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.

The 2007 Nobel science prizes

It's a knockout

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Prizes for genetically disadvantaged mice, computer hard drives and the basis of much of industrial chemistry

THE award of the Nobel science prizes often brings blinking into the limelight people who have laboured unknown to the wider world. Seldom, though, is there such a compelling human story to go with the intellectual one as that of Mario Capecchi, one of the winners of the medicine prize. His father was an airman who was killed in North Africa during the second world war. His mother was sent to Dachau concentration camp. He survived more than three years as a street kid in Italy before migrating to America after the war was over—and yet he ended up helping to develop one of the most important tools of modern biology, the knockout mouse.

It is not quite a rags-to-riches story. In truth, his family was well connected in a bohemian sort of way, and his mother (the daughter of a painter and an archaeologist) was an American. But it does make great copy for reporters covering an event that has the true characteristics of celebrity. For, like many of those who populate the pages of celebrity magazines, the Nobel prizewinners are most famous for being famous. In most years, the prize-winning work itself makes dull copy.

This year, however, the prize committees of the Karolinska Institute (Sweden's main medical school) and the country's Royal Academy of Science seem to have taken some lessons in public relations. Not only have they picked a researcher with an interesting back-story, but they have also cunningly disguised a deserved but possibly contentious award by bundling it in with something else. On top of that, one of the topics chosen for a prize has an obvious resonance with the public.

The bundling was done in the medicine prize. Dr Capecchi shares this with Oliver Smithies, another immigrant to America (he was born in Britain) and Sir Martin Evans, a Briton who stayed at home. Working independently, these three men provided the parts that, when put together, enable the elimination of one gene at a time from the genetic make-up of a mouse. That is of medical significance because it allows mouse “models” of human genetic diseases to be made—and most diseases have at least some genetic component.

The contribution made by Dr Capecchi and Dr Smithies was to work out how to define and excise particular pieces of DNA from a cell while leaving the rest intact. It is Sir Martin's role, however, that is of most interest, for he discovered what are now known as embryonic stem cells and thus opened a field of endeavour that has had political as well as medical ramifications.

The first practical application of embryonic stem cells was to provide a way for the gene-targeting trick invented by Dr Capecchi and Dr Smithies to be used to produce adult mice lacking particular genes—or knockout mice, as they are now called. You do this by crossbreeding mice that have had some of their cells treated this way when they were embryos, and have thus developed sex cells that lack the knocked-out gene. Certain of the offspring of these crosses will inherit the lack of the gene in question from both parents, and thus it will be entirely absent from them. That was what the Karolinska gave Sir Martin his prize for. But although he discovered the cells in mouse embryos, human embryos have them too, and that is leading to trouble as the desires of researchers butt up against the fears of ethicists.

The physics prize, by contrast, has nothing but feel-good about it. It is for giant magnetoresistance—the basis of modern computer hard-drive memories. The phenomenon itself was discovered, independently, by Albert Fert, a Frenchman, and Peter Grünberg, a German, in 1988. Its significance is that a small magnetic field can induce a large change in the electrical conductivity of an appropriately designed material. (Appropriate design, in this context, means layers of different substances assembled in a way reminiscent of molecular puff pastry.) That means individual bits of data can be stored as magnetic domains on a spinning disk, and the changes in conductivity they induce in a reading head held over the disk can be turned into signals that a computer can process. The result has been that the amount of data computers can store has grown even faster than their ability to process it. The discovery made by Dr Fert and Dr Grünberg has thus out-Moored Moore's law.

Only the chemistry prize has preserved the traditional aura of obscurity. It

goes to Gerhard Ertl, another German, and is for his studies of the role of surfaces in catalysing chemical reactions. Since an awful lot of industrial chemistry is catalysed this way, and the chemical industry lies, one way or another, at the base of most manufacturing, there is a good argument that this is the most important prize of the lot. But glamorous? Sadly not.

