Original scientific article
Izvorni znanstveni članak

Acta Med Hist Adriat 2022; 20(1); 27-50
https://doi.org/10.31952/amha.20.1.2

# THE ORIGINS OF THE BLOOD TRANSFUSION: EUROPEAN LITERATURE AND ITALIAN DEBATE ON NEW INNOVATIONS (1667-1668)

# PODRIJETLO TRANSFUZIJE KRVI: EUROPSKA LITERATURA I TALIJANSKE RASPRAVE O NOVIM INOVACIJAMA (1667. – 1668.)

**Silvia Marinozzi[*], Daniela Messineo[**], Giuseppe Sanese[***]**

SUMMARY

*This paper deals with the literary debate on the first experiments regarding blood transfusion on human beings between 1667 and 1668 in Europe, with particular attention to the less-known experimental research, carried out in Italy. The authors examine the details of the experimental developments, focusing on the techniques and instruments used by physicians involved in this new surgical approach, with special attention to the Italian debate and experimentations. The article suggests that transfusion was considered a part of what we could call "emergency surgery". In this framework, Italian transfusional pioneers played a central role in the improvement and transmission of a discipline that was still in its dawning throughout Europe. Moreover, the manuscript highlights the contribution of the "chirurgia infusoria" as an innovative therapeutic system for an immediate and rapid recovery. From this perspective, blood transfusion represents a surgical practice for reanimation and resusci-*

[*] Department of Molecular Medicine, Unit of History of Medicine and Bioethics, Sapienza University of Rome, Rome, Italy. ORCID: https://orcid.org/0000-0002-4571-343X
[**] Department of Radiological, Oncological and Pathological Anatomy Sciences, Faculty of Medicine and Dentistry, Sapienza University of Rome, Rome, Italy.
[***] PhD School on Medical-Surgical Applied Sciences-Plastic Regenerative research area and Department of Plastic and Reconstructive Surgery, School of Medicine and Surgery "Tor Vergata", University of Rome, Rome, Italy.
*Correspondence Address*: Daniela Messineo, Department of Radiological, Oncological and Pathological Anatomy Sciences, Faculty of Medicine and Dentistry, Sapienza University of Rome, Viale del Policlinico, 155, 00161 - Roma, Italy. E-mail: daniela.messineo@uniroma1.it.

*tation. The objective of this work was to analyze the importance of foreign literature and the English and French disputes presented by Davia in Italy, which made them known. Despite foreign prohibition in Italy, experiments with animal-to-human transfusions continued after 1648. A papal bull excommunicating scientists for conducting such research has never been found.*

***Keywords:*** *blood, transfusion, European literature, transfusion history, Italian culture, human transfusion, animal transfusion*

## Introduction

This article is a comprehensive and more detailed version of the first steps in blood transfusion research in Italy, focusing on the debate about this new practice and the views of other international scholars (Marinozzi et al., 2018).

In the ancient medical tradition, the vital spirit was a vapor of pure, thin, and warm blood, produced by the action of the heat of the heart on the most subtle and airy part of the blood. When this vapor reaches the brain, it comes into contact with the soul. What is perceived by the body is transmitted by the spirit to the soul, which processes the sensations by transmuting them into "imagination". As the seat and vehicle of the spirit, the blood vitalizes and transmits movement to the body and becomes an expression of the moral and spiritual qualities of the individual. The ancient tradition is full of similar examples: Democritus claimed that for some diseases, it is useful to take the skull, duly treated, of a condemned person, while for others, it is useful to take the skull of a friend or relative of the patient; Apollonius used a tooth extracted from a corpse to scarify the gums; Meletus recommended human bile to cure cataracts; Artemone made people suffering from epilepsy drink water poured and left overnight in the skull of a man who had died a violent death, just as Antaeus used the skull of a hanged man as an antidote to the bite of rabid dogs.

In Roman culture, moreover, several sources attest to the custom of drinking human blood to treat epilepsy: A. C. Celse[1] (1st century B.C.–1st century A.D.), in his manuscript "*De re medica*", reports that in Rome it was customary to collect and drink the still-warm blood that flows from the wounds of gladiators, selected based on their young age, physical power, strength, and gymnastic ability. They represented an exemplary model of men from whom blood is drawn, which, as the seat and vehicle of the vital spirit, infuses those

[1] "*Quidam iugulari gladiatoris calido sanguine e poto tali morbo liberarunt; apud quos miserum auxilium tollerabile miserius malum fecit.*" (Celsus, Aulus Cornelius, *De re medica*, III,23,7)

who absorb it with the *vigor* and physical energy proper to the individual from whom it was extracted.

Pliny the Elder (23–79 A.D.) also reports on the use of drinking the blood of wounded gladiators to treat epilepsy since it is rich in vital warmth, the soul of life (Moog & Karenberg, 1758; Galassi et al., 2019).

Through the popular magic-religious traditions and the philosophical-alchemic traditions of Arabic and neo-platonic matrix, the therapeutic use of human blood filters became an official practice in iatrochemistry. In Paracelsian doctrine, the intellectual life of the soul is the spirit of God; since the celestial spirit dwells in the body and works continuously, man is himself the firmament and welcomes the spirit, the divine intellectual "verb". The eternal Man lives in the soul, and the soul is the dwelling place of God. Therefore, man, the perfect complement to every divine work, the complete image of the entire universe, the simulacrum of God, contains everything.

So, in man coexist the three worlds, the *tria prima* of world and heaven, and the fourth world, which is in all things, that is the spirit or mind of God. The spirit of man, the *verus internus homo*, is, in fact, an invisible body which, constituted of reason and the astral spirit, is similar to angels. It is part of the elements, and from these, it receives the mortal earthly physical body. Blood is a material vehicle of contact between the various constituent parts of the human universe, and it is the seat of the vital spirit that participates in the divine and the universal soul.

For Andreas Tentzel (fl.1625), the blood, a vital principle, contains the four natural elements since it is composed in a small part of the earth, in a more significant measure of water, mainly of air, and it receives heat from the heart. In the Paracelsian philosophical conception, the body also contains the first principles of earth and sky (i.e., sulfur, mercury, and salts), which can be identified through "alchemical" processes that allow their extraction.

The wisdom and knowledge of alchemical processes for the transformation, combination, and extraction of the elements, allowed the elaboration of new drugs derived from the mineral, vegetable, and animal world, including man. Every part of the human body can be subjected to "officinal" processes of distillation and purification to extract the vital or spiritual essence that reconstitutes the original *archeo* of the sick part or element.

Alongside pharmacological preparations that involve the use of animal blood, there are also extracts of human blood.

Johann Schroder (1600–1664) indicated the "*officinal parts*" of the body to be used in therapy, including blood. When drunk, still fresh and warm, it is good for epilepsy resuming the motion more vigorously and the course faster until the onset of sweat, and sedates any bleeding. However, drinking blood requires great caution, as it can induce violence and even cause epilepsy. Moreover, when used externally, it soothes blood rashes, especially from the nostrils. The blood of childbirth heals scabies.

