‘LA TRASFUSIONE DEL SANGUE’

By: Dr MALACHIA DE CRISTOFORIS (1875)

A TRANSLATION OF PAGES 1-90 BY PHIL LEAROYD

A copy of the book ‘La Trasfusione del sangue’ by Malachia de Cristoforis, published in 1875 in Milan [by Fratelli Rechiedei] can be viewed or downloaded from the following sites:

https://wellcomelibrary.org/item/b22369971#?c=0&m=0&s=0&cv=0&z=-1.3775%2C-0.095%2C3.7551%2C1.9

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I have translated the ‘historical sections’ of this important 159 page book on blood transfusion from the original Italian into English in the hope that the content may be appreciated by a wider audience. It is one of a relative few number of Italian books on transfusion that were published in the 19th century and as such provides a different viewpoint on many of the issues relating to the history of blood transfusion. Whilst I am obviously aware that instantaneous computer-generated translation is possible, this process struggles with specialist terminology and also produces a ‘colloquial style’ not always representative of the original text. I have purposely produced this translation to be ‘un-interpreted’, in that I wanted to maintain the author’s original meaning / wording as much as possible. As with any translation the wording may be purposely or inadvertently altered to ‘make it read better’ but in doing so there has to be an element of personal interpretation involving something on the lines of ‘I believe that this is what the author is actually trying to say’. I wanted to avoid that as much as possible and try to present what the author actually wrote and as a result the reader may find that the English text does not ‘flow’ as well as it could. Although I have taken great care not to misrepresent the author’s original wording I cannot guarantee that this work does not contain ‘translational errors’ and the reader is recommended to check specific details against the original Italian text.

Cristoforis includes a variable and extensive use of italics throughout his book to represent names, places, references and certain wording that I frequently found confusing (and occasionally rather irritating). I have therefore not reproduced this within the translation, using the author’s italics only within the references. The references are presented as written in the original text. Any personal comments made by myself regarding the text or translational problems are included in square brackets.

I must emphasise that the names of researchers and authors are variably and frequently incorrectly spelt within the book – sometimes a person’s name is spelt differently a number of times on the same page! I have faithfully reproduced all of these spelling variations in my translation text (as I am unsure how their names would have been correctly interpreted in Italian in the 19th century) and would therefore stress that these spelling variations are the original author’s and not produced by myself within the translation. I did start to use the term ‘[sic]’ to highlight these variations but found that this resulted in too large a number being included, which detracted from the original text and therefore I decided not to use this option.

At the end of the introduction to his book, Cristoforis states that his method for presenting the ‘history of transfusion’ was the result of a competition by ‘the

Honorable Lombard Institute of Sciences and Letters', resulting in him dividing the history into three distinct periods, which he identifies as:

1. The mythological, ahead of the discovery of blood circulation
2. The experimental, or almost exclusively such, which embraces from the historical origin of the transfusion at the end of the 18th century
3. The practical or therapeutic, in which this operative act finds its logical applications and which from the end of the 18th century, continues to the present day.

Effectively therefore he has followed the pattern of many other authors of that period by breaking the history down into three time periods! It does however mean that his third section is somewhat lengthy, complex and a 'recent history' in that he later states that it covers the period from 1783 to 1874. As such, the three sections are rather unbalanced with regard to their content, with the first section being covered in 5 pages, the second in 36 pages and the third in 49 pages, which together means that the 'history section' takes up nearly two-thirds of the book's total content of 159 pages.

This is in a large part due to the fact that the third section is not a history as such, which one would expect to be covered in chronological date order. Instead Cristoforis provides summaries (and some personal comments) of the work performed and the results obtained by different people during this 90-year period. As a result, it means that a large part of this third section is presented more as a commentary on the work performed rather than as a summary of notable historical events.

Within the first 'Antiquity-Mythological' period the author argues convincingly that the theories that were believed at that time regarding the role and movements of the blood in the human body together with the function of the heart mitigates even the thought of blood transfusion let alone the possibility of it being carried out prior to Harvey's discovery of the circulation of blood.

Cristoforis starts the second 'Historical-Experimental' period (1628-1700) by arguing that the two Italians Giovanni Colli and Fernando Folli 'discovered' blood transfusion by the fact that they thought of it first, even though they did not put their words into actions – especially since he believes that they have been either ignored or only briefly mentioned by other contemporary authors. The details of the roles of these two people have been explored in detail more recently by other authors, e.g. Gilder (1954), Marinozzi, Gazzaniga and Iorio (2018) and Simli (1933).

Although Cristoforis follows this by giving the Englishman Clarke priority for the first infusion of blood, he states that as an "impartial reporter" he can give no one in particular credit for performing the first blood transfusion! Though he credits Richard Lower's work, he also includes Magnari's transfusion experiments on dogs as equally important. He then provides information on the human transfusions performed in France as well as also including those performed in Italy by Guglielmo Riva d' Asti and Paolo Manfredi. He covers the disputes following Denis' transfusions in France, championed especially by Lamy, as well as providing information regarding similar disputes that occurred in Italy, principally championed by Raimondo Gianforti and Bartolomeo Santinelli. The obvious 'Italian bias' to some of the history is excusable but is also very interesting, providing additional information regarding the history of transfusion frequently ignored or only briefly referenced by many other English, French or German authors of the 19th century.

Cristoforis identifies the sentence given to Châtelet by the lieutenant of criminal cases on the 17th April 1668 in Paris (i.e. that 'in the future, transfusion could not be done in humans without the approval of a doctor from the Faculty of Paris') following the court case brought by Denis, but unlike many other authors discussing this same period, instead of saying that this ruling effectively stopped transfusions in France,

Cristoforis identifies that they were not banned but limited and states that for example Denis did obtain permission to transfuse a woman after this ruling but that he did not perform it and that other research work on animals continued – a statement though that has a notable paucity of references.

This second section suffers somewhat from the fact that details are not necessarily provided in chronological order, with the author digressing into different areas of experimental research – for example those involving injecting air into animals to establish its effect.

He starts the third section by proposing that Michele Rosa resurrected blood transfusion rather then James Blundell – something commented on by Pierre Oré in the 1876 version of his book 'Historical, physiological and clinical studies on blood transfusion'. The author's meandering writing style continues in section three, which is essentially a number of summaries (with his own comments) of the transfusions and experiments performed by different researchers. As such it is presented as 'areas of research' rather than pieces of historical information in date order and therefore as a 'history' is presented rather differently from that of other authors. It does however obviously include important historical information, including such topics as defibrination, the use of 'alkaline salts' to prevent coagulation, etc. Cristoforis also includes 'transfusion methods' within this section but again rather confusingly having discussed direct and indirect techniques includes his own indirect method using defibrinated blood later in the book (pages 118-121). I have included this section at the end of this translation as I believe it to be historically interesting to identify the actual practical details relating to blood transfusion performed nearly 150 years ago.

MALACHI DE CRISTOFORIS (1832 – 1915)

Cristoforis was born in Milan on the 9th November 1832; one of the nine children of Giovan and Adelaide Battista. His father died when Malachi was 6 years old and a year later in 1839 his mother sent him to the Boselli Institute boarding school where he was described later by a colleague as being 'a thin, pale boy with two big swollen hands, red and bloody from chilblains'. He then became a private student at the Liceo di Porta Nuova and in November 1850 enrolled at the University of Padua for the first course of Medicine.

The university years appear to have been crucial for his personal and professional development that later enabled him to combine professional, clinical and scientific interests with a strong inclination for civil and patriotic commitment. He graduated with a degree in medicine on 25th April 1856 with a thesis on uterine deviations and their treatment; he subsequently graduated with a degree in surgery on the 6th August 1857.

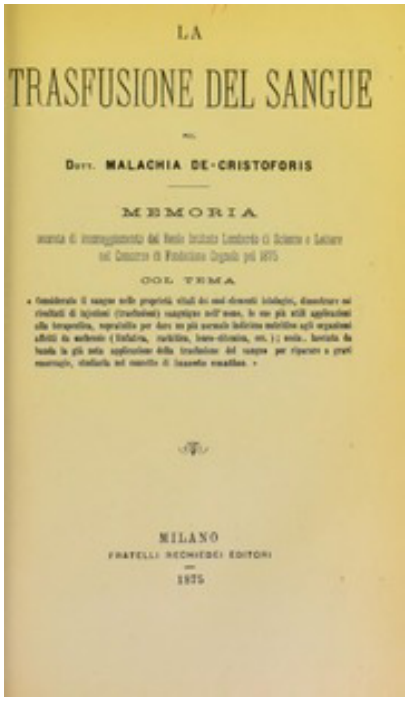
He enlisted as a volunteer medical officer in Garibaldi's forces at the start of the 1859 second war of independence, during which time he became a medical captain and earned the silver medal for military valour. In 1866 he was appointed assistant physician at the Ospedale Maggiore in Milan and a year later he was appointed primary physician.

In 1867 he visited England where he met Charles West and subsequently translated and published an Italian version of the book *Lessons on the diseases of women* (Milan 1868) that included many personal observations, clarifications and additions not present in the English edition. A few years later in 1885 he produced a greatly revised version of the book that contained additional new chapters.

In 1873 he resigned from the Ospedale to operate on his own and in 1875 became the director of the *Universal Annals of Medicine* journal, a post that he held

for three years. As a result of his personal clinical reputation he became a free lecturer in medicine at the University of Naples in 1883. His interests expanded outside his specialty, as testified by his numerous publications on a variety of clinical subjects, including his memoir on blood transfusion, for which he received an award. From 1890 to 1897 he was the director of the *Journal of Midwives*.

Beyond his roles as a doctor and scientist, Cristoforis was a very prominent figure in the social and political life of Milan. In 1886 he unsuccessully stood as a candidate for Parliament but later, in 1895, he was successful, standing as a radical democrat he was elected to the 19th legislature and was subsequenbtly re-elected to the 20th and 21st legislatures. It is believed that his position as president of the Milanese Freemasonry had an influence on his political positions. He was a member and also president of a variety of scientific societies and academies. In 1906 he chaired the first international conference on occupational diseases in Milan and in 1907 he chaired the first national congress on occupational diseases in Palermo. He died in Milan on 28th December 1915.


LA

TRASFUSIONE DEL SANGUE

Dott. MALACHIA DE-CRISTOFORIS

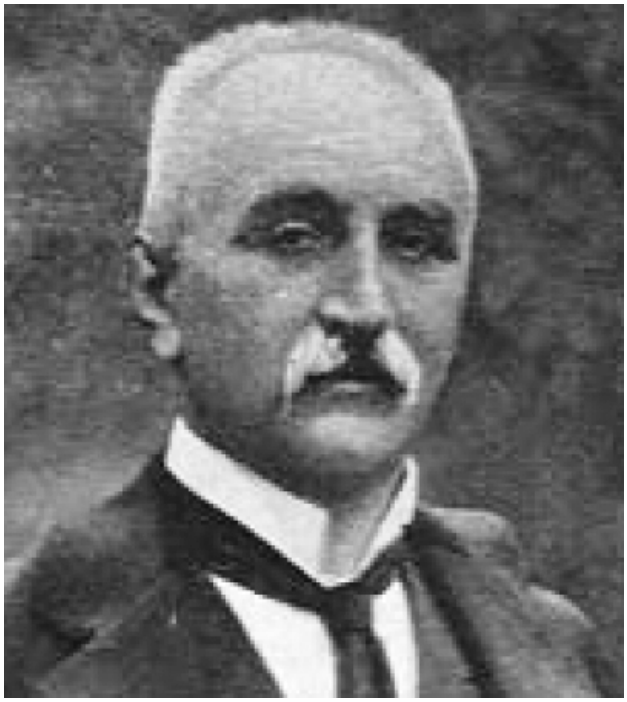
MEMORIA

COL TEMA

MILANO

1875

La Trasfusione del Sangue (1875)
(Image credit: Wellcome Collection)



Malachia de Cristoforis
(image credit: galileumautografi.com)

FIRST PERIOD: MYTHOLOGICAL ERA OF TRANSFUSION

Some historians believe that blood transfusion was known from the most remote antiquity, and Olao Borricchio narrates that the ancient Egyptian priests used it to revive their languid princes. According to legend, one of them, having been horrified to see a man near death in his arms, forbade transfusion and ordered that human blood baths be replaced. It is said that Tanaquilla (Book of Wisdom of Tanaquilla) gave her blood to her husband Tarquinio Priscus. The sorceress Medea would have learned the art of transfusion from the Egyptian priests; and, according to traditions, she would have rejuvenated Jason's old father by letting the aged blood out of his vessels and injecting her own. Some lines of Ovid (*Metamorphosis*, Book VII, verses 285-388) which seem to foreshadow a distant idea of the transfusion, serve as evidence for the supporters of this opinion.

All these vague traditions seem to have as their basis the concept that blood has its own vital force for the whole body, and that blood is the soul itself.

In the fifteenth century of the vulgar era, stories report that Marsilio Ficino from Florence discovered blood transfusion, and they cite his work as confirmation: *De vita sana, longa et coedesti*, published in Florence in 1489. But it is easy to see how Marsilio Ficino speaks of blood-sucking, which he advises to old men by removing it from the bodies of young men: “Cur non et nostri senes crani videlicet auxilio destituti sanguinem adolescentis sugunt? volentis inquam adolescentis, sani, Iseti temperamenti, cujus sanguis quidem sit optimus sed forte nimius. Sugant igitur more hirudinum, ex brachii sinistri vena vix aperta, unciam uuam aut duas.”

Many consider Peglielio Magno, doctor of medicine and professor of mathematics in Rostok as the inventor of transfusion. The traces of his discovery would be found in these words of his book, *Thesaurus rerum selectarum*, published in 1604: "Ratio chirurgica insignis et rara komini communicaus extera quae ipsi bona, et interna multa quse noxia avertens.” But as Scheel, Dieffembach, and more recently Scalzi ably observe, in these words nothing else is to be seen except an infusion, that is to say, a surgical introduction of remedies designed to amend various diseases. No allusion in his work is made to the true blood transfusion.

The famous Andrea Libavio of Halle, doctor of medicine, director and professor of the Coburg high school, is considered by many to be the inventor of transfusion. They rely on some words from his book, *Appendix syntagmalis arcanorum surgicorum*, 1615. He speaks of his own contemporary empiricist idea, without stating whether he considered it executable. Libavio then shows himself against it, going so far as to declare anyone who has tried it worthy of hellebore (See: Scheel, *Die transfusion des blutes*). Many writers, both Italian and foreign, mention a blood transfusion that was allegedly given to Pope Innocente VIII in 1492 by a Jewish doctor, of unknown name, who allegedly used the blood of three children. They rely on the authority of the historian Sismondi, who narrates the fact, adding that the three children died from the beginning of the operation due to the introduction of some air bubbles in their veins. (See: Sismondi*, History of the Italian Republics of the Middle-Ages*, Volume II, p. 416. – Diary of Stefano Intesfan, p. 1241)

But Sismondi was wrong, since in the *Ecclesiastical Annals of Raynaldus*, which go up to the year 1534, on page 412, we find it said: “Laboraverat diutino morbo, a biennio enim, quo torpore soporifero vigiliti horis sine vitse signis jam erat, adversa valetudine fuerat usus; acciditque tum, ut cum vis morbi medicam artem eluderet, judeus impostor qui valetudinem pollicebatur, a tribus pueris annorum decem, qui paulo post mortui sunt, sanguinem exbauserit; ut ex eo farmacum stillaticum, chimica arte paratum, propinandum pontifici, conficeret; quod cum Inuocentius suspicisset execratum nefas, judeum jussit facessere, qui mox fuga supplicio se subduxit.” From this passage the fact of the introduction of blood, chemically prepared, is evident, not for the ‘circulatory tree’, but through the ‘executive streets’.

Without further over reaching myself in reviewing all the authors who are wrongly considered as inventors of transfusion, I declare that blood transfusion was probably glimpsed by the ancients, but not as an injection into the bloodstream, then not yet known; and that the true thought of such an operation arose after the discovery of the circulation of the blood, being an immediate consequence of it.

And in fact it is easy to prove that in no way could a transfusion be conceived with the then dominant doctrine on the movement of blood in the human body. According to the ancient doctrine of Aristotle, the heart prepares the blood in its own cavities; the blood flows as food for all parts of the body, it soaks it in the same way that the gardens are watered by streams of water: but the blood never returns to the heart. The heart is likewise the source of heat for the whole body, the seat of the sentient soul, the most important organ that it contains in itself and the impulse of its movements. With blood, all parts of the body receive from the heart the power to feel and move. At each respiratory motion, the vital breath gives this force to the heart: by way of the air canals and lungs, and from the lungs by means of vessels, it reaches the cavity of the heart, from which it spreads through the blood to all parts of the body (de partibus animce - de respiratione - de generatione animce, etc.).

Even less could the ancient doctors come to the thought of transfusion, after the two renowned professors of the Alexandrian School, Herophilus of Chalcidonia and Eristratus of Keos (about 300 years BC), teaching how blood flow is carried out, taught the universally accepted doctrine that only air is contained in the arteries, which comes from the lungs upon respiration.

Galen shows experimentally that the arteries contain blood, and explains the motion of this by saying that: "the blood reaches the right heart through the hollow vessels, and there the heat of the heart separates the usable parts of the blood from the useless ones. The useless parts are led to the lungs by means of the pulmonary arteries, and from the lungs they are emitted in the form of soot. The servable parts reach the left ventricle through the hole that exists in the septum. In the left heart the blood receives the life force."

As we can see, Galen corrected the first of the three fundamental errors in which the theory of circulation was wrapped, that is, that the arteries contained air; but two other errors still remained, namely that the septum separating the two ventricles was perforated, and that the veins carried the blood to the parts instead of bringing it back.

Vesalius clarifies the second error (*Opera omnia anatomica*, 1572, tom. 1, p. 157, 19). He says that the substance of the inter-ventricular septum is so large, compact and dense that he could never understand how the slightest amount of blood can pass through it.

It was therefore necessary to look for another way for the blood to pass from the right heart to the left, when Michele Serveto, who was publicly burned as a sorcerer, on 27 October 1550, discovered the 'small circle'. In his writing *Restitutio chrystianismi* he says: "Fit autem comunicatio haec (that is, between the cavities of the two halves of the heart) not per parietem cordis mediani, ut vulgo creditur, sed magno artificio a destro corde, longo per polmones ductu agitatur sanguis subtilis, a pulmonibus preparatur, flavus efficitur et a vena arteriosa (art. polm.) in arteriam venosam (pulmonary veins) trasfunditur."

Six years later Realdo Colombo, without knowing about Serveto's book, also discovered the pulmonary circulation.

Andrea Cesalpino describes in turn and without citing Columbo (who he certainly did not know) the flow of blood from the right ventricle of the heart to the lungs to the left ventricle, and is the first person to use the name 'circulation' (see: *Quaestionorum peripateticorum*, lib. 2, chap. 17 and lib. 5, chap. 4).

In 1574 Fabrizio d'Acquapendente, a follower of Falloppio, discovered the valves of the veins.

Finally, the Englishman Harvey, who was a pupil of Fabrizio d'Acquapendente and studied in Padua, once the venous valves have been discovered, finds it easy to destroy the third error concerning the circulation; creates the centripetal movement of the blood flow in the veins, and clearly speaks of two circulations, the large and the small (1616-19-28).

