic method available to detect virus at a level of 10 to the 6 or lower. Stated that it would be highly problematic that in the near future they would have serologic tests that would be able to find many, if any of the plasma that are contaminated with non-A, non-B hepatitis virus.

Stated the importance of chimpanzee ~~model~~ model for evaluating methods to inactivate non-A, non-B hep. Discussion of experiments done w/ chimpanzees inoculated w/ inactivated materials.

Discussion of approaches to be taken in designing inactivation experiments - stating that out of three -

approaches - the best is to evaluate inactivation in the Final product.

P 71 Stated that it would be desirable IF they had a serologic test that was generally accepted for antigen & antibody. D Stated that, that was NOT the case AT That time -

Stated that an additional problem is designing studies to evaluate inactivation procedures is the possibility that there is more than one non-A, non-B hep. agent & as time passes this possibility becomes stronger. Evidence from this came from humans & Chimps that we had

multiple ~~epo~~ episodes of non-A, non-B hepatitis ~~that~~ which were a somewhat a different form of non-A, non-B hep. in hemophiliac patients w/ multiple exposures to blood + blood products who first exposed to anti hemophilic factor developed a slightly different form of non-A non-B hepatitis — strongly suggesting that there was a different agent in the anti hemophilic factor.

Discussion of evidence ~~to~~ supporting existence of more than one agent.

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The challenge for investigators designing inactivation studies for non-A,

non-B hepatitis includes the design of study, selection of susceptible

p. 75 Chimpanzees, selection of suitable titered inocula & investigators.

~~& Those~~

p. 79 afternoon session

Committee asked to think about whether or not studies w/ marker viruses can replace the clamp. tests -

* 80 ? Dr. Bove stated that the whole point of their meeting on ~~to~~ marker viruses was to give confidence about inactivation of dangerous viruses - & there are at least the hepatitis group & maybe another group of agents that

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some people think might be associated w/ AIDS.

D stated that if Office of Biologics adopts the concept that testing w/ marker viruses has some value because it tells you something about what happened to the hepatitis or other potentially dangerous viruses, then you should let the public know that. If marker virus testing has value then it should appear on the Labels - if you can't use it in the labeling that means you don't have faith in the process.

It had been proposed that

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at some point that the manufacturers must state that the product is heated - & that would be the only claim - however this is WAS felt to be unsatisfactory.

Reason they want to use marker viral studies is because they can do them in their laboratories whereas it is difficult to do clamp studies in labs.

With their present information they felt ~~the~~ to protect the public safety they must continue using the clamps.

P. 95 It WAS stated that at the present they should figure out how

to correlate a marker battery of viruses to the characteristics they were interested in in the known viruses they considered hazardous - meaning hepatis B & non-A, non-B at that time - & perhaps some other viruses in the future.

Statement re: known hazardous viruses in plasma at that time being hep B, non-A + non-B.

P100

P101 Stated that - we all know there's a hidden agenda + that is hep + AIDS & the Bureau has an obligation to see that the labeling does it -

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allow that hidden agenda to

Become important to

the user -

In discussing labeling of products it was

stated that they didn't

know what HBOS agents are.

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