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Contents lists available at ScienceDirect

Transfusion and Apheresis Science

journal homepage: www.elsevier.com/locate/transci

Review

Transfusion – Whence and why



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ARTICLE INFO

Keywords:

Blood transfusion
History
Paradigm shift
Blood conservation
Patient blood management

ABSTRACT

The past is prologue. Reviewing the history of transfusion tells us how far we have come, but also where we need to go. The past has been filled with innovation and important discoveries, but is also fraught with stumbling blocks and unintended side effects. Although much has been achieved and transfusion is safer today than ever, nonetheless we are recognizing new potential concerns with transfusion and we are undergoing a paradigm shift in our attitudes, approach and patient management in regard to blood transfusion.

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- Patients think blood transfusion is special and beneficial, but have difficulty accepting small risks they cannot control.
- Blood donors believe their contribution is a gift to the community that will be used appropriately and safely.
- Clinicians think blood is ordinary, take blood transfusion for granted, benefit is assumed and risks regarded as minimal.
- Governments view blood as a commodity and transfusion medicine as an expensive support service which should be regulated and funded in a cost-effective manner (James Isbister).

The patron saint of blood transfusion is St Januarius (St Gennaro), a bishop of Benventum in southern Italy, who was beheaded in 305 for refusing to worship pagan gods. Vials of his blood and his head were put in the Cathedral at Naples in 1497 and it is said that these resulted in mirac-

ulous deliverance from eruptions of the nearby volcano of Vesuvius (e.g. 1631 and 1707). On his feast days, these relics are examined. The congealed blood may liquify, 'boil' & re-solidify and this may occur as much as 18 times during the year when exposed and put near his head. Hence he became the patron saint of blood transfusion.

An early mention of 'transfusion/infusion' is from Ovid's metamorphoses (seventh book) in 43 BCE, when Jason pleaded that Medea restore the youth of his father, King Aeson. "*Medea took her unsheaved knife and cut the old man's throat, letting all of his old blood out of him. She filled his veins with a rich elixir, which he received through his lips and wound. His beard and hair, no longer white with age, turned quickly to their natural vigour, dark and lustrous; and his wasted form renewed, appeared in all the vigour of bright youth*". What did Medea use? A mixture of "root herbs, seeds and flowers, strong juices and pebbles from the farthest shores of oceans east and west, hoarfrost taken at full of moon, a hoot owl's wings and flesh, a werewolf's entrails, the fillet of a snake, the liver of a stag, and the eggs and head of a crow which had been alive for nine centuries". We have come a little way since then (although perhaps not as far as we think).

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The Bible tells us about blood, e.g. Leviticus 17:11 “*the life/soul of the flesh is in the blood*”, and Matthew 26:28 “*...take drink...this is my blood, which is shed for you ...*”. In China, 1000 BCE, it was believed that the soul is contained in the blood. Egyptian kings and the Romans (taurobolium) bathed in blood. Pliny described Romans drinking the blood of gladiators to gain strength and to cure epilepsy. Galen advised drinking the blood of a weasel or a dog for rabies and ancient Norwegians drank seal and whale blood for epilepsy and scurvy [1]. Of the drinking of blood, the 13th century Italian physician Pietro di Abano said: “*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 bathe in tepid water & to copulate with girls according to the law natural, and to play with pretty girls & young boys; and ... to eat serpents whose heads & tails have been cut off with the edge of a palm frond*” [1].

Often stated as the first transfusion, in 1492, the aging Pope Innocent VIII is said to have received a transfusion of the blood of three 10-year old boys, each of whom was paid a ducat and all of whom died [2,3]. The Pope died, the donors died, and the physician fled the country. Probably the blood was intended to be taken orally. Indeed, there is no reliable evidence that the sickly pope accepted the blood at all. This story has been told and retold over the last half millennium. It is most likely apocryphal and has the flavor of an early legend in its details and its antisemitic and anti-catholic overtones [4].

