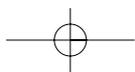
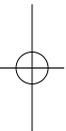
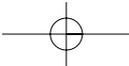
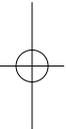
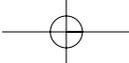


*Part 1*

---

**Basic principles of transfusion**





# Chapter 1

## Introduction

---

*Ian M. Franklin*

Nearly 4 years have elapsed since the first edition of this book. Has anything occurred in the world of transfusion medicine to alter the concepts that were important then? In the past 12 months, a number of crucial events have occurred that have again acted to increase global anxiety about the safety of blood transfusion. The arrival of severe acute respiratory syndrome (SARS) and its prompt recognition as a novel coronavirus in early 2003 focused attention on the difficulties of maintaining blood safety in the face of an unknown emerging infection. In the absence of any knowledge of the epidemiology of the infection, it had to be assumed that there was the potential for SARS to be transmitted by blood. This remains an unresolved issue that will have to await a better understanding of the virus, which perhaps may be obtained in any new outbreak in 2004 or later. Anxieties over SARS were followed quickly by the expected US summer epidemic of West Nile virus (WNV), known to be a transfusion-transmitted infection, and for which precautions in the USA and Europe were urgent and needed to be robust. These included the use of nucleic acid testing for WNV genome in all donations in the USA, Canada and Mexico. In Europe, recent visitors to North America were not accepted as donors for 4 weeks after return.

Most recently, after a few years in which the expected major epidemic failed to materialize, the possibility that variant Creutzfeldt–Jakob disease (vCJD) may well be a transfusion-transmitted infection in humans became more likely, following worrying results in sheep transfusion studies some years ago. A patient, one of only 48 known to be at risk through receiving a labile blood component from a donor who later developed vCJD, devel-

oped and died of vCJD in 2003, 7 years after receiving the blood. The donor was healthy at the time of donation in 1996, but became unwell and died of vCJD in 2000. In the absence of a blood test for vCJD, and with no way of confirming that the two patients had the same or different ‘strains’ of vCJD, this is not conclusive evidence for transmission. On the balance of probabilities, however, it seems likely that the transfusion recipient acquired vCJD from the blood transfusion. This event has triggered a further round of new initiatives in the UK to protect blood safety and retain confidence in the transfusion of blood. In addition to leucocyte depletion of blood components and importing both plasma for fractionation and fresh frozen plasma (FFP) for those born after 31 December 1995, it appears likely at present (January 2004) that the exclusion of donors who have received a transfusion in the UK since 1980 will be added to this list. Renewed efforts to reduce inappropriate transfusion because of concerns about the impact of this new measure on the sufficiency of the blood supply is also probable. Perhaps the one cause for optimism comes from the failure of a massive epidemic of vCJD to develop in the UK, at least to date, and most estimates of the ultimate size of the epidemic have been reduced considerably. This makes it even more important to minimize secondary cases acquired from blood transfusion. As the UK blood services prepare for additional precautions to prevent vCJD, through deferral of transfused persons as donors, fears over ‘chicken flu’ are beginning to dominate the headlines and once more pictures from Asia show citizens wearing masks as they go about their daily lives. Although this is currently topical, it may appear

out of date later in the year and over the next 2–3 years.

Other crucial events have included the relentless march of two new technologies aimed at improving blood safety. The first, nucleic acid testing (NAT) for viral pathogens, is already established, although concerns over cost–benefit analyses, at least where NAT is a second-line test to a highly effective antibody detection system, may lead to review. The second, pathogen inactivation (PI) also appeared to be heading for implementation, and one system, Intercept, had been licensed for treatment of plasma in the EU. However, after a few patients developed antibodies to aspects of the agents of the system, a delay in further trials is inevitable until the safety profile can be assessed further. Another, different, PI system has developed similar problems with neoantigen formation. Although other PI systems are continuing to be developed, all of these work by using a chemical agent to prevent nucleic acid replication, and so each must have a potential for antigenicity that will require extensive study before any such system could be introduced for large-scale use.

The above events continue to make safety and supply the main priorities of blood services and this has changed little from where they were 5 or even 20 years ago. Therefore, the four key areas considered in the previous edition still appear to be as relevant now as then and are listed below. The four principal areas to be considered are:

- blood safety;
- the appropriate and effective use of blood and blood products;
- donor recruitment and retention; and
- informing patients about blood transfusion.