From this quick outline of the theories and errors that prevailed around the movement of blood before the complete theory of the circulation became known, it seems quite proven that doctors and practitioners prior to this moment could not even come up with the idea of a transfusion; and at least they had such an abstract and confused concept of it that they didn't have to take it into account.

With the knowledge of the blood circulation, the period we have called mythological ends, and the historical era of transfusion begins; the 2nd period begins, the experimental, which from the discovery of the circulation of blood goes up to the 18th century; a period that we like to call such, because transfusion was almost always done more as an experiment than for a real therapeutic purpose.

SECOND PERIOD: THE EXPERIMENTAL ERA OF TRANSFUSION FROM 1628 TO 1700

If the merit of a great discovery lies in the idea, in the first concept, if the implementation is a consequence of designing, then transfusion should be kept as an Italian creation.

It is Giovanni Colle from Padua who in his book *Methodus parandi jucunda, abbigliamento et nova medicamenta*, published in Venice in 1628, discussing foods and medicines designed to prolong life, expounds the thought that to obtain such an aim more readily and securely, should be to immediately transmit the blood of a healthy young man into the body of an old man.

In that book he poses a question to himself which contains precisely the ideal concept of transfusion; that is, the method that is achieved with medicines, would be better and more easily obtained by passing the blood through a channel that from a perfectly healthy young man enters an old man.

Here are his words: “Denno insurget aliquis, frustra hsec esse tentanda, dum per pauciora seque et bene valemus consequi optata, veluti si quis sanguis e vena exibiens juvenis admodum salubris, per fistulam in venam seuis permeet, insufflante juvene et sene attrahente et inspirante; ut sanguis juvenis intus attrahatur a sene, ne hujus egrediatur. Nam hic sanguis potest reparare humidum primigenium et temperamentum, docente Aristotile. Si senex haberet oculum adolescente, non ne videret ut adolescens? Non sentiret et rationaretur ut juvenis, si cor et cerebrum juvenis possideret? ergo etiam si sanguinem juvenis obtineret, viveret ut juvenis.”

To this question Colle hastens to reply: “Respondendum haec minime veritatem attingere, quoniam in uutritione et vita vegetali actu requiritur sanguificatrix actu expeditur nutritiva facultas et genuinum calidum temperamentum, quod trasmutat sanguinem illuni introductum; necessario etiam desideratur ut continuo non effluat illum umidum et calidum temperamentum quod, teste lppocrate et Galeno, incessanter ab intimis principiis et ab aere lambiente lacessitur; actiones vero sensuum et intellectus non conficiunt sibi propria objecta, sed sollummodo ea recipiunt aut illustrant; non potest quod dissimiles mores babet in discordibus locis permanere; discordia rebellant, pugoant, atque inter se dissident ignis et aquae temperamento: haec sunt philosophiae raedicse arcana.”

It is very true that Colle has not translated his thought into action, and that in the course of his book he expresses words of distrust about the applicability of the medium: yet it is an absolute fact that from the mind of this Italian came the first impulse, the first light, and that after him there was nothing left to do but

courageously follow the concept and put it into practice in any way. The great idea had been thrown into the scientific field, and the great idea was from an Italian.

If the name of the Paduan Colle is not enough to give the Italians the right of priority in proposing and conceiving transfusion as a means of reforming and medicating the human body, another Italian's name immediately records the history, with even greater evidence of tradition, if it is possible to say, truncating any dispute in this regard.

This is Francesco Folli from Poppi, Province of Arezzo, whom we read in his work *Stadera medica, in which, in addition to infusion medicine and other innovations, the favorable and contrary reasons for the blood transfusion already invented by Francesco are balanced and now described and dedicated by the same to the Most Serene Prince Francesco Maria of Tuscany*, Florence, 1680.

In his work, at Ponderazione II[a], [*sic*] he speaks of blood transfusion. He begins to consider the causes of the greater or lesser length of life, and comes to the conclusion that the different quality of blood makes the time of life of the animals diversify, the diversity of the sauces the plants, and the different mixture of mercury and sulfur the metals (op. cit. page 19). He passes onto the examination of the various substances that according to the dominant doctrines at that time make up the blood, briefly describes the circulation and concludes by saying that the blood, so necessary for life, for the continuous circulation of several years, exhales the hottest, thinnest and witty part, it becomes big, black and easy to freeze; in a word it ages and dies; therefore in good or bad blood constitutes the length and brevity of life, aging and graying. And if, as Cicero said, "senectus ipsa es morbus", why won't it be permissible for every doctor to seek the remedy to keep it away?

And here I think it appropriate to reproduce the words of Folli verbatim, because they prove the accuracy of my assertions. On p. 35 it is expressed thus: "In the year 1652, I read the English book by Guglielmo Arveo, which deals with the movement of the heart and blood; which reading, with some news that he had about grafting plants, produced this problem in my fantasy: that given the circulation of the blood, transfusion was possible with which not only could some ills be cured, but rejuvenated and magnified. I mentioned this in my booklet on the cultivation of the vine, which I published only to make it clear to everyone that the blood transfusion had been invented by me and until the year 1654 manifested to the Serene Highness Ferdinand II Grand Duke of Tuscany: his very pleasant genius and profuse magnificence was pleased with the novelty of the experience, nor did I ever communicate this thought of mine to others, giving myself to believe that if this invention were successful it was only worthy of monarchs."

Folli then mentions how he dedicated and presented his memoir on transfusion to the Grand Duke in the year of 1665, when he learned from a friend of his, Ippolito Tei da Bibbiena, that in England they had found a beautiful invention of rejuvenating by transfusing the blood of young men in the veins of the old (op. cit. p. 37). Folli suspects "that being at the Court of Florence some Englishmen, having been present on many occasions, as attested by Mr. Redi, among which Mr. Finchio ambassador at the door, they could have overheard it in the court, understood and carried it into practice." In his work, Folli calls the Grand Duke as a witness of the priority of his discovery and exclaims, "With reason, I can therefore call it mine as it is, and as mine I must by nature's obligation defend it and protect as best I can; that however I began to write this third booklet in his grace, if not with a certain faith to credit it as successful, to show the world at least that the reasons that led me to hope for it were not of such little weight, as they have been up to now judged by many." (op. cit., p. 38)

Folli then goes on to answer all the objections raised against transfusion by Mr. Raimondo Gianforti, in his book of medical consultations and responses; objections that we will mention by discussing in a specific chapter the supporters and opponents of the transfusion in Italy.

Folli then describes the method to be followed in a transfusion, the quality and quantity of blood to be transfused, the appropriate instruments, the operative act (op. cit., p. 91).

As for the instruments, lancets are required to incise the vein, then a funnel to transfuse the blood. This funnel consists of three parts; the sharpest part, which must enter the patient's vein, will be made of gold and silver, but according to Folli it would be better to take the quill of a crow or raven wing feather, somewhat folded in the middle, placing a ribbon over the fold in order to then tie it to the arm. The second part of the funnel is a hare, cat or dog gut, of the width of the little finger of the hand, as long as four fingers; and this is tied from the longest part of the quill or pen, so that it cannot slide. The third part is a small ivory or bone funnel, with a large rim on the widest part to be able to drill it with a drill to take out the air and make other holes in it to fit a ribbon so that it can be tied to the arm of the young man. The quill is introduced into the cut across vein of the individual that is to receive the blood and is fixed to the arm by means of a ligature. Placed in a comfortable position, the young man who has to administer the blood, the vein is incised and the other part of the funnel, that is the bottle, is attached to it, keeping it fixed by means of a ligature around the arm. The surgeon embraces the gut with his hand, and as he feels it fill he will press it slowly as if he were milking it.

Finally Folli comments on the season in which transfusion is best suited, of the diet to which the patient receiving the blood must be subjected, and of other incidental things.

However, it seems that Folli has never performed it since on page 98 he says: "Finally I know that I have said too much about the way of containing oneself in the operation, not having experienced it." Even from this quick mention it is clear that he, as early as 1652 (24 years after Colle), proposed blood transfusion for therapeutic purposes; and that in 1680 not only did he still remember the thought he had already had and manifested previously, but also showed that he had made it the subject of theoretical study and that he could consequently dictate precepts in an operative and a therapeutic application line.

I had to render such an act of justice to the Italian Folli, as it is not even mentioned by some authors and by others mentioned only briefly without even attributing any merit to him. What is strange is that Italian writers contemporary to Folli do not even mention him, I don't know if they are unwilling, or because they really didn't know the memoir presented to the Grand Duke in 1665. In fact, Paolo Manfredi, in his book *De nova et inaudita medica chirurgica operatione sanguinem transfundente de individuo ad individuum*, published in Rome in 1668, does not speak of Folli. Bartolameo Santinelli, in his book *Confusio transfusionis*, published in Rome in 1668, does not speak of Folli; and indeed he claims that blood transfusion originated in England, from where it passed to France, and then came to Italy. Merklin in his book *Tractatio medicocuriosa de ortu et occasionu transfusionis sanguinis* published in Nuremberg in 1669 attributes almost no part in the discovery of transfusion to Italy and makes no mention of Folli.

To come to more recent authors, Scheel and Dieffembach, though not excluding the possibility that Folli is the inventor of transfusion, say, and not wrongly, that Folli published his discovery much later than the others. L'Oré in his book entitled *Etudes historiques et phisiologiques sur la transfusion du sang* makes no mention of Folli.

And after so much knowledge on the part of some, and after the doubts issued by others, these facts always remain as incontestable:

1. That in 1628 Colle of Padua is absolutely the first to talk about transfusion, and that he proposes it at a time when such a thought could have a basis for criteria, since the discovery of circulation was already in the scientific world.
2. That Folli of Poppi in 1680 (*Stadera medica*) asserted that in 1652 he had already expounded and published (in the book on the Culture of the Vine) his thought of

the possibility and purpose of a blood transfusion; it was never contradicted by any writer, doctor or historian; so that his statements must be believed to be true, because of this fact and because of the authority of the testimonies he cites in his favor.

3. That the English never hesitated to oppose these observations and to accuse Folli of falsehood in those words, for which he accuses the English themselves as frequenters of the Florentine Court, as having stolen the thought of transfusion from his ceremonial testimonies to the Grand Duke Ferdinando II.
4. That Prof. Scalei, from 1866 onwards, never included a denial in his historical research (Giornale di Roma, April 1866, issue 4. *Esperienze sulla trasfusione del sangue in Roma*), in which he states how Folli should be given credit for having proposed the transfusion of blood from one individual to another as being possible and useful.

It is therefore reasonable that the conception of this operative act can be attributed to Folli since he lived in the era in which Harvey made known his studies on circulation and having followed the progress and discoveries that the anatomists and physiologists of the Florentine school of that epoch, he could on these bases devise a transfusion into his physiological and therapeutic truth and rationality.

Folli was also a scholar of agronomy and by practicing plant grafts he could very well deduce from these acts the possibility of transplanting the element of one organism into another, of bringing vital and radical modifications, of directing the organization in his own manner.

Lastly, it should be added that Folli knew about the attempts of infusion in medical circles, he was a partisan of them and then described the methods with full knowledge of the subject.

And after the evidence of these chronological dates related to Colle and Folli, why can historians and doctors propose other names and claim that these preceded the two Italians in the study of blood transfusion?

And even if one wants to question whether Folli is telling the truth by asserting (as he does in the writing of 1680) that he proposed transfusion as early as 1652, the fact still remains that Colle Padovano wrote about it as early as 1628 with indisputable evidence of meaning and words.

But after this is it then true that the names cited by some historians as predecessors to Folli in the study of transfusion are really so by date of time, by intention of concept, by breadth of views? Let us see.

Meanwhile, when Leonardo Landois (memoir in the *Medical Gazette* of Vienna, 1867) says that the theologian Potter in 1638 in a conference of the Royal Society of London expressed the thought of the possibility of replacing animal blood with the blood of another animal, it does not destroy the precedence of Colle (1628), and still leaves the merit of Folli intact, of having widely spoken about it and of having a broad theoretical study of it, very worthy of admiration. And it helps to believe it was a simple nod to Potter, since most do not remember it at all and take very little account of it.

It is necessary to move to 1657, five years after Folli's work, to feel the transfusion remembered again; since after Colle (1628), before and after Folli (from 1652 to 1657) we only see studies and experiences of medicinal infusion

I believe that English historians are mistaken when they say that Christopher Wren in Oxford, in 1656, was involved in transfusion; since, even as written by Boyle (*Philos. Transact.*, 1665. Vol. 1, p. 129), an eyewitness of Wren's experiences, it never appears that he injected blood, but rather that he infused only medicinal substances (crocus metallorum, or antimony oxysulfide, etc.)

On the other hand, I think Clarke is the first who in England perceived the uselessness of infusions and abandoned them; indeed, he was deeply impressed by the struggle, then fervent and universal, which was stirring around the composition

and mystical power of the circulating blood, he turned his investigating instinct to this element and handed over to history the first experimental fact of blood transfusion.

In 1657 he transfused blood using a direct method from one dog into another dog, by means of a cannula bent at both ends: and without being given sufficient information to take away from his writings on the method carried out in his attempts, we can say (on the contrary to Scheel's assertion) that not all of them failed; since writing in an editorial. Oldemburg, first editor of the *Philosophical Transactions Med. Journal*, No. 35, puts it this way: “Tu nobiscum vidisse, vir amicissime, animla largo sanguinis profusione fere exangue redditum, et eonvulsionibus lethalibus piane moribundum, sanguine alterius animalis, ejusdem speciei in illuni transfuso, intra septem borse minuta ad pristinum et perfectum vigorem restitutum.”

It was therefore a direct transfusion of blood between animals of the same species, for the purpose of reimbursing the one artificially taken from one of the two; it is the first thought of recasting, of replacing blood, considering this as an essential element of life.

At the same time as him, Dr. Henshaw gives the annals an equal experience; which seems not to have had a lucky outcome, as Merklin says in his book *De ortu et occasionu transfusionis sangumis*, November 1674.

I think it is very difficult to specify, after Clarke, who really has the priority of having carried out conclusive and coordinated experimental tests. The first signal was given, from all sides instructive elements had to arrive, demonstrative proofs, more or less defined facts, different and opposite concepts, which all had to refer to a single center, the last true, which is no one in particular but of all the scholars together.

So it is that now we will see theory and fact walking hand in hand with regard to transfusion, and therefore speeches, lectures, writings on the one hand, experimental tests of all kinds on the other, in the various scientific centers of all nations, within a short period of time from each other, putting the impartial reporter in great difficulty.

France begins only in this time to wake up and take part in the subject: and the first word from there is that of the monk Roberto de Gabets, who from July 1658 made a speech on transfusion in an assembly held by Mr. Montmar. Gabets narrated how Harvey's discovery made him think of a new kind of blood circulation, namely the communicative circulation between one animal and another. "For this, two small silver channels are enough; one of them has a funnel-shaped opening to receive blood to be introduced into the open vein of an animal; the other smaller tube to be introduced into the vein of the animal or man that must receive the blood: these two tubes are joined with a third intermediate channel of skin, which, in addition to other advantages, also has that of allowing the course of the blood to be accelerated, when alternating pressure is applied to it with the fingers." According to Gabets, the operation is not dangerous, it can be of great advantage to revive individuals exhausted by haemorrhage, disease, old age, to correct malignant diseases and to repair the lack of blood, but when the viscera are not yet affected, such as for example in the incipient etisia. [Progressive wasting diseases like tuberculosis - PL]

Transfusion should have come into favour with French doctors of the time, due to the writing and the judicious indications of Gabets; but this was not so, indeed a complete forgetfulness followed, perhaps because Gabets had not corroborated his precepts with experimentation. In addition, Landois cannot support his assertion that Gabets did a transfusion on a man, since the evidence is neither provided by him nor is it apparent from the writings of the monk himself and his contemporaries.

Just as Clarke's early experimental studies, popularized by Oldemburg's pen in his periodical, occupied much of the London scholars and scientific bodies; so in 1662 we immediately see Hoffmann from his chair at the University of Pavia discussing transfusion, dictating an immediate method, proposing it for melancholy, mania and leprosy, already presenting the therapeutic approach that could and should have made such a powerful impact.

In September 1663 the Philosophical Society of London examined the two topics of infusion and transfusion, and delegated to this purpose doctors Wilkins, Daniele Coxe, Thomas Coxe, and Hook: so that on the 31st of the following May the Society observes Thomas Coxe transfusing a pigeon; after he bled it to death, he injects it with blood from another pigeon, revives it for 1/2 hour, but it then dies.

Coxe, tempted by this first test, from which immediate and evident effects had been obtained, on 7 June 1665 took a dog, and by means of a bladder fitted with a cannula he injected two English ounces of another's blood into the dog's crural vein without the slightest consequence.

But, in this experimental era of transfusion and infusion, the English anatomist-physiologist Richard Lower is certainly the one who brought the greatest light, the greatest clarification; and we see it stimulating his two pupils Boyle and King to investigate new points, to establish new clues to the importance and value of the transfusion.

At the end of February 1665, Lower performed his transfusion experiments on dogs. But while, with the exception of Clarck, the indirect or mediated method was used in blood transfusion, receiving the blood of an animal first in drops and then injecting it into the veins of another animal, Lower returns to the direct method from vessel to vessel. At first he tried to pass blood from a jugular vein into the jugular of another animal; but seeing that the blood easily coagulated in the tubes, he passed the blood from an artery into the vein. In the presence of doctors Wallis, Millington and others, at the end of February 1665 (and not in 1666, as Scheele said) in Oxford, he opened the jugular vein of a medium-sized dog and let so much blood flow until the dog was exhausted and close to falling into convulsions. He then opened the cervical artery to a large dog that had been tied close to it, and from the open cervical artery of the large dog he passed as much blood into the open jugular vein of the other dog that it was filled with it, as could be possible, perceived from its anxiety and restlessness; Lower then stopped the entry of the foreign blood and let blood flow from the vein again. This he repeated several times, until the two large dogs had gradually given their blood to the small dog, and according to Lower the blood mass had completely changed. He tied the wound of the little dog and let him free; he jumped off the table, appeared cheerful and even afterwards suffered no fatal consequences.

Here is the exact and detailed description of the Lower method (6 July 1664) of direct transfusion. "The carotid is revealed to the animal that must give its blood for about an inch, then a knot is made with a thread in its upper part, a knot well tightened and that cannot be untied. One thumb length under that, towards the heart, another knot is made which can then be tightened and released at will. Two threads are passed between these two nodes under the artery, then the artery opened and a small cannula is placed within the incision; the well tightened artery above the cannula is tied with two threads and closed with a small cork. Once this is done, the jugular of the other animal is exposed for an inch and a half and a slip knot is made at each end, and between these two knots two threads are passed under the vein; then the vein is cut and two tubes are introduced, one in the lower part to receive the blood of the other animal and bring it to the heart, the other in the upper part that comes from the head, allows the blood to flow out. The two tubes are closed with a stopper. Having done this, the two dogs are tied towards each other so that other tubes can be passed between the first two since the necks of the two dogs cannot be brought close enough to each other, it is necessary to use intermediate tubes. Once this is done, the stopper is removed from the tube that descends into the jugular vein of the receiving dog, and the stopper from the tube that comes out of the artery of the offering dog; they are joined to each other by means of three or four intermediate tubes, the running knot is released and the blood will rush through the tubes, as if through an artery. At the same time the stopper of the tube coming from the upper part of the jugular of the receiving dog is removed (having first made a

ligature around its neck, or at least pressing the other jugular vein with the fingers), and the blood of this into a dish (but not continuously) until the dog offering arterial blood begins to scream, weaken, fall into convulsion and is about to die. Then the two tubes of the jugular vein of the receiving dog are raised, and having completely tightened the two last knots, the vein is cut at the intermediate point, the skin is joined and the dog is let free."