Schroder indicated the procedures for the elaboration of distillate, oil, balm, spirit, and the arcane of human blood. The distilled oil was obtained from the blood of young people, extracted during the winter, left to digest in wine alcohol, and then macerated in ashes for about 40 days. Then, it was distilled in a still that will produce a substance composed of water and oil, which were rectified by distilling in the ashes, the first in a *bain-marie* and the second in a retort. This oil, taken every day for a month, starting from the new moon, in the amount of half a scruple at a time, and then in the amount of one scruple at each new moon for one year, was recommended to treat epilepsy. It was also good for paralysis, apoplexy, pleuritis, and pulmonary inflammations.

About the remedies extracted from man, Moyses Charas (1618-1698) believed in the principle that God created man so that he could find his remedies in his body.

That blood must be taken from young, healthy men who do not have red hair, then poured into glass containers soaked in ashes over a moderate fire until the watery part, drying out, solidifies. The dried blood will then be put into a horn and cooked again until it is possible to extract the oil and volatile salt, which will then be stored in a flask for rectification in a sand bath. The volatile blood salt was used as a remedy against epilepsy. It promoted circulation and had healing properties for malignant and contagious fevers. It was also used for gout and hydropsy.

Georg Wolfgang Wedel (1645-1721) inserts human blood to treat epilepsy among the "*liquores animalium spontanei succos aemulantur, expressi minus usitati*" that find pharmacological use (Wedel, 1686). However, it seemed to him that the intake of blood extracted from the vessels was a cruel custom, so he denied what Marsilio Ficino claimed about the power of human blood to prolong life. Wedel thus reported the therapeutic virtues of animal blood, such as goat's blood to cure the traumas of falling from a height, pleurisy, and calculus, donkey's blood for melancholy, hare's blood against dysentery. However, since dried and baked in the oven, the blood takes on another char-

acter, and the essence degenerates into something else (i.e., it lacks therapeutic virtues). The intake of fresh blood was recommended.

The human blood that Wedel used, as it is identical to "*substantia et essentia*", was the female menstrual blood that could be used to treat moles for its nitrous, cooling, and positive virtues. The blood of women, deprived of that vital principle proper to man, is cold by nature.

Still, in the 18th century, Robert James (1703-1776) reported that

> *" [...] The fresh and warm blood, drunk, is told to be effective against epilepsy; provided that the patient, after drinking it, makes a lot of motion, running until he sweats. It also stops all sorts of bleeding. Used externally, it represses every blood flow, and especially that of the nose. [...]"* (James,1758; Himmelmann & Kenneth, 1997).

Thanks to studies on anatomy, new methods and different infusion instruments were also created and perfected to study the anatomo-physiology of the blood system and for anatomical preparations. Regnier de Graaf (1641–1673) developed a siphon to infuse a preservative liquid, colored according to the vessels and organs to be prepared, to illustrate the ramifications of the vessels and the mutual interconnections in the individual parts of the body (De Graaf, 1677). Siphons for anatomical preparations were also used by Thomas Bartholin (1616–1680), Louis De Bils (1623?–1669), Frederik Ruysch (1638–1731), Jan Swammerdam (1637–1682), Alexander Monro (1697–1797), who in Essays and Observations of Medicine of the Society of Edinburgh (Venice, 1753) describe in detail the process of intravascular injection of preservative liquids into different parts of the body for anatomical preparations. The experiments to study the physiology of the blood system led to new developments both in the therapeutic use of blood, thanks to new instruments, and in the affirmation of 'infusional surgery', which allows the injection of pharmacological liquids into blood vessels. The affirmation of the therapeutic value of blood came after the invention of transfusion (Marinozzi & Conforti, 2005).

## Methods

For the study, we analyzed historical sources from the archives of the Sapienza University of Rome between 1600 and 1800. This period was chosen because of the innovative prodromal transfusion techniques that were found. No patients were involved or examined in this study. The study did not examine what pertains to the practices of cannibalism or ingestion of powders or oils from cadavers that were reported in the same historical period and

predominantly from Egypt and the Near East (Montanari, 2015). The history of blood transfusion has been widely discussed in the literature of medical history (Giangrande, 2000). Indeed, many papers have highlighted the controversy over the origins of its application to humans, a debate that arose between English and French authors who were experimenting with transfusion at the time (Johns, 2000). There is a little history of experiments carried out in Italy after publication of the work carried out by doctors from beyond the Alps. The authors have analyzed the Italian studies.

The authors analyzed the Italian studies to reconstruct a real picture of the medical environment of the time, in search of objective data demonstrating the therapeutic value of transfusion (Farr, 1980; Hall & Hall, 1980). The descriptions of the experiments conducted by surgeons between 1666 and 1668 also provide accurate information to better understand the methods, instruments, and techniques used by different surgeons during this period (Giordano, 1931; 1932; 1939).

## Discussion

In the 16th century, the demonstration of the circular movement of blood also led to the search for new therapeutic methods. The most innovative method was "Infusional Surgery" - the direct introduction of pharmacological liquid into veins and arteries - tested and applied in the mid-17th century, especially by C. Wren (Clark, 1668) and widely written about in the works of J. D. Major (Majoris, 1667). This method was quickly modified with the use of blood. Starting in 1663, some doctors of the Philosophical Society of London, among whom John Wilkins, Thomas Coxe, and Robert Hooke, experimented with a series of procedures for blood transfusion in animals. In 1667, Richard Lower applied this procedure on humans (Fastag et al., 2013), simultaneously with those practiced by J.B. Denys in France (Hoff & Guillemin, 1963; Picard & Schneider, 1996), followed by G. Riva's experiments in Rome, Italy (Romano, 2009; Scalzi, 1871; Riva et al., 2014).

### Arguing on the paternity of blood transfusion - Who were the earliest proponents of this practice?

The attribution of the primacy of this invention is controversial. Already in 1628, G. Colle (1628) was the first to hypothesize that infusing blood taken from the vein of a young man to that of an older person was the best cure for the diseases of old age, "*nam hic sanguis potest reparare humidum et temperamen-*

*tum, professor Artistotele*", yet he never carried it out. One has to wait for the Harveyan revolution to see the rise of surgical infusion. J. D. Major claims to have been the first to propose blood transfusion (Majoris, 1667) and to have already practiced this procedure between 1664 and 1665 – however, when he published his works in those years, there was no mention of transfusion. Thus, it was only in his book, *Chirurgia Infusoria*, from 1667 that he finally dealt with transfusion when also experiments were performed in France, Italy, and England.

Francesco Folli, an important physician of the 17th century, a member of the *Accademia Sperimentale* [Experimental Academy] of the Grand Duke of Tuscany Ferdinando II and the *Accademia del Cimento* [Cimento Academy] of Leopoldo I, stated that he was the first to use blood transfusion to treat elderly patients and prolong life. In his treatise, he affirmed that he had expressed this idea to the Grand Duke Ferdinand of Tuscany in 1654, long before British surgeons performed their first experiments. However, there is no evidence that any experiments were conducted, and no account of his theory was published any time before 1680 when he published his *Stadera Medica* (Folli, 1780).

