

AUTOLOGOUS BLOOD TRANSFUSION

NGP SLATER, FRCPath

Division of Haematology, United Medical and Dental Schools of Guy's and Sr. Thomas's Hospitals, London

Summary

Autologous blood transfusion - transfusion to the patient of his or her own blood - is of increasing importance in transfusion practice. There are three main techniques: pre-deposit, in which patients donate blood over a period of time in preparation for elective surgery; preoperative isovolaemic haemodilution, in which blood is removed in theatre immediately preoperatively and volume replacement is given, the blood being reinfused postoperatively; and salvage transfusion - the harvesting of blood shed at surgery or in similar circumstances, which is reinfused immediately or after concentration and purification. All these techniques can play a part in rendering transfusion safer and in economising on scarce supplies of donor blood.

Keywords: Blood transfusion, autologous, blood donation. viruses, blood salvage, safety.

INTRODUCTION

Autologous transfusion, or autotransfusion, is a term used to describe a number of different techniques in which patients receive a transfusion of their own blood. The concept is one of some antiquity; the first transfusion of a patient's own shed blood, in a case of post-partum haemorrhage, is attributed to the English obstetrician James **Blundell**,¹ who performed many crucial experiments on blood transfusion, used it clinically with some success, and certainly experimented with autologous transfusion in animals.¹ The idea was not adopted in his time, and in 1874 **William Highmore** published in *The Lancet* his "Practical remarks on an overlooked source of blood supply for use in postpartum haemorrhage," in which he described the case of a woman who died of **exsanguination** and whom he might have saved if he had had the equipment by him to give her a transfusion of her own blood. The first transfusion of blood shed during surgery followed soon afterwards, when blood drained from an amputated limb was successfully reinfused.³

At the time, the argument for autologous transfusion rested on the scarcity of donor blood and the risk of incompatibility, which was well recognized though not understood. At the present time, the growing worldwide interest in autologous transfusion is sustained by many different considerations, the most important of which relate to infection, immune **function** and logistics.

Infective complications

The list of infections that can be transmitted by blood transfusion is long and increasing. Table 1 shows the main organisms causing concern; many others are not included because of their rarity or trivial consequences. In principle, any blood-borne pathogen can be transmitted by transfusion; fortunately, however, most people suffering from acute viraemia or bacteraemia feel too ill to donate blood at the time. Furthermore, one consequence of the explosive spread of HIV infection among haemophiliacs before the risk was recognized, was a realization that still-unknown viruses may contaminate donor blood and cause disease with a delayed onset. (For instance, fears have been expressed about the possible transmission by transfusion of slow viruses such as that of Creutzfeld-Jakob disease).

Immunological effects

Blood transfusion can affect the immune system in many ways. Foremost among them are the results of red cell incompatibility - haemolytic transfusion reactions, which continue to cause deaths wherever transfusion is practised. This and other problems of red cell alloimmunization, and immunization to HLA antigens, platelet antigens and others, are too well known to require detailed discussion here. The possibility of transmitting immunological diseases such as allergic asthma or urticaria is also well established,

and affected individuals are discouraged from donating blood. Much less well understood are the immunosuppressive and immunomodulating effects of blood transfusion. These first came to prominence with the finding that renal transplant rejection was less frequent in patients who had received a **blood transfusion**.⁴ It has since been shown that **transfused patients show** various in-vitro anomalies, such as a **decreased** ratio of helper to suppressor **lymphocytes**, and decreased natural killer cell activity.¹ Many reports have also appeared suggesting a clinical counterpart to such findings; for instance, transfused patients appeared to have a higher risk of recurrence following cancer surgery, a higher risk of postoperative infection, and a higher risk of progression from **HIV positivity** to AIDS, than non-transfused **patients**.^{6, 7, 8, 9} Much remains to be clarified in this context, but some effect of transfusion (possibly of plasma, or white cells and their debris, rather than red cells) on the immune system appears to be beyond doubt. Finally, the rare complication of graft-versus host disease directly induced by transfusion (especially the transfusion of fresh blood from a family donor) has been established beyond doubt, though its frequency is **unknown**.¹⁰

