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Hypoxanthine in stored blood

To the Editor:

The enzymes that degrade hypoxanthine (HX) are known to be lacking from human red cells (RBCs).[1] Thus, HX becomes the terminal product of the catabolism of ATP in RBCs. Consequently, its concentration increases steadily during storage of whole blood or RBC concentrates in common preservatives (Fig. 1). The extent of accumulation of HX may depend on several factors including hematocrit and pH, but in no instance was its level less than 1.5 μmol per g of hemoglobin (Hb) by the 35th day of storage, the expiration date with some of the preservatives tested. HX efflux from RBCs had half-times of 15 and 45 seconds at 37 and 4°C, respectively, as measured by mixing equal volumes of RBCs with high HX and normal saline and assaying HX in the supernatant after rapid centrifugation at preselected times.

Whereas the high permeability of the RBC membrane may allow removal of HX by washing the RBCs with normal saline, it may also result in an increase in HX in the circulating blood after transfusion of nonwashed blood or RBCs. Indeed, on transfusion, the HX that had accumulated in the RBCs during storage may enter the plasma due to the concentration gradient between the RBCs and the plasma (HX is virtually absent in the circulating blood). Further, HX cannot be metabolized in the circulation because the activities of xanthine dehydrogenase and xanthine oxidase (XO) are near zero in fresh and outdated human plasma or blood.[1] Thus, if a patient with 5 L of blood is rapidly transfused with 1 L of blood containing 3 μmol of HX per g of Hb, the concentration of HX in the patient's blood could theoretically peak at 0.096 m*M*.

A level of 0.1 m*M* HX in the vascular space was found to exacerbate severely the reperfusion injury after ischemia or hypoxemia in isolated perfused rat hearts.[2,3] If it is considered, first, that some human tissues, including liver and intestine, may have higher XO activity than the rat heart;[4] second, that transfusion with RBCs is usually given after hypovolemic shock that leads to ischemia in the organs; and third, that patients receiving transfusions may have less than 5 L of blood, we would like to raise consideration of the possibility that HX released in the circulatory system, from the stored RBCs, may exacerbate the contribution of XO to the reperfusion injury.

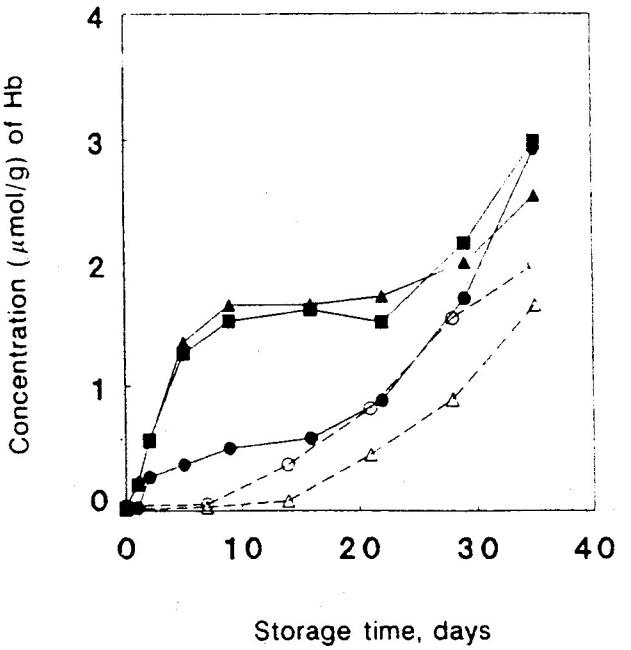

FIG. 1. High-performance liquid chromatography[5] determination of hypoxanthine (HX) in blood or red cells (RBCs) stored in common preservatives (n = 6 for each group). —●— ACD blood; —▲— CPD blood; —■— CPDA blood; —△— CPDA-RBCs; —○— SAGM-RBCs.

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