THE EARLY HISTORY OF BLOOD TRANSFUSION

THE HISTORY OF BLOOD TRANSFUSION BEFORE THE 20th CENTURY

COMPILED AND WRITTEN
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This document was originally written for training purposes and as such includes material of 'general interest' related to the early history of blood transfusion and is not therefore intended to be a 'review article' on the subject. As such, this document does not contain references.

INTRODUCTION

The practice of blood transfusion, that is the transference of blood from the circulation of one individual to that of another for practical therapeutic purposes, is of relatively recent origin. Although it only became a practical possibility during and shortly after the Second World War the concept of 'transfusion' has a longer history. The practicality of transfusion has to some degree paralleled and in many instances been the consequence of, developments in other sciences. The idea though of the theoretical beneficial effects of blood transfusion has been recognised for over three centuries. This older history is based on the traditional idea of blood as being the 'living-force' of the body. Man must have recognised that loss of blood was frequently associated with weakness and death. This was manifested by Greeks and Romans committing suicide by 'opening a vein' (involving cutting their wrists). Blood was recognised as having numerous mysterious properties, including initially that of carrying both the mental and physical characters of its owner. Early attempts at replacing lost blood involved the drinking of blood by the patient. By choice, this was from a young, healthy, fit person or animal. The legend of the vampire originates from this concept. This somewhat mystical fascination with the properties of blood is to some degree still with us today.

EARLY BEGINNINGS

There are many early documented references to the use of blood, for what can be at best described as 'medicinal' purposes. One of the first of these relating to a 'transfusion' is contained in the *Seventh Book of the Metamorphoses* by Ovid, who in 43BC wrote how the witch Medea rejuvenated Jason's aged father Aeson as follows:

> "Medea took her unsheathed knife and cut the old man's throat letting all of his blood out of him. She filled his ancient veins with a rich elixir. Received through his lips and wound, his beard and hair no longer white with age, turned quickly to their natural vigour, dark and lustrous; his wasted form renewed, appeared in all the vigour of bright youth".

Ovid (43BC – 17AD)[1]

Engraved frontispiece of *Ovid's Metamorphosis* (1632)[1]

Medea's apparent remarkable success was achieved with an ‘elixir’ brewed in a bronze cauldron containing the following ingredients:

> "... root-herbs, seeds and flowers, strong juices and pebbles from the farthest shores of oceans east and west; hoar-frost taken at the full of the moon, a hoot owl's wings and flesh, a werewolf's entrails, a fillet of a snake, the liver of a stag and the eggs and head of a crow which had been alive for nine centuries."

Medea's practice as a ‘transfusionist’ was not confined to this single event, since she is later reported to have killed Pelias by pretending to perform a similar miracle on him, having first gained his confidence by apparently changing an aged sheep into a lamb.

Medea
(by Anthony Sandys - painted 1866-68)[1]

In addition to these early mythical writings, there are several noted citations in the Old Testament indirectly bearing on (blood) transfusion. These have a social impact to the present day, relating to the denial of a blood transfusion by certain persons on religious grounds.

It is believed that the ancient kings of Egypt apparently bathed in blood, believing such baths to *"… resuscitate the sick and rejuvenate the old and incapacitated"*, as well as believing it to be a cure for elephantiasis! In classical times the Romans and Greeks, as well as bathing in blood, also reportedly drank it. Pliny the Elder wrote in the 1st century AD, describing how spectators rushed into the arena to drink the blood of dying gladiators. These people did this because they felt that such blood was especially beneficial since the athletes were strong and brave, qualities that they believed were present within, and therefore transmissible by, the blood of the person concerned. The situation apparently became so bad that by AD193, a decree was issued by Septimus Severus prohibiting this practice.

Pliny the Elder also wrote: *"... a man's blood rubbed upon himself will relieve him of pain"* and that the drinking of blood *"... as if out of a loving cup"* was a cure for epilepsy. About the same time, the writer Galen advised that the drinking of the blood of a weasel or a dog was a cure for rabies. Similarly, ancient Norwegians reportedly drank the blood of seals and whales as a remedy for epilepsy and scurvy.

Although these references refer to the drinking of blood or the application of blood to the skin, an ancient Hebrew manuscript refers to an actual possible transfusion as follows:

> "Naam, leader of the armies of Bed-Adad, King of Syria, afflicted by leprosy,

consulted physicians, who in order to cure him drew out the blood from his veins and put in that of another."

Pliny the Elder (23AD – 79AD)[1]

An early recognition of the dangers of the custom of 'ingestion' of blood, as well as probably the first rather fanciful description of what could be described as the management of an adverse reaction, is contained in the works of the 13th century writer Petro de Abano, who wrote:

> "He who drinks of menstrual blood or that of a leper will be seen to be distracted and lunatic, evil minded and forgetful, and his cure is to drink of daisies powdered and mixed with water of honey, and to bath in tepid water and to copulate with girls according to the law natural, and to play with pretty girls and young boys; and the antidote is to eat serpents whose heads and tails have been cut off with the edge of a palm frond."

Since most of the ancient and medieval references probably refer to the ingestion of blood rather than to its infusion it is difficult to determine when the first authentic attempt at transfusion was actually performed. One of the most frequently quoted candidates for this noteworthy honour is Pope Innocent VIII, Giovanni Battista Cibo (or Cybo), who was reputedly 'transfused' some time between 1490 and 1492. Villari, some considerable time later recounted the incident, claiming that the Pope had some sort of illness that rendered him semi-comatose (in the light of present knowledge this was probably chronic renal disease). This was described as being so profound at times that the Pope was mistakenly thought to be dead.

On one occasion, after all means to revive the Pope had failed, Vallari reported that a physician (or mystic) called Abraham Meyre appeared in the court and promised to save the Pope's life by transfusing him with the blood of young 'donors'. Apparently, three young (10-year-old) shepherd boys were selected as donors and he states that the blood of the dying Pope was passed into the veins of one of the boys, *"… who gave him his own in exchange"*. The process was apparently repeated with the other two boys. All three boys reportedly died shortly after the procedure, possibly as a result of air embolism, but there was no change to the Pope's condition.

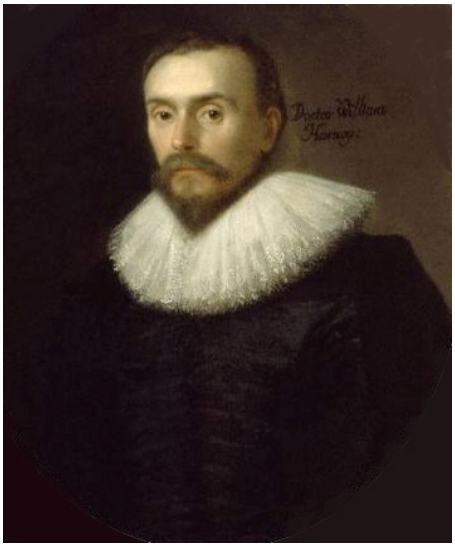
This story is however controversial and open to interpretation, being based on translations from the original script. It is probable that this presumed 'transfusion' stems from an incorrect interpretation by Villari of an earlier account of the Pope's illness. If

this is the case, what is likely to have happened is that the Pope was asked to drink the blood. In any event, all authors seem to agree that the three boys, *"… costing one ducat apiece"*, died shortly after the procedure, as eventually did the Pope (presumably from his underlying renal condition).