Also, R. Lower (1728), in his *Tractatus de corde* of 1669, claims to have been the first to attempt transfusion on a dog in 1665 by connecting the cervical artery of the donor to the receiver's jugular artery.

According to historians, among the first to experiment with injecting drugs into veins was C. Wren, who in 1663 also carried out blood transfusion, opening the way to the experiments in this direction for the doctors of the Royal Society of London (Sprat, 1667).

T. Clark, in a 1668 letter to Oldenburg, the first editor of Philosophical Transactions, states that "praterea sanguinis etiam ipsius transfusionem saepius tentaverim" starting in 1657, from an animal artery to the vein of another.

The first experiments were published in the Philosophical Transactions of 1666, when Lower highlighted the success of a blood transfusion between two dogs carried out in February 1665 (Lower, 1666; Fastag et al., 2013). R. Boyle, who appreciated Lower's experiments, immediately posed some questions on the use of transfusions; the most striking questions concerned the effects on the blood and the body of the recipient, specifically whether the quality of the blood changes and how when the animals belong to different species. Moreover, he wonders if the blood of a healthy young subject can be thera-

peutic for an older animal and induce greater vigor and growth. These would be the most debated issues between opponents and supporters of transfusion. A central point is found in the theme of the prolongatio vitae and how blood infusion can revitalize the sick and offer such potent nourishment to induce even disproportionate and excessive growth in the individual who receives the transfusion (Knight & Hunter, 2007).

Scientific reports about transfusion experiments

Between 1666 and 1668, in the *Philosophical Transactions*, we find numerous references to experiments carried out in England and France. Their description makes it possible to derive the surgeons' techniques and instruments. T. Birch (1752) reports that in 1666, on behalf of the Royal Society of London, E. King performed several experiments on animals, along with Balle, Coxe, and Hooke, and he was the first to try heterogeneous transfusion, infusing sheep blood into a dog. His idea was to transfuse blood in humans, although the first physician to experiment with it would be J.-B. Denys in France. We also found his transfusion experiment from a veal's vein to a sheep's one, injecting a large amount of blood. However, this caused convulsions at first, leading to the animal's death. We also learned of Thomas Coxe's experiments, with blood transfused from one dog with mange to another healthy dog, without the latter having contracted the disease, and the donor would even be cured in two weeks (King, 1666-1667). Moreover, we found the publication of extracts from Denys' letters, Professor of Philosophy and Mathematics in Paris, already published in the *Journal des Sçavans (Journal des savants)*, which describes his blood transfusion experiments between three veals and three dogs (Denis, 1667), as well as his first transfusion on a human, carried out to cure A. Mauroy, suffering from a "delirium", with two blood transfusions from the femoral artery of a calf. In the first procedure, Denys transfused blood into the vein of the right arm, while in the second into the left arm in December of 1666 (Denis, 1666–1667). There is also news of a transfusion experiment on a man carried out in November 1667 in London by R. Lower and E. King, from the carotid artery of a sheep to the vein of the arm of a man named Arthur Coga, who had been unsuccessfully treated for a long time. Firstly, they drained the blood of both with bloodletting through silver pipettes inserted in their respective vessels, which vented into a basin. Then they connected the pipette inserted into the artery of the sheep to the one introduced in the man's vein through a feather, probably from a goose, and infused approximately 9 to 10 ounces of blood into the patient, who had no trouble and was

in excellent health. Through his experiments on animals, Clark was able to see the benefits this practice could offer because it acts immediately. However, he also highlighted some issues on the possible effectiveness as a therapy in humans. He also wondered if a young man's blood can give force to that of an older person, as well as the benefit or damage, concerning blood from animals of different species (Clark, 1668).

In the *Journal des Sçavans (Journal des savants)* from 1667 and 1668, we find the letters of J.B. Denys, Doctor of King Louis XIV, who from 1666 experimented with this practice on animals, as well as work from other supporters of the new method. We also found some authors who opposed this practice, like G. Lamy, the greatest opponent of this "*nouveau moyen de tourmenter les Malades, que de les guerir*" (Le Journal des Sçavans, SA, 1668). In 1668 in Rome, Italy, the *Giornale de' Letterati* was founded, offering a report on the experiences of transfusion performed at that time in France, Italy, and England. Translating reports of the *Journal des Sçavants (Journal des savants)* and drawing upon the work from *Philosophical Transactions*, the printer of the "Giornale", N. A. Tinassi, drafted a monographic work entitled "*Relatione dell'esperienze fatte in Inghilterra, Francia ed Italia. Intorno alla celebre, e famosa trasfusione del sangue per tutto Gennaro 1668*" (Tinassi, 1668) printed in Rome, while V. M. Davia (1668) published the same work in Bologna.

They translated into Italian extracts of letters and communications across the Alps of the authors who published work and experiments on transfusion, as well as news from the experiments carried out in Italy, making it possible to outline a comprehensive picture of the work and techniques used by different physicians (Castelnuovo, 2011).

In *Journal des Sçavants (Journal des savants)* and *Giornale de' Letterati,* Denys' works were reported, starting from the experiment performed in March 1667 with the surgeon P. Emmerez on two dogs of different gender and breed, with a blood transfusion from the femoral artery of the female to the male's jugular vein. The technique was as follows: two ligatures were made at the donor's crural artery, the lower with a tight knot to hold the blood flow, the higher with a sliding knot, and then it could be loosened if necessary. Then, they perforated the artery and fitted a small brass tube with the curvature in the direction of the heart to receive blood after loosening the upper knot. They made similar ties to the jugular of the receiver, both with sliding knots that are loosened after making the hole in the vein and having inserted two pipes, one with the curvature towards the heart to push the blood in that direction, the other curved toward the head to evacuate the excess blood.

After, they combined the tube placed in the artery of the female dog to that penetrated the jugular of the male dog, towards the heart. Six days later, they repeated this using the same dog as a donor that had previously been on the receiving end and transfused this blood to a third dog. They concluded that by using the femoral artery and not the carotid artery like the British, the donor animals survived, and it was better to use short tubes to preserve the natural heat of the blood.

