Medicina Historica 2023; Vol. 7, N. 3: e2023049

History of the first organ transplant: Blood transfusions

Karidia Karaboue
University of Campania "Luigi Vanvitelli", Naples, Italy

Abstract. The term transplantation refers to various situations which differ in the type of biological material involved, how it is performed and the type of donor. We usually refer to the experience of transplantation in terms of a gift that one person donates to another: the risk, however, is that this concept is used automatically, uncritically, without any prior reflection on its characteristics. The origins and development of the first type of transplantation are found in blood transfusions, and there were numerous scientific discoveries and technical innovations at the turn of the 19th and 20th centuries which enabled transfusions to become an established practice. The common thread running through this analysis is the figure of the blood donor, initially flanked by that of the paid donor, and only since 1990 recognised as the sole legitimate source of blood and its components.

Key words: blood transfusions, transplantation

Introduction

It is complicated to reconstruct the exact chronology of events that make up the history of blood transfusion, much as it is equally difficult to establish who the first person was to come up with the idea of transfusing blood from one individual to another and subsequently put this into practice. Within this uncertain history, however, it is possible to identify a crucial event after which the first transfusion attempts were to begin: the discovery and accurate description of the human circulatory system by William Harvey (Figure 1) in 1628. Before this discovery, there was abundant evidence of the use of blood during rituals and celebrations in various cultures and religions. For example, in Mesopotamia and Ancient Greece, the blood of sacrificial victims was offered to the gods or used during divinatory practices to read the outcome of battles or the development of events (1). In the Bible, blood is regarded as a means of purification and atonement for sins, and in the New Testament the blood of Christ, shed to atone for the sins of the world, became a symbol of the covenant between God and humanity. Various sources also report that blood was used for medical purposes: for example, in Ovid's Metamorphoses (1st century B.C.), to rejuvenate old Heson, Medea cuts his throat in order to remove the old blood; Hippocrates (390 BC) (2), Celsus (c. 60 A.D.) and Tertullian (c. 150 AD) refer to the use of blood as a medicine. These accounts show how blood has always been associated with an individual's vitality, strength and vigour while lack of blood in the body implies weakness and, in some cases, death (3). In the Old Testament, for example, there were references to the life-giving properties of blood: "Of your blood indeed, that is, of your life, I will require account (4). The life of every living thing is its blood since it is life; and I said to the children of Israel: you shall not eat the blood of any living thing, for the life of every living thing is its blood, and whosoever eats of it shall be cut off (5)". Due to this, blood was believed to have properties (6) which meant it could determine not only physical characteristics but also those of character and temperament, a feature we still find today in a number of commonly used expressions such as 'good blood?, 'bitter blood', and 'blue blood' (7). For this reason, it was customary to cleanse one's skin or ingest the blood of strong and vigorous people to acquire these characteristics. According to Pliny the Elder (23 A.D. - 79 A.D.), spectators in the arena habitually drank the blood of dying gladiators to become similar to them (8).

In the ‘humoral’ theory of Hippocrates, adopted and modified by Galen in the 2nd century A.D., blood was considered one of the fundamental elements of the body, along with phlegm, yellow bile and black bile: a balance of these four elements was understood as a good mixture (eucrasia) and ensured an individual’s health. At the same time, an excess or deficiency of one of these affected character and physical health. On this basis, Galen justified the idea of bleeding out poor blood, performed through bloodletting and applying leeches to the skin. These practices remained in use until the 19th century (9). In none of these testimonies does the idea of transfusing blood from one person to another seem to have been considered, at least until 1492, the year that is generally referred as that of the first ever transfusion. According to reports by Pasquale Villari (1827-1917), the recipient was the old Pope Innocent VIII, afflicted with an illness that had reduced him to a semi-comatose state, but was treated with the transfusion of blood from three young boys of about ten years of age. According to Villari’s testimony, all three transfusions were unsuccessful and the boys and the Pope died shortly afterwards. Numerous doubts surround this episode, which has not surprisingly been the subject of much controversy and debate among historians as it is implausible that a transfusion could have been carried out in complete ignorance of the existence of blood circulation. What seems more likely, however, is that the term ‘transfusion’ was misused, perhaps due to a mistranslation of the Pope’s illness. For more reliable evidence, it is necessary to refer to the 17th century: as mentioned, 1628 represented a turning point in the history of blood transfusions (Figure 2). In his work from that year entitled *De Motu Cordis* (Figure 3)

