

INTRODUCTORY NOTES

The book 'The Blood Bank and the Technique and Therapeutics of Transfusion' by Robert A Kilduffe and Michael DeBakey was originally published by The C.V. Mosby Company, St Louis, USA in 1942. The first chapter of this book (pages 17-45 inclusive) is titled 'History' and provides an extensive overview of the 'history of transfusion'.

Whilst publishers Elsevier (who I have identified to now hold the copyright for the C.V. Mosby Company) have provided their permission to reproduce this chapter, they are unable to identify for certain if they are the legal copyright holders of this material. As such, this article is presented in this format for personal study only and must not be downloaded, copied, modified or reproduced further – it is provided here as an additional source of information relating to the history of blood transfusion.

Although chapter 1 of the book is reproduced here for convenience, the whole book can be accessed via:

[https://babel.hathitrust.org/cgi/pt?id=uc1.\\$b595310&view=1up&seq=21](https://babel.hathitrust.org/cgi/pt?id=uc1.$b595310&view=1up&seq=21)

This 'history of blood transfusion' concentrates principally on describing the methodologies of blood transfusion that were employed by early researchers such as Lower, Denis, Heister and Blundell, together with the later methods described by Roussel, Aveling, Gesellius and others. It also provides an excellent source of information regarding the direct transfusion techniques employed mainly in the US by Payr, Crile, Bernhelm and others. These different methodologies are profusely illustrated within the text. The chapter also includes an extensive bibliography.

THE BLOOD BANK AND THE TECHNIQUE AND THERAPEUTICS OF TRANSFUSION

Robert A Kilduffe and Michael DeBakey

CHAPTER I - HISTORY

The development of blood transfusion, from the vague allusions in the early mythological period to the present-day scientifically established and ubiquitously employed therapeutic procedure, forms one of the most fascinating and romantic chapters in medical history. It would be inexpedient to attempt here a detailed account of the story of blood transfusion for indeed, it reflects the historical development of medicine. However, those interested in this phase of the subject may refer to a number of previously published comprehensive treatises.^{6, 28, 44, 49, 51, 85, 100, 106, 113, 127, 130, 142 150, 155, 165, 169, 174, 183}

The antiquity of the concept of blood as a therapeutic agent is difficult to establish. It probably antedates even civilization and certainly it began with the origin of medicine itself. The ancient Egyptian princes used blood baths for resuscitation and recuperation, and the custom of rushing into the gladiatorial arena to drink the freshly flowing blood of dying victims prevailed among the Romans. The Egyptians, the Hebrews, and the Syrians are supposed to have practiced "transfusions", and Greek and Roman writers have been credited with witnessing it. However, as one reads this early history, he is impressed with the obscure references and the vague

and contradictory literature. This confusion apparently arises from the fact that during the Middle Ages the drinking of human blood was popularly considered a health restorative measure, and in the older records the ingestion and the transfusion of blood were frequently confused. Moreover, it is difficult to conceive how blood transfusion, as we understand the procedure today, could have been practiced at a time when the circulation of blood was not recognized. For this reason it has been difficult to determine with any degree of exactitude just when the transfusion of blood in the modern sense was first performed, and considerable controversy exists regarding claims of priority. The oft-quoted and now famous "transfusion" of Pope Innocent VIII, in the year 1492, must be considered in the light of these facts. According to Villari, the Pope, who had had an apoplectic stroke the year before, "had for some time fallen into a kind of somnolency, which was sometimes so profound that the whole Court believed him to be dead. All means to awaken the exhausted vitality had been resorted to in vain, when a Jewish doctor proposed to do so by the transfusion, by a new instrument, of the blood of a young person; an experiment which hitherto had only been made on animals. Accordingly, the blood of the decrepit old Pontiff was passed into the veins of a youth, whose blood was transferred into the veins of the old man. The experiment was tried three times, and at the cost of the lives of three boys, probably from air getting into their veins, but without any effect to save that of the Pope." However, this story has always been the source of controversy, and there are several different versions.^{28, 126, 142} Probably the most truthful account is that given by Mathews, in which it is stated that the blood was administered as a draught. Be that as it may, all seem to agree that the three boys as well as the Pope died, and the Jewish physician quickly disappeared.

Approximately a century elapsed before the reappearance of the subject of blood transfusion, and it is during this period that the greatest controversy regarding claims of priority existed. Although Hieronymus Cardanus (1505-1576) has been credited with mentioning the possibilities of blood transfusion, according to Ullersperger, "the idea and theory of transfusion, etc., appertains by full right to Magnus Pegel," whose work "obtained the privilege of being printed already in 1593, under the Emperor Rudolphus II, but was not published before 1604." On the other hand, the first definite application of blood transfusion, with a detailed description of technique, has been credited to Andreas Libavius, a chemist of Halle. This arouses more than passing interest, because it appears to antedate Harvey's discovery of the circulation and because of the surprising similarity of the technique to that advocated comparatively recently by Bernheim.¹¹ The following description of transfusion appears in Libavius' writings, in 1615: "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 into it one of the tubes, fastening it in. Let him immediately after open the artery of the old man, and put the female 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 weakness will be dispelled." Whereas some⁶⁷ believe that Libavius was a serious advocate of transfusion, others^{28, 142} think that he considered the procedure as ridiculous and contemptible and the extravagance of his claims was merely an expression of irony. The Italians' claim to priority lies in the writings of Jean de Colle, of Padua, who, in 1628, described a method of transfusion and seriously mentioned the procedure as a valuable aid in prolonging life.

In the evolution of the modern practice of blood transfusion, there are certain outstanding historical landmarks. The first important contribution which made possible blood transfusion as it is known today was the announcement of the theory of circulation of the blood by William Harvey,⁷⁴ in 1628, a theory first propounded in his lectures in 1616. It is perfectly obvious that without knowledge of the circulation of the blood, transfusion as it is known today cannot be considered possible, and all

references to the procedure prior to the announcement of the theory of circulation are necessarily regarded with considerable doubt. Following Harvey's epochal exposition, popular imagination, which had always attributed mystic powers of resuscitation to blood, immediately began to seek a method for the transfusion of blood from a vigorous to a debilitated subject. This immortal contribution paved the way for investigators throughout the world to begin energetic experiments on infusions of various substances into the blood stream and it was the direct stimulus of coordinated and scientific studies on infusion and transfusion.



Fig. 1: William Harvey (1578-1657) of Folkstone, England, was the discoverer of the circulation of the blood (1616). His famous *De Motu Cordis* (Frankfurt, 1628), which summarised his epoch-making concept and stirred opposition among his adversaries, opened the way for experiments in blood transfusion. (From Royal Society Portrait.)

However, it is not until after the middle of the seventeenth century that authentic references to blood transfusions are to be found. According to some writers, Francesco Folli, a Florentine physician, is supposed to have performed the first transfusion on Aug. 13, 1654, in the presence of Grand Duke Frederick II. He employed a silver tube inserted in the artery of the donor and connected to a cannula of bone in the vein of the recipient, by means of a hollow pipe made from the blood vessel of an animal. On the other hand, Mayerhofer, in an investigation of this subject, expresses the opinion that Folli merely described the method to Grand Duke Frederick but never actually performed the operation. The French, in their claim to priority, state that a Benedictine monk of Cluny, Robert des Gabets, first demonstrated the possibility of transfusion in 1653, and performed the operation five years later.^{38, 158} The instrument he employed and which he invented, in 1651, consisted of two small silver tubes "connected by a leather ball, the size of a walnut, and each contained a valve to regulate the flow of blood." Also of interest from the viewpoint of the French is the priority claim of Tardi. In his "Traité des l'Ecovlement

du Sang d'un Homme dans les Venes d'un Autre et ses Vtilitez," written in 1667, Tardi stated that he was one of the "inventeurs" of blood transfusion and described in detail the procedure of artery-to-vein human transfusion. In a letter to LeBreton, written in 1667, Tardi spoke of this paper on blood transfusion and stated: "Lacking a capable surgeon, I can myself perform the transfusion alone, having practiced all my life, not only at operations on the dead, but also on living bodies."^{2, 43}



Fig. 2: Sir Christopher Wren (1632-1723), English architect, astronomer, and author of the illustrations in Willis' *Cerebi Anatome* (1664), was one of the earliest investigators of infusing medicaments and transfusing blood into animals.

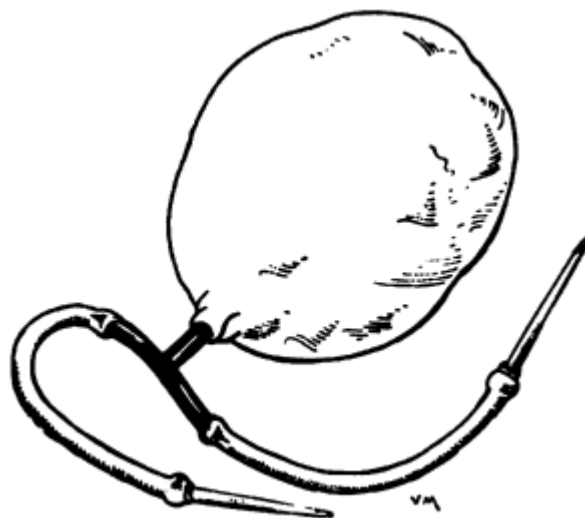


Fig. 3: An animal's bladder to which two quills were attached (devised by Wren) served as a receptacle and a means of injecting medicaments into the veins of animals.

In the year 1656, Sir Christopher Wren, the astronomer and architect, while at Oxford, in an endeavour to develop a new method of administering blood experimented with dogs by injecting various medicaments, such as ale, wine, scammony, and opium, into the veins. Further experiments of this character were continued at Sir Christopher's suggestion by Timothy Clarke, Robert Boyle, and Nathaniel Henshawe, with indifferent success. He writes further that in his first attempts at transfusion he "connected the jugular vein of one dog with that of another by means of a cannula. However, the comparatively slow-flowing venous blood immediately coagulated and obstructed the lumen of the tube. Then I decided to try another plan, one that would more closely follow nature, and convey the blood of one animal into the vein of another." The experiments soon attracted the attention of the Royal Society and at a meeting of this group, in 1665, it was proposed to try the transfusion of blood.



Fig. 4: Richard Lower (1631-1691) of Cornwall, England, physician and anatomist, performed the first direct transfusion of blood between animals (1665). (Only known portrait of Lower from the first edition of "Receipts," London, 1700.)^{60a}

Owing to lack of proper apparatus, there were several unsuccessful attempts. However, in February, 1665, Richard Lower, together with E. King, performed the operation of transfusion successfully.¹²⁴ Quills were employed, and later a silver tube to convey blood from the carotid artery of one dog to the jugular vein of another dog. Lower reported the cure of a mangy dog in ten days after transfusion from a healthy one. He also relieved the acute anaemia of a dog exsanguinated following splenectomy. It is of interest to note Pepys' quaint allusion in his diary to Lower's experiment on transfusion. On Nov. 14, 1666, he writes: "Here Dr. Croone told me that at the meeting at Gresham College tonight, which, it seems they now have every Wednesday again, there was a pretty experiment of the blood of one dog let out, til he died, into the body of another on one side, while all his own run 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." In the latter part of November, 1667, Lower transfused Mr. Arthur Coga, "a mildly melancholy insane man," using the blood of a lamb. Again we find a reference to this in Pepys' diary: "November 30, 1667. But here, above all, I was pleased to see the person who had his blood taken out. He speaks well, and did this day give the Society a relation thereof in Latin, saying that he finds himself much better since, and as a new man, but he is cracked a little in his head, though he speaks very reasonably, and very well. He had but 20 s. for his suffering it, and is to have the same again tried upon him: the first sound man that ever had it tried on him in England, and but one that we hear of in France, which was a porter hired by the virtuosos."

