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Blood Matters

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NATIONAL BLOOD SERVICE

NHS

Editorial

This issue of Blood Matters will focus on appropriate use of autologous blood and other alternatives such as preoperative assessment clinics and the potential of recombinant factor VIIa. Thirty per cent of the red cells issued to hospitals are used in Cardiothoracic, Orthopaedic, Vascular and General Surgery. The use of some of the practices described in this issue could have a significant impact on conserving allogeneic blood.

The pros and cons of Predeposit autologous donation (PAD) are addressed in this issue, raising the question of whether or not the patient would be better off with or without PAD.

Despite its introduction over two decades ago, acute normovolaemic haemodilution (ANH) has neither emerged as a standard intervention nor has it been discredited. Its use has largely been a matter of personal preference on the part of anaesthetists or surgeons and its use is not discussed further in this edition.

Unlike PAD, where 30 – 50% of the units collected may not be transfused, the major advantage of peri-operative cell salvage is that shed blood which usually goes to waste can be processed and returned to the patient. One of the key issues concerning the use of cell salvage is obtaining a safe, high quality component for transfusion in sufficient quantities to reduce or avoid the use of allogeneic blood. There are several large series published that demonstrate the efficacy of intra-operative cell salvage. The 1998 Consensus Conference on Autologous Transfusion stated that peri-operative cell salvage with a wash cycle provides a high quality product that is safer for the patients than allogeneic blood.

A survey of English hospitals in 1999 showed only 23% of hospitals were using intra-operative cell salvage (IOCS). In June 2002 at the Cell Salvage Meeting, held at the Royal College of Pathologists, Dr Virge James identified the following factors as constraints to IOCS, lack of awareness, lack of confirmatory evidence, contradictory reports and 'hassle factors' such as funding and organising of training. Jo Lamb in her article 'How to make cell salvage happen' gives a practical guide on how to tackle these hurdles, together with a follow on article on how to provide an online assessment and training programme. This training package will soon be widely available.

Another article by Bernard Crotty and Joan Jones describes how financial incentives can be used to promote autologous transfusion programmes within a Trust. The contentious issue of whether or not infected and malignant operative fields are an absolute contraindication to IOCS is also addressed in this issue.

Post-operative cell salvage (POCS) involves the collection of blood from surgical drains followed by reinfusion, with or without a wash cycle. Although there have been concerns about the safety of transfusing unwashed red cells, POCS is used routinely in orthopaedic surgery in a number of hospitals in the country and the NBS is not aware of any serious untoward incidents associated with its use.

Along with the different modalities of autologous transfusion, other techniques or strategies to reduce allogeneic blood usage are discussed in this issue. There is an article on the value of pre-operative assessment clinics and a description of an individual hospital strategy, which resulted in reduced blood usage. The judicious use of recombinant factor VIIa to control bleeding is also given an airing. A national survey of transfusion practice in elective orthopaedic joint replacement surgery clearly demonstrated that a combination of strategies resulted in significant reductions in the use of allogeneic blood. However this survey also showed that there was great scope for improvement, as only half the hospitals had two or more blood usage reduction strategies in place.

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Fitness For Surgery

Surgical departments in some hospitals have been running pre-surgical clerking clinics for routine elective surgical patients for many years. Sometimes this practice is perceived as creating extra work for hospital staff as well as resulting in an extra journey for the patient to attend the hospital. The alternative approach is for everything to be done on the day of admission, which is usually the day prior to the intended surgery date.

With increasing pressure on beds the luxury of a day, or even part of a day, in hospital prior to surgery is a thing of the past. Patients are admitted the evening prior to surgery, putting pressure on 'on-call' staff by using emergency or 'out of hours' time to perform routine blood tests, x-rays and ECGs. The escalating 'out of hours' workload of non-urgent work required for the next morning's theatre list is causing huge staffing, morale and practical problems in hospital departments, not to mention putting patient safety at risk as the chance of errors increases. At present, with recruitment so difficult especially amongst BMS and radiographic staff, moving to a partial or total shift system is impossible. Apart from costing more, there are simply not enough personnel available for such a rota.

The current situation results in patients going to theatre without investigations having been performed. This is unacceptable and often results in last minute changes to theatre lists which is potentially dangerous, with delays and cancellations to routine surgery because of unforeseen problems detected on routine tests. Failure to complete day ward procedures within the working day results in over night stays or readmission the following day. The knock on effects for the NHS Trust are huge in terms of risk management as well as costs and effective use of beds.

It is time for a real investment to be made in setting up 'fitness for surgery' clinics which would take place six to eight weeks in advance of the planned surgery date. This would make sense in terms of resource allocation, medical management of the surgical patient and risk management. It would improve outcomes, reduce mistakes and improve morale amongst overworked junior doctors, laboratory and other support staff who are currently expected to perform routine work, in addition to emergency work, out of hours.

A global assessment of patients' physical state and anticipated needs can be made in advance of surgery. This

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then has the effect of reducing cancellations, reducing unnecessary prolonged in-patient stays and of course reducing the need for blood transfusion, as time can be taken to consider how to minimise the chance of requiring allogeneic blood.

The purpose of pre-operative assessment clinics

- The identification of an unsuspected condition which may require treatment pre-operatively or a change in anaesthetic or surgical management pre-operatively.
- An opportunity to explain and discuss the surgery and the possible outcomes and complications to the patient.
- Identification of psychological or social factors which could impact on recovery or outcome.
- The prediction of post-operative complications.
- The establishment of 'base line' measurements for later reference.
- Opportunistic screening unrelated to the surgery in question

HISTORY:

Taking a thorough history should allow significant co-morbidities to be detected and evaluated, such as sickle cell disease, diabetes, respiratory problems, immuno-suppressive disorders (e.g. MDS or CLL), or illnesses which can put staff at risk such as viral hepatitis, HIV infection or prion disease. Current medications can be reviewed and a plan made to stop those which increase bleeding tendency, e.g. aspirin, NSAIDS and warfarin, if this is at all possible. Long term steroid medication may be noted and appropriate action can then be taken. History of previous surgery may allow insight into potential anaesthetic problems or bleeding tendencies and a history of blood transfusion and pregnancy will be relevant events if blood may be required.

