

A brief historical account of blood transfusion

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SUMMARY

Apart from the obvious - that people were weakened and often died following blood loss, the manipulation and use of blood originated from two concepts - 'bad blood' (which physicians tried to treat by bloodletting) and 'deficit of humor' (which was combated with blood drinking, bathing and infusion). Although in ancient times, there were accounts of 'transfer of blood' from one person to another, it was the discovery of blood circulation in the seventeenth century (which was swiftly followed by the development of intravenous infusion devices) that paved the way for practical attempts at intravenous blood infusion. The development of intravenous infusion devices facilitated many transfusion experiments evolving through animal-to-animal, animal-to-human then human-to-human. The many adverse outcomes associated with inter-species transfusion led to the prevalence of human-to-human blood transfusions. However, as well as the propensity of blood to clot, the poorly understood issues of selective compatibility of blood posed significant challenges to the establishment of transfusion as a routine medical procedure. This article presents the first of a two-part account of major milestones in blood transfusion, highlighting how ancient discoveries, observations, inventions and experiments have collectively overcome these challenges, allowing for blood transfusion to be established in modern medical practice.

EARLY ACCOUNTS OF BLOOD MANIPULATION AND TRANSFERENCE

Humans have, very long ago, identified the value of blood - the loss of blood was frequently associated with weakness and sustained or 'heavy' bleeding eventually led to death. The concepts of '*blood is life*' and '*blood and soul*' are reflections of the importance associated with blood.^{1,2} A reference to the high regard for blood is also available on the account of Publius Ovidius Naso (43BC - 18AD) who described how Medea (wife of Jason of the Argonauts) 'restored' her aged father-in-law's youthfulness by infusing his veins with elixir.³ In addition, Hippocratic theory of '*humorism*' stated that the body was filled with four fluids (blood, phlegm, yellow bile and black bile) which are 'balanced' in a healthy person, but a deficiency or excess of any would cause disease and disabilities.⁴ An example of the medical application of this theory (pioneered by Galen, 129 - 201AD) is the practice of bloodletting with the use of leeches to alleviate ailments such as 'excess blood' by restoring the balance between body fluids.⁵ The belief that physical and mental illnesses were caused by 'bad humours', and removal of which is expected to cure the patient allowed the practice of bloodletting by venesection and leeches to persist throughout the middle ages.^{6,7} Arabian physicians also attempted to treat diseases by venesection, leeching and cupping. Abu Al-Qasim Al-Zahwari (936 - 1013) gave descriptions of indications and procedures for cupping in his book '*Kitab al-Tasrif*'.⁸ On the other hand, early attempts to replace lost or replenish deficiency of blood involved the drinking-of or bathing-in a healthy person or animal's blood. Gaius Plinius Secundus (Pliny the Elder) who lived from AD23 to AD79 was said

to have given account of how spectators used to drink the blood of dying gladiators, on the belief that they would acquire the gladiator's attributes of strength and bravery by drinking their blood.⁹ Similarly, ancient Norwegians were reported to have drunk the blood of whales and seals as a treatment for scurvy and epilepsy, because they believed it to be a source of 'power'.⁹ There are also accounts of ancient Egyptian kings bathing in blood, on the belief that such act would resuscitate and rejuvenate the sick and the aged.⁹

The first recorded event of a deliberate blood transfer, as a medical procedure is available in ancient Hebrew accounts that Naam, King of Syria and leader of the armies of Bed-Adad, who was rid of his own, and infused with blood of another, in order to cure him of leprosy.¹⁰ Although, the authenticity of this transfusion-event is debatable,⁹ a more frequently reference event is the transfusion of Pope Innocent VIII (Giovanni Battista Cibo) who was reported to have been transfused in 1492. The Italian historian, Pasquale Villari (1827 - 1917) who provided this account stated that the Pope received blood from three 10-year old boys, one of whom was also transfused with the semi-comatose Pope's blood. The Pope's condition however did not improve, and eventually died, so did the three boys.¹¹ Some scholars contested the authenticity of this transfusion incident and suggested that the Pope could have drunk the blood instead,¹² the account however holds some logical conviction, as it is unlikely that a semi-comatose individual would be capable of swallowing.

