INTRODUCTION

Blood transfusion is a very effective form of medical treatment. It began as a result of intellectual curiosity during the Renaissance but developed rapidly along with the general expansion in scientific knowledge in the middle of the twentieth century. Necessity in times of war was a powerful stimulus. The wide availability of safe blood transfusion facilitated countless developments in medicine from open heart surgery to curative treatment for leukaemia. Demand for blood and blood products continues to rise but in recent years there has begun to develop a more critical attitude towards transfusion. Many of the more subtle effects of transfusing blood have only come to light recently. Whilst the use of blood transfusion in the emergency situation is not in dispute, the indications for elective transfusion are being examined more closely. Transmission of disease and possible damage to the immune system are the major worries. Previously assumed benefits are being questioned.

In this article, I will describe changing attitudes towards the practice of blood transfusion from early, experimental days, through the period of rapid technological development to a golden age and finally to the more cautious era which we are entering.

EARLY DAYS

The first [exchange] transfusion is attributed to the witch Medea who according to Ovid [Metamorphosis 43BC] rejuvenated Aeson, Jason’s father, by replacing his worn out blood by her own magic brew. Attempts were said to have been made to save the life of the dying Pope Innocent VIII by blood transfusion from three healthy youths.

The first credible attempts to transfuse blood directly into the circulation occurred, however, during the seventeenth century when the observations, ingenuity and urge to experiment of a variety of Renaissance men led to attempts at blood transfusion in animals and occasionally humans. Christopher Wren, architect, astronomer and anatomist, and Francis Potter, an eccentric rector from Somerset were amongst the first English experimenters. The first human transfusions occurred in England just after the Plague of London and the Great Fire, and in Paris at about the same time. Richard Lower had experimented on dogs, exsanguinating and then resuscitating them by direct artery to vein transfusion. Curiously the first human recipients were transfused for psychiatric reasons [in order to bring about a personality change] and the donor was usually a sheep. The first well documented transfusion involving a human was carried out as a demonstration before the Royal Society and in the audience was Samuel Pepys. The news therefore spread far and wide and even provoked a scene in a satirical play of the time in which cross transfusion between a mangy spaniel and a healthy bulldog resulted in the former turning into the latter and vice versa.

The French experiments were also carried out for psychiatric indications with variable success. The fourth subject was a lunatic, a violent maniac, who died after his third transfusion [from a gentle calf]. The ensuing scandal, despite the revelation that the patient’s wife had poisoned him with arsenic, led to the French Parliament banning human transfusions. There soon followed similar disapproval from the Royal Society in London and from the authorities in Rome. Few transfusions were tried over the next 150 years but scattered reports suggest that the main indications were still insanity, mania or, sometimes, chronic disease. Animals served as donors.

That the blood was carrying oxygen to the tissues was not appreciated until the end of the eighteenth century following the work of Priestley and Lavoisier on oxygen and respiration. The effects of acute blood loss and the logical application of blood transfusion as treatment for blood loss formed the basis of the work of James Blundell, an obstetrician at Guy’s Hospital. After experiments in which he resuscitated exsanguinated dogs, in the early 1820’s he transfused women bleeding to death from post-partum haemorrhage and had considerable success. Despite his clear exposition of the indications, rationale and practice of transfusion for blood loss, others were reluctant to follow his lead.

By the turn of the century, however, developments in both understanding and technique were combining to make transfusion increasingly common. The need to avoid clotting meant that most transfusions were via direct artery to vein anastomoses. Alexis Carrel, a French surgeon working in New York, was asked to transfuse a 5 day old girl, herself the daughter of a well-known surgeon. The baby was dying from Haemorrhagic Disease of the newborn but Carrel anastomosed her father’s radial artery to the baby’s popliteal vein. This operation, carried out on the kitchen table, was triumphantly successful – the baby making a complete recovery. Wide publicity helped both the popularity of blood transfusion and those fighting an antivivisectionist bill. Carrel’s techniques had been learned exclusively in animal experimentation. Similar direct transfusions were carried out by Crile who reported on 55 patients thus treated. Despite the lack of any grouping or crossmatching tests, the treatment was successful in most patients. Reactions occurred in about one in three which is much as expected in the light of subsequent knowledge. The ABO blood groups were defined by Landsteiner at about this time. The development of this new and exciting form of medical treatment stimulated research and the problem of clotting was largely overcome by the introduction of citrate in 1915. As with many other developments, this occurred simultaneously in at least three widely separated centres: Belgium, Argentina and New York.
The ability to store blood immediately found application on the battlefield and in military hospitals both during World War I and the Spanish civil war.

MODERN TIMES

The first hospital blood bank was developed in Chicago in 1937 and over the next 50 years blood transfusion assumed a fundamental place in the practice of medicine and surgery. In all developed countries, a blood bank became an integral part of any hospital and, whether voluntary or paid, the blood donor became a familiar part of society.

Almost no-one thought ill of transfusion. Donors were [and are] seen as good citizens. Many lives were saved and surgery became safer. In Britain, the National Blood Transfusion Service became a highly efficient scientific organisation producing blood and blood products of very high quality and engaged in major research. New technologies such as plastic packs were adopted and fractionation of donations was increasingly refined to ensure the patient received only what he lacked. The combination of research and availability of blood and blood products virtually abolished Haemolytic Disease of the newborn as a cause of stillbirth and infant mortality.