EXAMINATION:

Examining the patient generally reinforces the information from the history and allows assessment of the severity of concurrent conditions as well as noting of other problems such as venous access, obesity or cachexia (which may affect wound healing) or dental problems (which can affect anaesthesia). A need for further special investigations may be apparent and these can then be done as an out-patient prior to surgery instead of delaying surgery once the patient is admitted. These investigations may include special x-rays, endoscopy, angiography, cystoscopy or respiratory function assessment.

INVESTIGATIONS:

Routine pre-operative investigations generally include full blood count, U&Es and liver function tests, clotting tests (if there is an indication), plus chest x-ray and ECG in older patients or those with a history of respiratory or cardiac problems. It is of paramount importance that a mechanism is in place for the test results to be reviewed following the pre-admission clinic. One stumbling block of such clinics is that although the tests are done, results and abnormalities are not noted until the patient is admitted later for surgery.

Additional aspects which may come to light in a pre-surgical clerking clinic and which may have a significant bearing on the outcome include emotional, psychological and social problems. Some patients may have difficulties coping with the consequences of surgery, or problems at home which require extra support, counselling or home visits. Other patients may need time and help to sort out care for small children or elderly relatives of whom they are the sole carer. Identifying such problems in advance helps to smooth admission and discharge and avoid last minute cancellations by the patient if they are mentally or socially unprepared.

Detailed information regarding the nature of the surgery, the expected outcomes and possible complications can be given to the patient at the pre-surgical clerking clinic and leaflets may be issued making informed consent immediately prior to surgery a more meaningful task.

BLOOD TRANSFUSION:

In the specific area of blood transfusion the pre-operative haemoglobin and body weight can be used to calculate how much blood can safely be lost by the patient (and replaced by colloid or crystalloid) maintaining a haemoglobin safely above 8g/dl. Subnormal pre-operative haemoglobins can be detected and appropriately investigated and treated. Iron deficiency may be treated with oral ferrous sulphate or intravenous iron sucrose. Anaemia of chronic disease, a frequent accompaniment of malignancy and chronic inflammatory disease, may respond to erythropoietin plus iron supplements. The surgical team can also consider the appropriateness of various methods of reducing the likelihood of allogeneic transfusion. These may include the use of intra and post operative cell salvage, acute normovolaemic haemodilution, intra-operative pharmaceutical agents such as aprotinin, tranexamic acid, fibrin glues and sealants. Some patients may benefit from pre-operative autologous deposit (PAD) and this can be organised at a pre-assessment clinic and take place in the four weeks prior to surgery if appropriate.

A number of recent studies have shown that nurse led pre-operative assessment clinics are at least as efficient, possibly more so, than those conducted by pre-registration house officers or senior house officers. Studies have shown that nurse led pre-assessment or 'fitness for surgery' clinics probably increase level of satisfaction for patients with improved patient care, improved sense of informed choice for patients, decreased cancellation rates, more efficient use of theatre time and a decrease in the complication rate following surgery. Nurses can also monitor waiting lists, removing those who no longer require or wish to have surgery.

I am sure that in the next few years the belief in the benefits of an up front assessment in pre-operative surgical assessment clinics will result in investment being made in this area. Ultimately, money will be saved and the NHS would run more smoothly with fewer causes for complaints and litigation.

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The Pros and Cons of Predeposit Autologous Donation & Transfusion (PAD)

Both public and professional attention has recently been drawn to autologous transfusion. Predeposit autologous transfusion (PAD), has the longest history of the different varieties of autologous transfusion. Interest first soared in the 1980s with worries surrounding HIV transmission, again in the 1990s with concerns about HCV transmission and now, once again, with the vCJD 'cloud' hanging over transfusion. Whenever autologous transfusion is mentioned in the media, PAD is the only type discussed.

What is PAD?

PAD is a process whereby blood is collected from a patient, stored and retransfused to the patient during or immediately post surgery. The very concept of "get your own back" is attractive. Collecting blood from a patient and reinfusing when needed is a neat and deceptively simple idea.

The main advantages are that it is emotionally satisfactory. Patients feel it removes all risk of transmissible infections. It is perceived as a safe form of transfusion. Possibly the fact that it is not easily available within the UK and that most doctors prescribing transfusions know little about it, has increased its desirability!

However we need to look much more closely at this apparently simple and obvious form of autologous transfusion.

First hurdle: the procedure itself. Blood, to be safe, needs to be collected by an experienced team according to the principles of GMP. This requires dedicated staff and training.

Second hurdle: only a limited number of patients are suitable; basically, fit patients who can spare blood prior to elective surgery and whose surgery time is guaranteed. Autologous red cells also only last 35 days! In the 4 weeks prior to surgery usually only 2 and sometimes 3 units can be collected with any ease. This results in a chronically haemodiluted patient going to theatre.