Lower believes that blood transfusion is very effective in getting an exhausted person back from excessive bleeding. He thinks it would also be effective for curing the insane and arthritics, but only when they have healthy viscera. But, according to Lower, all the sick whose blood is rotten due to putrefaction or some contagion coming from inside, or are suffering from chronic bowel failures, should not expect the least benefit from a transfusion, because the new blood introduced would soon be corrupted by coming in contact with broken blood.

Clarcke lived in the time when opposition arose as a reaction to the system of natural faculties of Galen and to archaism in physiology, and against chemistry and the excesses of humor. In fact, in the therapeutic indications of transfusion, Clarche is more forthright than ever, and predicts that attempts at blood grafting are in vain where the material condition of the organs is irreparable. Great concept and precept together, unfortunately too forgotten there and then.

Boyle took the most active part in Lower's experiments and did his best to make transfusion successful. In a session of the Philosophical Society he proposed various problems, of which I mention only the more important ones, because they are directed towards the search for knowledge and physiological and pathological facts:

1. Will a dog whose blood has been mixed show any changes in pulse, urine, excrement, perspiration?
2. Will a hungry dog lose its appetite when injected with chyle-rich blood from another well fed dog?
3. Will it be possible to keep a dog alive by injecting it with the chyle of another animal?
4. Will a dog with blood diseases be cured by replacing you with healthy blood?
5. Can medicines be combined with the transfused blood, and is the action of these medications different from when they are given by mouth?
6. By injecting a dog with the blood of another dog that has been given a purgative, will the first be purged?
7. What are the results when transfusion is done between animals of different species?

As can be seen from his report, Boyle intended transfusion as possibly the most perfect replacement, as a complete exchange of blood, as a true blood graft. The bad thing is that not all these questions had a solution for corresponding experiences; and only King on 8 December 1666, in the presence of Daniele and Thomas Coxe, Hook and Pope, transfused the blood of a sheep to a dog, making it an absolute replacement without any accident, thus answering the question that blood of a herbivore does not harm a carnivore; and later in 1667 Thomas Coxe showed the harmlessness of the transfusing blood of a mangy dog into another healthy dog.

But the Philosophical Society of London was not satisfied with the replacement, they wanted a reparation: they had a dog bled and reduced to near death to then introduce sheep's blood: the experiment was done by King and succeeded without harm to the transfused dog.

Other experiments that King performed for the Society had an unfortunate outcome: in one he let calf's blood flow into a small sheep, another in which he bled out a sheep and transfused it partly with arterial and partly venous blood from a dog, and finally another in which a fox was transfused with lamb's blood, in which he found

bloody serum and blood pouring into the serous cavities. In these attempts, the cause of the unfortunate outcome was either the difference in the volume of blood cells (1/168 for the sheep, 1/196 for the calf, 1/139 for the dog) or was the excessive amount of blood injected.

A great step had therefore been taken by June 1667 and largely by the English. It could be assumed by definition that bleeding until apparent death had found in transfusion a quick and excellent aid: that an excessive amount of injected blood was not tolerated, producing alarming phenomena, that had to be artificially removed by subtraction; that the blood of animals of one species was tolerated by the blood of animals of another species; that the transfusion could equally be accomplished with an immediate and mediated method; and finally that blood clots had sometimes prevented the progress and completion of the operation (Lower).

Certainly not second to the Italians, indeed some of them even before Coxe, King and Boyle himself, they give hand to a series of experiments, whose purpose and outcome must be highly taken into consideration.

The first Italian animal transfusion experiment was by the famous Geminiano Montanari, former professor in Bologna, then in Padua. On 28 March 1667 in Bologna at Cassini's house, after having measured the amount of blood that a lamb could give, he bled another one of equal size until death and to this he transfused blood from another lamb, removed from the carotid: the jugular vein through which the blood was introduced was then completely cut off, closing the two stumps with two laces; without appearing weaker the animal soon followed those who had operated on it; and eight months later, put to death, the stumps of the jugular vein were found adhering to the nearby muscle and communicating the two branches by means of a small venous branch which could in a certain way make up for the lack of continuity of the jugular trunk. (*Journal des Savants*, 17 November 1668, p. 85)

Except that the transfusions, hitherto remained in the purely experimental sphere; in the hands of the Italian Griffoni of Udine marks the first step towards the therapeutic application; because in May 1667 he set out to heal a hunting dog of mediocre stature, 13 years old, therefore already old, very weak in strength, which can hardly walk and is more deaf; the little lamb's blood given without accident, on the contrary, it sees the animal rise, walk, run, gain an excellent appetite and partially regain its auditory faculty, which was then completely recovered a month later. (*Journal des Savants*, 19 November 1668, p. 88)

Daniele Major, although he never carried out transfusion experiments in animals and much less in man, in his work *Delicia hiberna* he describes a particular method of his that I love to reproduce because it was used later by other experimenters, and it is in my belief that it is the first note given for the semi-direct or instant transfusion of which Moncoq recently became the inventor.

"We have two men ready, one of whom is athletic, robust and abundant with blood, the other sick from bad moods: a mild purge being promised, one and the other should have a ligature in the right arm or in the left: then with a lancet a vein is opened to the sick man and three to four (English) ounces of blood are allowed to flow. Introduce the thinnest part of the instrument to be used for the transfusion in this vein incision, then make a ligature of the arm under the vein incision to prevent more blood from escaping and to hold the instrument in place. The vein of the healthy man is then opened in the same way and the other end of the instrument is applied to this vein, so that the blood, without coming into contact with the external air, passes from the vein of the healthy man into the vein of the sick man. The instrument used for this kind of transfusion is the following: a canal or silver tube about two fingers long, of equal width: one end of this tube or cylinder is briefly curved with an opening shaped like a cup, so that this extremity fits exactly to the arm of the healthy man and receives all the blood that comes out of the vein: the other extremity of the instrument ends in a thin and short cannula, and this extremity is introduced into the vein of the sick man."

Major then says that to prevent the blood from coagulating in the cavity of the cylinder, a few grains of deer antler salt or ammonia flowers can be introduced.

In this turn of time, a fact that, although not belonging to the history of transfusions, deserves our attention is the one handed down to us by Cristiano Federico Garmann of Schemnitz, who explains to Major in his letter of June 1667 the thought of recalling to life children born asphyxiated, by injecting a few drops of Malaga wine into their umbilical vein. And he translated his concept into an experiment when injecting a small quantity of Rhine wine into the umbilical vein of a newborn dog saw him become very animated, while he made it fall into drowsiness by pushing a narcotic liquid along the same route, and then promoted alvine discharges by introducing a purgative liquid. This was perhaps the starting point of another bolder thought born in the mind of a distinguished modern surgeon; that of resuscitating a newborn by transfusing blood through its umbilical vein. I mention this association of ideas without taking away the slightest part of the merit of the fact I am referring to.

It is Garmann himself who judges transfusion to be very beneficial after violent haemorrhages, while he considers it perfectly useless in consumption, emaciation and similar diseases.

And what does France do? We will see it now in all its glory.

Denis begins transfusion experiments on animals. From a letter he wrote on 9 March 1667 to M.… about blood transfusion, he notes that on March 3 of the same year he performed a transfusion experiment on two dogs. The transfusion was made from the crural artery of a bitch into the jugular vein of a dog, to avoid convulsions if possible: the method he used was that of Richard Lower: the two dogs were kept alive. The bitch later gave birth to a dead dog, in which only three or four drops of blood were found.

Denis together with Emmerets on 8 March 1667 undertakes a new transfusion experiment. He uses a dog that had been transfused in the previous experiment, and passes its blood into another dog; with this he so weakened the first animal as to appear dead, having lost about 12 ounces of blood. The two dogs recovered perfectly.

Denis concluded from this that transfusion is not harmful as claimed by some, because the blood, which in less than six days had been found in three different bodies, did not cause any inconvenience to the one who had received it last.

And here we have to observe that the experiments took place between animals of the same species, therefore without any difference in the properties of the blood, between what is given and what is received.

In a letter he wrote to M.… in April 1667 (see Oré, page 10) he tells how he passed the blood of three calves into three dogs, to see the effects deriving from the mixture of two very different bloods. The three dogs recovered well and thrived.

Denis and Emmerets performed numerous other transfusion experiments on dogs, from artery to vein, then from vein to vein, and always with success. They transfused the blood of animals of different breeds into the dogs, and did not loose a single one of the 19 dogs they experimented on. However, there is no detailed description of the studies and the tests they made.

Yet they had become masters of the act and of the accidents: and therefore they had gained the courage to attempt the experiment in man for therapeutic purposes.

In fact, Denis, after having answered all the objections that arose from all sides made against transfusion, performed the first transfusion on a man using lamb's blood in conjunction with the surgeon Emmeretz. It was a young man aged 15 to 16, to whom doctors had done twenty great bloodlettings due to a hot fever that had lasted two months according to the Gui-Patin school. For this treatment a very marked prostration of forces followed, exquisite anemia with a comatose state. Denis admitting that the great loss of blood was the thing that had demolished the

patient's constitution thought of carrying out a transfusion, which was performed on 15 June 1667 at 5 am.

At first, three ounces of blood, which seemed to be defective, were extracted from the patient, and from the carotid of a lamb, by means of a cannula, about nine ounces of blood were immediately passed into an arm vein: then he was bandaged as after a bloodletting and laid in bed. The patient during the operation said he felt a sensation of heat that ascended down the arm, along the course of the vein. At ten hours the patient felt well, wanted to get up and was cheerful. At 4 pm he had an epistaxis, but only of a few drops of blood. The following days he gradually improved, the sleepiness disappeared and he was completely cured. Denis attributed this happy and wonderful result to the fermentation and development of vital spirits or the product of the arterial blood of the animal in the viscous blood of the patient.

So Denis was encouraged to carry out a second transfusion experiment on a man in the same month of June. Here it was more of an experiment than a real cure. He was a robust and healthy porter from Paris, aged 45, who underwent this operation for a given sum of money. As he was healthy and had no contraindications for the operation, it was decided to have a large transfusion. About ten ounces of venous blood were extracted and about 20 ounces of blood, removed from the crural artery of a lamb, were transfused. During the operation he was in a good mood, he made his own reflections on this new method of treating the sick, he did not complain about anything, only that he felt a great heat from the point where the vein was cut ascended to the armpit. After the operation he himself wanted to slaughter the lamb that had supplied him with the blood, he went to the tavern to drink the money he had earned with his friends and resumed his usual occupations. (See “Lettre à M. de Montmort touchant deux experiences de la transfusion faites sur les hommes.” Paris, 1667, *Journal des savants*, p. 44-65)

These two brilliant results only exacerbated the opponents of transfusion more, who arose most viciously against Denis and all the followers of transfusion. We will talk about them when we deal with the opponents and supporters of transfusion in a specific chapter; it is enough, however, to mention right now that they were unable to oppose facts other than by unfounded hypotheses and theories.

The method followed in these two transfusions, as in the following ones, is described by Denis himself in a letter written to Monsieur De Sorbière: we will find it further on: here suffice it to say that it was a direct transfusion method.

But the opposition against transfusion continued; Lamy was the toughest opponent. In a letter that Gadrois wrote on 8 August 1667 to the abbot Bourdelot to answer Lamy's objections, we find the following experience of transfusion with calf blood made by Gadrois: it was a sick man who had not taken food for three months, he had lost knowledge and speech. After the first transfusion, his pulse raised, speech and consciousness returned and the diarrhoea stopped; but after 24 hours it returned to its pristine state. A second transfusion was made which gave him new vigor, but only for a short time because after 12 hours he died. At the cadaveric section it was found that his intestines were gangrenous. Nor, we note, is it the first time (as will be seen below) that in this historical period we see a successful transfusion by an operative act, but performed without indication, therefore failed in its final purpose.

Denis in July 1667 performed other experiments on animals, to answer the objections that were made against transfusion; as a result, animals with foreign blood kept well after five months.

Soon Denis and Emmeretz were offered a new opportunity to experiment with blood transfusion on man. It was Baron Bond, prime minister of the King of Sweden, who for three weeks had been suffering from liver failure with diarrhea and violent fever. He was treated with numerous bloodletting to the arms and feet, purgatives and enemas, so that he was so weakened that he could not stand, that he was

without speech and knowledge, suffering persistent vomiting. A transfusion was thought of; and although Denis and Emmeretz opposed it, judging it to be completely useless, yet they finally decided to do it. It was performed on 24 July 1667, injecting a small amount of calf's blood into his vein. Although the patient was unconscious with convulsions and almost imperceptible pulses, even as a result of the introduction of six waves of blood the pulse became stronger, his strength recovered, the patient recognized the people around him; he then fell asleep and was quiet. After three quarters of an hour he woke up, took various broths and herbal teas, without having any vomit or alvine discharge. This state of well-being lasted for 24 hours; but then his strength decreased again, the pulse dropped, he fainted. Then Denis repeated the transfusion: the relief was momentary, as after 11 hours death followed, without convulsions. The cadaveric section was found to have intussusception of the ileum, an extraordinarily hard and degenerated pancreas, a four-fingered spleen, a very large liver, discolored in many places, the veins and ventricles almost empty of blood.

The issue of transfusion was too important for no other experiments to be made. The Società Reale di Scienze in Paris took part in the dispute, and also made numerous tests. Of these we find only a brief mention in Du-Hamel's History of the Royal Society. A somewhat more extensive report is found in a work on Perrualt's transfusion published in volume IV of the book *Essais de physique* of 1688. - Here are these experiments:

On 22 January 1667, a transfusion was performed from the crural artery of one dog into the crural vein of another dog: the tubes that were used for the operation, however, were not made as the experimenters wanted, and there was a doubt that much blood had been taken.

On 24 January 1667 the experiment was repeated. The blood easily passed from the artery into the vein, but too much blood meant that the dog died on the spot: the section found that the right ventricle and superior vena cava were filled with coagulated blood.

On 23 February 1667 the experiment was repeated, but not having injected the blood so suddenly and in large quantities as in other tests, the dog did not die. It was precisely to demonstrate the damage of too abundant a transfusion that Dr. Gajant made many experiments on the subject, among which I quote the following: a dog, which he had been transfused with one and a half pounds of blood more than he had lost, fell into a swoon which lasted about 7 minutes, and died 5 days later.

During this same period, Italy does not fail to be worthily represented, since transfusions on animals are soon followed by transfusions on humans, some of which were crowned with splendid success.

The first in Italy to perform a transfusion on a man was Guglielmo Riva d'Asti. This information about Riva, who was surgeon of the King of France and of Clement IX and who died in Rome on 17 October 1677, was communicated by Antonio Masinucci and inscribed in the Roman Anthology of July 1788. The only document that survives of the experiments of transfusion made by Riva is a report printed on a fly-sheet which is preserved in the Catanatense of Rome, written in Latin and authenticated by four eyewitness doctors. In this report it is said that Riva transfused the blood of three castrated men into three men in the December 1667 in Rome. Riva gave great solemnity to his experiences by instituting them publicly and in the presence of the most distinguished doctors: among them Giovanni Maria Costanti, Antonio Egidio Petraglia, Giovanni Trulli, Giacomo Sinibaldi and various foreigners. Esler, who was present in the audience, gives a description of these experiences with the title: "Trium sanguinis transfusionum ex animalium triura viventium arteriis in triam laborantium morbis diversis venas celebratarum, anno 1667, mense decembre, Romae non bestiali more sed feliciori et kumano methodo prosperoque eventu a Joanne Guillelmo Riva ac principalioribus conprofessoribus qui priesentis operationibus interfuere suscriptae ac testificale."

The first subject on which Riva performed a transfusion was Francesco Sinibaldi, professor of medicine, suffering from very serious tuberculosis: “et cimi phtisicus ipse derelictse spei et destitutus et morituriens esset.” As for the method used and the quantity of transfused blood, neither Esler, nor Tiraboschi, nor others mention it. Only in Esler (*Miscel. Acad. Natur. cur*. Paris 1772) is it identified that these experiments were carried out with a simpler method than that used in France, that is: “sine vence extraelione vel exoriatione”, i.e. simply pricking the vein, and only for a little longer than what you do in bloodletting.

The consumptive patient died after a few months, as was to be expected: but of this outcome it is said as follows: "Sinibaldum post menses non ratione doloris vulneris inflicti vive sanguinis infusi vel diffusi in transfusione, sed illius anno XIV interpolate per tracheam rejecti, catarrho, febri, et ulcere polmonum glaciali tempore corraumptum obiisse.” An even more glaring mistake than the error of indication made by Riva; and in fact Dieffembach says and believes that the transfusion has prolonged the life of that patient by a few months.

The second individual on whom Riva gave a blood transfusion to had been suffering from continuous malignant fever for sixteen days. From the brief mention that Tiraboschi gives in his *Storia della Letteratura Italiana*, volume VIII, p. 468, it is noted that after the transfusion the fever ceased; then he left Rome, and there was no more news of him. Scalzi in his valuable article on transfusion does not mention it. Dieffembach only says how he improved after the transfusion. It is a surprise to find in Merklin (op. cit.) that this transfused individual died. I do not know which of the two narratives are correct; however, it is unfortunate that we do not have exact information and documents of this case.

The third subject to whom Riva transfused had been suffering from intermittent tertiary-type fever for 36 days: the patient, as all writers assert, recovered completely. Merklin, with his spirit of systematic opposition, also in this case says he is of the opinion that this individual would have recovered equally well even without the transfusion; moreover, he expresses doubt that, having recovered from the fever, he could later suffer damage from the transfusion; damage that, according to him, will have been carefully kept silent by Riva. An accusation that is absolutely unjust, or at least unfounded, since one of Riva's great merits was precisely that of giving maximum publicity to his experiments.

Meanwhile in Rome in 1667 Ippolito Magnani or Magni as some call him began to experiment with transfusion. He did not publish any writings, but the report of his experiences is found in *Confusio transfusionis*, Rome 1668, by Dr. Santinelli, a contemporary to his.

In the first, a dog to which he transfused lamb's blood, Magnani carefully noticed the phenomenon of the passage of blood in the urine a few hours later; and having found in the section that all the vessels and the bladder were distended and filled with blood the fine physiologist concluded "that too much blood had been transfused."

In another, a scabby dog gave the transfusion, and after it the animal appeared much livelier than before; but then it urinated blood and died, it seems, of haemorrhage because the animal lacerated the vein with its paw. It is not known how much blood was extracted and how much was transfused in both of these experiments.

In a third, a bloodless dog was transfused with lamb's blood: this also emitted a lot of blood in the urine on the following night, and then died. At the section the abdominal cavity was found filled with bloody serum. A slightly darker serum in the stomach, intestines and kidneys also contained a vinous as well as bloody fluid, as did the heart, the bladder and the left side of the skull. Magnani again attributes death to too much blood having been injected.

