

DE LA TRANSFUSION DU SANG

By: Dr. E. LABBÉE

A TRANSLATION BY PHIL LEAROYD

The review article 'The Transfusion of Blood' by Dr. Ernest Labbée, published in the *Journal de thérapeutique* in 1875 in ten separate parts, can be read or downloaded from the following sites:

Part 1: Volume 2, pages 556-565.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=658>

Part 2: Volume 2, pages 599-610.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=701>

Part 3: Volume 2, pages 641-649.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=743>

Part 4: Volume 2, pages 676-688.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=778>

Part 5: Volume 2, pages 716-724.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=818>

Part 6: Volume 2, pages 757-770.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=859>

Part 7: Volume 2, pages 796-807.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=898>

Part 8: Volume 2, pages 835-845.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=937>

Part 9: Volume 2, pages 873-886.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=975>

Part 10 Volume 2, pages 911-923.

<https://babel.hathitrust.org/cgi/pt?id=mdp.39015070505006&seq=1013>

I think that I should start the summary of this review paper by saying that although it is a 'lengthy read', this is because its content is extremely comprehensive and I believe it to be one of the most insightful and well balanced reviews of blood transfusion written in the 19th century, which accurately documents and summaries the information regarding blood and blood transfusion known at that time. It is very well presented, written in an uncluttered open style, in which the debatable points of research are clearly argued in a balanced / unbiased manner – though this does take its toll in the last part, where the author identifies that he is running out of space! My one main criticism is the lack of accurate references.

Labbée begins the first part by commenting on the movement away from bloodletting (championed by Bousais) and identifies Billroth as a dissenter of this move. He then sets out to review the early history of the subject of transfusion, critically examining the ancient references to transfusion initially identified by La Martiniere. He dismisses Casse's claim that Folli made the earliest attempts at transfusion in 1652 but argues that transfusion, after the explanation of the circulation, was 'a small step' from infusoria surgery, i.e. a gradual process of development. He discusses the various arguments between supporters and detractors of transfusion, that eventually became insults, especially aimed at Denis and identifies the effects of the decision by the Châtelet in Paris on 17 April 1668 had in effectively stopping transfusion being performed on humans until 1818, which he identifies as being 'truly the time of transfusion's rebirth'.

Part two, titled 'Considerations of Experimental Physiology' starts by looking at 'the role of blood in transfusion', beginning with the pivotal experimental work of Blundell and the

influential work of the physiologist Legallois, who identified the importance of blood flow in maintaining movement and sensibility in the body. The author identifies that although the early transfusion experiments between animals of different species or classes were initially successful, the animals did not survive and that the greater the difference between the animal species, the more toxic the blood became. Labbé then discusses at length why this infused blood is toxic, identifying that it is not just the size and shape of the different blood cells that is the cause, but also, as initially described by Landois in 1873, the problem of 'inter-species incompatibility' (now known to be antibody induced) and the subsequent disruptive effects caused by the destroyed red cells within the recipient's circulation.

In part three the author continues to the information on experimental physiology by examining the relevant importance of the different constituents of blood, i.e. the red cells or the serum/plasma, in regenerating the recipient's vital properties. He reviews the research that shows that serum/plasma has no revitalising properties and that experiments demonstrate that it is the oxygen charged red cells ('globules') that restore the recipient's vital functions. He therefore identifies that from a purely physiological viewpoint defibrinated blood is as effective as whole blood – the beating process charging the cells with oxygen. He identifies however that the defibrination process alters the 'special density of the red cell suspending medium', but he believes this to be of importance only with injections of large volumes of transfused blood.

Part four starts with an examination of the relevant physiological benefits of arterial c.f. venous blood, concluding that at the practical level of small volume transfusions the difference is somewhat academic as the donated venous blood is rapidly oxygenated in the patient's lungs. Labbé then looks at the reasons behind who is the best blood donor, identifying that to be young men (based on them having the greatest number of red cells) and then the effects of temperature on blood coagulability and how 'chemical agents' can inhibit coagulation – though these have a detrimental effect on the red cells (and would appear to be toxic!). He concludes this section by looking at the published research into how coagulation is activated and by presenting a number of conclusions based on the information provided in the preceding chapters.

Part five begins the discussions on the therapeutic applications of transfusion, starting with its use in serious haemorrhages, which the author starts by commenting on the inability of people in recognising that the obvious treatment is to replace the lost blood – which he credits started with Blundell. Traumatic haemorrhage is discussed, identifying that it is better to use normal blood, as transfusion with defibrinated has led (not unexpectedly) to bleeding in animal experiments. He then deals with the use of transfusion in cases of puerperal haemorrhages, starting with the comments of some eminent obstetricians who believe that the women would have been saved anyway by existing methods, but he identifies that these comments are not supported by any demonstrable facts. By comparison, the author presents the results of over 100 cases of the use of transfusion in puerperal haemorrhages with over 70 reported successes – a large number of the failures being due to severe childbirths or 'time delay' in performing the transfusion.

'Operating Manual' is the heading that starts part six, opening with identifying the symptoms of puerperal haemorrhage, a condition that different authors have definitely ascribed to needing timely transfusion intervention. The author states that a specialist transfusion device is not required, identifying that 'an ordinary syringe that is perfectly clean' is all that is needed in an emergency, but he stresses that the injection should be done with 'excessive slowness', using a small amount of blood, giving examples of the most commonly used doses that have been successful. The phenomena usually observed in patients after the transfusion are listed. He then describes sub-acute anaemia (hyphemia) resulting from repeated less abundant blood loss, primarily non-puerperal metrorrhagia, where transfusion has been shown to be less successful due to the underlying conditions of the patients, but can still be identified to be of value in some cases.

Part seven continues the general heading of 'Operating Manual' by the author recommending the use of normal human blood for transfusion and then identifying the categories of various 'external haemorrhages' that cause anaemia sufficient for the use of a

transfusion. The author identifies that these include epistaxis in haemophiliacs (epistaxis being recognised as the most frequent haemorrhagic diathesis – more common than bleeding from the mouth or intestine). Other sub-acute anaemic conditions identified as requiring transfusion intervention that are discussed in some detail are haematemesis, traumatic haemorrhages of diverse origins, excessive bloodletting, enterorrhagia, haemoptysis and haemorrhoidal bleeding. Labbée concludes this section by stressing that the transfusion of normal (non-defibrinated) blood needs to be performed in good time in the presence of a worrying state of acute or sub-acute anaemia as well as in cases of uncontrollable haemorrhage.

In part eight, the author examines the role of transfusion in 'dyscratic constitutional diseases', purpura, scurvy and leukocythemia, which, although he identifies that some successes have been reported with scurvy patients, he believes that the effect of transfusion is only palliative. The treatment of anaemia in chlorosis patients, dealt with in a separate section, is stated to have been shown to be mainly successful. Although the treatment by transfusion of severe anaemia associated with certain dyscrasias, e.g. suppurations, excessive breastfeeding, inanition and serious fevers, is identified to be mainly palliative, though in some suppurations for example it is identified to possibly allow time to rectify the underlying causative condition. Finally, transfusion in some cachectic states is also stated, by its very nature, as only being palliative, though he states that transfusion can be used to keep a patient alive longer in special circumstances, e.g. in a pregnant woman.

Part nine is essentially a summary list of the other clinical disorders in which blood transfusion (using human blood) has been tried, invariably with only a palliative effect. This part starts by looking at depletory transfusion (i.e. transfusion preceded by a bloodletting) in cases of poisoning, the first section of which includes information regarding cases of poisoning by chemical agents, e.g. coal vapour (carbon monoxide), mephitic gases, phosphorus and asphyxia in newborns (strangulation by the cord). The next section, titled morbid poisonings, includes cases of cholera, diphtheria and malarial fevers where transfusion has been used, followed by a section titled virulent diseases, which includes cases of rabies, smallpox and syphilis. This part concludes with information regarding transfusion in nervous diseases that includes convulsive neuroses, eclampsia, hysteria, epilepsy, tetanus and neuroses of the intellect.

The tenth and final part starts with the major heading of 'transfusion in man with the blood of animals' that includes the use of lamb's blood in acute and chronic anaemias, pulmonary phthisis and mental alienation, concluding that the effects are at best palliative, stating that its advantages are 'doubtful, limited or non-existent' and its use has neither the reasoning, based on the theoretical considerations, nor the support of clinical facts. Labbée identifies and discusses the symptoms seen after a transfusion of animal blood. He then discusses 'transfusion devices', which in his opinion are all 'too complicated, difficult to use, subject to alteration, highly priced and not convenient' and believes, as stated earlier, that the syringe is the easiest and most convenient device to use. He identifies mediate and intermediate transfusion options and then discusses the choice of blood (whole rather than defibrinated), the quantity to use (small volumes between 50-200 grams) and the temperature (close to normal) – somewhat repetitive of information provided in part six.

This section concludes with identifying the accidents associated with blood transfusions, i.e. infusion of air, embolisms and others. It is a shame that this last section is so briefly covered compared with the earlier sections of this review, which the author states is due to space limitations!

Because of its overall size and the space requirements of the separate parts, the different topic areas covered within this review do not necessarily coincide inclusively to be within a particular part. As such, it is difficult to identify and clearly follow the separate topic areas covered by the author that are included within the different parts. This is compounded to some degree by the fact that not all of the headings and sub-headings are not consistently numbered / listed in the same way within the different parts of the original text. I have tried to ensure that this is more uniformly presented within the translation.

Similarly, due to its size and format it is difficult to locate the different individual topics within the original as well as the translated text. As would be expected of a review published in ten separate parts, the author does not include a contents list. However, to enable the locations of the different topics to be identified more easily, I have created one using the different headings used by the author that includes the part and page numbers of the original publication as well as the page numbers of them within this translation *:

TOPIC	PART – PAGES
Introduction	1 - 556 / 7
Historical	1 - 558 / 8
 First Part: Considerations of experimental physiology	
Chapter 1: The role of blood in transfusion	2 - 599 / 13
§ I. Transfusion between animals of different species or classes	2 - 601 / 15
§ II. Accidents caused by transfused blood in animals	2 - 605 / 17
§ III. Which, of the main elements that make up blood, are those that can regenerate the vital properties?	3 - 641 / 20
a) Transfusion with blood serum	3 - 642 / 21
b) The role of blood globules in transfusion - Properties of defibrinated blood.	3 - 643 / 21
 Chapter 2: The qualities that blood intended for transfusion must possess	 4 - 676 / 25
§ I. Should arterial blood or venous blood be transfused?	4 - 676 / 25
§ II. Who are the best blood donors?	4 - 679 / 27
§ III. At what temperature should the blood be transfused?	4 - 680 / 28
§ IV. Can blood made incoagulable by chemical agents be transfused? – Some indications on blood clotting.	4 - 682 / 29
Conclusions to be drawn from the previous chapters	4 - 687 / 33
 Second Part: Therapeutic applications	
Chapter 1: Transfusion in serious haemorrhages	5 - 716 / 33
§ I. Traumatic haemorrhages	5 - 717 / 34
§ II. Transfusion in puerperal haemorrhages	5 - 720 / 36
Operating Manual	6 - 757 / 39
§ III. Transfusion in sub-acute anaemia resulting from repeated blood loss or rapid hypemia	6 - 761 / 41
I. Non-puerperal metrorrhagia	6 - 763 / 43
Operating Manual	7 - 796 / 47
II. Various haemorrhages	7 - 798 / 48
a) Epistaxis and haemophilia	7 - 798 / 48
b) Haematemesis	7 - 802 / 51
c) Traumatic haemorrhages	7 - 804 / 52
 Chapter 2: Transfusion in some constitutional diseases and certain anaemias due to dyscrasia	 8 - 835 / 55
§ I. Transfusion in purpura, scurvy and leukocythemia	8 - 836 / 55
a) Purpura	8 - 836 / 56
b) Scurvy	8 - 837 / 56
c) Leukocythemia	8 - 837 / 56
§ II. Transfusion in chlorosis and chloro-anaemia	8 - 838 / 56
§ III. Transfusion in certain anaemias due to dyscrasia	8 - 840 / 58
a) Prolonged suppuration	8 - 840 / 58

b) Prolonged breastfeeding	8 - 842 / 59
c) Inanition	8 - 842 / 59
d) Severe fevers. Intestinal disorders	8 - 843 / 60
e) Purulent fever, septicaemia	8 - 844 / 60
§ IV. Transfusion in some cachectic states	8 - 844 / 61
 Chapter 3: Transfusion in poisonings	9 - 873 / 61
§ I. Poisoning by various toxic substances of a chemical nature	9 - 874 / 62
a) Poisoning by coal vapour	9 - 875 / 62
b) Poisoning by mephitic gases or vapours	9 - 877 / 64
c) Poisoning by phosphorus	9 - 878 / 64
d) Various poisonings	9 - 878 / 65
e) Asphyxia of newborns	9 - 879 / 65
§ II. Morbid poisonings	9 - 880 / 65
a) Cholera	9 - 880 / 65
b) Diphtheria	9 - 881 / 66
c) Maremmatic fevers	9 - 881 / 66
§ III. Virulent diseases	9 - 882 / 67
a) Rabies	9 - 882 / 67
b) Smallpox	9 - 882 / 67
c) Syphilis	9 - 882 / 67
 Chapter 4: Transfusion in nervous diseases	9 - 883 / 67
§ I. Convulsive neuroses. – eclampsia, hysteria, epilepsy, tetanus	9 - 883 / 67
a) Eclampsia	9 - 883 / 67
b) Hysteria	9 - 883 / 68
c) Epilepsy	9 - 883 / 68
d) Tetanus	9 - 884 / 68
§ II. Neuroses of the intellect	9 - 884 / 69
 Third Part: Transfusion in man with the blood of animals	10 - 911 / 70
Chapter 1: The transfusion of lamb's blood in various anaemias and cachexias	10 - 912 / 71
§ I. Acute anaemia, chronic anaemia	10 - 912 / 71
§ II. Pulmonary phthisis	10 - 913 / 71
§ III. Mental alienation	10 - 914 / 72
§ IV. Symptoms observed after the infusion of lamb's blood	10 - 915 / 73
 Fourth Part: Transfusion devices – Operating manual	10 - 917 / 74
§ I. Devices	10 - 917 / 74
§ II. Operating manual	10 - 918 / 75
a) Immediate transfusion	10 - 918 / 75
b) Mediate transfusion	10 - 919 / 76
c) Choice of blood	10 - 921 / 76
d) Quantities to inject	10 - 922 / 77
e) Temperature	10 - 922 / 77
§ III. Transfusion accidents	10 - 922 / 77
a) Entry of air into the veins	10 - 922 / 77
b) Embolisms	10 - 923 / 78
c) Phlebitis	10 - 923 / 78
d) Accidents and various phenomena following transfusion	10 - 923 / 78

I have produced a translation of this review article from the original French into English to enable its content to be appreciated by a wider audience. Whilst I am obviously aware that instantaneous computer generated translation is available, this process however struggles with accurately reading the original text and interpreting specialist terminology, as well as producing a 'colloquial style' not always representative of the original text. In addition, an 'automatic translation' may either purposely or inadvertently alter the wording to 'make it read better' but in doing so there has to be an element of interpretation involving something on the lines of 'I believe that this is what the author is actually trying to say'. I want 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 in accurately identifying the original text and producing a true representative translation of 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 text.

I have tried to reproduce the original paragraph settings, line spaces within the text and the general layout as accurately as possible and maintained within the translation the words that are originally printed in italics. The spelling of people's names and the dates of events are reproduced as originally printed. The author frequently uses the word 'globule', which is believed to equate to a corpuscle – though given that there is no other translation option for this word, I have left it as being 'globule' within the translation as well. A very small number of words are not able to be translated – I have placed these within square brackets in the translation.

Dr. ERNEST LABBÉE

I have unfortunately been unable to identify any information from the internet relating to the author of this review article. There is however a 'Special Correspondence' report (no author given) published in the *British Medical Journal*, 9th January 1875, 1, 57, that has the sub-title 'Notes in the Hospitals of Paris', which includes comments relating to a M. Labbé, working at the Pitié. Given the different spelling of the name I am unsure if this is the same person, however he is described in the article as follows: '*M. Labbé is one of the more practical of the hospital surgeons of Paris – active, intelligent, well-read and a man of the world. He shares, with most French surgeons, the habit of teaching well and clearly; of laying stress on the particular points on which he wishes to express his views; and of interesting his auditory by vivacity of manner, and by the evident interest which he takes himself in the subject of which he is talking*'.