The opinions expressed in this introduction are those of the author alone.

Blood has been assumed to have mystical qualities from the early days of transfusion experiments in the seventeenth century by Lower in England and Denis in France. A number of predictable disasters caused the subject to fall into disrepute, and progress in transfusion had to wait until there was adequate understanding of blood groups to enable safe transfusions between individuals. The imperatives of the Second World War were also important in emphasizing the need for transfusion services

and for providing the clear logistical base from which they might be organized. The early transfusion services, certainly in the UK, were often related to military practice and modern practitioners might be forgiven for believing that the sole objectives were collection, process and supply of (at that time) bottled blood and plasma. There also seems little doubt in retrospect that there was great profligacy in the use of blood and in particular plasma. Some of this stemmed, no doubt, from inadequacies in surgical practice and an equivalent lack of understanding of blood coagulation, but the failure to collect even the most basic evidence of any benefits of blood or plasma transfusions has bedevilled the field ever since. Following a consistent increase from the 1950s, blood usage in the USA has shown a downward trend in the past decade from a peak in 1986, and demand has been decreasing for the last 3 years in the UK. The reasons for this are probably multifactorial, but include improved surgical techniques as well as concerns about blood safety. Despite this, there is evidence for disparities in blood usage between surgeons and between hospitals, for similar activities. There is also wide variation in the use of blood avoidance strategies such as autologous transfusion using cell salvage and preoperative deposit. There is, in the UK, little use of preoperative clinics to enable haemoglobin correction with iron, other haematinics or erythropoietin. In the UK, these issues will be addressed over the next few years by ‘Better Blood Transfusion’ initiatives.

### **Blood safety**

Trends in transfusion practice in the past two decades, since the identification of acquired immunodeficiency syndrome (AIDS), have been in the general direction of enhanced safety of plasma products and cellular components, as well as improved purity. With pooled fractionated plasma products there was a shift from low, then to intermediate and eventually to highly purified factor VIII, for example, which provided many benefits in safety and specificity of treatment. Together with the development of the necessary technology, these advances led to the realization that recombinant

products, ideally free of any added human or animal proteins such as albumin, were the ultimate expression of the drive towards total safety and absolute purity.

This success in improving the safety of plasma products by eliminating donor-derived material seemed to have encouraged the view that the goal of zero risk from transfusion was to be required by regulators and governments. Although there have been no specific statements to change this, a trend seems to be emerging in favour of a 'balance of risk' approach. In the Netherlands, the health minister has made clear that optimal, not maximal, safety is the goal. Although it is not clear what this means precisely, the inference is that some form of cost-benefit judgement must be included in the equation for achieving blood safety. The European Union (EU) Commissioner for Health and Consumer Protection, David Byrne, who has a portfolio that includes food and blood safety, stated in a speech entitled 'Irrational Fears or Legitimate Concerns' on 3 December 2003 that zero risk cannot be achieved. And in the UK, ministers have begun to question how much must be spent on the safety of the railways before this becomes excessive. The inference is that other areas of public life must achieve a balance between delivering an effective service without crippling costs arising from chasing absolute safety.

Prior to these public statements, it appeared that the provision of blood by national blood services was almost unique in the political imperative that required total safety, at whatever cost. This obsession with reducing risks to zero led to there being a perception that there are problems with the safety of blood. Some of this came about because of later criticism of earlier decisions, in particular in the UK over delays in implementing hepatitis C virus (HCV) testing (discussed in detail in the first edition). The failure to introduce the first-generation test for HCV antibody led to a delay in the effective testing for this known transfusion-transmitted virus, and there is no question that some patients acquired HCV during this period. This delay was strongly criticized in the judgement in the English courts by Justice Burton, who considered that testing should have been introduced in January 1991 and not September as happened.

One obstacle to early implementation was the desire to have the whole of the UK introducing the test at the same time, so that there would be no difference in quality of component anywhere. Although in an ideal world all parts of an individual blood service would implement testing of a new agent at the same time, this seems inappropriate when a significant delay is introduced thereby. It would seem to be preferable for larger blood services to begin testing as soon as possible in some parts of the service, even if others are not yet ready. At least in this way some donations would be protected. In countries where there is no single authority managing blood services, this already happens. In the UK, leucocyte depletion of all labile blood components was implemented to prevent the then 'theoretical' risk that vCJD might be transmitted by blood transfusion. Leucocyte depletion was phased in as soon as it was possible operationally – there was no 'big bang' before which components were not leucocyte depleted and after which they were. New virus or other tests and safety measures should be managed similarly in future.