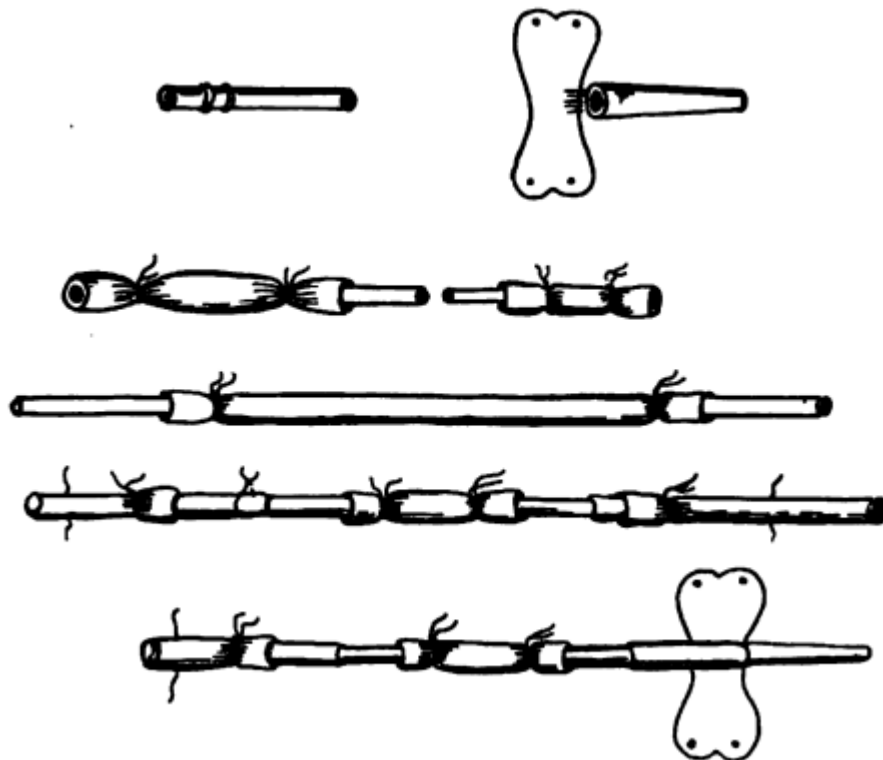


Fig. 5: Drawing from etching in Lower's articles on blood transfusion in *Philosophical Transactions*, showing silver cannulas and quills used to transfuse blood; the double leaf has perforations through which threads fix the cannulas in position.'

In the meantime somewhat similar investigations were being done in other countries, and in Paris, Jean Baptiste Denis, the Montpellier philosopher and mathematician and the physician to Louis XIV, performed the first authentically recorded successful transfusion on human beings, in June, 1667. The patient was a youth 15 or 16 years of age who had some obscure fever which had been treated by repeated venesections until he was in a state of extreme exhaustion. The boy made a remarkable recovery following the administration of 9 ounces of blood from the carotid artery of a lamb. Denis successfully performed his second transfusion simply as an experiment on a perfectly healthy older subject who consented to the experiment after being remuneratively persuaded. Denis' renown as a transfusor brought on a storm of opposition, hatred, and jealousy, and further investigations got him into difficulty. His third attempt on a moribund patient did little more than delay death a few hours, and his tragic fourth transfusion which ended fatally, apparently because of an incompatibility reaction, resulted in his arrest and trial for murder. This

last patient, who was a lunatic and had been previously transfused by Denis with apparently temporary success, was transfused the third time at the request of the patient's wife. Denis' enemies conspired with the widow to charge the transfusor with murder. Following a prolonged legal battle, Denis was eventually exonerated. However, because the influential members of the Faculté de Médecin, in Paris, were leaders of the opposition to transfusion, the procedure was decreed criminal except with their sanction. About ten years later an edict of Parliament, the results of which were far-reaching, specifically prohibited the operation in France. The procedure also was abolished as far as the Royal Society was concerned, and the action of the Parisian court so impressed the magistrates of Rome that they also forbade the operation. Accordingly, interest in transfusions quickly abated throughout Europe.



Fig. 6: Matthias Gottfried Purmann (1649-1711), author and surgeon, describes transfusion of blood from animal to man as performed in the seventeenth century. Purmann, with Balthasar Kaufman, is credited with curing a case of leprosy by repeated transfusions of lamb's blood.



Fig. 7: Blood transfusion from animal to man as practiced in 1672 (Lamswerde). (Drawn after Scultiti.)

Of particular interest is the trend of thought and speculation as regards transfusion and the indications during this early period. Although little or no consideration was given this procedure in the treatment of acute loss of blood, it was the possible mental effects that appealed most strongly to the imagination and interests of these early investigators. Mania and melancholy ranked as prime indications and considerable importance was given the procedure in the restoration of youth to the senile and the alleviation of advanced lung and bowel disease, apoplexy, itch, epilepsy, and fistulous ulcers. There was great speculation as to whether a dog transfused with sheep's blood would grow wool, hoofs; and horns. It was proposed that the phlegmatic be corrected with blood of a choleric, and that marital discord be settled by reciprocal transfusions of husband and wife. In the light of present-day knowledge, these transfusions based upon such ludicrous naiveté and irrational indications obviously resulted in few, if any, beneficial effects. Moreover, the complete ignorance of asepsis, of immunology, of the process of coagulation, of blood groups, and of incompatibility inevitably caused severe and fatal reactions. In addition to its eventual consideration as a disreputable and hazardous procedure, ecclesiastical disapprobation and administrative disfavour finally produced a gradual dying of interest which caused blood transfusion to be relegated to almost complete desuetude for nearly a century and a half in spite of the initial impetus given it by the meritorious works of Lower and Denis.

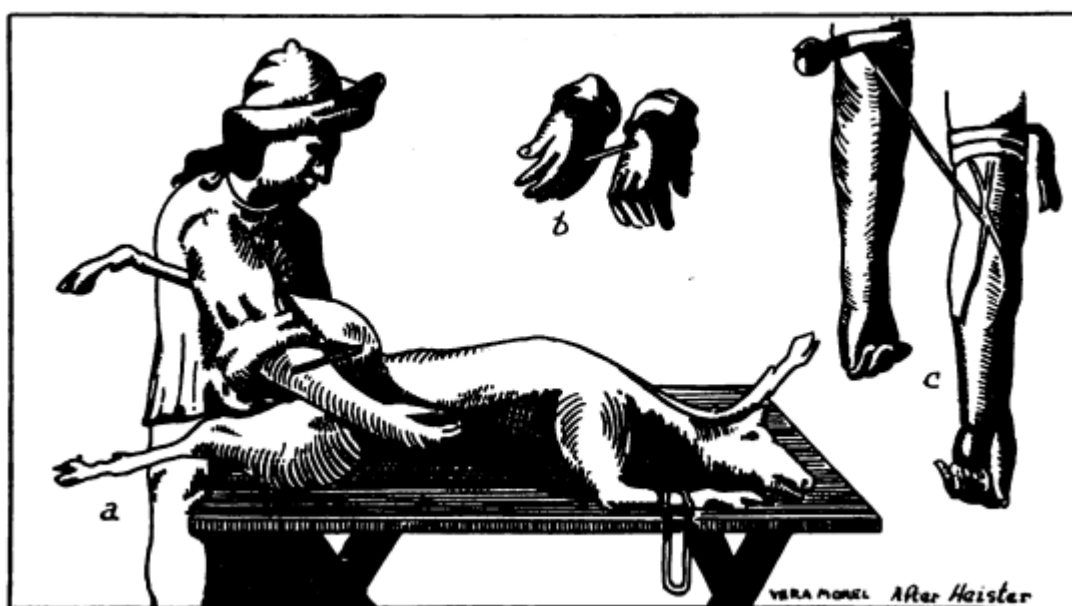


Fig. 8: Transfusion of blood conceived and described by Lorenz Heister. *a* "Shews the Transfusion of Blood from the crural Artery or Vein of an Animal into the Arm of a Man, by the Intervention of the Tube." *b* and *c* "Exhibit the Transfusion of the Blood from the Veins of one Man into those of another." (From Heister.^{77a})

A few sporadic efforts appeared during this period. In 1683, Kaufman and Purmann transfused a leper with lamb's blood. Nuek, in 1714, and Cantwell, in 1749, stated that the procedure was valuable in severe hemorrhage and extreme emergencies. In 1783, Michel Rosa of Modena performed extensive investigations on blood transfusion. In 1792, Harwood of Cambridge also experimented with transfusions in dogs, and Russell, of Suffolk, is credited with curing a boy of rabies by transfusion of lamb's blood. In 1802, Paul Scheel, of Copenhagen, published an extensive monograph in which he reviewed in great detail the previous work on blood transfusion and strongly advocated the procedure. However, with the exception of

these occasional attempts and lamentations, no constructive work was done until the early nineteenth century.



Fig. 9: Lorenz Heister (1683-1758) of Frankfort-on-the-Main, whose *Chirurgie* (1718) was the most popular work of the eighteenth century, made the first post-mortem section on appendicitis (1711), introduced the term “tracheotomy” (1718), and was one of the earliest advocates of the procedure of blood transfusion in the treatment of shock.

It remained for another Englishman, the London physiologist and obstetrician, James Blundell, in 1818, to revive the interest of medical investigators in blood transfusion. Stimulated by the appalling helplessness and inefficacy in combatting overwhelming and fatal puerperal hemorrhage, Blundell directed his attention to the possible expediency of replacing the blood of the exsanguinated patient. In a truthfully scientific spirit, he began a series of experimental investigations on the dog to determine “whether the blood would remain fit for the animal functions after its passage through the instrument.” After studying the effects of passing blood through a syringe, he concluded that it lost none of its vital properties by such manipulation, and that venous blood was as satisfactory as arterial. He devised an apparatus, consisting of a funnel-shaped receptacle for the blood, connected by a two-way tap with a syringe from which the blood was injected through a tube and cannula into the recipient. This was fixed to the back of a chair for support and was referred to as Blundell’s “impellor.” Convinced by his investigations that the procedure was practicable and “with a mind rationally prepared to the best of my power by previous reflection and experiment,” Blundell attempted transfusion in the human being. His first four unsuccessful attempts were desperate resorts in moribund patients, but he was later successful with three women in whom death from postpartal hemorrhage seemed certain. He performed the operation in ten cases, five of which were successful. Great credit is due Blundell for reviving the procedure and placing it upon a sound, clinically rational, and scientific basis.¹⁰² Moreover, his technical developments are reflected in some of the present-day methods.