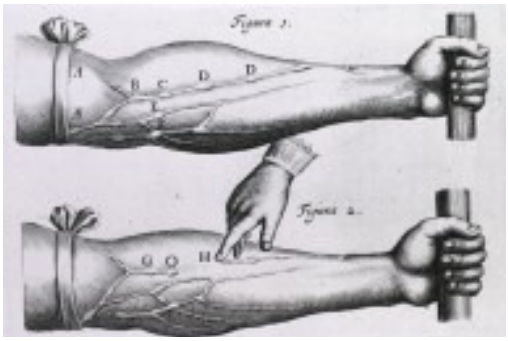
Pope Innocent VIII (1432-1492)[1]

THE FIRST TRANSFUSION - CLAIMS FOR PRIORITY

After the apparent incident involving Pope Innocent VIII, few references regarding the 'administration' of blood can be found until early in the 17th century. One of the most important discoveries permitting the transfusion of blood was then made, that of the formulation of the theory of the circulation of blood, discovered by William Harvey in 1613.



William Harvey (1578-1657)
(1627 – by Daniel Mytens)[1]



Circulation of the blood
De Mortu Cordis (1628, page 184)[3]

William Harvey was a doctor who identified that blood flowed through blood vessels in one direction. Up until then blood was assumed to wash forwards and backwards in the vessels, like 'the tides of the sea'. Harvey lectured on the subject of blood circulation for a number of years and finally published his findings in a book entitled *De Motu Cordis* (published in 1628) where he described the human circulatory system in detail, including the true role of the heart. It is likely that all references to the transfusion of blood before this date must be considered at best questionable.

Harvey's discoveries initiated considerable speculation regarding not only the possibility of the transfusion of blood, but also the infusion of other medications or potions. It is thought unlikely that Harvey himself used blood transfusion in relation to his medical practice, though there is evidence that in order to test his theories he pumped water through the circulation of a dead man.

In 1628 Johannes (Giovanni) Colle, a professor at the University of Padua (who may well have had knowledge of Harvey's work), whilst writing on the 'methods of prolonging life', mentioned blood transfusion as a possible means of achieving this goal. There is however no evidence that he ever attempted to carry out a transfusion in practice. Similarly, a decade earlier in 1615, Andreas Libavius, a renowned chemist of his day, wrote the following (satirical) comments while defending his chemical theories against critics:

> "Let there be a young man, robust, full of spirituous blood, and also an old man, thin, emaciated, his strength exhausted, hardly able to retain his own soul. Let the performer of the operation have two silver tubes fitting into each other. Let him open the artery of the young man, and put it into one of the tubes, fastening it in. Let him immediately after open the artery of the old man and put the other tube into it, and then the two tubes being joined together, the hot and spirituous blood of the young man will pour into the old one as if it were from a fountain of life, and all of his weaknesses will be dispelled. Now, in order that the young man may not suffer from weakness, to him are to be given good care and food, but to the doctor, hellebore."

Based upon his readings of Ovid's story of Medea, Francis Potter is thought by some to possibly be the first person to conceive of transfusion on a practical basis. Potter was the vicar of Kilmarton in Somerset and apparently something of an eccentric and recluse whose efforts were documented in the writings of his contemporary and friend, John Aubery. According to these writings, Potter originated the idea of transfusion as early as 1639, and devised quills (as 'needles') and tubes for the purpose. In 1649 he wrote to John Aubery reporting that he had attempted the procedure of transfusion between two chickens, though it is likely that because of the size of such birds, it was probably unsuccessful:

> "I am as yet frustrated in ipso limine, but it is my owne inexpertness, who never attempted any such thing on a creature before; for I cannot, although I have tried divers times strike the veine so as to make him bleed in any considerable quantity. I have prepared a little cleare transparent vessel (like unto a bladder) made of the craw of a pullet; and I have fastened an ivory pipe to one of the neckes of it, and I have put it into a veine which is most conspicuous about the lower joint of the hinder legges; and yet I cannot produce above 2 or 3 drops of blood to come into the pipe or bladder."

The above account is reported to have been written in December 1652, but it cannot however be claimed that the Reverend Francis Potter greatly advanced the science of blood transfusion to any great degree!

During the 25 years or so following the publication by Harvey of the description of the circulation of the blood and the role of the heart, it is only to be expected that several

people in different European countries should be thinking along similar lines. This gave rise to conflicting priority claims as to the first person to actually transfuse blood. One certainly false claim is made by Florentine physician, Francesco Folli, who published a book in 1680 setting out his claim to be the originator of blood transfusion. He stated that he read of Harvey's work in 1652 and thereupon formed the idea that the transfusion of blood should be possible to cure diseases and to rejuvenate the aged. In 1654 Folli wrote:

> "This I pointed out in my pamphlet on life culture which was published for no other reason than to make known to all that blood transfusion had been invented by me at the end of 1654 and demonstrated to his Serene Highness Ferdinand II, Grande Duke of Tuscany, of undying memory. The novelty of it had pleased him, or the fascinating ingenuity or the considerable experimental elaboration. To no one else did I impart my idea, believing that if such an invention were successful, Monarchs alone were worthy of it."

Francesco Folli (1624-1685)[3]

Later Folli described in some detail the apparatus required for a blood transfusion and the method of using it. He even postulates the presence of twenty young men as blood donors so that the patient may receive blood of a fresh donor every day over a considerable period. The apparatus apparently consisted of a funnel connected by a tube formed from a goat's artery with a gold or silver cannula to be inserted into the patient's vein. Though Folli describes the theory of transfusion, near the end of the book comes the confession, which spoils it all from a practical viewpoint, where he identifies that he did not actually carry out the process:

> "Finally I know that I have said too much concerning the manner of carrying out the operation, not having made the experiment….. but I have done it solely so that everyone, however simple or ignorant, could understand, be inspired, and even make the experiment with the least possible expense, and to this end only I have written in the vulgar tongue."

A French Benedictine monk may also lay some claim to being the first to perform a transfusion. At a meeting of a learned society, held in Paris in July 1658, Robert des Gabets discussed the discovery of the circulation of the blood by Harvey and claimed that he was convinced that he could establish another type of movement of the blood.

He termed this *"communication"*, by which he meant *"… the effective passage of blood of a healthy man or other animal to the veins of an individual weak or diseased"*. He also claimed that seven years earlier, a Friar called Pichot, had prepared an instrument consisting of two small silver tubes connected by a leather purse about the size of a walnut, which could be used for this purpose.

The established priority claim however for proposing and demonstrating the intravenous administration of medications (into the veins of dogs) is made by Dr (later Sir) Christopher Wren (1632-1723), who was to achieve far greater fame as an astronomer and architect. He developed (in 1656) an animal bladder attached to two quills for this purpose. Dr Thomas Sprat, in his history of the Royal Society in 1657, records the following about Wren:

> "… he was the first author of the Noble Anatomical Experiment of Injecting Liqors into the Veins of Animals: an experiment now vulgarly known, but long since exhibited to the Meetings at Oxford, and thence carried by some Germans, and published abroad. By this operation, Creatures were immediately purged, vomited, intoxicated, killed or revived, according to the quality of the Liquor injected. Hence arose many new experiments and chiefly that of transfusing blood, which the Society has prosecuted in many instances, that will probably end in extraordinary success."

Wren's experiments were later to be described in some detail by his associate Robert Boyle, in his book *Usefulness of Experimental Philosophy* (published in 1663).

Sir Christopher Wren
(Godfrey Kneller's portrait of 1711)[1]

The Royal Society was founded in London during 1661 and received its Royal Charter in 1662. It was this 'philosophic assembly' of distinguished scientists that witnessed the beginnings of blood transfusion experiments in animals. It was the practice of the time that experiments should first be demonstrated in front of colleagues and peers and then written down and published (usually by the Royal Society itself). Among several persons involved in these experiments was Richard Lower, then a doctor practising in Oxford, who claims priority for the first animal-to-animal transfusion.