The other obstacle to new tests or safety measures is the impact on supply, i.e. on donors. There is no doubt that blood donors are the essential cornerstones of a transfusion service. Nevertheless patients expect and believe that the transfusions or tissues they receive will be as safe as possible, and that those donors who may pose an additional risk to safety should not be accepted. The range of risks for which donors are deferred continues to increase, and significant numbers are turned away because of recent tattoos or body piercings, or travel to areas where there are concerns about old or emerging agents, such as WNV, malaria or *Trypanosoma cruzi* exposure. Testing is becoming more complex and extensive and the prospect that PI might achieve the same result as more testing, in a single manufacturing process, is most attractive. On the face of it, PI of cellular components, e.g. of platelet concentrates using the psoralen S-59 and ultraviolet A light, holds great promise by preventing virus and bacterial replication. Removing the risk of transfusion-transmitted graft-versus-host disease by preventing T-cell replication would be an added bonus. Unfortunately, the occurrence of antibodies to blood cells produced by two of these

systems may well prove a major, if not fatal, blow to this approach for the time being.

### Regulation of blood services

Blood service regulation developed following a number of episodes of transfusion-transmitted infections that occurred in the 1960s and 1970s. In the USA the responsible body is the Food and Drug Administration (FDA), through its Center for Biologics and Research (CBER) division. In the UK the regulator has been the Medicines Control Agency, mainly for the production of pharmaceuticals from plasma, as cellular components were not considered to meet the requirement for a 'product'. This latter nicety was dealt with by Justice Burton in his HCV judgement, which confirmed that cellular blood components were indeed products. The Medicines Control Agency merged with the Medical Devices Agency in 2003 to form the Medicines and Healthcare products Regulatory Agency (MHRA). For Europe, there is an overarching medicines safety body, the European Agency for the Evaluation of Medicinal Products (EMA), but no unifying EU legislation until the EU Blood Directive entered EU law in January 2003. This will be implemented by the end of 2004 by EU member states, and requires defined standards for all aspects of the blood supply chain. For the first time in the UK there will be a legal requirement to trace blood donations to the recipient, which will take regulators into hospitals for the first time. There are still no legal requirements to consider transfusion alternatives or to implement optimal blood-use programmes.

### Risk management

Awareness of the importance of protecting patients from potential risk following transfusion has taken a much higher profile recently. Ten years ago there were delays in introducing tests that would clearly have impacted significantly at the 1 in 1000 or 1 in 10 000 level for HCV transmission. Now, blood services in Europe and the USA are implementing tests using nucleic acid amplification by polymerase chain reaction (PCR) where it is possible to detect events with an incidence of

between 1 in 300 000 and 1 in 2 000 000. These risks are now perceived to be politically and economically worth preventing. Sir Kenneth Calman, the former Chief Medical Officer of the Department of Health in the UK, addressed issues of risk in a series of articles. He provided examples of activities associated with moderate risk, such as smoking 10 cigarettes a day (1 in 200 chance of death in any one year), to infinitesimal risks, such as being struck by lightning. Schreiber and colleagues, writing on behalf of the US Retrovirus Epidemiology Donor Study, estimated the risk for transfusion-transmitted virus infections at between 1 in 63 000 for hepatitis B virus (Calman risk level, very low) and 1 in 493 000 for human immunodeficiency virus (HIV) (Calman risk level, minimal) (Table 1.1). There are no equivalent figures for the UK, although an estimate for HIV can be made from evidence of only two known transmissions of HIV since the introduction of testing in 1985. During that time some 30 million donations have been transfused. In the first year of testing for HCV RNA using PCR, only one true PCR-positive, HCV antibody-negative donation has been detected, during a period when about 3 million donations were tested. Although PCR testing for HCV RNA was initially introduced for testing plasma donations, it has been a mandatory release criterion for cellular components since 2000, in order to remove a risk of around 1 in 2 000 000 or less. The number of NAT-positive, HCV antibody-negative donations has been very small since then, and the cost of each transfusion-transmitted case avoided has been immense.