Some patients did develop jaundice after transfusion but exclusion of Hepatitis B carriers from donation kept donated blood in Britain safe, or at least meant that it was perceived as safe by both doctors and patients.

DOUBTS APPEAR

Concern began amongst haemophiliac patients. Their lives had been transformed by the availability of effective treatment with factor VIII. Inescapable pain and ultimate crippling were replaced by normal development and unrestricted activity.

This small but vocal group has often determined the policy of the transfusion service. Their ever-increasing need for Factor VIII has been the driving force behind the desire for self-sufficiency in plasma. Before this could be achieved, HIV appeared and a cohort of patients was infected by material from non-UK donors.

When this was widely reported, attitudes began to change. Notwithstanding effective testing and a vanishingly small risk of acquiring HIV from transfusion in the UK, the two have become inextricably linked in the minds of many.

Two areas must be examined. Firstly, what really are the risks of transfusion and how are they perceived by medical and by lay people? Secondly, are the indications for elective transfusion correct? Could we transfuse less without doing any harm to patients?

RISKS AND PERCEPTION OF RISKS

The main areas of risk are summarised in the table. It is hard to quantify them as they are not notifiable conditions. Absolute risk estimates can only be guesses. The relative incidences are probably fairly good estimates. It is often pointed out that about half of the blood transfused [and about 80% of the platelets] goes to patients whose survival is short – perhaps less than one year. Long term sequelae are therefore irrelevant for many recipients but there remain

<table>
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<th>SOME COMPLICATIONS AND RISKS OF BLOOD TRANSFUSION (Excluding &quot;Medical&quot; Problems such as Fluid Overload)</th>
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<tr>
<td>1. Inevitable - Iron Deposition</td>
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<tr>
<td>2. Common - Alloimmunisation to WBC and Plasma Proteins leading to Febrile Reactions</td>
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<td>3. Uncommon - RBC, Platelet Alloimmunisation leading to Haemolytic Reactions</td>
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<td>4. Rare - Transmission of HIV, Yersinia</td>
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<td>5. Unexpected - Immune Suppression leading to Metastasis of Cancers</td>
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Undergraduate medical education in this field is sometimes poor [personal observation] and I thought it would be illuminating to make enquiries amongst the house staff. A brief questionnaire circulated to junior doctors in Lancaster and Kendal addressed the question of discussion of risks and benefits and also examined the doctors’ perception of transfusion-associated risk (Fig. 1). A reassuring majority do discuss the treatment with the patient beforehand and most of these emphasised the benefits (Fig. 2).

![Figure 1 - Blood transfusion: doctors' anxieties](image)

![Figure 2 - Attitude towards transfusion: junior doctors](image)
Less than half discussed the risks, however, and disturbingly, whilst a quarter worried about mistakes [in reality the most dangerous aspect of transfusion] one fifth worried about HIV transmission which in the UK is an infinitesimally small risk.

One explanation may be that many people, both lay and medical, conflate numerical risk and consequence of risk. Thus although the chance of catching HIV from transfusion in the UK is vanishingly small, the consequences are very great. Overall, therefore, it is seen as a sizeable risk and well worth worrying about. This is a difficult area and patients will vary in the extent to which they might wish to discuss it. They should certainly be given the opportunity. In Australia, every blood pack bears a “health warning” stating that it may transmit infection. This may well soon become the case in the UK.

TRANSFUSE LESS BLOOD?

Finally, do we need to transfuse so much? In Lancaster, we spend nearly £400,000 annually on blood and blood products. If a proportion of transfusions can be safely dispensed with, not only will patients be exposed to less risk but resources can be diverted to other aspects of patient care. Jehovah’s Witnesses attract media interest out of proportion to their numbers in the UK and usually this is because of their refusal to accept blood transfusion in dramatic circumstances. However, because of their stance, it has proved possible to study the effects of removing blood transfusion from the equation in various surgical procedures – almost permitting a trial of surgery with and without blood. One review cites 16 such series involving 1404 operations of all types. Some of these studies have approached the standard of a controlled trial, with all variables comparable [age, disease state, surgeon, institution] except transfusion. No difference in outcome was observed between 100 Jehovah’s Witnesses receiving hip prostheses without transfusion and 100 similar patients transfused “normally”. Overall, in all types of surgery, there was a small increase in deaths directly [0.6%] or partially [0.8%] attributable to blood loss. No increase in morbidity from infection, stroke, renal failure or myocardial infarction was found in the non-transfused groups and their length of stay in hospital was the same.

CONCLUSION

Blood transfusion, the earliest and most successful form of transplantation therapy, has evolved and flowered over less than 100 years. It is entirely possible that it is now overused and that more critical assessment of benefits and risks could lead to its more selective use. This would reduce risk to patients and save money.

The key must lie in better education of doctors both in the area of the use of blood and blood products and most importantly in the need to discuss carefully the risk/benefit balance of elective transfusion before prescribing this form of treatment.

References