In the letter to Montmor, Advisor to the King, in June 1667, Denys informed him that he had performed another experiment on dogs from vein to vein and from the crural and the carotid artery to the jugular vein, without ever having caused the death of animals. Along with Emmerez, they then transfused blood from a calf to a dog with good results, confirming that the blood of a donor animal of a different species does not harm the recipient nor alters its nature and that the passage in the small tubes does not change the quality of the blood. Denys responded to objections raised by opponents of transfusion who argued that different blood types could not be homogenized in a proportionate mixture and that donated blood may even be toxic to the recipient. Instead, the author considered the blood from a different individual as therapeutic since it acts as a food, which is different in quality, nature, and substance from the blood, but that it is processed and assimilated until becoming part of it. This is true, as supported by Hippocrates, namely that when blood is stagnant and decanted, it can be harmful. However, the transfusion is not exposed to air, and it is fast flowing without the loss of heat and does not interrupt the natural motion. Circulation, with the continuous passage of the blood between the two vascular systems, ensures a perfect mixture between the donor and the recipient so that the blood extracted from a healthy individual vivifies the corrupted one of a sick individual who undergoes transfusion because it acts as a powerful and immediate drug in the therapeutic action. Therefore, the transfusion is the most reliable and effective therapy in cases of chronic diseases, for which the digestion and absorption of drugs taken orally are impaired for altered processes, thus preventing proper assimilation.

Following a *leit-motive* that was typical of this new practice proponents, Denys highlighted that it is Nature itself that indicates how transfusion is an entirely natural process because it follows what happens during pregnancy when the *fetus* is formed, developed, and fed on the blood of the mother. This is only a quicker way to bring nourishment and vitality to the body, and it is more effective than bloodletting to purify the blood.

He argues that the blood of an animal can be transfused to humans, as long as it is less corrupted than the human blood, which undergoes altered digestion processes due to the intemperance of food and excessive variety of foods, as well as unruliness of lifestyles. In contrast, animals ingest healthy and natural foods and lead a more balanced life.

Furthermore, we can carry out transfusions from artery to artery, vein to artery, and vein to vein. The blood of a young individual can benefit the elderly because it gives life, and that of a healthy animal can treat one that is sick. In June of 1667, the first transfusion of human blood was performed – that of a young man suffering from months of a violent fever and whom doctors had subjected to frequent bloodletting until he had become weak and intellectually unresponsive. After having taken out 3 ounces of blood and transfusing it from the carotid artery of a lamb to the vein of the boy's arm, the young patient survived and showed signs of improvement. The success of this experience led the author to repeat it on a strong, healthy man, drawing the first ten ounces of blood and then replacing it with an equal amount transfused from the crural artery of a lamb.

## The European debate about transfusion efficacy

Lamy responded with a letter addressed to Dr. Moreau, from the School of Medicine in Paris, in July 1667, opposing transfusion as a therapy, pointing out that, since nearly all internal diseases result from the impurity or the overabundance of blood, it is harmful to transfuse more. In addition, many diseases are caused by an excess of heat, for which adding further arterial blood would only increase it, while the venous system, due to its nature, cannot mitigate that of the receiver. Furthermore, the blood of a boy cannot give force to that of an older adult because the nature and temperament of a young individual are very different from that of older people. Blood is made up of many different particles, each intended to feed specific body parts, and all contribute to generating semen. Therefore, those that are suitable for feeding the parts of an animal cannot be suitable for man, which has a different constitution. Transfused blood is of such a small amount that it can only be corrupted by the recipient without offering any benefit at all. As a matter of fact, this old idea has recently found a new appreciation in the therapeutic use of plasma (Sha et al., 2019).

Doctor Gadoys responded to Lamy in a letter of August during the same year, directed at the abbot Bourdelot, from the Medical School of Paris. He reminded him that before infusing new blood, draining is carried out to evac-

uate the bad or corrupted blood as much as possible, and enter new blood again from a healthy individual, thus balancing what remained of the recipient. Human blood is not incompatible with animal blood because man feeds on many different foods, which are different from that of the blood but are absorbed and converted into the same substance after being processed by digestion. Similarly, blood transfused from animals, passing through the heart, is also digested and transformed until being assimilated by the recipient's blood. It also refers to the case of a man suffering from bilious dysentery, fever, and hepatic flow, treated for three weeks with enemas, bloodletting, and purges, with no results. Denys and Emmerez transfused the calf's blood, but the patient died. During the autopsy, they observed that the death was not the result of the intervention but gangrene caused by the illness. In light of the little amount that remained in his veins, the transfused blood was completely absorbed. The experiments carried out by Gadoys and Denys can also be found in the *Philosophical Transactions* of 1666.

Lamy, in a letter addressed to Moreau, tries to undermine the real basis of the doctrine behind transfusion (i.e., whether it is a process that is the same as what happens during pregnancy when the mother transmits her blood to the fetus). He states that there is no conflict between the nature of the woman and that of her child because the mother's blood is specifically composed to nourish the *fetus*. On the other hand, the substance and nature of animals' blood are quite different compared to that of humans. In addition, during transfusion, even good blood turns bad when it passes into parts of a patient's body.

### The Italian experience with transfusion

Tinassi reported an extract of discourse from an anonymous doctor and philosopher (perhaps P. Petit) (Castelnuovo, 2014; Lancetti, 1836) using the pen name Eutifrone, who argued that bloodletting is necessary to remove the impurities of the blood and that if you want to perform a transfusion, you must use human blood.

C. Tardy, a doctor of the medical department in Paris, writing to his colleague C. Le Breton, also argued that the blood of animals does not undergo a complete digestion process. Therefore, it does not help man, and only human blood must be used for transfusions. The transfusion can be harmful in pleurisy and warm diseases in general, as the arterial blood would increase the heat, but it is "*necessaria all'intera perfettione della Medicina*" [necessary for the complete perfection of medicine] (Tinassi, 1668).

On December 19th, 1667, Denys and Emmerez performed another transfusion on a man suffering from periodic insanity for about eight years. They removed about ten ounces of blood through bloodletting and then transfused about six from the crural artery of a calf. A few days later, they carried out a second operation, this time transfusing a pound of blood, and the patient healed.

Concerning the work in Italy, and specifically in Rome, Tinassi does not mention that of G. Riva, a surgeon at the *Ospedale della Consolazione* [Consolation Hospital] and chief physician of Pope Clement IX. On December 10th, 1667, Doctor Riva carried out in Rome three transfusions on humans. One of the patients was Francesco Sinibaldi, Professor of Medicine at the *Studium Romano*, who suffered long from consumptive disease and was transfused with sheep blood from the carotid artery to the vein of the arm; the operation was successful, although Sinibaldi died of his illness in February 1668. The second patient had been "sick for 16 years, suffering from continuous fever", and the third suffered from tertian fever. These experiments were conducted in the presence of the chief physician Giovanni Maria Costanzi and collegiate doctors Giovanni Trulli, head physician and theoretical medicine lecturer, Antonio Egidio Petraglia, head of general medicine, and Giacomo Sinibaldi, Lecturer of the *"Semplici"* in the *Studium Romano*. They then drafted a report, which was signed and notarized. Riva carried out arterial transfusions from animals to the patients' veins, presumably those of the arm, although the documents do not refer to exactly where. There are also discordant sources on the outcomes of the interventions on the last two patients. They are believed to have survived for a few months (Sprengel, 1841).