Units are collected at weekly intervals and the patient is put on iron therapy. But, in general, the haemoglobin does not 'pick up' between donations. Twenty recent cases referred to NBS Colindale, North London for autologous blood collection, have been analysed. The haemoglobin level was measured using a HemoCue haemoglobinometry prior to each autologous blood donation. Sixteen of the 20 patients had a lower haemoglobin one week after blood donation on every occasion that a unit of blood was collected from them. One patient showed no fall in haemoglobin between donations and the other 3 had a very slight rise in haemoglobin between donations. For the 16 patients who had a fall in haemoglobin between donations, the mean haemoglobin 1 week after an autologous donation was 11.75g/l lower than the predonation value (range 0.5 – 25g/l).

The mean starting haemoglobin for all 20 patients was 130g/l (range 110-165g/l), and the mean haemoglobin prior to the donation of the last preoperative autologous unit was 118g/l (range 106-140g/l).

Hospitals in the North West Thames Region are asked to provide a report giving information about the fate of autologous units collected by NBS Colindale. Twenty reports were received from hospitals between October 2000 and June 2002. These showed that of 46 units of autologous blood collected, only 18 were transfused (39.1%).

Third Hurdle: Adverse events of donation such as fainting and bruising happen to autologous donors as well as to all donors, but if the donor is also a patient the consequences can be more inconvenient and even serious. Experience from Southampton with patients undergoing oro-maxillary surgery and ideal for a PAD programme (young and fit and definite operation time) showed that approximately 10% reacted badly to the autologous donation; furthermore none of 28 such donor/patients actually needed their donation as the calculated post operation haemoglobin was no lower than 80g/l in any.

Fourth Hurdle: the one not understood by those not intimately concerned, consists of the administrative problems; labelling, testing, transport and storage .

Is it worth it? And here we have many well entrenched opinions, but few facts. The clinical benefits are in doubt, cost benefit analyses are unsatisfactory and contradictory.

Some people who have set up large PAD services, responding to public demand say "don't". Administrative costs in time, money and energy outweigh the unknown benefit of a 2 or sometimes 3 unit transfusion. If patients bleed heavily, they almost inevitably need more than the number of autologous units deposited. In the NBS, overall experience suggests that, approximately 50% of the units collected are not reinfused, as either they are not needed or there is an administrative problem. Another concern is that, if autologous units are available they may be reinfused whether needed or not, thus incurring the risks of such transfusions.

What are these risks? Although the remaining small risk of infections from donor blood are eliminated, bacterial contamination of the units remains a hazard and so does the greatest of all current transfusion hazards, "getting the wrong blood."

Finally, adverse events may occur as the result of donation, possibly more so in patients requiring surgery than in the healthy volunteer donor. It is worth pointing out that Jehovah's Witnesses do not normally accept PAD, although most will accept intraoperative cell salvage.

Having said all this, there are still definite indications where PAD is the transfusion process of choice. These are patients receiving autologous marrow transplants, patients with very rare antibodies for whom donor blood is difficult or impossible to find, and perhaps patients who have a morbid fear of donor blood should be included, if intraoperative cell salvage or other blood conservation procedures are not available.

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It must also be acknowledged that, should donor blood sources 'dry up', then extensive use may need to be made of PAD. But for that a total rethink will be required. A safe, dedicated PAD service similar to the current donor blood service would need to be set up. All current guidelines for the use of PAD would need to be dramatically changed, from acceptability of patients for this procedure, through supplementation with erythropoetin and other haematinics, to testing of donations and even possibly cross over from one service to another.

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Reducing Blood Usage – An "Electronic" Approach With Fast Issue

Blood is a valuable resource, which if misused is potentially hazardous. This has recently been re-emphasised in the new Health Service Circular on Better Blood Transfusion[1], where the importance of avoiding unnecessary transfusions is again addressed. Provision of compatible blood requires not only an adequate supply of cells to transfuse, but laboratory time to manage the blood stock efficiently and carry out pre-transfusion compatibility testing.

We recognised that much time was wasted in cross matching blood that was unlikely to be transfused. Therefore in line with many hospitals we introduced a maximum blood order schedule (MBOS) for elective surgery in 1989[2]. This improved our cross-match transfusion ratio to 68%. However we were concerned that the ready availability of compatible blood meant that it was still being transfused unnecessarily. If we could guarantee rapid provision of compatible blood on request, this would not only reduce time invested on unnecessary cross-matching and blood stock management, but might also prevent unnecessary transfusion.

As a first step, in January 2000, we introduced the issue of blood via the electronic crossmatch[3]. The technology in use in the laboratory is an IBG Multisampler performing ABO and Rh group, and three cell solid phase antiglobulin test (SPAT) and enzyme antibody screen all on microplates. This method has been fully validated and performed well in NEQAS exercises over the last 12 years. The ABO and Rh groups are read and interpreted automatically on an IBG Multiskan Plus Reader and the antibody screens are read and entered manually. The results are then transmitted to the APEX computer system, which has been fully validated for ABO and Rh compatibility. As our current system is semi-automated, we only issue blood by this method when we have a current tested sample in the laboratory and a previous sample has been tested by automated means as an historical record.

Initially blood was issued electronically according to the MBOS, but as user confidence grew, we were able to introduce a fast issue system. With the fast issue system, operations where blood would be issued routinely according to MBOS are reported as "Units available for FAST ISSUE". Blood is not issued until the decision to transfuse is made. When blood is required it is requested via telephone and issued promptly - we are fortunate that the laboratory is less than 5 minutes from theatre. To facilitate fast issue, occasional extra samples are requested when a preadmission sample is received and the patient has not been tested previously.

To demonstrate current practice, information was gathered over a four-week period in January 2002, considering elective operations requiring transfusion cover.