THE FIRST REAL ATTEMPTS

Sir Christopher Wren is considered to have been a genius, being one of the scientists who, in the 17th century, not only laid the foundations for calculus but also made fundamental contributions to astronomy. He will however always be remembered for his architectural genius, having designed over 20 churches in London, including St Paul's Cathedral. Although not as well recognised, his description of intravenous injection to the Royal Society was an important forerunner to the initial efforts to perform blood transfusions at that time. The following excerpt from the Philosophical Transactions of the Royal Society (1665) indicates the priority of Wren's contribution and also the possible use of this technique for the injection of blood. The note also indicates the role that was played by Robert Boyle, a noted chemist and physician of the time, now famous amongst chemistry students for his description of the compressibility of gases, i.e. 'Boyle's Law'.

> "Whereas there have lately appeared in public some books, printed beyond the seas, treating the way of injecting liquors into veins; in which books the original of that invention seems to be ascribed to others besides him to whom it really belongs, it will not be thought amiss if something be said whereby the true inventor's right way, beyond exception, be asserted and preserved... 'Tis notorious that at least six years have passed since the learned and ingenious Sir Christopher Wren did propose in the University of Oxford (where he now is the Professor of Astronomy) to that noble benefactor of experimental philosophy, Mr Robert Boyle, Dr Wilkins, and other deserving persons, that he thought he could easily contrive a way to convey any liquid thing immediately into the blood. This involved by making ligatures on the veins, and then opening them on the side of the ligature towards the heart, and putting into them slender syringes and quills, fastened to bladders, containing the material to be injected."

Robert Boyle (1627-1691)[1]

The manuscript continues with an account of Boyle's experiments using this technique for the injection of opium and also Crocus metallorum (an antimony sulphate preparation used at the time as an emetic) into dogs. It also contains a description of the injection of Crocus metallorum into 'volunteers' taken from the inmates of a London prison, one of who was described as a *"… malefactor who was an inferior servant of his".* The article states:

> "Some may conceive that liquors thus injected into veins without preparation and ingestion will make odd commotions in the blood, disturb nature and cause strange symptoms in the body, yet they have other thoughts of liquors that are prepared of such things that have passed the digestion of the stomach; for example, of spirit of urine, of blood, etc; and they hope likewise that beside the medical uses that may be made of this invention, it may also serve for anatomical purposes by filling the vessels of an animal as full as they can hold, and by exceedingly distending them, discover new vessels.... The reader may securely assume that this narrative is the naked real matter of fact, whereby it is clear as Noonday....that to Oxford, and in it, to Dr Christopher Wren, this invention is due."

Many of the early experiments were performed on dogs using *"liquors"*, which included such substances as ale, wine and opium. Although the practice at the time, the animals used in these experiments were obviously treated unacceptably by present day standards since they were reported to have undergone *"... suffering vomiting, intoxication and I fear death"*.

These and many other various entries in the *Journal Book of the Royal Society*, record the earliest suggestions and attempts to carry out blood transfusions in animals or birds. In a report dated 31st May 1665, there appears the first mention of a direct artery-to-vein transfusion from an animal to a human. After Robert Boyle's experiments, the major part of future work was done by Dr Richard Lower, whose first statement, written in a letter to Boyle, was read to the Royal Society on the 26th September 1666. Lower's book on the heart *Tractatus de Corde* (published in 1669) proves him to have been one of the great pioneers in anatomy and physiology. In it he makes the following statement about blood transfusion:

> "... to reveal the conduct of the whole affair and at the same time show by what train of thought reasoned it out and undertook it, and finally, by what means and aids it was carried into effect."

He then proceeds at great length to give an account of the first (published) description of a successful direct transfusion from artery to vein (having first attempted vein to vein direct transfusion and failed due to the blood clotting in the silver tubing used for the purpose).

Richard Lower (1631-1691)
Oil paining by Jacob Huysmans[2]

It seems clear that Lower was the first to define the appropriateness of transfusion for the replacement of blood in severe haemorrhage, since he was able to demonstrate that a dog could be exsanguinated to the point of near death and then be completely restored by transfusion.

The diary of Samuel Pepys provides valuable insight into Richard Lower's early experiments in blood transfusion and the public interest occasioned by this revolutionary technique. Pepys' (now famous) diary, in the entry of 14th November 1666, describes one of these transfusions, performed in London by the Royal Society, as follows:

> "Dr Croone told me that at the meeting of Gresham College tonight, which it seems they now have every Wednesday, there was a pretty experiment of the blood of one dog let out till he died, into the body of another on one side, while all his own ran out on the other side. The first died upon the place, and the other very well and likely to do well. This did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like; but as Dr Croone says, may, if it takes, be of mighty use to man's health, for the amending of bad blood by borrowing from a better body."

Lower's efforts were the stimulus for a series of experiments on animals by various people throughout Europe, which eventually led to the transfusion of blood from an animal to a man. The priority of this procedure occasioned a somewhat heated debate between Lower and a man he described as *"a certain Denis",* who was actually a Frenchman called Dr Jean-Baptiste Denis (also called Jean Denys), a young physician on the large staff attached to King Louis XIV. On the 23rd November 1667, Lower, assisted by Dr Edmund King, transfused a man named Arthur Coga. The interest in this event being again described by Samuel Pepys as follows:

> "We discoursed a man that is a little frantic, that hath been a kind of minister, that is a poor and debauched man, that the College have hired for twenty shillings to have some blood of a sheep let into his body; and it is to be done of Saturday next. They propose to let in about 12 ounces; which they compute, is what will be let in a minute's time. They differ in the opinion they have of the effects of it; some think it may have a good effect upon him as a frantic man by cooling his blood, others that it will not have any effect at all. But the man is a healthy man, and by this means will be able to give an account of what alteration, if any, he do find in himself, and so may be useful."

The event was also later detailed in the *Philosophical Transactions of the Royal Society*. The initial part of the account describes the quills and silver pipes used to carry the blood between the carotid artery of the donor sheep and a vein of the recipient's arm. The account however concludes:

> "The blood did run all the time of those two minutes and we concluded .... upon the man's saying he thought he had enough. The man after this operation, as well as in it, found himself very well, and hath given in his own narrative under his own hand, enlarging more upon the benefit he thinks he hath received than we think fit to own as yet. He urged us to have the experiment repeated upon him within three or four days after this, but it was thought advisable to put it off somewhat longer."

This second experiment did in fact occur (the following month) and apparently proceeded without mishap. Afterwards, the subject Arthur Coga said he felt better, although Pepys later wrote in his diary *"… he is cracked a little in the head"*. This second experiment was not recorded in the *Transactions of the Royal Society* possibly because of events occurring almost simultaneously in France involving *"… a certain Denis"*.

It should be remembered that these early 'transfusion' experiments were carried out at a time when the popular medical procedure used by doctors to treat many illnesses was 'blood letting', i.e. bleeding the patients rather than transfusing them.

THE FIRST FALTERING STEPS

Dr Jean-Baptiste Denis read of Lower's experiments in the *Journal des Savants* of 31st January 1667. In association with a surgeon, Paul Emmerez, Denis initiated his own trials approximately a month later, performing numerous dog-to-dog transfusions. On the 15th June 1667, Denis was asked to treat a 15-year-old boy who had suffered from a fever for many months, for which he had been bled by his physicians twenty times, *"... to assuage the excessive heat"*. Denis wrote:

> "Before this disease, he had not observed to be of a dull spirit, his memory was happy enough, and he seemed cheerful and nimble in body; but since the violence of his fever, his wit seem'd wholly sunk, his memory perfectly lost, and his body so heavy and drowsie that he was not fit for anything."