'THE TRANSFUSION OF BLOOD'

By: ERNEST LABBÉE

PART 1

The reaction against Broussais' system has led the doctors of our time in a path quite opposite to that to which the illustrious reformer wanted to lead them in his wake. To the antiphlogistic methods so much vaunted, and, shall I say it? so ruthlessly applied when physiological medicine flourished, almost always given way to tonic and restorative treatments in the curation of diseases; and if some disciples of the professor of Val-de-Grâce still follow the errors of the master today, it must be recognized that the majority of practitioners proscribe blood emissions from the treatment of diseases, and endeavour to spare, with a sort of bias, the blood of the patients entrusted to their care.

Even acute affections, phlegmasias, rheumatism, pyrexias, etc., so often combated by leeches, bloodletting and debilitating diet, are only rarely opposed by such means; and as for chronic diseases, they are subject to antiphlogistic methods only in truly exceptional circumstances. Today, the tactics are not only different, but also absolutely opposite to those prescribed by Broussais, and much more attention is paid to repairing and regenerating the blood impoverished by disease, than to reducing its quantity. This is the will of the human mind, generally passionate about contrasts and clear-cut oppositions, and which, enthusiastic about doctrines, quickly tires of them, soon abandons them, and finds nothing better to do than to occupy itself with the contrary thesis.

Thus it is that *irritation*, a formula now forgotten, has given place to *anaemia*, and that to combat the new enemy we are trying new weapons.

Therapeutics, and history shows us this, willingly follows systems: sometimes it is inspired by the ideas of Brown, Broussais, Rasori, the ontologists; sometimes it becomes eclectic and defiant. And yet it is progressing. In truth, it has taken great time to try in turn the medications directed against sthenic or asthenic affections, antiphlogistics, stimulants and counter-stimulants, the specifics; but it has not wasted its time; and the attentive observer who follows its progress finds a profit by its more or less skilful evolutions. Today, I say, it has become eclectic, sceptical perhaps; it searches a great deal, studies, handles medicines with skill without too much bias and goes, confidently or incredulously, to ask a thousand hygienic modifiers, a thousand cures of various importance, the resources that the *materia medica* could not provide it. However, it has its preferences, and it is here that we see the spirit of the system reappear and willingly direct itself in certain paths opened to it by pathologists. There is no doubt that it is at this moment pursuing *anaemia* and is striving to combat with advantage this morbid state so often invoked today, as was the *plethora* in the time of Broussais.

These tendencies of the art of healing towards methods which perfect and secure the craving of the blood, and, on the other hand, the profoundly developed spirit of scientific curiosity, the proofs of which we see every day, will doubtless explain why this great question of the *transfusion of blood* has been studied anew. What a wonderful way would it not be, in fact, if it were not so terrible to contemplate, difficult to implement, to come to the aid of a faltering body? Unfortunately this operation is still poorly known; its degree of importance and its value are unknown, and it has the unfortunate gift of moving even the doctor, who considers it only as an extreme resource, hardly indicated in the most serious haemorrhages. Moreover, it has its more or less vehement detractors who condemn it, want to exclude it from science, and attach themselves to demonstrate that it is only a ridiculous conception and a dangerous means.

A German surgeon, Billroth, one of the most passionate opponents of transfusion, said a few months ago that this method could only be considered as one of those crazy ideas, accepted by nations or corporations suffering from psychological disorders. *Modestly*, he added that for him he was, with regard to this operation, "in the state of a surgeon who still enjoys the fullness of his good sense" (*Revue méd. de l'Est*, July 1875.) This epidemic

monomania, to use Billroth's language, has been affecting Germany and Italy for some years now, because from these two countries have come the greatest number of works on this subject; France, England and America have been more spared. But let us leave aside the quip of the learned author of the *Elements of General Surgical Pathology*, and conclude that transfusion is a question that is entirely on the agenda and that imposes itself on the reflections of doctors. I will try to set it out in detail from its origin to the present day, multiplying quotations and facts, assembling as much material as possible, in order to make the reader of the *Journal of Therapeutics* penetrate more deeply into this subject. I shall consider myself fortunate to have spared him long and painful research, if I have been able to inform him sufficiently, in this *Review*, about the pending trial, the vicissitudes of which are now unfolding before the eyes of the medical profession. In this presentation I will follow the order adopted by Professor Gubler in his learned lectures on transfusion, given this year at the School of Medicine, certain that I will not go astray as long as I allow myself to be guided by my eminent master.

HISTORICAL

An anti-transfuser better known for the violence of his language than for his solid erudition, La Martinière, who wrote in 1668, imagined for the needs of a bad cause to give transfusion an ancient origin. Desirous of depriving Denis, his adversary and the one who first had the audacity to perform this operation on man, to the merit of the idea of a new mode of treatment, he consulted ancient and modern authors, poets, historians and scientists, and drew up a long list of works in which the transfusion is mentioned.

I will not follow our scholar on this voyage of research, to make sure that Tanaquila, wife of Tarquin the Elder (Book of Wisdom), Ovid, the anatomist Herophilus, the Egyptian or Jewish physicians, Pliny and Celsus, Marcus Ficino, the abbot Trithemius, Aquapendente, Harvey, Frapaolo, etc., practiced or pointed it out; it would be a waste of much time without profit. I cannot, however, resist the urge to point out in this historical work two errors which are still transmitted from one author to another, with a really distressing obstinacy. An episode taken from Ovid's *Metamorphoses* (*Metamorph.*, 1. VII) has been misinterpreted. Medea, solicited by the daughters of Pelias to rejuvenate their father, speaks thus:

Stringite, ait, gladios; veteremque haurite cruorem
Ut repleam vacuas juvenili sanguine venas.

These verses are quoted everywhere to show that the poet knew transfusion. The mistake is strange! Medea has no other object in giving these treacherous counsels to the daughters of old Pelias than to make them commit murder; she deceives them, of course Pelias succumbs to the blows inflicted on him by his daughters; then the enchantress disappears, carried away by the winged dragons, fleeing the vengeance of her victims. It takes a certain amount of goodwill to see this parricide as an example of transfusion.

Another passage in the same book VII of the *Metamorphoses* is no more conclusive. Medea, in order to rejuvenate Eson, indulges in a host of magical practices, implores the gods and prepares a powerful potion, the power of which she tests on a withered olive branch. This twig in contact with the potion having immediately been covered with leaves and fruit, Medea no longer hesitates; she opens the old man's throat, lets his aged blood flow and replaces it with juices:

Stricto Medea recludit
Ense senis jugulum; veteremque exire cruorem
Passa, replet succis...

The operation was a marvellous success this time. Jason's father regains vigour and youth:

Adjectoque cavæ suppletur sanguine venæ,
Membraque luxuriant. Æson miratur, et olim
Ante quater denos hunc se reminiscitur annos.

Here again I find only pleasant fictions, insufficient proofs to show that, in the time when Ovid lived, transfusion was known.

Pliny the Elder does not speak further of this operation, he simply recalls that epileptics descended into the arena to drink the blood of dying gladiators.

Moreover, the author of the article TRANSFUSION in the great *Encyclopaedia* (1765), vol. XVI, has ascertained that a good number of quotations from La Martinière are false or misinterpreted. On the other hand, if he quotes wrongly, he is incomplete and forgets to talk about Libavius (1615) who would have real rights to the priority of the invention, if he had spoken of it seriously. He mentions an operation by means of which the blood, transfused from the artery of a young man into the vessels of an exhausted and weakened subject, revives and comforts him; but he laughs, with reason, at the audacious man who would advise such a remedy, and prescribes to him *hellebore* in advance.

Another more important fact would certainly have interested La Martinière; it is the one quoted by Sismondi, according to Raynaldus (*Ann. eccles.*, 1492). The learned author of the *History of the Italian Republics* relates that Pope Innocent VIII "allowed himself to be persuaded by a Jewish physician to try the remedy of blood transfusion, often proposed by charlatans, but which had never before been tried except on animals. Three young boys, aged 10, were successively, in return for a reward given to their parents, subjected to the device which was to pass the blood from their veins into those of the old man and replace it with their own. All three died at the beginning of the operation, probably by the introduction of a few air bubbles into their veins, and the Jewish doctor fled rather than try his hand on new victims." (Sismondi, *Hist. des répub. ital.*, 1807-1818, t. VII, p. 289.)

It seems to me useless to add to these historical data, pure curiosities incapable of furnishing us with very great lessons. It may be concluded, however, that if antiquity suspected the possibility of transfusing blood, if some Egyptian, Hebrew, or Greek priests applied the method, this tradition has been of no resource to the moderns. In such a matter it was necessary to have more than ideas, more than the suspicions or reveries of a poet, it was indispensable to speak of proven facts, to cite at least one operative procedure; well!, the ancient authors do not inform us on any of these points, their narratives are only fictions which science cannot adopt. Another conclusion: the more modern times, up to the time of Harvey's great discovery, teach us nothing serious about transfusion. As long as the circulation of the blood remained unknown, doctors could not form very correct ideas about this operation and believe in the possibility of carrying it out. It was therefore not until 1619 that truly scientific studies appeared on this subject.

Joseph Casse, in a recent work (1875), cites with praise the work of the Italian Francesco Folli, 1652, who, inspired by William Harvey's book on the movement of the heart and that of the blood, describes a process of transfusion and attributes to this means the power of healing, rejuvenating and making strong. This simple document and some essays indicated in the works of Folli (*Stadera medica...* 1680) seemed sufficient to Mr. Casse to allow him to award the Italian author the honours of the discovery of transfusion. This judgment seems to me to be absolutely arbitrary. In fact, if Folli had made some attempts as early as 1652 to transfuse blood, he would have spoken of it explicitly, and above all he would not have dared to write that this was a means of rejuvenating and making strong; moreover, when his main work was published, in 1670, transfusion had been carried out throughout Europe and was hardly practiced anymore.

Moreover, he had been preceded in this field of hypothesis by our compatriot Dom Robert des Gabets (See: *J. des savants*, 1667) who in 1650 was already thinking of transfusion. This Benedictine monk even gave a real lesson on this subject in July 1658 at Mr. de Montmor's house, in the presence of a large audience of French and foreign scholars. On the other hand, Potter and Clarck (*Philosophical transactions*, 18 May 1668), Tardy and the Abbé Bourdelot, well before 1652-1658, were theoretically familiar with transfusion. Finally,

should we add that, in the works published at the time of the great vogue of this operation (1665-1670), the name of Folli is not mentioned, in connection with the history?

I sum up by saying that this much-disputed priority, claimed successively by the Germans, the English, the French, the Italians, or else offered to the different peoples of antiquity, probably belongs to everyone and cannot be conceded to one man alone. The idea came to several scientists after the discovery of circulation, and the execution originated in another discovery made about 1656, *infusoria surgery* or the art of administering medicines by intravenous injection.

Science progresses slowly; one idea gives rise to another, and it takes many steps to reach the goal. Was the circulation, for example, proven from the outset by Harvey? Not at all. It took the labours of Galen, Servetus, and others to prepare for his coming. Only, perhaps, the discovery of auscultation would be an exception to the rule, and yet we oppose it, without any serious reason, with the sound of Hippocratic succession.

I come back to infusoria surgery. The venous injection of medicines was devised at the end of the year 1656 by Dr. Christopher Wren, professor at Oxford, and performed on dogs by Boyle, according to the indications furnished by C. Wren. The following year, 1657, the operation was performed on a man condemned to death, at the France embassy in England; the patient received emetic wine in a vein. The experiment was a success and the condemned man, who was very little tried by this attempt, was pardoned.

Infusoria surgery then became fashionable. Clarck, in a letter of May 18, 1668, states that he had been practicing it for more than two years, injecting into the veins diuretics, emetics, purgatives, cardiac drugs and opiates. Doctors were even seen to apply the method to patients whose lives were seriously compromised. A Doctor Smith, of Danzig, in a letter of 18 August 1668, announced to Boyle the success of the medicinal infusion in some of his patients. One of them, "so infected with pox" that it was considered incurable, was cured by venous injection; and the same treatment succeeds at will on a gouty one, in an individual suffering from an apoplectic state and on a third patient affected by Polish plique. In Danzig also, Fabricius ascertained the efficacy of the purgatives, administered through the veins. Two drachms of a purgative solution acted at the end of four hours; the patient had five toilets (Jan. 1668); and two women with epilepsy were purged in the same way. So infusoria surgery had indeed entered into practice at that time.

From the infusion of medicines into the veins to the infusion of blood or transfusion, the distance is short, and it required very little effort of imagination to go from one to the other. Clarck (1657) and Boyle himself point out this application. This is why we see a first unsuccessful attempt at transfusion in England in 1658 by Handsham (*Encyclopédie Diderot*); a new unsuccessful attempt also, in 1665 (Potter, who wrote in 1668, places Henshaw's experiment around 1658), by Timothy Clarck and Dr. Henshaw (H. Quinche); and, in the same year, February 1665, the favourable experiment of Richard Lower, who passed the blood from the carotid artery of one dog into the jugular of another dog.

We then enter the experimental period of transfusion. From 1666 onwards, animal testing multiplied in England, under the impetus of Lower's work; and, in 1667, we witness such an outbreak of experiments and communications on this operation that we even refrain from mentioning them under the name of their authors alone. In France, England, and Italy, is practised the passing of the blood of one animal into another, either by following the Lower process and making the carotid artery of one animal communicate with the jugular of another animal by means of small feather pipes (*J. des Scavans*, Monday 16 January, 1667), or by any other method.

In Paris, Denis, a professor of philosophy and mathematics, was especially noted for his enthusiasm and activity. His name is now inseparable from the history of transfusion. On 3 March 1667, with the help of a surgeon named Emmerez, he managed to change the blood of three dogs without making them sick. Other experiments having taught him the harmlessness of transfusion, he published his intention to test it on man with the avowed aim of arousing criticism and seeing if serious objections would not be addressed to his project. A certain number of arguments directed against his idea failed to convince him, and on

Monday, 28 June 1667, Denis wrote to Mr. de Montmor: "At last the transfusion has fortunately taken place on two men."

In the first case, it was a young teenager aged 15 to 16, exhausted by a severe fever and 20 bloodlettings. With the help of Emmerez, he draws 3 ounces of blood from his vein and infuses him with arterial lamb blood. The operation was a marvellous success; the young boy had no other accident than an insignificant epistaxis and soon recovered his strength and a good appetite.

In the second, it was a chair-bearer, aged 45, a robust and healthy man, who submitted to the operation in return for payment. Denis bleed him 10 ounces and infused him with the same quantity of lamb arterial blood. The experiment was so successful that this man ran to the cabaret shortly afterwards to spend his salary and offered himself for new trials.

Denis had thus just demonstrated the safety of transfusion in humans and its therapeutic value. Emboldened by these attempts, he practiced it several times more on humans.

On 19 December 1667, at the home of a lunatic named *Mauroy*, who had been suffering from periodic madness for eight years, and was very agitated, Denis bleed 10 ounces and injected him with six ounces of calf's arterial blood: the outbursts were immediately moderated. Three days later, another transfusion of a pound of calf's blood. The patient experiences *severe pain in the kidneys*, has large *evacuations from above and from below*, produces the next day two large glasses of *blackish urine, nosebleeds*, but recovers.

On 10 February 1668, Denis operated on a paralytic woman with complete success. But setbacks come soon. Denis did not succeed in saving, *in extremis*, the son of the Baron de Bond, who was suffering from hepatic and diuretic flow. Finally, performing a third transfusion on the insane Mauroy, he had the misfortune to see him succumb before his eyes during the operation (poisoned by his wife, according to Denis). On the other hand, the paralytic patient had only had a momentary benefit from the transfusion; she died shortly afterwards.

In England, Denis had had imitators. Richard Lower and Edmund King gave the transfusion to a man of letters, Arthur Coga, who was suffering from madness. A bleeding of 7 ounces was performed on him, and 10 ounces of sheep arterial blood was injected in its place (23 November 1667). Arthur Coga remained mad, but tolerated the operation perfectly well.

In Italy, the first transfusion in humans was made in December 1667, in Rome, by the famous anatomist G. Riva.

We are in the midst of a period of infatuation. We see in the new method a mode of treatment that can be heroic; we go so far as to believe in the possibility of giving strength to the weak and rejuvenating the old. Cl. Tardy, one of the most enthusiastic transfusers, writes: "Old men and those whose vessels are full of bad humors and corrupt blood can preserve themselves from the evils with which they are threatened." (1667) An experiment made on 20 May 1668, at Griffoni's, could support this view. An old pointer dog, very weak, almost impotent, deaf, was transfused with lamb's blood: his vigour returned, and his deafness partly disappeared. Medea was equalled!