THE UNDERSTANDING OF BLOOD CIRCULATION; A 'STEPPING STONE' FOR BLOOD TRANSFUSION

In 1628, William Harvey (1578 - 1657) described cardiac function,¹³ which, with the later work of Marcello Malpighi (1628 - 1694), led to the understanding of how the pumping the heart allows the flow of blood within vessels throughout the body.¹⁴ It should however be noted that there are a number of previous works in this area, for example, as early as AD923, Al-Akhawayni had described the pulmonary circulation in his book, '*Hidayat al-Muta'lemin fi al-Tibb*', which translates to 'A Scholar's Guide to Medicine'.¹⁵ Ibn Al-Nafis (1210 - 1288) had previously described the pulmonary and coronary transit of blood but this information was largely unknown in Europe.^{16,17} Also, Michael Servetus (1511 - 1553) and Realdo Colombo (1515 - 1559) were stated to have independently described pulmonary circulation in 1552¹⁸ and 1559¹⁹ respectively. This knowledge of blood circulation not only initiated the prospects of the infusion of potions, medications and blood, it also ushered in an era of the development of various devices, instruments or equipment to be used for these purposes.^{6,9}

EARLY ACCOUNTS OF BLOOD TRANSFUSION

Not long after Harvey's description of blood circulation, the idea of blood transfusion was suggested by Francis

Potter (1594 - 1678) in 1639.²⁰ Potter was said to have devised quills as needles and pipes as tubes for the purpose of blood transfusion and he attempted transfusing chickens using these devices but he was not satisfied with his achievement.²¹ In 1680, Francesco Folli (1624 - 1685) published a book that provided a description and instructions for use of a blood transfusion device.²² This device was described as a funnel that was connected to a cannula by a tube (fashioned from a goat's artery). The cannula itself was said to have been made of gold (or silver) and was for insertion into the patient's vein. Folli however clearly identified that he did not actually perform a procedure using the device.^{22, 23} In 1658, Robert des Gabets stated that Eloy Pichot had created an apparatus that consisted of two small silver tubes connected to a small leather pouch which could be used for blood transfusion.²⁴ In 1642 however, Georg von Wahrendorff was reported to have successfully injected various substances, including wine and medication into the veins of dogs using chicken bones.⁹ Jonathan Daniel Major (1634 - 1693) was said to have also achieved intravenous infusion of medication and even suggested that blood transfusion was possible, using his equipment which consisted of a silver cylinder with a cannula-like spout at the base, by ejecting the contents into the recipient with the aid of a piston.⁹ In 1656, Christopher Wren (1632 - 1723) also developed and successfully used a device made out of animal bladder, to which two quills were attached, for intravenous administration of medication into the bloodstream of a dog.²⁵ Wren's work was continued by Richard Boyle in 1663. Boyle's experimentation of injecting substances into dogs was witnessed by members of the Royal Society (London), including Richard Lower, who also participated in the procedures.²⁶

Subsequently, there were a series of attempts to perform blood transfusion in animals. Notable among these, and probably the established claim for the first successful animal-to-animal blood transfusion, was the work of Richard Lower, in 1665 in England.²⁶ Lower's account of artery-to-vein transfusion of one dog to another was also credited to be the first to define the appropriateness of blood transfusion.⁹ Lower's success stimulated a series of experiments which later led to animal-to-human blood transfusion. In 1667, Lower and Edmund King transfused a human with blood of a sheep.^{26, 27} Samuel Pepys, who recorded the event made mention of the quills and silver pipes that were used to convey blood from the carotid artery of the sheep to a vein in the man's arm.²⁷ In the same year in France, Jean-Baptiste Denys and Paul Emmerez had also performed dog-to-dog and sheep-to-man transfusions.^{28, 29} However, one of their works resulted in what can today, be called inter-species incompatibility, but the recipient survived. Several months later, Denys and Emmerez transfused the same patient again, although the transfusion session was uneventful (apart from stopping the transfusion mid-way due to 'poor flow of blood'), the recipient died in the following evening.⁹ This could be a result of a haemolytic reaction, following sensitisation from previous transfusions, but a court exonerated Denys on the grounds that the recipient had died as a result of poisoning instead.⁹ This incident led to the French Parliamentary and Papal prohibition of transfusion in 1678 and 1679 respectively.³⁰ These

probably resulted in the collapse of interests in the field of blood transfusion.