The last experiment was done on a very thin old greyhound dog, with a happy outcome, since this time he tried to avoid overfilling the vessels: lamb's blood was used.

The tireless industriousness and laudable daring of Denis and Emmerets around this time gives us another therapeutic transfusion in man. The waiter Antonio Mauroy, aged 34, had been suffering from recurrent furious madness for about eight years: he had been free from such attacks for some time, he married and the old disease reappeared for 4 months.

On 19 December 1667 at six o'clock in the morning Denis gave him a transfusion; ten ounces of blood were extracted from the patient, and they gave him 5-6 ounces that is 150-180 grams (exuberant quantity!) of blood removed from the crural artery of a calf, giving the patient tranquility and improvement. The operation was repeated on the other arm, in the presence of doctors Bourdelot, Lallier, Vaillant, etc.; during the operation, the patient felt a sense of heat: then he complained of pain in the kidney region, oppression in the chest, irregular heartbeats, and the next day, nosebleeds and bloody urine. Every phenomenon stopped and his mental health improved, but for a short time, since in June 1668 it recurred. His wife wanted the transfusion to be repeated, but it could not be performed because the patient was seized by violent convulsions and general tremor. The patient died in March 1669 probably from poison administered by his wife; Denis could not do the section of the corpse.

The last case recorded in those days also belongs to Denis. (*Abregé des transact. Phylos. de la Société Royale de Londres*, part 6, 1790, p. 387. – *Diction. des Sciences de Neufchatel*, vol. 26)

In February 1668 he was called to a paralytic woman for apoplexy: the right half of the body was devoid of sense and motion. She was previously treated by other doctors with five bloodletting, innumerable medicines, enemas, vomitories, but to no avail. Denis transfused her 12 ounces of calf arterial blood over two occasions, healing her paralysis.

And this must have been, by then, the last transfusion in France, since the lethal and mysterious case of the waiter Mauroy aroused a great dispute, due to rumors and arguments, as a result of which the Lieutenant of criminal cases on 17 April 1668 issued a sentence prescribing that "à avenir la transfusion ne pourrait e'tre faite chez l'homme sans approrobation d'un medicin de la Faculte 'de Paris." (Tesi di M. Nicolas, *Essai sur la transfusion du sang*. Paris 1860)

Scheel is not wrong to point out that the writers who claim that transfusions were absolutely forbidden in France by that decree were mistaken: its application was only limited and conditioned to avoid abuses and its reckless practice. So much so that after that sentence Denis had intended to give a transfusion to a paralytic woman, and obtained permission from eight doctors; only he did not perform it, it is not known why.

Meanwhile, Italy, excited by Riva's daring, continued to work not only on experiments but also with a therapeutic transfusion on a man, performed by Paolo Manfredi. He wrote two treatises, one in Italian: *Summary of the experiments carried out under the direction of Paolo Manfredi*, Rome 1668; the other in Latin: *De nova et inaudita medico-chir. operatione sanguinem transfundente de individuo ad individuum prius in brutis et deinde in homine*, Romae experta, 1668.

In these works, Manfredi, speaking of the invention of blood transfusion, admits that the first foundations of this discovery were laid by Daniele Major, followed by the English, then the French and finally the Italians. In another chapter he describes the method followed by the French in transfusion, then goes on to narrate the method he followed in performing blood transfusions on animals, assisted in this by doctors Giovanni Camaj and Bartolomeo Simoncelli.

He performed his first transfusion experiment on two dogs by passing blood from the crural artery of one into the jugular vein of the other, according to the method

used in France; but he became convinced that this method of transfusion was much more difficult and time-consuming, so in another experiment, in December 1667, he passed blood from the carotid artery of one dog into the jugular vein of the other - he used glass tubes in these animal transfusion experiments.

After the experiments on animals were happily successful, Manfredi thought, in conjunction with the aforementioned doctors, to also perform a transfusion on a human. It was performed on 2 January 1668. The report he gives us is very incomplete: he says that it was a certain Angelo di Udine, but he does not mention what disease he suffered from and why he was given the transfusion: the method followed is like that used in France, direct: only that, to make the skin incision and uncover the vein, an assistant raised a fold of the skin transversely to the course of the vein with his fingers; lamb's blood was transfused, but the amount is not even documented. The author does not even identify the outcome of this operation; it seems, however, that it was favorable, since Esler (op. cit.), sees this man some time later alive and flourishing, and writes: “Feliciter autem isthanc operationem cessisse ipsemet ego fideliter contestavi possum, qui hominem sanum et valentem post aliquot menses ejusdem anni Patavi offendi exercentem in pubblico operas suas veterinarias emuque aliis pluribus ostendi.”

Only by way of digression and to show how faithfully and accurately the history is written by some, will I say how Oré in his work completely forgets these cases of transfusion, which, although incomplete, are also always important. In his history, Dieffembach (*Handbucli theoretisch-praktischcs der chirurgie*; by Dr. Rust), noted as Griffoni in 1668 states that he had transfused calf's blood into a deaf dog of 13 years of age; and says that for it he became lively and later completely regained his hearing (!).

But Riva's failure in treating his patient Professor Sinibaldi resulted in a bitter war being waged with unjust accusations and false writings against transfusion being made by many, which engendered such a distrust in the public and in the doctors themselves that the experimenters were discouraged, feared for their reputation and eventual unfortunate accidents, and they stopped after having traveled so far with so much courage.

We see not only silence following in terms of experimentation and application: but voices rise from various quarters to openly condemn the ingenious therapy. While Folli proclaims that "if" the soul is in the blood, we will be able to conclude that in the blood, good or bad, consists the length and brevity of life, aging and graying; and if old age is a disease, why "will it not be permissible for every doctor to seek the remedy to keep it away?" (op. cit., p. 34) and elsewhere while expressing "that the old man can improve his condition and reincarnate through the transfusion" (p. 51); while Manfredi describes the proper advantages of transfusion with the words "Plethoricos exinanit: atrophicos humido rore conspergit, putredines abluit et duplici benificio pravum depulsum meliori communicato supplet, extinctam fere caloris flammam accendit": while, I say, all these authorities so strongly support transfusion; the opponents of it use all their influence in Italy to discredit it.

Raimondo Gianforti in his book of *Consulti e risposte medicinali* [Consultations and medicinal answers], admits that "blood transfusion would be beautiful and very useful, if, on the contrary, no short-term difficulties arise during the operation and even more serious after it.” His main objections to the transfusion boil down to the following:

1. The blood to be transfused must be extracted from the vein or artery: if from the vein as impure there will be difficulty in completing the transfusion, if from the artery everyone knows the danger of aneurysm and death.
2. If one has to infuse good and pure blood into a sick body with spoiled blood, one will first have to extract the bad blood, and this is several times less dangerous; that however the patient will lose so much spirit in opening the vein and will lose

so much of his own blood that what will then be introduced will not be enough to restore him.

3. It is difficult to find an exact similarity between two men, but very difficult between man and animals; which analogy in transfusion and nutrition is necessary; but, however, it is difficult using transfusion to separate the bad body habit of a cachetic and restore it from an atrophic one and feed it, since it is necessary to extract the blood from several young bodies to introduce enough of it.
4. If, according to Galen, the milk used for feeding must be sucked from the udder immediately; if the semen out of the seminal vessels loses its strength: what should be said of the transfused blood which does not enjoy the operation of the stomach and liver like milk?; and if the semen sometimes remains infertile for the length of the virile vessel from which it comes out, what will one have to judge of blood transfused by a canal?

Bartolomeo Santinelli was another great opponent of transfusion and in his work *Confusio transfusionis*, Rome 1668, he attempts to demonstrate how blood transfusion is uncertain, useless and harmful. To prove his assertion, he relies on some experiences made on animals by his friend Ippolito Magnani: he compares the transfusers to Circe who changed the worshipers into fish: he says that transfusion is "quaedam veluti barbaries"; his writing is full of futile and pedantic sophisms, useless to the solution of such an argument.

But Santinelli's work raised a great deal of noise and certainly contributed to discrediting this practice.

Some writers also speak of a government bill of Rome, which, issued in 1679 with the intention of absolutely outlawing transfusion, would also have resulted in cutting off all study and progress on the subject. But authentic quotations are lacking in these same authors who claim its existence, and it must be believed that an error by Merklin in this regard has been repeated by Sprengél and Maclcenzie without a deliberate search for the truth. If Scalzi (*Experiences on the transfusion of blood in Roma*, Medical Journal of Rome, April 1866), then placed in the best position to consult the ancient historical writings of local libraries, strongly denies that the veto on transfusion was issued by the Court of Rome, and we must value his statement more than any other.

Elsewhere, we saw Denis's failures as a stimulus to Châtelet's decree in France. Here the dispute between supporters and opponents of transfusion was much fiercer. The main opponent of transfusion in France was Dr. E. Lamy, or better still M. Moreau, doctor of medicine of the Faculty of Paris, who used the name of his pupil Lamy.

The main objections raised by Lamy against transfusion are: (1) that the new blood that is transfused, in its path to reach the heart, mixes with the old blood so that it cannot therefore act on the heart; (2) the transfusion cannot benefit against diseases dependent on excess blood nor on diseases dependent on excessive heat or corruption of the blood. With these and other arguments, Lamy tries to prove not only the futility but the harmfulness of the transfusion. Denis responded with arguments and experimental facts, until the failure provoked the Châtelet decree; after that, transfusion falls into complete oblivion.

The Châtelet decree not only dropped transfusion into discredit and oblivion in France, but also resonated in other countries; so it is no wonder that, continuing the history of transfusion, for 13 years, from 1667 to 1680, we can only record the three transfusions of Baldassare Kauffmann and the three of Purmann, which were also the first and only operations in Germany in this 2nd historical period. Apart from these, the study was limited to medical infusions in humans, experimental transfusions in animals, and experimental infusions in humans performed by King. There are a few more facts to tell before closing the experimental period of transfusion.

In June 1667, the Englishman Major transferred blood from another animal (it is not indicated of which species) to a dog that was short of breath. As soon as the arterial blood, and therefore more oxidized, reached his veins, it began to breathe quietly.

At its meeting on 17 October 1667, the Philosophical Society of London proposed to carry out the following experiment: to pass the blood of a dog from its pulmonary vein through a tube into the aorta of the same, without letting it circulate through the lungs, and commissioned Dr. Lower and Hook to perform this experiment. But the experiment failed, and was resumed in another respect on 4 November 1667 by Lower: he communicated to the Philosophical Society the happy outcome of the experiment he instituted, with which he made a dog immediately pass blood from the carotid artery into its jugular vein on the same side, without any accident.

These experiments, as can be seen, aimed to demonstrate the safety of mixing arterial with venous blood, pushing the first into the veins with a transfusion.

In England, where transfusion into humans had not yet taken place, Edward King expresses the idea of attempting it and plans to do so in April 1667 (*Philos. Transact*. 1667, No. 25, p. 449), but he does not do it for lack of opportunity. After in a letter to his friend Oldemburg on 21 October 1667, he communicated his method and described his apparatus, on 22 November 1667, he performed it purely as an experiment on a healthy individual not suffering from any disease, compensating him with a guinea.

He was a 32-year-old bachelor in theology named Arthur Coga, with a bizarre mood, so Lower calls him “hominem amabilis qusedam vesanise affectum”. Before undergoing the operation, Coga wanted to drink wine, and was then transfused using King's method: he inserted a slightly curved silver tube into the carotid of a lamb, and let its blood flow into a cup for the space of a minute to be able to determine how much blood was flowing at a given time: in an minute 12 ounces came out. This done, we move onto the operative act: a vein in the patient’s arm was opened as if for bloodletting, and 6 to 7 ounces of blood were let out of him, then a small tube was inserted through the same vein.

The tube introduced into the man’s vein was connected by means of a quill with the tube introduced into the carotid artery of a lamb. During the operation, the patient did not feel that sense of heat along the course of the vein that had been mentioned by the French experimenters and this was perhaps because the blood had cooled due to the length of the communication tube. The patient received approximately ten ounces of lamb's blood. After the operation he felt perfectly well, and drank two glasses of absinthe. He had a full and strong pulse and strong appetite, greater than before, and had three or four ‘scariche’ [possibly should be ‘discharges’ - PL]. That night he slept peacefully, and the next morning he sweated for three hours. Two days after the operation the arm wound was completely healed.

Coga made repeated requests for another transfusion to be performed. In fact, on 12 December of the same year, Dr. King gave him another transfusion; he extracted only eight ounces of blood and with the same method introduced 14 ounces of lamb's blood. This time the patient was also perfectly well, except for a few slight feverish fits. King, however, believed that this feverish state was not due to the operation, but to a lot of vinegar wine he drank after the operation.

In spite of this favorable result, the transfusion of blood in man also fell into disrepute in England: the failures in France contributed greatly to this.

However, transfusion experiments on animals were still continued, especially from a physiological viewpoint: and in this respect they are very important.

For example, Dr. Thruston in Chester did the following experiment on a pair of dogs. After weighing a dog before the operation, he found it weighed 15 pounds; then he transfused it with sheep's blood in such quantity, that after the operation the dog weighed 2 pounds more, i.e. 17 pounds.

Because of this increase in his blood mass, the dog felt very ill, became breathless and died. At the section there was coagulated blood in his heart, black and bloody liquid in his stomach, all the veins so filled with blood and so dilated that circulation had been prevented; and then the animal suffocated. An experiment of great significance; which would have been even more so if he had used dog's blood instead of sheep's blood, i.e. blood of the same species as the animal on which the test was made.

On 14 January 1669, Dr. Cronne expressed the idea of carrying out experiments to see if it was possible to keep an animal alive for some time, with repeated transfusions at short intervals, without giving it any food. These experiments were not carried out to full effect, as transfusions were already beginning to fall into disrepute.

About this time, and specifically in 1680, Folli published his Treatise on transfusion (op. cit.) which is intended to be considered as the first complete work on the subject, and which as such became a guide and instruction to the experimenters and scholars of the art. Courage and true conviction must have inspired Folli in spreading the written one, in which there is a wealth of knowledge and no neglect of the issues relating to the transfusion, since it was at the time of the fight between the supporters and detractors of this therapy. This is another debt that the Italians have towards him, and which is therefore also recognized by most of the foreign writers and historians.

Ettmuller also cared about transfusion; and one of his memoirs published in 1682 (*Ueber die transf.*) bears witness. He warns of the danger that exists in transfusion due to the mixture of blood of different species: he considers it indicated in certain forms of melancholy and mania and in violent bleeding; however, according to him, small amounts of blood should always be transfused at a time; as for the method he prefers that of Denis; this dissertation does not contains any experiments.

Finally, in Germany too, blood transfusions were performed on humans. It was done in 1668 by the regimental surgeon Baldassare Kaufmann in conjunction with his pupil Matteo Purmann. The patient had suffered from malignant fever for three months, from whom an abundant amount of blood was extracted first and then replaced by a corresponding amount of blood taken from the carotid artery of a lamb: he was cured.

Other transfusions were made by the same author, that is, in two soldiers suffering from scurvy and in a fisherman suffering from a corroding lupus, but which resulted in a worsening of the patient's conditions.

As for his ideas on infusion and transfusion, he agrees perfectly with the ideas of Elsholz and Ettmuller, except that he also proposes (and I think he is the first one to do so) an injection into the arteries so that the remedy goes immediately to the sick part. But he himself agrees that this method is dangerous and difficult and only in rare cases practicable. He says that the transfusion could be done much better from one vein to another, by means of a tube that is placed inside another tube filled with hot water to prevent blood clotting as much as possible.

And as the last experimental transfusion of this era, we are left to remember that of Giovanni Boleo in 1690: after taking blood from a young dog, he injected it into another old dog, so thin due to mange (!) that it seemed close to dying: after the transfusion the dog was well, the mange healed in a few days and the dog became fat.

Giovanni Brunner, professor in Heidelberg, Giovanni Corrado Peyer, Giacobbe Wepfer and Harder, all performed experiments on the action of air in the circulation, in order to somehow calm the doubters who, moved by fear of the possibility that a column of air is injected with the blood into the circulation, used this as a weapon to oppose the use of transfusion.

The first of these experimenters in 1682 injected into a dog, via a tube into the crural vein, so much air and with such violence that one could hear the gurgling of

the air blown in the vein. The dog began to breathe more rapidly and became labored: tied the vein released itself: it was soon attacked by tetanus like convulsions; but gradually it recovered and became as lively as before. After about half an hour, Brunner again blew the air through its crural vein with such violence that he could hear its gurgling in the precordium; the dog died after having emitted feces and urine, and at the autopsy he found the stomach and intestines very contracted and red, spleen and liver very congested, veins and heart stretched by air, as well as the heart, especially the right ventricle; in the stomach there was a little bile, and the very red urinary bladder still contained a lot of urine, although the animal had urinated abundantly before death.

In the writings of the Schaffhausen doctor, Giovanni Corrado Peyer, we find the following experiments made in 1682.

For anatomical studies he blew so much air into the cisterna chilifera [*sic* - possibly meaning lymphatic system - PL] of a cat that had aborted and seemed completely dead as to penetrate the heart and make it beat again; and this for several hours. He also repeated these experiments on human corpses; he obtained this effect more easily if the air was hot. The movements of the heart had a different duration according to the kind of death to which the animal was subjected; they lasted longer in the strangled; even the blowing of air into a vein produced the same effect.

Giovanni Jacobo Wepfer, a physician from Schaffhausen, wrote in 1863 to his friend Rodolfo Giacomo Camerarius that he had killed an old castrated and a pregnant cow through the insufflation of air into the jugular vein.

Camerarius performed the following experiments which are of great interest: to two bitches he violently blew air into the jugular vein, and saw death rapidly follow. Then he performed a new experiment: at first he drew a little blood from a young dog, then injected a little air into the jugular vein with little force: after the operation the animal remained calm, without strength, with half-open eyes, with paralytic and numb extremities: it remained in this state for about seven minutes, then returned to being as lively as before.

To the same dog some time later he blew air into the other side of its jugular vein with great violence; frequent pulse followed, general relaxation of the limbs, without convulsions, the animal screamed and finally died quietly; from the wound flowed foamy blood: the heart with its vessels was dilated by the air, but especially the right atrial auricle in which there was no blood: in the ventricles there was foamy fluid blood mixed with air: the coronary vessels of the heart contained more air what blood; air bubbles were contained in all the veins and arteries of the body. Camerario repeated this experiment on another dog with the same result, and the conclusion he drew is that a great distension of the heart can produce swoon.

Finally, in October 1864, Dr. Garder in the presence of doctors Burgower, Stéhél and Tonjola, blew air vehemently into the jugular vein to a medium-sized dog. The animal died instantly, and the heart was very relaxed and containing only a little frothy blood.

I think that the importance of these experiments should not be overlooked, which allow us to easily deduce the vivifying action that oxygen has on the blood mass if air is caught in it to even a mediocre degree, and the mechanical paralyzing action that it exerts on the circulatory center if injected in an excessive volume.

But man easily forgets the past: and therefore we will see later in the 3rd period doctors and physiologists offer, as if they were new, experiments and facts which already were thrown into the history of transfusion in the 2nd period with much sense and rectitude of concept.

