Killing Yersinia enterocolitica

In a recent article, Gibb et al1 presented studies dealing with the role of Yersinia enterocolitica in transfusion transmitted disease. They proposed that the increased frequency of reported transfusion complications during recent years, caused by Y enterocolitica infected blood components, is related to the use of additive solutions for red cell storage, which brings about a decrease in complement activity. They showed that dilution of plasma with an additive solution to a concentration corresponding to that in red cell units decreases complement killing of Y enterocolitica strains at 20°C. These authors assume that the blood of subjectively healthy donors contains Y enterocolitica organisms which possess a virulence plasmid rendering them resistant to complement. The organisms are thought to be present free in the donor's plasma. When collected blood is cooled to 20°C, the plasmid is no longer expressed and the organisms become sensitive to complement. The authors suggest that the normal two to six hour delay before separation into components may not be enough for complement killing.

This hypothesis is very interesting and Gibb et al presented some evidence in support of it. They do not mention, however, that there is another possible explanation. We have suggested that Y enterocolitica organisms are transferred intracellularly in donor leukocytes, where they are obviously protected from the action of plasma complement.2 After days or weeks of storage, any leukocytes present in red cell units will begin to disintegrate, releasing any organisms they contain. Y enterocolitica can grow rapidly at 4°C. Whether the storage medium is undiluted plasma or plasma diluted with an additive solution, no killing by complement will be expected at this temperature, particularly if the bacteria are released after more than a week of storage.

This alternative hypothesis is compatible with the observation that most of the severe complications seen with Y enterocolitica units stored for ≥21 days. That no Y enterocolitica complications were reported before 1975 may be explained by a combination of insufficient identification of species before the 1970s and that red cells were generally stored for less than 21 days at that time.

The mechanism by which Y enterocolitica causes these complications is not just of academic interest. As suggested by Gibb et al, the length of time collected blood is held at 20–25°C is important, whether bacteria are present free in donor plasma or whether blood has been contaminated during collection or component separation. Complement killing can be done quickly in Gibb et al's study and in a previous study by my group.3 Removal by phagocytosis is likely to be slower. However, if the major mechanism of transmission of Y enterocolitica is via leukocytes, then there is no real basis for the view that this way of overcoming this problem would be to remove the leukocytes from the red cell preparations, either by removing the buffy coat layer, as is done in some European countries, or by leukocyte filtration.

When discussing possible ways of improving the safety of transfusion, it should be remembered that severe transfusion complications as a result of Y enterocolitica infected blood products are extremely rare. The interested reader is referred to a recent review of the subject.4

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1 Gibb AP, Poling N, Murphy WG. Failure to kill Yersinia enterocolitica is due to contamination of red cell units stored at 4°C. J Clin Pathol 1996;49:434–6.

Dr Gibb comments:
Professor Högman’s hypothesis was discussed in a previous study by myself and colleagues.1

Professor Högman and I agree that those Y enterocolitica cells which go on to multiply in donated blood probably survive for some time inside human cells. We disagree about the location of the bacterium at the time of blood collection. As this is such a rare event, we may never know the answer with any certainty, but evidence from animal models suggests that invading Y enterocolitica is an extracellular pathogen.2,3 The plasmid borne, temperature regulated virulence factors of Y enterocolitica code for resistance to phagocytosis, as well as complement resistance at 37°C.4 These virulence factors are not expressed at low temperature so that complement mediated bacterial killing, or entry into cells, might occur some hours after blood has been collected. If complement mediated killing is impaired by plasma dilution, then this would presumably increase the probability that bacteria could reach a safe intracellular location.

The point in history at which Y enterocolitica become a problem is important because of its possible relation to changes in blood transfusion practice. There was an isolated case in 1975, but no further cases were reported until 1982, about the time when additive solutions were introduced into practice.5 This suggests that growth of Y enterocolitica in blood was exceptionally rare before 1982, but that it could be detected if it did occur.

Readers will be aware of the major contribution of Professor Högman to the development of additive solutions for red cell storage.6 It is clear that this work has had important benefits in improving the supply of red cells and plasma products. I have speculated that this process may also have contributed to the growth of Y enterocolitica in donated blood. I agree with Professor Högman that this speculation is not proven. Even if there is a link, however, the benefit from improved red cell and plasma supply outweighs the possible harm from the rare occurrence of transfusion related Y enterocolitica infection.

The harm done by Y enterocolitica in blood transfusion is small when compared with other current problems. Nevertheless, we should attempt to understand what has happened and consider strategies to prevent it.