There followed a 150-year near-complete hiatus in transfusion work, but, in 1615, Libavius advocated transfusion, but is not known to have actually done one. He said: “*Let there be a young man, robust, full of spirituous blood, and also an old man, thin, emaciated, his strength exhausted ... open the artery of the young man, and put it into one of the tubes, fastening it in ... immediately after open the artery of the old man, ... then the two tubes being joined together, the hot and spirituous blood of the young man will pour into the old one as it were from a fountain of life, and all of his weakness will be dispelled. Now, in order that the young man may not suffer from weakness, to him is given good care and food, but to the doctor, hellebore*” (hellebore: a plant causing violent vomiting, diarrhea, vertigo, etc.) – it is not easy to be a doctor, but even today, the donors are provided with juice and a biscuit.

In the 17th, many infusion experiments performed e.g. by Christopher Wren and Robert Boyle. These included intravenous wine, beer, opium, emetics, water, nitric acid, and sulfuric acid. Understanding the concept of circulation (Harvey 1613) was, however, critical to developing the reality of blood transfusion and Richard Lower, in Oxford, is credited with performing, in 1665, the first authentic blood transfusion (animal to animal). He kept exsanguinated dogs alive by connecting the carotid artery of the donor dog to the jugular vein of the recipient dog with a quill. He was preceded by six months in his first human transfusion by Jean-Baptiste Denis in Paris [5]. Denis was a young physician of Louis XIV who said he preferred animal (rather than human) blood for his experiments, as he believed it less likely “to be rendered impure by passion or vice”. Denis and Emmerez performed a transfusion of lamb

blood into a young woman in June 1667. Denis’ 4th transfusion recipient suffered from syphilitic madness and it was thought that the tranquil blood of an animal might alleviate his symptoms. After a symptom-free transfusion of calf blood, he was again transfused 3 days later, giving rise to the first description of a hemolytic transfusion reaction: “*As soon as the blood began to enter into his veins, he felt ... heat along his arm and under his arm-pits ... his pulse rose ... we observed a plentiful sweat over all his face ... he complained of a great pain in his kidneys, and that he was not well in the stomach, and that he was ready to choke ... he vomited of bacon and fat ... he found himself urged to urinate and asked to go to stool ... when he awakened ... a general lassitude he felt in all his limbs ... he made a great glass full of urine, of a color as black as if it had been mixed with soot of chimney ... bled at the nose very plentifully ... his urine cleared up and after ... resumed little by little its natural color*”. He improved, however, so another transfusion was done, which proved fatal. The patient’s wife then charged Denis with poisoning her husband. Denis was exonerated (and the wife was charged with poisoning her husband!), but this incident led to prohibition of blood transfusions: in 1678 by the French Parliament, in 1678 by the British Royal Society, and in 1679 by the Vatican, and, again, a 150-year near-complete hiatus in transfusion work followed. The importance of Lower, however, is that he was the first to define the appropriateness of transfusional replacement of blood in severe hemorrhage; this was in marked contrast to the standard cure-all treatment of the day, phlebotomization.

In the 18th century transfusions were done only sporadically; generally animal to human. They were thought of as a cure for mental aberration or as a youth potion for the aged, rather than treatment for blood loss. Reciprocal transfusions between husband and wife were suggested as a cure for marital discord. Blood was thought to carry characteristics of the donor to the recipient: sheep blood would make a dog grow wool, hooves and horns; and cat blood would make a girl feline, etc [1].

In 1818, James Blundell (obstetrician, Guy’s Hospital, in London) attempted human-to-human transfusion. He preferred human donors, because “*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 better suited for the purpose, but then it has not been taught to walk properly up the stairs.*” Between 1825 and 1830 he performed 10 transfusions, five beneficial, and he stated: “*The fact that life may be saved by transfusion of blood into the veins will be beneficial a thousand years hence as it is on this day*” [6]. And blood could indeed be ‘good stuff’. Following transfusion of a woman with post-partum hemorrhage with her husband’s blood ... after six ounces had been administered, the woman, previously semicomatose, suddenly exclaimed “*By Jesus, I feel as strong as a bull*” [7].

However, it was not without danger and in 1849 Routh reviewed all reported transfusion patients to that date. There were 48 cases, of which 18 had had a fatal outcome, which he estimated was a mortality “*rather less than that of hernia, or about the same as the average amputation*” [8].

Transfusions in the 1800s were plagued by complications. Panum and Landois showed that same species trans-

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