Number of cases	265
Eligible for Electronic Crossmatch	245 (92%)
Units issued	151
Units transfused	129 (85%)

During this time period 72 extra samples were requested and processed. The current cost per group and antibody screen is 72p excluding BMS time and the cost of the equipment, thus resulting in a total cost of £51.84. Under the previous MBOS, 530 units would have been issued but still possibly only 129 transfused (24%). Reasons for not being able to use electronic crossmatch were as follows: 9 patients had atypical antibodies, 12 had not had previous samples tested and 20 were received late in the day or overnight when automation is not in use.

A comparison was taken between the last quarter of 1999 (prior to the introduction of the electronic crossmatch) and the last 4 months of 2001.

	1999	**2001**
Units Issued	3325	2993
Units Transfused	2274 (68%)	2285 (76%)
Crossmatches	960	787
Units dereserved	1039	677

Assuming the biomedical scientist (BMS) time per serological crossmatch to be 20 minutes, the above amounts to a BMS saving of (960-787) x 20 = 3460 minutes (231 hours per year). Also, of the 787 crossmatches performed in 2001, approximately 86% (699) would be electronic crossmatch. Assuming the BMS time to be 5 minutes per electronic crossmatch, this results in a further saving of 669 x 15 = 10035 minutes. (669 hours per year). This amounts to a total saving of 900 BMS hours per year; approximately half a full time BMS post. In addition the number of units requiring dereservation fell from 1039 in 1999 to 677 in 2001.

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Assuming a dereservation time of 2 minutes per unit, this amounts to a saving of 1039 – 677 x 2 = 724 minutes (48 hours per year). Saving is also made in that shelf life of units of blood is not being "wasted" in the blood bank. Assuming each unit is kept in the blood bank for 48 hours before dereservation, the reduction in units dereserved from 1039 to 677 represents a saving of 17 units of blood (assuming each unit has a 35 day shelf life).

The introduction of the MBOS, electronic crossmatching and fast issue have produced a significant reduction in our overall blood usage despite increasing activity.

	1999/2000	2000/2001	2001/2002
Units of red cells	7943	6823	7610
Cost per unit (£)	77.88	82.50	84.56
Total cost (£)	6186.00	5628.97	6435.01
Elective activity	5719	5903	4996
Emergency activity	22376	23899	25726
Total activity	28095	29802	30722

These changes have been introduced in the setting of an active Trust-wide education programme on blood transfusion, recently facilitated by the appointment of a Nurse Specialist in Blood Transfusion. Further recent innovations include pre-operative iron for elective orthopaedic surgery and post operative cell salvage on total knee replacement.

The introduction of new technology and laboratory blood stock management procedures, electronic crossmatch and fast issue, together with an active education programme, facilitated by a Clinical Nurse Specialist, have resulted in significant reduction in blood usage within our Trust, despite increasing activity. Not only does this indicate that many unnecessary transfusions are being avoided, but it also optimises the use of the scarce blood stock and permits the limited number of trained laboratory staff to deal with an increasing workload.

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Recycling Blood - Sharing the Benefits

One key objective of HSC 2002/009, "Better Blood Transfusion - Appropriate Use of Blood" (July 2002), is for NHS trusts to avoid the unnecessary use of blood in clinical practice. There is an action on Trust Chief Executives to "Review and explore the use of effective alternatives to donor blood". The primary driver behind this objective is that donated blood is a limited resource. Additionally the associated unknown risk of vCJD transmission by blood transfusion may lead to future limitations on the number of blood donors. Utilising alternatives will therefore place less demand on the UK Blood Services.

An alternative to a blood transfusion utilising donated blood is via an autologous transfusion. The patient's own blood is collected and utilised to substitute or augment donated blood. These practices are common in the USA and account for over 5% of blood usage. Autologous transfusions are most widely used in elective surgery and evidence from clinical trials (BMJ 2002;324:772-5) shows that autologous transfusions are more cost effective than a blood transfusion utilising donated blood.

The development of autologous techniques in the UK is sporadic and relies primarily on the enthusiasm of the medical staff. Financial issues have not been considered by most Trusts. Swansea NHS Trust is at the forefront of utilisation of cell salvage techniques whereby the patients' blood is recycled during and post operation. Given that a unit of donated blood costs £100 (a 160% increase since 1998) there is a developing financial argument to invest in these alternative techniques. This argument carries additional weight within English Trusts where the National Blood Service (NBS) charges £100 per unit of blood supplied via an internal market. Each acute Trust will therefore hold a budget for blood purchases from the NBS. Savings within this budget will be realisable within the Trust.

Swansea Blood Bank collected data and costs associated with cell salvage utilisation in the financial year 2001/02. Putting this data into an English NHS market setting would yield :

	£'000	£'000
505 donated units saved via cell salvage		50
Cost of consumables	12	
Maintenance and running costs of machinery	6	
Staffing	16	
Capital Charges	3	
Total costs		37
Saving on Blood Budget		**13**

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This analysis includes an estimate for the capital charges of holding the machinery. These charges will fall as the price of the machines is reducing, and will soon fall under the £5,000 capital threshold. The savings for a large Trust like Swansea would therefore seem small. What they indicate, however, is that if there were a further increase in the Swansea cell salvage programme then the potential for savings would be accentuated. An operation requiring three units of blood would save £300 for an additional consumable cost of approximately £65.

On the other side of the fence the NBS would be faced with an income shortfall under the internal market so, in the short term, there would be no significant gain to the NHS as a whole. Over the longer term, however, some significant savings could be made if the autologous programme was more widely extended. For example:

- The NHS could utilise its buying powers to obtain the necessary autologous equipment and consumables at significantly reduced prices, thereby enhancing savings.
- More "self sufficiency" in blood requirements for elective surgery would smooth out peaks and troughs in demand patterns allowing the development of a smoother blood collection programme.
- There is evidence that clinical outcomes are improved by adopting autologous techniques over donated blood. This will have a favourable cost impact, of more relevance to health economists and NHS accountant.