Logistical considerations

The availability of donor blood varies strikingly from country to country. Shortages have generally been uncommon in Western countries, though with the self-exclusion of many former donors because of homosexuality or other risk factors, and the exclusion of others because of abnormal liver function tests or positivity for hepatitis C antibody, such shortages are now beginning to appear (particularly at certain seasons of the year). In other countries, where the tradition of blood donation is less deeply rooted, the patient's relatives are often under pressure to donate - sometimes inappropriately. There has also been a progressive rise in the cost of a unit of blood due to the increasing complexity of the tests required. Autologous donation, particularly in preparation for elective surgery, can provide a way round many of these problems.

A more specialized **indication** for autologous transfusion is acute severe haemorrhage (e.g. intraoperative), where adequate amounts of matched donor blood may not be readily available, leaving a choice between reinfusion of salvaged autologous blood and death from exsanguination.

TABLE 1
INFECTIONS TRANSMITTED BY BLOOD TRANSFUSION

<i>Viral</i>	Hepatitis B
	Hepatitis C
	Cytomegalovirus
	HIV1
	HIV2
	HTLV I
	HLTV II
<i>Parasitic</i>	Malaria
	Chagas' disease
	Babesiosis
<i>Bacterial</i>	Syphilis

TECHNIQUES OF AUTOLOGOUS TRANSFUSION

Three techniques are generally distinguished (Table 2); they are mutually complementary, and all three may sometimes be used in a single patient.

Pre-deposit

This describes the collection of one or more units of blood from a patient in anticipation of a future need. The blood is stored until required, and then reinfused.

Frozen storage. The greatest flexibility could theoretically be achieved if the blood was frozen. It could then be stored for an indefinite period, and thawed only when required. A single patient could lay down a large volume of blood, collected over an extended period, for an operation of any magnitude. Unfortunately, current techniques of blood freezing, involving repeated washing before **glycerolization**, and the same process in reverse when the blood is recovered, are so time-consuming and expensive as to make this form of predeposit impractical in most transfusion services. This situation may change, however.

TABLE 2
TECHNIQUES OF AUTOLOGOUS TRANSFUSION

Pre-deposit	Frozen storage
	Leap-frog technique
	Short-term (blood bank) storage
Preoperative	isovolaemic haemodilution
	Salvage transfusion

when a recently developed, simplified technique for blood freezing is introduced." In this technique, separated red cells are simply suspended in a hydroxyethyl starch solution and frozen over liquid nitrogen, in which they are then stored; recovery involves no more than placing the frozen pack in a 42°C waterbath for a minute or two, after which the contents are infused without further manipulation. This would make frozen storage of **predeposited** donations an attractive option.

The leap-frog technique. This is a rather cumbersome way of making large volumes of autologous blood available for surgery. The patient donates his first unit in the usual way; **at a second (or later) session, he donates two** units instead of one, and receives his original donation back again. Thus he has effectively just lost only one unit of blood, but two fresh units are available with a full shelf life ahead of them. **This process can be repeated as necessary. Needless to say, it is also labour intensive, and in practice it is rarely needed**

Blood bank storage. This is the backbone of most autotransfusion programmes. The patient donates a unit of blood on a number of occasions during the five weeks prior to an elective operation, and the units are stored in the blood bank until needed. It is usually possible to collect up to five units in this way, so most elective operations can be covered.

The eligibility criteria for autologous donors are much wider than those for ordinary donors. Standard regulations for ordinary blood donors are partly designed to protect the recipient against transmitted pathogens, malignant cells, "allergic" antibodies, or drugs in the donor's blood, and partly to provide the donor (a healthy volunteer) with every possible protection against the risks of donation (hence the exclusions for pregnancy, cardiovascular disease, old or young age, etc). In the case of autologous donors, most of these precautions are either irrelevant or at least less compelling, and in practice very few restrictions are applied. **Table 3** shows a set of criteria representing a compromise between those of the British Committee for Standardization in Haematology,¹² which are stricter, and those of the AABB,¹³ which are less strict. It will be noted that cardiovascular disease is not mentioned; patients with a wide variety of cardiovascular disorders have been successfully venesected. **though** some situations (such as significant angina or borderline heart failure) represent a real risk. The lack of fixed rules obviously lays a greater responsibility on the clinician to satisfy himself that his patient is actually fit to donate blood.