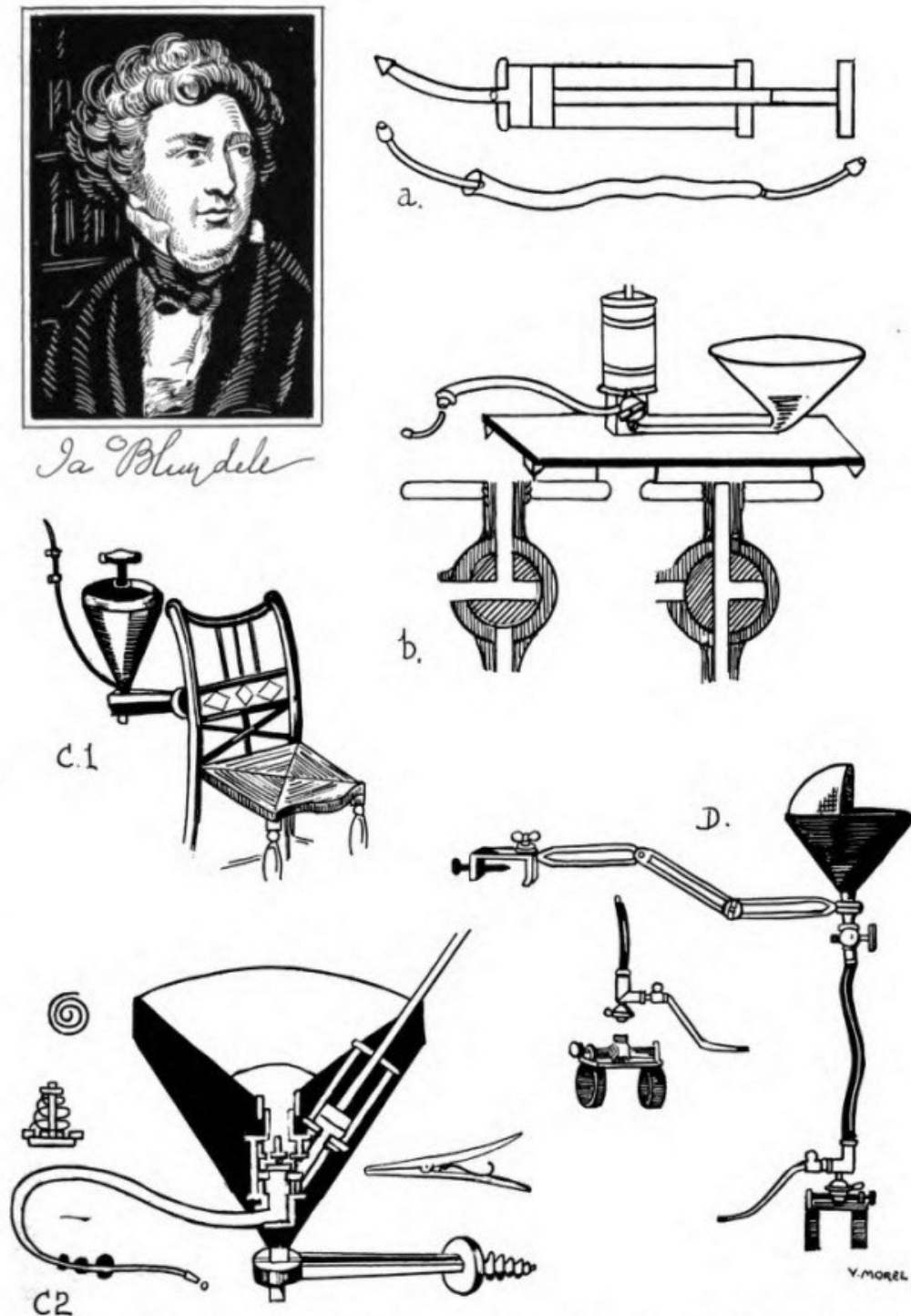


Fig. 10: James Blundell (1790-1877), London obstetrician and physiologist, “rediscovered” blood transfusion and devised several instruments for performing the procedure which are reflected in many of the present-day methods, *a*, Simple syringe used to suck blood into a glass tumbler before injecting it into the vein. The cannula or tube is for direct transfusion from artery to vein (1825). *b*, A modified syringe (about 1818) with a three-way valve; the blood is directed into a cup, the piston of the syringe is pulled upward, and the blood is forced into the barrel of the syringe. Cross section shows the stop-cock which is turned, thereby forcing the blood into the vein of the patient. *C1*, Blundell’s “Impellor” (1824) attached to a chair in which the donor is seated. The inner cup contains warm water to exclude air. *C2*, Cross section of “Impellor” showing syringe and valve mechanism for changing direction of flow. Blood is impelled by “long strokes and sharp movements.” *D*, Blundell’s “Gravitator” is his fourth method.

Although a number of surgeons and obstetricians attempted to follow Blundell's example, four obstacles, namely, agglutination and haemolysis from the admixture of incompatible blood, infection, and blood coagulation, hindered the successful application of this therapeutic procedure which occasionally yielded such brilliant results. The last hindrance, coagulation, was first overcome in 1835 by Bischoff with the utilization of defibrinated blood, although Dumas, Prevost, and Dieffenbach had previously performed experiments with defibrinated blood. In 1847, Larsen, at the suggestion of Panum, performed one of the earliest transfusions with defibrinated blood.

Although some^{69, 111} objected to the use of defibrinated blood, others^{21, 83, 136} staunchly supported its value. In 1874, an editorial⁵³ appeared in the *Philadelphia Medical Times* in which the pros and cons of defibrinated blood were discussed. Freer presented experimental evidence of the innocuity of defibrinated blood and concurred with McDonald that "blood is rendered more suitable for the purpose of transfusion by being deprived of its fibrin." Further attempts to overcome coagulation consisted of the addition to the blood of chemicals, such as sodium bicarbonate,¹⁴⁰ sodium phosphate,⁸⁰ and ammonia.¹⁵⁶

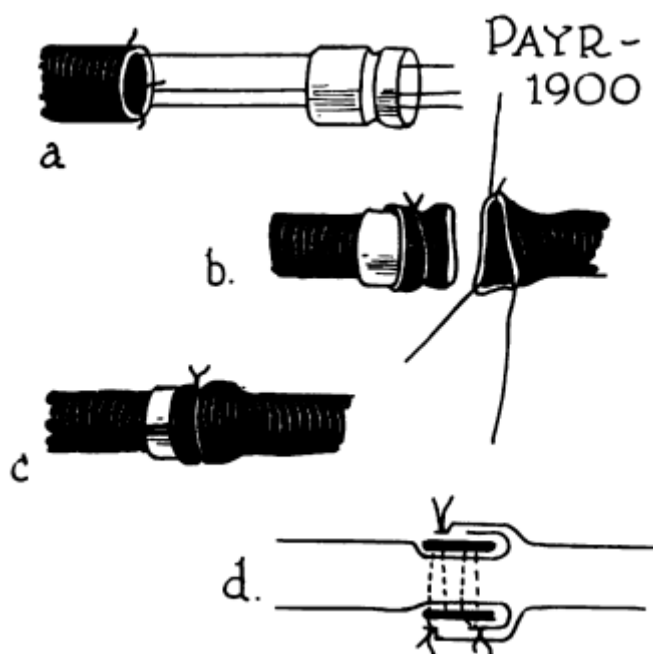


Fig. 11: Methods for direct transfusion (Figs. 11-17). Erwin Payr (1900).^{149a} Technique for using metal tube to facilitate continuous intimal contact in vessel anastomosis. Based on this principle, various methods of direct transfusion were devised. *a*, Vein is threaded through metal tube; *b*, vein is cuffed back and tied in groove of tube; *c*, other end of vessel is drawn over vein and tied in groove, completing anastomosis and making continuous intimal contact as shown schematically in *d*.

In America, it would appear that little knowledge or interest was shown in this subject prior to the publication of Blundell. As one reads the early history of blood transfusion, one is impressed with the profound influence of this London physiologist and obstetrician on medical investigators in blood transfusion throughout the world. Certainly, in America Blundell must be given credit for initiating interest in this subject. Following his publication, numerous reports appeared in this country commenting upon the subject and advocating the procedure. In 1828, Channing directed attention to Blundell's article, presented abstracts of some of his cases, and concluded that "there seems full evidence enough to recommend it to the attention of the profession." Jackson also discussed the procedure and stated that it was

particularly indicated in postpartal haemorrhage. Similarly, Benedict and Rouanet advocated the procedure in such cases. In 1859, Haughton proposed it in the treatment of "tuberculosis phthisis," and its various indications were discussed further by Kay and Meyer.

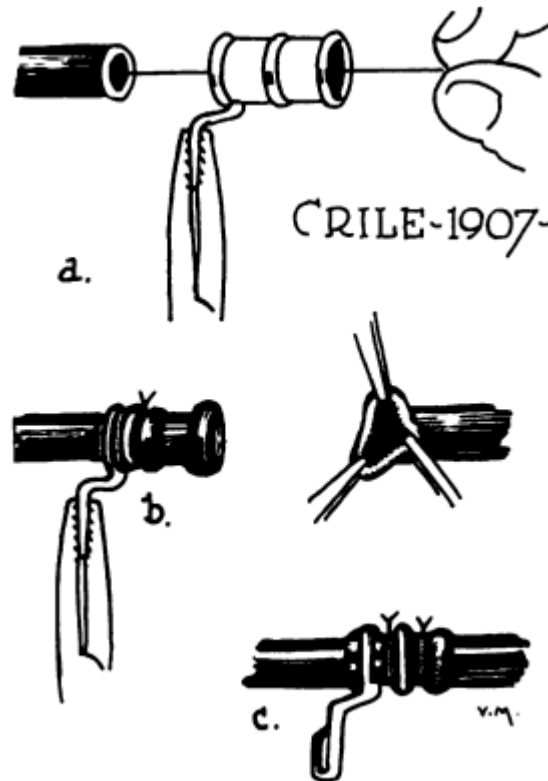


Fig. 12: George Washington Crile.⁴¹ Artery-to-vein method with cannula. *a*, Pulling vein through cannula. *b*, Vein cuffed and tied into place in groove near handle of cannula; artery ready to be drawn over vein. *c*, Completed anastomosis of artery and vein.

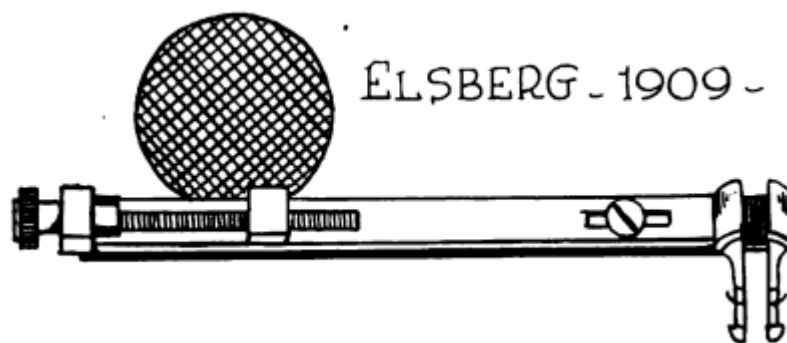


Fig. 13: Charles Elsberg.⁵⁵ Cannula built on monkey-wrench principle with screw at end for enlargement. From the cone-shaped tip is a ridge with four small pin points directed backward. The lumen of the cannula is larger at the base than at the tip, and has the advantage of being adjustable to fit vessels of various sizes.