Space dust

Blowing in the wind

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The building blocks of planets and people come from black holes

WHEN the writer of Genesis said man was made of dust, he spoke true. And not just man. The whole Earth was made from dust particles in orbit around the primitive sun, as were all the other solid objects in the solar system. But how did the dust itself come into existence?

That is a puzzle. Modern space dust blows off stars that formed about 10 billion years ago. These stars would have been too young to have shed much of the stuff by the time that the solar system formed, 4.5 billion years ago. The universe's primordial dust must therefore have come from somewhere else—and a team of researchers led by Ciska Markwick-Kemper of the University of Manchester think they know where. The answer is from black holes.

The black holes in question are at the centres of quasars. These formed shortly after the universe began and they came to the attention of earthling astronomers because quasars are powerful radio sources. The radio waves (and lots of other radiation) are the result of matter being drawn into the black hole and releasing energy as it falls. But not all this matter is swallowed. Some is baked, transformed and spat out again. It was this transformation that interested Dr Markwick-Kemper.

Suspecting that it might be the source of primordial dust, she recruited a space telescope called Spitzer to look at a quasar called PG 2112+059 in more detail. Spitzer is tuned to pick up infra-red radiation—the sort of radiation emitted by dust that has been heated. And the details of the spectrum of infra-red radiation given off by a speck of dust will betray its composition.

Dr Markwick-Kemper and her colleagues report their findings in a forthcoming edition of Astrophysical Journal Letters. The dust around PG 2112+059 contains large quantities of rock-forming minerals, including crystalline forms

of silica (essentially, small sand grains), a form of aluminium oxide called corundum (better known on Earth as the principal ingredient of rubies and sapphires) and a form of magnesium oxide called periclase (which is present in marble).

These minerals must have been produced by the quasar, Dr Markwick-Kemper argues, because their crystal structures would not survive long in the hostile conditions of outer space. Cosmic rays would zap them into an amorphous, glass-like state. Moreover, corundum and periclase have not been detected in space dust before. Their association with the quasar is therefore strong evidence that this is the object that created them. A human being may still be a handful of dust. But that dust has had an exciting history.

Human evolution

Hidden charms

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Lap dancers earn more when they are most fertile

“BECAUSE academics may be unfamiliar with the gentlemen's club sub-culture, some background may be helpful to understand why this is an ideal setting for understanding real-world attractiveness effects of human female oestrus.”

No doubt readers of The Economist are equally unfamiliar with this sub-culture, but for Geoffrey Miller of the University of New Mexico, who penned the words above in a paper just published in Evolution and Human Behaviour, such clubs are a field site as revealing of human biology as the Serengeti is of the biology of lions and antelopes. Dr Miller is an evolutionary psychologist—and the author of the theory that the large brains of humans evolved to attract the opposite sex in much the same way that a peacock's tail does. His latest foray, into the flesh-pots of Albuquerque, is intended to investigate an orthodoxy of human mating theory. This is that in people, oestrus—the outward signs of ovulation—has been lost, so that men cannot tell when women are fertile.

This theory is based on the idea that in evolutionary terms it benefits women to disguise when they are fertile so that their menfolk will stick around all the time. Otherwise, the theory goes, a man might go hunting for alternative mating opportunities at moments when he knew that his partner was infertile and thus that her infidelity could not result in children.

However, this should result in an evolutionary arms race between the sexes, as men evolve ever-heightened sensitivity to signs of female fertility. Dr Miller thought lap-dancing clubs a good place to study this arms race, because male detection of female fertility cues would probably translate into an easily quantifiable signal, namely dollars earned. He therefore recruited some of the girls into his experiment, with a view to comparing the earnings of those on the Pill (whose fertility was thus suppressed) with those not on the Pill.

The results support the idea that if evolution has favoured concealed ovulation in women, it has also favoured ovulation-detection in men. The average earnings per shift of women who were ovulating was $335. During menstruation (when they were infertile) that dropped to $185—about what women on the Pill made throughout the month. The lessons are clear. A woman is sexier when she is most fertile. And if she wishes to earn a good living as a dancer, she should stay off the Pill.