These exaggerations compromised the method. The transfusers were sharply attacked in a host of letters and pamphlets, and when war was declared, they stopped discussing to insult each other. The main objections had been the following: "From the mixture of the two bloods may result a dangerous fermentation" (Gurye, 1668). "It is not true that most diseases come from the blood; they almost all have their source in the disturbance of the solid parts, in the increase or decrease of the play and activity of the different viscera ... the blood of a man with scabies, a person with pox, etc., is just as pure as that of a healthy man." (Eutyphro, pseudonym of Pierre Petit.) This objection is one of the most serious that I have found, with the following: Blood passing through inanimate conduits must coagulate and cause fatal palpitations when passing through the heart; the others, for the most part, do not deserve to be reported. What do we think of the arguments provided by Lamy? Just as, he says, the semen of an animal cannot be used to beget an animal of another species, so the blood loses its properties when it is transfused from one species into another, and

becomes a poison. Besides, what fate awaits the particles of calf's blood destined to form the horns of the animal, when this blood circulates in man?

An objection of the illustrious Perrault, produced in the Academy of Sciences, is not of very great value either: "It is very difficult," he says, "for an animal to accommodate blood that has not been cooked and prepared at home. You can't change blood like you can change your shirt."

Against these or other reasons, most often bad, it was enough to invoke the facts. This is what C. Gadroys did, who showed that dogs transfused by him with the blood of calves or goats lived very well at the end of five months. He might also have cited the favourable and analogous experiences of Denis; those performed at Bologna (28 May 1667), under the eyes of Cassini, on two lambs; those of Riva and Manfredi (1668), of King (1668), where the transfusion is made from a calf to a sheep; of Thomas Coxe (1668), who operated on two dogs, one of which was mangy; etc.

But Lamy replied by saying that the transfused men and animals had resisted and had *purged themselves of foreign blood*. This answer was quite judicious.

The adversaries, of course, could not convince themselves and, at the end of their arguments, they came to insults. The transfusion, under the pen of the "verbose La Martinière", became a barbarous operation from Satan's shop; and those who exercised it were only executioners worthy of being sent back among the cannibals..... etc..

Denis was especially strongly attacked; and they went so far as to have a lawsuit brought against him by the widow Mauroy. The leader of the transfusers was scarcely more inspired in his replies than his enemies; he treated them as jealous, envious, and scoundrels, and called La Martinière, a miserable tooth-puller, operator of the Pont-Neuf. Fortunately, he won his case. But, in the midst of these disputes, transfusion received a terrible blow, and if, like emetic, it did not have the honours of a decree of parliament or a decision of the faculty to proscribe it, it was regulated by a *sentence of the Châtelet*, on 17 April 1668. The criminal lieutenant decided "*that in the future the transfusion could only be done on men with the approval of a doctor from the faculty of Paris.*"

Denis, a doctor of Montpellier, could no longer practice transfusion without submitting to the new formality; he preferred to abstain.

From that date on, silence was kept around this operation. In England, there is no longer any question of it; in Italy, it was banned in 1679, following an unfortunate attempt by Riva, in Rome; in Germany it is easily forgotten. Transfusion had, in fact, never been much in honour in the latter country. Purmann had indeed transfused the blood of a lamb into the veins of a leper. Daniel Major, to whom the discovery of transfusion is often attributed without valid reason, had, in truth, published his two famous dissertations so favourable to transfusion:

Prodromus a se inventie infusoriæ, sive quo pacto agonisantes quidam, pro deploratis habitis, servari aliquamdiu possint, infuso in venam sectam liquore particulari (Leipsig, 1664); and

Deliciæ hybernæ, sive inventa nova tria medical (Kiel, 1667). But Purmann had had no imitators, and Major had not convinced his compatriots, despite his talent and its notoriety.

It is difficult to explain the disfavour which reached transfusion in England. R. Boyle, who sponsored this operation with his great scientific authority, had, however, indicated many experiments to be made, which might become the origin of interesting discoveries.

In 1667 he recommended to Lower that after the transfusion he should study the pulse, the humors, the secretions; to see whether certain diseases could be transmitted by the blood and whether others attributed to this humor were not modified by the addition of a new blood; to examine whether the blood of an animal which has taken a purgative does not determine purgation when it is infused into the veins of another animal; to practice transfusion with the blood of warm-blooded animals of different species; and, in warm-blooded animals, with the blood of cold-blooded animals; finally to perform the operation on a pregnant female dog to judge its effect on small dogs.

This rich mine was not exploited, and it is the modern experimenters who will take charge, as we shall see, to answer these questions so well posed by Boyle.

A singular thing! For a century and a half, there was no longer any question of transfusion. It will only be spoken of as a worthless curiosity, a daring fantasy that has fallen into oblivion.

Was such a discredit deserved? No; no valid reason can be adduced to justify this abandonment. If the transfusion had not given the marvellous results that certain enthusiastic minds had promised, it had not been compromised by serious accidents, and its beginnings remained on the whole very honourable. From the attempts made in France, two important lessons could be drawn:

1° Transfusion is possible from animal to man or between two animals of the same or different species; 2° it is most commonly harmless. And, on the other hand, Clarck, in England, had clearly specified one of the capital therapeutic indications of transfusion by saying that it could be applied *in magnis et subitaneis profusionibus, ad vires subito instaurandas*. He adds the proof of this assertion by relating that an animal bled white owed its salvation to the transfusion and had *perfectum vigorem restitutum*.

From 1670 onwards, we entered into a long and absolutely sterile period for transfusion and in which it is quite impossible to point out any significant progress. Doubtless the operation was not absolutely buried in oblivion from 1670 to the beginning of the 19th century, since there are some attempts towards the end of the 18th century, but, I repeat, we find nothing important to collect in these very few observations, published by Michel Rosa (Naples, 1782), Russell and Harwood (1792), etc.

In his *Recherches sur la vie et la mort*, which appeared in 1799, Bichat mentions real examples of transfusion in dogs, intended to demonstrate the action of two bloods (arterial or venous) on the brain, and which prove that the illustrious physiologist was well acquainted with this operation because he had performed it. However, he draws no other conclusion than those which are peculiar to the subject he treats, namely, that red blood maintains cerebral activity and that black blood extinguishes it.

It is necessary to arrive at the year 1818 to find a date that marks in the history of transfusion; it was truly the time of its rebirth.

PART 2

FIRST PART: CONSIDERATIONS OF EXPERIMENTAL PHYSIOLOGY.

CHAPTER 1

The role of blood in transfusion

In 1818, the new impulse which was to give transfusion such a great development and to lead it from the shifting ground of empiricism into the surer path of experimentation was born in England. It was in this country, as in the 17th century, that a learned physiologist had the happy idea of rehabilitating this important operation and drawing the attention of practitioners to it. Blundell's labours inaugurated that beautiful and truly scientific period, which extends from 1818 to the present day, and in which we see the many combined efforts of physiologists and clinicians throwing an entirely new light on transfusion. No doubt Blundell's task was easy at that time, for the experiments of Bichat, the important historical researches of Paul Scheele (*Die Transfusion des blutes und Eispritzung der Arzeneyen in die Adern...*, Copenhagen, 1802-1803), the studies of Hufeland (1815), etc., had singularly prepared minds; but it is fair to acknowledge that the English doctor's memoir had the merit of showing a new path and of attracting experimenters to it. It was after having seen a woman in childbirth perish before his eyes, from a formidable uterine haemorrhage, that Blundell resolved to ask through experimentation what resources the transfusion of blood could provide to the practitioner who would find himself faced with such terrible loss of blood. Performing enormous bloodletting on dogs, which reduced these animals almost to the state of corpses, he saw that the transfusion of a few ounces of blood, made with the help of a syringe of his invention, revived these unfortunate victims in a few moments and saved them

from death. He was then convinced of the possibility of using this excellent therapeutic method for humanity.

Blundell's original idea had been to use a special device for the operation which made it possible to infuse into the veins, like a medicine, the blood drawn from the body. Until his time, it had been limited to making the blood donor's artery communicate with the vein of the recipient by means of tubes, that is to say, to practice, according to Dieffenbach's expression, the *immediate transfusion*. Blundell's experiments inaugurated a simpler method of operation, called *mediate transfusion*, the only one possible for medical practice, at least in the greatest number of cases, and which is generally adopted today by surgeons and physiologists.

This momentous fact, now known to everyone, even to people who are not connected with medicine, and which shows us that an animal that has been bled dry can be resuscitated, so to speak, by transfusion, indicates to us on the one hand the value of this method, and on the other the special role of the blood in awakening vital manifestations that are numb or on the point of dying out.

A physiologist of great talent, unfortunately a little too forgotten nowadays, Legallois, had admirably understood one of the modes of action of the blood on our tissues and foreseen the theories which have been given, more than 40 years after his work, to explain the role of this humor in transfusion.

In 1809, in one of his remarkable memoirs on *The Principle of Life*, he wrote that "life is due to an impression of the arterial blood on the brain and spinal cord, or to a principle resulting from this impression." As proof in support of this view, he cited the well-known experiment of Sténon. In an animal, the aorta is linked to the level of the 1st lumbar vertebra, and soon a complete paralysis of movement and feeling in the hindquarters is seen; then the ligature is removed, and immediately movement and sensibility return to the paralyzed parts.

Thus, when the blood ceases to flow in a region, life instantly disappears; this is what led Legallois to say that by "binding all the arteries that go to the head, we would reduce this part to a state of death, and all the intellectual functions proper to the animal would be totally annihilated. ... These same functions would then be reborn, after the arteries had been untied." For Legallois, the blood is therefore charged, among other functions, with animating the tissues, and the skilful physiologist develops this idea in a passage which I quote *in extenso* in spite of its length, for I see clearly indicated in it those curious experiments of Brown-Séguard which have had a deserved repercussion, and which I will recall later.

"If one could supply the heart with a kind of injection, and at the same time if one had, in order to supply the injection in a continuous manner, a supply of arterial blood, either natural or artificially formed, supposing that such a formation were possible, it would be easy to maintain life indefinitely in any section (of the body) whatsoever, and consequently, after decapitation, it would be maintained in the head itself, with all the functions proper to the brain. ... We could recall life in any portion of the body, after its complete extinction; we could recall it in the same way in the whole body, and thereby bring about a true resurrection and in all the force of expression." And, further on, he adds: "If there were some means of supplementing the natural circulation ... it is certain that a corpse could be resurrected some time after death; a time which would be limited by several circumstances, and variable depending on the species, the age of the animal, the causes of death, the seasons, etc."

There is reason to be surprised that a physiologist as skilled an experimenter as Legallois did not think of using blood transfusion to demonstrate the accuracy of these beautiful conceptions. Are we to believe that at that time the operation was so forgotten or taken so little seriously that no one thought about it anymore; or should we think that death did not leave Legallois (died in 1814) time to verify these beautiful aims of his insightful mind? That is what I will not decide. Another physiologist of great talent was to accomplish this task; I have already named Brown-Séguard. This is not the place to recall the beautiful experiences to which I allude; they will find their place in another part of this review. For the moment, I simply draw from the previous considerations the conclusion that blood is a special stimulant capable of reappearing vital manifestations on the point of dying out or

already apparently disappeared. Now, we need to study under what conditions such a phenomenon can occur.

Blundell having bled a dog dry, injected it at the moment when it showed no more signs of life, 6 ounces of the arterial blood of another dog into the femoral vein; in a few moments the animal recovered and seemed to have come out of *a deep sleep rather than from agony*.

This experiment called for new research. Could a bloodless dog, for example be recalled to life by any blood, that of man or of another mammal? This is what we will examine in the following paragraph:

§ I. TRANSFUSION BETWEEN ANIMALS OF DIFFERENT SPECIES OR CLASSES.

The first transfusion operators taught us that the blood of calves, lambs and sheep can be injected with impunity, in a certain quantity, into the veins of a man or a dog; and some have affirmed that it is capable of restoring energy to a faltering body. Blundell wanted to verify this assertion. He injected human venous blood into the veins of a bloodless dog; the animal revived but expired shortly afterwards. Varying this experiment in several ways, for example infusing into the veins of dogs exhausted by haemorrhage, more or less large quantities of this same blood (100 to 300 grams), etc., this doctor never succeeded in saving their lives: all died after a few hours or a few days. Conclusion: it is dangerous to substitute high proportions of human blood for the dog's blood. "*The human blood cannot be safely substituted, in large quantities for that of the dog.*"

At the same time, Goodridge and Leacock, of Barbados, arrived at the same results by transfusing the blood of man or sheep into dogs.

Soon, in 1821, the question was taken up again by Prévost and Dumas, who concluded, like the previous observers, that the transfusion made on an animal with blood of a different species most commonly failed; the recovery of animals is only imperfect, and rarely can they be kept for more than 6 days, whether fresh blood or defibrinated blood is used. The pulse becomes frequent, the temperature drops, the droppings are mucous and bloody and life is extinguished.

These accidents are nothing extraordinary and can be explained; but one is surprised at the conclusion drawn by the two eminent observers, namely, that transfusion on man, that "operation unfortunately too famous, and which has been so abused in an ignorant and barbarous century, must be condemned as absurd and dangerous, so long as we are not more advanced in the intimate knowledge of the active principle of blood."

As far as I know, we had not used transfusion more than ten times in the space of a century, so the criticism was wrong. This is what Milne Edwards understood perfectly, who, two years later, included in his inaugural thesis (*Th. de Paris*, 1823, no. 73), this proposition: "in desperate cases of haemorrhage, we can try transfusion blood."

I leave this incident aside and continue the exposition of the main works relating to this question of *transfusion with the blood of animals of different species*.

Dieffenbach examined it with great perseverance in 1829, and came to formulate an opinion absolutely similar to that of the preceding authors: for him, in the case of fatal haemorrhage, the blood transfused between different species can momentarily revive an animal, but cannot preserve its life. Let us pause for a moment on these works of Dieffenbach, which are not lacking in interest, and in which we will find useful information.

He practiced especially in animals the *mediate transfusion* and he saw that, in bloodless dogs, the infusion of the blood of the species awakens life and preserves it in *half* of the cases; on ewes or calves, in more than $2/3$; and on cats and birds, such as pigeons, hens, ducks, geese, crows, which have suffered an exhausting haemorrhage, which it *fails* most often or always.

With blood foreign to the species, the results are no less decisive: most of the transfused animals perish quickly in the midst of violent convulsions when the dose is strong enough and they are healthy, and if they have been bled white, they experience almost no benefit from the operation. This distinction is important to make in Dieffenbach's observations between animals that have been bled and those that have not. The latter tolerate the addition of foreign blood fairly well in many cases: sheep, ox's blood; the dog as well; cats,

pig's blood, etc.; but this is only a simple tolerance, and it is undisputed that, when these animals are exhausted by haemorrhage, the transfusion of foreign blood is of no use to them.

However, the author makes a very fair remark, which is that moderate bleeding allows animals to easily tolerate the infusion of blood of different species; and this could allow us to understand why the first transfusions succeeded in passing, without accidents, herbivore blood through the veins of a carnivore: almost always, in fact, before the operation, they drew blood from the animal that was going to be transfused.

In summary, according to Dieffenbach, blood transfused between animals of different species can never preserve the life that will disappear as a result of a loss of blood; and if some mammals, in such cases, benefit from the transfusion of a blood peculiar to their species, others (cats) are only rarely saved by it; finally, in birds, such an operation would always be powerless.

Dieffenbach's experiments were subject to two objections: on the one hand, he used defibrinated blood; on the other, he had recourse to mediate transfusion. If it is easy to destroy or dismiss the first by saying that Blundell had not been more fortunate in using ordinary blood, or by arguing more recent facts which demonstrate the value of blood deprived of fibrin to restore vital functions, it is less simple to respond with advantage to the second.

It is known, in fact, that as early as 1667, King, in England, and Denis, in France, revived by *immediate transfusion*, with blood foreign to the species, animals bled white; and that Rosa, in Naples, verified these observations in 1782 by successfully transfusing carotid blood from a calf to a lamb made bloodless by the opening of the jugular, or by performing the same operation from sheep to calf. We also see modern experimenters casting doubt on the assertions of the German physiologist and countering his negative experiments with positive facts. I need not insist on the importance of this subject, and to point out that, from the point of view of practice, transfusion with blood foreign to a species would offer immense advantages if its safety and efficacy were demonstrated, and I therefore dwell with some complacency on the observations capable of throwing light on these controversial questions.