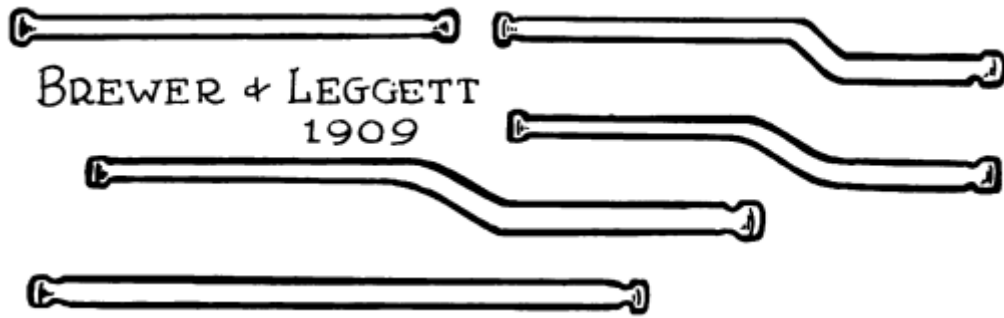


Fig. 14: George Emerson Brewer and Noel B. Leggett.²⁶ Simple cylindrical glass tubes coated with paraffin. Set includes some of uniform caliber; others are bayonet-shaped and others are tapering in shape and in caliber. Notch at extremities is for ligatures.

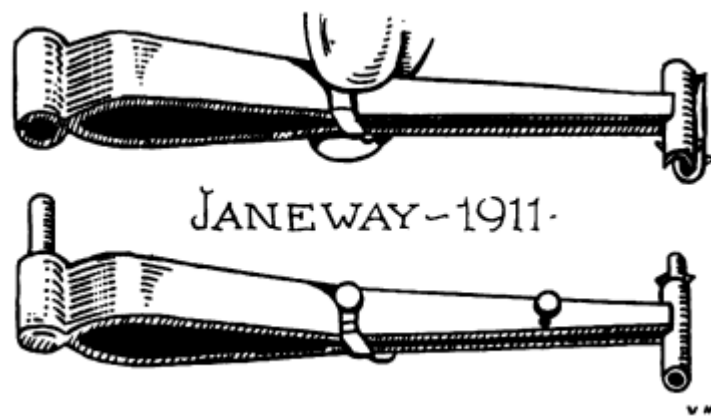


Fig. 15: Henry H. Janeway.⁹⁷ Improved device for end-to-end method, showing male and female halves of instrument. Hemicylinders with points for catching the turned back cuff of the vessel are separated by pressure on knobs.

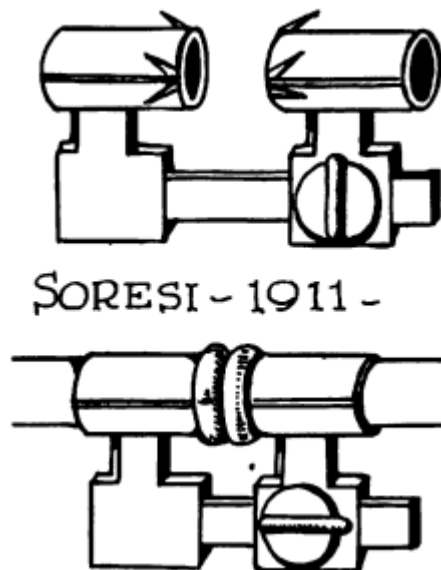


Fig. 16: A. L. Soresi.¹⁷⁰ Blood vessels are cuffed over hooks and openings are approximated by sliding clamps together.

However, despite the early interest and discussion instigated by Blundell's publications, blood transfusion does not appear to have been actually performed for some time. It is difficult to determine exactly when the procedure was first employed in this country. In 1853, Benedict, in New Orleans, presented the report of a committee investigating this subject and stated that they "were not aware of the operation having ever been performed in America." A similar opinion was expressed by Jackson in 1828. However, in commenting upon a recent report of a case described by Blundell, the editors⁵² of the *Philadelphia Journal of the Medical and Physical Sciences*, in 1825, stated that thirty years previously, Dr. Physic performed "the experiment of transfusion of blood under precisely the same circumstances." One of the earliest accounts of its successful application is the report of Jones, in 1833, who employed the procedure in a 50-year-old female with "tubercular disease of the lung," who had "every symptom of approaching dissolution." Following the operation, "the countenance was relieved and the next day she was much better and able to take food."

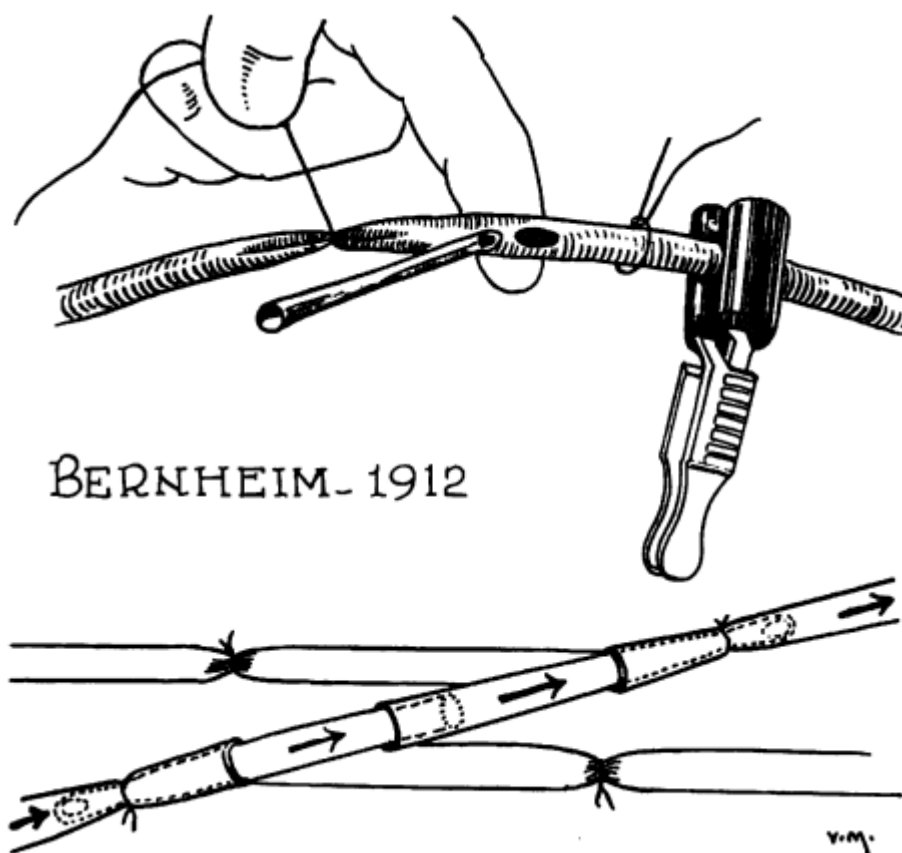


Fig. 17: Bertram M. Bernhelm.¹¹ Male and female cannulas consisting of two hollow tubes (4 cm. long), one for artery and one for vein. Tubes are bulbous at one end to form neck for retaining ligature and are believed to facilitate entrance into vessel. Other ends are tubular and fitted for invagination.

Another early report is that of Flint, who stated that in New Orleans during the winter of 1860 to 1861 he performed the operation in a moribund patient "by means of an ordinary injecting instrument. The blood to be injected was taken in a full stream from a vein in the arm of the husband, received in a vessel which was immersed in water at 100° F., immediately taken from the vessel into a fine syringe, and injected as quickly as possible into the veins of the patient. About seven ounces of blood was thrown into the veins at three different operations, with a few minutes interval." Although the patient improved immediately following the procedure, death

occurred twenty-four hours later. In 1867, Braman described a case of excessive hemoptysis following exertion in a circus rider, and after various forms of therapy had been tried in vain, a blood transfusion was done and the patient recovered. Two years later Buchser reported another successful case in a young female who apparently had purpura hemorrhagica. He utilized the Enlenburg-Landois syringe and remarked that the \$80.00 cost of this instrument was one of the principal reasons for the infrequent use of the procedure. During the same year, Hoehling reported two cases in which defibrinated blood was employed, and Morton in a subsequent publication stated that he believed these were the first successful transfusions in America. That there were few cases performed prior to this time is shown by the fact that in a series of 170 cases collected from the world literature, in 1872, Drinkard could find only four cases performed in America, and these were done by Drs. King, Allen, and Hunter.

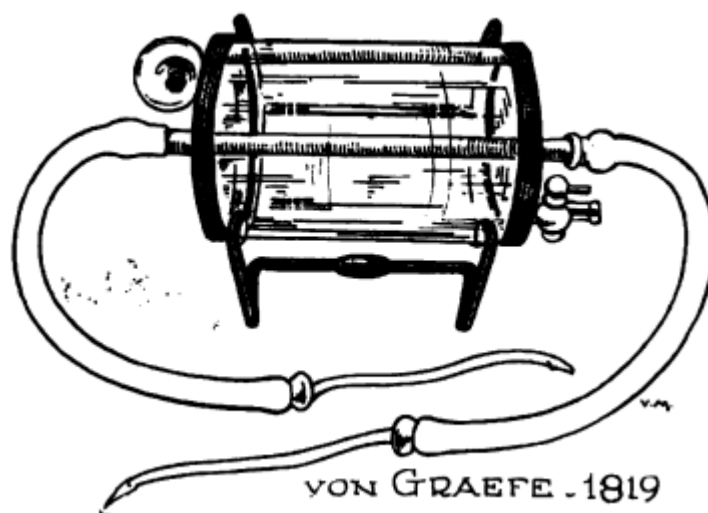


Fig. 18: C. F. von Graefe. Instrument for blood transfusion with tube brought through a glass chamber containing hot water to prevent coagulation of blood during procedure.

During the third quarter of this century transfusion was performed with increasing frequency. Up to the year 1859, Edward Martin had collected fifty-seven cases of transfusion for postpartal bleeding and stated that recovery occurred in forty-five of these with no fatalities attributable to the transfusion. In 1863, Blasius recorded over 116 transfusions performed during the previous forty years, with sixty-six successful results; and, in 1869, von Belina-Swiontkowski had collected 155 cases of blood transfusion. In a comprehensive monograph, Landois, in 1875, brought the literature up to date and found that there had been 347 human transfusions and 129 cases in which animal's blood was used. A number of reports appeared in which the rationale, indications, and technique were discussed.^{21, 24, 48, 65, 68, 71, 77, 79, 88, 134, 153, 154, 166, 167}

Apparently a more physiologic approach to the problem was being sought and significant investigations on the physiology of the blood were performed by Magendie, Brown-Sequard, Panum, Landois, Mueller, Berns, and von Bergmann. Chadwick classified the cases in which transfusion was indicated into four groups and predicted that "further researches of physiologists will render a much closer discrimination possible, and lead to a much more rational use of transfusion." Because the procedure was considered a *dernier resort*, Barker made a plea for its earlier application and remarked that it "should be employed not exclusively in those desperate cases where favorable results are hardly looked for but should be resorted to before patients have arrived at, and fallen into this desperate condition." He

preferred the use of whole blood, and in commenting upon the physiologic benefits, he stated: "There is doubtless diminished power in the blood for carrying oxygen to the tissues in the cases in which transfusion is ordinarily resorted to, and that necessitates a few additional ounces of blood to give an impulse to the circulation, bridging over, as it were, for a time by furnishing it with a fresh supply of oxygen."