In this experimental period, although confusion and indeterminacy of experiments are manifest, however empirical, their direction is badly carried out most of the time and the results are improperly interpreted: yet it is necessary to concede that in this

period some laws regarding the theory of transfusion were identified that have remained unchanged up to our day, and in its study marked a real advance.

And they are: mediated transfusion to replace immediate (Lower, Feb. 1665); the resuscitation of an animal bled to death apparently merce [*sic* - translates as 'goods, commodity or merchandise' - PL] by introduction of new blood (King, 1667); the damage of an excessive introduction of blood, by which the animal suffocates, the motions of the heart are stopped by repletion (Gajant, June 1667); the passage of blood through the kidneys through the urine and into the cavities for the serosa when the introduction of blood was greater than the need (Magnani Magni, 1667 Rome); the tolerance that animals of a given breed have for the blood of animals of different breeds (Denis, July 1667); the tolerance that man has for the blood of herbivores, calves and lambs (Denis and Emmeretz, July 1667): the beneficial modification made to the greatest of cerebral disturbances, madness, through the introduction of blood into the circulation (Denis, December 1667); the return of the forces lost as a result of serious illnesses (Denis and Emmeretz, July 1667); the obvious, but fleeting refreshment of life close to dying out as a result of irreparable visceral failures (Grandojs, August 1667 and Diva, December 1667); finally, how innocent a small column of air injected into the circle is, immediately lethal if enough to fill the cavity of the heart.

The thought Garmann had (1665) of repairing asphyxiation of newborns using infusion via the umbilical vein is also worthy of the utmost remark; an idea supported by successful experiments in animals, and which must have suggested to modern operators to use this route to perform transfusion in asphyxiated newborns.

Therefore, good progress has already been made in this second phase of transfusion, and it was then established with the clinical fact (Denis and Emmerets, June 1667) that blood transfusion in man is possible, which is useful in acute anemia and which can be done with a successful result, using herbivore blood (calf).

But the incomplete knowledge of the physiological doctrines around the circulation and breath, their functional action, the special function of the blood cells, the sources of their reproduction, the reciprocal action between the blood elements and the stem elements, made transfusion take empirical and erroneous directions, to the point of succeeding in its attempts to be often useless and irrational, sometimes harmful, rarely useful.

The restraint that was imposed on this act was therefore prudent and justified, and on the other hand the time elapsed between the last attempts of the experimental period and the first of the following period was certainly not fruitless; from the progress of the physical sciences, from the ever increasing positivism of human and comparative physiology, transfusion had to be and was led back to a better and more useful direction.

THIRD PERIOD: THE PRACTICAL-THERAPEUTIC ERA FROM 1783 TO 1874

Before proceeding in this third period according to the order established in my preface, I must also do justice to the factual truth for this historical phase, erasing with absolute evidence an error that until today weighed disadvantageously and wrongly on the merits of the Italians.

Marked by all, a silence of 150 years, the writers of the subject (Marmonier, Scalzi, D'Oré, De Bellina, Paolo Scheel, Schilz, Dressen) all start the third period with Blundell: my task is to render justice to those medical experimenters who dealt with the question before Blundell, and it is certainly without temerity or fear of erring that I assert that it was the Italian Michele Rosa da Modena in his experiences who preceded Blundell by thirty-five years, who occupied it from 1783 to 1785.

The proof of my assertion lies in the chronological dates: in fact Michele Rosa delivers in his *Lettere sopra alcune curiosità fisiologiche* (Volume 1) his many experiences of transfusion in animals, and on page 288 of the same volume he summarizes them in three fundamental conclusions worthy of much commendation; while it was only in 1818 that Blundell published his experiments on animals for which he raised so much cry in the *Med. chir. trans*. Vol. IX (Esper. on the transfusion of blood) - See also *Ann. Univers. di Med*. Vol. XII, 1819.

It is therefore indisputably proved that the transfusion was re-established, after 150 years of forgetfulness, by the Italian Michele Rosa, and so I feel that in my research I have fulfilled a chronicler's debt and a duty towards my country, since the quotation history no longer allows foreigners and nationals to put other names before that of Rosa.

Here I begin the proposed division of the third period, not by chronological dates, but according to the concepts and clinical and therapeutic directions for which the doctors implemented it, both experimentally and clinically in animals and men.

Transfusion can be defined as the operational act by which a given copy of blood administered by another individual is introduced into the circulation of an individual (man or animal).

In this act the following are considered: the species on the naturalistic scale of the individual who receives in comparison with the subject who lends the blood; the quality, quantity, physical condition of the blood being transfused; the species of the blood vessel from which it is removed to that of the vessel into which the blood is introduced; the manner of the transaction, including the instrument used; the dangers and the accidents; finally, the aim or direction both experimental and therapeutic.

I will study these different moments of the transfusion one by one in the most useful details, in the criticism, in the appreciations, leaning as much as possible on the results obtained so far from the experiments and therapeutic applications. I will digress little in recalling the individual studies of all the experimenters, and much instead in exhibiting the demonstrative evidence in support of the practical conclusions which gradually came.

The species of the individual who receives compared to that of the subject who gives blood

It is very difficult to formulate an exact concept on the subject since it is not yet proven whether in itself the blood of one species in animals of a different species is absolutely harmful.

The experiments in this line of concept have produced results too different from each other to be able to deduce positive and convincing corollaries. In my opinion, the conditions under which the tests were carried out were so different that in no way it is possible to form an absolute, definitive idea. – Now the jugular injection was made with damage to the action of the heart; now with an exaggerated amount of blood to have apoplectic phenomena; who used direct method, who indirect with defibrinated blood or not; sometimes it was omitted, sometimes bleeding was allowed, now partial, now extreme. Blundell (*Med. Chir. transact*. 1818) was happy in his tests using animals of different species, while Dieffembach (*Ardi, de Muller* and *Arch. de Medecine*, 1818) says he has never managed to obtain a favorable outcome: calf or lamb reanimates a bled, dog (Panum) and a rabbit (Belina): pigeon blood is perfectly tolerated by a dog (Brown-Sequard) and so on, having very disparate conditions with outcomes, now the same, now different, sometimes even indefinable and uncertain, as Prevost and Dumas tried it, they saw (*Biblioteque de Genève*, Volume XVII, 1821) that blood from a different species is capable of only imperfectly and with difficulty in keeping the animal who receives it alive

The only true and acceptable conclusion was the one that we learned from globulimetric observation, and for which it was believed that, under equal experimental conditions, the most important element one needs to consider when calculating the result is the size of the blood cells; in regard to which it is not possible to forget two facts: obstruction of capillaries when the injected blood cells will have a volume greater than the lumen of those of the recipient, and diapedesis when the size will be smaller: which, taking place in the visceral vessels, will have a lethal outcome in the first case, interstitial effusions and infiltrations in the second case.

Not only the size, but also the shape has to be evaluated: the elliptical blood cell (camel, dromedary, birds, reptiles) having two diameters can be stopped in the middle of its course, when in the vortex of the wave or by impact of a nearby cell to arrange itself with its major axis transversely to the light of the vessel in which it had circulated freely for a certain distance, as long as it was placed lengthwise. Prevost and Dumas (*Biblioteque Universelle de Genève*, volume XVII, 1821) killed a bird with sheep's blood; Magendie sees a dog die after 15 hours from infused turkey blood, another dog from frog blood, a goose from dog blood, a cat from turtle blood; Bischoff (*Arch. de Muller*) loses a young rooster given calf's blood, a hen for dog's blood, a dog for chicken's blood, a rooster for cat's blood once and rabbit's blood another time. Brown-Sequard has given us a series of very useful and conclusive experimental tests (*Comptes rendus Acad. Des Sciences*, 1857), from which we have learned that the blood of a vertebrate animal of one species is not venomous for vertebrate of even a very distant species. But after all, for physical reasons, it is indisputable that the donor should not differ in form and should deviate as little as possible in size from that of the subject who receives it; therefore the supposition that in transfusions between animals of different species the disproportion in the volume of the blood cell may have been the cause of the unsuccessful experiment is not unfounded; while that, if this sometimes succeeded well in spite of similar globulimetric differences, the explanation of the fact lies perhaps in having injected a very small amount (sometimes only ½, 1 or 2 drams only) of foreign blood; and this often only obvious by careful reading of the works that refer to this topic.

Why the ancient blood transfusors, which science had not yet learned that the blood cells in different animal species differ in volume, used calf and lamb blood rather than that of any domestic animal, is difficult to say. Perhaps, taking the blood as the seat of the soul, the docility and timidity of these animals were the only reasons for the preference in comparison to the power, indomitable, uncertain and often unknown nature of the horse, bull, ox, dog etc. From no concept in fact in the choice of blood do they say that the transfusors of the second period departed: Denis who for the first in France, on 15 June 1667, remediates a man given lamb's blood, Riva d'Asti in Italy (October 1667) with sheep's blood; Kauffmann in Germany (1668) with lamb's blood and Edward King (April 1667 – purely by experiment) with lamb's blood. Only in the third period, after the applications of the microscope and the first histological studies, did the use of the blood of the aforementioned animals become justified, although the previous facts (just mentioned) were enough to accept such a procedure.

The first transfusion with lamb's blood in this third period was made by Russel in 1828, in a hydrophobic, using an indirect method, and after bleeding the patient (*Allgemeine repertorium*, March 1868): nor do recent writer speak of this case, wrongly believing and letting believe that Esmarck in 1860 had preceded everyone in the use of calf's blood.

Today we can count ten transfusions with calf or lamb blood for the second period, and seven (to be added later those of the Freniatric Congress) from 1828 onwards - 17 in all, of which we have the following data: the first ten all succeeded well – they are from: Denis and Emmeretz (1667), Gadrois (1667), Denis and Emmeretz (1667 and 1668), Riva d'Asti (1668 – three), Paolo Manfredi (1668), Kauffmann (1668), King (1667) – Of the other seven, one died when the operation

started (Esmarck – *Archiv de Virchow*, vol. 27 p. 241), the second died a few hours later (Dressen – *Dissert. de transf. Sang*. 1861) with anatomical findings that do not blame the transfusion, having indeed obtained from it very advantageous direct phenomena, such as energetic contractions of the heart, frank respiratory motions, pupils less mydriatic and reactive to light, radial pulse returned: death occurred amidst convulsions such as occur in extreme slow agony. – The other five, of which two from the Albini of Naples (Rendic. della R. Accademia scienze fisiche e mat. File XII, December 1872), one from Bliedunq (*Gaz. des Hopit*. 1839, p. 766), one of the Wilminton Hospital in North Carolina (*Louisville courier journal*, June 1871) one by Russel (*Allgemeine repertorium*, March 1868) had very satisfactory physiological effects.

It should be noted that Esmarck mentioned above, contains a grave error, that of having injected 420 grams (14 ounces) of blood – an enormous amount in itself, but even more out of respect for the atony in which the heart of that poor oligemic must have been, who had suffered haemorrhages from a disarticulation of the thigh and consequent profuse suppuration.

More recently a last series of transfusions with lamb's blood in Italy consigned to history the alienist doctors as a therapy for certain phrenitis (D.G.L. Ponza - *Della trasfusione del sangue praticata negli alienati del Manicomio di Alessandria*, 1874. Prof. Azzio Caselli of Reggio d 'Emilia - *Considerazioni sulla trasfusione del sangue*, 1874); none of which count, by any chance, that undermines the concept that lamb's blood is harmless to man.

When I speak of the result of the transfusion, I mean only the direct result of the operation, its harmlessness in the moments of which it is established, and therefore I count among the successful ones also those that had an unfavorable outcome with regard to the therapeutic purpose, for which I placed last in the chapter of practical applications and clinical purposes of transfusion.

Therefore in this sense the many transfusions with lamb's blood were all successful, not having to take into account the one in which the patient died at the very beginning of the operation. In all of them out of tolerance to foreign blood, the awakening of cardiac life and of the centers was obtained, although more or less lasting and sometimes very fleeting. Therefore, it is believed that calf, lamb and sheep blood in a given measure can be used in humans, because it is tolerated by him and felt by him as a physiological stimulus.

No doubt therefore can remain that the shape and size of the blood cells of these animals have an adequate proportion with the lumen of human capillaries - that the cell and serum are tolerated by the human body and also by the blood tissue within which they come to mix.

But will the blood of calves, lambs and sheep be able to replace that of man in everything, as some would like? Does it have a reconstituting and lasting virtue equal to the human? Is it absolutely harmless to our species? We will respond to these doubts later - Choice of blood quality.

So far I have talked about transfusion between different species, now I will talk about this therapeutic act between the same species.

Who is not born ready, naturally frank, the thought that no blood, no matter how excellent and similar, can equate in virtue an equal blood, the blood of an animal of the same species?

This is not the place to talk about the experiments made between animals, because, as well as ultimately they were not very demonstrative due to their infinite variety, they are of little use at least to clarify the subject I am now dealing with. I will restrict myself to speaking of transfusions among the human species, the number of which is now very large, such that no one can refuse to enter this path, from accepting what has already been shown to be positive, from hoping that new tests can increase the extent of therapeutic applicability of the transfusion. Although it seems to me that I have spent any word in vain to show how it is for man to prefer

that of his species to any other blood, I cannot refrain from making known the latest experiences of Landois of Greifswald aimed at ascertaining the physical effects on blood elements in transfusions between humans and different animals.

He saw that the blood serum of many mammals dissolves the blood cells of other mammals; the blood cells of rabbits he saw less resistant than those of the dog and cat, using both prone blood and defibrinated blood: he showed that the blood cells of mammals introduced into the bloodstream of the dog soon dissolve; and under this relationship he asserts that the sheep's blood cells resist less long than those of man; that the dissolved blood cells are excreted mainly by form but still by the intestines and the serous cavities. It is a pity that he does not mention the way of behaving with respect to each other of blood cells and the serum of lamb and man.

The same Fiedler and Birch-Hirschfeld who found numerous red blood cells of less than human diameter in patients transfused with lamb's blood hasten to say that this finding is of no value, since these smaller forms of blood cells are also seen in different proportions in individuals who did not receive animal blood. They found that lamb cells did not dissolve in the human serum, but turned pale: while the human blood cells in lamb serum became more marked, with a wrinkled surface, took on a serrated edge and gathered in more or less large groups. Hasse thinks that haematuria sometimes occurs due to the wasting of red blood cells.

Such experiments lead to conclusions, certainly not made to be accepted with closed eyes, neither to demonstrate the physiological harmlessness of mixing blood of different species together. Similarly, the conclusions reached by Fiedler and Birch-Hirschfeld of Dresden (*Deutshes Archiv für Kliniche Medicin*. Leipzig, July 1874 p. 545) with their transfusions in man made with lamb's blood must be accepted (more on this later).

It seems useless to say that the little essential difference between the blood of a woman and that of a man leaves full power to exchange it between the two sexes, provided that the physiological knowledge is not forgotten that the blood of a woman is generally less rich in blood cells and contains relatively greater quantity of water and albumin: what leads to always preferring male blood whenever the choice is possible.

The same norm must be followed for age, knowing how the two extremes of life offer less suitable blood than the average age.

The choice between venous and arterial blood

This has kept experimenters and practitioners divided in different fields, as would be natural, given that the different quality of blood implies different operating modes, more or less exact, that are differently assessed, and therefore constitutes differences of opinion in operators and clinicians.

Bichat in 1811 was the first to study the action of venous blood on brain functions: injecting it into the carotid artery of a dog he noticed restlessness, shortness of breath, amazement, as if the animal had breathed carbon vapors (Lessons on life and on death) for which he contrarily concluded “that life could be restored to the asphyxiated by transfusing their brain with arterial blood which is its natural excitement, but only in the first period of asphyxiation when the brain function is only suspended."

Bichoff (1838) sees a bird reanimated given arterial blood from a mammal, but dying from venous blood. But the most conclusive and wise experiments are those of Brown-Sequard (*Compt. Rendus de l'Academie*, vol. XXXII. - *Journal de Physiol*. 1857-58) and those of Eulembourg and Landois (*Gaz. Med. de Paris*, 1865). The first proved: (1) that vertebrate blood, both arterial and venous, if it is loaded with oxygen so as to have a glowing color, can be injected without damage into the veins of another vertebrate; (2) that vertebrate blood, both venous and arterial, when

saturated with carbonic acid so as to become black, cannot be injected into the veins of a warm-blooded animal without producing phenomena of asphyxiation and death, dependent on the toxic action of carbonic acid. These facts were also experimentally confirmed by Eulenburg and Landois who came to say that the lack of oxygen excites the respiratory center of the medulla oblongata is the agent of the rhythmic movements of the muscular inspirations; that in acute anemia the animals die of asphyxiation because the loss of a large number of oxygen-carrying red blood cells first produces excessive irritation, then paralysis of the said center; that the transfusion of vermilion and oxygen-laden blood decreases these irritations up to the degree of normal, physiological excitation, and therefore respiratory motions restart; that arterial blood produces this effect by acting directly on the medulla oblongata.

Therefore the choice between arterial and venous blood could not be uncertain after such demonstrative tests. However, lateral considerations, of expediency, of practical application on humans, and still dependent on the operative modality, had to keep opinions divided from the beginning and keep them until today. From whom though should we draw arterial blood – perhaps from man? To easily accept such a thought, one would have to forget many grave considerations which I believe are so severed in their significance as to disprove any contrary opinion.

Next, consider the seriousness of the injury that would go to the individual who gives the blood, to get to the artery, which is almost always under aponeurotic and therefore requires an ever deeper wound than that which occurs when the blood is removed from a vein; in addition to this from surgery and physiology it is known that it is not possible to stop the blood from an injured artery without its total closure, nor is it always easy, safe, complete, to establish a collateral circulation sufficient to nourish the parts below the binding point. Add that when we want to overcome these grave doubts, these radical objections, we still have to ask ourselves how we should transfuse this arterial blood from the healthy to the sick? If you want to do it directly, you will have to follow the same procedures as for direct arterial transfusion between animals, that is, it will be necessary to first discover a large tract of artery in order to free the blood from the lower stump; secondly to secure the afferent cannula within the vessel of the recipient of the blood. With these operative acts such sufferings and dangers are inflicted on the generous individual who gives his blood that every word aimed at stigmatizing such a practice is superfluous.

If you want to use an indirect method, that is by defibrinating human arterial blood in order to prevent it from clotting, you will certainly not have achieved greater operational perfection than if you had drawn venous blood and beaten, adhered and defibrinated it; you would have added the risks and seriousness of the arteriotomy of the donor, thus completely invalidating the supposed advantages of transfusion with human arterial blood.

So all that remains for man is to ask for venous blood, knowing that the incision of a vein, always available on the surface, is easy, safe and free from consequences.

But soon the serious objection of the toxic action of venous blood enters the scene to arouse doubts and fears; an objection that would indeed be very valid if the transfusion of venous blood were to be done directly from man to man in the thought of thus preventing its coagulation.

But since Prevost and Dumas (*Bibliol. Univ. de Geneve*, 1821, issue 17) have expressed the idea that the oxygenated blood for beating is capable of reviving an animal bled with haemorrhage; since Dieffembach (*Archiv. de Muller*, 1828) and Bischoff (*Beitrage zur Lehre von den Blut-Archiv, Muller*, 1834, p. 347; and 1838, p. 351) contrary to Magendie's opinion, arrived with their numerous and convincing experiments to pronounce in favor of the beating of blood; we are absolutely authorized to believe that the venous blood oxygenated by beating is put in chemical and physiological conditions equal to that of the pure arterial.