Accordingly he was bled to the extent of about three ounces and received in exchange nine ounces of blood from the carotid artery of a lamb. The change that ensued in the patient was described as *"startling"*, and presently the boy was showing *"… a clear a smiling countenance"*, where previously he had apparently passed the time *"… in an incredible stupidity"*. The boy had also felt *"… a very great heat along his arm"* (a present-day indication of an incompatible transfusion reaction), but there were apparently no further ill effects.

Denis's second transfusion was performed on a 45-year-old man using a reported 20 ounces of lambs' blood and described the man as feeling stronger than before the transfusion. Further transfusions were performed; one of which involved the description of a variety of reactions in the patient that would nowadays be indicative of a severe haemolytic transfusion reaction. Denis submitted a report of his transfusion of the teenage boy to the Royal Society in July 1667, which due to the editor of the Journal being detained in the Tower of London at the time, was not published until the 23rd September 1667. Therefore, although Lower performed the first animal-to-animal transfusions, Denis is credited with performing the first animal-to-human transfusion (Lower in fact performed his first animal-to-human transfusion in November 1667).

Denis favoured the use of animal blood for his transfusion experiments because he believed it less likely *"… to be rendered impure by passion or vice".* This way of thinking about blood, as carrying a person's (or in this case an animal's) temperament, beliefs, strength or courage, was typical of the time. Following the transfusion of a number of individuals, Denis and his associate performed a further transfusion in 1668, which was to have far-reaching and significant repercussions, and in fact determined that the practice of transfusion was to lay dormant for nearly one hundred and fifty years.

A 34-year-old man, Antoine Mauroy, was described by Denis as suffering *"a severe phrensy",* which apparently had lasted seven or eight years and had reportedly been due to an unfortunate love affair. One day the man was said to have escaped from his wife's control and paraded through the streets of Paris clothed *"… only in nature's garb, followed by an admiring throng"*. Such an opportunity was apparently not to be lost by the enthusiastic researcher such as Denis, who was asked to transfuse this luckless fellow to allay the *"… heat in his blood"*. As a result, on the 19th December 1667, ten ounces of blood were removed from the vein of his right arm, being replaced with five or six ounces of blood from a calf, with no obviously untoward (or beneficial) effects. Two days later, the man was transfused a second time. This resulted in what would now be

recognised as a haemolytic transfusion response. Denis's description of this second transfusion could in fact be considered to be a classic medical description of this phenomenon:

> "As soon as the blood entered his veins, he felt the heat along his arm and under his armpits. His pulse rose and soon after we observed a plentiful sweat over all his face. His pulse varied extremely at this instant and he complained of great pains in his kidneys, and that he was not well in his stomach, and that he was ready to choke unless given his liberty. He was made to lie down and fell asleep, and slept all night without awakening until morning. When he awakened he made a great glass full of urine, of a colour as black as if it had been mixed with the soot of chimneys."

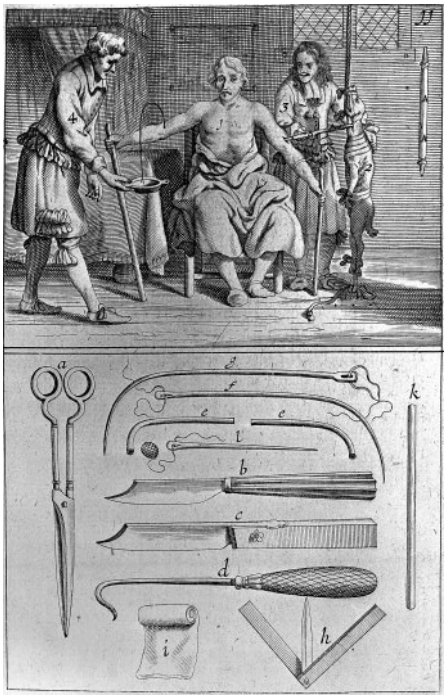
Denis also recounts that the following morning (the second day) Mauroy had further haemoglobinuria and epistaxis. However, by the third day his urine had cleared and his mental state having apparently improved, the man returned to his wife. Denis attributed the colour of the urine to a *"black choler"* which had been retained in the body and had sent *"vapours to the brain"*, causing the patient's mental disturbance. About one month later Antoine Mauroy again became violent and irrational and his wife persuaded Denis and his associate Emmerez to repeat the transfusion. A transfusion was attempted, but since the flow of blood was poor, it was apparently abandoned. Mauroy died the following evening.

Through their transfusion experiments, Denis and Emmerez had acquired many enemies among the physicians of Paris, since the 'approved' medical practice of the day frequently involved bleeding the patient, principally by the use of leaches. Three of these physicians persuaded Mauroy's widow to accuse Denis and Emmerez of contributing to the death of her husband by the transfusion. Other physicians in the Faculty of Medicine of Paris, an apparently extremely conservative body who refused even to recognise Harvey's theory of circulation, were opposed to transfusion and published pamphlets condemning the practice. At one point Mauroy's widow offered to withdraw the lawsuit provided she would receive payment from Denis, however he replied *"That those physicians, and herself, stood more in need of the transfusion than even her husband had done"*. Denis lodged a counter-complaint against the widow, so that when the trial came to court, he appeared as the plaintiff not the defendant. Following a prolonged legal battle, the final outcome was that Denis was exonerated and Mauroy's widow was apparently shown to have poisoned her husband with arsenic. More importantly however, due to the enemies that Denis had made, the adjudication included a statement that in future the procedure of transfusion was not to be performed without the permission of a member of the Faculty of Medicine. Since the Faculty was bitterly opposed to the whole idea, this permission was never given and the practice of transfusion rapidly fell into disuse. Eventually, an edict from the French parliament ruled transfusion to be a criminal act if performed in France. This ruling also had repercussions in London where the Royal Society rapidly washed its hands of transfusion as well. As a result, quite understandably, interest in transfusion rapidly waned.

Now that the various problems associated with the transfusion of more than a very small quantity of blood from any animal into a human are known, the outcome described by Denis was inevitable. Animal blood, whether from a dog, lamb or calf contains proteins totally incompatible with those of human blood. If transfused a second time, the transfused animal red cells are therefore rapidly destroyed, haemoglobin appears in the urine (which it discolours) and the symptoms of anaphylaxis follow. If a transfusion is repeated using a large enough volume of blood, it can be fatal.

Although the practice of transfusion had essentially ceased, some text books

published in the 17th and 18th centuries still included classical accounts of how the procedure could be accomplished, mainly it is now thought due to the fact that transfusion could be so admirably sensationally illustrated! One notable illustration in the textbook *Armamentarium Chirurgicum* by Scultetus (published in 1693) identifies a dog bound tightly to a stake as the donor, whilst the patient is being transfused via a direct artery to vein tube. This illustration however also identifies that whilst the patient is being transfused into the left arm, he is being bled from the right arm into a bowl (i.e. bleeding a patient was still the accepted medical practice).



Dog to human transfusion
(Scultetus 1693)[2]

Lamb to human transfusion
(Purmann 1705)[2]

Apart from Lower's comments associated with his initial dog experiments, during this period little consideration was given to the use of transfusion for the replacement of blood loss. The most popular use for transfusion was the possibility of it being able to alter the mental state of the patient. Considerable importance was attached in contemporary writings to the possibility of restoring youth to the aged and it was even suggested that marital discord might be settled by the reciprocal transfusions of the blood of husband and wife! In line with the mysticism associated with the act of transfusion, it was for instance speculated that a dog transfused with the blood from a sheep might grow wool, cloven hooves and horns. There was apparently even an account of a young girl who received blood from a cat and was quickly endowed with feline characteristics.