As seen so far, the animal-to-human blood transfusions given in the accounts were not performed for the purpose of treating blood loss, rather they were based on the concepts of transferring vigour, personality or treating symptoms of physical or mental unwellness. In 1749 however, a recommendation was made to perform blood transfusion in dire situations such as severe blood loss.³¹ This recommendation, and the work of James Blundell (1790 - 1877) re-ignited experiments in blood transfusion. Blundell was an obstetrician whose interest in transfusion originated from his desire to treat postpartum haemorrhage. He successfully exsanguinated and revived dogs by transfusion from other dogs.³² During his experiments, he also identified the dangers of inter-species blood transfusion, this made him pursue human-to-human blood transfusion. For this reason, Blundell is regarded as the 'father of modern blood transfusion'.³² It must however be known that Blundell's work was influenced by John Henry Leacock's manuscript on the subject of transfusion, which also contained arguments to discourage the mixing of blood from different species.³³ In fact, Leacock should be credited for recognising what is today known as 'risk-benefit assessment' of blood transfusion. Leacock's concluding remarks of his 1817 dissertation state "The consequences of haemorrhages where the functions are not dangerously affected, do not of course, require transfusion, since other remedies will suffice...". He also recommended that the 'other remedies' should be considered before having recourse to the 'last hope' (i.e. blood transfusion).^{9, 33}

Although the first human-to-human blood transfusion is said to have been carried out in Philadelphia by Syng Physick in 1795,³³ a more popular record states that, on 22nd December 1818, in England, Blundell successfully performed human blood transfusion.³² Within 11 years, Blundell and colleagues carried-out ten additional human blood transfusions. Although not all of these were successful, some deaths could have been the result of circumstances other than transfusion. However, Blundell gave an account of patients suffering fever, head and back ache and passing dark urine.^{9, 32} These clinical observations would, today suggest a haemolytic transfusion event. Human blood transfusions in other parts of the world happened soon after. Andrei Martynovich Wolff performed human-to-human blood transfusion in Russia in 1832,³⁴ while in 1849, New Mexico, William Hammond is said to have transfused soldiers.³⁵

EARLY ATTEMPTS TO ESTABLISH TRANSFUSION DEVICES AND PROCEDURES

During Blundell's experiments, he was challenged with the impracticability of vein-to-vein transfusion due to blood clotting, but he had observed that using a direct method of transfusing blood from donor's artery to recipient's vein did not have this problem.³² Blundell's initial transfusions were achieved by an indirect approach of using needle and syringe to withdraw blood from a donor's vein and immediately injecting it into the recipient's vein. In

addition to avoiding blood clots, Blundell also pointed out the necessity of expelling air from the syringe before transfusion³⁶ - what would today be described as avoiding air embolism. Another transfusion device called an 'impeller' was described by Blundell in 1829. The device comprised of a funnel and a pump which was used by allowing the donor's blood to flow into the funnel (which was enclosed in a jacket containing warm water - to 'keep the blood in a fluid state'). The action of the pump would force the blood along a tube then into a cannula which is inserted into the recipient's vein.³⁷ Blundell later invented a variant of the impeller, called the 'gravitator', the difference being that gravitational force was employed for blood flow, rather than the use of a springed-pump.³⁷ Samuel Armstrong Lane, in 1840, used a modified syringe that comprised of a three-way valve and a funnel to collect blood from the vein of a donor and transfer into the vein of the patient with haemophilia.³⁸ Routh (1849) was able to achieve transfusion by allowing blood to flow from the donor's vein directly into a receptacle (sort of a basin) and from this, a syringe was used to collect blood for injection into the recipient's vein.³⁹