The NBS in collaboration with a number of Trusts in the Trent region has just completed a pilot study promoting the use of cell salvage techniques to evaluate the difficulties associated with this change in surgical and anaesthetic practice and the effectiveness of the intervention. The aim is to publish the results of the study by the end of 2002.

There has been discussions on the possibility of patients being infected with vCJD via donated blood. So far there in no evidence that any patient has been infected with vCJD after receiving donated blood. This potential problem would be circumvented if the patient's blood were recycled.

The above basic financial analysis only scratches the surface of the financial impact of what would be a fundamental change in practices for a large number of NHS Trusts. Autologous programmes have an almost unique characteristic in that they offer potential financial savings and, at the same time, provide a forum where accountants and health economists are in agreement. The indications from Swansea are that there will be a financial incentive for Trusts to expand and develop their autologous programmes in line with HSC 2002/009.

The promotion of the autologous techniques in "Better Blood Transfusion - Appropriate Use of Blood" therefore offers a unique opportunity to enhance standards and be cost effective for the NHS as a whole.

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How To Make Cell Salvage Happen

The technology for intra-operative cell salvage has been available since the 1960's and it is widely used in North America and continental Europe, where up to 20% of transfusions are autologous. In the UK, the Health Service Circular "Better Blood Transfusion", published in 1998, asked hospital Trusts to explore the feasibility of autologous transfusion and consider the introduction of peri-operative cell salvage by the year 2000. Partly as a result of this, awareness of the technique of red cell salvage grew, but its routine use in the UK remains disappointingly patchy. The recent circular "Better Blood Transfusion II" published in July 2002, has prompted hospitals again on this issue, requesting that Trusts review and explore the appropriate use of autologous transfusion. This article will examine some of the barriers in the path of cell salvage development and offer advice on "how to make it happen".

THE PATIENTS

The UK population has great confidence in a safe donor blood supply and autologous transfusion in this country has never been consumer led. Despite this apparent lack of demand, most patients will intuitively recognise that receiving their own blood rather than donor blood will have at least less potential for harm. Patients are almost universally accepting of and enthusiastic for intra-operative cell salvage when it is offered.

PROJECT LEADERS

Active involvement of key individuals is needed to develop the project.

- A lead clinician
  Ideally the clinician should work in the operating theatres, coming from an anaesthetic or surgical background. There are examples of a clinical lead from a haematologist but this may be difficult in practice.
- A manager
  Active involvement of a member of the hospital management team is helpful. This person will be able to assist with the business case and financial planning.
- A key member of the theatre staff
  This individual may be a theatre nurse, operating department practitioner (ODP) or perfusionist. He or she will be invaluable in helping to identify training needs and planning for what will work in practice.

ESTABLISHING THE POTENTIAL DEMAND

Theatre activity data must be analysed to estimate the number of suitable cases and the pattern of the demand.

Intra-operative cell salvage is indicated during "clean" surgery where the anticipated blood loss is >20% of the patient's blood volume, that is one litre for a 70kg man. Cell salvage will not always replace the need for donor blood, particularly with large volume losses, but may make a contribution to the transfusion requirements.

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The hospital case mix is important. Some types of elective surgery will guarantee a supply of suitable cases. Examples of these include:

- Open cardiac surgery
- Vascular surgery
- Major orthopaedic surgery particularly revision arthroplasty and spinal surgery

At this stage the difficult issue of cell salvage in tumour surgery must be faced. This remains controversial and there has been no clear lead from national bodies. Medical and theatre staff will need clear guidance on what is acceptable in their Trust and this has clear implications for the caseload.

Having established an estimate of case numbers, the pattern of the demand should be examined. For hospitals with a significant emergency workload 24-hour availability must be the gold standard. At present there are probably only a handful of hospitals in the UK that are able to guarantee this. Even if this standard cannot be met at the outset, it is worth building it into the plan.

OVERCOMING THE FINANCIAL HURDLE

In many hospitals money from the budgets of surgical directorates is "topsliced" to pay for transfusion services. There will as a result be no incentive for surgical teams to use less blood and a disincentive to spend valuable resources on cell salvage. Even if a capital sum is identified to pay for machines, the disposables will be a significant recurrent cost. There are a number of potential solutions to these difficulties, for example:

- Moving money from the transfusion budget into the theatre budget.
- Ordering disposables via blood transfusion so surgical teams request these from the blood bank as they would donor blood.
- Persuading theatre departments to accept cell salvage as a necessary extra cost.

CHOOSING EQUIPMENT

There are three main companies commercially active in the field of intra-operative cell salvage in the UK – Dideco, Fresenius Kabi and Haemonetics. When choosing a supplier the costs that need to be taken account of include:

- The cost of the machine
- The cost of disposables for collecting blood
- The cost of disposables for processing blood
- The cost of machine maintenance

It is also important to have a contract for what is on offer in terms of a training package. Machines will be an expensive wasted resource without trained operators.

The flexibility of the equipment must be examined. Check that there are software programmes for different rates of blood loss and different types of surgery. One important feature is the capacity to purchase separate disposables for the collection and the processing of blood. When this facility exists, the opportunities for cell salvage are maximized. Collection only sets should be inexpensive, making them freely available for staff to set up for collection in cases where the blood loss is difficult to predict or may be borderline. If there is insufficient blood collected to make processing worthwhile, little has been lost. If blood is never collected in these cases valuable opportunities for cell salvage will be missed.