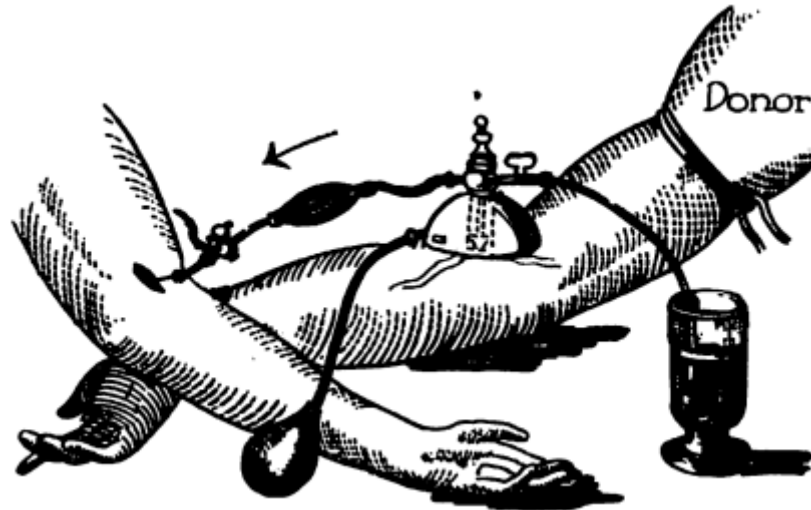


Fig. 19: J. Roussel (1867). Instrument devised for transfusion of unmodified blood with rubber bulb for suction and pressure and suction chamber over donor's vein for collection of blood.

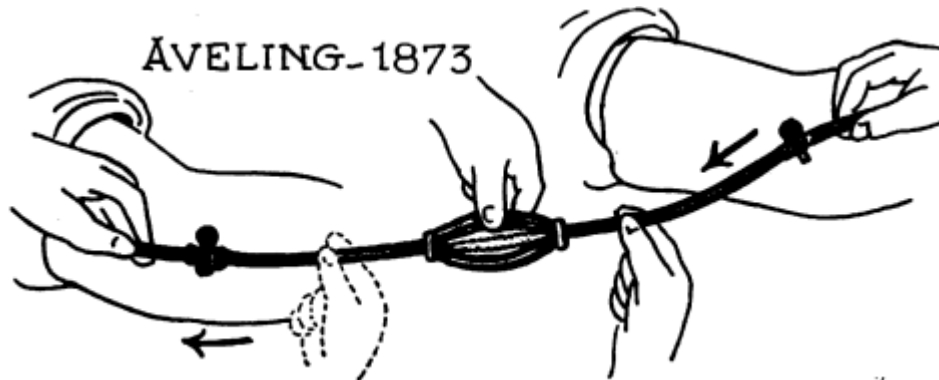


Fig. 20: Aveling. Apparatus for transfusion of blood with rubber bulb for aspiration and ejection of blood.

Thus, it appears that the indications and rationale of blood transfusion were amazingly well understood, and with the gradually increasing use of the procedure at this time, the technical considerations in its actual performance were becoming important problems. In an attempt to facilitate these technical difficulties innumerable ingenious instruments were devised, many of which were rather bizarre and complicated in character.^{3, 9, 64, 66, 81, 82, 87, 93, 107, 171, 173} Chadwick classified the principal methods in use at that time into four groups: (1) transfusion with defibrinated blood; (2) mediate transfusion with pure blood; (3) immediate transfusion from vein to vein; and (4) immediate transfusion from artery to vein. In employing the method of "mediate transfusion," the only special instrument that was required was a syringe, but complicated devices were proposed and particular emphasis was placed upon the avoidance of cooling the blood and contact with air.^{93, 171} The majority of

instruments proposed at this time were devised for the purpose of “immediate transfusion” from vein to vein. Some of these were modifications of the Aveling apparatus,^{3, 64, 66} and others were more complicated and are reflected in some of the present-day instruments.^{9, 81, 87, 107}

That the technical difficulty in the performance of the procedure was one of the most important hindrances to its general use is shown by the statement of Thomas, in 1878, that “transfusion of blood into the human system holds the position of an operation the plausibility and theoretical advantage of which all admit, but the absolute utility and practical results of which amount to very little indeed. . . . The reason for the unfortunate fact that the transfusion of blood is rarely resorted to, and that it to only a very limited degree enjoys the confidence of the profession, is to be found, I think, in the inherent difficulties and dangers of the operation, almost all of which arise from the tendency to coagulation.” For this reason Thomas suggested the use of some other “vital animal fluid . . . which would fulfil the indications of increasing the amount and improving the quality of the blood and which did not possess the disadvantages of coagulation.” On this basis, he advocated the use of cow’s milk which was suggested to him by Hodder, of Toronto, who in 1850 had employed it in Asiatic cholera. Thomas reported twelve cases in which it was used and concluded that “the injection of milk into the circulation in place of blood is a perfectly feasible, safe, and legitimate procedure. . . .” In the light of subsequent developments, Brinton’s statement that “this new operation will, in a few years, have entirely superseded the transfusion of blood, which latter operation is even now being rejected as at once dangerous and unavailing in many parts of the country . . .” is interesting and amusing. Although several reports subsequently appeared,⁹⁴ fortunately the procedure did not gain favor and promptly disappeared from the literature.

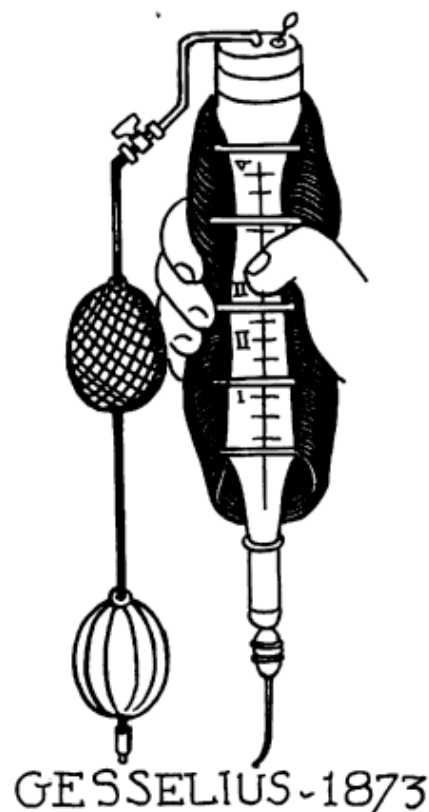


Fig. 21: F. Gesselius. Indirect method for transfusing whole blood with hot water in rubber bag over container to prevent chilling of the blood.

About this time the use of animal, blood, especially lamb's blood, was revived, probably because human donors were obtained with difficulty. This was apparently due in great measure to the influence of Gesselius, in St. Petersburg, and Hasse, in Nordhausen. The latter author stated that he had performed transfusion with lamb's blood in fifteen cases, with only one fatality and with improvement in ten. He described in detail the characteristic manifestations of incompatibility reactions but attributed these to "acute plethora." Several reports of cases in which lamb's blood was employed appeared in the English and American literature.^{5, 70, 86, 99, 109, 168, 180} The consequent severe and even fatal reactions which occurred prevented its popular use and a number of investigators emphasized its dangers. Hotz employed lamb's blood in nine cases and stated that it was a failure in six and caused death in one patient. In commenting upon Hasse's recommendation of animal blood, Freer stated that he "was forced to the conclusion that he [Hasse] is strongly affected with a theory, which serves to warp his judgment." In 1874, this subject was discussed in an editorial in the *Philadelphia Medical Times* and the opinion was expressed that "the various experimenters seemed carried away by the clinical idea, without due regard for the very imperfect physiological basis upon which it rests." Cohnheim, in 1882, also discussed the dangers of heterogenous transfusion and emphasized the fact that "the serum of one species is a direct poison for the corpuscles of another." Agglutination and hemolysis of heterologous blood corpuscles were demonstrated by a number of investigators (Creite, 1869; Landois, 1875; Bordet, 1895; Ehrlich and Morgenroth, 1900).

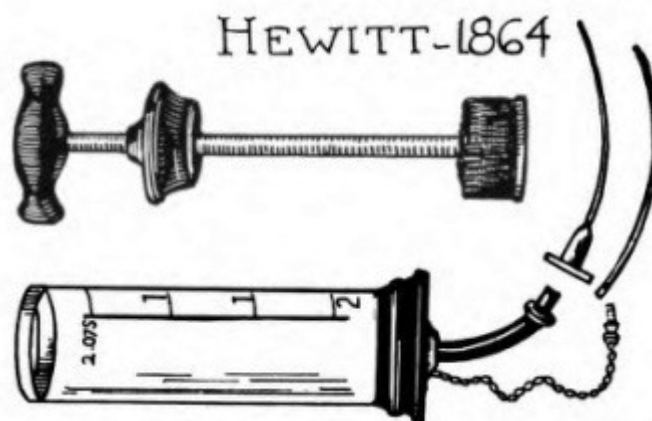


Fig. 22: Graily Hewitt. "Transfusion case" contains two-ounce syringe, piston, cannula, and plug.

Although the procedure was apparently gaining favor toward the beginning of the last quarter of the nineteenth century, the increasing interest and exaggerated enthusiasm seemed to produce an extraordinary departure from previously established fundamental principles. The indications began to comprise various vague infections and debilitating diseases including phthisis as well as uremia, syphilis, and insanity. As a consequence of its indiscriminate employment and of the lack of knowledge of blood compatibilities, the number of severe reactions and fatalities increased. This again resulted in the eventual consideration of transfusion as a hazardous and disreputable procedure, to be used only as a last resort and in extreme desperation. In addition to this, at about the same time physiologic saline solution was introduced and its safety and efficacy were demonstrated. Although a few reports^{57, 105, 137, 172, 179} appeared during the last quarter of the nineteenth century, the procedure was virtually abandoned and not seriously considered until the beginning century marked the next important historical landmark.

Probably the greatest achievement and the most important single discovery in the history of blood transfusion was the demonstration, in 1900, by Landsteiner of the presence of isoagglutinating and isoagglutinable substances in human blood. In the following year, Landsteiner divided the blood into three groups with regard to their agglutinating reactions, and indicated their practical significance. In 1902, DeCastello and Sturli added the fourth group. Hektoen further emphasized the significance of blood groups in the performance of blood transfusion, and Ottenberg and his associates first applied the procedure in actual transfusions. Jansky, in 1907, worked out the reciprocal agglutinating reactions of the four groups and classified them accordingly. Three years later, Moss, working independently, confirmed Jansky's findings. However, due to the relative inaccessibility of Jansky's publication, which was in the Bohemian language, it remained unrecognized until after Moss published his studies. Unfortunately, Moss, being unfamiliar with Jansky's work, transposed Groups 1 and 4 of the Jansky classification and although his classification received wide adoption, considerable confusion resulted. In 1921, the Committee of the American Medical Association⁹⁵ reviewed the question, and recommended that in view of priority of three years, preference be given to Jansky's grouping. Thus the greatest danger of blood transfusion, namely incompatibility, was explained and eliminated and the operation placed upon a firm foundation. The only remaining difficulty then became purely technical.