Patients making predeposit donations should be referred by the clinician in charge of them, and interviewed and examined by the haematologist responsible for the autotransfusion programme. A standard donation of 450 ml is usually taken into CPD anticoagulant. It is generally accepted that the blood should be tested for blood group, atypical antibodies (in case the patient needs additional homologous blood), hepatitis B, HIV1 and syphilis. Positivity for hepatitis or HIV is not a contraindication to autologous donation, but special precautions may have to be applied in storing the blood.

The interval between donations may be as little as 4 days, though a week is more usual. **The last donation should be taken not less than 4 days before surgery.** Oral iron (ferrous sulphate 200 mg b.d.) is normally prescribed during the venesection period.

There is no agreement as to whether the patient's blood should be made available for general blood bank use or not required by the patient himself. Although this would represent a useful addition to the nation's blood stocks, much autologously donated blood would be unsuitable, and many transfusion services (including the British National Blood Transfusion Service) have chosen to avoid potential risks by stipulating that unused autologous donations must be discarded. However, many transfusion services in the USA have taken an opposite view, and actively encourage "crossover" transfusion of such blood, subject to appropriate precautions.

The potential blood savings achievable by a predeposit programme vary widely. In many parts of the United Kingdom, for instance restrictions on the availability of surgical beds interfere with forward planning, so that much autologous blood could be wasted due to last-minute cancellations of surgery. More

TABLE 3

TYPICAL CRITERIA FOR AUTOLOGOUS DONORS

Age:	no limit
Body size:	no limit (children and other small patients may donate smaller volumes)
Haemoglobin:	110 g/l (males and females) (lower in pregnancy: e.g. 100g/l)
Exclusions:	Ongoing bacterial infection Use of antibiotics History of fits History of adverse reaction to blood donation

wastages occurs when blood is drawn for operations where it is unlikely to be needed (e.g. cholecystectomies, caesarian sections). Recruitment of autologous donors may also be a problem when a hospital has a wide catchment area, rather than serving a relatively compact community. With these and many other variables, estimates of blood savings achieved by predonation have ranged between 2% and 20% of all blood transfused. A recent study by the College of American Pathologists¹⁴ found a national mean saving of 5.3% in the USA.

Obstacles to predonation programmes. Many obstacles stand in the way of more widespread use of autologous transfusion. The recent expansion of such programmes in Western countries was largely fuelled by the fear of AIDS, leading to consumer pressure for maximum safeguards against it. AIDS has now largely lost the impact of novelty, and public anxiety about it - at least in the UK - seems to be at a much lower level than before; while hepatitis has never worried the general public. Accordingly, there has been a fall in patient-led demand for autologous transfusion in many countries.

Predonation is also often unattractive for the patient, involving travelling (perhaps over long distances, perhaps in discomfort or pain - many suitable patients are awaiting cardiac or orthopaedic surgery), not to mention the potentially frightening experience of blood donation itself.

For a hospital transfusion service, autologous transfusion represents a considerable extra burden. To make it acceptable, an appropriate financial structure must exist. The advent of clinical budgeting in the UK has been a first step in this direction; a hospital blood bank can now attempt a rational comparison of the costs of providing homologous and autologous blood, and introduce a predonation programme if it can be done economically. Many problems remain: the logistics of running a blood donor service are unfamiliar to most UK hospitals, though routine for hospitals in many other parts of the world; unexpected difficulties arise in ensuring that available autologous blood is not forgotten when the patient gets to theatre; and the division of clinical responsibility for the autologous donor (between surgeon or physician and haematologist) must be clearly delineated.