Why should such minimal or even infinitesimal risks be unacceptable in blood transfusion? There is no doubt that the appalling stigmatization of individuals that occurred during the development of the AIDS epidemic in the USA and Europe has some part to play. Descriptions of transfusion-transmitted infections in the media invariably use words such as 'tainted' and 'contaminated' in relation to the blood supply. The invasion of the body by an unseen, unknown and unwelcome virus or other agent may explain some of the psychological revulsion. Commissioner Byrne alluded to this issue in his 3 December speech, and suggested that the control that individuals can exert over a risk is

**Table 1.1** Descriptions of risk in relation to the risk of an individual dying (D) in any one year or developing an adverse response (A). (From Calman 1996 with permission.)

<i>Term used</i>	<i>Risk range</i>	<i>Example</i>	<i>Risk estimate</i>
High	> 1:100	(A) Transmission to susceptible household contacts of measles and chickenpox	1:1–1:2
		(A) Transmission of HIV from mother to child (Europe)	1:6
		(A) Gastrointestinal effects of antibiotics	1:10–1:20
Moderate	1:100–1:1000	(D) Smoking 10 cigarettes a day	1:200
		(D) All natural causes, age 40	1:850
Low	1:1000–1:10000	(D) All kinds of violence and poisoning	1:3300
		(D) Influenza	1:5000
		(D) Accident on road	1:8000
Very low	1:10000–1:100000	(D) Leukaemia	1:12000
		(D) Playing soccer	1:25000
		(D) Accident at home	1:26000
		(D) Accident at work	1:43000
		(D) Homicide	1:100000
Minimal	1:100000–1:1000000	(D) Accident on railway	1:500000
		(A) Vaccination-associated polio	1:1000000
Negligible	< 1:1000000	(D) Hit by lightning	1:10000000
		(D) Release of radiation by nuclear power station	1:10000000

crucial in the acceptance of that risk. So accepting a lift in a car enables a person to decide whether the car seems roadworthy, the driver sober and likely to be a safe choice. Similarly perhaps with issues such as home versus hospital child birth, where a significant minority of women choose home delivery despite evidence of greater risk. With a blood transfusion, or a food additive, no such choice is possible. The recipient or consumer must accept the safety of the blood or food at face value. If that acceptance is later found to have led to a transfusion-transmitted infection, then anger, compensation claims and litigation are the common responses.

Unfortunately, there is no arena in which a dispassionate discussion about blood safety can be held. It would surely be helpful to discuss these important issues in a forum in which patient groups, transfusion professionals, clinical users of blood and those responsible for funding new developments could consider the issues outside the blame culture that follows a perceived transfusion problem. Involvement of 'stakeholders' in deciding the principles by which new, expensive and perhaps only moderately effective measures should

be introduced might be interesting and educational for all concerned.

Issues to be considered when deciding whether to implement new testing or other safety measures for a transfusion-transmitted infection include the following.

- 1 Nature of agent being tested for, and the disease it causes.
- 2 Is there effective treatment?
- 3 How much does that treatment cost?
- 4 Is there perceived stigmatization or implications for subsequent lifestyle, e.g. sexually transmissible.
- 5 What compensation might be payable if no testing is implemented?
- 6 What is the potential loss of reputation to the blood service?
- 7 How much does the test or intervention cost?
- 8 How effective is the test or intervention at preventing future transmission?

#### **vCJD precautions**

The publication of the results of experiments in sheep which showed that vCJD could be transmitted by whole blood transfusion suggested that it

would be only a matter of time before vCJD was transmitted by blood transfusion between humans. Although the case reported in December 2003 remains only 'possible', the acquisition of vCJD by one of only 48 patients being followed who were known to be at transfusion risk is highly suggestive. The extension of the risk reduction measures already introduced (importation of plasma from countries with no or low vCJD, universal leucocyte depletion of fresh components and importation of FFP for children born after 31 December 1995) to include the deferral of all previously transfused donors is imminent. This will put pressure on supplies at a time when donor attendance seems to be falling.

As was the case 4 years ago, a more appropriate move in terms of addressing concerns about safety would be a more rigorous process of thought for each and every transfusion, especially in those individuals who are likely to have a long survival after it. This would include all children and those adults who do not have life-threatening diseases, such as candidates for replacement hip surgery. The very large sums of money allocated to vCJD prevention in the UK (£70–100 million per year) might have been better spent, for example, by investing in an educational programme for hospital workers at all levels. The introduction of hospital transfusion teams to ensure that patients get the right blood and are not excessively or unnecessarily transfused would have been another approach that should have been considered.