IDENTIFYING MACHINE OPERATORS

The individual tasked with setting up and operating the equipment will usually be a theatre nurse, ODP or perfusionist. Some enthusiastic anaesthetists train to operate the equipment themselves, but others find this less than ideal and a potential distraction. If an extra person is added to the usual team solely to operate the equipment, cell salvage becomes much more expensive and staff shortages inevitably limit its use. An extra person is not usually necessary, although may be invaluable in more acute emergency situations.

EDUCATION AND TRAINING

Some means should be found to provide information about cell salvage to all relevant theatre staff, including surgeons and anaesthetists. The aim is to develop a broad understanding of the place of cell salvage, the contraindications and what the end product actually provides.

Parallel to this, the specific training of identified machine operators must run. This should be given high priority and is a key element of a successful programme. There is no nationally recognised qualification and most training is done by the provider company. It is essential to build up local expertise allowing a core group enough access to cases to build up confidence with the technique. Training may then be "cascaded down" in house, although some form of competency assessment may be needed to meet the requirements of clinical risk management. Only named trained operators should be permitted to use the equipment.

STANDARD OPERATING PROCEDURES

It is recommended that a local standard operating procedure be drawn up giving clear guidelines to staff using cell salvage.
Areas covered may include:

- Indications and contraindications
- Rules about trained operators
- Warnings about prohibited contamination of the surgical field
- Rules on blood "expiry time"
- Blood labelling requirements
- Documentation requirements

This information should be easily accessible – laminating the document and attaching it to the machine is one solution.

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AUDIT AND MONITORING

Ensuring completion of a simple audit sheet for each case serves a number of purposes:

- Data is collected for activity analysis
- The process is monitored for untoward incidents or problems
- Use of disposables is monitored
- A record of case numbers is kept for machine operators
- An individual patient event record is made

Useful information is gathered if the audit sheet is completed for all cases where blood was collected, even for those not proceeding to processing.

CHANGING PRACTICE

For cell salvage to work, medical and theatre staff will have to accept a change in practice. Whilst some will be enthusiastic, there will be others who have reservations. Some surgeons regard transfusion issues as low priority or feel criticism is implied of their surgical skills. Some anaesthetists regard it as of limited use and too much hassle. Members of staff may feel uncomfortable transfusing a product that is unfamiliar to them.

Time and energy are needed to "make it happen", however many staff do find involvement in cell salvage a positive experience. Even for those less keen, encouraging a team to consider or try cell salvage undoubtedly focuses attention on the issues of blood conservation.

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Intra-operative Cell Salvage Techniques (ICS) – A new online assessment and training programme

The University Hospitals of Leicester (UHL) NHS Trust started a pilot of Intra-operative Cell Salvage (ICS) in March 2002, along with other hospitals in the Trent region. Each hospital was equipped with ICS machines and consumables, funded by the National Blood Service, for a 6-month trial period. A key element in the success of the pilot proved to be staff training, mainly Anaesthetists, Operating Department Practitioners (ODPs) and nurses, in the use of cell salvage techniques. Unless clinicians understood the need and the ODPs and Nurses were able to operate the equipment, the trial would not achieve its goals.

The UHL Autologous Transfusion Subcommittee has developed an on-line training package to train the UHL staff in ICS techniques. The package provides the required background information, ICS equipment specific training, and links to a number of full text articles and educational materials as well as links to on-line training videos. There is a built-in quiz feature to stimulate further interest in the subject. The on-line training can be undertaken in approximately one hour and can be completed in more than one stage. The training package has the potential for a built-in assessment tool that could formally certify successful completion of training and the degree of individual's understanding of ICS techniques. The on-line training package would allow such training to be logged in order to maintain accurate records. The successful completion of on-line training would be a pre-requisite for a live training session using the actual ICS apparatus.

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Infected and Malignant Fields are an Absolute Contra-indication to Intraoperative Cell Salvage: Fact or Fiction?

Introduction

Since the technique of intraoperative cell salvage (ICS) was introduced, it has been held that infected surgical fields, or those contaminated with malignant cells, are absolute contraindications to its use. In an attempt to scientifically validate this statement, I performed a MedLine search. In total, 513 citations were studied and the evidence was presented to the Consensus Conference at the Royal College of Physicians of Edinburgh on 11th November 1998. This review is a précis of that presentation[1].

Infected Fields

Routine Surgery

Although 12.7% of samples of the blood salvaged from 401 patients undergoing cardiac surgery were infected, there was no correlation between the incidence of infectious complications and positive blood cultures. In maxillo-facial surgery, ICS was used and patients received between 1 and 10 million organisms. In 15 patients blood cultures were positive but no infectious complications were seen.

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Trauma

The risk of infectious complications, following trauma to the colon, in the absence of multiple injuries and injury to the spleen is low. There is no correlation between the degree of soiling and the incidence of infection. Of 70 patients, admitted with penetrating abdominal injuries, in whom the Penetrating Abdominal Trauma Index score > 20, 50 received allogeneic blood and 20 received ICS salvaged blood, which was potentially infected. The wound infection rates were identical (25% in both groups) and no correlation was found between the organisms cultured from the salvaged blood and those causing postoperative bacteraemias, pulmonary or urinary tract infections. In a trial of 11 patients with penetrating thoraco-abdominal trauma, who received enteric contaminated ICS blood, and who received parentral broad-spectrum antibiotics, 3 patients developed wound infections but none developed intra-abdominal sepsis and no deaths were reported. The use of ICS in trauma patients with gastrointestinal injuries is safe, as long as they receive perioperative broad-spectrum antibiotics. Another trial studied 20 cases of gunshot injuries in which there were penetrating bacterially contaminated abdominal injuries. ICS was used and was life-saving in many of the cases.