Some autotransfusion services are run by a regional transfusion service rather than the hospital to which the patient will be admitted. This solution has been rejected by the British National Blood Transfusion Service because of the logistical problems it would involve; one

could also predict a possible conflict of interests.

Surgeons, too, may be unenthusiastic about sending their patients for predonation, because of the additional time, responsibility and logistical difficulties involved.

Even when a patient has accepted autologous donation and has entered a program, success is not certain. Some patients react badly to donation; others cannot regenerate red cells sufficiently rapidly after donation to enable an adequate volume of blood to be collected. (Erythropoietin has been used experimentally to stimulate erythropoiesis in autologous donors, with success in many cases; because of the expense and possible side-effects, its place here is not yet clear).

Preoperative isovolaemic haemodilution

Many of the disadvantages of predeposit donation are avoided in this procedure, in which a volume of blood (typically 500 - 1000 ml) is removed from the patient in the anaesthetic room immediately preoperatively, and replaced with an equal volume of colloid, or a somewhat larger volume of crystalloid solution. The blood is collected in standard CPD blood packs, and kept beside the patient for reinfusion at the end of the operation. The aim is to achieve a preoperative haematocrit of around 0.30.

The foremost advantage of this technique is that blood is made available for transfusion that is completely fresh, with a full complement of clotting factors, platelets, and red-cell 2, 3-DPG, not to mention all the other advantages of autologous blood mentioned above.

An additional apparent advantage is that of haemodilution itself, resulting in a decrease in blood viscosity and consequent enhancement of blood flow, so that tissue oxygenation is maintained unchanged or even improved. This effect was originally described after haemodilution in dogs,¹⁵ and similar benefits have been shown in humans.^{16, 17} Because the compensatory increase in blood flow requires an increase in cardiac output, severe cardiorespiratory disease and conditions in which the cardiac output cannot be increased are contraindications to haemodilution (see Table 4).

A further (somewhat paradoxical) advantage is that following haemodilution, operative loss of a given volume of blood entails less red cell loss. Numerous studies have shown that haemodilution itself does not increase subsequent blood loss.¹⁸

Preoperative haemodilution is practised routinely in cardiothoracic units, but has also

TABLE 4

**CONTRAINDICATIONS TO
PREOPERATIVE HAEMODILUTION**

been used successfully in many types of surgery including vascular and orthopaedic procedures.

Intraoperative blood salvage

This was the type of transfusion envisaged by proponents of autologous transfusion in the last century - the immediate reinfusion of blood shed during surgery, intraperitoneal haemorrhage e.g. from a ruptured ectopic pregnancy, postpartum haemorrhage, and the like.

The theoretical attraction of the technique is clear. The more the patient bleeds, the more blood is available for reinfusion; problems related to the time needed for emergency crossmatching, shortages of donor blood, or incompatibility do not arise. The theoretical drawbacks are also evident: blood lost during surgery may be contaminated (e.g. by bacteria or malignant cells), or it may have undergone activation of the coagulation system, haemolysis, or other changes; and collecting it in a usable form is not always simple or even feasible. Operations suitable for salvage autotransfusion are those in which significant blood loss can be expected, and the blood is likely to be uncontaminated (see Table 5). It should also be noted that Jehovah's Witnesses, who cannot receive ordinary transfusions of stored blood (whether homologous or autologous), are usually willing to accept direct reinfusion of salvaged blood.

The earliest steps in salvage transfusion in modern times were taken by American surgeons during the Vietnam war. The first practical device, the Bentley autotransfusion system, enabled shed blood to be aspirated, filtered and reinfused, and many lives were saved by it. It was abandoned because of a relatively incidental fault, namely that blood was reinfused under pressure, and this had given rise to a number of fatal air embolisms.

Subsequent developments have followed two main paths. A simple and relatively inexpensive technique is to apply suction so that shed blood is collected directly into a soft plastic blood collection bag suspended inside a rigid canister. It is reinfused from the bag through an ordinary giving set under gravity. Examples of such system are the Receptal systems (Abbott Laboratories, Abbott Park, IL, USA) and the Solcotrans system (Solco Basle Inc, Rockland, MA, USA). Blood is anticoagulated (normally with a citrate solution) as it enters the suction line, which is made with a double lumen for this purpose.