### **Appropriate and effective use of blood and blood products**

Recent studies indicate that the most important effect on the effective use of blood within a hospital or group of hospitals seems to be its culture of transfusion. It has been known for some years that blood transfusion activity is based more on local custom and practice than on evidence. Clear differences exist in transfusion practice and blood usage between individuals and between hospitals. Although there has long been an assumption that blood must be a good thing, recent evidence suggests that even moderate transfusion practices may

in fact carry risks. A 1999 randomized trial of red cell transfusion thresholds in the setting of intensive care suggested that less was best, and a systematic review of albumin use in critically ill patients strongly suggested an adverse outcome in those patients who received albumin rather than crystalloids. The vested interests of those on either side of the albumin controversy demonstrated the difficulty of both collecting evidence that would be believed universally and in the acceptance by clinicians of the possibility that they may have been wrong all along. It has been well known for some time that individuals who reject blood transfusion for religious reasons, such as Jehovah's Witnesses, can undergo open heart surgery with a reasonably high degree of safety. This in itself might suggest that for many years there has been a greatly excessive use of blood (as perioperative red cell transfusions). This is not to say that blood transfusion has not enabled new and innovative surgical procedures to be initiated. Blood remains essential for many cardiac surgery operations and for liver surgery, to cite but two, and of course many patients with malignancy could not receive chemotherapy without the use of blood components to support them. Even in situations where blood transfusion is life-saving, risks remain from errors in the transfusion process, leading to the 'wrong blood [being] given', issues highlighted in the UK Serious Hazards of Transfusion (SHOT) reports.

In the face of an increasing body of evidence suggesting that blood transfusion carries both known and unknown risks, surely we should be seeking to eliminate unnecessary transfusion. Evidence of the clear benefits of red cell transfusion from good randomized trials is lacking, although there is now evidence that patients with cardiac decompensation tolerate anaemia badly and do benefit from transfusion to higher haemoglobin levels. It is therefore incumbent upon clinicians to think once, twice and three times before transfusing patients and serious consideration must be given to involving patients in these decisions (see below). One thing that does seem clear is that now vCJD seems likely to be transmissible through blood transfusion then there will be an interest in each and every transfusion received by a person who contracts

vCJD (or even tests 'positive' for it if and when there is a test). Clinicians responsible for prescribing blood must be able to justify each transfusion.

The appropriate and inappropriate indications for transfusion are covered elsewhere in this book. However, the evidence continues to accumulate that there are still hazards of blood transfusion that it is not possible to avoid, and that blood transfusion will never be zero risk. The time is overdue for a concerted effort to reduce the use of allogeneic blood to those situations where it is essential to saving or prolonging life, or the quality of life. Since the previous edition of this book, the four UK Chief Medical Officers convened a further seminar in September 2001 to consider the issue of 'Better Blood Transfusion'. This was followed in 2002 by a further Health Service Circular (HSC) to the chief executives of hospitals in the UK, setting out an agenda for hospitals to follow. This second seminar was held partly because of a generally disappointing response to the first in 1998! Although the second HSC provides a clear toolkit for implementation of better transfusion practice, hospitals have many competing priorities, and it is still difficult to maintain blood transfusion at a high enough level of urgency for hospitals to respond in a consistent way. The cynic might be forgiven for believing that only if there is a blood shortage, sufficient to impact on surgical activity, will hospitals really tackle the issues of best transfusion practice.

### Reducing wastage

A discussion about the disparity between the demands for blood placed on transfusion services by clinicians and the true needs of the patients being treated is beyond the scope of this chapter. However, one good first step towards ensuring that there is always sufficient blood would be to check that no blood donation is wasted. Unfortunately, this is far from the case and figures of between 5 and 40% are quoted informally for different regions, hospitals or blood groups. The loss of potential donations begins as soon as a prospective donor arrives to offer a donation. An increasing proportion of individuals who come forward offering themselves as donors are unsuitable for reasons of low haemoglobin, lifestyle issues

known to be associated with a higher risk (e.g. transmissible infectious disease) and other temporary reasons for deferral such as body piercing, tattooing and international travel. Technical difficulties in the process of donation may also impair the percentage of units going forward for patients, such as low volume donations, long donation time and technical problems with leucocyte filtration, to give some examples.