Figure 1. Portrait of William Harvey (1578–1657), the English physician who revolutionized the understanding of human anatomy and circulation. His work laid the foundational basis for modern prenatal diagnosis.

Figure 2. 17th-century illustration depicting an early experiment in blood transfusion, using the blood of a dog to attempt a medical procedure on a human, a practice that paved the way for modern transfusion medicine.

Figure 3. A page from ‘De Motu Cordis’ by William Harvey, published in 1628, showcasing his groundbreaking research on blood circulation, which laid the groundwork for modern medical science.

William Harvey detailed the way blood flows through the body: it is pumped from the heart within a system of channels (veins and arteries) in one direction only, thanks to the presence of special valves that prevent reflux. In addition, Harvey demonstrated that the pumped blood is not entirely consumed by the body to be replaced by new blood but returns to the heart itself, i.e. it circulates (Figures 4, 5, 6). This discovery was of great importance: the fact that blood moved in a circular direction made it possible to infuse medicines or other substances that would reach the whole body through the bloodstream (10). The leap would have been short from here to the idea of 'transferring' blood from one individual to another. It is virtually impossible to establish who the first person was to develop the idea of performing a transfusion, although there are various descriptions after 1628 of the procedure and instruments needed to perform it. In that year, Richard Lower, a member of the Royal Society, carried out the first homologous transfusion, i.e. between individuals of the same species: it involved two dogs, one of which, bleeding to death, was saved by transfusing blood from the other animal. Lower carried out numerous additional experiments on dogs and went so far as to perform repeated transfusions of sheep's blood on a man, Arthur Coga. Despite the probable inauspicious outcomes, Lower's experiments gave rise to many other European transfusion attempts. These, too, were unsuccessful, as most transfusions were indiscriminately carried out between individuals of different species, initially only between animals and later from animals to humans (11). In France during the same period one of

Figure 4. Engraving of William Harvey presenting his discovery of the circulatory system to a group of physicians, a seminal moment in medical history that redefined our understanding of human biology.

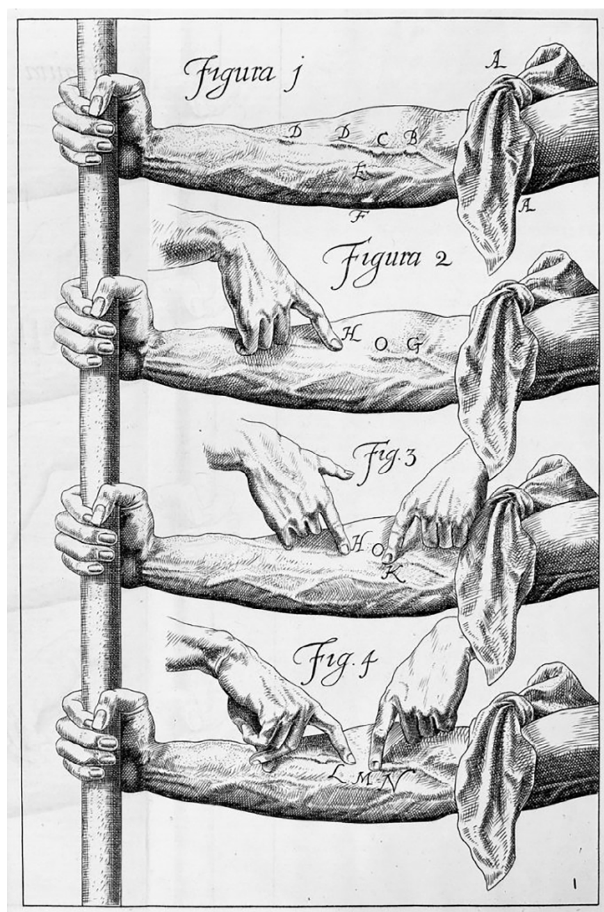

Figure 5. Depiction of William Harvey's experiments demonstrating the mechanics of venous valves, from his influential work 'Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus'.