Only sporadic attempts at transfusion were undertaken during the remainder of the 17th century and throughout the 18th century. All were animal-to-human transfusions and were performed with no knowledge of immunity or anticoagulation. None of the events involved the clinical practice of blood replacement after haemorrhage and were usually based on the popular concept of transferring personality, vigour and/or youth. All were performed without any practical or functional equipment and many must have involved blood that was already in the process of clotting. Not until 1749 did a Dr Cantwell, a member of the Faculty of Medicine in Paris, state that transfusion was valuable in extreme emergencies involving severe blood loss.

RENEWED INTEREST

Following the decrees of the mid-17th century forbidding blood transfusion throughout most of Europe, the practice fell into general disrepute for more than a century and a half. The credit for placing transfusion on a scientific basis and re-awakening interest in its use must be given to Dr James Blundell (1790-1877).

James Blundell was a noted physician, physiologist and one of the outstanding obstetricians of his day. He is credited with rekindling interests in blood transfusion in the second decade of the 19th century and providing it with a semblance of a rational scientific approach. Many people in fact regard Blundell as the 'the father of modern blood transfusion', though the *Dictionary of National Biography* makes no reference at all to his work on transfusion, but does note that he left a fortune (especially for the time) of £350,000 when he died in 1877.

James Blundell (1790-1877)[2]

Blundell initially became interested in transfusion as a method of treating post-partum haemorrhage, being *"appalled at my own helplessness at combating fatal haemorrhage during delivery"*. His experiments began by exsanguinating dogs and then reviving them by the transfusion of arterial blood from other dogs. From his experiments he concluded that the blood from one animal could not be substituted for that of another with impunity and he therefore turned to the use of human blood for human transfusion.

It must however be noted, that Blundell received his medical degree from the University of Edinburgh and was undoubtedly influenced in his early experiments by the work of Dr John Henry Leacock. Although Leacock's manuscript on the subject of transfusion was written later when he was in Barbados, his experiments were performed during his time in Edinburgh, where one of his contemporaries was Blundell. Utilising a six-inch length of ox ureter (as the 'tube') with crow quills (as the 'needles') attached to both ends, Leacock operated on dogs, resuscitating exsanguinated animals by transfusion. Although Leacock did not perform a human transfusion, he argued against the mixing of blood from different species and his experiments quite clearly pointed to the advantages of such a treatment. In 1817, Leacock eloquently concluded his dissertation on transfusion as follows:

> "The consequences of haemorrhages where the functions are not dangerously affected, do not of course, require transfusion, since other remedies will suffice. But when the danger is imminent, and the common means are ineffectual, as when a parturient women trembles on the brink of the grave from uterine haemorrhage, or when a soldier is at the point of death from loss of blood, what reason can be alleged for not having recourse to this last hope, and for not attempting the recruit the exhausted frame and turn the ebbing tide of life."

Blundell initially advocated direct transfusion; however, shortly after he introduced the use of the syringe to facilitate vein-to-vein transfusions. He described transfusion by syringe in several papers, noting the necessity of removing air from the instrument before transfusion as well as experiencing the problems of blood clotting, *"... the blood is satisfactory only if it is allowed to remain in the container for but a few seconds."*

Blood Transfusion Apparatus – Improved form of Dr Blundell's syringe by Savigny & Co[2]

The historic date assigned to the first documented transfusion of human blood is the 26th September 1818. The procedure was published in 1819, under the title 'Some account of a case of obstinate vomiting in which an attempt was made to prolong life by the injection of blood into the veins'. This case study describes how Blundell, with the help of the surgeon Henry Cline, transfused a 35-year-old man who was suffering from what would now be called gastric carcinoma, but was then described as *"scirrhosity of the phylorus*". When first seen by Blundell, the patient was near to death. Approximately 14 ounces of blood were administered by syringe in small amounts from several donors at intervals of 5-6 minutes. Despite temporary improvement in his condition, the patient died 56 hours later. His disease was incurable and nothing could really have been expected from the transfusion.

Between 1818 and 1829, Blundell and his colleagues performed a total of ten transfusions using human blood, of which no more than four can have been successful, as two patients were in fact noted to already be dead when the transfusion was commenced! The first 'successful transfusion' was of a woman who recovered from severe post-partum haemorrhage after receiving eight ounces of blood from Blundell's assistant during the course of three hours. This case was published in the journal *The Lancet* in 1829. Blundell still reported patients who *"... suffered fever, backache,*

headache and passed dark urine" (presumably due to ABO incompatibility). However, he still argued for the use of human blood in transfusions rather than animal blood, noting (somewhat amusingly) of the impracticability of the latter due to the difficulty of finding an appropriate animal in an emergency, as follows:

> "What is to be done in an emergency? A dog might come when you whistled, but the animal is small; a calf might have appeared fitter for the purpose, but then it had not been taught to walk properly up the stairs!"

Blundell was also aware that the operation of transfusion might be performed needlessly and emphasised that it should be reserved for desperately ill patients only. He also actively encouraged his contemporaries to practice transfusion. For the most part these were obstetricians who used the procedure in cases of postpartum haemorrhage. Two of the most active 'transfusionists' of the time were Dr Edward Doubleday and Dr Charles Waller. Dr Doubleday described in great detail the transfusion of a woman (suffering from postpartum haemorrhage) who was transfused with her husband's blood. He noted that after six ounces had been given the woman, previously semi-comatose, suddenly exclaimed, *"By Jasus, I feel as strong as a bull"*. Similarly, in 1829 Blundell, describing a transfusion of postpartum haemorrhage, claimed that:

> "... the patient expresses herself very strongly on the benefits resulting from the injection of the blood; her observations are equivalent to this - that she felt as if life were infused into her body".

To place this statement in the context of its time, it is of interest that this report, published in *The Lancet*, follows the thorough documentation of the murder trial of the resurrectionists Burke and Hare. Similarly, although Blundell showed remarkable insight into developing his techniques of transfusion, it should be noted that he also commonly applied leeches to the skin of both donor and recipient in an effort to prevent inflammation of the veins.

James Blundell established during his interest in transfusion so many fundamental points that it is difficult to exaggerate the importance of his work in the history of transfusion medicine. However, after 1830, James Blundell's interest in blood transfusion waned. He retired from medical practice in 1847 at the age of 57, undoubtedly well facilitated by a fortune which is recorded to have been accumulated from his medical practice and bequests. Although Blundell lived in comparative obscurity after his retirement he was a controversial figure, frequently at odds with the Medical Society of London and the Directors (and Treasurer) of Guy's Hospital.

During this period, considerable debate continued regarding the use of transfusion and various views being recorded in the minutes of the Medical Society of London. Many people felt that the procedure was dangerous and that it may have hastened the death of some of the patients in whom it was used. Furthermore, it was claimed that most of the patients who benefited from the procedure would have recovered anyway without the use of a transfusion. Dr Blundell argued strenuously however on behalf of the use of transfusions, noting repeatedly that the dangers of haemorrhage in these patients far outweighed the possible danger from transfusion.

This debate was still raging in 1849 when Routh reviewed all the published transfusions to that date in an article entitled 'Remarks, statistical and general on transfusion of blood', which was published in *The Medical Times*. He reported that he was only able to find 48 recorded cases of transfusion, of which 18 had a fatal outcome. This gave a mortality figure of approximately 1 in 3, which was reported as being *"… rather less than that of hernia or about the same as the average amputation"*. Furthermore, he noted that the mortality rate was unjustly high, for in many of these

patients death was due to causes other than the transfusion. Routh concluded that the greatest danger of transfusion was the transmission of air and suggested that the quantity of blood transfused should be *".... not less than 6 ounces nor more than 16 ounces".* Amongst the indications for transfusion cited by Routh were *"Severe haemorrhage, extreme exhaustion from dyspepsia, stricture of the oesophagus, collapse following long-continued fever, severe diarrhoea, dysentery or cholera"*. Finally, he described a method of transfusion using a syringe, which is of interest since many of the writings on transfusion of the period concentrated on the development of ingenious types of transfusion apparatus.