Where donors would find wastage unacceptable would be if they were aware that their donation might simply go out of date because nobody had used it or because it had been left carelessly out of a blood refrigerator. Improvements in crossmatch to transfusion ratios are continuing all the time but much more needs to be done because it is imperative that blood is not 'tied up' waiting for patients who are very unlikely to need it, and so unavailable to those who do. In this way so-called 'electronic crossmatching' holds out much hope and is already implemented safely in many parts of the world. Innate conservatism and lack of investment seem to have inhibited its more widespread acceptance. Many of these measures can be implemented if only there was a sufficient will to do so.

### Donor recruitment

After the end of the Second World War there was a strong sense of community, and in addition many people worked in large industrial settings with a strong sense of identity. This made blood collection easy, since workplace sessions readily recruited large numbers of willing donors. Gradually, many of the large industries have disappeared, and in their place service sector jobs more widely dispersed geographically have arisen. Competition, the changes in the place of women in society (most now work) and a perception that everyone now has less free time have provided challenges to which blood services have had to adjust. Sometimes these responses have been slow. For too long the premise seemed to be that individuals would tolerate a wait of many hours to donate, and the whole process was very centred towards the blood service collection system rather than donor requirements. Only recently has this been fully

acknowledged as inappropriate and moves towards donation by appointment, improving the processing of donors through the session ('donor flow') and an increased emphasis on the professionalism of donor staff have all helped to maintain the donor base.

It is essential that transfusion services continue to make it easier and more convenient for individuals to donate. There is now a more mature and active relationship developing between donors and the blood services, and this process should continue since it appears that donors are not solely motivated by general altruism – a non-specific wish to do a good thing – but are aware of specific issues. More might be done to strengthen this, perhaps by using advertising more targeted to providing information about the uses of blood and how it makes a specific difference, over and above the general exhortations such as 'we can't operate without you'. Is there really a reduction in altruism in the UK, as has been suggested? There may be a change, particularly in young people who perhaps appear rather more self-obsessed than previous generations. The lack of major conflicts such as wars and other common adverse circumstances, while most welcome, tends to reduce the opportunities for building community spirit. However, on reflection and reviewing some of the literature in the area, it is more likely that it is the change in society in terms of longer working hours and more commitment to careers in early adulthood causing less time to consider or attend for donation that is important. It is up to transfusion services, the healthcare industry in general and government in addition to generate and maintain interest in and awareness of the need for blood donation.

### **Informing patients about blood transfusion**

In many countries it has been a specific requirement that informed consent is obtained from each patient prior to blood or plasma transfusion. Difficulties in defining what constitutes informed consent and what information must be imparted are considerable. In the USA, a legal decision has meant that recipients must be given information about the alternatives to allogeneic blood transfu-

sion as part of the consent process. In the UK the consent issue has been considered repeatedly over the past few years and is one area where medical care is lagging well behind what is likely to be considered acceptable in the event of a legal challenge. The biggest difficulty appears to be dissecting the need to obtain informed consent and the resources required to provide staff with the time and expertise to discuss the issues. In the absence of any significant momentum to obtain consent as a matter of good practice, perhaps concerns over shortages of blood, the need to consider alternatives, and potential litigation might encourage some form of dialogue between recipient and the healthcare team. In an era of potential blood shortage, blood conservation measures might achieve importance and preadmission clinics, which would need to be a minimum of 3 weeks prior to surgery, might be one way for this to occur. Discussion of alternatives to transfusion such as correction of anaemia, perioperative salvage or predeposit donation all need time and could be combined with a formal agreement by the patient to receive allogeneic blood if that proved necessary.

Certainly the current situation where most patients receive little or no pretransfusion information or advice cannot be allowed to continue for much longer without a real risk of litigation in the future. Also, the lack of information makes it impossible to discover the true opinion of individuals about to have a transfusion, or the likely interest in alternative strategies such as autologous transfusion or other blood conservation approaches, or to deliver them nationally with equity. At present, well-informed individuals in major cities probably have a chance of accessing an autologous blood programme, but certainly not the great majority of potential recipients. The challenge for the transfusion services is to convince themselves and colleagues that delivering information about transfusion really is an imperative. What else might be done in the interim? Literature for patients already exists about blood transfusion and its risks, but these do not always reach the parts of the health service that most need them, i.e. the medical and surgical wards and clinics. Perhaps, rather like package inserts for pharmaceutical products that must contain a patient infor-

mation leaflet, a leaflet should be issued with each unit of blood, plasma or platelets and handed to the recipient. This might become tedious for blood and marrow transplant units with recipients of multiple transfusions but may be useful for the majority of patients, or their relatives, who receive blood for major surgery as a single event.