After Denis, King and Rosa, etc., Delafond and Milne Edwards had indicated a fact favourable to transfusion between different species: an ass deprived of its blood and dying was cured with defibrinated blood of horses; so that the experimenters concluded that "zoological kinship is favourable to transfusion."

Thus we find ourselves faced with two absolutely opposite opinions: 1° that of the first transfusions, which admits the possibility of obtaining good therapeutic effects by infusing the blood from one species to another; and 2° that of Blundell, Prévost and Dumas, Dieffenbach, P. Bérard, etc., which denies this possibility.

It was a Russian doctor, Gesellius, of St. Petersburg, who recently undertook to defend the first opinion. Unfortunately, while this defence was presented with conviction, it is not proven that he provided a strong case for it. The author shows us well, what was known and what remains, that lamb's blood is in no way fatal to the human body and that a quantity equal to the twenty-fourth part of its blood mass can be introduced into an animal without causing accidents, even though there has been no previous bleeding, but these are mere demonstrations of the harmlessness of the operation and not proof of its therapeutic value. Gesellius was anxious to inaugurate, by the transfusion of lamb's blood, a new era in the art of healing, and he had no doubt that this distribution of blood to phthisics and cachectics can render them significant service; but these assertions are still waiting to be supported by numerous and rigorously observed facts. We will return to these experiments in the therapeutic part of our study.

Another Russian doctor, Nikolai Tabure, of St. Petersburg, probably inspired by his compatriot Gesellius, published experiments of the same order in 1873-1874. Transfusing, after copious bleeding:

- 1° 2 cats, with dog blood;
- 2° 7 dogs, with calf's blood;
- 3° 1 dog, with cat's blood;

4° 1 sheep, with dog's blood;

He lost only two dogs, which had received calf's blood, and noted a marked benefit in the other animals. The conclusion to be drawn from these facts is that the cats, dogs, and sheep resisted, but it cannot be said that the transfusion would have prevented them from dying after a *serious haemorrhage*.

We shall in a moment bring other arguments against the thesis maintained by Gesellius; for the time being, we believe that we must abandon this discussion in order to complete more quickly the filling of the framework imposed on us by the title of this paragraph, by studying *transfusion between animals of different classes*.

In 1821, Prévost and Dumas observed that by injecting mammalian blood into the veins of a bird, determined nervous disorders and death, as if a violent poison had been introduced into the circulation. The following year, Magendie found, for his part, that a small quantity of turkey blood was enough to kill a dog; and Gaspard killed a hare in 12 hours with the blood of a [limaçon, i.e. cochlea!].

Later similar observations were collected by Dieffenbach and Burdach. The first indicated that a few drops of mammalian or fish blood were enough to kill a pigeon: the bird dies struck by lightning, as if it had been injected with prussic acid; the second showed that fish blood is toxic to dogs, cats and rabbits. Dieffenbach had reached the same results in his experiments as the previous author and had concluded that the more different the animal species, the more toxic the blood becomes. However, sometimes animals resist, and this experimenter noted that a young cat which had received 8 grams of turtle blood in its veins had serious accidents, but recovered after 24 hours.

This question was studied again in 1838 by Bischoff, who had occasion to make the following interesting remarks: birds tolerate the defibrinated blood of mammals fairly well;

Frogs are killed by mammalian blood, but tolerate fish blood well;

Finally, while the venous blood from dogs is toxic to geese or chickens, arterial blood does not cause these animals to die.

General conclusions: It seems to me that one is entitled to deduce from the facts set forth in the course of this long paragraph, that the transfusion of blood can only be attempted, to recall to life a subject exhausted by a haemorrhage, than between mammals of the same species; and that if it concerns animals of different species or classes it is powerless, useless or dangerous.

It is now necessary to study how infused blood becomes toxic; this is what we will try to explain in the following paragraph.

§ II. ACCIDENTS CAUSED BY TRANSFUSED BLOOD IN ANIMALS.

Before entering into the subject, I must specify that I am not at present concerned with those serious accidents which are usually reported in the study of transfusion: the entry of air into the veins, the injection of fibrinous clots; but only from the toxic action proper to the blood, considered as a medicinal substance. Now the harmful action of this liquid is exerted under certain conditions with which we are familiar; it certainly exists, without fail, and we must now try to interpret it, since, in the final analysis, man can be subjected, like animals, to the pernicious influence of the blood which is introduced into his circulation.

Death, in animals to which foreign blood has been infused, can occur in two ways: suddenly or slowly. In the first case, clonic convulsions, great anxiety and plaintive cries, dyspnoea or apnea, pupillary dilation, acceleration of circulation, and then complete cessation of vital functions are often observed.

In the second case, the same symptoms may present themselves with less intensity, and the agony lasts a few hours; but, sometimes, the animals survive for several days, during which they become weak and languid, shiver, vomit, have fever and mucous-bloody diarrhoea, make bloody or slightly bloody abundant urine, or have anuria, etc.

At the autopsy of these animals, the main lesions consist, in both cases, of visceral hyperemia of varying intensity: the lungs, liver and kidneys in particular are engorged with blood; and, when life has been prolonged for some time after the transfusion, sero-bloody effusions are found in the serosae; in the organs, various infarctions; congestion and blood

infiltration of the mucous membrane of the digestive tract; thrombosis and embolism in the pulmonary artery.

So that we can summarize the symptoms and the lesions in two words by saying that they both relate to sudden or slow asphyxia.

The mechanism of this asphyxia is easily understood in the case of transfusions on animals of different classes, for often then the blood globules have considerable differences in volume or shape. Thus the large elliptical corpuscles of birds and reptiles can only with great difficulty circulate in the capillaries of mammals, which have dimensions in proportion to the spherical and much smaller red blood cells of these animals, they stop in the small vessels of the lungs and become the origin of real capillary embolisms, which oppose an invincible obstacle to the pulmonary circulation. Thus, Plosz and Györgyai (1874), transfusing bird blood into rabbits, observed eleven times out of 14 experiments, death by thrombosis or embolism of the pulmonary artery.

But it is perhaps less simple, at first sight, to understand the circulatory disorders produced in an animal by foreign blood whose globules are smaller than those of its own blood. Well, here again we are dealing with mechanical obstacles determined by the figurative elements of the blood or their debris. *It is this proposition that must be demonstrated.*

From the time when Magendie was experimenting with animal transfusion (about 1822), the question was asked what became of the blood introduced into the veins.

The eminent physiologist made several attempts to resolve the question, and assured that the foreign blood disappeared fairly quickly. In support of this view, we will relate three of his experiences.

1° In a dog to which 15 centilitres of turkey blood are injected, the elliptical corpuscles of a bird are no longer found after a few hours.

2° Another dog, which had received in its veins the blood of 15 frogs, had quickly got rid of it because the elliptical amphibian globules had disappeared from its blood shortly afterwards.

3° A goose, which had been transfused with 4 centilitres of dog blood, had no more spherical mammalian corpuscles at the end of eight days.

Thus the red blood cells are destroyed, or at least disappear fairly quickly when transfusion is carried out between animals of different classes.

In recent years, the experiments of several physiologists have fully confirmed the results indicated by Magendie; and as they complete the question we are studying, it is necessary to speak of the most important.

A work by Professor Landois, of Greifswald, published in 1873, furnishes us with some interesting information. Injecting into the veins of dogs the blood of humans, cats, sheep, guinea pigs, pigs, calves and pigeons; to rabbits the blood of man, hare, calf, sheep; to sheep, human blood; to frogs, the blood of man and that of the animals designated above; to the *Rana esculenta*, the blood of the *Rana temporaria*, the German doctor noted in the transfused animal the *rapid disappearance* of the foreign blood. The blood cells are destroyed and the haemoglobin is released. In frogs, this effect occurs between 3 and 5 minutes, with rabbit blood; between 20 and 30', with the blood of other mammals; the urine is loaded with the albumin and the colouring matter of the injected blood. A very simple experiment shows what must happen in the circulatory torrent. If we study under the microscope the action of frog serum on mammalian blood, we see the globules being agitated by molecular movements, swelling, pale, shrinking, and disappearing, leaving debris which clumps together to form small masses of more or less volume.

The same phenomena are observed when mammalian blood is treated with the serum of other mammals.

There are, however, some nuances to be established: for example, while the serum of the dog dissolves the globules very actively, that of the rabbit is a solvent of little energy; moreover, while the red blood cells of the dog resist the serum for a long time, those of the rabbit are very quickly attacked and dissolved.

In the end, it becomes probable (one could say certain) that the globules of a transfused blood are destroyed by the serum of the animal which received this blood, and it is possible that in its turn the foreign serum destroys the transfused subject's own globules. If, in fact, a little serum of another frog is injected into the veins of a frog, haemoglobin soon appears in its urine.

The significance of these facts is not difficult to guess: the mixture of two bloods is bad or disastrous, either because these humors exert an endosmotic or other chemical action on each other, or because the body, poorly accommodating itself to this abnormal state, reacts and defends itself in its own way against the poison by destroying and eliminating it. It is therefore necessary that the economy should get rid of this foreign body, and that all the elements of the blood should be evacuated to the outside. Water and salts escape very easily, as well as albumin and globular detritus, at least under certain conditions, when the doses are not excessive.

In this respect, we are perfectly informed, and in an almost mathematical way, by the interesting experiments of Müller, of Stockholm, which are even more precise than the preceding ones.

By operating on dogs, whose blood mass he increased by 28%, he saw that at the end of 24 hours the number of blood globules was the same as before the transfusion. And he is careful to add that the greater the quantity of blood injected, within certain limits at least, the longer the elimination lasts and the more considerable the proportion of red blood cells remains and in excess of the original physiological figure. In a dog weighing 4,560 grams, which had received 290 grams of blood, the count of the globules still gave a higher figure after 4 weeks than that found before the transfusion.

However, it would be unwise to believe that things always happen so simply.

In many cases, especially when it is a question of injections of a blood very foreign to the animals in experiments and carried out in massive or strong doses, the infused liquid undergoes serious alterations, the red blood cells, as we know, are destroyed by the serum and leave a residue in the blood. Let us therefore see the consequences of this globular destruction.

When the debris of the red blood cells is not too considerable, it is eliminated or transformed in the circulatory torrent. According to Landois, elimination would take place through the kidneys, intestine, uterus, bronchi and serous membranes. At the end of an hour or two, haemoglobin and albumin show themselves in the urine, and for twelve hours these substances pass through this humor.

This elimination of the debris of the blood had been foreseen by Magendie and especially by Dieffenbach, and its consequences had not escaped this sagacious observer, for he had noted that the more evacuations there are in an animal transfused with foreign blood, that is to say, the more abundant its faeces, vomiting, and urine, and the more the danger of death is diminished for it.

Another physiologist confirmed, in 1873-74, the results obtained by Landois. A. Jakowicki has seen, in his experiments with the transfusion of normal or defibrinated blood, the decomposition taking place in the vessels and the residues escaping with urine, faeces, and vomited matter.

In short, if the materials from the decomposed blood can pass through certain emunctories in time and pass into the secretions, the animal will survive. This explains why not all animals to which foreign blood is infused into their veins die. But, more commonly, they succumb; it is because then the dose was too high, it will be said; so be it, I grant it; what happens then?

It has been thought that in such circumstances, the mass of the blood being considerably increased, there was a plethora and consequently the production of deep circulatory disorders. The fact is true in some cases, on condition that the quantity of blood circulating is increased in enormous proportions. Cl. Bernard has shown, in fact, that in the dog, water can be injected into the veins without serious danger, until this animal weighs 1/3 more, but that beyond this limit, convulsions occur, the secretions are dried up, and the animal dies. Ponfick and J. Bamberger have recently made an identical remark. Increasing the weight of

the blood of an animal by one-half, by the addition of an artificial serum, formed of a solution of albumin and sodium chloride, or by the injection of lamb's serum, they did not determine any accidents.

It is therefore not to the excess of vascular tension that we must attribute the serious phenomena caused by the transfusion of large doses of blood; there is another more real cause, which is the accumulation of the debris of globules in the vessels and their projection, in the form of innumerable embolic masses, into the capillaries of the organs. It seems to me that visceral congestions and infarcts can only be explained by a mechanical obstacle to circulation, produced by the obliteration of the capillaries. The transfused subjects would therefore find themselves in conditions similar to those of animals to which fine powdery matter has been injected into the veins.

Ponfick has given another explanation which seems to me less satisfactory. For him, it is the alterations of the kidneys that cause death. He saw, in fact, that these organs are very altered: they are swollen, congested, dotted on their surface with brown spots, and the examination under the microscope shows the urine tubes full of a substance which is none other than haemoglobin. The animals would die of haemoglobinuria. This theory seems questionable to me, at least for the majority of cases. Indeed, since the kidneys are the emunctories of haemoglobin, it is not surprising to find this material in the uriniferous tubes.

I therefore maintain my first proposition, stated above, namely that the serious symptoms observed after transfusion resulting from the destruction of the injected globules; the accumulation of their debris in the small capillary vessels of the viscera causes mechanical interference with the circulation, and asphyxia soon results from this cessation of the flow of blood, for it is most often in the lungs that such disorders occur. But all the organs: the kidneys, the liver or other glands and viscera, are exposed to this mechanical hindrance to their circulation.

Hence special effects, related to the role that the injured party plays in the functioning of the animal machine. The brain, the marrow, the intestines or the glands can cease their action, together or separately; we can also imagine the diversity of effects observed, which are absolutely different from one animal to another.

This is not the place to go further into this field of physiology, and I return to questions that are more directly of interest to therapeutics.

PART 3

The question of the *role of blood in transfusion* would be incompletely studied if I confined myself to the foregoing considerations. I must, therefore, embarking on a new direction, inquire, with the authors, what can be expected from the intravenous infusion of the principal elements which enter into the composition of the blood fluid: such is the aim which I propose to attain in the following paragraph, devoted exclusively to this important study.

§ III. WHICH, OF THE MAIN ELEMENTS THAT MAKE UP BLOOD, ARE THOSE THAT CAN REGENERATE THE VITAL PROPERTIES?

I recall that the fluid that circulates in the vessels of vertebrate animals can be considered as formed of two main parts: *plasma* and *globules*. In the fresh state, according to Professor Robin, in the adult man, the reciprocal proportions of these components would be 600 of the first against 400 of the last, per 1000 parts of blood.

The *globules* or *red blood cells*, well described for the first time by A. van Leewenhoeck a few years after the period of renaissance of transfusion (15 August 1673), have been the subject of numerous investigations during the course of the past two centuries, but, unfortunately, of no great importance from the point of view of the subject with which we are concerned; but we will not speak of them here, referring to the *classical treatises* those readers who would like to be informed about their form, their volume, their number, their composition, etc.

As for *plasma*, we will say only two words about it. It may be described as a special medium intended to contain red blood cells *in suspension*, to promote their functions and, probably, to nourish them. Its composition is excessively complex; however, we can give a fairly accurate idea of it by saying that it is a saline solution containing (Ch. Robin) from 14 to 16 grams 00/00 of crystallisable principles and 78 00/00, in the dry state, of a particular organic substance, coagulable by various reagents.

According to Denis, of Commercy, who has formerly done very remarkable work on this question, these 78 parts of organic matter could be decomposed as follows: 25 of *Plasmin*, an albuminoid substance which precipitates by the powder of sea salt, and 53 of *Serine*, which cannot be coagulated by this reagent. Finally, in its turn, plasmin would be formed of 3 of concrete or spontaneously *coagulable fibrin* and 22 of *dissolved fibrin*, differing from serine in that it precipitates by sulphate of magnesia. So that, according to Denis, fibrin does not exist in the blood in its normal state: what is designated by this name is only an artificial product resulting from the splitting of plasmin.

I finish here these considerations of biological chemistry, which will find their applications later, and I summarize the question by saying that, from the point of view of the subject with which we are concerned, it is sufficient to consider blood as a liquid formed of a plasma, *liquor sanguinis* if you will, and of globules. Let us now see what influence each of these two constituents can exert in transfusion.

As far as I know, the action of pure plasma has not been sought by infusing it into the vessels.

It is difficult, if not impossible to isolate it from the globules and to keep it as a liquid, because concrete fibrin solidifies very quickly and easily, so it is the *defibrinated plasma* or the plasma kept fluid with the help of certain chemical bodies (potash, soda, phosphate of soda, etc.) that was used in the experiments.