In the method described by Routh, blood is allowed to flow from the donor vein directly into a basin, from which the syringe was filled and then injected into the recipient. This is of particular interest since one of the major drawbacks to the further development of blood transfusion practice was that no successful method had been found to stop blood from clotting. The only practical method of transfusion was a direct one involving the joining of the artery of the donor with a vein in the recipient. This problem resulted in an interesting period with regard to some particularly odd, and in some cases rather bizarre, blood transfusion apparatus being described.

ESTABLISHING TRANSFUSION PROCEDURES

It is obvious that one of the first problems that had to be solved before blood transfusion could be placed on a practical footing was the prevention of coagulation or blood clotting. During the 19th century attempts to overcome this problem took several forms. James Blundell noted that vein-to-vein direct transfusions were impractical due to blood clotting, but attaching the artery of the donor to the vein of the recipient rendered the procedure feasible, i.e. a 'direct' transfusion. Alternatively, donor blood was collected into a vessel and then infused into the patient, i.e. an 'indirect' transfusion.

Considerable use was also being made around this time of using defibrinated blood, that is to say blood from which the (platelet-fibrin) clot has been removed, for indirect transfusions. This method began with the work of Prevost and Dumas in 1821 and was after that time employed by many others. A variety of techniques were described to achieve this goal, though the majority incorporated some form of blood stirring process. One of the first people to use an 'anticoagulant' additive was Neudorfer, who in 1860 recommended the addition of sodium bicarbonate as an anticoagulant. Two other physicians who actively sought an answer to the problem of coagulation were Dr Braxton Hicks, who used a solution of sodium phosphate (in six notably unsuccessful transfusions) and Dr E. Brown-Sequard, who used defibrinated blood for his experiments performed in the early 1850's. However, half a century was to elapse before a practical means of anticoagulation was devised. Efforts during the remainder of the 19th century were directed towards the development of (usually) unproved devices for direct and indirect transfusion or the refinement of surgical procedures to facilitate direct transfusion. Many of these devices were quite ingenious, attempting to incorporate the features of rapid administration, measuring the amount injected and, in some instances warming the blood.

James Blundell had first used a simple form of brass syringe and cannula, sucking blood out of the donor's vein and then injecting it immediately into the patient's vein. Blundell then invented a rather strange instrument called an 'Impellor', which was essentially a funnel and pump combined; a diagram of which appeared in his book, published in 1824. The outer compartment of the funnel was first filled with warm water (to help keep the blood fluid) and the donor's blood was made to flow into the funnel. The action of a pump (within the water filled jacket of the funnel) forced the blood along a tube to a cannula inserted in the patient's vein, by means of two oppositely acting

spring valves below the funnel. According to the illustration, the Impellor was designed to be fixed to the back of a chair to give the equipment stability (as well as possibly being for the benefit of the blood donor!). Later Blundell invented another instrument, the 'Gravitator', in which as the name implies, gravity provided the motive force for pushing the blood into the patient's vein. The equipment consisted of a funnel at the end of a long flexible bracket, which was again attached to a chair or similar object for stability. The funnel is connected to a tube with a cannula, which was buckled to the patient's arm. Illustrations published in 1829 show the blood donor standing by the equipment while he watched his blood gushing into the funnel.

Blundell's 'Gravitator' method of blood transfusion from: 'Observations on the transfusion of blood', *The Lancet* 1828, volume ii, issue ii, page 321[2]

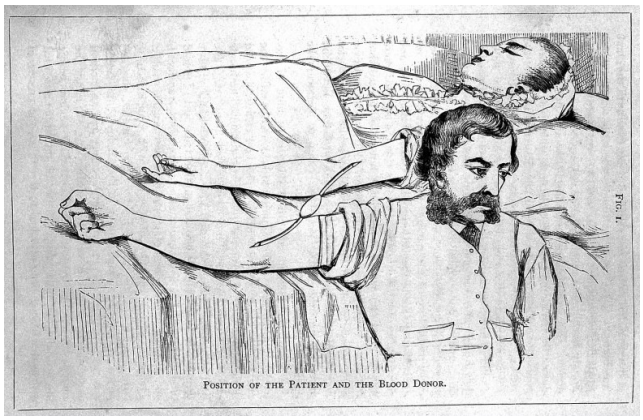
Blundell was at great pains, like a number of his contemporaries, to show (by extensive experiments) that the blood was not 'injured' by its passage through an instrument, though he thought that the introduction of *"a few air bubbles"* into the circulation was, contrary to the belief of earlier observers, *"quite harmless"*.

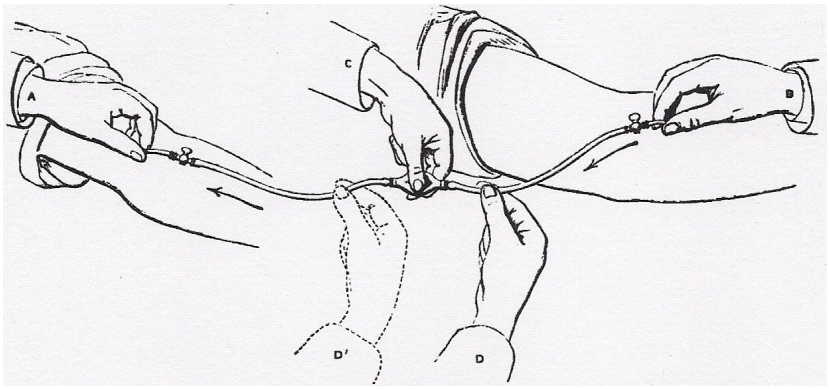
Although anticoagulation of blood was becoming more popular during the mid-19th century, one of the chief exponents of a direct or immediate manner of transferring blood was the English obstetrician Dr James H. Aveling. His apparatus was described and illustrated in an article published in 1873. It consisted of a simple tube with a central rubber bulb, which provided a pumping action produced by squeezing the bulb together with the tube at alternative sides of the bulb. Aveling described the apparatus as being extremely convenient, so much so that he wrote, *"I carried the apparatus around in my pocket to every confinement I attended for eight years until at length the opportunity for using it arrived"*. From this statement it may be correctly inferred that the concept of sterility was unknown at this time! Dr Aveling finally used his direct transfusion apparatus in 1872, when he attended a lady, aged 21 years, *"in extremis"* from postpartum haemorrhage. She received 60 drachms of blood from her coachman and apparently soon recovered, certainly enough to reportedly be able to remark that she thought that she was dying! Aveling added in his report that:

> "… the mental improvement of the patient was not as marked and rapid as I anticipated, but this was perhaps due to the quantity of brandy she had taken."

Aveling was 'pleased to record' that the coachman was not only *"collected and cheerful",* but able to make several useful suggestions during the transfusion process, though unfortunately he does not record what these suggestions actually were. No reason was given as to why this man was chosen as a donor other than presumably

because he was a servant and ‘available’; or even if he was a willing donor.