Bischoff after having proved that fibrin and serum (also oxygenated, as Brown-Sequard experimented) cannot recall a bled animal to life (*Archiv. Muller*, 1834,

1838) concludes that the blood cells alone constitute the active principle of the blood, and therefore came to support of the fact left to us by Dieffembach (*Arch. Muller*, 1828) who brought about the revitalization, although not lasting, of a bled animal by injecting it with dried blood then artificially re-dissolved.

Therefore the blood cell is the element to which the assimilation of oxygen to a venous blood which is mixed with atmospheric air by means of beating must be carried out: and it follows that the venous blood of man can therefore without exception be used in a therapeutic transfusion, when it is brought to enough oxygenation to make it vermilion, and to approach it, not only for appearances, but also for the physiological and chemical properties of the arterial.

Having accepted this fact, refused the use of human arterial blood, it remains for us to take advantage of the arterial blood of animals. And so far from the physiological side, no objection, yes to the volume of the blood cells, as long as it is a question of lamb or calf or sheep blood, yes to the vivifying power of its natural oxygenation. And the facts noted earlier prove it. But it is from the practical side that the most serious objections arise against the use of animal blood, in comparison with human blood, for the many accidents of which the operative act first consists, and for the office it fulfills in the body brute blood of man. This is not the point of enumerating the first ones since my objections and my comparisons must here be limited to the experimental and practical physiological side.

I will immediately say that when I reflect on the small number of transfusions performed with animal blood up to now, in comparison with the many made with human blood; when I think of the generic physiological concept for which I believe we owe preference to the latter; I believe that the transfusion of calf blood cannot be accepted for more than what it is really worth, that is, as a fallback, a substitute for that with human blood.

Dieffembach (*Arch. Muller*, 1828) asserts that he has never managed to keep any bled animal alive more than six days by injecting it with the blood of animals of a different species.

Panum (*Virchow's Archiv*., 1864) from his numerous and diligent experiments had to conclude that foreign blood can restore, but only briefly, the activity of nerves and muscles, respiration and the production of heat: he saw it dispersed partly due to haemorrhage and partly due to the decomposition of blood cells and the urinary tract. The products of decomposition, in which the absence of urea is noted, bring serious disturbances into the body which can be endured if a small amount of foreign blood is injected and if a sufficient copy of primitive blood remains: but if a lot of foreign blood is introduced and the subject has retained little of his own, death by extinction or death with nervous symptoms occurs. In his experiments, neither the excess of carbonic acid, nor the lack of oxygen, nor too much blood, nor fibrin could never be the cause of death or morbid symptoms; because the blood was defibrinated, oxygenated, and the transfusion was preceded by depletion: the only cause was the introduction of blood of another species.

Belina in experiments between rabbit, dog and calf by injecting only 45 grams of defibrinated blood of one into the other, had a very blackish urine evacuation without any accident: increasing the quantity of the injection to 66 gr., he had an increase in circulation and breath, and death an hour and a half later between convulsions, with partial infiltration of blood in the lungs, bloody serum in the stomach and intestines, blackish discoloration and renal hyperemia, engorgement and extravasation in the brain and a characteristic dark tint in the muscles.

Our physiologist Albini (*Rend. Accad. scienza fisica e matematica*, Naples, December 1872) expresses himself thus: "I am far from believing that blood of another species can always take the place of one's own lost, but I believe that its presence in the vessels, mechanically and chemically, is so beneficial to the new organism into which it is transfused that it revives the main organic functions and

especially those for the formation of blood, and thus gives time and place to reproduce the missing blood and regain health."

And after all this, tell me if the necessary apparatus for a blood transfusion with animal blood can always be appropriate? Leading the animal into the room, tying it on the table, keeping it absolutely fixed, bringing it close to the bed of the patient who hears its complaints, who may fear its proximity, who may have moral disgust at accepting its blood ... or many other small circumstances which, added to the first, make the direct transfusion between animal and man not an easy operation, not always convenient.

It is very difficult among relatives, bystanders, those interviewed even for adequate remuneration, one will fail to give his blood: less difficult still the doctor (or whoever for him) will be able to procure a subject, who for pecuniary compensation and persuaded of the harmlessness and his insignificant expenditure of strength let himself be practiced a little bloodletting. I and all those who practiced transfusion with human blood always found the subject who lent the blood quite easily, not infrequently for free, the most for even a modest fee.

Physical conditions of the blood

I already touched on the topic of blood oxygenation, which necessarily implies that of defibrination; act by which this animal tissue loses its natural physical conditions.

Lower (1665) had noticed that the blood outside the veins was coagulating; King and Fracassati (1667) noted that blood cells had sometimes prevented the progress and completion of the operation; Mayor (1667) proposed the introduction of a few grains of deer antler salt or ammonia salt flowers to prevent blood coagulation; Prevost and Dumas (*Bibl. Univers. de Geneve*, phase. XVIII) were the first to express the idea that defibrinated blood is capable of reviving an animal bled by haemorrhage; and finally Bischoff (*Arch. Muller*, 1838) established the need to defibrinate the blood in order to successfully perform the transfusion

Since then, and after the knowledge of the absolute parity of life-giving force between the arterial prectus and the venous oxygenated through the beating that defibrinates it, this practice always finds advocates in a progressive number, to the detriment of the other one that was used arterial blood of animals of different species: and in fact in the third period, if after 1828 little more than 28 transfusions of animal blood were made in man, well over 200 were operated with human blood, in just over half of the which preceded defibrination.

But objections arose from all sides against the use of human venous blood, not discrediting its effective excitatory power when mixed with oxygen and atmospheric nitrogen, but because this oxygenation implies an act, a manipulation that of some it alters the structure of this liquid, brings disadvantageous modifications to it, takes away those physical and physiological qualities that are necessary for an effective transfusion. And although the figures demonstrate the physiological superiority of human blood in comparison to that of an animal, it was also questioned by many, asserting that if it is ready it does not respond sufficiently to the purpose due to its wealth of carbonic acid, if it is oxygenated upon beating it loses an element of its own, fibrin, and is beaten up, bruised in its cellular part.

In enumerating the reasons that the detractors of defibrination claim in their favor, I love to follow the arguments of Dr. Moncoq (*Transf. Instant. du sang*. 2nd edition 1874), as the one who more than any other is opposed to this act, and because the reading of that book made a strong impression on me, showing me how much passion and preconceived ideas may lead us astray from the path of true and the just. "Le sang defibriné n'est plus du sang:" Moncoq proclaims highly, repeatedly and in abundance in his book, without however ever bothering to perform a transfusion with defibrinated blood. In support of his opinion he wants to recall an

experience of Magendie in which he unsuccessfully injected once, twice and three times, after a few hours, from two hundred to three hundred grams of defibrinated and filtered blood into a dog. But Moncoq does not think that with such large quantities of blood Magendie acted against one of the principal norms, the proportionate and moderate quantity of liquid to be injected, and that only for this reason he had blood imbibition of the viscera, extravasation in these and in the natural cavities. Does Moncoq not know the experiences of Prevost and Dumas and of Bichoff, which all had a successful outcome, even with defibrinated blood? Why does he not take into account the facts and experiences instilled with defibrinated blood by Belina, Polli, Panum and many others? Why doesn't he mention those of Brown-Sequard, who even manages to overcome the rigidity of a man made a corpse for 13 hours, reawakening his irritability for several hours? I invite Moncoq to carefully read the clinical cases and experiences noted by these authors, and I challenge him to maintain the concept he expresses on page 163: "l'operation antiphysiologique de l'injection d'un sang defibriné ne fait pas mourir par elle meme, elle est incapable de ramener à la vie" and that therefore "la defìbrination du sang doit disparaitre à tout jamais" (p. 165). And with what good faith on page 182, he invalidates the transfusion with defibrinated blood so well and boldly undertaken by Folli (*Ricerche ed esperienze sulla trasfusione del sangue*, 1852) on the young Maria De Filippi, considering that the seven grams of defibrinated blood injected "sont parfaitement etrangers à la guerison de là malade" while the second case of Polli himself is silent on the damsel T.P., in which four waves were injected with equal luck, that is 120 grams? It is regrettable that in order to support a preconception, we face the truth, the history of which belongs in everyone's domain, and which Moncoq should not have ignored! But let's get down to reasoning and let us criticize the aforementioned author so as not to spend other words in vain.

Is the presence of fibrin essential for the injected blood to maintain life-giving properties? Or in other words, does defibrinated blood lose its physiological faculty? The mere fact of the coagulability of ready blood, and therefore of the possibility of injecting fibrinous clots (emboli), would be enough to accept a priori the injection of a blood that does not clot, which is the defibrinated one.

But we must study this question from the physiological side and from the clinical side: and it is precisely here that every argument supports us in supporting the concept that fibrin is by no means indispensable to obtain the effects required by a transfusion. The origin and purpose of fibrin in the blood are still unknown, so much so that the greatest physiologists do not hesitate to say (Brown-Sequard) that it is a very difficult substance to characterize and to distinguish chemically and physiologically - that it seems there are two fibrins - which does not already exist constituted in the body, but is formed in it without knowing its origin.

In addition to this, it is necessary to consider how little part, proportional to the other elements, it has on the mass of the nutritional liquid: so much so that it represents from two to three decigrams per hundred grams of blood. And indeed if we defibrinate 200 grams of blood we see that the mass of fibrin obtained is limited to being reduced to the size of a core and no more, nor pure, but still mixed with blood cells and serum which we do not care to squeeze completely from that clot.

It would seem at first, accepting remote ideas, that by lending fibrin to give viscosity to the blood, it is the main cause for which this circulates (Magendie) and does not leak from the walls of the vessel: this opinion is the opponents of defibrination. Against such concepts we can today frankly declare: (1) that if it is deduced from some cases in which the injection of defibrinated blood was deleterious, this was when an exaggerated quantity of blood was injected to produce stasis, ruptures of vessels, haemorrhages; or because the vein chosen was the jugular (in animals) for which the action of the right heart was violently surprised, with the arrest of the cerebral venous return circulation; either when the indication was not the best (perforating stomach ulcer, intestinal haemorrhage), or finally when the

defibrination was not complete and therefore fibrinous emboli were injected into the circulatory branches. Nor should I mention the bad results that Neudorfer saw from transfusions of defibrinated blood in the Hospital of S. Spirito in Verona in 1860. Read carefully the cases reported and you will see that you have to conclude from them (as others think so with me) that those patients had reached extreme weakness, had been rendered marastic by suppuration, and that the only wrong thing was that transfusion was performed too late, while it cannot be denied that the direct effects were great and lasting enough; sleep, appetite and an improvement in general conditions were then undoubtedly verified.

If the failure were to be attributed to the defibrinated blood, the first beneficial changes would not have taken place, on the contrary, a continuous deterioration would have been seen; it is not to the quality of the blood, but to the disproportion between the exciting virtue of it and the susceptibility to suffer the effects on the part of the sick, that we must attribute the result had in those of Neudorfer. (2) That a single fact of excellent outcome with defibrinated blood would be enough to invalidate any doubt, any prevention; and that, moreover, there are nowadays too large a number of successful or harmless or happy defibrinated blood transfusions (Polli, Panum, De Cristoforis, Hasse, Marfell and Moleschott, D'Ore, Belina, etc.).

Therefore, if history records cases of harmlessness in spite of failure, or cases of fortunate outcome by means of transfusion with defibrinated blood, it is necessary to conclude that the ablation of fibrin does not harm the physiological qualities of this animal liquid - that its chemical composition - physical although changed it does not take away from it the vivifying virtue required by it, for the cases in which it is used. And Moncoq still says after this "l'experience à prononcé contre le sang defbriné" (p. 159).

Is it then true that the blood treated with the beating as necessary to be defibrinated suffers in its cellular part, which is violently bruised, altered in form and integrity? I have repeatedly subjected man's blood to the microscope, beaten vigorously beyond the necessary time to defibrinate it using a broom of many wooden rods joined together, and I never saw fragments of cells, forms detaching from the normal and in greater numbers than what is observed in a blood just removed from the circulation. When everything was ready for microscopic observation and my eye fell precipitously on the drop lying between the slides, I did not find an altered or wrinkled blood cell: when I reviewed the same preparation shortly afterwards, or observed another state that had been arranged for a few minutes, cells appeared to me wrinkled, deformed in equal measure and proportion of what happens to blood not beaten. I invite my colleagues to repeat these observations in the same way, and I am sure that their result will not in the least differ from mine.

Therefore I have the full and indisputable proof and certainty that the blood beaten for defibrination does not lose any of its physical properties in the solid part. Is it perhaps a reasoned comparison what Moncoq (page 157) makes of milk with blood by comparing casein to fibrin?

But beating and defibrination have a purpose that far exceeds the loss of fibrin in importance and proficiency; I mean the oxygenation of the cellular element. Since it was proved by exclusion and directly that the main function of the blood is supported by its solid part, the globule, intended to assimilate oxygen in the respiratory act and to translate it into every point of the organism for organic combustion, for stem cell excitation, for irritation of muscles and tissues (Brown-Sequart): since it has been proven that the serum does not awaken the blood: that by drying only the blood cells (Dieffembach) are removed from the blood mass, revived with little liquid, these can re-excite the heart of a bloodied person; it is necessary to conclude that the globular part is the most important, the most necessary part of the blood; that this liquid is not unlike any other tissue in which the protoplasm is represented by the serum, and the plasma by the globule or blood cell. And therefore it must be concluded that arterial

blood differs from venous in that it is the first load of oxygen and exciter more than the second.

When we subject venous blood to beating we already make it undergo an act of breathing, of artificial oxygenation with which we reduce it to the same physical and physiological conditions as arterial blood; and furthermore we remove an element from it, fibrin, which can be harmful for partial coagulations and therefore injection and transport of emboli, while it is neither necessary nor useful for the purpose we set ourselves. This is indisputably proven by an infinite series of facts.

Now therefore, since human blood is for physiological reasons preferable to that of an animal, since the use of human arterial blood must be excluded due to the seriousness of the lesion that is imposed on those who lend themselves to the purpose, it remains in the practical field as less difficult; the use of human venous blood is less objectionable, but it will have to be subjected to beating to be oxygenated and equalized in an exciting virtue to the arterial, and to be freed from fibrin which offers the danger of its coagulation and consequent embolisms. Hence it is that the Provost and Dumas proposal to defibrinate the blood (182) undoubtedly marks the brightest point in the history of transfusion.

And indeed the danger of the fibrinous clot worried all experimenters. Since Richardson expressed the concept of keeping the blood fluid in the circulation by mixing with a small amount of ammonia vapor, we first saw Neudorfer propose to add some sodium bicarbonate to the blood to be injected to prevent coagulation, and shortly after Branton-Hichs implement this proposal in three cases (*Guy's Hospital Reports*, 1869, Volume XIV).

Rautemberg in 1869 in a memorandum to the Medical Society of Petersburg also proposes to use blood that is not defibrinated, but kept liquid with the addition of sodium carbonate. However, these proposals are not new, since the ancients (Mayor for the first in 1667) used to put a little bit of volatile deer horn salt or flowers of ammonia in the tubes used for transfusion to prevent blood coagulation. But Branton's cases are certainly not made to prove the harmlessness of adding alkaline salts. Even if for other tests or substitutes for sodium phosphate achieved the intent, we should still respond to the other indication of the need for the transfused blood to be properly oxygenated. By adding alkaline salts, we achieve only one purpose and we forget that venous blood is mixed with a lot of carbon monoxide, and therefore in some cases harmful (in carbon monoxide poisoning) and always endowed with less vivifying power.

The addition of alkaline salts, if proven innocent, could be useful for transfusion with animal arterial blood in order to avoid coagulation; and then the direct method of transfusion between animal and man would diminish in importance and necessity, since with simplicity of apparatus and modality, without the presence of the animal and with the advantages proper to indirect transfusion with defibrinated blood we would have at our disposal coagulable arterial blood.

But experience has not yet pronounced the last word on the addition of alkaline salts to blood, not so much for the impediment to coagulation which is proved true, but for the harmlessness of the said salts on the transfused blood cells and on the mass of blood of the patient.

What I have said so far refers to the species and nature of the blood and its physiochemical conditions. But it is now time to consider another state of the blood still belonging to its physical condition; I mean the temperature it must have at the time of transfusion.

It was natural that it was thought to keep the extracted blood at its normal temperature until the moment of injecting it and during the operation itself; therefore in the injections of blood the instrument was heated and kept warm during the whole operation by keeping it wrapped in cloths wet with hot water at 36° or 37°, at least the blood was defibrinated in a vessel heated and surrounded by hot water to maintain an environment at 32°. All this in the concept that the introduction into the circulation

of a liquid lower than normal in temperature could harm, morbidly affect the heart and nervous centers (Darwin 1796). But experiences have shown the opposite of what was previously believed, and after Hunter, Blundell, Dawy, who had already seen blood clotting delayed as long as it was kept at a low temperature, we come to Giovanni Folli who had the merit in 1857 (*Research and experiences devalue blood transfusion*), when for over 50 years every rumor about the transfusion had been silent and even those few healthy precepts that history had already recorded were forgotten, to draw attention to the fact that blood coagulates more easily at the temperature of the human body, than at a lower one, and which becomes uncoagulable below zero: he concluded that he was "indifferent whether the blood is hot or cold, its vitality is preserved longer at a low degree of temperature than at a high degree." Nicolas made new experiences in this regard and came to the same conclusions, namely that the cold seems to prevent coagulation: - that to keep the blood liquid it is better to cool the jar and the syringe (page 39 – *Thesis*, Paris, 1860).

He bled out a large rabbit, injected 10 centim. into the jugular. cub. arterial blood from another rabbit by reducing its temperature by 8°C; six minutes later he detected weak heartbeats and low temperature, 30 minutes later less precipitous, more sensitive, almost normal beats, and an hour and a half later it returned to a complete physiological state.

In another experiment, the injected blood had a temperature of 9°C, and 20 minutes after the operation the beats and breaths, which had stopped at first, returned to normal. The same result was obtained with defibrinated venous blood at 25°C, i.e. for two hours the heartbeats remained weak, the temperature rose slowly, but the animal ended up recovering.

Panum (*Exper. Untersuk. uber die Trasf. Transpl. oder Supstit. des Bluter*, etc. 1863) declares that fresh and defibrinated blood then kept cold by means of ice is perfectly usable for transfusion as long as it is warmed up before using it to body temperature: a fact that has its confirmation in the 5° experiment of Polli (op. cit., page 8) in which blood extracted from a horse, beaten, defibrinated, poured, left in the air in a metal container held at 9°C for 24 hours, then stirred and heated to 35° to be injected into another horse, was very well tolerated.

Bellina (*Transf. du sang de fibrine*, 1871) expresses the concept that blood collected and placed in contact with air at average temperature remains invariable in its histological constituent parts and retains its chemical properties for two or three hours.

This applies to the influence that the temperature can have on coagulability of blood, having to believe that the risk of embolism is less as the blood temperature is lowered compared with its effect on its physiology. But from another point of view, it had to be seen that the introduction of injected blood at a lower the temperature does not affect the patient's blood mass, the heart and the nervous centres in particular.