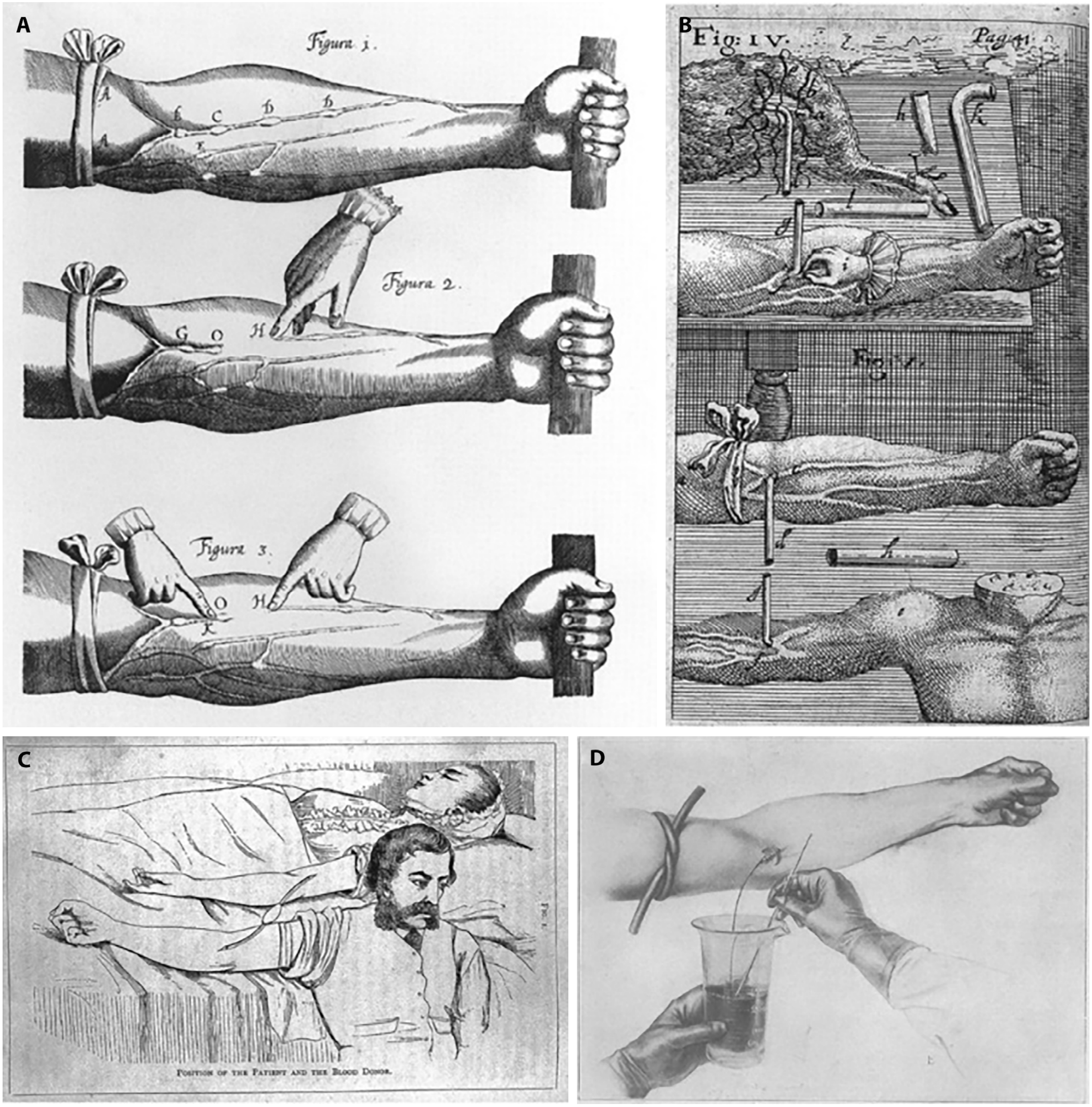

Figure 6. Series of illustrations depicting the progression of William Harvey's experiments on the circulation of blood and the function of veins, crucial to the understanding of human anatomy and physiology.

King Louis XIV's doctors, Jean-Baptiste Denys, performed several transfusions attempts on dogs before attempting the procedure on a 15-year-old boy. Again, the transfusion was performed using animal blood, specifically that of a lamb.

Denis stated that he preferred animal blood because it was 'less likely to be rendered impure by passions or vices than human blood': the old idea that blood conveyed an individual's temperament or strength was still firmly established. It is no coincidence that in 1667 Denys performed repeated transfusions on a man named Anthony Mauroy, who suffered from an unspecified madness. He used the blood of a calf, an animal considered to be calm, so that its mild disposition could appease the man's spirit. It is worth pausing briefly to consider the case of Mauroy: it has acquired specific historical importance since, due to its nefarious consequences, it was in all probability the last transfusion attempts to be carried out for at least one hundred and fifty years. Mauroy died following one of the transfusions he had undergone, which had not cured his madness. The members of the Paris Faculty of Medicine and the majority of doctors of the time believed that the only acceptable practice was still bloodletting and exploited Mauroy's death to condemn transfusions and those who practised them. Blood transfusions were still considered an experimental practice with too uncertain a consequence, and Denys himself, who had dedicated himself vigorously to the practice, used to subject his experimental patients to bloodletting before the transfusion (12). It was later discovered that Mauroy's death had not been caused by repeated transfusions but by cyanide poisoning caused by his wife, yet the ban on transfusions ordered by the Parisian Faculty of Medicine did not lapse. It was rendered official by a measure issued by the French Parliament in 1678 and adopted shortly afterwards by the Royal