Tinassi also does not report on P. Manfredi's experiments, perhaps because in the same year, the latter published a *Ragguaglio* [detailed report] on his experiences with transfusions on humans.

On the other hand, he does refer to the work of I. Magnani, a surgeon in the Conclave and to the Holy Spirit and chief physician of Pope Innocent XI, successfully experimented with transfusion between animals of different species, except in the case of a dog which had been transfused with veal blood. With his experiments, he demonstrated that blood revitalized the dying dogs.

In Italy, there was also a different instrument from the one generally used abroad, with two small pipettes joined together. B. Coluzzi connected the pipes to a small blower to better control and manage blood pressure, first with

a steady flow, then slower, managed with finger pressure. Magnani used three fragments of the animal intestine to avoid the cooling of the blood in passing from one individual to another. They used glass tubes to observe the transit from the donor's artery to the recipient's vein because the terse surface facilitates the passage of blood. Two tubes could be used, tucking the thinner into the wider edge of the other, or it is possible to use only one tube with double curvature at the ends, one right and one left, inserting it directly into the donor's artery and in the recipient's vein to prevent possible leakage of the vital spirits.

Based on the experience of the British and French, according to Magnani, there was no difference between blood transfused from the carotid or crural artery. Tinassi describes numerous animal transfusion experiments conducted in Rome in 1668.

## The importance of human blood use in transfusion medicine in Italy

We also found the letter from G. Montanari, a mathematician at the *Studium* Bolognese [Bologna], to G. D. Cassini, an astronomer at the same university, regarding an experiment he performed in May 1668 in Udine in the presence of Doctors G.B. Coris from Bologna, A. and G. Griffoni and the surgeon A. Cerassini from Udine, at the house of Mr. Savorgnano. They performed a transfusion from the crural artery of a lamb to the jugular vein of a dog. The lamb bled to death due to a large amount of blood flowing from the tube, while the dog survived. In another letter, he reported that Griffoni had performed similar experiments. In the *Philosophical Transactions* of 1668, there is also an extract from the report published in the *Giornale dé Letterati* regarding the transfusion experiment conducted in May 1667 in Bologna in the house of Mr. Cassini between two lambs, from the donor's carotid artery to the recipient's jugular vein. And in Udine, at the home of Mr. Griffoni, the experiment was performed from the artery of a lamb to the vein of a dog.

G. Tiraboschi (1822) confirms that the first experiment with blood transfusion in Italy was the one carried out by Montanari. Besides, Cassini, lecturer in philosophy and medicine at the *Studium bolognese*, described the aforesaid operation he had carried out with Montanari on the two lambs in his letters sent to Ambassador B. Chalks and Abbot M. Giustiniani in 1667. These letters were transcribed by A. Simili and archived in the manuscript 770 of the Bologna University Library. Cassini also reported another experiment carried out to analyze the effectiveness of the method used by the French to transfuse from the crural to the jugular, and if it would be better to use

the carotid artery. Montanari first used the crural and then the carotid artery for the same donor. He noted that one ounce of blood came out from the first, while the second led to eight ounces. For this intervention, he used hen feathers, which allowed the observation of blood flow from one animal to another. Moreover, he transfused the blood of a lamb to a deaf and sick dog, healing him (Simili, 1933).

Therefore, Italian doctors experimented with French and British methods, transfusing from the crural artery as well as the carotid on animals, although in *human* transfusion, the use of the latter was more frequent.

Manfredi, a student of Riva in 1668, carried out several experiments in Rome with C. Cannaj and B. Simoncelli, offering some reports on their work.

Working with Simoncelli, anatomist and surgeon of the *Ospedale della Carità* [Charity Hospital], in 1668, Manfredi practiced experiments on animals and humans in his home. According to the French method, he repeated the experiment on two dogs with a transfusion from the crural of one to the jugular of the other. On January 2nd, 1668, Simoncelli transfused blood from the carotid artery of a lamb to Angelo di Utina's arm vein. Manfredi defended the practice of transfusion, citing Hippocrates, the father of medicine, and a typical recurrent theme used by those who called themselves new Hippocratic physicians.

Indeed, much of seventeenth-century medicine used the authority of Hippocrates to confirm and give credence to new physiological discoveries. After the demonstration of blood circulation and the new embryological theories, Manfredi, as well as the English and French surgeons who practiced transfusion, explained that this therapy follows the rules of Nature. He argued that it is nothing more than an analogy of the natural and continuous movement of blood from the mother to the fetus to nourish, grow, and infuse the child with vital warmth.

Manfredi defended the practice of transfusion in the name of Hippocrates, who first explained how essential maternal blood through the umbilical cord was during pregnancy for nourishing, developing, and warming the *fetus*. It was considered an essential and effective therapy, especially in diseases in which the vital heat and the blood were weakened, becoming dirty due to humidity, like in atrophy or plethora, and for those pathologies that needed new nutrients when the body was consumed by a long-term illness untreatable with traditional remedies (Manfredi, 1668).

All advocates of blood transfusion based their doctrines on ancient medicine that had always identified in this fluid the most important essence of life, *essence par excellence* that also makes up seminal fluids in men and reproductive secretions in women. Moreover, it was considered essential nourishment for the *fetus* in its development and functions, transmitted from the mother to create its physical substance first, the nutrition after, and finally, the vital spirits.

In a human transfusion, Roman surgeons infused blood in the arm's vein. Manfredi transmitted us a detailed description of their method. The doctor tightened a tourniquet above the elbow to make the vein swell until it became hard. Then he made another tie below to prevent an excessive amount of blood from exiting after opening the vein. Using a curved needle, he passed a thread under the blood vessel to lift and separate it from the other parts. Then he cut the vein with a lancet, inserted a silver pin to dilate the walls, and introduced the tube with the curved part directed towards the shoulder to follow the natural motion of venous blood to the heart. With the thread, he bound the hole to allow the blood flow to come out from the lower part of the arm. Following this step, he united the other end of the small tube with the one inserted in the animal's carotid artery. He loosened the ties to get the blood flowing, but without entirely untying it, to control the amount of flow. Manfredi used glass tubes to observe and control blood flow and reported that the patient who had undergone this surgery on January 5$^{th}$ was still alive after twenty days. Similar to Denys, Manfredi replies to opposers of animal-to-man transfusion that animal blood nourishes and revitalizes them just like human blood does in humans. And animal flesh, nourished by the blood, is daily food. Simply a small amount of good blood from a healthy individual is enough to correct the problems of a sick body. Transfusion followed the rules of Nature because it was a direct analogy of the natural and continuous movement of blood from the mother to the fetus to nourish and infuse the child with *vital warmth*. According to him, the transfused blood revitalized the body. He explained some of his predecessors' failures, not for the technical errors or the use of animals, but for the excessive amount of blood transfused at a single time. In his opinion, it was safer to carry out multiple patient transfusions using small amounts of blood, as demonstrated by the experience of G. Riva, G.B. Pieri and I. Magnani at the Consolation (Manfredi, 1668).