I must say, however, that most physiologists have been content to operate with ordinary serum, which may be considered, to a certain point, as defibrinated plasma.

a) *Transfusion with blood serum.* – I have already had occasion to point out the disastrous effects on animals of the intravascular infusion of a serum foreign to the species: this liquid acts in the manner of violent poisons, causes the animals to perish in convulsions, probably by destroying their blood globules, and indirectly causing a generalized embolism.

When it comes to the serum of the species, the results, while not so disastrous, are not satisfactory. Magendie (1838) injecting dogs with dog serum, caused this animal to be in such a painful state that it became "*intact*"; and death occurred if the dose was a little high.

This fact should not surprise us, since we know that the serum of the blood exerts a destructive action on red blood cells. The debris of these will obliterate the vessels and give rise to the known phenomena of vascular obstructions.

In the less serious cases, the animals become haemoglobinuric, albuminuric. Sometimes their blood loses the ability to clot and many die from typhoid symptoms.

Moreover, according to Dieffenbach, Magendie, Bischoff, Brown-Séguard, etc., *hot serum is absolutely unfit to recall to life an animal exhausted by a loss of blood.* If, following the example of Dieffenbach, an artificial serum loaded with dissolved fibrin is made, in order to transfuse it, the extinguished vital activity is not awakened. Nor is the well-oxygenated serum useful. This last fact is not surprising, for serum does not dissolve more oxygen than ordinary water (Ch. Robin).

Ultimately, blood serum has harmful properties, and it has no useful properties, therefore its role in transfusion can only be bad.

At most it can be considered as a simple vehicle for the globules, which, as we will see, have a completely different importance.

b) *The role of blood globules in transfusion.* – *Properties of defibrinated blood.* – Some animals exhausted by haemorrhage, transfused with blood globules suspended in water (Oré) or in an appropriate liquid were brought back to life. For example, Oré, transfusing six bloodless dogs with water holding red blood cells in suspension, was able to revive them; three have recovered, slowly, it is true, but completely. Therefore, we must attribute to red

blood cells the capital and preponderant role in the curative effects of transfused blood, and admit, with Dieffenbach, "that the globules are the true active principle of this liquid."

This conclusion was the origin of an operation which is important from a practical point of view, transfusion with defibrinated blood.

In fact, as we shall explain later, one of the most serious pitfalls which stop the doctor from deciding to perform a transfusion is the fear of injecting fibrinous clots with normal blood. In a few minutes: 1¹/₂, 2, 3, small fibrinous concretions are seen to form in the blood drawn from a vessel, and the danger is great of throwing such particles into the circulatory torrent. Now the defibrination of the blood, when it is exactly done, absolutely removes this serious inconvenience; so many physiologists have multiplied experiments to investigate whether defibrinated blood enjoys, from the point of view of transfusion only, the revivifying qualities of normal blood.

It may be said that the demonstration of the physiological fact is now perfectly established; there is no doubt that defibrinated blood possesses the tissue-stimulating qualities attributed to non-defibrinated blood.

Before citing the proofs of this assertion, I wish to specify that I do not intend, for the present, to speak of applications and to maintain that transfusion in man, practiced with defibrinated blood, is a good operation, by no means; I always stand on the ground of pure physiology. A little later, it will be time to address this controversial issue. Here then is the thesis that must be defended, namely, that defibrinated blood, like blood which has its fibrin, is capable of providing the tissues of the organism and the organs and apparatus with the *stimulus* necessary for their functioning; finally, to restore to life the animal dying of haemorrhage.

After Dieffenbach, Bischoff, in particular, has applied himself to make the following opinion prevail:

The danger of transfusion lies in fibrin, because this substance is really toxic or can become so; on the other hand, the blood globules are the only reviving elements of this humor; hence the necessity, one might say the obligation, to *infuse only defibrinated blood*, since experimentation clearly proves that animals exhausted by haemorrhage are revived by such a transfusion and recover.

Not only, according to Bischoff, does defibrination not deprive the blood of its qualities, but also, I repeat, it strips it of its toxic properties. Thus, the defibrinated blood of mammals is well tolerated by birds, and, conversely, mammals tolerate the defibrinated blood of birds: the rooster, the hen, the duck are not killed by the blood of dogs, and the latter animal, in an experiment of Bischoff's, could be transfused without inconvenience with an ounce of hen's blood. These results have been more recently verified by Brown-Séguard, who declares that oxygenated defibrinated blood is not toxic and that it can be injected with impunity between different species; thus, the blood of the amphibian is very well tolerated by dogs, cats, and rabbits, to which it is transfused.

But we still know many other facts which testify in favour of the safety of defibrinated blood; I will mention some of the main ones:

Brown-Séguard reported, a few years ago (20 February 1869) before the Biological Society, that he had revived a dog bled dry with defibrinated blood of pigeons; the animal heals.

Oré tells us that he was able to inject into the veins of a dog, from 15 to 20 grams of duck blood without testing it much, and into those of a duck, 30 grams of dog blood, without killing it.

These results are worthy of attention and deserve to be contrasted with the serious facts which we have previously pointed out in speaking of transfusion between different species.

However, it seems to me difficult to make fibrin responsible for all the accidents observed and noted during transfusions with blood foreign to the species, and I think that serum is no less guilty. Moreover, I find in a work by Ladislav de Belina (1873), one of the convinced supporters of blood defibrination, proof that defibrinated blood is not absolutely harmless, even in moderate doses: 60 grams of calf's blood cause rabbits to perish in convulsions, and at autopsy, the lungs are found to be engorged with blood, the digestive tract filled with

bloody mucus, the kidneys hyperemic and the muscles infiltrated with black blood. I see, moreover, that Worm Muller has not been more successful with the defibrinated blood of lambs in dogs; he killed these animals by injecting them with such blood and noticed when opening them pulmonary, intestinal, renal congestions, etc.

It therefore seems to me more accurate to conclude that if defibrinated blood does not have the serious harmful properties of normal blood when it is transfused between different animal species, it is far from harmless: it is a matter of dose. Perhaps the transfused globules disintegrate more quickly and more deeply after defibrination than when the blood has not been beaten, which would facilitate the elimination of haemoglobin: this would be one of the explanations for this relative safety, apart from the opinion which rightly attributes unfortunate effects to fibrin. The simple mixture of two heterogeneous bloods is sufficient, in fact, to determine the almost instantaneous appearance of fibrinous flakes in the mass; consequently the disastrous effects of fibrin cannot be disputed. Whatever these explanations may be, we are entitled, I think, to make this proposition: defibrinated blood, without being absolutely harmless, appears to be less toxic in transfusion than normal blood.

I will now endeavour to establish that it possesses, apart from this negative property, real positive qualities, as Dieffenbach and Bischoff affirm. It will suffice, for this purpose, to give here the summary of Polli's experiments, published in 1852, and to add to them some other facts no less convincing observed since.

The learned Italian doctor bleeds a dog white; he carefully collects the blood, defibrinates it by beating, filters it and injects it into the jugular of the inanimate animal: immediately the dog is pulled from the collapse, and later it recovers. Polli is careful to add that not all dogs treated in this way recover, but that in the end, quite often the transfusion succeeds.

In another circumstance, Polli removes 10 kilograms of blood from a mare, then, after 20 minutes, he injects into her vein 5 kilograms of this liquid, defibrinated and filtered through a stocking. The injection lasts $\frac{1}{2}$ hour; the beast is revived and does not die until after seven hours.

The success was complete in another horse which had lost only five pounds of blood: this humor, well defibrinated and injected in a dose of 1 kilogram 35 grams recalled him to life, and he recovered. A little later two kilograms of blood were drawn from the same animal, then this liquid was defibrinated, put in a tinned copper vessel and, after 24 hours, it was transfused; the horse was not inconvenienced.

A French physician, H. Quinche, 1858, made some similar experiments on 13 rabbits. He bled them white and gave them back their defibrinated blood. Six, who underwent this operation, revived and recovered. However, the other seven, not transfused, also recovered, albeit very slowly. While the former could eat after a few hours, the latter remained without food and in pain for 24 hours.

In 1860, Dr. Nicholas made similar experiments on rabbits, which it seems to me useless to report, as they only confirm the previous facts. Here are now other experimental results no less conclusive, and which we owe to Brown-Séguard.

Following the example of Kay (1834), he showed that defibrinated blood made rigor mortis disappear and restored muscular contractility and the excito-motor properties of the nerves. On the corpse of a tortured victim, Brown-Séguard, by transfusing his own defibrinated blood into the artery of a limb, restored the muscles of the latter to their irritability and motor nerves to their motor skills.

In a striking experiment, absolutely confirming the predictions of Legallois, he observed that by injecting defibrinated blood into the four encephalic arteries of a dog that had just been decapitated, he determined the appearance of *apparently voluntary* movements in the face,: calling the dog by its name, Brown-Séguard saw the *eyelids of this head open and the eyes turn towards him!*

One would therefore have no hesitation in accepting the conclusion of the skilful physiologist, namely that "the motor and sensory nerves, the spinal cord, can, after having lost their vital properties, in consequence of an interruption of the blood circulation, recover them under the influence of the oxygen-charged blood."

To this nomenclature of organs, we must necessarily add the brain, as the remarkable experiment of Brown-Sequard, which we have just reported, demonstrates this to us, and, moreover, mention the glands. It is known, in fact, that Ludwig, practising artificial circulation on a liver, made it secrete bile (1868).

Ultimately, defibrinated blood is a perfect exciter of vital functions, and it owes this property to the *globules charged with oxygen* (Brown-Séquard, 1855.)

The oxygenation of the blood is the capital fact; defibrinated blood loaded with carbonic acid kills the animals, and death is preceded by a period of convulsions (Eulenburg and Landois, 1865).

In summary, and to conclude, I will say, with Bischoff, Polli, and Brown-Séquard, that defibrinated blood can revive an animal thrown into the collapse by a serious haemorrhage, and that in losing its fibrin it is not stripped of its peculiar exciting qualities; I will say, with Panum (1863), that it is as invigorating as normal blood.

I will add, according to Polli, that fibrin is only an accessory element in the blood destined to be eliminated, which, in any case, is easily regenerated in the circulatory torrent. Is it necessary to say, moreover, that defibrination by beating promotes the oxygenation of the blood, and charges the red blood cells with large proportions of this gas? - The fact is beyond doubt.

Finally, it is not useless to point out with Dumas, Muller, Brown-Séquard, etc., that the *beating of the blood does not alter the microscopic characters of the globules*.

All the proposals and conclusions set out in the preceding pages are very attractive and constitute a plea of great value in favour of transfusion with beaten blood. However, serious objections may be placed in the face of the good reasons invoked and produced by the authors who support the cause of defibrination; I will list the main ones, without developing them much, reserving myself to return to this subject when I deal with transfusion in man, practiced with defibrinated blood.

Magendie condemns defibrination on the grounds that the blood deprived of fibrin loses its viscosity, extravasates into the tissues, circulates wrongly in the vessels, even stops in the capillaries, and usually causes visceral congestions and sero-bloody effusions in the serous cavities. For the eminent physiologist, it is the viscosity of the blood that makes it circulate in the vessels.

This opinion is also that of Poiseuille: "Without fibrin," he says, "the life of animals would often be compromised, because the blood slows down its course in the capillary vessels as it becomes poorer in fibrin."

Without doubt, red blood cells remain suspended in the blood fluid only by the special density of the plasma, and it is quite obvious that if this density decreases they will no longer remain in suspension; this is what happens when they are put in water or even in serum. However, the argument is not absolutely decisive; the blood can be greatly expanded with water without ceasing to circulate, and animals tolerate well the introduction of enormous quantities of water into their blood. So that Magendie's objection, serious as it is, can only be applied to cases where large proportions of defibrinated blood are injected, which is not realized in the normal practice of transfusion.

Here is another argument which seems to me to be absolutely theoretical; it was given by Devay and Desgranges. Beaten blood is no longer blood; and when it is transfused, only a medicinal infusion is actually injected. It doesn't matter if the medication is effective. However, physiological experiments seem to demonstrate excellent properties in this medicinal infusion.

Are we really entitled, moreover, to admit that the ordinary blood that has passed through transfusion machines is still living blood? Is not this mediate transfusion rather be a real medicinal infusion? This seems to me probable.

In my opinion, blood cannot be infused alive, at least by mediate transfusion; it is therefore only a medicine that this operation introduces into the economy, often a heroic agent, but which has only a fleeting role: like a good number of agents of the *materia medica*, it is destroyed in the organism and eliminated by various emunctories.

It is a real stimulant, by its oxygen-charged red blood cells; but its materials can hardly be used for nutrition. I can give proof of this.

Attempts have been made in vain to feed animals deprived of food by transfusion. Thus Blundell was only able to keep a dog for 3 weeks to which he injected, in several times, 84 ounces of blood. Eulenburg and Landois (1865) were not much happier; injecting a certain quantity of blood every 48 hours, from the 6th day, into a dog deprived of food, they could not prevent its death; the animal lived only 24 days, and had lost 36% of its weight. However, we know that dogs have been able to resist a rigorous diet for up to 29 days (Carville). It seems, therefore, that transfusion, as a means of feeding an animal, is more harmful than useful.

Joseph Casse carried out, in 1874, some experiments which demonstrate the probability of this harmfulness. In three observations which he reports, the transfused animals lost their weight during the absolute diet; and the loss was greater than during simple starvation, when he injected defibrinated blood. Worm Muller has also indicated that after transfusion the urea increases greatly in the urine: a dog whose blood mass had been increased by 28% gave up twice as much urea as the normal level.

Therefore it is indifferent, from the experimental and therapeutic point of view, that beaten blood is no more than a medicine, as soon as it is proven, and I believe the fact beyond doubt, that its stimulating properties remain with it.

It acts topically on the tissues, excites them, galvanizes them and restores their functioning. Once this impulse has been given, its role ends and it disappears. Transfused blood does not bring life, as the ancient transfusers thought, it only provokes vital manifestations thanks to its special dynamic qualities. Certainly, with Monneret, transfusion should be considered as an *anti-physiological operation*, if its pretensions went so far as to want to make the most of the life of the blood. "There is," he says, "in the blood, something other than albumin, fibrin, globules, physical, chemical and microscopic properties; *it has a life of its own.*" But, I cannot repeat it too often, this is not its purpose; the transfused blood excites the vessels, the heart, the glands, the nervous system, the haematopoietic organs perhaps, as electricity stimulates the muscular fibres; oxygen, lungs; food, the digestive system; etc., - it excites them, - I say, mechanically and by physical impression, rather than by virtue of its vital energy.

Consequently, and this is how I summarize these refutations, I conclude that from the *pure physiological point of view* the transfusion with defibrinated blood is a perfectly justified operation. We shall see later whether it is necessary to deduce from animal experiments that this operation is also applicable to the human species as a therapeutic method.

PART 4

CHAPTER 2

The qualities that blood intended for transfusion must possess.

Several of these qualities have already been pointed out, and we know that it is necessary to choose the blood of the species and inject it only as long as it is perfectly fluid, the presence of small fibrinous concretions being the source of serious dangers. There are, however, other peculiarities, useful to know, which we will study in the various paragraphs that follow.

§ I. SHOULD ARTERIAL BLOOD OR VENOUS BLOOD BE TRANSFUSED?

This question may seem rather naïve, after the ideas we have just put forward on the action of blood and the preponderant role of *oxygenated globules* in transfusion. They alone possess, in fact, the property of exciting the vital properties, and it seems that we are entitled to draw from this fact the conclusion that arterial blood must be used exclusively since its red blood cells are perfectly charged with oxygen. However, this is only a simple theoretical view, which cannot resist the very peremptory argument, namely, that venous blood

introduced into a vein passes rapidly into the right heart, and from thence into the lungs, where it undergoes haematosiis, and becomes arterial blood. Consequently, we can already say that the oxygenation of the blood is only a secondary question, because it is necessarily accomplished as soon as this humor has penetrated the circulatory torrent, so that it is indifferent, from the point of view of the final result, to practice the *mediate transfusion* with arterial blood or venous blood.

In *immediate transfusion*, on the contrary, there is only one resource, that of opening the blood donor's artery, because so far no authentic example of *veno-venous transfusion* has been cited done with full success.

A certain number of more or less solid reasons have been given by the authors in favour of the choice of arterial blood. Its red blood cells are more resistant and circulate better in the vessels; they are more regular in shape and more elastic, as a result of the presence of oxygen. Therefore they prevail over the globules of venous blood, which are softer, easily stretched, viscous, and less suitable for circulating conveniently, and even very capable of clumping together, and of obstructing the capillaries.