Society in England and the Papal Court. This measure decreed the abandonment of experiments on transfusions and the study of circulation physiology (13) for over a century and a half. The studies and experiments of an English obstetrician named James Blundell renewed interest in the practice of transfusion. Two significant milestones can be attributed to Blundell: the first is that he paved the way for the revival of transfusion studies within a cultural context (14) where it was still viewed with suspicion. The second is that he recognised the danger of heterologous transfusion (15) (i.e., between individuals belonging to two different species) and decided to abandon the use of animal blood in transfusions on humans. Blundell used to perform transfusions with an instrument of his invention named the Impellor, which consisted of a combination of a funnel and a pump: extracted blood was collected in its funnel and subsequently pushed through the pump into a syringe, which was inserted into the patient's vein (16). The impellor was designed to be fixed to the back of a chair, thus forcing the blood donor to remain seated at the patient's side for the duration of the transfusion. Although it was an impractical tool, Blundell and his colleagues used it in an attempt to overcome a problem that made any transfusion difficult, namely that of blood coagulation. The funnel was surrounded by two outer membranes, in one of which hot water was collected, necessary to keep the blood fluid and thus prevent clots from forming. This solution only delayed clotting for a short time: a definitive remedy would only be discovered a century later. Despite the renewed interest in the topic, the practice of transfusion continued to be a rare occurrence. Blundell regarded the procedure as a last hope i.e., treatment to be used exclusively on patients in a desperate condition (for example, in cases of post-partum haemorrhage) and no longer as a means of curing insane temperaments. Bloodletting remained the standard treatment for all kinds of illnesses, along with leeches, which were applied to the skin of both the blood donor and the recipient to prevent inflammation of the veins.

