Safety of Stored Liquid Plasma - A Clinical Study

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Introduction

The use of pooled plasma has been discarded by most physicians, chiefly because of the high incidence of serum hepatitis in recipients. The realization that hepatitis was being transmitted in epidemic proportions by plasma from large pools came in World War II. Later efforts to inactivate the virus with ultraviolet irradiation have failed, as demonstrated by the Korean experience and more recently by laboratory and clinical investigation. Irradiated pooled plasma prepared for commercial distribution has produced hepatitis in 7 to 9 % of recipients. Garrott Allen has proposed that the storage of liquid plasma at room temperatures for six or more months inactivates the virus of hepatitis. The validity of the
method has been investigated by inoculating human volunteers with known contaminated plasma, before and after prolonged storage. Human transmission experiments are of necessity limited, and those performed to date have not been conclusive.

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The period since World War II has seen the development of many hospital and community blood banks. Progress in achieving a good plasma product has lagged in many of these operations because of the concern over hepatitis. Concurrently, a large amount of plasma which should be salvaged from outdated blood and suspended cell preparations is being thrown away due to lack of demand. The waste is enormous, considering that outdating losses of whole blood range from 10 to 20 % if inventories are maintained at a high enough level to meet a reasonable percentage of requests.

At the University of Cincinnati Blood Bank, from 1941 to 1952, the gamut was run from large pools to small pools of six units, the purchase of irradiation equipment, and finally to group specific plasma in attempts to minimize the occurrence of hepatitis.

Method

A program was planned in January of 1952 to determine the value of Allen’s method. Plasma was again prepared from large pools of from 30 to 72 donors but stored at room temperatures for six months before release. All plasma was obtained from carefully screened donors and the processing conformed to the standards of the N.I.H., except that the requirement of ultraviolet irradiation was not employed. Bacterial contamination was detected in less than 1 % of the plasma, human pyrogen tests were negative for all lots, and transmission of bacterial disease was not encountered.

The storage beginning in January, the first lot was issued in July, and contact with recipients began in January 1953. It has taken a long time to accumulate enough data to be of value. Plasma was requested infrequently because of the fear of hepatitis and the group of patients subjected to this risk had injuries and diseases which often resulted in early death.

The survey for incidence of jaundice began with a form letter and questionnaire sent to each recipient six months after transfusion. Later, a house visit was made by a graduate nurse to confirm the information supplied. Detailed records were kept and the data was tabulated.

Results
In the entire study there were 1275 recipients of plasma from pools with a
donor population of 4652. There were 433 early deaths, leaving 842 believed still
living for follow-up. Data was obtained in 629. The whole blood exposure for the
group of 629 totalled 1532. The donor population of the plasma used for the 629

**Table I**

Incidence of Hepatitis in all Recipients of Plasma and Plasma and Whole Blood

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totalled 4494. The donor exposure remained high because while many recipients
escaped follow-up, others were available for study of the effects of the same pools of
plasma. 5 of the 629 developed jaundice.

Recipients were then divided into two groups: group I received plasma and
whole blood; group II received plasma only.

**Table II**

Group I Recipients

Incidence of Hepatitis in Recipients of Plasma and Whole Blood

In group I there were 929 recipients of plasma from pools with a donor population
of 4537. These patients also received 3285 units of whole blood. There were
321 deaths, leaving 608 for follow-up. Contact was made with 432. These 432
patients were exposed to a plasma donor population of 4414 and to 1532 units of
whole blood. The 5 who contracted jaundice were in this group.
The causes of the hepatitis in the 5 can only be surmised since each received
whole blood and plasma. They received 1,9, 1, 1 and 4 units of blood, respectively,
and 1, 3, 2, 1, and 1 units of plasma. No two of the patients with jaundice received
plasma from the same lot. Of 50 patients followed who received plasma remaining
from these same lots, none contracted hepatitis.
The hepatitis occurred in a group of 432 followed patients who received 1532
units of whole blood, an incidence of infectivity of 0.3 %, which could be expected
from the whole blood exposure. The group of 432 was also exposed to plasma of

**Table III**

Group II Recipients

Incidence of Hepatitis in Recipients of Plasma only

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Table IV

Transfusion Data in the Five Cases of Hepatitis

* No two of the patients with hepatitis received plasma from the same lot.
** Of 50 patients followed who received plasma remaining from these lots, none contracted hepatitis.

4414 donors. If the plasma were responsible, the incidence of infectivity would be 0.1%. This figure is contrary to all experiences with untreated or irradiated pools of plasma, being even lower than that encountered with group specific plasma or whole blood. Analysis of results to this point indicates that the blood was most likely responsible for the jaundice and is strong evidence that the stored plasma can be used with reasonable safety.

The most positive information concerning the safety of this plasma comes from analysis of results in recipients of plasma only. In this group, there were 346 recipients of plasma from pools with a donor population of 4067. There were 112 deaths, leaving 234 for follow-up. Data was definite in 197. Among these, no jaundice occurred, although they were exposed to plasma of 3846 donors.

Here 81% of the entire plasma donor population is converted to donor exposure of 197 recipients who were followed. None received whole blood and none developed jaundice.

Table V

Significance

Existing blood bank organizations have a vast potentiality for the production of plasma for civilian and military use. Solution of the plasma-hepatitis problem should restore the confidence of physicians and return plasma to its appropriate place in hemotherapy.

In ordinary civilian use it is simple to employ room temperature storage. As outdating losses of whole blood ordinarily exceed the demands for plasma, reserves may be expanded for emergency use and maintained by gearing production to suit the demand. In the event of need for larger stockpiles for mass casualties, plasma stored as a liquid for six or more months could be frozen and dried for longer storage. Adequate stores of safe plasma would be of tremendous importance in
civilian practice and for any type of mass casualty, military or civilian.

Table VI

Conclusion

The storage of liquid plasma at room temperatures for six or more months has eliminated activity of hepatitis virus in pools of plasma in a clinical trial which exposed 197 patients to the plasma of 3846 donors. It is believed that such plasma may be given to patients without concern for serum hepatitis.

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