This argument would be of some importance if it were based on well-proven facts and, moreover, if the injections of blood were to be copious; now, with a few grams, an ounce of this humor, excellent results are obtained, real resurrections are effected in animals bled white; consequently it is useless to concern ourselves with the resistance of venous red blood cells, especially since the haematosiis will restore them, with oxygen, to their regular shape and elasticity.

Moreover, arterial blood coagulates, say most physiologists, more quickly than venous blood; this is a severe disadvantage to be taken into serious consideration, as it appreciably reduces the short time available to the operator to transfuse a very fluid blood.

A difference of one less minute, out of three or four to which one can claim, singularly complicates the operation or makes it very dangerous. In truth, there is not much agreement as to the respective rapidity of the coagulation of the two species of blood, and while the greater number of physicians or physiologists admit that arterial blood coagulates more rapidly than venous blood, Blundell and Davy want the reverse to be rather true, and they point out a two-minute delay in the coagulation of the arterial blood of man, compared to that of venous blood; finally, Berthold and Saissy also speak of a similar difference of $\frac{1}{2}$ minute in calves or goats.

The first opinion seems to me to be the best, or, at least, the one that is most often verified. Besides, how can we get along? - the conditions which cause the proportions of fibrin in the blood to vary are so diverse and numerous that it is difficult to lay down fixed rules as to the relative quantities of fibrin contained in the two bloods, black or red. Fibrin does not normally exist in the blood as fibrin properly so-called, as I have said from Denis, but there is a substance fibrinogen, which is absolutely different from it, even from the chemical point of view, and whose variations are enormous from one vein to another. For example, it is a certain fact, easy to verify and generally admitted, that fibrin is lacking in the blood of certain veins; Lehmann and Brown-Séguard have noted this for supra-hepatics: their blood no longer gives fibrin when beaten and is not coagulable.

For the renal veins or for the veins of other glands, it is the same thing, according to Franz Simon, Cl. Bernard, Brown-Séguard. So that it could be said, in a general way, that the blood loses its fibrin by passing through the secretory glands. On the contrary, this substance would regenerate in the blood that passes through a muscle, because Lehmann found more fibrin in the superficial veins of the limbs than in the arteries.

Many other circumstances or conditions may vary the proportions of fibrin in the blood, so that we should only place relative confidence in the various analyses which inform us of the exact composition of this humour; they give only averages or approximations.

How can we be surprised, then, at the absolutely opposite opinions expressed on this apparently very simple subject of blood coagulation! All observers saw it correctly, there is no doubt about it, but they have made the mistake of generalizing and of wanting to draw from a particular fact an invariable rule.

If the fact pointed out by Lehmann, of the greater proportion of fibrin in the blood of the superficial veins, is very constant, we might deduce the consequence that the blood of the superficial arteries coagulates more slowly than that of the veins. On the other hand, on the basis of the experiments of Brown-Séguard, Cl. Bernard, etc., one would be entitled to affirm that the blood of the deep veins is less coagulable than that of the corresponding arteries. Thus, agreement would be possible between the contradictory statements that we have pointed out.

I will not dwell any longer on this subject, which is of interest only from the point of view of experimental medicine. In man, in fact, it is impossible to think of using arterial blood for transfusion; and, despite several successful attempts in Germany, we believe that this practice has no chance of being adopted in our country

To return to the question that concerns me in this paragraph, and to summarise the main facts which emerge from the preceding considerations, I will say that we point to the advantage of arterial blood is the better condition of its red blood cells, its richness in oxygen, its stimulating qualities, its delayed coagulation, and, finally, the greater number of its globules.

Let us now see whether these qualities are important enough to make it preferred to venous blood. Theoretically, arterial blood is better; practically, it is no better than black blood. In fact, by defibrination one can load red blood cells with oxygen and rid the blood of its fibrin, which immediately makes it a kind of arterial blood that is incoagulable or rather poorly coagulable. If this defibrination is feared, well, with a little activity it is possible to inject a perfectly fluid venous blood; and after a few moments this blood will undergo haematoses in the lungs and become arterial blood.

A good reason has even been given in favour of the choice of venous blood, namely, that it is more stimulating to the veins and right chambers of the heart than would arterial blood be to these tissues. If the demonstration of this theoretical idea has not been made, it has probability on its side. Moreover, black blood is a physiological stimulant of the chambers of the heart, right or left; the experiments of Haller and those of Bichat clearly prove this. The illustrious author of the *Researches on Life and Death* concludes that "black blood excites almost as much as red blood the internal surface of the cavities which ordinarily contain the latter....." and he thinks that if there is a difference, it is reduced to very little.

Brown-Séguard is even more affirmative than Bichat, and he attributes to venous blood greater exciting qualities than to arterial blood; for this distinguished physiologist, venous blood gives tissues life *in action*, while arterial blood would give them life *in potential*.

Consequently, I think I can conclude that the choice between venous or arterial blood is, from the point of view of the success of the transfusion, almost indifferent. It seems even more rational to take the latter, as it is more stimulating of the veins and right chambers of the heart and more capable of mixing easily with the blood of the transfused animal.

§ II. WHO ARE THE BEST BLOOD DONORS?

In human transfusion, as we shall see later, one is not always spoiled for choice; a devoted person offers his blood, the doctor accepts it without worrying much about the theoretical considerations put forward by the authors. If the subject appears to him to be healthy, he will ask no more, happy to take advantage of this generous sacrifice and to offer the benefit of it to the patient who is about to succumb, if one does not try to apply this last resource. But, when studying transfusion from the experimental point of view, it is advisable to mention certain indications that have their small value.

We know that the number of blood cells is important, since these are really the active elements of the blood; so the richer this liquid is in red blood cells, the more reviving properties it will have.

The richness of globules is very variable; however, there are some facts beyond doubt, which we must quote. Thus, the younger an animal is, the more red blood cells its blood contains. For example, while the blood of the newborn contains from 600 to 700 parts of cells to 300 or 400 of plasma in 1,000, that of the adult man consists of only 300 to 400 red blood cells to 600 or 700 of plasma, which is a completely reversed proportion (Robin).

Hence it follows that the blood of a very young animal should be taken above all to practice transfusion; generally again, in such cases, the dimensions of the globules are a little smaller.

In addition, it is said that the blood of young animals is less easily coagulable and that it absorbs oxygen better than that of adults.

Finally, it is necessary, as far as possible, to take the blood of a male, which is always richer in figurative elements than that of the female.

In men, there are 141 00/00 globules and in women only 127 (Becquerel), figures which agree with those given by Lecanu in 1831, 149 in men and 129 in women.

§ III. AT WHAT TEMPERATURE SHOULD THE BLOOD BE TRANSFUSED?

It is natural to think that the closer the blood temperature is to body temperature, 37.5°, 38°, 39°, the more favourable the chances will be. This is not the case, as we will see. In the past, when an immediate transfusion was done, we did not fail to surround the container containing the blood to be transfused with hot cloths, in order to delay coagulation. Malgaigne was the first to combat this practice, showing that the closer the temperature gets to zero, the more slowly the blood coagulates. In fact, first Hewson, then Hunter, were the first to teach us that cold does not produce blood clotting. Hewson freezing the blood made it fluid by warming it and soon saw coagulation will occur. In one of his interesting notes appended to Hunter's works, Palmer mentions that Sir C. Scudamore observed that "cold retards coagulation, in about the same proportion as heat accelerates it."

More recently, various experimenters have made the same remarks. Professor Robin has noted that the blood which falls into a refrigerating mixture at 0° coagulates only very slowly, and Dr. Oré points out this peculiarity, that "the more the blood is cooled, after it has left the vessels, the longer time it takes to coagulate," a fact based on his numerous experiments. Here, moreover, according to Robin, the progress of coagulation at various temperatures: very slowed down to zero, it increases appreciably between 12 and 14 degrees and does not increase much until 30°, then obviously slows down from 30 to 40 degrees.

Let us go into the details of the facts for a moment. At 8° above zero, Hunter saw the coagulation of human blood take place only after twenty minutes, and at 0°, Davy (1820) noted that it was delayed by an hour.

If the blood is subjected to higher temperatures, the following is noted: at 45°, the blood of animals overheated in an oven remains incoagulable (Cl. Bernard), but at 50°, heated in a vessel, it coagulates more rapidly than at 38° (Polli). Finally, to conclude this question of the influence of heat, let us quote the opinion of Prater, who maintains that very high temperatures, as well as low temperatures, render the blood incoagulable.

What results from this data? The following two facts seem to me to be the best answers to this question: 1° to delay the coagulation of the blood this liquid can be heated to between 30 and 40 degrees; 2° or cool it to between zero and 12 degrees. The cooled blood remains perfectly reviving, when the cold does not fall below zero; and on the other hand, when it is heated too much, it completely loses its special properties (P. Bert).

A number of experiments have been carried out to demonstrate that blood cooled between zero and 10 degrees is capable of regenerating vital properties.

In 1860, Dr. Nicolas did some work in this direction, after having been inspired by this sentence of Malgaigne: "It is not cooling that brings about the coagulation of the blood, quite the contrary; and when one wishes to try transfusion, one will henceforth know that, to keep it liquid, the best thing to do is to cool the vessel and the syringe."

Here is one of his experiments. The carotid artery of a rabbit is opened, and thus completely exhausted; then, when the heart has ceased to beat and the respiration has been accomplished, it is transfused with 10 cc of arterial blood cooled to 8°. Soon the animal comes back to life and recovery takes place, complete and easy. Two other similar experiments (observations XIV and XV of the memoir) are reported by Dr. Nicolas, which show that the cooled blood has not lost its stimulating qualities for this reason. At 8 degrees,

says this experimenter, the coagulation of the blood is very delayed: at the end of an hour, it is far from complete, which makes the operation considerably easier.

Dr. Oré has achieved identical results by operating on dogs.

Three of these animals, rendered bloodless, were revived by the injection of 100 grams of blood cooled to 6°; they recovered.

It was natural to wonder whether the injection of blood whose temperature is well below normal does not cause any disorder. Joseph Casse has more particularly studied this question recently, and gives us interesting experimental information on it which we are going to report. It should be noted first that in all the observations reported it is a depletive transfusion.

1° Into the veins of a dog he infuses 150 grams of blood cooled to 5°, but whose temperature rises to 10° during the operation; the disorders are zero and the dog's temperature is not noticeably modified.

2° In a second experiment, he injects a small dog with 150 grams of blood at 3°. The temperature rises a little, the pulse increases in frequency, in a word, the animal has a fever. These accidents do not last and the dog is not otherwise tested.

3° A dog receives 150 grams of defibrinated blood at 27°, without experiencing the slightest inconvenience.

4° Another experiment identical to the previous one.

5° On a dog, 110 grams of defibrinated blood is first transfused, then shortly afterwards 40 grams of the same blood cooled to 27°; slight fever.

6° 160 grams of defibrinated blood with a temperature of 47° is transfused into the veins of a dog. The pulse is affected and accelerates slightly.

7° In a similar experiment, 160 grams of defibrinated blood at 50° is injected. Breathing and pulse accelerate, temperature rises, and then everything returns to normal.

8° 160 grams of defibrinated blood is injected at 55°; the effects are the same as before.

In all these experiments we have never observed any serious phenomena; the dogs tolerated the introduction of cooled or heated blood well. When the blood is very cooled the temperature first drops, the pulse decreases in frequency a little, then there is a sort of febrile reaction and the animal recovers. When it is heated, the animal heat rises a little, but it does not take long to return to its physiological level.

However, are not these thermal variations due to the operation, to the trauma? This is unlikely, because Frese's observations demonstrate that transfusion of up to $\frac{1}{10}$ of the total mass of blood does not raise the temperature. The elevation is only shown when $\frac{1}{4}$ or $\frac{1}{3}$ of the mass of the blood is infused.

To conclude, I will say that the lowering of the temperature of the blood to be transfused does not modify its revivifying properties and that the accidents to be feared are zero or insignificant when a depletive transfusion with such a liquid is practiced. Nor is defibrinated blood warmer than the blood of the body dangerous to the animals into which it is injected.

§ IV. CAN BLOOD MADE INCOAGULABLE BY CHEMICAL AGENTS BE TRANSFUSED? – SOME INDICATIONS ON BLOOD CLOTTING.

A certain number of chemical agents have, as is well known, the property of retarding or preventing the coagulation of the blood. The question to be solved is whether the liquid thus obtained is still suitable for reviving the tissues. Before giving the solution, let us briefly examine what are the agents which oppose coagulation and recall the main facts known about the interesting phenomenon of coagulation; it is important to describe them well when dealing with transfusion.

For a long time now, Prévost and Dumas have taught us that a thousandth of potash or soda is enough to prevent the blood from coagulating, and, according to the same authors, Boyle and especially Richardson, ammonia has the same property. According to the latter experimenter, who published in 1858 an important memoir on this subject, analyzed in the *Journal de la Physiologie*, by Brown-Séguard (1858, 1st year), the blood is, in the normal state, kept fluid by a gaseous body which can only be ammonia in different combinations according to the animal species. This principle, he says, is eminently volatile. For if the

blood is compressed and thus prevented from being released, there is no coagulation, and there is no more coagulation if it is cooled. On the contrary, by promoting the release of this body, by raising the temperature of the blood, or by placing it in a vacuum, coagulation is made more rapid. Unfortunately Richardson's ideas are open to attack and have been successfully fought; so that today his theory is no longer adopted. The result, however, is that the mixture of 1 part of ammonia to 500 of blood remains fluid.

Among the other substances that prevent blood clotting is sodium chloride (Hewson), active at a dose of 20 grains (1^{gr}20) per ounce of blood (Richardson). In a very recent study (See: *J. de Pharmacie*, of September 1875), Gautier indicates that sea salt, in the proportion of 4%, prevents or delays coagulation without altering the corpuscles. These retain their general shape, do not lose colouring matter, but seem to contract slightly. By filtering the mixture at 6 or 8°, the plasma is easily separated from the globules.

Finally, I will mention, among the chemical agents used to retard the coagulation of blood intended for transfusion, sodium sulphate (Figuier, Lecanu, Denis, Desgranges), sodium phosphate and sodium carbonate.

It is quite obvious that all these chemical bodies act on the concrete fibrin and keep it fluid; we have ascertained this directly.

But let us enter further into this study of blood coagulation, which is a question on the agenda, as evidenced by the numerous works recently published on this subject.

When left to itself, in any vessel, blood draws from the vessels, it does not take long to form in the fluid mass a fibrinous network, with increasingly narrow meshes, which traps the globules to form the clot. I have just said that heat, cold, certain chemical agents accelerate or activate the phenomenon, I do not have to return to these points and I move on to enumerating the other conditions which influence its development.

In the various animal species the clot forms more or less rapidly; thus the blood of the dog and that of birds coagulates almost as soon as it leaves the vessels; on the contrary, the horse's blood remains fluid for a long time.

Tackrah tried to establish some kind of law governing this phenomenon by saying that the clotting of blood in the various animals is due to size. Without taking Tackrah's assertion literally, which is too absolute, we can nevertheless rely on the following figures: the coagulation of horse blood is complete between 5 and 13'; that of ox's blood, between 2 and 10'; that of sheep's, pig's, rabbit's blood, between $\frac{1}{2}$ and 1'; that of dog's blood, between $\frac{1}{2}$ and 3'; duck, between 1 and 2'; of the hen, between $\frac{1}{2}$ and 1 $\frac{1}{2}$ minutes; finally, the coagulation of the mouse blood is almost instantaneous.

The same author, continuing his researches on the coagulation of blood, observed that the shape of the vessel containing this liquid, and especially the nature of the walls of the vessel, exerted a certain influence on it. In effect, the more flared the container, the more rapid the coagulation and, conversely, the smaller it is, the less quickly it takes place. A copper vessel delays coagulation, while a tin vessel facilitates it. These data are of some importance from the point of view of the construction of transfusion devices. Generally their containers are cylindrical, in the shape of a test tube, and made of glass, circumstances favourable to non-coagulation.

In the past, it was believed that contact with air greatly encouraged the bulking of blood. The illustrious Hunter has easily refuted this opinion, particularly supported by Hewson, by showing that blood put in a vacuum coagulates more rapidly than that which is left in the air; and Davy has shown that this liquid, received under a layer of oil, behaves as in the open air. Therefore, air has nothing to do with the phenomenon of blood clotting. However, Oré reports that the blood received in a rubber ampoule is sheltered from the air and coagulates a little more slowly than under ordinary conditions.