Between the second half of the 19th and the beginning of the 20th century, important discoveries meant that it was possible to overcome those obstacles that prevented transfusions from establishing themselves as a valid form of treatment. First and foremost, Louis Pasteur's discoveries on bacterial contamination (1865) contributed to the introduction, albeit gradual, of instrument sterilisation and other antiseptic methods and in general to greater focus on the risk of infection during transfusion.

Another critical success was reported in 1894 when Sir A. E. Wright demonstrated that soluble salts of certain acids could delay blood clotting indefinitely, although at least twenty years were to pass before this discovery was put into practice. This period also represented a turning point in understanding interspecific incompatibility, mainly due to the studies of Emile Ponfick (Figure 7) and Leonard Landois. They both noticed that upon contact with human serum the red blood cells of animal blood underwent lysis i.e., were destroyed and then eliminated through the urine of the recipients (a phenomenon termed 'haemoglobinuria'). On the one hand, this explained the side effects often found in heterologous transfusions, such as dyspnoea, cyanosis, vomiting, convulsions and kidney congestion (17); on the other hand, it provided a scientific justification for the impracticability of this type of

Figure 7. Portrait of Emil Ponfick (1844–1913), a renowned German pathologist who made significant contributions to the study of blood diseases and transfusion medicine.

transfusion, which was soon abandoned (18). Ponfick and Landois' studies did not explain why homologous human-to-human transfusions could also have dangerous or fatal consequences. This problem was solved at the beginning of the 20th century when, in 1900 Karl Landsteiner (Figure 8) discovered and demonstrated that one person's serum could agglutinate another's red blood cells, leading to the formation of clots. This did not happen due to disease as had been believed up to then, but because of specific proteins, the A and B antigens, present on the membranes of the red blood cells (19) of different individuals. Landsteiner showed that the presence or absence of these antigens (20) differentiated human blood into three different groups (which he called A, B and 0) and the possibility of 'interaction' between these groups and thus the success of the transfusion depended on it (21-25). In 1902, von Decastello and Sturli discovered the existence of

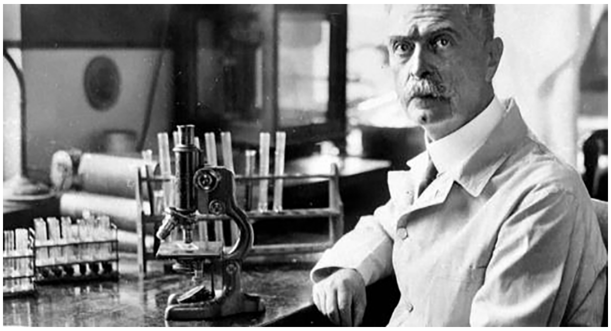

Figure 8. Karl Landsteiner (1868–1943), Austrian biologist and physician, in his laboratory. Landsteiner's pioneering work in identifying the major blood groups laid the foundation for safe blood transfusions.

a fourth group which Landsteiner had not noticed (A.B.) (Figure 9) the least common of all. Several years later, in 1908, Ottenberg and Epstein discovered that, like other traits, blood groups are heritable according to Mendel's laws. During the First World War, discoveries concerning the anti-coagulant properties of sodium citrate began to be applied in field hospitals, with a vital consequence: the possibility of delaying blood clotting made it possible to separate the collection and transfusion phases in both space and time. In short, blood could be collected, stored in natural banks, and transfused later without forcing the donor and recipient to be present simultaneously. During World War I and World War II, blood transfusions became critically important in military medicine and the treatment of wounded soldiers. In World War I, the innovation of sodium citrate as an anticoagulant by Richard Lewisohn transformed the feasibility of blood transfusion in field conditions, saving countless lives on the frontlines. This advancement was hailed by contemporary physicians as revolutionary, likened to 'stopping the sun' (26). World War II witnessed an exponential increase in the demand for blood, prompting widespread donation campaigns (27, 28) where millions of units of blood were donated, particularly in the United States and the United Kingdom (29). The establishment of blood banks and the refinement of methods for blood preservation and transportation played a pivotal role in supporting the war efforts (30). However, transfusions during this period were not without risks, as issues related to blood compatibility and transfusion safety were not yet fully resolved (Figure 10) (31, 32).