Polli has already proved any fear in this regard to be erroneous; but these days from the valuable work of G. Casse of Brussels (*De la transfusion du sang*, 1874) we see a very diligent series of experiments with very demonstrative thermographs on the subject. The author very reasonably deduces from these that the temperature of the animal changes with the degree of temperature of the liquid to be injected - that the temperature of the injection at a lower degree of the thermometric scale produces a lowering followed by a much more lively reaction - that in the case of injection below the average normal temperature there is an increase in heat in the subject, but the thermometric oscillation is less marked than in the case of cold injection - than with at the injection temperature close to the normal average the effects are not very marked.

On the one hand, therefore, we have: (1) the physical experiences on the preservation of blood and its lesser disposition to coagulate when kept at a low temperature: (2) the experiences given by Casse on the evident and absolute fleeting impression that the organism receives for a transfusion done with blood at a lower

than normal temperature. On the other hand, we have the fact of the organism's tolerance for blood introduced 24 hours after its extraction and defibrination. For all this I believe there is no objection to concluding that the transfusion is not an operative act in which readiness is required, to cure the temperature of the liquid to be injected for fear that this will break down and lose its virtues if kept exposed to the air and used a few hours after being extracted and defibrinated.

A better demonstration of this second fact, that is of the length of time in which the blood retains its vivifying property, are Dieffembach's experiments, from which he deduced that the vitality of the blood decreases from the third hour after its exit from the vessels: that it is rarely possible to revive an animal by injecting it with blood that has come out of the circulation for some time: that this revitalization is of very short duration when one injects blood exposed to the air for more than six hours, and finally that blood extracted for a longer time awakens only very faint signs of life, as any lukewarm liquid injected into the veins would do, but it serves no purpose in recalling life.

This would be in complete contradiction with the results obtained by Blundell, who completely reanimated dogs that had bled to death with blood drawn for over 24 hours; and it is not at the same time in agreement with the other assertion already cited by Dieffembach himself, which he saw obtaining revitalization, albeit incomplete, of bled animals to which he injected re-dissolved artificially dried blood cells.

But *in medio stat virtus*, so without any other support than that given to us by common sense, we will have to believe that the less time we lose, the fewer physicochemical changes will have occurred in the elements of the blood disposed for transfusion.

Of the use of pure human venous blood

The thought of defibrinating blood was, as we have already seen, inspired by its coagulability when, without any manipulation when removed from the vein, it was left to rest for a few minutes. And certainly, even when one wished to neglect for a moment the second reason for defibrination, that is, the re-oxygenation of venous blood, the only doubt that a clot could be injected and embolism occurs, would suffice to conclude with Bischoff "on the indispensable need to defibrinate blood in order to successfully perform a transfusion." But is he really condemning a transfusion of pure human blood? Is the danger of injecting fibrinous clots inevitable? I can answer these questions on my own account in the negative. Considering the question from the physiological point of view whether the blood rendered arterial is preferable to the pure venous and for this reason it does not cease to be equally useful in given circumstances.

The question is solved by the indication that I will develop in due time, but which can now be stated in these terms: when the patient's adynamic state is not acute, therefore an energetic and prompt re-excitation of the centers is not required by him without which he will run the risk of seeing cardiac activity cease at any moment; that is when it is a state of chronic anemia, then even venous blood may be useful because it will be changed into arterial as soon as it passes through the lung. Of course, the operative act acquires greater importance in this case with ready venous blood, since it will have to be faster in order to avoid the formation of clots during the time required for its injection.

Of course, if a not infrequent accident occurs during a transfusion (venous thrombus, swoon, convulsive motions, etc.), for which the injection must be suspended for a few minutes, we will soon face the doubt that in that lost time clots have formed within blood contained in the syringe. Reason dictates that in a case where this occurs, that then defibrination of that same blood takes place, because

the time elapsed is sufficient for the formation of the first fibrinous clots and because it will be convenient for us to take advantage of that blood we have at our disposal. And here is time wasted doing what had to be done before.

Nothing less can be said since it was made and it was successful (see my two pious cases below) that the practice of transfusion with venous blood is possible; that it is only necessary to prepare and prevent everything so that by dividing the tasks it is certain that from the moment in which the syringe is filled to that in which all the required mass of blood has been transfused, no more than 15 minutes have passed. In fact, everyone can be sure of two things, that in a human venous blood some fibrinous glomeruli begins to form between the 10th and 15th minutes of its extraction, if this was wide-spread, and that in less than 10 minutes it can be done in all its various acts (from the deliberate extraction of the blood to its complete injection) in the transfusion of 150 grams of blood.

And after all and in spite of my clinical facts (narrated later) I think it is always wise and provident to defibrinate the blood in order to be sure not to introduce clots, so as not to be obliged by any accident to go to defibrination later; and finally to give the patient more blood to excite his fiber.

Schilz and after him Martin are wrong when they state that they prefer the injection of pre-venous blood to defibrinated, saying that a lot of precious time is lost by defibrination.

If, while the blood flows from the vein of the donor into a basin, it is beaten with the broom, we already begin to gain two or three minutes of time, so that another five minutes is enough to complete the defibrination, and three minutes to pass it through the sieve to fill syringe and have it ready for injection. So 10 minutes or at most 12 are spent on these preparations, but only relatively spent, since this manipulation can be done while another surgeon isolates the vein and fixes the cannula into which to insert the end of the syringe. That if we had to operate alone, as did Marmonnier in 1851 without technical assistance based on the knowledge previously developed on defibrination and the temperature of the blood to be injected, we will always be able to carry out all the bloodletting, then defibrinate the blood and pour it, then keep it with impunity in a vessel exposed to the air during the time that the patient's vein is prepared, and lastly when the syringe is filled, go to the injection.

The importance of the case that occurred to Marmonnier cannot really be overlooked, and no one will deny that he, with his daring, with his energy on that occasion almost without his knowledge, accomplished an act that was very extensive in teaching doctors, and proved to them the few difficulties of transfusion, no need for special devices in spite of using venous blood, and finally the effectiveness of this surgical dressing.

Dechambre and Diday reflect in the right words on that case of Marmonnier, “un beau et legitimate succès; une ferme et prudente decision .... la conduite de M. Marmonnier aurà sourtout le grand avantage d'inspirer aux praticiens une consiance dant, ils manquaient, et il aura mieux deserved de la Science qui il ne esperait peut-etrè lui meme par l'exemple à la fois plein de hardiesse et de circonspection qu'il lui a etò donné de fournier.” (*Gaz. Med*. Paris, 3 January 1851)

Blood from capillaries or mixed arterial-venous

We saw that the two objections made against human venous blood are those of the lack of oxygen and the alteration that is made to it in stripping it of fibrin.

Fred. Geselius in 1868 condemning both the section of the artery in man used to draw arterial blood and bloodletting from the vein to use venous blood, proposed in his book Capillar-Blut. undefibr. zur Transf., St. Petersburg 1868, the use of blood removed from the capillaries, i.e. mixed venous and arterial blood. He extracts it

from the skin by operating on it various scarifications and sucking it with a special device.

He does not say in favor of his method other than, the capillary blood is clearer, richer in oxygen and therefore more suitable for transfusion, he does not deal with its coagulability, which is equal to that of venous blood, and his device would transfuse it freely and by gravity alone into the patient's vein. He republished his work in 1873, expanding it, but he did not implement his concept; and therefore no judgment can move in this regard because there are no supporting clinical cases.

Placental blood

One fact in the history of the transfusion strikes us with true admiration; it is the one that belongs to L. De Belina in 1869. (*Gazette med. de Paris*, N. 2, 1870) and which is so far the only one known. The spark of the man of genius, of the physiologist, of the practical man, sure of his concepts because he was largely educated in science, was fully revealed in his clinical case.

He was assisting a Russian lady who was giving birth prematurely in the eighth month, due to an impact received in the railway; when the fetal head comes out of the vulva, the neck is tightly secured by two turns of the umbilical cord, so much so that it is born asphyxiated, anemic and purple in color, with near signs of extinction of life. The usual means of reviving him are useless; then De-Belina thinks about the transfusion; but there was no time to waste, it was urgent to have blood, and he takes the placenta between his two hands, squeezes it, defibrinates the expressed blood, and with a glass syringe injects it into the umbilical vein in the newborn. Immediate awakening, return of the rosy skin color, raised wrists, free breathing and the child's life was thus completely saved. Therefore, De-Belina found a new source of blood, and thus gave the most useful teaching to the doctor and obstetrician in particular.

Amount of blood to be transfused

If the most remote transfusion experiments are diligently examined, it is soon seen that in most cases the amount of blood injected is so high that it must be attributed solely to this failure; especially since for the most part the transfusions were made into the jugular veins, therefore with less probability of resistance on the part of the right heart to the injection, which came so quickly and surprised it into paralysis.

Physiology later stated that the ratio of the mass of an animal's blood to its body weight to be 1 to 13.14; therefore we, behind this fundamental data, can as of now believe that a greater quantity of blood to l / l3 of the weight of a subject will be harmful: and this, given and not granted, that it can be completely deprived of his blood.

But when we reflect on the many indications that the clinic offers us for a transfusion, we must necessarily and without any difficulty, believe right now that the volume of blood to be injected must be proportionate to the current need, it must be regulated by the therapeutic need, by the special indication.

I reserve the right to go down to particular teachings, the result of the experience and practice of today, when I discuss the individual morbid conditions in which the transfusion is applied. Here it is enough for me, about the quantity of blood to transfuse, to talk about it in a generic way with the sole stock of physiology and physiopathology.

The first tells us that the normal average of vascular tension is the normal average of cardiac activity: the second gives us frequent examples of the alteration of this activity due to modified tension of the vascular system.

By filling the right atrium excessively, we expose ourselves to the danger of cardiac paralysis: accumulating too much blood in the venous shaft, internal and interstitial bleeding can occur, all the more easily when blood pressure has decreased due to morbid weakening of the heart. Hence the fundamental practical teaching for transfusion is not to fill the vascular system more than normal so that the heart's energy is not altered. That if the tension of the venous system were excessive in spite of our diligent work, there is no better advice than to open the patient's vein and remove the excess blood.

Let the pulse be the thermometer of vascular tension, and we will always take the norm from it to continue or stop the injection or to counterbalance the excess mass introduced by subtraction.

Casse, in a dog weighing 6895 grams, therefore having about 530 grams of blood, injects 368 grams of blood twice at 24 centigrade, seeing no other morbid phenomenon being produced than vomiting (perhaps from cerebral congestion) and chills. The next day, the animal is fine: 575 grams of defibrinated blood is injected, and it vomits food, emits clear urine, but later groans, intestinal liquid discharges, killing and death 20 hours later; the section shows injection of the subcutaneous tissue, lungs redder than normal, the right more intensely, pink foam in the trachea, ecchymotic congested auricles of the pericardium, dense black blood in the right ventricle, right endocardium with more marked bruising than in the left, the trunks large veins heavily engorged, red epiploon, bruising on the colon, caecum, small intestine, liver and kidneys strongly congested, ecchymotic renal calyxes, filled cerebral venous sinuses, dark red tint of the gray matter, haemorrhagic focus in both cerebral lobes, blood in the fourth ventricle.

In a third experiment, Casse injects 710 grams of blood to a dog weighing 4800 grams, that is a little less than the 7th part of its weight: it becomes drunk and paralyzed in the hind limbs; killed, there is hyperemia of the serous, bloody mucus in the stomach, congested liver, mild renal hyperemia, cerebral sinuses filled with blood, ecchymosis of the left choroid plexus.

Finally in a fourth experiment on a dog weighing 4700 grams, he injects 375 grams of blood, that is just over the tenth part of his weight, death a few minutes later, blood effusion in the abdomen, coming from the liver, which is bulky and cracked in many places: general hyperemia.

These experiences lead Casse to reasonably deduce that under the influence of a large amount of blood added to the total mass of its own, the animal can live; but that in these conditions haemorrhages occur in the tissues - that the capacity of the circulatory system is considerable - that it is not always on the breathing side that accidents occur in cases of great repletion.

Finally, experience has shown that for man 60 to 100 grams are always sufficient for any indication and that with this quantity, if the injection is properly done, it is certain that there will be no morbid functional phenomena or material injuries.

However, the quantity to be injected is also related to other conditions - to the patient's build - 25 or 35 grams may be sufficient in neonates, 30 to 60 grams in children: - to the general frailty of the tissues, to the functional state of the heart, so that in weak subjects, anaemic for a long time with a tendency to haemorrhages, with a weak heart, it will be necessary to limit the mass of blood to be transfused - finally to the pathological indication (of which I will speak later), which regulates this point of the operative act in a fairly fixed way.

Of the vessel from which to remove and in which to inject blood

I have already said how the proponents of animal blood transfusions must by logical and physiological necessity prefer arterial blood, transmitting it directly to the patient and thus avoiding manipulations and preparations of the blood.

Therefore, in an animal destined to give blood, the vessel to be opened is always any artery of the body, of sufficient caliber to receive a cannula; in general the carotid artery is preferred. But I already said that when it comes to using human blood it is certainly not allowed to expose the subject who lends himself to an arteriotomy, since we would inflict an injury that is always too serious, which would have no compensation measure, and to which anyone who was informed of the sacrifice asked of him would refuse.

Less would be the price of the work to damage an artery of the bidder to use his blood without fibrin; since then we can replace venous blood made arterial by beating.

The cephalic vein of the thumb, the median basilica or the median cephalic, are the preferred ones for bloodletting: only an easy and wide jet is required to save time.

And now we discuss the way by which the blood must enter the recipient's circulation.

From the most remote experiences, the atrium for a transfusion was the venous: the reasons for this choice lie in the superficiality of the vessel, in the harmless lesion, in the easy healing, finally in the physiological suggestion to transmit blood by the shortest way to the heart; which was believed to be the organ that was first revived in cases of bleeding.

That if an injection was sometimes devised and implemented for the jugular, this was done only in experiments on animals, given the superficiality of the vessel. In man, knowing what serious danger is accompanied by the incision of this large venous branch, the entry of air, no one attempted this way; the only exception was made by Jevel and Bayle (*London medico-physical Journal*, 1826) who transfused a patient through the jugular, died from it, and found large air bubbles in the right ventricle.

No less trouble was found in the injections of this vein in dogs; the too direct arrival of the blood to the right heart (however studied the pressure and thrust given to the blood column), causes it to be very easily surprised and paralyzed.

Those who, like me, have had the patience to go through a good part of the experimental facts on animals will have seen that injections of the jugular often had an inauspicious or uncertain outcome for the above reasons, to the detriment of the purpose for which they were instituted.

These considerations have led transfusors to prefer a vein in humans farthest from the heart; and it was obvious that the internal saphenous vein was first used for this purpose in its journey from the internal maleolus to the middle of the leg - the cephalic from the carpus up to the fold of the cubit - finally the two medians - since they are all the most striking and most luminous.

Out of respect for the surgical needs, we will keep as a precept the wearing of a shallower lesion, less wide, therefore choose a superficial vein - physical needs reflect the need for the lumen of the vein to be sufficient to receive the delivery cannula - finally, the physiology of the transfusion requires the farthest point from the heart to be chosen.

With these rules, we will be sure to have surrounded the operational act with all the precautions necessary for its success.

Transfusion by the arteries

Except that, in spite of the ancient and widespread practice, Dr. G. Huetter of Greifswald (*Die arterielle Transf. - Centralblatt fùr die Medicin. Wissenschaft*, 1869, N. 25) proposed that the injection be made for the arteries whereby, forced to cross the network of capillaries, it undergoes the action almost of a filter, by which it is impossible for clots to reach the heart. He chooses the radial artery or the posterior tibial and asserts that it is possible in a short time to push enough blood from a small

artery through the capillaries; he says it is possible but not frequent, tearing of the vessels follows the outflow of blood.

The only reason that militates in favor of his proposal is the sweet and divided arrival of the new blood into the circulation, via a very indirect route to the heart. However, he adds that the "arterial transfusion does not give any guarantee with regard to the overload of blood and its rapid arrival to the heart, with central disturbances."

This, I believe, is the greatest condemnation of his method, which he instituted to ensure that there was no surprise to the heart.

That if we reflect on one of his clinical cases in which the unmarked artery was still beating (thus marking the persistent action of the heart) and we remember that in spite of the arterial transfusion the blood reached the heart too soon (as the author himself confesses) to beat entirely, we must conclude that the danger of cardiac paralysis also exists when transfusing through the capillaries.

And the frequent lacerations of vessels with intercellular spreading, which occurred in Hueter and Prof. Albanian (*Gazzetta Clinica di Palermo*, 1870) - and suppuration consecutive to this accident, the severity of the injury, why inflicted on an artery and why deep? - are considerations to be neglected?

I believe that as it was born such a procedure will die, which in every way does not satisfy neither physiologist nor surgeon.

Injection by the umbilical vein

I said earlier that Garmann (1665) already glimpsed how the umbilical vein route could be used to give you injections of exciting wine for the purpose of reanimating asphyxiated babies.

Dieffenbach (1830) Blasius (1832) Benecke (1867) De Belina (1869) carried out the transfusion for the umbilical vein: Benecke repeated it twice in the same subject; with the exception of the case of De Belina mentioned above, the others had no result.

Nonetheless, the principle is to be accepted and will want to be applied whenever the indication is needed, since it is a naturally prepared way, for which the direction of the current is centripetal, and the injection point sufficiently far from the circulatory center.

Obstetricians in their clinics and in their private practice will be able to benefit from this teaching, often with profit, always with full justification of their work.

Methods of transfusion and different devices

Transfusion is perhaps the operation that has the largest number of execution processes in surgery; which differ from each other essentially because of the different and disparate concepts to which it is intended and the special intentions of each individual operator.

Defending the blood from contact with air, preventing the formation of clots, keeping it at its natural temperature, regulating the pressure with which it is to be injected, using animal blood rather than human blood, and pure venous rather than defibrinated - are so many reasons of modification in the operative act and in the instrumental apparatus, which we will now pass in review.

There are two fundamental concepts that inform transfusion: that of the duet passage of blood from vessel to vessel and that of the indirect passage, i.e. extracting the blood in the desired quantity, loading it en masse into a special device and thereby introducing it into the patient's circulation. The first kind of transfusion is called direct or immediate, the second indirect or mediated.

The ancient experimental method was also followed by doctors in therapeutic transfusions to humans, so we see the first ones always performed with the direct method. Only later, after Blundell made the first experimental transfusion with an indirect method, do we see it performed by him for therapeutic purposes in the year 1825, thus giving the first impulse to the cancellation of many prejudices about the influence of air on blood, to its lost vitality as soon as it left the circulation. Later, when the cause of blood coagulation in the coagulability of fibrin was recognized (as Bischoff proved in 1835), greater reason was added to the possibility and convenience of the indirect method, and the evidence multiplied.

Now it is up to us to describe these acts in their two main concepts.

Direct transfusion and methods

It was in Italy, at the Pavese University, for the theoretical teaching of Hoffmann (1662) and in England for the practical application made by Lower (1666) that the direct or immediate method of transfusion imposed a silence of more than 150 years (up to Blundell, 1818) to the ancient indirect or mediated system, used until then.

The false concepts that the air exerted a malefic influence on the blood, and that this, once released from the circle of the living, became dead matter, lost its physiological properties, were the main reasons that suggested the direct passing of the animating liquid from individual to individual – and from here studied all the physical and surgical ways that best and more easily respond to the purpose.