To realize this curious property of the blood, we must seek its explanation in the intimate modifications which take place in the fluid blood itself.

Scudamore, basing himself on the fact that carbonic acid gas advances the coagulation of the blood, thought that he found in the release of this gas the essential condition for the production of this state of the blood. This opinion has recently been taken up and developed with great conviction in a well-done work by Messrs. Mathieu and Urbain. The authors have

accumulated in their memoir a host of arguments in favour of this thesis, which they maintain, namely, that "the spontaneous coagulation of fibrin is a true chemical precipitation, determined by carbonic acid normally contained in the blood."

"If," they say, "this gas does not act on the blood contained in the vessels, it is because it is retained by the corpuscles, which have a great affinity for it. But if this gas accumulates in the blood, as happens during asphyxia, we will see many coagulums form in the vessels."

One of the strongest proofs which the authors give in support of their theory is that the coagulation of the blood can be prevented by removing its carbonic acid.

It is not for me to decide whether the opinion of Messrs. Mathieu and Urbain is the right one; these authors rely mainly on chemical data, and I decline all competence on this subject, but I can say that their thesis is provided with solid arguments. As for the explanation which these experimenters propose to explain why the blood remains liquid in the vessels, it seems to me difficult to accept. Until further notice it seems to me prudent to hold to the old opinion of Hunter, and to admit with that great physician that "it is the vitality of the body or the vessels that maintains it in a liquid state. For it, he adds, the vessels have the ability to keep the blood in a fluid state." The fact relating to this influence of the vascular walls is indisputable, as is proved by Hewson's old experiment: blood enclosed in a vessel between two ligatures remained $\frac{2}{3}$ fluid for $3\frac{1}{4}$ hours; and it has been confirmed time and time again.

More recently, F. Glénard has come up with new experimental evidence to support Hunter's opinion and give it a new interest. We are going to relate in some detail the interesting experiments of the French physiologist, because of certain applications that have been made of them to transfusion.

If we force the blood to accumulate in a vessel, between two ligatures, and then remove this sort of aneurysmal pouch, we have what Glénard calls a *segment*. Now this experimenter has seen that the blood contained in an arterial or venous segment, detached from a living animal, does not coagulate, whatever the capacity of the segment, and that if evaporation is prevented on the surface of the bag, it remains liquid for the space of 12 to 15 hours. So that, according to Glénard, the blood outside the vessels coagulates by the mere fact that it is in contact with a foreign body; while, as long as it remains in contact with the vascular walls, it retains its liquidity, on condition, however, that it does not concentrate by evaporation. The gases, moreover, cannot act on it, and one can place filled segments in atmospheres of carbonic acid, oxygen, hydrogen sulphide, etc., without observing a more rapid coagulation of their contents.

In summary, the vascular walls enjoy the property of acting by impression on the blood and of keeping it liquid: the experiments of Hewson, mostly those of Glénard, put the fact beyond doubt. Now, can we hope that by making segments on the animal according to the Glénard method, we will be able to prepare real reservoirs of liquid blood, the contents of which the doctor will use to perform transfusion? This question has not yet been resolved.

Many times, indeed, Glénard has used the blood of segments to transfuse it into animals, and he has almost always succeeded. For example, by injecting into the veins of a dog bled white the blood of a segment taken from an ox, he was able to recall the animal to life; or else practising transfusion between very different animal species, he remarked on the complete harmlessness of the injection of foreign blood. But it is unlikely that these laboratory experiments will ever receive good clinical applications and that the blood of the segment taken from an animal: sheep, lamb, calf, etc., will be infused into the veins of a man. It would be better to have recourse to immediate transfusion, which is not difficult to practice, if it were judged that the blood of animals could be useful to man. Do we really know, in fact, what is contained in the segment which is emptied into the veins of a subject, and does not the blood have in its mass fine particles of fibrin? Glénard's experiments perhaps answer this question themselves: several times, by transfusing animals with blood foreign to their species, he made them very sick or killed them. We therefore do not conceive the usefulness of vascular segments in transfusion, and this operation is just as simple and effective, performed with defibrinated blood and, above all, when direct communication is established between the vessels of the animals.

In short, we see that in order to keep the blood fluid artificially, apart from defibrination, it is necessary either to cool it or heat it a great deal, or to add chemical agents to it, or finally to keep it enclosed in segments. What value do these various processes offer from the point of view of transfusion?

I have said that by lowering the temperature of the blood to 4° above zero, or by raising it to 40°, a perfectly reviving liquid could be obtained; I have also just shown on the other hand that one could not rely on segments; it is therefore only a question of examining whether the blood rendered incoagulable by chemical substances can be useful. Well, my answer is no. Most of them, one might say all, attack the blood cells. Potash, soda, ammonia deform them, give them viscosity and, consequently, make their circulation in the fine capillaries difficult or impossible; consequently these are bad means. Thus it is necessary to renounce the sodium phosphate, advocated by Braxton Hicks; three times this physician failed in man by transfusing blood kept fluid by this salt (*Guy's hosp. Rep.*, 1869). Also the use of soda ash, which was rightly rejected by Pavy (*Guy's hosp. Rep.*, 1869), must also be abandoned; to sea salt, for which Higginson himself did not praise in a case of transfusion in man.

Without doubt, the experiments attempted with sodium phosphate and sodium chloride are not yet numerous and there would be interesting experimental studies to be carried out in this direction; but it may be said, *a priori*, that somewhat concentrated saline solutions, such as must be prepared to prevent the coagulation of the blood, must be harmful to red blood cells, and that, in short, it is better to practice the beating of the blood than to expose it to the physicochemical actions of phosphate or sodium chloride.

To conclude this long study of *transfusion from the pure experimental point of view*, I have only a few words left to say about the operating manual. I will be brief, for I am willing to remain in the field of physiology proper so called only as far as I can find explanations or applications from which therapeutics can profit. However, as the doctor may be tempted to repeat the operation on animals before performing it on humans, I will briefly indicate the main operating methods used in transfusion in animals.

I have said that transfusion is *immediate* or *mediate*, depending on whether the blood from the donor's artery is passed directly into the veins of the recipient, or according to whether the blood collected in a transfusing device is injected into the latter. *Immediate veno-venous* transfusion has been tried in vain (Camille Morel, 1856); it is a process whose material impossibility is easily understood, the blood can never be thrown with sufficient force from one vein into another.

To do the *immediate arterio-venous transfusion*, the large vessels of the neck or thigh jugular and carotid artery and femoral vein, are carefully uncovered and stripped to a certain extent: the artery in the animal that supplies the blood, the vein in the one who receives it.

This done, two ligation wires are passed under the vessels, which will serve to lift and bind them; then the artery is clasped between two ligatures very close to each other, it is cut between the wires, and its central end is joined to the simply incised vein, by means of a small very short conduit, pipe or cannula, held securely attached to the two vessels. The arterial ligation is then released: the blood fills the conduit and passes into the vein in a quantity that varies according to conditions foreseen in advance by looking for how much blood flows in the space of a minute through the gaping unfinished artery. This is approximately the procedure described by Lower in 1667 (See: *J. des scavans*, 16 January 1667) and which has since received only modifications of detail. The English physician joined the carotid artery to the jugular by means of feather tubes, and he placed in the cephalic end of the transfused animal another feather tube intended to give the blood a free flow in order to avoid plethora. Lower's aim was, as we see, to demonstrate that the blood of one animal could be passed to another without compromising the existence of the latter.

Today, in laboratories, mediate transfusion is more often practiced, either by means of the devices used in humans, or by injecting defibrinated blood by means of a syringe. I will talk about the devices later. For the moment I am content to say that I give preference to the simplest method, to the ordinary syringe which is loaded with normal or defibrinated blood and the contents of which are emptied into the vein incised in a V shape or mounted on a small cannula.

I finish here these considerations of experimental medicine, which have taken me far too far. Unfortunately, it was very difficult for me to pass them over in silence or to shorten them, since they are the best guide for the doctor who wants to see beyond the simple application of a therapeutic method. From this study, in fact, result a certain number of interesting facts which I think it good to summarize in the form of conclusions and which will recall the main discussions in which we have engaged in the two preceding chapters. By retracing our steps quickly in this way, we will better see the milestones left from distance to distance on the path travelled.

Conclusions to be drawn from the previous chapters.

1° The transfusion of blood is an operation whose value is put beyond doubt by experimental physiology: it revives bleeding animals and facilitates their recovery;

2° It is inapplicable between animals of different species, although nevertheless some favourable observations have been reported. The best thing is to infuse only the blood of the species;

3° In the blood, the active element is the globule; plasma has no reviving properties; therefore it is possible to operate with defibrinated blood;

4° If the question of the superiority of defibrinated blood over normal blood has not yet been demonstrated, it is nevertheless proved that it has a real value in reviving an exhausted animal, and that, moreover, as blood foreign to the species, it is less toxic than non-defibrinated blood;

5° The blood acts as a stimulant of the vital properties of the tissues; but it is not a food, and still less the vehicle of a vital principle capable of regenerating or transforming a weakened body;

6° The infused blood, after having acted as a stimulant, is eliminated (the globules) by various emunctories, the principal of which are the kidneys and the intestine;

7° It is preferable to choose the blood of a young animal, because its globules are smaller and more numerous, and it is immaterial whether arterial or venous blood is taken when the mediate transfusion is practiced;

8° According to Dieffenbach, neither age, nor sex, nor the different states of the body determine any change in the action of the transfused blood;

9° The temperature of the blood can be lowered to 4° without inconvenience; but it cannot be raised much beyond 37°; between zero and 40°, the blood nevertheless retains its reviving qualities;

10° The injection of blood kept liquid by the addition of certain chemical agents is dangerous and probably devoid of useful effects;

11° Mediate or immediate transfusion can be practiced in animals indifferently; but it is possible that the former is more effective than the latter.

PART 5

SECOND PART: THERAPEUTIC APPLICATIONS

CHAPTER 1

TRANSFUSION IN SERIOUS HAEMORRHAGES

It is really strange to see how difficult it is for the most elementary facts, in medicine as in all things, to impose themselves on the attention of observers. A man has a considerable haemorrhage and is about to die bloodless; what could be more natural than to think of giving him back a part of what he has lost! No doubt the idea is simple; well, it has taken centuries to achieve this, and I hardly dare to say that even today it is much discussed and even treated as chimerical by some physicians.

The first transfusions, in the 17th century, blinded by their bizarre conceptions of transfusion, which they considered as a remedy for the deterioration of our body, only very vaguely glimpsed the application of this operation to acute anaemia. Led astray by a seductive mirage, they wander about on adventure, seeking the impossible, and are careful not to worry about that rational application which could be imposed on them by the most vulgar common sense.

However, at the end of the 18th century, some Italian doctors, Michel Rosa in particular, and the Englishman Haarwood, revived bleeding animals by giving them blood, and thus showed the excellence of the method. But in man, no transfusion was reported in a case of sudden haemorrhage before 1825. It is true to say that Denis, our compatriot, performed his first operation on a young man exhausted by a long illness and repeated bloodletting; this, however, was only a case of ordinary anaemia, which could be cured by simpler means, and this bold innovator did not go any further in this direction.

It is to Blundell that we must attribute the merit of having revealed the value of transfusion in serious haemorrhages, either by his fine experiments on animals, which I have already made known, or by his audacious attempts on man, fortunately crowned with complete success.

In a woman suffering from an excessive haemorrhage which had plunged her into a state of apparent death, he had the happiness of seeing the transfusion of 180 grams of blood prevent the fatal outcome.

From then on, the main indication for this operation was formulated and its effectiveness highlighted.

Since 1825 the observations of successful transfusion in abundant haemorrhages have multiplied, and we already possess sufficient data to establish in principle that this is the best therapeutic resource we can have at our disposal in such cases.

Let us now see to the clarification of the facts by studying the applications of this method in each of the varieties of serious haemorrhages in which it has been used.

§ I. TRAUMATIC HAEMORRHAGES.

It is not difficult today to cite facts in which it is reported that subjects rendered bloodless by an injury have been revived and cured by transfusion. A few examples are even absolutely comparable to those curious experiments which are carried out in physiological laboratories on animals bled white, and which are cured by the injection of blood.

In 1839, Doctor Samuel Lane performed strabismus surgery on an 11-year-old boy. The patient unfortunately suffered from haemophilia and during the operation he suffered repeated losses of blood which put him in the most worrying state: he was without a pulse, had lost consciousness; excessive pallor, cooling. A syringe is loaded with human blood and five and a half ounces are injected into him in 4 times. Immediately the patient is revived, his pulse and his intelligence reappear; soon he is out of danger. He later recovered from his strabismus and haemophilia.

Other cases are no less curious; I mention them in substance so as not to lengthen this study.

In 1829, Philpott cured a fat woman who had become bloodless as a result of a ruptured varicose vein, by transfusing 120 grams of blood into her.

In 1833, Walton also succeeded in reviving by transfusion an operated phimosis patient who had been exhausted by excessive blood loss.

Then come other similar facts from Astley Cooper, 1840 haemorrhage during the removal of a tumour of the back; - by Blasius, 1842: haemorrhage after an injury to the lower limb; - by Michaux, 1860, haemorrhage during the removal of a nasopharyngeal polyp; - by Higginson, 1868 haemorrhage in a subject suffering from phlegmon of the forearm; the operation was so successful that this man was able to bear the amputation a little later; he heals.

Other doctors have reported some successful transfusions in cases of traumatic haemorrhage: Furner, 1844; Sacristan, 1851; Kwasnicki, 1868; Braman, 1868; Leisrink,

1872; Albanese, 1873, in amputees or subjects affected by wounds of large arterial or venous vessels (varicose veins).

Unfortunately the transfusion has not always been successful, and we must not omit to point out its failures. In 1829 Danyau, in London, transfusing an individual weakened by a great loss of blood resulting from a serious wound in the leg (a complicated fracture), was able to galvanize him sufficiently to enable him to undergo amputation, but it did not prevent his death. The following year, Roux failed even more completely in a wounded man who had his subclavian open, death immediately followed the transfusion. In 1833, Scott saw a young girl die before his eyes who he was operating on for a neck tumour, despite the transfusion. Finally, Maison-neuve (1854), Neudorfer (1860), Simon (1865), Lister (1869) and Maurice Raynaud (1871), reported similar failures.

In short, we can now bring together twenty-two cases of transfusion performed on subjects suffering from serious haemorrhage after a trauma, and singularly compromising their existence. Thirteen recovered, i.e. a little less than 60%; nine succumbed, i.e. a little more than 40%.

I could point out, as other authors have no doubt already noted, that transfusion is not absolutely responsible for the nine failures. In fact, Scott's patient had his jugular open during the operation, and may have died as a result of the entry of air into this vessel; Simon's was suffering from pneumonia; that of Lister, of tuberculosis in the 3rd degree; finally, Mr. Raynaud, who operated on a soldier affected by a carotid wound, with the help of defibrinated and filtered blood, accuses himself of having taken a long time to transfuse. When one waits too long, he says, there can occur between the time of haemorrhage and that of death a generalised steatosis that the transfusion cannot cure and which makes its success impossible.

Ultimately, transfusion can be considered a first-rate remedy for blood loss that follows trauma. It would be difficult to understand if it were otherwise, and it seems to me that it is not rash to state this proposition, theoretically, in a case of traumatic haemorrhage threatening the life of a subject, the transfusion well done must always ward off the danger if it is carried out in time. The organs are healthy, and if they have ceased to function, it is because they lack their natural stimulant, oxygenated blood. It would be very strange if this stimulus were restored to them, while they are still impressionable, and their vital properties remained powerless to recover.

It must be admitted, and Professor Gubler has developed this idea at length which is personal to him, in his course at the Faculty this very year, it must be admitted, I say, that the blood rapidly infused from one body into another continues its role completely in the latter: "it fulfils all the functions of personal blood; its globules continue to be the vehicles of gases, the agents of exchange essential to respiration and nutrition, the centres of attraction for plasmin, fixing albumin and opposing its exit from the vessels."

Therefore both the clinical facts, and the physiology, and the reasoning lead us to consider transfusion as perfectly indicated in the haemorrhages of the wounded; it is truly curative and capable of producing those resurrections which we know in transfused animals.