Aveling’s transfusion apparatus
(*The Lancet* 1823, volume 2, page 148)[2]

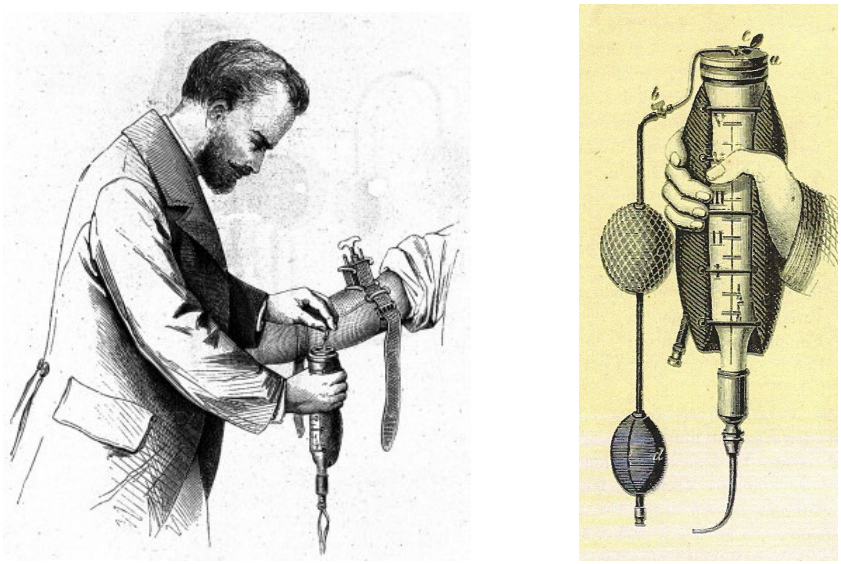
Defibrinated blood was used by Sir Thomas Smith, who in 1873 used it in St Bartholomew’s Hospital for the first reported case of a transfusion to an infant (who was suffering from Haemolytic Disease of the Foetus/Newborn). His defibrinating apparatus on this occasion included a wire eggbeater and a hair sieve with which to remove the fibrin clot. Defibrinated blood has been used until relatively recent times by various operators but the process results in the removal of a large part of the protein content of the blood as well as some of the cells. It is also time consuming and difficult to perform correctly, as well as of course posing sterility problems.

A somewhat important instrument modification was introduced in 1857 by Higgingson, who applied the principle of a rubber sealed syringe with ball valves for transferring the blood from the receptacle into which it was drawn to the vein of the patient. ‘Higginson's syringe’ was later used for a somewhat different purpose (i.e. in the treatment of syphilis in men) but it was successfully applied by its inventor in a series of seven transfusions. One of these transfusions is recorded to have been given to a woman, who, having been transfused with about 12 ounces of blood from a healthy servant, fell into *"… a state of quietude following her previous restlessness".* A few minutes later the patient was seized with a rather severe rigor. It did not last long, but led to a state of reaction and excitement during which she *"sang a hymn in a loud voice".* Although this is a somewhat unique description of a patient probably experiencing a transfusion reaction, the final outcome was apparently satisfactory and Higginson reported that some benefit was obtained from five of the seven transfusions he performed.

ONE STEP FORWARD, ONE STEP BACK

Although so much of the early work on blood transfusion had been performed in England and its revival during the 19th century was started in the United Kingdom, most of the references to transfusion up to 1874 are to be found in continental publications. This is somewhat unfortunate due to the fact that, although Blundell in his initial experiments had shown that the blood from one species of animal was potentially fatal to another, for the next fifty years continental writers were continually attempting to re-assert the possibility for using animal blood for the transfusion of humans. As a consequence of this obsession, a great deal of their writings are rendered valueless. Even as late as 1874, two treatises were published by Franz Gesellius and Oscar Hasse, advocating the use of lamb's blood.

In 1868, Gesellius, apparently an opponent to the use of defibrinated blood, sought to introduce the use of what he called ‘capillary-blood’ obtained by means of a rather ingenious if somewhat bizarre piece of apparatus, which simultaneously punctured the skin at numerous sites on the donor's back. Blood was then sucked from the punctured surface and allowed to run into a receptacle from which it was transferred to the recipient's vein. The apparatus, though rather graphically described and illustrated in Franz Gesellius' (German) publication of 1873 does not however merit closer study. Subsequently, and rather understandably, he (and presumably the donors) found it simpler to fill his receptacle directly from the donor's vein.



Syringe transfusion apparatus described by Franz Gesellius[2]

However, from this somewhat promising start involving human blood donors, Gesellius passed rather confusingly onto supporting the use of animal donor blood and in a somewhat over elaborate investigation tried to demonstrate that greater dangers were associated with the use of human rather than animal donor blood.

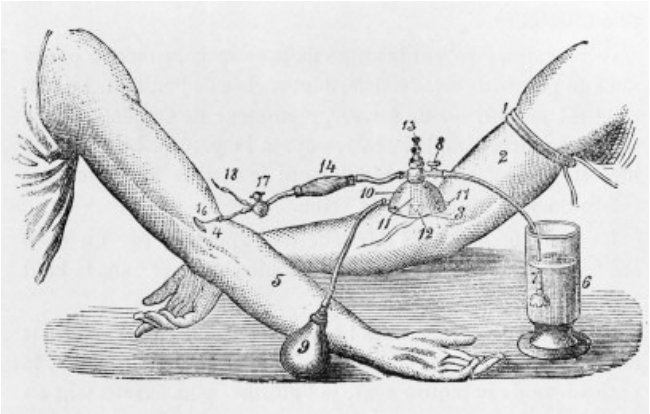
Hasse had also been an exponent of the use of human venous defibrinated donor blood and in fact performed 16 transfusions with this product. However, though apparently outwardly content with his results, after reading a publication by Gesellius on the use of arterial lamb's blood, he resolved to practice this method instead, and finally in 1874 advocated its use in both acute and chronic anaemia and other diseases. Hasse illustrated the method used to perform the transfusions in the frontispiece to his treatise, which involved a simple short cannula connection between the animal's carotid artery and the patient's antecubital vein.

Less was heard of the use of lamb's blood for transfusion after this date. Sentiment, if not science, seems to have had its effect, since a publication of the same period described the process as *"only taking lamb in another form".* It however seems more likely that common-sense was the motive power in the decline of the use of animal blood (especially in Germany) since the number of fatal reactions (not unexpectedly) increased.

The application of more recognisable scientific experimentation was however beginning to be occasionally applied to transfusion. The earlier recognition by various workers regarding inter-species incompatibility was resolved by the experiments of Dr Emile Ponfick who reported the dangers of transfusion between species in 1874 and Dr Landois who published details of the effects of cross-species experiments in 1875. This work finally put an end to the use of animal blood for transfusion. Ponfick was also the first to note that the dark urine produced, following what would now be recognised as an incompatible transfusion reaction, was in fact haemoglobinuria (and not haematuria as previously reported), resulting from the destruction of the donor red cells and not those of the recipient.

During the final quarter of the 19th century, frustration and discouragement with blood as a transfusion product resulted in a brief period of enthusiasm for the transfusion of milk, which was thought of as a 'blood substitute'. This form of treatment achieved its greatest popularity in the United States between 1873 and 1880, with the milk of cows, goats and humans being used. The most outspoken advocate of milk transfusions was T.G. Thomas, who was discouraged by the use of blood because of its *"tendency to coagulation"*. J.S. Prout supported Thomas and even postulated a medico-legal use for milk transfusion in that it might prolong life for a sufficient time to permit *"the victim of an assault to identify his assailant"*. By 1878, J.H. Britton, also writing in the *New York Medical Record*, predicted that transfusion using milk would entirely supersede transfusions of blood. However, by 1880 increasing numbers of adverse reactions associated with the administration of milk led to its general abandonment. A major contributing factor in the final decline of the use of animal blood and milk for transfusion must however have been the introduction, between 1875-1880 of physiological saline solution for infusion use, with its associated convenience and lack of danger to the recipient.