Fields Containing Malignant Tissue

The given reason for not using ICS, in a field where malignant tissue is present, is that tumour cells could be aspirated, reinfused into the patient and be carried around the body implanting in distant organs generating metastases. This worry needs to be confronted in three areas, the practical, *in vitro* experimentation and *in vivo* experience.

From a practical point of view, malignant cells are found in the circulation prior to surgery and many more are driven into the circulation as soon as the surgeon touches the tumour. This occurs both in patients who do and do not develop metastases. Using nested PCR, malignant cells have been identified circulating in patients with colorectal carcinoma and also in breast and gastrointestinal cancer. Recent work on colonic tumours shows that these secrete enzymes, which loosen the surrounding tissue, allowing malignant cells to escape into the circulation prior to surgery. In colorectal cancer intravascular spread is far less important than local spread within the peritoneum where tumour cells become entrapped by fibrinous accumulations. Such cells become strongly adherent within minutes and cannot be dislodged by irrigation. By contrast, few intravascular tumour cells express adhesion molecules so intravascular cell spread is less important than stimulation of the previously dormant cancer cells, which were disseminated prior to surgery.

The relative importance of surgical trauma, as measured by technical expertise, is emphasised by the local recurrence rate in patients undergoing anterior resection for rectal adenocarcinoma, being 17% when a consultant performed the operation as opposed to 51% when the resection was done by a senior registrar.

In vitro studies

Units of blood spiked with malignant cells were processed through a Cell Saver. The red cell concentrate was filtered with either a standard 40 transfusion filter or a Pall RC100 filter. Although abundant tumour cells were found in samples using the 40 transfusion filter, no cells were identified, either microscopically or on culture, from units filtered using the RC100. In post-filtration blood irradiated with 50 Gy all the tumour cells were shown to be in mitotic arrest.

In vivo data

There have been a number of small, nonrandomised studies and one prospective, but not randomised trial, reported. Most have been in urological surgery and show no differences in recurrence rates between patients receiving ICS blood and those receiving allogeneic blood. In addition two UK groups have a large amount of unpublished data, especially in urological surgery and there have been a number of case reports.

The prospective, consecutive non-randomised trial showed that 54 patients who underwent hepatectomy and received ICS had a better 3-year survival than those who did not. Similar results have been shown for colorectal tumours. The blood that was not transfused was examined cytologically for malignant cells and none were found. Others have used ICS blood, salvaged from the tumour field and then irradiated in more than 300 patients.

Discussion

There appears to be virtually universal agreement that ICS is a valuable technique in the treatment of trauma, even when the surgical field is contaminated. When considering the use of ICS in a malignant field, it would appear from the *in vitro* data that its use, combined with a LDF, and/or irradiation produces a product, which is either free of malignant cells or the cells are non-viable.

When evaluating the possible role of ICS in the production of distant metastases, many other problems have to be considered. In what percentage of cases will cells have already been disseminated? Will dormant cells be awakened simply by surgery? What effect does the skill of the surgeon contribute? Is intravascular spread less important than local deposits?

The majority of *in vivo* studies on ICS in malignant fields are small, retrospective and non-randomised. They appear to support its use, but the follow-up has been too short and the design inadequate to allow drawing a firm conclusion. There were no reports of *in vivo* trials in which filtration was used in addition to ICS, but those using irradiation and filtration suggest that this is safe.

In summary, the issue is one of balancing risks. ICS can be lifesaving in trauma and the risks due to bacterial reinfusion can be mitigated by adding an antibiotic to the anticoagulant. Even if sepsis occurs, I have always maintained that it is better to have a live patient with bacteraemia than a dead patient with sterile blood cultures. The problem with using ICS in malignant fields is less clear-cut. It is highly unlikely that, for both ethical and practical reasons, a definitive trial could be mounted. However it seems that the use of filters and/or irradiation, produces a product that is as safe, if not safer, than allogeneic blood. If the advantages of reduced risk of

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postoperative infection, reduced cost and the theoretical possibility of a reduction of malignant recurrence, are taken into account, I personally would opt for ICS in malignant surgery.

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Further Information:

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A novel approach to inducing haemostasis

The recent article by Dr Clare Taylor 'Reducing surgical blood usage and bloodless surgery' (Blood Matters (September) 2001;8:5-7) was a much needed practical guideline on steps to improve transfusion practice and reduce surgical blood usage.

While the article considered the role of bloodless surgery, it did not review emerging evidence which suggests that prudent use of recombinant factor VIIa (rFVIIa) offers a novel approach to inducing haemostasis, so preventing or controlling severe, intractable bleeding in surgical and trauma patients with no pre-existing coagulopathy.

Readers of 'Blood matters' will be familiar with rFVIIa and its role in the management of bleeding episodes and provision of surgical cover in haemophilia patients with inhibitors, but may not be aware of recent literature and a growing number of case reports suggesting that a single dose of this agent can rapidly control intractable bleeding in cases without coagulopathies that have not responded to standard management of haemorrhage, including repeated blood transfusion (1).

A recent article by UK haematologist Maadh Aldouri (2) considers the current literature regarding this 'off-label' use of rFVIIa and reports experience in 5 patients with uncontrolled bleeding during open-heart surgery, where a single dose of rFVIIa (30ug/kg) resulted in a mean reduction in blood loss from 4170ml to 262.5ml (2,3).