## The opposition to traditional medicine

The spread and publication of documents and literature that provided information on this new surgical practice truly shocked a medical culture that was still tied to tradition at a time when Harveyan theories on blood flow and circulation had not yet penetrated traditional medicine, and were still a matter of debate. In April 1668, the court of Paris decreed a ban on practicing transfusion on humans, which was considered a cruel and harmful practice. During the following years, the ban seemed to involve all European countries, even if some authors still *encourage* this kind of treatment in Italy to get the job you were hoping for to perform experiments and use blood transfusion as a good therapeutic practice. Despite the medical thought, animal testing continued for a century and a half but transfusion on humans was no longer done, while *chirurgia infusoria* [infusion surgery] was still practiced.

In 1668, B. Santinelli published his *Confusio transfusionis*, denouncing it as a practice that was still uncertain in the technical sense, a useless and ethically unacceptable therapy, cruel, and inhuman as drinking blood. R. Gianforti was also contrary, opposing the transfusion after having analyzed the results of this operation on patients in detail, concluding that it is not useful and may instead be harmful. However, he praised the experiments carried out. Still, in his *Stadera Medica*, Folli reiterated the therapeutic value of transfusion since blood serves to restore digestion so that the blood from a young person can heal the dry and bilious older patient. It is so powerful in its vital and nutritive properties that, if transfused repeatedly in a young man, it would disproportionately increase his or her growth. He believed that surgeons should always have young people available to practice transfusion in urgent cases, withdrawing blood in small quantities from each of them as a single donor could become too debilitated and sick (Folli, 1780).

Folli affirmed that vein-to-vein transfusion was the best alternative and created his instruments and tools. He made a bag from a hare, cat, or dog bowel connecting it to a funnel that ended with a thin gold or silver nozzle or a crow feather inserted into the donor's vein. The other funnel spout was made of bone or ivory and connected to another tube inserted into the vein of the recipient. The bag created from the animal's intestines allowed him to control the quantity and flow of the blood from the donor to the recipient by simply pressing on it. Instead of the intestines and the funnel, he also used the artery of a goat or other animal, soaked in spirit or fat, to preserve it and keep it soft (Castelnuovo et al., 2014).

Transfusion was also used in German medicine. According to Sprengel (1668), the first to practice blood transfusion were B. Kaufmann and M. G. Puirmann, who in 1668 transfused the lamb's blood on a leper. However, Kaufmann is considered the first to have transfused the lamb's blood in arteries rather than veins, carrying out this experiment on four men (Simili, 1933).

However, although no longer practiced, the theoretical seed of this practice had sprouted and continued to be strongly supported by numerous authors with absolute certainty, according to the knowledge and the doctrines of the time, based on the therapeutic success in specific diseases, and its ineffectiveness or danger for other diseases. A solid demonstration is found in the work of M. Etmuller, who, while never having practiced it, in his *Dissertatio de Chirurgia Transfusoria* from 1682, traces the history of transfusion and discusses its absolute effectiveness, and stresses that this is not only a concrete demonstration of the progress of anatomical and physiological knowledge but has itself contributed to the improvement of medical practice. He reinforces its therapeutic usefulness, as it rejuvenates the old, cures fevers, regenerates the debilitated body, and restores the body parts that have failed due to pathological processes, thanks to the restoration of the right digestive process, and infusion of heat and vital spirit. On the other hand, it is dangerous in case of cachexia, hypochondria, scurvy, and heart palpitations. This therapy is ineffective, or at least doubtful, in the therapeutic outcome for those suffering from melancholy or mania, inflammations and abscesses, atrophies, arthritis, and epilepsy, as well as scabies, syphilis, and leprosy (Etmuller, 1728).

The doctors would continue experimenting with techniques and tools on animals in the eighteenth century. However, we would have to wait until the beginning of the 1800s, when J. Blundell began transfusing human blood. By developing the mediated technique, transfusion would become a recognized medical practice.

Why did the transfusion find such strong opposition?

A central issue is the use of animal blood in human transfusions. Because blood nourishes parts of the body, the blood of an animal, which forms and nourishes hair, horns, hooves, tails, and organs of different anatomical configurations concerning humans, could not be transfused into humans. Opponents even warned of the risk of infusing the beastly spirit during the transfusion, which would transform the real nature of man, acquiring the instincts and behavior of the donor animal. This led the way to philosophical interpre-

tations of the spiritual essence of blood as the substrate of the soul; therefore, the transfusion from animal to man as practiced in the seventeenth century would have violated the very essence of a person, corrupting body and spirit. In the more purely medical field, the real issue is that transfusion represented a true break from tradition (Moore, 2003).

Infusion surgery and blood transfusion were the synthesis of this new perspective of medicine in the middle of the 1600s, as well as the application of the scientific method to medical and clinical science. Based on the works of the surgeons who practiced transfusion, it is quite clear that this operation was considered an *ante litteram* emergency intervention because it was carried out on patients who were considered incurable, in need of immediate resuscitation, through the use of rapid revival of the blood, and therefore the body itself. This action represented an epistemological revolution in medicine.

In ancient medical thinking, the concept of immediate therapeutic effect, intended as an intervention aimed at an immediate and rapid recovery, is absent. The Hippocratic physician treats diseases by following the natural course of events, and therefore he avoids intervening in those who are not amenable to be saved. The disease should take its course, grow and reach *the crisis*, the time of definitive change that leads to either death or recovery. The doctor acts to restore the original balance of the body. The timing of the medical interventions follows those of the disease's course, without any forced action that stops the natural evolution of the process.

It would be necessary to wait for the development of anatomy and anatomical knowledge in the sixteenth century, to devise new therapeutic approaches, and, above all, the onset of surgery, which allowed a different approach to treatment in order to counter the process of death and take prompt actions (Learoyd, 2012).

## Conclusions

Transfusion was a measure used to face a process of a disorder that would otherwise lead to the patient's death.

Therefore, these approaches represented a shift from the old approach to a new therapeutic concept of care, that of a rapid intervention that immediately restores the natural state of the body when traditional long-term therapy has not been effective. In conclusion, infusion and transfusion represent an epistemological revolution that marked the shift from gradual cure to that of immediate action – an emergency treatment for the revitalization and res-

toration of natural functions, opening the way to research on techniques and systems for resuscitation that would later emerge in the eighteenth century (Marinozzi et al., 2011).

In this framework, Italian transfusion pioneers, like Folli, Montanari, Cassini, and Manfredi, played a central role in the improvement and transmission of a discipline that was still in its dawning throughout Europe. Especially, there is no evidence that the pope issued a papal edict excommunicating or impeding blood transfusion (Bomba, 1873).

