Better blood assessment

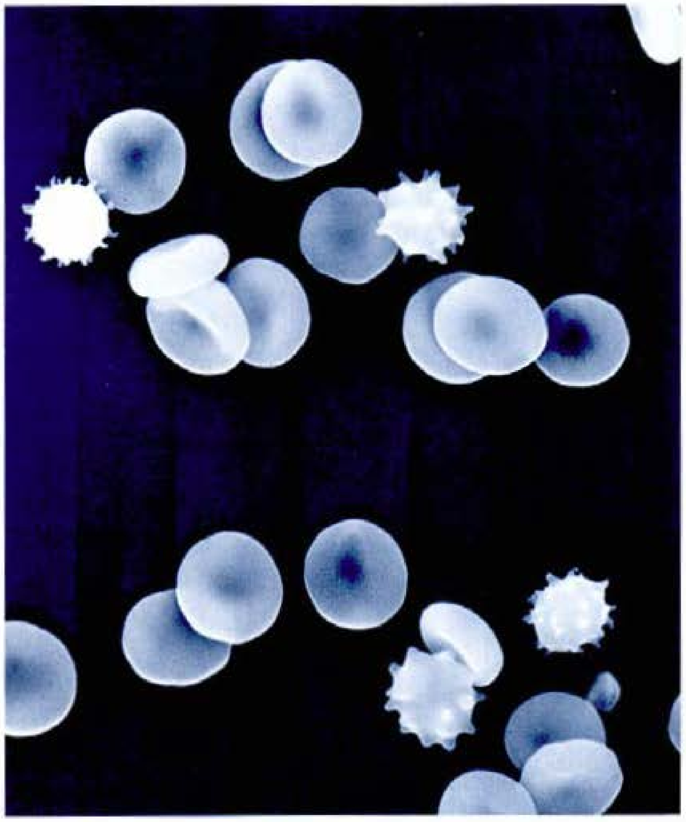
Thoughts of fresh human blood are not confined to certain Transylvanian counts. Anybody unfortunate enough to be the victim of major injury or undergo surgery will need to receive transfusions of several litres of the stuff.

We tend to take for granted the life-saving availability of blood on demand, but to be effective this living fluid must not be 'stale' — and so considerable research has been conducted over the years into how to keep blood in a state that's fit to use, and how to know when it's not.

From the point of view of blood's main function — carrying oxygen — the red blood cells are its most important part. Over time, whether in the body or stored in a blood bank, they age — but the body makes many millions of new ones every day to replace the old ones that die. In the blood bank, of course, this rejuvenation doesn't happen. The aging brings about changes to the membrane and/or shape of the cells.

Nearly every text-book describes a red blood cell as a biconcave disc — think of a flying saucer with a bulbous rim. The cells are bags of the oxygen-carrying pigment haemoglobin, confined within a very stretchy membrane. When healthy, they can be deformed and bounce back into shape, which is just as well, as their passage through the body's smallest capillaries — with a diameter less than the cells themselves — squeezes and pummels them.

Healthy (disc-shaped) and abnormal 'prickly' red blood cells, seen under the electron microscope. The abnormal cells have lost their flexibility.



Cells with unusual shapes, or that are not easily squeezed, can block small capillaries. The result is serious for the tissue downstream, which will die from lack of effective blood flow. Stiff red blood cells carry and release oxygen less efficiently. They are also more likely to fragment as they are buffeted in the bloodstream. The cells' 'deformability' is, therefore, a vital property of healthy blood.

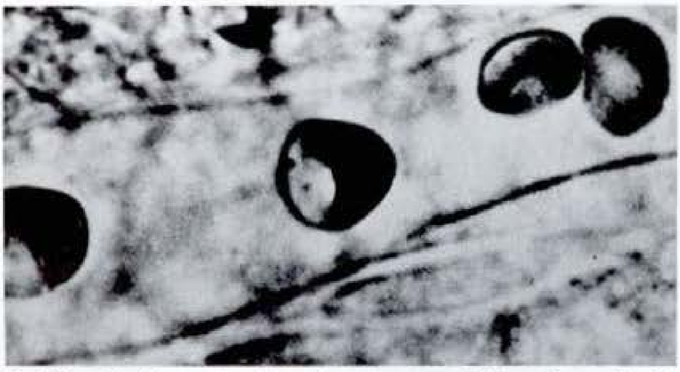
Despite special procedures to extend its shelf-life, blood cannot be stored for more than 3–6 weeks at 4°C because of the changes to the red cells. (Freezing blood is possible, using glycerol to prevent ice crystals damaging the cell membranes, but is expensive and not feasible for general blood-banking.)