Our own experience in cardiac surgical patients with severe perioperative bleeding is that use of rFVIIa dramatically reduced bleeding rates and was of clinical benefit in 5 of 7 subjects. Three patients had aortic root surgery (one for the third time), two had coronary bypass graft surgery (CABG, one re-do), and two had mitral valve replacements (one combined with a CABG). All but one patient (who had an INR of 2.3) had normal pre-operative coagulation parameters. All patients received either Aprotonin or Tranexamic acid intravenously. The mean blood loss of the survivors prior to giving NovoSeven^{R}/rVIIa was 1,013mls per hour (range 182-1500 mls), falling to 22 mls per hour (range 7-41 mls) after a median dose of 2.4mg (mean also 2.4mg, range 1.2 to 6mg) at a cost of £1,300 (range £700 to £3,500). All patients received the drug as a result of excessive bleeding either intra-operative (n=4) or post-operative (n=3) bleeding. The patients had all been given varying quantities of fresh frozen plasma (n=4), cryoprecipitate (n=4) and pooled platelets (n=7) as well as prothrombin complex concentrate, Beriplex^{R} (n=6) prior to rVIIa administration. No thrombo-embolic complications occurred among these patients. One patient died from on-going massive haemorrhage whilst still on the operating table, and the other death, on the 5th post-operative day, was due to multiple organ failure.

Other case reports of use of rFVIIa to reduce surgical blood loss include patients with Crohn's disease, false thoracic aneurysm, chronic myeloid leukaemia (post-splenectomy haemorrhage) and following Caesarean section. A small-scale on-going study (PROSE) in patients requiring transabdominal prostatectomy, also indicates that mean blood loss can be significantly reduced in patients who receive rFVIIa as compared with placebo.

In trauma, there are also reports that use of rFVIIa is a valuable resort in patients with intractable and life-threatening bleeding. Cases in the literature include subjects with gun-shot wounds and multiple stab wounds. In addition, rFVIIa has been used in the management of life-threatening upper gastrointestinal haemorrhage that proved unresponsive to extensive surgery and massive transfusion.

In each of these cases, subjects had no history of coagulation disorders, but all represent patients in whom measures such as reoperation and further transfusions were deemed unsuccessful or inappropriate.

The rationale for using rFVIIa in patients as described here is based upon current understanding of coagulation and haemostatic mechanisms and the known mode of action of rFVIIa.

Patients with profuse bleeding due to extensive surgery or trauma often develop a complex coagulation pattern, which includes reduced plasma levels of fibrinogen, factor VIII and Factor V and decreased platelet counts. These patients are thought to have an impaired capacity to generate thrombin and consequently stand to benefit from introduction of rFVIIa since this will assist in achieving a thrombin peak sufficient to allow formation of a firm, stable fibrin haemostatic plug.

Thus, while randomised controlled trials are now required to confirm these case observations and small cohort reports, there is a suggestion that rFVIIa could play a role in managing cases of intractable bleeding. Although rFVIIa is not yet licensed for the management of major haemorrhage associated with surgery or trauma (probably until 2005), we, as clinicians, need to be able to identify high-risk patients in whom this agent could be used to induce haemostasis, since there is scope both to improve patient outcome and to preserve valuable blood resources through careful use of rFVIIa.

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For a complete bibliography please contact Denise O'Shaughnessy.

Frequently asked questions

Does the NBS test for HTLV?

Until now, the UK has not screened blood donors for antibodies to HTLV, but 2 pilot studies have demonstrated seropositivity rates of 0.0013% to 0.005%, which is ten times lower than among pregnant women in the same regions. This difference probably reflects donor exclusion criteria and under-representation of ethnic minorities in the donor population. A recent study of Afro-Caribbean donors in the UK has shown prevalence of 0.11-0.55%. An anonymised pilot study in the UK of 87,792 samples tested in pools of 48 samples has revealed one true HTLV positive sample. This prevalence of 0.0011% is almost identical to that found previously in the same area by testing of single donations.

Following advice from the Microbiological Safety of Blood and Tissues Committee (MSBT) the Department of Health has instructed the NBS to introduce testing for HTLV. We are planning to complete this introduction as soon as satisfactory arrangements can be made to ensure safe operational implementation. Implementation will be phased by geography and component type and is expected to begin in August 2002.

The test will be applied as a release criterion to components, which expire after midnight on the day following donation, and will be managed automatically within the NBS core computer system (PULSE).

The time required to complete the test will not result in a delay to the release of components but the following components will be released prior to an HTLV test being available:

- Hyperconcentrated (IUT) platelets
- Apheresis Granulocytes
- Buffy coats, gamma irradiated and issued for clinical use
- Any other white cell components
- Heparin Whole Blood (Adult and Neonates)

The source donations for all of the above will normally receive an HTLV test but the result will not be available prior to issue of the component.

There will be no withdrawal of untested blood components associated with the introduction of these changes. This includes frozen plasma components. As HTLV is a white cell associated virus, and all plasma components are in any case leucodepleted the risk of transmission of HTLV infection associated with these components is considered negligible.

The estimated number of positives detected is expected to be in the order of 100 donors in the first 2 years of testing.

Protocols have been drawn up for the counselling and management of HTLV positive donors and for lookback.

News Flash – NBS extends the use of US Plasma

Public Health Minister Hazel Blears announced on 15th August 2002, that Fresh Frozen Plasma (FFP) for new-born babies and young children born after 1st January 1996 will be obtained from the United States as an additional precaution against the unknown risk of vCJD transmission through blood.

This imported FFP will be pathogen inactivated using Methylene Blue technology. The NBS estimates that two tonnes of plasma will be imported and treated with methylene blue per annum.

The NBS's prime concern has always been and will continue to be the safety of patients and donors and the quality of blood and blood products. As an integral part of the NHS, the NBS is working closely with the NHS, Department of Health and medical and scientific experts to continue making blood and blood products even safer for patients.

Over the coming months we will keep you updated as to the progress of this project and when importation of US FFP will commence.

Blood Matters is prepared and issued by the National Blood Service, Oak House, Reeds Crescent, Watford, Herts WD24 4QN (Telephone 01923 486800)