It can be said, however, that since the first implementation of this concept the intent was achieved very well, and so much so that the subsequent and modern modifications do not have the value attributed to them by the authors.

Lower describes his method of direct transfusion.

"The carotid is exposed for about an inch to the animal that has to give its blood, then a knot is made with a thread in its upper part, well tightened and that cannot be untied; a thumb below, towards the heart, another knot is made which can then be tightened and released at will. Two threads are passed between these two nodes under the artery, then the artery is opened, a small cannula is placed against the incision, the artery tightly tightened above the cannula is tied with the two threads, which is closed with a small cork. Once this is done, the jugular of the other animal is exposed for an inch and a half and a slip knot is made at each end, and between these two knots two threads are passed under the vein; then the vein is cut and two tubes are introduced, one in the lower part to receive the blood of the other animal and bring it to the heart, the other in the upper part to translate the blood that comes from the head; the two tubes are closed with a stopper. This done, the two dogs are tied towards each other in such a way, however, that other tubes can be passed in the first two, since, not being able to bring the two dogs close enough to each other by the neck, it is necessary to put intermediate tubes. Once this is done, the stopper is removed from the tube that descends into the jugular vein of the receiving dog, and the stopper from the tube that comes out of the artery of the offering dog; they are joined together by means of three or four intermediate tubes, the slipknot is released and the blood will rush through the tubes as though through an artery. At the same time the stopper of the tube coming from the upper part of the jugular of the receiving dog is removed and the blood of this is allowed to drip into a dish, but not continuously, until the dog offering arterial blood begins to cry out, to weaken, falls into convulsions and dies. Then the two tubes are removed from the jugular vein of the receiving dog, and having fully tightened the two slip knots, the vein is cut in the intermediate section, the skin is joined and the dog is left free."

Denis followed the same method three years later; the cannula was silver and no other intermediate tubes were used: the lamb was placed on the table and the patient's arm rested against his neck: Denis preferred small tubes because they more

easily prevent blood clotting, he gave to the patient enemas, and he kept him fasting before the operation in order to avoid alvine discharges or vomiting: he had identified that his tubes in a first minute gave six ounces of blood.

Riva d'Asti, as Esler writes (*Michel. Acad. natur. cur*. Paris, 1772) wanted this act to be carried out with a milder method than that used in France, which is, since it is done for bloodletting opened the vein with a lancet “sine vaens extractione vel excoriatione.”

Returning to the practice of uncovering the vein, Manfredi (2 January 1668) wanted the cut to be made on a fold of skin that was raised transversely to the course of the vessel.

C. won Graefe did not want to forget the decrease in temperature that the blood must suffer when passing through the cannulae and so as not even needing to monitor the current in them, is the reason why he designed his instrument.

D'Ore was very concerned about the vacuum that he pre-established in the cannulas in order to avoid the introduction of the air contained in them, and he devised three different devices designed to create a vacuum throughout the entire travel of the instrument.

And Moncoq in 1862 had Mathieu make the ‘hematophore’ in which the principle was to imitate the systole and diastole of the heart; its role entrusted to a plunger which is raised and lowered alternately by a toothed wrench: with the first movement it creates a vacuum in the tube that starts from the donor and thus pulls the blood, which with the lowering of the plunger goes to the recipient almost for a systole cardiac: two valves at the connection of the tubes close and open alternately for the direction of the current.

Albini in Naples in November 1873 presented a very simple instrument for direct transfusion to the Naples Surgical Medical Academy, equipped with a long elastic tube; he fills the device with a sodium solution and drives it out with the arterial wave given by the animal: a delicate and simple device stops the current and shows if it has accidentally stopped; the whole device is opaque.

Caselli (*Bullettino delle se. med. di Bologna*. Serie 5a, vol. 18, p. 334) also in the last year replaced another instrument that is well evident in its composition and in its mode of action as soon as the figure is seen.

Luciani, Ruggi and others study other more or less complicated devices, which have nothing special to be described here.

Without returning to the question of the value of direct transfusion, the critique offered by all and individual instruments of these types are reduced to:

1. To be constructs of opaque substances so that it is not possible to monitor the current trend within them
2. The impossibility of measuring the amount of blood that passes from the animal to the patient; although the lumen of the cannulae is known and it is possible to establish how much liquid passes through them in a given time, the calculation will always be approximate and often fallacious, since the cardiac power varies from animal to animal, it varies in the same animal in different moments of suffering, and of fright
3. To the uncertainty that the animal is quiet and does not distract the device in its convulsive movements
4. Finally, that there is no security, in a moment of forced suspension of the operational act, a small clot forms in the conjunctures of the matter and is subsequently thrown into the circulation.

Except that all the mechanical efforts to strictly adhere to the precept that blood does not come into contact with the air, and that it naturally and directly has no time to coagulate, met with strong objections on other sides; of which the main one, in my

opinion, is that of the incoagulability of the blood and its un-alteration when it is defibrinated, indeed of being equalized to arterial if oxygenated with beating.

So it is that, when Prevost and Dumas in 1821 demonstrated that beaten venous blood is capable of vivifying an individual, the thought of indirect transfusion was born and had a de facto life.

Indirect transfusion

Blundell, as I already said, in 1818 (*Diss. inaug. de sang, trans*. 1824. Tietzel) had the merit of bringing to life the ancient method, Tindiretto, instructed by the conclusions reached by the physiological experimenters of his time, and precisely for this purpose he replaced a copper syringe with the graduated plunger rod to determine the amount of blood that is injected: the tip of the syringe is equipped with two elastic straws, one ending in a funnel-shaped vessel intended to collect the blood to be injected, and the other into a tube that must be introduced into the vein of the recipient of the blood.

With a key system that is at the point of union of the two tubes, it is made so that, by pulling the plunger upwards and turning the key, the blood passes from the funnel-shaped vessel into the syringe; while with another turn of the key and pushing the plunger down, the blood is pushed into the other tube and then into the vein. As seen, Blundell did indirect transfusions with pre-venous blood.

Graefe (*Journ. der Chir. und Augenheillcunde, von Graefe und v. Welther*. Bd 55, 8. fi37. 1824) used an apparatus similar to Blundell's in construction, but which he immersed completely in a glass tank containing water at 32°. Nor was it long to see the simple syringe replaced in all these by complicated mechanisms, driven by the knowledge that blood coagulates less easily at a temperature below the physiological one.

And father Marmonnier, (*Gaz. des Hôpit*., 1851), gives us a splendid example using a metal enema syringe for a child; the only one he had available at that time. He isolated the basilica vein and exposed it for three centimeters, and passed a single thread through it in order to fix the end of the cannula within the vessel.

The modifications that the operational act and the instrument subsequently underwent are reduced to the following:

The first concerns the way of opening the vein, which for some operators should be done by means of a trocar, or a sharp lanceolate cannula like a writing pen; while for others it should be performed methodically by first incising the skin parallel to the vein, then exposing it for a very short stretch, and finally passing through it both a common pin on which it is turned with a digit 8 thread, and the only thread to tighten it around to the cannula: some add a second thread to obstruct the trunk below this.

Each operator prefers his method, either for the sake of fatherhood, or for a contracted habit: and we let each one boast his own; we will say only from factual experience.

1. That rarely, especially in an anemic, the vein can be so artificially inflated by means of a lace that it is certain to injure it in a single blow with a lanceolate cannula.
2. That this penetration can injure and puncture the internal wall of the vein.
3. That if to remedy this inconvenience, a tubular counter-cannula is introduced into the perforating cannula (after this is hidden in the lumen of the vessel), this must necessarily have a large diameter, or at least such that in several cases it will not be used. Thus, Caselli's cannula is too large, extremely exaggerated in its diameter to be useful in an anemic subject, with small, retracted veins. Several times, even with the smallest of the cannulae I use, and which is half the diameter

of Caselli's in cases of slow anemia, of chlorosis, penetration into the lumen of the vein was very painful.

4. The uncovering of a small stretch of the vein (everyone asserts it, and I too) is never followed by unpleasant accidents, while it ensures and allows you to clearly see the tissue of the vein covering the cannula; thus we are made sure of avoiding the big mistake of having penetrated only into the cellular mesh, with complete failure of the operation, and we will have avoided producing a thrombus that is always difficult to resolve, often even a suppuration center to the serious detriment of the patient.
5. It is necessary to fix the instrument to the vessel either with a thread or with turns of thread on the needle subjected to it: often, especially in the carpus, it is useful to prepare another thread to close the lower trunk of the vein in order to prevent or stop the loss of blood that can be had, due to the many anastomoses.

Dr. Casse of Brussels uses a bulging glass cannula, very commendable; which allows the blood flow to be seen and is sufficiently robust; but it can only be used for your device, it cannot be adapted to the end of a metal syringe and has the drawback of being a bit large. I add that his instrument is equipped with a long elastic rubber tube, just long enough to allow the blood vessel to be raised in order to increase pressure and current speed; the tube does not add advantages, in my opinion, to the device because it veils the blood flow for a long distance.

The other modifications in indirect transfusion concern the mechanism by which the blood is injected.

We can see devices with a simple plunger, simple syringes in all their primitiveness (Martin, Marmonnier) - syringes whose plunger is moved by a toothed wheel with key (De Cristoforis) - vessels in which the impelling force is constituted by air, which in the tube loaded with blood is pushed by means of both a single rubber balloon (Helmoltz), and by means of two balloons, one of which acts as a reservoir of compressed air (Richardson) - vessels finally, equipped with elastic, from which the blood only by the law of gravity flows and enters the patient's circulation (Casse).

Almost all of these devices carry a scale marked on the vessel for evaluating the amount of blood collected and injected - a tap to intercept the current for this purpose, and are constructs in the back to monitor the decrease in blood mass, air emboli, blood clots.

Generally, in my opinion, the long elastic tubes betray the need for transparency in the apparatus, and give rise to a leap within the lumen, to a discontinuity where the elastic tube closes on the small cannula: the point where the blood collides and is beaten in a way that leaves no security, using pure blood, that no clots will form there.

It is not strictly useful to imitate systole by means of elastic balloons, because a common plunger moved by the hand can make this alternating movement, and because the pressure made by the hand that pushes the liquid from the balloon into the vessel cannot always be of equal strength and it cannot completely imitate in power and mode that of the heart ventricle.

No valve can be accepted in an appliance, due to the ease, in closing and opening, that it agitates or retains particles of blood which would end up coagulating.

Semi-direct or instant transfusion

It seemed that a myriad of instruments and mechanisms were not enough, and a third kind of transfusion was devised: which, due to its modality, I believe, can be considered as an intermediate, as a link between direct and indirect transfusion.

Thus, while in the first the blood is guided from the circulation of the donor to that of the patient with tubes that are fixed in a blood vessel of both of them: while in the

second only the desired quantity is extracted and injected in another time of the operation in the recipient's circulatory tree (pure or manipulated, it does not matter): this third method firstly spares the cannula infixion to the donor, and secondly does not collect the volume of blood en masse which draws from this, but constitutes an extrinsic communication to the wounded vessel of the donor by bringing a tube or vessel near the point of the limb from which the blood comes out; as this flows it is guided both by the law of gravity and by mechanical pressure in the patient's circulation. It is a transfusion of human pre-venous blood which is performed in this way.

Moncoq calls this process instant; but the epithet does not correspond to its essence; since the difference is not in the time it takes in comparison with the other methods, but in the principle. For the reasons set out here reflecting the modality of the operation and the improperness of the epithet with which the author wanted it designated, I substituted the term semi-direct, which I believe is the most appropriate.

This method, which he attributed to himself as his own invention, is nothing more than the reproduction of what Daniele Major (*Delìcìa hyberna*) proposed for transfusion in 1667 with the following words: "a gentle purging of both men and make a ligature in the right or left arm of the sick man, and let three or four ounces of blood flow; the thinnest part of the instrument that must be used for transfusion is introduced into this vein incision, then the arm is ligated under the vein incision to prevent more blood from escaping and to hold the instrument in place; the vein of the healthy man is then opened in the same way and the other end of the instrument is applied to it so that the blood, without coming into contact with the outside air, passes from the vein of the healthy man into the vein of the sick man. The instrument used for this kind of transfusion is the following: a canal or silver tube with a length of about two transverse fingers, of equal diameter and which can contain 5 or 6 ounces of liquid; one end of this tube or cylinder bends briefly at its opening like a cup so that it fits exactly to the arm of the "healthy man" and immediately receives all the blood that comes out of the vein; the other end of the instrument ends in a thin, short canal, and this end is introduced into the vein of the sick man."

From the figure of Moncoq's instrument it can be seen that the concept of this differs from that of Major only for a complication of no importance; that is the plunger that presses and pushes the blood column, since by the law of gravity alone the blood can flow into the patient's circulation, as Gasse's instrument proves it. What is more, there is the presence of a valve at the juncture of the crystal dome and the transparent cylinder which, using ready venous blood can cause (as I have already said) stopping of blood and clot formation.

Mathieu in 1853 (see Goulard, *Thèse*, p. 49) offered doctors an instrument of his that had a similar function.

Later, perhaps to follow the wishes of those who fear harm from cooling the blood within the transmitting tube, he coated it with a glass channel containing a thermometer.

Moncoq, always keeping to the principle of intermittence in the injection of blood to imitate the systole and diastole of the heart, as if to interpose (as he puts it) a mechanical heart between the donor and the recipient, equips his apparatus with a pump moved by degrees by a key (fig. 2a, page 200 of his op. cit.). And later on tirelessly looking for an instrument that fully satisfied his aims, he built another one in 1863, which he used several times and is very tender in praising them (fig. 5a page 222, op. cit.).

There is also a semi-direct transfusion syringe that was the subject of serious controversy between its inventor (a manufacturer of surgical instruments) and Moncoq. He wants it rejected from practice - but the fact is that it can serve without being commendable. It is a plagiarism to Moncoq's tool; hence the anger of Moncoq and the polemics.

Here ends the myriad of distractions, among which only the main ones I have mentioned; while there is another long series that for small, insignificant modifications of mechanics, not of principle, differ from each other and multiply the already superfluous paraphernalia by the transfusion operation.

Ancillary instructions for indirect transfusion

The indirect transfusion apparatus, in addition to the proper instruction of injecting the blood, requires other instruments intended for the act of manipulating the blood, for its defibrination.

And these are: a basin that receives venous blood from the donor; a broom of thin wooden sticks with which the blood is stirred and shaken as it falls into the basin; a glass cup, preferably with a spout, into which the blood flows which, stripped of the fibrin, is poured from the basin over a fine horsehair sieve.

I reserve the description of the operative act of indirect transfusion in the last chapter for reasons of brevity.

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Operative process in indirect transfusion to defibrinated venous human blood

I love to describe this process because I do not find it in full or in other authors, and because it is the one I prefer to follow; it precedes the narration of my clinical cases almost as an introduction.

1. Preparation of the patient. If the indication is not urgent, the patient must not have eaten for 3 to 4 hours before the transfusion, and the food will be low in volume and exciting (good brolo, egg yolk, wine); no notice will be given of the time of the transfusion so that the patient can spend the night before and the emotion lasts as little as possible; a moment of apyrexia will be chosen; the degree of heat will be detected in the days before and the morning of the operation, and with the same norm detected will be the pulsations and respirations; it will be necessary to calculate the emotion that will have accelerated the wrists, and it will not fail to detect the sphygmographic traces prior to the operation; a hand bath or foot bath will be done a few hours before the transfusion and bandaging of the limb above the incision point of the vein, so that this cloves more prominently; the limb will be placed on a pad, and the trunk kept a little raised.

2. Preparation of the blood. After bleeding with a large jet, collect the blood in a basin; as it flows, shake it with the broom; once 120 grams have been collected, entrust the bandaging of the bled arm to an assistant and continue the beating of the blood, for which in 6, 8 minutes all the fibrous core will have gathered between the legs of the broom; stir again vigorously to better oxygenate the mass; the core of fibrin is squeezed so that the globules contained in it are not lost; with one hand hold a fine sieve of horsehair, with the other pour the blood from the basin over it, making it fall filtered into a chalice; from this pass the end fitted with a tap into the syringe; if the piece including the tap is removed from my syringe, there is an opening shaped like a funnel and large enough to comfortably pour the blood into it while the plunger is completely withdrawn backwards; this done, reapply the tap piece, with the toothed wrench the plunger is raised until all

the air that is above the blood column is removed; and so loaded the instrument closes the tap: needless to say that defibrination should be done by the surgeon himself who carries out the transfusion for his own guarantee that he himself must have made sure that all objects and containers are clean and that no corpuscles fall into them while they are arranged for the operation: this is achieved by keeping them upside down and covered with cloths.

3. Preparation of the patient's vein. Once the vein has been chosen and inflated by means of a lace tightened to the top, the skin is cut longitudinally and, once the vein is exposed, it is isolated by tearing the cellular tissue that surrounds it; with a thin scissors it is opened in the longitudinal direction and, both immediately and after having crossed it in its lumen neck of the probe for greater safety, the selected and proportioned cannula is introduced; then the lace around the limb is untied, the vein is pulled out or a pin is then turned to the top and then the thread is pulled up to number 8, or only a thread is passed to knot it over the point of the vein containing the cannula, in order to secure this within it; a second thread will be useful to pass under the peripheral stump of the vein and tighten it there to prevent the reflux of blood: if there were not an assistant for all these offices, the operator after loading the syringe would think about preparing the vein, not taking care that the blood changes its temperature. The difficulty of penetrating the vein with the cannula may make a first attempt unsuccessful; the surgeon chooses another vein and how many are needed, but does not defer the operation so that the already weak patient is not discouraged.

4. The operator withdraws the buttoned probe that occludes the lumen of the cannula, with one hand he makes the blood of the prepared vein flow from top to bottom so that it enters from the covered end of the cannula and fills the lumen up to the outer end, then he quickly joins the end of the syringe to the free end of the cannula and begins the injection keeping the instrument slightly inclined from bottom to top from front to back so that the flute-beak opening of the cannula is not occluded from the upper wall of the vein obstructing the course of the injection.

   An assistant and the same operator monitor the pulse for instructions to continue or stop the injection.

   If the cannula is really in the lumen of the vein, if the injection is not forced, if the blood was well defibrinated, we will not have thrombus or interstitial blood flow; we made sure of the air embolism when we filled the syringe.

5. After the injection, the pin is withdrawn from the dissection of the vein and with it the thread, or the two threads that have been attached to a lace are cut and withdrawn, then the cannula is slowly extracted; a finger is slid from top to bottom towards the wound on the portion of the vein surrounding the cannula in order to let out the drops of stagnant blood that could be in the process of congealing; he dries the wound and closes it with strips of plaster, then making a discreetly compressive bandage on the top, which is left for a few hours until the thrombus is made in the vein and reassured by blood loss; finally, the cold epithem is applied to the top of the patches, which are not removed until the third day.

   It is not uncommon, especially in anaemics and cachetics, to have the wound reunited by secondary intention: a consequence of no value ever.

   The observations of the pulse, breath, temperature will be continued during the operation and for two or three consecutive days, for the evaluation of the direct effects of the transfusion.

   Once the disturbance of circulation and soul has calmed down, the patient can take food, preferably preceded by some stimulating wine.