This more modern period in the development of blood transfusion was characterized by various attempts to facilitate the transfer of blood. Obviously coagulation presented the chief difficulty, and the attempts to overcome this took several directions: (1) prevention by permitting the blood to come in contact only with intima; (2) rapid transfer of blood; and (3) use of anticoagulants. The direct method, that is the anastomosis of the vessels of the donor and the recipient, was based upon the fact that, normally, blood remaining within the intimal coating of vessels does not coagulate. The technical features of vessel anastomosis had been previously perfected and developed by Murphy, Carrel, and Guthrie, and transfusions were performed by this method for several years. Because it was a formidable operation requiring considerable skill and technique, the procedure gained little popularity. However, in 1907, Crile, on the basis of a principle previously developed by Payr (Fig. 11), described a more practicable technique which facilitated the procedure considerably by using the clever device of a cannula through which the vein of the recipient was drawn and cuffed back. The donor's artery was then drawn over the vein thus establishing a continuous intimal lining (Fig. 12). This gave impetus to the direct method and numerous modifications rapidly followed (Figs. 13-17).^{30, 55, 56, 60, 73, 97,}

^{115, 118, 131, 170} The obvious unfavorable features of this method, i.e., the sacrifice of an artery and the inability to measure the amount of blood transfused, together with the advent of the simpler and more reliable indirect methods of transfusion, caused its popularity to decline rapidly.

The previous demonstration by Freund, Bordet, and Gengou that the coagulation of blood received in vaseline and paraffin coated vessels is delayed formed the basis for the introduction of another group of instruments advocated in blood transfusion. Based on this principle Brewer and Leggett, in 1909, developed their paraffin-coated glass tube, and Curtis and David, in 1911, devised an apparatus consisting of a paraffin-coated glass tube having two outlets on one end for the donor and recipient and connected on the other end to a syringe. This same principle was utilized by Kimpton and Brown two years later in the development of their tube, and by numerous others^{39, 110, 135, 152, 162, 177} in subsequent modifications. Whereas these methods enjoyed considerable popularity, their disadvantages lie in the facts that the tube and its connections must be smoothly and accurately coated with paraffin, and that the procedure is necessarily operative.

Another means of overcoming coagulation, namely, by the rapid transfer of the blood, consisted of Lindeman's revival and technical improvement, in 1913, of von

Ziemssen's vein-to-vein method with multiple needles and syringes. Although this method yielded good results in expert hands, it could never become popular because of its awkwardness and the necessity of coordinated action by a skillful team of workers. However, its historical importance lies in the fact that it indicated the way to the syringe-valve method.

The introduction of the syringe-valve methods marked another advance in the simplification of the technical difficulties of blood transfusion. The essential features of this method consist in the utilization of a syringe and some type of valve for the change in the direction of flow from donor to recipient. Among the earliest of these syringe-valve apparatuses were those of Freund,⁶² Unger, Bernheim, Kush, and Miller. Subsequently, a multitudinous variety of modifications were devised and advocated, but the majority are basically the same. The method in principle has continued to enjoy a wide popularity because of its obvious advantage in transfusing unmodified blood.

The addition of anticoagulants is the final method of overcoming coagulation. The use of hirudin as an anticoagulant was suggested by Landois¹¹⁴ in 1892, and tried by Satterlee and Hooker in 1914, but its toxicity furnished a serious objection. An important advance was made in this direction by Hustin of Belgium, in 1914, when he reported his experiments on the use of sodium citrate and glucose in the prevention of coagulation of the blood. On Nov. 14, 1914, Agote in Buenos Aires performed the first transfusion in which citrate alone was used. Then in the following year, in the United States, Lewisohn and Weil independently perfected the technique and standardized the dosage. Of interest in this regard is Rueck's claim to priority in originating this form of transfusion. However, a careful investigation of this subject leaves little doubt that full priority in citrate blood transfusion belongs to Hustin. One of us (M. DeB.) possesses a photostatic copy, kindly sent by Hustin, of progress notes made on the chart of a patient transfused by this method in March, 1914. This method, by rendering the procedure extremely simple and practical, placed blood transfusion at the disposal of the majority of physicians. Its standardized use in military service during the World War increased its popularity and gave it the impetus for wide adoption.

References

1. Agote, L.: Nuevo procedimiento para la transfusión de sangre, *An. Inst. modelo de clin. med.* 1: Nos. 1 and 3, 1915; Nouveau procédé pour la transfusion du sang. Travail présenté au Deuxième Congrès Scientifique Pan-Américain, Dec. 27, 1915, to Jan. 8, 1916, Washington, D. C., National Capitol Press; La transfusion du sang. Un curieux cas de coincidence apparente. Travail présenté au Deuxième Congrès Scientifique Pan-Américain, Dec. 27, 1915, to Jan. 8, 1916, Washington, D. C., National Capitol Press.
2. Annan, G. L.: Claude Tardi, 1607-1670; early advocate of direct transfusion of human blood, *Bull. New York Acad. Med.* 11: 700, 1935.
3. Aveling, J. H.: Aveling's apparatus for immediate transfusion, *M. Rec.* 9: 190, 1874.
- 3a. Aveling, J. H.: On immediate transfusion, *Tr. Obst. Soc. Lond.* 6: 126, 1864.
- 3b. Aveling, J. H.: Successful case of immediate transfusion, *Lancet* 2: .147, 1872.
- 3c. Aveling, J. H.: An improved apparatus for immediate transfusion, *Tr. Obst. Soc. Lond.* 14: 100, 1873; 15: 164, 1873.
4. Barker, Fordyce: Transfusion, *M. Rec.* 9: 187, 1874.
5. Barnes, Robert: A contribution to the theory and practice of transfusion, *Lancet* 1: 6, 1874.
6. Beck, A.: Die Methodik der Bluttransfusion und die Vermeidung ihrer Gefahren, *Ergebn. d. inn. Med. u. Kinderh.* 30: 150, 1926.
7. von Belina-Swiontkowski, L.: Die Transfusion des Blutes, Heidelberg, 1869.
8. Benedict, N. B.: On the operation of transfusion, being the report of a committee, *New Orleans M. J.* 10: 191, 1853.

9. Berens, J.: Transfusion of blood; a new apparatus, Philadelphia M. Times 9: 126, 1878.
10. von Bergmann, E.: Die Schicksale der Transfusion im letzten Decennium. Rede gehalten zur Feier des Steftungstages der militairärztlichen Bildungsanstalten, Aug. 2, 1883.
11. Bernheim, Bertram M.: An emergency cannula; transfusion in a 36-hour-old baby suffering from melena neonatorum, J. A. M. A. 58: 1007, 1912.
12. Bernheim, Bertram: A modification of the Crile transfusion cannula, Ann. Surg. 50: 786, 1909.
13. Bernheim, Bertram: A simple instrument for the indirect transfusion of blood, J. A. M. A. 65: 1278, 1915.
14. Berns, A. W.: Beiträge zur Transfusionslehre, Dissertations Freiburg i. Br., 1874.
15. Bischoff, T. H. W.: Beiträge zur Lehre von dem Blute und der Transfusion desselben, Arch. f. Anat. Physiol. u. wiss. Med., p. 347, 1835.
16. Blasius: Statistik der Transfusion des Blutes, Monatschr. f. med. Statist. u. oeff. Gsundheitspf. Berl., pp. 77, 1863.
17. Blundell, James: Experiments on the transfusion of blood by the syringe, Med. Chir. Tr. Lond. 9: 56, 1818.
18. Blundell, James: Lectures on the theory and practice of midwifery, delivered at Guy's Hospital: Management of the more copious floodings, Lancet 1: 609, 641, 676, 1827-1828.
19. Blundell, James: Observations on transfusion of blood, Lancet 2: 321, 1828.
20. Blundell, James: Successful case of transfusion, Lancet 1: 431, 1828-1829.
21. Boisnot, J. M.: A case of purpura haemorrhagica requiring transfusion, Philadelphia M. Times 5: 371, 1874-1875.
22. Bordet, J.: Les leucocytes et les propriétés du sérum chez les vaccinés, Ann. Inst. Pasteur 9: 462, 1895; also ibid. 12: 688, 1898.
23. Bordet, J., and Gengou, O.: Recherches sur la coagulation du sang et les serums anticoagulants, Ann. Inst. Pasteur 15: 129, 1901.
24. Bowditch, H. P.: Recent progress in physiology (transfusion), Boston M. & S. J. 94: 67, 92, 1876.
25. Braman, C. B.: A case of transfusion, Boston M. & S. J. 77: 533, 1867-1868.
26. Brewer, George Emmerson, and Leggett, Noel B.: Direct blood transfusion by means of paraffin coated glass tubes, Surg., Gynae. & Obst. 9: 293, 1909.
27. Brinton, John H.: The transfusion of blood and the intravenous injection of milk, M. Rec. 14: 344, 1878.
28. Brown, H. M.: The beginnings of intravenous medication, Ann. Med. Hist. 1: 177, 1917.
29. Buchser, Joseph: A successful case of transfusion, M. Rec. 4: 337, 1869.
30. Bryan, R. C. and Ruff, F. R.: Modification of Crile transfusion cuff, J. A. M. A. 58: 1443, 1912
31. Cantwell: Quoted by Dutton.⁵¹
32. Cardanus, Hieronymus: Quoted by Zimmerman and Howell.¹⁸³
33. Carrel, Alescis: The surgery of the blood vessels, etc., Bull. Johns Hopkins Hosp. 18: 18, 1907.
34. Chadwick, J. R.: Transfusion, Boston M. & S. J. 91: 25, 1874.
35. Channing, W.: On the transfusion of blood, Boston M. & S. J. 1: 97, 1828.
36. Chereau, V.: Note sur deux pointes dans l'histoire de transfusion, Union méd. 18: (3dds) 373, Sept. 8, 1874.
37. Cohnheim, J.: On the transfusion of blood, Med. News 40: 313, 1882.
38. de Colle, Jean: Methodus facile parandi incunda, tuta et nova medicaments, Venetiis 7: 170, 1628.
39. Corbett, J. F.: A substitute for the syringe used in the David and Curtis equipment, St. Paul M. J. 16: 594, 1914
40. Creite: Quoted by Zimmerman and Howell.¹⁸³
41. Crile, George: Technique of direct transfusion of blood, Ann. Surg. 46: 329, 1907.
42. Curtis, Arthur H., and David, V. C.: Transfusion of blood by a new method, allowing accurate measurement, J. A. M. A. 56: 35, 1911.
43. Dally, P.: Claude Tardi, précurseur de la transfusion, Semaine d. hôp. de Paris 12: 560, 1936.