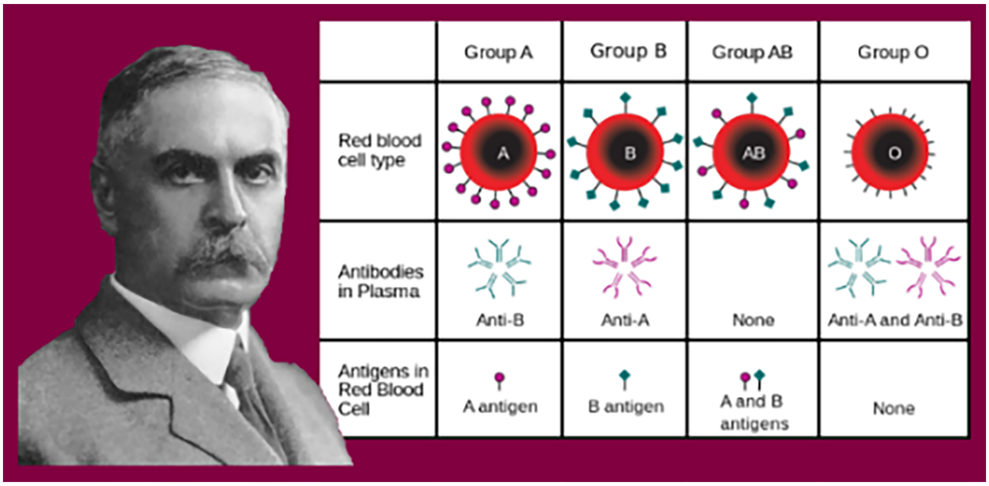

Figure 9. Karl Landsteiner, depicted alongside his groundbreaking discovery of the ABO blood group system, which revolutionized medical transfusions and won him the Nobel Prize in Physiology or Medicine in 1930.

Figure 10. A medic administers a blood transfusion to a soldier during World War II, a poignant reminder of the critical role that medical intervention plays in times of war, and the beginnings of mobile medical units in combat zones.

In addition to the advancements during the World Wars, the Spanish Civil War (1936-1939) also saw significant developments in the field of blood transfusion, spearheaded by notable figures such as Hervás Moncho, Elósegui Sarasoga, and Durán Jordá. These medical professionals played a pivotal role in establishing mobile blood transfusion services, which were crucial in treating wounded soldiers rapidly on the battlefield. Their innovative approach in setting up these mobile units marked a significant advancement in wartime medical care and highlighted the growing importance of blood transfusions in saving lives during armed conflicts.

Furthermore, the Soviet Union also made notable strides in the field of blood transfusion, particularly through the work of Sergei Yudin. Yudin's contributions were groundbreaking, as he developed techniques for blood transfusion that were used on both sides of the Soviet Union during its internal and external conflicts. His work not only saved countless lives but also paved the way for future research and development in blood transfusion and storage techniques. The efforts of these individuals during the Spanish Civil War and in the Soviet Union underscore the global impact and evolution of blood transfusion practices during the tumultuous times of the early 20th century.

Conclusion

Bernard Fantus created the first blood bank in Chicago in the 1930s, but a decisive development came in the 1950s thanks to the discovery and use of multiple plastic bags by Carl Walter. These were more practical and advantageous than glass bottles as they allowed blood to be collected in a closed system which avoided contact with air and were thus more antiseptic.