## Conclusion

The past two decades have seen blood transfusion services in developed nations trying desperately to minimize the risk of the next transfusion-transmitted infection, one of which seems to appear every 5 years or so. Douglas Starr, in his book *Blood: an Epic History of Medicine and Commerce*, spells out most forcibly the errors of omission and commission made over the years. These were more usually due to a combination of denial and naivety rather than gross negligence. Five years on, and it still makes compulsory reading for anyone working in a senior position in a blood service (see Further reading). Attempts to educate the public about risk will fail as long as blood transfusion mishaps are newsworthy, even where they occur by chance in an otherwise effectively functioning system. The only realistic way forward is to engage all participants in the blood transfusion process in active discussion. The most obvious way to begin such a dialogue would be through a pretransfusion interview that would bring physician/surgeon together with the patient to discuss blood safety, and as an obvious prerequisite would require the blood services to provide training and information for colleagues in hospitals. Such an innovation might just pave the way for a realistic debate about the wisdom of further attempts to reduce the risks of transmission of known viruses by blood transfusion to an unattainable singularity of zero risk.

Much of this introduction has focused on the problems and challenges that face blood services as we enter the new millennium. That there are plenty of opportunities as well as threats is certain, and the very dependence of blood services on good manufacturing practice and good laboratory practice is opening doors for crucial collaborations in the related fields of cellular immunotherapy, gene

transfer, tissue engineering and tissue and organ banking. Exciting developments in virus inactivation and in blood cell substitutes continue to provide research opportunities at the clinical interface, and improving the education of donors and patients will provide great opportunities for those in donor and patient care services. Transfusion medicine will continue to be a little like walking through a tropical rainforest, where the known paths are clear but still require careful navigation, and new and unseen threats may still lurk around the next corner to trap the unwary. But just as the rainforest contains a huge biodiversity to keep the most jaded traveller interested, so the field of transfusion medicine can never be anything other than a fascinating and rewarding area in which to work.

## Further reading

- Bird SM. Recipients of blood or blood products 'at vCJD risk'. *Br Med J* 2004; **328**: 118–19.
- Calman KC. Cancer: science and society and the communication of risk. *Br Med J* 1996; **313**: 799–802.
- Calman KC, Royston G. Personal paper: risk language and dialects. *Br Med J* 1997; **313**: 939–42.
- Chalmers I. Human albumin administration in critically ill patients. I would not want an albumin transfusion (letter, comment). *Br Med J* 1998; **317**: 885.
- Cochrane IGAR. Human albumin administration in critically ill patients: systematic review of randomised controlled trials (see comments). *Br Med J* 1998; **317**: 235–40.
- Goodnough LT, Shander A, Brecher MA. *Lancet* 2003; **361**: 161–9.
- Hebert PC, Wells G, Blajchman MA *et al*. A multicentre, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion requirements in Critical Care Investigators, Canadian Critical Care Trials Group (see comments). *N Engl J Med* 1999; **340**: 409–17.
- Hunter N. Scrapie and experimental BSE in sheep. *Br Med Bull* 2003; **66**: 171–83.
- Llewelyn CA, Hewitt P, Knight RSG *et al*. Possible transmission of variant Creutzfeldt–Jakob disease by blood transfusion. *Lancet* 2004; **363**: 417–21.
- McClelland B. Albumin: don't confuse us with the facts. Rather than fulminating, seek to answer the questions raised (editorial, comment). *Br Med J* 1998; **317**: 829–30.

Chapter 1

---

Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted virus infections. *N Engl J Med* 1996; **334**: 1685–90.

Serious Hazards of Transfusion. Annual Report 2001–2002. [www.shotuk.org](http://www.shotuk.org)

Sharp Research Ltd. *Altruism and Blood Donation. Qualitative Research Report*. London: Research

Division, Central Office of Information, November 1998, Report No. SR0015.

Starr D. *Blood: An Epic History of Medicine and Commerce*. London: Little, Brown, 1999.

Wu YY, Snyder EL. Safety of the blood supply. Role of pathogen reduction. *Blood Reviews* 2003; **17**: 111–22.