44. DeBakey, Michael, and Honold, Edith: Blood transfusion, *Internat. M. Digest.* 33: 301, 367, 1938; *ibid.* 34: 49, 1939.
- 44a. DeBelina, J.: *Die transfusion des Blutes in physiologischer und medicinischer Beziehung*, Heidelberg, 1869.
- 44b. Debelina, J.: *La transfusion du Sang appliquée au traitement des blesses*, Paris, 1870.
- 44c. DeBelina, J: *De la transfusion du sang défibriné*. Paris, 1873.
45. DeCastello, A., and Sturli, A.: Ueber die Iso-agglutinine im Serum gesunder und kranker Menschen, München. *Med. Wchnschr* 49: 1090, 1902.
46. Denis, Jean Baptiste: Extract d'une lettre de M. Denis, Professeur de Philosophie et de Mathematiques, touchant la transfusion du sang, *Journal des Scavans*, p. 86 (March 9), 1667; pp. 123, 178 (April 2), 1667; also in *Philosophical Tr. Roy. Soc. London* 1: 617, 1665-1666; 2: 453, 1667; 3: 710, 713, 1668.
47. Dieffenbach, J. F.: *Die Transfusion des Blutes*, Berlin, Theod. Christ. Fr. Enslin, 1828.
48. Donaldson, F.: Case of transfusion of blood for uterine hemorrhage, *Tr. Med. & Chir. Fac. Maryland* 78: 53, 1876.
49. Dorrance, G. M., and Ginsburg, N.: Transfusion; history, development, present status and technique of operation, *N. York M. J.* 87: 941, 1908.
50. Drinkard, W. B.: History and statistics of operation of transfusing blood, *Richmond & Louisville M. J.* 13: 20, 1872.
51. Dutton, Walton Forest: *Intravenous therapy: its application in the modern practice of medicine*, Philadelphia, 1924, F. A. Davis Co., Chap. I.
- 51a. Early history of blood transfusion, *Lancet* 2: 792, 1939.
52. Editors: *Transfusion of blood*, *Phila. J. Med. & Phys. Sciences* 11: 205, 1825.
53. Editorial: The present status of transfusion, *Philadelphia M. Times* 5: 89, 106, 1874-1875.
54. Ehrlich, P., and Morgenroth, J.: Ueber Haemolysine, *Berl. klin. Wchnschr.* 36: 6, 481, 1699; 37: 452, 681, 1900.
55. Elsberg, C. A.: Simple cannula for direct transfusion of blood, *J. A. M. A.* 52: 887, 1909.
56. Fauntleroy, A. M.: Reports of four transfusions by the vein-to-vein method with curved glass tubes, *U. S. Nav. M. Bull.* 5: 47, 1911.
57. Fitch, L. P.: A case of transfusion, *Tr. Iowa M. Soc.* 4: 169, 1880.
58. Flint, Austin, Jr.: Transfusion, *M. Rec.* 9: 189, 1874.
59. Folli, Francesco: Quoted by Cox, B., Blood transfusion in 19th century, *J. A. M. A.* 62: 222, 1914.
60. Frank, Robert T.: A new method for the transfusion of blood, *N. York M. J.* 88: 1023, 1908.
- 60a. Franklin, K. J.: Some notes on Richard Lower (1631-1691) and his "De Cordi," London, 1669, *Ann. Med. Hist.* 3: 599, 1931.
61. Freer, J. W.: Transfusion of blood, *Tr. Illinois M. Soc.* 25: 77, 1875.
62. Freund: Quoted by Zimmerman and Howell.¹⁸³
63. Freund, H. A.: A method for the transfusion of fresh normal blood, *J. Michigan M. Soc.* 12: 459, 1913.
64. Fryer, B. E.: A few remarks on the transfusion of blood, with a modification of the apparatus of Aveling, *M. Rec.* 9: 201, 1874.
65. Gallaher, Thomas J.: A case of leucocythaemia with great exhaustion, following diarrhea; transfusion of human blood; death, *N. York M. J.* 22: 395, 581, 1875.
66. Garrigues, H. J.: Apparatus for transfusion, *Am. J. Obst.* 11: 754, 1878.
67. Garrison, Fielding H.: *An Introduction to the History of Medicine*, ed. 4, Philadelphia, 1929, W. B. Saunders Co.
68. George, C.: Physiological considerations in transfusion of blood, *Buffalo M. & S. J.* 15: 366, 1875.1876.
69. Gesselius, F.: *Capillar Blut zur Transfusion*, St. Petersburg, 1868.
70. Gradle, H.: Two cases of direct transfusion from animal to man, *Med. Exam, Chicago* 16: 294, 1874.
- 70a. von Gräfe, E.: Beschreibung des neuen v. Gräfe'schen Transfusionapparats, *J. d. Chir. u. Augenh. Berl.* 20: 637, 1833.
71. Gregory: Hemorrhage; transfusion, *Missouri Clin. Rec.* 1: 169, 1874-1875.

72. Guthrie, C. C.: Blood-Vessel Surgery and Its Applications, New York, 1912, Longmans, Green & Co.
73. Hartwell, John A.: The operation of direct blood transfusion; description of a simple method, *Am. J. Surg.* 23: 92, 1909.
74. Harvey, William: Works, translated by Robert Willis, Sydenham Society, London, 1847.
75. Hasse, Oscar: Die Lammblood-Transfusion beim Menschen St. Petersburg, Edward Hoppe, 1874.
76. Houghton, B. E.: A consideration of the pathology and treatment by transfusion of blood in tuberculosis phthisis, *Cincin. Lancet & Obst.*, n.s. 2: 647, 1859.
77. Haynes, F. L.: A case of direct transfusion, *Philadelphia M. Times* 5: 420, 1875.
- 77a. Heister, Lawrence: General System of Surgery (translated from Latin), 5th ed., W. Innys and J. Richardson, London, 1753.
78. Hektoen, Ludvig: Iso-agglutination of human corpuscles, *J. A. M. A.* 48: 1739, 1907.
79. Heldrel, C. C.: On the abstraction and on the transfusion of blood, *Am. J. M. Sc.* 63: 101, 1872.
- 79a. Hewit, G.: On the operation of transfusion in obstetric practice, with description of a more convenient transfusion-apparatus, *Bnt. M. J.* 2: 232, 1863.
- 79b. Hewit, G.: Apparatus for the performance of transfusion, *Tr. Obst. Soc. Lond.* 6: 136, 1864.
80. Hicks, J. Braxton: On transfusion and new mode of management, *Brit. M. J.* 2: 151, 1868.
- 80a. Higginson, A.: Report of seven cases of transfusion of blood, with a description of the instrument invented by the author, *Liverpool M. Chir. J.* 1: 102, 1857.
81. Hodgen, J. P.: Apparatus for the transfusion of blood, *St. Louis M. & S. J.* 11: 473, 1874.
82. Hodgen, J. P.: Another apparatus for transfusion, *St. Louis M. & S. J.* 18: 1, 1876.
83. Hoehling, A. A.: Transfusion by Mader's method, *Med. & Surg. Reporter* 20: 379, 1869.
84. Hollingsworth, Merrill W.: Blood transfusion by Richard Lower in 1665, *Ann. M. Hist.* 10: 213, 1928.
85. Holmes à Court, A.: The history of blood transfusion, *M. J. Australia* 2: 528, 1927.
86. Hotz, F. C.: On the transfusion of lamb's blood in the human subject, *Med. Exam.*, Chicago 16: 20, 1875.
87. Howe, Joseph W.: A new method for the transfusion of blood, *M. Rec.* 9: 170, 1874.
88. Hunt, W. C., and Wadsworth: Two cases of transfusion, *Chicago M. J.* 28: 205, 1871.
89. Hustin, M.: Principe d'une nouvelle méthode de transfusion muqueuse, *J. méd. de Brux.* 12: 436, 1914.
90. Hustin, A.: Note sur une nouvelle méthode de transfusion, *Bull. soc. roy. d. sc. méd. et nat. de Brux.*, No. 4, April, 1914.
91. Hustin, A.: Court aperçu historique des débuts de la transfusion citratée, *Arch. Franco-Belges de chir.*, January, 1923.
92. Hustin, A.: Personal communication to the author.
93. Hutchison, Joseph C.: A new apparatus for transfusion, with remarks on the intravascular injection of blood and other fluids, *N. York M. J.* 40: 656, 1884.
94. Hutchison, Joseph C.: Transfusion of blood (Aveling's method); transfusion of milk (King's County Hospital, Flatbush, L. I.), *Med. & Surg. Reporter* 40: 230, 1879.
95. Isohemagglutination. Recommendation that the Jansky classification be adopted for universal use, *J. A. M. A.* 76: 130, 1921.
96. Jackson, Samuel: On the safe delivery of the placenta, with some observations on transfusion, *Am. J. M. Sc.* 2: 77, 1828.
97. Janeway, Henry: An improved device for transfusion, *Ann. Surg.* 63: 720, 1911.
98. Jansky, Jan: Haematologicé, studie u phychotikú (Études hématologiques, dans les malades mentales), *Sborn. Klin.* 8: 85, 1907.
99. Jenkins, J. H.: Transfusion of lamb's blood in typhoid fever, *North Car. M. J.* 26: 446, 1890.
100. Jennings, C. E.: Transfusion; its history; indications; and modes of application, London, 1883.
101. Jones, William: Successful employment of transfusion, *Med. Magazine* 1: 567, 1833.

102. Jones, Harold W., and Mackmull, Gulden: The influence of James Blundell on the development of blood transfusion, *Ann. M. Hist.* 10: 243, 1928.
103. Kaufman and Purman: Quoted by Dutton,⁵¹ and Mayerhofer.¹²⁷
104. Kay, J. P.: Transfusion, *Cyclopedia of Practical Medicine*, Philadelphia, 1854, Blanchard and Lee, vol. 4, p. 468.
105. Keegan, P. J.: A case of transfusion of blood, *Albany M. J.* 10: 78, 1889.
106. Kerr, W. M.: A history of blood transfusion, *U. S. Nav. Med. Bull.* 16: 465, 1922.
107. Kiernan, J. K.: A new transfusion instrument, *Chicago M. Rev.* 5: 134, 1882.
108. Kimpton, A. R., and Brown, J. H.: A new and simple method of transfusion, *J. A. M. A.* 61: 117, 1913.
109. King, J. F.: A case of transfusion of arterial blood from the carotid of a lamb into the cephalic vein of man, *Tr. M. Soc. North Car.* 14: 40, 1872.
110. Kreuzscher, Philip H.: A new blood transfusion method, *J. A. M. A.* 70: 223, 1918.
111. Kuester: New facts on transfusion with lamb's blood, *M. Rec.* 9: 515, 1874; also *Arch. f. klin. Chir.*, Berlin 17: 385, 1874.
112. Kush, Morris: A automatic transfusion apparatus, *J. A. M. A.* 65: 1180, 1915.
- 112a. á Lamzweerde, Johannes Baptista: *Chirurgiae, veteris ac modernae promptuarium tabulis viginti novem exornatum, instrumenta varia, eorumque usum exhibentibus, necnon observationum medico-chirurgicalum centuria illustratum*, Amstelodami apud J. à Someren, 1672.
113. Landois, Leonard: *Die Transfusion den Blutes*, Leipzig, 1875, S. C. W. Vogel.
114. Landois, Leonard: Quoted by Zimmerman and Howell.¹⁸³
115. Landon, L. H.: A simplified method of direct blood transfusion with self-restraining tubes, *J. A. M. A.* 61: 490, 1913.
116. Landsteiner, K.: Zur Kenntniss der antifermentativen, lytischen und agglutinisrenden Wirkungen des Blutserums und der lympe, *Zentralbl. f. Bakt.* 28: 357, 1900.
117. Landsteiner, K.: Ueber agglutinationserseheinungen normalen menschlichen Blutes, *Wien. klin. Wchnschr.* 14: 1132, 1901.
118. Levin, Isaac: A clamp for direct transfusion of blood, *N. York M. J.* 88: 669, 1908.
119. Lewisohn, Richard: A new and greatly simplified method of blood transfusion, *Med. R.* 87: 141, 1915.
120. Libavius, Andreas: Quoted by Zimmerman and Howell.¹⁸³
121. Lindeman, Ed.: Simple syringe transfusion with special cannulas, *Am. J. D. Child.* 6: 28, 1913.
122. Lindeman, Ed.: Blood transfusion, report of 135 transfusions by the syringe-cannula method, *J. A. M. A.* 62: 993, 1914.
123. Lower, Richard: *Tractatus de corde; item de motu et colore sanguinis, etc.*, London, 1669, Jacobi Allestry, chap. 4.
- 123a. Lower, R., and King, E.: Transfusion practiced upon a man in London, *Phil Tr.* 3: 231, 1700.
124. *Philosoph. Trans. Roy Soc.*, London 1: 128, 352, 353, 1665-1666; 2: 557, 1667.
- 124a. Major, J. D.: *Chirurgia infusoria*, Kiloni, 1667.
125. Martin, Eduard: *Ueber die Transfusion bei Blutungen Neuentbundener*, Berlin, 1859, August Hirschwald
126. Mathews, A. H.: *Life and Time of Rodrigo Borgia*, p. 60, Brentano's, New York, 1912.
127. Mayerhofer, B.: Einige Klarstellungen zur Geschichte der Bluttransfusion, der subkutanen Injektion und der intravenösen Infusion, *München. med. Wchnsehr.* 84: 1417, 1937.
128. Mayerhofer, B.: Hat wirklich der Italiener Franz Folli die überhaupt erste Bluttransfusion ausgeführt, diese bereits von Mensch zu Mensch *Med. Welt.* 12: 473, 1938.
129. Mayrhofer, B.: *Die Medicina infusoria des Franz Folli*, *Med. Welt.* 12: 1299, 1938.
130. McClure, Roy D., and Dunn, George B.: Transfusion of blood; history, methods, dangers, preliminary tests, present status; report of one hundred and fifty transfusions, *Bull. Johns Hopkins Hosp.* 28: 99, 1917.
131. McGarth, Bernard Francis: A simple instrument for transfusion, *J. A. M. A.* 62: 40, 1914.
- 131a. Mercklinus, G. A.: *De ortu et occesu transfusionis sanguinis*, Norimbergae, 1679.
132. Meyer, W. W.: Transfusion in anemia, *Med. & Surg. Reporter* 15: 255, 1866.
133. Miller, G. I.: Blood transfusion; indications and technique, *M. Rec.* 88: 425, 1915.