- Severe anaemia
 - Severe ischaemic heart disease
 - Cardiac dysfunction (e.g. arrhythmias)
 - Treatment with beta-blockers or other cardiac depressant drugs
 - Emphysema
 - Chronic obstructive airways disease
-

When a worthwhile quantity of blood has been collected, the bag is disconnected and the contents reinfused. To prevent infusion of tissue fragments and blood clots, the blood is passed through a microaggregate filter (20 or 40 μm pore size).

This technique requires no expensive hardware, most of the equipment used being disposable. It is quite quick to set up, and can be brought into use whenever there is a suspicion that blood loss may be heavy. The disadvantages lie in the quality of the blood that is collected. It is diluted to a variable and somewhat unpredictable extent by the anticoagulant solution; it may contain free haemoglobin due to lysis of erythrocytes as they are aspirated (particularly if a surface-skimming suction technique has been used); and it is almost certain to contain activated coagulation factors, and possibly large and small clots as well. In practice, the major drawback relates to coagulation: abnormal clotting results are regularly found after reinfusion of significant quantities of such blood, although clinically significant disseminated intravascular coagulation has been reported surprisingly rarely. The technique is particularly useful in major vascular surgery where the patient is systemically heparinized, so that partial clotting does not occur and haemodilution by anticoagulant solutions is less of a problem.

Blood that collects in serous cavities such as the pericardium or pleural cavity is naturally defibrinogenated and incoagulable; it may be directly infused without further anticoagulation. This is frequently done, for instance, with mediastinal blood following open-heart surgery; or following traumatic haemothorax or ruptured ectopic pregnancy. Reinfusion of large amounts of such blood may cause a dilutional coagulopathy, but more serious adverse effects on coagulation are not seen.¹⁹

TABLE 5
USES OF BLOOD SALVAGE

Liver transplantation
Cardiac bypass
Peripheral vascular surgery (dissecting aneurysm)
Orthopaedic surgery (e.g. spinal)
Ruptured liver/spleen
Ectopic pregnancy

The second line of development in blood salvage is that of cell washing to remove activated clotting factors, platelet and leucocyte debris, anticoagulant solutions, and other unwanted components before reinfusion. The washed concentrated red cells are then reinfused in saline suspension. The technique was introduced by the Haemonetics Corporation (Braintree, MA, USA) and numerous machines are now marketed by this and other companies, for low and high blood loss situations.

Such systems have the obvious disadvantage that they require a significant capital investment; the disposable software is also expensive, and it may be necessary to salvage a significant volume of blood at operation to recoup the cost. Their advantage lies in the greater purity of the salvaged blood. There have been few reports of clinically significant adverse reactions to washed autologous red cells, though experimental studies have suggested that coagulopathy and platelet dysfunction are more severe after autologous transfusion (whether of unwashed or washed blood) than after homologous transfusion.²⁰ (Furthermore, it must be remembered that coagulopathies are likely to occur, irrespective of the type of blood transfused, in patients with multiple trauma or receiving massive blood transfusions). There is a limit to the degree of red cell purification that can be achieved, and bacteria, white cells, platelets and anticoagulant cannot be entirely eliminated. A specific hazard associated with activation of platelets and leucocytes by the centrifugation process has been described."

CONCLUSION

Autologous transfusion, by any of these techniques, requires a significant commitment by medical and technical staff if it is to be practised efficiently and to make a worthwhile impact - therapeutic or economic. One of the most potent motivating factors in the past has been the fear of AIDS. A potent motivating factor in the future may be the fear of litigation. It may already be possible, in some countries, to prove medical negligence

if a patient comes to harm from transfusion and was not previously informed of the possibility of autologous transfusion (or if autologous transfusion was not available). It appears certain that the advantages of autologous over homologous blood will continue to increase as methods of salvaging and processing it improve, and it is incumbent on all haematologists involved in blood transfusion to inform themselves about autologous transfusion and to promote its use where practicable.