In addition, this facilitated the separation and collection of blood components (platelets, white blood cells, red blood cells and plasma). This led to both the development of targeted therapies, where each patient was transfused with only what he or she needed, and the possibility of multiple transfusions from a single blood sample. In addition to these discoveries, more recent developments from the second half of the 20th century included the discovery of the Rh factor of red blood cells (1940, Landsteiner and Wiener); the HLA system of white blood cells (1954, Dausset et al.), a fundamental discovery for bone marrow transplants; the introduction of the use of liquid plasma and the discovery and development of methods for fractioning plasma proteins (22, 33-35) (1940s); the introduction of ACD solution, which allowed blood to be stored for up to 21 days (1943) and the most recent discoveries in the field of haemopoietic (23, 36) stem cell storage from peripheral and cord blood (1990s). As a result of these breakthrough discoveries and the development of regulations governing the collection and use of blood and blood components, transfusion became a key procedure during the 20th century in surgery, the treatment of oncological and haematological diseases (including haemophilia, anaemia, thalassaemia) and in transplantation and first aid (23, 37).

References

1. Zonza M. Breve storia delle pratiche trasfusionali e della donazione di sangue. La donazione in Italia, Milano: Springer; 2011.
2. Greenwalt TJ. A Short History of Transfusion Medicine. Transfusion 1997; 37(5):550–63.
3. Bernetti A, La Russa R, De Sire A, et al. Cervical Spine Manipulations: Role of Diagnostic Procedures, Effectiveness, and Safety from a Rehabilitation and Forensic Medicine Perspective: A Systematic Review. Diagnostics (Basel) 2022; 12(5):1056.
4. Genesi 9,5, La Bibbia, Milano: Edizioni Paoline; 1987.
5. Levitico 17, 14, La Bibbia, Milano: Edizioni Paoline; 1987.
6. El Ghouzzi MH, Rebibo D. Blood transfusion and residual risk. Rev Francoph Lab 2010; 426:79–83.
7. Karaboue MAA, Ferrara M, Bertozzi G, et al. To vaccinate or not: literacy against hesitancy: Vaccination hesitancy. Med Histor 2022; 6(1):e2022014.
8. Greenwalt TJ. A short history of transfusion medicine Transfusion 1997; 37(5):550–6.
9. Njah M, Noulra A, Yacoub S, et al. Tranfusion practices and attitudes. Tunis Med 2002; 80(6):306–11.
10. Giaconi C, Manetti AC, Turco S, et al. Post-mortem computer tomography in ten cases of death while diving: a retrospective evaluation. Radiol Med 2022; 127(3):318–29.
11. Pereira A, Sanz C, Tàssies D, Ramírez B. Do patient-related blood donors represent a threat to the safety of the blood supply?. Haematologica 2002; 87(4):427–33.
12. Learoyd P. The History of Blood Transfusion prior to the 20th Century – Part 1. Transfus Med 2012; 22(5):308–14.
13. Granata V, Coppola F, Grassi R, et al. Structured Reporting of Computed Tomography in the Staging of Neuroendocrine Neoplasms: A Delphi Consensus Proposal. Front Endocrinol (Lausanne) 2021; 12:748944.
14. Karaboue MAA, Milone V, La Casella GV, et al. What will our children do when we are gone? Italian legislature does not tackle the worries of parents of disabled children. Reflections on disability. Med Histor 2022; 6(1):e2022013.
15. Mazzei MA, Guerrini S, Cioffi Squitieri N. Reperfusion in non-occlusive mesenteric ischaemia (NOMI): effectiveness of CT in an emergency setting. Br J Radiol 2016; 89(1061):20150956.
16. Iacobellis F, Segreto T, Berritto D, et al. A rat model of acute kidney injury through systemic hypoperfusion evaluated by micro-US, color and PW-Doppler. Radiol Med 2019; 124(5):323–30.
17. Fiorini F, Granata A, Battaglia Y, Karaboue MAA. Talking about medicine through mass media. G Ital Nefrol 2019; 36(1):2019-vol.1.
18. Op Den Winkel R, Brunner F, Harder F. Blood transfusions and kidney transplantation: Selection or conditioning of recipient?. Helv Chir Acta 1980; 47(1-2):227–30.
19. Granata V, Morana G, D'Onofrio M, et al. Structured reporting of computed tomography and magnetic resonance in the staging of pancreatic adenocarcinoma: A delphi consensus proposal. Diagnostics (Basel) 2021; 11(11):2033.
20. Mazzariol B, Karaboue M, Di Luca A, Di Luca NM. Guidelines, good practices and best clinical health practices: Valuable guidance for physicians and judges?. Clin Ter 2018; 169(6):292–6.
21. Mueller-Eckhardt C. Risks in Tranfusion Therapy. Anasth Intensivther Notfallmed 1980; 15(3):179–88.
22. Cantisani V, Iannetti G, Miele V, et al. Addendum to the sonographic medical act. J Ultrasound 2021; 24(3):229–30.
23. Raos M, Nemet D, Bojanić I, et al. Collection and composition of autologous peripheral blood stem cells graft in patients with acute myeloid leukemia: Influence on hematopoietic recovery and outcome. Coll Antropol 2010; 34(1):105–15.
24. Lacasella GV, Karaboue K. Nutrition and hydration of patients in a persistent vegetative state. Progr Nutr 2022; 24(2):e2022136.
25. Lacasella GV, Karaboue K. A short history of human nutrition from prehistory to ancient civilisations. Progr Nutr 2022; 24(2):e2022135.
26. Landsteiner K. On agglutination of normal human blood. Transfusion 1961; 1:5–8.