The shelf-life of blood varies with different donors, as some people's cells are in a better state to start with than others'. However, the blood-bank cannot assess every donation for this and so must standardise its operating procedures, which may mean that some blood only a few days old is already less than optimum and that still-acceptable blood of 4 weeks' age is thrown out. (The precise age at which blood is deemed to have passed its 'use-by date' varies between different countries.)

If red-blood-cell deformability could be readily assessed, this problem could be overcome. Also, such a test would have much wider applications, as assessing the loss of shape in red blood cells is important in the diagnosis and monitoring of a number of diseases. Examples are genetic diseases — like muscular dystrophy, sickle-cell anaemia, and thalassaemia — and many infectious conditions too.

But measuring the flexibility of such tiny cells (the average diameter is about 8 μm) is far from easy. Agreement between the various methods used to date has been poor, although the end-results of the loss of flexibility are clear enough under the microscope because the cells turn into spheres or 'prickly pears' (illustrated on this page).

Now Dr Tony Collings and his team at the CSIRO Division of Applied Physics in Sydney have devised and patented a unique and accurate way of assessing red-blood-cell deformability, using ultrasound. Reasoning that healthy red blood cells will absorb more sound than stiff ones, which will reflect it like baffles, Dr Collings first simply measured the extent of sound absorption in samples of



Red blood cells passing through a narrow capillary, the walls of which can just be discerned as thin dark lines.

fresh and over-aged stored blood, using sound at frequencies of 25–65 MHz.

The clear difference in the results indicated that the technique would indeed be effective, so he continued with more detailed experimentation. He found that the discrimination improved with higher frequencies, making it possible to distinguish between samples 1, 2, and 6 weeks old. Sound with frequencies lower than 20 MHz failed to detect any differences.

Dr Collings appeared to have found a discriminating and foolproof method of detecting 'old' blood; to ensure its usefulness, though, he had to be certain that it was the change in red-blood-cell deformability that genuinely led to the observed differences. Many biochemical processes can go on when blood is stored; could some of these be responsible for the decrease in sound absorption?

An easy way existed to check this. Blood experts (haematologists) had known for years that when fresh blood is heated to 50°C the red blood cells become spherical and lose their deformability, in a process mimicking what occurs during storage or disease.

Dr Collings found that, as he had expected, heating caused an identical change in sound absorption to that brought about by aging. Blood from which the cells had been removed (plasma) did not show this effect, thereby proving that it didn't stem from biochemical changes there.

Dr Collings and his collaborators hold a patent on their process, and hope to find backing for commercial development of their technique. It has a big potential market, as blood-banking is a multi-million-dollar business. Conservative estimates suggest that each unit of blood (about 350–400 mL) costs at least $40, and Sydney alone uses 300 000 units a year.

Assessment of blood on its merits would allow a bank to keep some that is past an arbitrary cut-off point but still has flexible cells — and considerable savings may ensue. The ultrasound method should work through the blood's plastic containers, avoiding any need to take samples. This added quality control in blood-banks would also ensure that they do not use blood that goes stale before the blanket cut-off date.

A simple means of obtaining reliable measurements of red-cell deformability also has plenty of clinical applications. It can help to assess the effectiveness of drugs designed to counteract the condition, and the efficiency of preservatives used in blood storage.

Dr Collings' work continues in the area of using ultrasonic techniques to measure changes in the red blood of athletes and of sheep subjected to heat stress, in collaboration with Dr Bob Hales of the CSIRO Division of Animal Production. The increased body temperature may bring about shape changes that are important in the problems that heat stress combined with excessive exercise can cause. It seems that ultrasound has more uses in medicine than just scanning.

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The development of an ultrasonic method for measuring red blood cell deformability. N. Bajenov and A.F. Collings. *Proceedings of the Fourth Australasian Heat and Mass Transfer Conference, Christchurch, New Zealand, May 1989*, 503–8.

Ultrasonic studies of human blood, or Dracula goes high-tech. A.F. Collings. *Search*, 1987, **18**, 248–51.

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