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269

Recent Experiences with Transfusion Therapy in PTC-Deficiency

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The mode of action of PTC or Christmas factor has been studied extensively since its discovery in 1952. Only sparse and contradictory evidence has been published, however, with respect to its stability under conditions of the blood bank[1, 2, 3].

Our work was undertaken with the limited objective of determining the PTC content of plasma prepared from out-dated blood, i.e. plasma reclaimed after its parent blood has been stored 19–25 days at 4° C. It is obvious that, should such plasma prove to be rich in PTC, the therapy of patients with PTC deficiency would be greatly simplified.

We began our work by determining the PTC levels of 23 "reclaimed" plasmas obtained from the deep-freeze at the blood bank. The parent blood donations had been collected through polyethylene tubing into ACD solution in polyethylene bags and stored at 4° C for 19–25 days. When the parent blood had been considered too old for transfusion, the plasma had been withdrawn, frozen and stored at –20° C.

[Our assay procedure for PTC is an adaptation of the one-stage AHF assay and is to be described elsewhere. The control for our PTC assay procedures was lyophilized plasma from one of us (J. D. G.) whose PTC level was found to be almost exactly the mean of a large population of normal student nurses.]

We found that 14 of the 23 individual samples of frozen, "reclaimed" plasma from the blood bank had PTC levels greater than 100 %, and 9 had levels less than 100 %. The highest activity of an individual plasma was 158 %, the lowest, 75 %. All PTC values fell within the wider range which we had previously found in a population of 89 apparently normal student nurses. Furthermore, there was no clear trend with time of storage, either at 4° C or at –20° C. If our results are accepted at face value, the implication is that plasma reclaimed from outdated bank blood has a full complement of PTC. The PTC content of the 5 plasmas stored more than 100 days at –20° C was high. This suggests that PTC may be stable for prolonged periods at –20° C.

(Four plasmas stored at room temperature for 6 months to inactivate hepatitis virus were also tested, and none contained measurable PTC activity.)

We felt that our conclusion, arrived at by an *in vitro* assay, required *in vivo* confirmation. This was achieved by transfusing large quantities of similar "reclaimed" plasma to a person with PTC-deficiency.

This patient was a 40-year-old man with severe, sex-linked PTC deficiency and PTC level of less than 5 %. Diagnostic studies on this man (J.J.T.) have been described previously[4].

On January 22nd, 1958, the patient was given 1500 ml of plasma. His partial thromboplastin time decreased sharply, and his PTC level rose from less than 5 % to 30 %. Nine upper teeth were extracted, and a dental splint was applied. He was given 750 ml of plasma the day of operation and 1 liter each day on the 3rd, 4th, 7th, 8th, and 9th post-operative days. Significant bleeding did not occur, and he was discharged 13 days after operation with healed gums.

He was readmitted 6 weeks later for removal of the 11 remaining teeth. On March 20th, he was given 8 units of "reclaimed" plasma, 6 before and 2 after tooth extraction, and a PTC level of 25 % was achieved. Eleven lower teeth were removed; a splint was applied, and the same uncomplicated course was observed. Six days after extraction, 4 units were given to prevent oozing when the dental splint was removed. The patient was discharged 11 days after the second extraction with healed gums.

It is possible to test arithmetically whether this *in vivo* experiment was consistent with the notion that reclaimed plasma is rich in PTC as follows:

The man's plasma volume can be estimated roughly from his body weight and hematocrit, assuming blood volume to be 10 % of body weight and blood to have a density of 1.0. If the following additional assumptions are made, the expected PTC level can be compared with the observed level.

1. The plasma transfused is assumed to have an average PTC content of 100 %.
2. It is assumed that no utilization of PTC occurs during the several-hour period of transfusion, and that none leaks out of the intravascular compartment.
3. Maximum and minimum assumptions can be made about plasma expansion, that is, there may have been (a) no expansion or (b) complete

expansion. The overall effect of these assumptions probably is to give a somewhat high expectation.

Using these assumptions, it can be calculated that the PTC level on January 22nd should have lain between 31 % and 43 %. It was in fact observed to be 30 %. Similarly, the PTC level on March 20th was expected to rise to between 39 % and 62 %. Actually a 25 % -level was detected.

While expectation and observation did not agree perfectly, we believe the *in vivo* data substantiate our *in vitro* data. It appears, therefore, that plasma prepared from out-dated blood is rich in PTC, possibly as rich as fresh plasma. Furthermore, this PTC activity appears stable for considerable periods at –20° C. This conclusion, it should be emphasized, has important practical implications.

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