27. Karaboue MAA, Massaro M, Lacasella G. Artificial nutrition and hydration: Bioethical and biolegal profiles: Artificial nutrition. Progr Nutr 2023; 25(2):e2023034.
28. Karaboue M, Massaro M, Karaboue K. When nutrition becomes artificial: A bioethical issue. Progr Nutr 2023; 25(2):e2023033.
29. Fantus B. The therapy of the Cook County Hospital. Journal of the American Medical Association 1937; 109:128–31.
30. Wright AE. On a Method of Determining the Condition of Blood Coagulability for Clinical and Experimental Purposes, and on the Effect of the Administration of Calcium Salts in Haemophilia and Actual or Threatened Haemorrhage: [Preliminary Communication]. Br Med J 1893; 2(1700):223–5.
31. Blundell J. Experiments on the Transfusion of Blood by the Syringe. Med Chir Trans 1818; 9:56–92.
32. Karaboue M, Casella GL, Karaboue K, Cipolloni L, Bosco MA, de Simone S. Il dibattito in Bioetica Health and disease: a multicultural dichotomy. Medicina e Morale 2023; 72(2): 207–12.
33. De Luca L, Veneziano FA, Karaboue M. Late Presenters with ST-Elevation Myocardial Infarction: A Call to Action. J Clin Med 2022; 11(17):5169.
34. Palaia G, Bossù M, Pranno N, et al. Oral Pathologies in Migrants: The Experience of the "PROTECT". Project in 3023 Patients Appl Sci 2022;12(24):12621.
35. Zanza C, Tornatore G, Naturale C, et al. Cervical spine injury: clinical and medico-legal overview. Radiol Med 2023; 128(1):103–12.
36. Russo A, Reginelli A, Lacasella GV, et al. Clinical Application of Ultra-High-Frequency Ultrasound. J Pers Med 2022; 12(10):1733.
37. Cappabianca P, Russo GM, Atripaldi U, et al. Universal Access to Advanced Imaging and Healthcare Protection: UHC and Diagnostic Imaging. Med Sci (Basel) 2021; 9(4):61.

Correspondence:
Karidia Karaboue
University of Campania "Luigi Vanvitelli" Via S. Maria di Costantinopoli, Naples, Italy
E-mail: info@karaboue.it