Medicine

Blood simple

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Because they lack an essential component, blood transfusions may be killing some of the people they are intended to save

IF THERE were any sure bets in medicine, you might think that "blood transfusions save lives" would be one of them. But there aren't. Even though deaths caused in the 1980s by accidental HIV infection mean that donated blood is now screened meticulously to keep it free of infectious agents, there is still a nagging feeling that something is wrong.

In 2004, for instance, Sunil Rao of Duke University Medical Centre, in North Carolina, carried out a study of people suffering from acute coronary syndrome (a specific type of heart attack). One conclusion that could be drawn from his research was that unnecessary blood transfusions might be causing tens of thousands of deaths in America alone. Dr Rao found that patients who had had a transfusion because of a low red blood-cell count had an 8% chance of dying within 30 days. Without a transfusion, only 3% died. Those numbers need to be treated with caution. As Dr Rao points out, the patients who underwent transfusion were, on average, sicker and older than those who did not. Nevertheless, his study is not the only indication of something amiss.

In recent years, research has suggested that transfusion is not necessarily a good thing for patients suffering from serious injuries, for those who have undergone surgery and even for those who are anaemic. And a study carried out earlier this year found that critically ill children whose red blood-cell counts had dropped by half fared no better after a transfusion than those who did not receive one.

As a result of all this, questions are being asked about whether something happens to blood when it is banked that causes it to stop working properly. What that might be has remained a mystery. But it may be one no longer. A group of Dr Rao's colleagues, led by Jonathan Stamler, think the answer is a gas called nitric oxide—or, rather, a lack of it.

Out of gas

The main reason for giving a patient blood is that it carries oxygen. It carries lots of other things, too, such as glucose. But it is a lack of oxygen that will kill you quickest. However, as Dr Stamler points out, what determines whether transfused blood works as a treatment is not merely how much oxygen it is carrying, but whether that oxygen can reach the tissues that need it. This is where nitric oxide comes in.

Nitric oxide increases the flow of blood to tissues by dilating the arteries that penetrate those tissues. The best known example is the erectile tissue of the penis (Viagra works by sustaining the signal that the gas gives). However, it is not just penile blood vessels that nitric oxide relaxes. When a red blood cell reaches any tissue in need of oxygen it releases nitric oxide in order to dilate the capillaries. Only then can it deliver its cargo. And that is doubly true of the cells in stored blood since red blood cells become less flexible with age, and thus less able to squish into capillaries. Dr Stamler thus wondered if a lack of nitric oxide was causing the problems associated with transfusions.

What he and his colleagues discovered, and published this week in the *Proceedings of the National Academy of Sciences*, was that the amount of nitric oxide in stored blood does indeed decrease—and does so rapidly. Within a day of storage, blood loses 70% of its nitric oxide. After a few days, up to 90% has been lost.

A second paper in the same journal, by Dr Stamler's colleague Timothy McMahon, confirmed this result (in fact, it showed that the initial drop of around 70% happens within three hours of collection) and showed that it was not caused by the way blood is processed, but merely by the passage of time. Dr McMahon also established that stored blood does indeed lose its ability to dilate blood vessels.

Dr Stamler is in little doubt about the significance of these findings. Furthermore, he warns that putting blood lacking nitric oxide into the body does not merely dilute what gas is already present in the bloodstream. Blood that is poor in nitric oxide will scavenge the gas from other tissues, causing the vessels in those tissues to constrict. If the tissue in question is heart muscle, the result will be a heart attack.

These papers, therefore, make a strong case that a lack of nitric oxide is creating the problems with transfusions—though as Michael Strong, the president of the American Association of Blood Banks, points out, they do not settle the issue once and for all. That would require a proper, randomised clinical trial.

And therein lies the rub. Because blood transfusion is such an old practice (it dates back to 1818) it has never been subjected to modern clinical standards. Nobody is questioning whether car-crash victims, say, should have transfusions after massive blood loss. Without it they would undoubtedly die. But for those not threatened with exsanguination it is far less clear whether a transfusion is a good idea. There are no rules about when to transfuse and who to do it to. These are matters of judgment, and knowledge is typically passed from doctor to doctor.

The good news from this study is that the problem should be easy to correct. If nitric oxide is what is needed, it can be added to banked blood just before transfusion. As part of the project, Dr Stamler tried this with dogs. He found that old blood replenished with nitric oxide is as good as fresh blood at relaxing blood vessels. And that, he thinks, points to a bigger possibility than merely returning blood to normal. Blood boosted with nitric oxide might be used as a therapy for people who have had heart attacks by providing extra oxygen in the crucial minutes after an attack, before the affected heart muscle has died. At that point, blood transfusions would no longer be part of the problem: they would be part of the cure.