Although indirect methods of blood transfusion were gaining popularity, Roussel's direct arm-to-arm technique for transfusion was recorded in 1865. This technique involved the use of a device called the 'transfuseur', which was a water-filled vessel attached with two-way cannula and pump. The donor's vein was punctured with a lancet and one cannula was inserted. By using a pump (attached to a tubing on the vessel) to 'eject the water' via one cannula, blood would flow from the donor into the cannula that was inserted into the vein of the recipient.²² In an 1873 article, J.H. Aveling was said to have designed a direct method of transfusion by using a device that consisted of rubber tubing with a bulb in the middle. The central bulb functioned as an 'auxiliary heart'. The device was also described to be portable enough for carrying about in the 'pocket'. In fact, it was recorded that Aveling used the device to transfuse a 21 year old woman who suffered postpartum blood loss.⁴⁰

In an attempt to bypass the problem of the clotting of donated blood, prior to transfusion, Alexis Carrel (1873 - 1948) developed a surgical technique that involved the anastomosis of donor's artery to the vein of the recipient. This technique permitted 'larger' quantities of blood to be transfused without clotting, but it required the presence of a donor and, as it was difficult to determine how much blood had passed from donor to recipient,

the donors often became hypotensive and the recipients showed signs of what is today known as transfusion-associated circulatory overload.⁴¹ Additionally, there was the challenge of transfusion-associated infections, but after the identification of microbial contamination as the cause of putrefaction by Louis Pasteur in 1865, antiseptic techniques began to be introduced, notable among these was the 1867- work of Joseph Lister who used antiseptics to control transfusion-related infection.^{42, 43} An alternative approach to resolving the issue of blood clotting was the use of defibrinated blood. This technique involved collecting blood into a vessel and made to clot. The fluid that remains after the clot is removed is then used for transfusion. However, this method involved a series of stirring procedures, using non-sterile equipment such as wire egg-beater, hair-sieve, glass syringe, aspiration cannula and various vessels. All these contributed to the microbial contamination of blood.⁶ In addition to the accounts of the early observation of James Lacy who was said to have made blood incoagulable in 1722 by mixing it with black bohea tea, various chemicals such as oxalic acid, bicarbonate of sodium and sodium phosphate had been investigated as candidates for the prevention of blood coagulation, but there were concerns of poisoning.⁴⁴ Braxton Hicks (1823 - 1897) had in 1868 campaigned for the use of chemicals as anti-clotting agents of blood and, on the recommendation of Frederick William Pavy (1829 - 1911), who had also been experimenting to anticoagulate blood with sulphate of soda,⁴⁵ Hicks conducted human transfusions using phosphates of soda as anticoagulant in 1869.⁴⁴ The transfusion of phosphate-anticoagulated blood was adopted in Edinburgh from 1883 to 1892. However, adverse outcomes such as patient's fainting, development of rigors, acute back pain, fever and death were attributed to the use of 'incorrect quantities' of the anticoagulant.⁴⁶ These observations, in coincidence with the introduction of more readily available saline infusions in 1980 led to a fall of interest in blood transfusion.^{47, 48} However, later, in 1915 sodium citrate was devised as a safe and effective means to achieve anticoagulation.⁴⁹ The second part of this article reviews the safety aspects of the development of blood transfusion.

REFERENCES on request from author

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ANY CHILD WHO:

- 1 Is breathing very fast
- 2 Has a 'fit' or convulsion
- 3 Looks mottled, bluish, or pale
- 4 Has a rash that does not fade when you press it
- 5 Is very lethargic or difficult to wake
- 6 Feels abnormally cold to touch

MIGHT HAVE SEPSIS
Call 999 and ask: could it be sepsis?

The UK Sepsis Trust registered charity number (England & Wales) 1158043

ANY CHILD UNDER 5 WHO:

- 1 Is not feeding
- 2 Is vomiting repeatedly
- 3 Hasn't had a wee or wet nappy for 12 hours

MIGHT HAVE SEPSIS
If you're worried they're deteriorating call 111 or see your GP.

JUST ASK
"COULD IT BE SEPSIS?"
IT'S A SIMPLE QUESTION, BUT IT COULD SAVE A LIFE.