Again in 1930, he claims that among the edicts and papal bulls at the Casanatense, there was no one on a ban on transfusion. The authors mention the poem in praise of blood transfusion by Padre di Acquaviva, which he would not have written in 1687 if there had been a papal bull prohibiting the practice. However, according to Tiraboschi, the poem was not published until later. In the article, it is said that they requested the Vatican Archives to find the document, which was never traced anyway. Maybe, for this reason, the Italian authors continued to describe experiments and propose this therapeutic method until the 18th century. For these reasons, the Italian contribution was not only theoretical but also practical, despite the international interdiction, as it is deducible in Folli's work, which clearly shows that transfusion experiments continued in Italy, as it is demonstrated by the description of the instrument that he suggested using for the direct arm to arm transfusion. Animal-to-human transfusions proved ineffective, however, and especially found aversion because of the question of the soul from brute to human and also about the mixing of human and human in the hypotheses of success (Di Segni, 1930).

## No competing interests

All authors have read and understood BMJ policy on declaration of interests and completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf. They all declare: no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

## Translation

Valeria Pasquali, BD-Baccalaureate in linguistic and philological studies.

## References


1. Birch, T. (1752). *The history of the Royal Society of London.* London: A. Millar.
2. Bomba, D. (1873). The Direct Transfusion of Blood. *Glasgow Med J.*, *5*(3), 353–360.
3. Castelnuovo, G., Menici, R. & Fedi, M. (2011). *La donazione in Italia: Situazione e prospettive della donazione di sangue.* Milano: Springer.
4. Castelnuovo, G., Menici, R. & Fedi, M. (2014). *La donazione in Italia: Situazione e prospettive della donazione di sangue.* Milano: Springer-Verlag.
5. Del Chiappa, G. A. (1838). *Della Medicina di Aulo Cornelio Celso*, lib. III,23,7. Venezia: Tip. Giuseppe Antonelli, 119.
6. Clark, T. (1668). One of His Majesties Physicians in Ordinary, Concerning Some Anatomical Inventions and Observations, Particularly the Origin of the Injection into Veins, the Transfusion of Blood, and the Parts of Generation. *Phil. Transact., 3*, 172-682.
7. Colle, G. (1628). *Methodus facile parandi.* Venetiis: Evangelistam Deuchinum, 170.
8. Davia, V. M. (1668). *Relazione dell'esperienze fatte in Inghilterra, Francia e Italia intorno alla celebre e famosa trasfusione del sangue per tutto maggio 1668.* Bologna: Per Manolesi.
9. Denis, J. B. (1666). An extract of a letter of M. Denis Doctor of physic and Professor of philosophy and the mathematicks at Paris, touching a late cure if an inveterate phrenfy by the transfusion of blood. *Phil. Transact, 2*, 617-623.
10. Denis, J. B. (1667). An extract of a letter of M. Denis Prof. of philosophy and mathematics at Paris, touching the transfusion of blood, of April 2 1667. *Phil. Transact, 2*, 453.
11. Di Segni, M. (1930). Il contributo italiano alle origini della trasfusione del sangue e della iniezione di medicamenti nelle vene, *La Rassegna di clinica terapia e scienze affini*, *XXIX*(Appendix), 66-90, 179-199.
12. Etmuller, M. (1728). *Opera Omnia.* Neapoli: Typ. Novelli de Bonis, 1467-1509.
13. Farr, A. D. (1980). The first human blood transfusion. *Medical history*, *24*(2), 143–162. https://doi.org/10.1017/s0025727300040138
14. Fastag, E., Varon, J. & Sternbach, G. (2013). Richard Lower: the origins of blood transfusion. *The Journal of emergency medicine*, *44*(6), 1146–1150. https://doi.org/10.1016/j.jemermed.2012.12.015
15. Folli, F. (1780a). *Stadera Medica.* Firenze, Alla Condotta: G. F. Cecchi, 35, 84-95.
16. Galassi, F. M., Habicht, M. E., Killgrove, K., De Carolis, S., Polidoro, M. & Haeusler, M. (2019). The Gladiator's Tears: Epiphora from Ancient Rome. *The Journal of craniofacial surgery*, *30*(7), 1938–1940. https://doi.org/10.1097/SCS.0000000000005902
17. Giangrande P. L. (2000). The history of blood transfusion. *British journal of haematology*, *110*(4), 758–767. https://doi.org/10.1046/j.1365-2141.2000.02139.x
18. Giordano, D. (1931). *Sulla trasfusione del sangue. Cenni storici. Estratto della Rassegna clinico-scientifica dell'istituto biochimico italiano*. Milano: Istit. Bioch. Ital., 11-12.

19. Giordano, D. (1932). *Sulla trasfusione del sangue dal 1700 ai giorni nostri. Estratto della Rassegna clinico-scientifica dell'istituto biochimico italiano*. Milano: Istit. Bioch. Ital., 9-10.
20. Giordano, D. (1939). La trasfusione del sangue e i suoi precursori in Italia. In *Estratto dal volume del decennale dell'A.V.I.S.* Milano: AVIS.
21. Hall, A. R. & Hall, M. B. (1980). The first human blood transfusion: priority disputes (Henry Oldenburg). *Medical history. 24*(4), 461-465. https://doi.org/10.1017/s0025727300040588
22. Himmelmann, P. K. (1997). Il corpo medicinale: An Analysis of Medicinal Cannibalism in Europe, 1300-1700. *Dialectical Anthropology: una rivista internazionale indipendente nella tradizione critica impegnata per la trasformazione della nostra società e l'unione umana di teoria e pratica*, *22*, 183-203.
23. Hoff, H. E. & Guillemin, R. (1963). The first experiments on transfusion in France. *Journal of the history of medicine and allied sciences*, *18*, 103–124. https://doi.org/10.1093/jhmas/xviii.2.103
24. James, R. (1758). *Nuova Farmacopea Universale.* Venezia: appresso Niccolò Pezzana.
25. Johns, A. (2000). Miscellaneous Methods: Authors, Societies and Journals in Early Modern England. *The British Journal for the History of Science*, *33*(2), 159-186.
26. King, E. (1666-1667). An account of a more accessible and safer way of transfusing blood out of an animal into another, viz. by the veins, without opening any artery of either; An account of another experiment of transfusion, viz. of bleeding a mangy into a sound dog. *Phil. Transact., 2*, 449-452.
27. Knight, H. & Hunter, M. (2007). Robert Boyle's memoirs for the natural history of human blood (1684): print, manuscript and the impact of baconianism in seventeenth-century medical science. *Medical history, 51*(2), 145–164. https://doi.org/10.1017/s0025727300001162
28. Lancetti V. (1836). *Pseudonimia: ovvero Tavole alfabetiche de' nomi finti o supposti degli scrittori.* Milano: L. di Giacomo Pilora.
29. Learoyd, P. (2012). The history of blood transfusion prior to the 20th century-part 1. *Transfus Med., 22*(5), 308-14.
30. *Le Journal des Sçavans*. (1668a). Paris: Iean Cusson, III, 16.
31. *Le Journal des Sçavans*. (1668b). Paris: Iean Cusson, III, 15-34.
32. Lower, R. (1666). The method observed in transfusing blood out one live animal into another. *Phil. Transact.*, *1*, 353-358.
33. Lower, R. (1728). *Tractatus de corde, item de motu, colore, et transfusione sanguinis*. Lugduni Batavorum: J. et H. Verbelk, 198.
34. Majoris, J. D. (1667a). *Chirurgia Infusoria.* Kiloni: J. Lüdervvald, VIII, p. 212.
35. Manfredi, P. (1668). *De nova et inaudita medico-chyrurgica iperatione sanguinem transfundente de individuo ad individuum*. Roma: N. A. Tinassi.
36. Manfredi, P. (1668). *Ragguaglio degli esperimenti fatti sotto la direzione di Paolo Manfredi… circa la nuova operazione della trasfusione del sangue da individuo a individuo e in bruti e in huomini.* Roma: Ignatio dé Lazari.
37. Marinozzi, S. & Conforti, M. (2005). Dal sangue come terapia alla terapia attraverso il sangue nel XVII secolo [Blood as therapy, therapy through the blood]. *Medicina nei secoli*, *17*(3), 695–719.