During the latter part of the 19th century, the Franco-Prussian war was raging in Europe and the possibility of using blood transfusions on the battlefield naturally came to the fore. The chief authority at the time was Dr Joseph Roussel, of Geneva, who had first used his method of direct arm-to-arm transfusion with success in 1865 for a patient with puerperal haemorrhage. The apparatus he used was described in the *Gazette des Hospitaux* in 1867 and later in various other publications, though Roussel complained in an article written in 1876 that the apparatus was *"insufficiently noticed"* and was not used as it might have been in the Franco-Prussian war.



Roussel's apparatus for direct transfusion (1876)[2]

Roussel rightly emphasised the importance of using only human and not animal blood for transfusion and claimed that his method was without danger either to the donor or the recipient. The basis of the transfusion technique was to place a glass vessel over the donor's arm, the apparatus was filled with water and a lancet (operated through the top of the vessel) then punctured the donor's vein. The operator, by means of a two-way tap, then rejected the water through one cannula and injected the blood into the recipient through a second cannula inserted in a vein. The motive power for the operation was supplied by means of compressing a rubber bulb between the two arms.

In 1867, Roussel claimed sixteen successful transfusions out of thirty-five performed for the treatment of a variety of conditions. In 1882, in Paris, he reported on a total of thirty 'complete successes' from sixty transfusions performed since 1865 in Switzerland, Austria, Russia, Belgium, England and France. Roussel's 'transfuseur' apparatus was subsequently officially adopted for use by the Austrian-Hungarian, Belgian and Russian armies, though there are no reports of it being used for battle casualties.

The dangers of infection (both local and systemic) relating to safe transfusion methods started to be resolved when in 1865 Louis Pasteur recognised that bacterial / fungal contamination causes putrefaction, and the work of Joseph Lister, who in 1867 discovered antiseptics. As a result, the sterilisation of instruments and antiseptic methods of working began to be introduced.

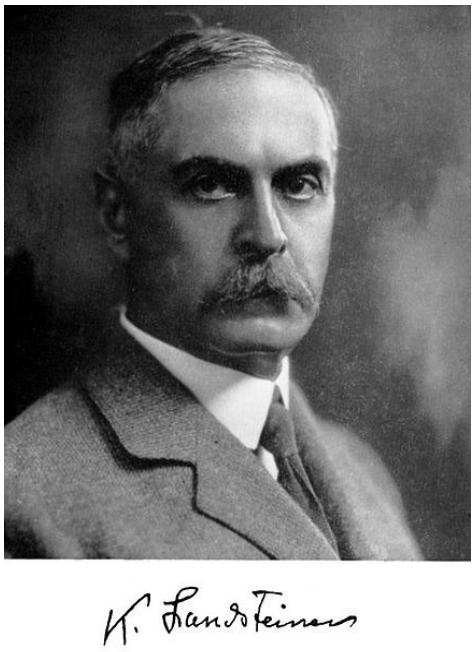
Throughout the 19th century, the main use of transfusion was however in the treatment of obstetric cases and in 1873 an enquiry was carried out by the Obstetrical Society of London into the merits of transfusion. The result was not very encouraging, recognising that due to its inherent dangers, the procedure was only used as a last resource. By the end of the 19th century, the practical use of blood transfusion was only slightly less primitive that it had been two and a half centuries earlier. The principle accomplishment during this period was the recognition, by the majority of people in the field of transfusion, of the inappropriateness of the use of animal blood for human transfusion. Beyond this fact, a number of major practical problems remained to be solved.

One of these was the number of severe reactions (graphically described in some reports) and even deaths of some patients, which followed the transfusion of not only animal but also human blood in some cases. These effects were for a long time attributed only to the introduction of air bubbles into the recipient's circulation. The discovery (in 1900) of the human ABO blood groups by Dr Karl Landsteiner in Vienna was the major step in understanding that these reactions were in fact due to what is now known to be blood group incompatibility (probably associated with intravascular haemolysis). It should be noted that many of the early transfusion experiments were performed using dogs, who do not have a major blood group system equivalent to the ABO system in humans and therefore did not produced these same (random) incidence of post-transfusion effects.

Landsteiner discovered the ABO blood group system by mixing the red cells and serum of himself and each of his colleagues. He demonstrated that the serum of some people agglutinated the red cells of others. From these early experiments he identified three groups, called A, B and C (C was later to be re-named O). The fourth much rarer blood group AB was discovered a year later. Landsteiner identified that most people had 'naturally occurring' antibodies in their serum that reacted with the antigens present on the red cells of a person of a different blood group. The presence of these antibodies, together with the variable frequencies of the different blood groups in European populations, identified why blood transfusion from one person to another had been so unpredictable, as receiving the "wrong ABO group blood" can be fatal.

For example, if a group O person receives red cells from a group A person, the antibodies present in their plasma will react with and destroy the donor red cells, releasing the haemoglobin out of the red cell into the person's circulation. If present in large amounts, the free haemoglobin is poisonous, possibly resulting in renal failure and

death. However, it wasn't until 1907 that an American surgeon Reuben Ottenberg suggested that it might be a good idea if both donor and recipient were ABO grouped before transfusion and their blood mixed in the laboratory ('crossmatched') to ensure compatibility. It is worth noting that the early animal experiments, which were invariably performed using dogs-to-dog transfusions, did not identify such transfusion reactions because dog red cells do not express blood group antigens equivalent to human ABO groups.



Karl Landsteiner (1868-1943)[1]

One of the other previously identified practical problems associated with blood transfusion was that of blood clotting (coagulation), which effectively meant that blood was transfused by direct techniques and could not be stored for even short periods. In 1915 Richard Lewisohn's research in the USA identified the optimum dose of sodium citrate needed to produce anticoagulation (though the anticoagulant effect of sodium citrate was also simultaneously and independently described by Albert Hustin in Belgium and Luis Agote in Argentina). Rous and Turner then described the use of a glucose additive as a red cell energy supplement to improve red cell preservation. These developments were given a major impetus by the tragic events of the 1st World War. But even so advances in the area of transfusion were relatively slow to develop. Dr Oswald Robertson reported transfusing only 20 casualties on 22 occasions during the Battle of Cambrai in November 1917, a somewhat small drop in a very large ocean.

Science and technological developments became more and more involved in the development of transfusion during the 20th century. The voluntary blood donor scheme was pioneered in London by Mr Percy Lane Oliver (1921) following a request of the Red Cross Service to provide two blood donors at short notice. The development of electrical refrigeration resulted shortly after in the first 'blood bank' being set up in Barcelona in 1936. In 1941 Dr Phillip Levine discovered the 'Rhesus' (now termed Rh) blood group system associated with the potentially fatal condition of Haemolytic Disease of the Foetus/Newborn. Many of the other major developments in transfusion medicine during the 20th century were given impetus by wars and major conflicts. Freeze dried plasma was developed in 1940, acid-citrate-dextrose (ACD) anticoagulant solution was developed for the storage of blood by Loutit and Mollison in 1943 and plasma fractionation was developed by Edwin Cohn in 1944, to be followed by the development of a method of freeze-drying plasma and of freezing red cells.

Current sophisticated methods for the collection, storage, processing and testing of blood required by the complex medical and surgical procedures of the present day are a long way from the early beginnings of drinking the blood of gladiators. However, it remains a fact that most of the important medical and scientific developments in transfusion have only been achieved in the last half of the 20th century and during the 21st century – but that is not the 'early history of blood transfusion'.

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3 Image from: National Library of Medicine – NIH (stated to be in the Public Domain)

References and additional information relating to the early history of blood transfusion can be found in:

Learoyd, P. (2012) The history of blood transfusion prior to the 20th century – Part 1. *Transfusion Medicine*, 22, 5, 308-314.
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