REFERENCES

1. Allen JG. Discussion. *Ann Surg* 1963; **158**:337.
2. Blundell J. Experiments on the transfusion of blood by the syringe. *Med Chirurg Trans* 1818; **9**:56-92.
3. Duncan J. On re-infusion of blood in primary and other amputations. *Br Med J* 1886; **1**:192-3.
4. Opelz G, Terasaki PL. Improvement of kidney graft survival, with increased numbers of blood transfusions. *N Engl J Med* 1978; **299**:799-803.
5. Kaplan J, Sarnaik S, Gitlin J, Lusher J. Diminished helper/suppressor lymphocyte ratios and natural killer activity in recipients of repeated blood transfusions. *Blood* 1984; **64**:308-10.
6. Foster RS, Costanza MC, Foster JC, Wanner MC, Foster CB. Adverse relationship between blood transfusions and survival after colectomy for colon cancer. *Cancer* 1985; **55**:1195-201.
7. Blumberg N, Heal JM, Murphy P, Agarwal MM, Chuang C. Association between transfusion of whole blood and recurrence of cancer. *Brit Med J* 1986; **293**:530-3.
8. Tartter PI, Quintero S, Barron DM. Perioperative blood transfusion associated with infectious complications after colorectal cancer operations. *Amer J Surg* 1986; **152**:479-82.
9. Blumberg N, Heal JM. Transfusion and host defences against cancer recurrence and infection. *Transfusion* 1989; **29**:236-45.
10. Vogelsang GB. Transfusion-associated graft-versus-host disease in non-immunocompromised hosts. *Transfusion* 1990; **30**:101-3.
11. Thomas MJG. Military experience in blood supply applicable to disaster medicine. In: Castelli D, Genetet B, Habibi B, Nydegger U, eds. *Transfusion in Europe*. Paris: Arnett, 1990: 237-43.
12. British Committee for Standardization in Haematology, Blood Transfusion Task

- Force. Guidelines for autologous transfusion. *Clin Lab Haematol* 1988; **10:193-201**.
13. Schmidt PJ, ed. Standards for blood banks and transfusion services. **11th** ed. 1984. Arlington, VA: American Association of Blood Banks.
 14. Renner SW, Howanitz PJ. **Autologous** blood utilization data analysis and critique. In: Q-Probes: short-term studies of the laboratory's role in quality care. **No.90-11A**. College of American Pathologists, **1990:1-16**.
 15. Messmer K, Lewis DH, **Sunder-Plassmann** L, Klovekorn WP, Mendler N, **Holper** K. Acute normovolemic hemodilution: changes of central **hemodynamics** and microcirculatory flow in skeletal muscle. *Europ Surg Res* 1972; **4:55-70**.
 16. Shah DM, Prichard MN, **Newell** JC, Karmody AM, **Scovill** WA, Powers SR. Increased cardiac output and oxygen transport after intraoperative isovolemic hemodilution. *Arch Surg* 1980; **115:597-600**
 17. Messmer K. **Haemodilution** - possibilities and safety aspects. *Acta Anaesthesiol Scand* 1988, 32 (**suppl.89**):**49-53**.
 18. Lilleaasen P. Moderate and extreme hemodilution in open-heart surgery. Blood requirements, bleeding and platelet counts. *Scand J Thorac Cardiovasc Surg* 1977; **11:97-103**.
 19. Schaff HV, Hauer JM, Gardner TJ et al. Routine use of autotransfusion following cardiac surgery: experience in 700 patients. *Ann Thor Surg* 1979; **27:493-9**.
 20. Silva R, **Moore** EE, Bar-Or D, **Ben-Galloway** W, Wright ED. The risk:**benefit** of autotransfusion - comparison to banked blood in a canine model. *J Trauma* 1984; **24:557-64**.
 21. Bull BS, Bull MH. The salvaged blood syndrome: a sequel to mechanochemical activation of **platelets** and leukocytes? *Blood Cells* 1990; **16:5-23**.