134. Moore, Prof. E. H.: On transfusion, *M. Rec.* 10: 348, 1875.
135. Morrison, William Reid: An improved blood transfusion tube, *Boston M. & S. J.* 176: 468, 1917.
136. Morton, Thomas G.: On transfusion of blood, with a report of 8 cases, and a description of a convenient apparatus for performing the mediate method, *Am. J. M. Sc.* 68: 110, 1874.
137. Morton, T. G.: Transfusion of blood (6 cases), *Surg. Penn. Hosp.* 65: 74, 1880.
138. Moss, W. L.: Studies in iso-agglutinins, *Bull Johns Hopkins Hosp.* 21: 63, 1910.
- 138a. Müller, Jacob Worm: *Transfusion and Plethora*, Christiana, 1875.
139. Murphy, J. B.: Resection of arteries and veins injured in continuity, end to end suture; experimental and clinical research, *M. Rec.* 51: 73, 1897.
140. Neudorfer: Ueber Transfusionen bei Anaemischen, *Oesterr. Ztschr. f. prakt. Heilk.* 6: 124, 1860.
141. Nuck, Anthony: *Operationes et experimenta chirurgica*, J. T. Brem. Med. Stud. Lugdun. Batavorum, 1692.
142. Oré, P. C.: *Transfusion du Sang*, ed. 2, Paris, 1876, Baillière.
- 142a. Oré, P. C.: *Etude historique, physiologique et clinique sur la transfusion du sang*, ed. 2, Paris, 1876.
143. Ottenberg, Reuben: Transfusion and arterial anastomosis, *Ann. Surg.* 47: 486, 1908.
144. Ottenberg, Reuben: Transfusion and the question of intravascular agglutination, *J. Exper. Med.* 13: 425, 1911.
145. Ottenberg, Reuben, and Kaliski, D. J.: Accidents in transfusion; their prevention by preliminary blood examination, *J. A. M. A.* 81: 2138, 1913.
146. Ottenberg, Reuben, Kaliski, D. J. and Friedman, S. S.: Experimental agglutinative and hemolytic transfusions, *J. Med. Research* 28: 141, 1913.
147. Ottenberg, Reuben, and Thalheimer, W.: Studies in experimental transfusion, *J. Med. Research* 38: 213, 1915.
148. Ottenberg, Reuben: Reminiscences of the history of blood transfusion, *J. Mt. Sinai Hosp.* 4: 264, 1937.
149. Panum, P. L.: Experimentelle Untersuchungen ueber die Transfusion, Transplantation oder Substitution des Blutes in theoretischer und practischer Beziehung, *Virchows Arch. f. path. Anat.* 27: 240, 433, 1863.
- 149a. Payr, Erwin: Beiträge zur Technik der Blutgefäß- und Nerven-naht nebst Mittheilungen über die Verwendung eines resorbirbaren Metalles in der Chirurgie, *Arch. f. Chir.* 62: 67, 1900.
150. Pemberton, J. deJ.: Blood transfusion, *Surg., Gynec. & Obst.* 28: 262, 1919.
151. Pepys, Samuel: *The Diary of Samuel Pepys*, edited by Henry B. Wheatley, London, 1928, G. Bell and Sons, Ltd., vols. IV to VI (1664-1667); vols. VII to VIII (1667-1669).
152. Percy, Nelson Mortimer: Simplified method of blood transfusion with report of 6 cases of pernicious anemia treated by massive blood transfusion and splenectomy, *Surg., Gynec. & Obst.* 21: 360, 1915.
153. Prewitt, T. F.: Transfusion; its history and present status, *St. Louis M. & S. J. n.s.* 13: 169, 1876.
154. Proegler, C.: Transfusion of blood, *Chicago M. J.* 28: 595, 1871.
- 154a. Purmann, Matthaeus Gottfried: *Chirurgische Lorbeerkrantz*, Halberstadt, 1684.
155. Razzoli, E.: I prodromi della pratica della trasfusione di sangue e della "chirurgia infusoria," *Policlinico (sez. prat.)* 40: 1014, 1933.
156. Richardson, B. W.: The cause of the coagulation of blood. The Astley-Cooper prize essay for 1856, quoted by Pemberton.¹⁵⁰
157. Rouanet: On abortion and transfusion of blood, *New Orleans M. & S. J.* 9: 111, 1852-1853.
158. Roussel, J.: *Transfusion of Human Blood by the Method of Roussel*, translated by C. H. C. Guinness, London, 1877.
- 158a. Roussel, J.: Nouvel instrument pour in transfusion du sang, *Gaz. d. hôp.* 2: 549, 1867.
- 158b. Roussel, J.: La transfusion, *Arch. générales d. méd.* 25: 129, 443, 690, 1875; 26: 204, 320, 570, 672, 1875.
- 158c. Rousel, J.: Presentation d'un appareil pour opérer la transfusion directe de bras à bras, du sang vivant et intact, *Bull. Acad. roy. de méd. de Belg., Brux.* 10: 624, 1876.
159. Rueck, G. A.: Transfusion of blood by the gravitation method, *M. Rec.* 87: 354, 1915.

160. Rueck, G. A.: The method of transfusion of blood treated with sodium citrate, *M. Rec.* 89: 688, 1916.
161. Sollmann, Torald: Jacob Worm Mueller; on transfusion; a retrospect, *Cleveland M. J.* 14: 546, 1915.
162. Satterlee, Henry S., and Hooker, Ransom S.: Experiments to develop a more widely useful method of blood transfusion, *Arch. Int. Med.* 13: 51, 1914.
163. Satterlee, Henry, and Hooker, Ransom: The use of hirudin in the transfusion of blood, *J. A. M. A.* 62: 1781, 1914.
164. Satterlee, Henry, and Hooker, Ransom S.: Transfusion of blood with special reference to the use of anticoagulants, *J. A. M. A.* 68: 618, 1916.
165. Scheel, Paul: *Die Transfusion des Blutes und Einspritzung der Arzneien in die Adern, historisch und in Rücksicht auf die practische Heilkunde bearbeitet*, Copenhagen, 1802.
166. Schriver, C.: Case of transfusion in diabetes mellitus, *Cincin. Lancet & Obst.* 18: 533, 1875.
167. Sedgwick, S. P.: Transfusion, *Chicago M. Times* 7: 1, 1875.
168. Sittel, Theo: Lamb's blood transfusion, *Clin. Cincin.* 7: 157, 1874.
169. Slocker, E.: Contributions to the history of blood transfusion, *Siglo méd.* 83: 75, 1929.
170. Soresi, A. L.: A new method of direct transfusion of blood, *N. York. M. J.* 93: 622, 1911.
171. Sternberg, George M.: Transfusion of blood and other liquids, *M. Rec.* 4: 22, 1869.
172. Taylor, G. G. S.: Accidental hemorrhage; transfusion, recovery, *Am. J. Obst.* 30: 190, 1894.
173. Thomas, T. Gaillard: The intravenous injection of milk as a substitute for the transfusion of blood; illustrated by seven operations, *N. York M. J.* 27: 449, 1878.
174. Ullersperger, Jean Baptiste: *Ancient transfusion and infusion compared with modern transfusion, infusion, and hypodermic or subcutaneous injections*, translated by Charles P. Wittig, Philadelphia, from Chaille, S. E., *Miscellanies*, 1867-1869.
175. Unger, Lester J.: A new method of syringe transfusion, *J. A. M. A.* 64: 582, 1915.
176. Villari, Pasquale: *The History of Girolamo Savonarola and His Times* (translated from the Italian by Leonard Homer), London, 1863, Longmans, Roberts & Green, vol. I, p. 144.
177. Vincent, Beth: Blood transfusion with paraffin-coated needles and tubes, *Surg., Gynec. & Obst.* 23: 360, 1915.
178. Weil, Richard: Sodium citrate in the transfusion of blood, *J. A. M. A.* 64: 425, 1915.
179. Whittle, A. P.: Blood letting and transfusion, *Pacific M. & S. J.* 28: 340, 1885.
180. Winants, J. E.: Case of transfusion, *Am. J. M. Sc.* 63: 108, 1872.
181. Wren, Sir Christopher: *Sir Christopher Wren and Medical Science*, *Brit. M. J.* 1: 386, 1923; also *Med. Life* 30: 307, 1923.
182. Ziemssen, V.: *Ueber die subcutane Blutinjection und ueber eine neue einfache Method der intravenoesen Transfusion*, *München. med. Wchnschr.* 39: 323, 1892.
- 182a. von Ziemssen, H.: *Klinische Vorträge, 3. Vortrag, 2. Abteil. 2. Ueber subcutane Blutinjektion, Salzwasserinfusion und intravenöse Transfusion*, Leipzig, 1887; *Abst., J. A. M. A.* 9: 35, 68, 1887.
183. Zimmerman, L. M., and Howell, K. M.: History of blood transfusion, *Ann. M. Hist.* 4: 415, 1932.