38. Marinozzi, S., Bertazzoni, G. & Gazzaniga, V. (2011). Rescuing the drowned: cardiopulmonary resuscitation and the origins of emergency medicine in the eighteenth century. *Internal and emergency medicine, 6*(4), 353–356. https://doi.org/10.1007/s11739-010-0495-1
39. Marinozzi, S., Gazzaniga, V. & Iorio, S. (2018). The Earliest Blood Transfusions in 17th-Century in Italy (1667-1668). *Transfusion medicine reviews, 32*(1), 1–5. https://doi.org/10.1016/j.tmrv.2017.09.003
40. *Miscellanea Medico-Physica Academiae Naturae Curiosorum Germaniae*. (1668). Paris: L. Billaine, 237, 289-294.
41. Montanari, A. (2015). *Il fiero pasto. Antrofofagie medievali*. Bologna: Il Mulino.
42. Moog, F. P. & Karenberg, A. (2003). Between horror and hope: gladiator's blood as a cure for epileptics in ancient medicine. *Journal of the history of the neurosciences, 12*(2), 137-143. https://doi.org/10.1076/jhin.12.2.137.15533
43. Moore, P. (2003). *Blood and Justice: The 17 Century Parisian Doctor Who Made Blood Transfusion.* Chichester: J. Wiley & Son.
44. Picard, J. F. & Schneider, W. H. (1996). L'Histoire De La Transfusion Sanguine Dans Sa Relation à La Recherche Médicale. Vingtième Siècle. *Revue d'Histoire, 49*, 3-17.
45. Regnier de, G. (1677). Tractatulus de usu Siphonis in Anatomia. In: *Opera Omnia*. Lugduni Batavorum: Officina Hackiana.
46. Riva, M. A., Benedetti, M., Vaglienti, F., Torre, C., Baggieri, G. & Cesana, G. (2014). Guglielmo Riva (1627-1677) and the end of hepatocentrism: a 17th-century painting. *Vesalius: acta internationales historiae medicinae, 20*(2), 69-72.
47. Romano, A. (2009). *Rome et la science moderne entre Renaissance et Lumières*. Roma: l'École française de Rome.
48. Scalzi, F. (1871). *La scoperta della trasfusione del sangue.* Roma: Tipog. G Via Corso, 387.
49. Sha, S. J., Deutsch, G. K., Tian, L., Richardson, K., Coburn, M., Gaudioso, J. L., Marcal, T., Solomon, E., Boumis, A., Bet, A., Mennes, M., van Oort, E., Beckmann, C. F., Braithwaite, S. P., Jackson, S., Nikolich, K., Stephens, D., Kerchner, G. A. & Wyss-Coray, T. (2019). Safety, Tolerability, and Feasibility of Young Plasma Infusion in the Plasma for Alzheimer Symptom Amelioration Study: A Randomized Clinical Trial. *JAMA Neurol. Jan., 76*(1), 35-40. 10.1001/jamaneurol.2018.3288
50. Simili A. (1933). *Origine e vicende della trasfusione del sangue.* Bologna: Cooperativa Tipografica Azzoguidi, 97-100.
51. Simili, A. (1933). *Origine e vicende della trasfusione del sangue*. Bologna: Cooperativa Tipografica Azzoguidi, 115.
52. Sprat, T. (1667). T*he history of the Royal Society of London, for the improving of natural knowledge*. London: F. Martyn at the Bell.
53. Sprengel, C. (1668). *Storia prammatica della medicina* (Vol. 4). Firenze: Tip. Della Speranza, 1841, 272-275.
54. Sprengel, C. (1841). *Storia prammatica della medicina* (Vol. 4). Firenze, Tip. Della Speranza, 272-275.
55. Tinassi, N. A. (1668). *Relatione dell'esperienze fatte in Inghilterra, Francia ed Italia. Intorno alla celebre, e famosa trasfusione del sangue per tutto Gennaro 1668*. Roma: Tinassi.

56. Tiraboschi G. (1822). *Storia della letteratura italiana* (Vol.14). Milano: Società tipografica de' Classici Italiani, 467.
57. Wedel, G. W. (1686). *Pharmacia Acroamatica.* Ienae: J. Bielckii, lib.II, sect. IV, cap. VI, par.8.

## SAŽETAK

*Ovaj članak bavi se književnom raspravom o prvim eksperimentima vezanim uz transfuziju krvi na ljudima između 1667. i 1668. u Europi, s posebnim osvrtom na manje poznata eksperimentalna istraživanja provedena u Italiji. Autori ispituju detalje eksperimentalnog razvoja, fokusirajući se na tehnike i instrumente kojima se koriste liječnici uključeni u ovaj novi kirurški pristup, s posebnim osvrtom na talijansku raspravu i eksperimente. U članku se sugerira da se transfuzija smatra dijelom onoga što bismo mogli nazvati "hitnom operacijom". U tom su okviru talijanski pioniri transfuzije imali važnu ulogu u poboljšanju i prenošenju discipline koja je još uvijek bila u nastajanju diljem Europe. Štoviše, članak ističe doprinos "chirurgiainfusoria" kao inovativnoga terapijskog sustava za trenutačan i brzi oporavak. Iz te perspektive, transfuzija krvi kirurška je praksa za reanimaciju i oživljavanje. Cilj je ovog rada bio analizirati važnost strane literature i engleskih i francuskih rasprava koje je Davia predstavio u Italiji, čime su oni postali poznati. Unatoč stranoj zabrani u Italiji, eksperimenti s transfuzijama sa životinje na čovjeka nastavljeni su i nakon 1648. Papinska bula koja je ekskomunicirala znanstvenike zbog provođenja takva istraživanja nikada nije pronađena.*

***Ključne riječi:*** *krv, transfuzija, europska književnost, povijest transfuzije, talijanska kultura, ljudska transfuzija, životinjska transfuzija*