Unfortunately, it is only applicable in a very limited number of cases. The doctor does not always arrive in time; he does not have at hand the few indispensable instruments; blood is lacking; he hesitates to try the latter resource; soon it is no longer time, and, if he has made up his mind, it is on a corpse that he operates, as some observations testify. It is important, in such circumstances, that the practitioner resolutely takes his side and finds in this rapid decision the means of making up for all that he lacks. A syringe of some kind, a scalpel, a lancet will constitute for him a sufficient instrumental device; and as for blood, he will easily find it: grave dangers easily inspire the devotion of all and no one will shrink from the inconvenience of bleeding to save the life of an exhausted wounded person.

Maurice Raynaud did not hesitate to have his vein opened and to give his blood for one of his patients. This generous sacrifice, although very worthy of admiration, is not to be imitated, unless the doctor can take a back seat as an operator in front of one of his colleagues and has no other way of intervening usefully in the operation.

There are certain circumstances in which transfusion can become a great therapeutic resource, and that is during surgical operations which are suddenly complicated by lightning haemorrhage. As soon as haemostasis is achieved, the patient must be transfused if his condition is alarming.

The use of defibrinated blood has been indicated in serious haemorrhages, but it seems to me safer to inject only normal blood. Defibrination wastes precious time, and when it is necessary to count per minute in an operation, it is a great deal to waste five or six minutes beating the blood and filtering it. And then the blood deprived of fibrin is less plastic. A few experiments by Nicolai Tabouré, of St. Petersburg, would seem to demonstrate this. On dogs that had undergone amputation he injected defibrinated blood; but all of them were dying of haemorrhages that were impossible to stop. So that for him the mass transfusion of defibrinated blood causes a kind of haemophilia in animals. Therefore, it is better to use only normal blood in humans.

The quantity to be injected will never be considerable; it is obviously not a question of restoring to the subject the blood he has lost; it is only important to stimulate his nervous system and to "set in motion cogs that have ceased to function, so that the individual who has been subjected to transfusion can then form blood by his own activity." (Gubler.)

In the observations we have cited, the maximum quantity or the fortunate cases was 360 grams (Walton) and the minimum 105 grams (Leisrink). Eight times at least no more than 200 grams were exceeded. I will add, without attaching much importance to this remark, that in the event of the failure of the transfusion the quantities of blood injected were always considerable: minimum 240 grams; and, more often than not, the figure of 400 grams was reached or exceeded. In Maisonneuve's observation, we are talking about a considerable quantity that has not been evaluated in a precise manner.

High doses seem to me to be contraindicated, it is better to return to transfusion than to stupefy the heart and other organs by injecting a large proportion of blood.

§ II. TRANSFUSION IN PUERPERAL HAEMORRHAGES.

Loss of blood that occurs in the course of pregnancy, as a result of abortion and vicious insertion of the placenta; during labour or after delivery, as a result of various causes, can be compared to traumatic haemorrhages, and must be compared with it when dealing with the indications for transfusion. In both cases, these are subjects *accidentally* rendered bloodless by vascular lesions; and, at a pinch, the two paragraphs could be made into one. Our division has no other goal than clarity and simplification of the description.

In this variety of haemorrhage, the transfusion triumphs as well as in the preceding one; and before going any further, we are not afraid to say that it is one of its happiest applications. This mode of treatment now has at least *sixty-seven successes*, several favourable observations have probably escaped me, and hardly more than 40 failures have been published. I grant that there have been many omissions among the latter, for it is not easy to bring oneself to disclose the negative facts; - and this is wrong, in my opinion: they have their value as well as the positive ones; but in the end if there were twice as many of these unfortunate cases, which is unlikely, the result considered as a whole would not be the less important.

Many operations that we do not hesitate to perform every day are far from being as successful as often; and, to give only a few examples, I will say that tracheotomy, amputation of the thigh, operation of the strangulated hernia, etc., could not even furnish analogous or comparable statistics.

So we hardly dispute these figures now, but a serious objection to transfusion, almost impossible to refute, is made with regard to any treatment, the following, no doubt, it is said, you show a number of convincing facts and you necessarily conclude: *post hoc, ergo propter hoc*; but where is the proof that the transfused women would not have cured spontaneously, excessive puerperal haemorrhages are not inevitably fatal. It is therefore necessary to present your figures more modestly, and probably relate to the *vis medicatrix naturae* the cures with which you do credit to transfusion.

For my part, I am far from despising this argument, I even make use of it willingly quite often, and I am disposed to give it all the more value because we absolutely lack certain prognostic signs to establish that a serious haemorrhage must end immediately in death. Nevertheless, I think that experience, medical tact, in the absence of more positive scientific data, make it possible to a certain extent to judge the seriousness of a case, according to a symptomatic group. Well, this is what guided the practitioners who dared to give the transfusion; and when they affirm that their patient was dying, we can take their word for it, accept their interpretation as really serious, and consider the favourable results they have obtained as pure of all illusions. One dies so well of puerperal haemorrhage that we spoke only a moment ago of more than 33 cases of death in spite of transfusion. Moreover, how can we think that an operation considered (wrongly) by those who have practiced it as an *ultima ratio* in circumstances almost beyond the resources of art, has been undertaken lightly?

At any rate, the objection which we seek to refute has taken on more importance, formulated as it has been by an authority in obstetrics, Professor Depaul, who does not hesitate to say with regard to fortunate cases of transfusion that "the women operated on would have been cured without it". Thus we see it accepted by Dr. Liégard, of Caen, with the most complete enthusiasm, as the following sentence demonstrates: *No, certainly, this so-called heroic remedy is only a sad illusion, reserved for practitioners only a deplorable disappointment; and I am convinced that ... transfusion is useless.* This is the language formally used by anti-transfusers, however in less moderate terms.

It is regrettable that such a clear opinion is not based on any demonstrative fact. Liégard cites two cases of excessive losses with a worrying general condition, ending in recovery, thanks to enemas of Bordeaux wine and the administration of generous wines; but these are not valid proofs, since it could also be objected that the illnesses of the Caen doctor *would have been cured without it.* I prefer to say, however, that in the cases of fortunate or unfortunate transfusions, we had tried, before resorting to the operation, the means reputed to be the most energetic, without obtaining anything. In addition, many women could no longer swallow or vomited constantly, so it would have been a wasted effort to prescribe them the stimulants.

I end this discussion here; it has only a secondary interest and could carry me far without any benefit to the reader. Professor Depaul and Dr. Liégard maintain intuitively that transfusion is useless; it is their impression, so be it; but scientific methods condemn *a priori* reasoning and they willingly accept well-observed facts; these are the arguments we are going to make.

A woman aged 41 years, treated by Klett (January 1828), had excessive metrorrhagia which put her after 18 hours in a state of apparent death; complete collapse, obscuration of vision, dizziness, chill, cold sweat, cadaverous pallor, hiccups, feeling of imminent death. Dr. Schrägle then performed transfusion, because neither the astringents nor the tonics had been able to do anything against this condition.

Barely has he injected two ounces of blood when the eyes open, the pulse reappears, the heat is restored, the face is coloured, the *haemorrhage ceases*; and this woman, when asked about the sensations she experienced, replied that she felt "a beneficent current of warmth towards the heart, which had given her a new life." The healing was complete.

The observation of Dr. Marmonier senior is remarkable among all, and I cannot resist the urge to recall it in just a few words, since it is reproduced or analyzed in all the medical journals of 1851-52.

On 3 January 1851, Marmonier was assisting a woman in labour and was obliged to do the version. After delivery, a terrible loss, which immediately plunges the patient into the most serious state: fatal pallor, cold, insensible pulse, obscuration of vision, repeated syncope: imminent death. A woman provides blood, and 90 grams are injected with *the help of a bad little child's syringe in two batches.*

Soon a considerable improvement appears: strong pulse, regular breathing, less blurred eyesight, no more syncope. At the end of two hours the patient fell asleep, and three weeks later she was completely cured.

Finally, I will summarise a fact no less conclusive, observed by Desgranges and Devay, 1852. This is a case of metrorrhagia following abortion in a 27-year-old woman. When she entered the hospital she was in the following state: collapse, pallor, cold, pulse small to 130, aphonia, vomiting, etc. She is injected in two and a half minutes, using a hydrocele syringe with 180 grams of normal blood. Then she revives, opens her eyes, attends to what is happening, stops vomiting, etc. A little later she had a somewhat sharp reaction with sub-delirium, probably as a result of an over stimulating action of the blood; but she recovered despite the subsequent appearance of *phlegmatia alba dolens*.

It seems to me useless to continue the enumeration of these curious facts, they all look the same; moreover, they are found summarized and collected almost everywhere, and I refer to three special works the readers who wish to know them. They are: 1° Dr. Oré's memoir on transfusion (1865); 2° the inaugural thesis of Marmonier junior (Montpellier, 1869, n° 49); 3° the more recent work of Joseph Casse (Brussels, 1874).

In doing my research in the main works published on transfusion, I found, reported at different times, the statistics of the main cases of puerperal metrorrhagia treated by this operation. I reproduce them here to clearly show the increasing progression they have followed.

Soden, in 1852, speaks of 36 observations, of which 29 were favourable.

Professor Martin (of Berlin), in 1859, cites 57 cases, of which 43 were favourable; and, regarding the failures, he mentions that 7 patients died *several days after* the transfusion, for one cause or another, unrelated, of course, to the operation.

Oré, 1863, analyzes 45 observations of transfusion, including 36 for haemorrhages during or after delivery, and 9 during the course of pregnancy. There are 12 deaths, of which barely 7 could be attributed to the transfusion, for in five cases the patients succumbed to accidents of peritonitis, metroperitonitis, uterine phlebitis, suppurative metritis, or to the entry of air into the veins.

Marmonier (1869), in his interesting work, relates 94 observations of transfusion, classified as follows:

7 before childbirth	2 failures	5 healings
8 during childbirth	4 -	4 -
57 after childbirth	20 -	37 -
11 after abortion	4 -	7 -
7 during pregnancy (in the third month)	0 -	7 -
3 during pregnancy (in the eighth month)	3 -	0 -
1 premature delivery	1 -	0 -
Total: 94	34 failures	60 healings

Finally, here is a last statistic from J. Casse, 1874:

1° Transfusions before childbirth and the term of pregnancy, successfully completed:	16
2° Transfusions after childbirth, and the term of pregnancy, successfully completed:	50
3° Unfortunate transfusions, before and after childbirth:	32
Total: 66 successes and 32 setbacks, out of 98.	

This enumeration, although very exact, is however not complete, and some cases have escaped the attention of the author; such are those reported to the Dublin Obstetrical Society, 1871-72, by John and Hill Ringland, two in number, of which a fortunate case the transfusion had been made with defibrinated blood; such is that of J.-H. Aveling, 1872, of which here is the summary: woman of 21 years, suffering from excessive loss after delivery and as a result of adhesion of the placenta; the usual means of haemostasis having failed, Aveling was called in to do the transfusion. The patient is exhausted, pale, cold, without pulse, with dilated and insensible pupils, unconscious, etc.; 210 grams of blood were infused into her veins: the pulse reappeared, the face became better, the intelligence awoke, and after a few hours the patient was able to take food. She heals.

I will add three more observations, quoted: one by John Aikman (*Glasgow. Med. J.* 1873), the success was only momentary and the patient died on the twelfth day; the other two by Robert M'Donnel, one of which was a success.

In short, I can affirm that in more than a hundred cases of puerperal haemorrhages transfusion has been attempted and that *seventy times* the operation has certainly succeeded as desired. As for the setbacks, which could be contrasted with this encouraging statistic, they cannot all be attributed to the method. A large number of cases of death have been the result of severe childbirth, and others are attributable to time delay. If I add that only one case of death is cited as a result of the entry of air into the vein, that of Jewell, in 1826, who had the mistake of transfusing through the jugular; that the facts of phlebitis have been *very rare and always blessed*; that, finally, there are no well-observed cases of embolism, I think that I will not be accused of an unthinking enthusiasm for the method when I have said that it seems to me to be rational, effective and worthy of the attention of doctors. It is applicable to all cases of puerperal haemorrhage, even to those of placenta previa, where there are 8 successful and 10 unsuccessful (Belina).

We therefore strongly urge French accoucheurs to study attentively, with their methodical spirit and their talent for observation so developed, transfusion from the practical point of view, and to inquire directly about the confidence it deserves.

There is a lack of documents to establish the frequency of cases of death by puerperal haemorrhage in France, but it appears that in England there are 365 cases per year (Graily Hewit). It is not surprising therefore, that our colleagues across the Channel have experimented with the method of treatment that we recommend; and it is to be hoped that if it is less on the agenda here, it is because we are more favoured than our neighbours. This would not, however, be a sufficient reason for us to be completely disinterested in this study, for, as a learned gynaecologist, Dr. Chailly-Honoré, has said, "Whatever we do, the transfusion alone can leave some chance of salvation. It is there that gives the midwife that security, that confidence so necessary in such a case."

PART 6

Operating Manual. – Transfusion has been made in puerperal haemorrhages with normal blood, defibrinated blood and even animal blood. Some English accoucheurs, Ringland, Higginson, and especially Robert M'Donnell, recommended defibrinated blood. The latter is of the opinion that from the surgical point of view it is healthier than normal blood, and that from the physiological point of view it is better, because fibrin is an excrementitious element. Martin, of Berlin, is said to have obtained twelve successes with defibrinated blood. I repeat that non-defibrinated blood seems to me to be better, because it is more plastic and more quickly prepared for injection: it takes at least 5 minutes (De Belina) to defibrinate and filter the blood, while ordinary blood can be infused into the vein almost as soon as it leaves the vessel.

But what are the symptoms that should guide the conduct of the accoucheur? I have already said that we do not know any absolutely characteristic features; however, there is a symptomatic set that does not deceive.

Here, for example, according to Cazeaux, are phenomena that announce imminent danger and imminent death: "Violent shivers, ever-increasing dyspnoea, convulsions, prolonged syncope, violent and continuous pains of the kidneys, and, in addition, glare and more or less complete blindness." The author adds to this pupillary dilation, which is all the more pronounced, according to Madame Lachapelle, as the syncope is deeper. (Cazeaux, *Tr. d'Accouch.* 1862, p. 932.)

Graily Hewit also indicates the following disorders as signs of the seriousness of a haemorrhage: cooling of the body and extremities, jactitation, complete obliteration of the pulse, unconsciousness, repeated syncope, uncontrollable vomiting, successive convulsions following prolonged collapse, pupillary dilation and insensitivity, conjunctival insensitivity.

On the contrary, the following symptoms would have a less unfortunate prognosis for him and would allow him to postpone the operation or, at least, to rely more on the action of medications: obtundation of sight, ringing of the ears, deafness, yawning, dull eyes, precordial anguish, sensation of constriction around the chest; anxiety painted on the face, unawareness of what is happening or indifference to those around them, subdelirium.

By comparing these two sets of symptoms, it is easy to note in each of them differences characteristic enough to guide the practitioner. I call attention to convulsive phenomena: they are very serious. Professor Bert has observed that any bloodless dog, which has convulsions when put on its back, is inevitably doomed to death; only transfusion can save him. Clinicians therefore agree with physiologists that this symptom is a phenomenon of exceptional gravity.

Dr. Hewit still considers the state of shock (we would say *nervous haemorrhage shock* or deep collapse) observed in a patient, even after a relatively minor loss, as a formal indication for transfusion. (See: about shock, the *J. de thérapeutique* of 1874, p. 115.)

Soden, in a circumstance of this kind, obtained a remarkable, almost miraculous, result from the transfusion.

Now let us see how the blood should be infused. I leave aside the details of the bleeding, of the patient's preparation, on which I will explain later, and I suppose that everything is ready and that it is only a question of introducing the borrowed blood.

Is it absolutely essential to have a special device? No, it is just as easily dispensed with as with the tonsillotome, when the tonsils are removed, or with any other instrument acting automatically in certain operations; all that is needed is a simple syringe that works well and is very perfectly clean.

The blood donor's vein being open, the liquid is received in the pump body of the syringe, previously soaked in hot water and surrounded by heated cloths. "By this process," say Devay and Desgranges, "the point of contact between the blood and metallic bodies is diminished; the harmful action of the air is reduced to almost nothing, and the chances of coagulation of fibrin diminished as much as possible." These doctors condemn, and they are quite right, the special apparatus, which offers long tubes "whose inert walls can only alter the life-giving fluid."

Therefore, we opt for the ordinary syringe; and those of our colleagues who wish to give an exact account of the value of this simple method will have only to refer to the conclusive observations of Blundell and Waller, Savy, Goudin, Schneemann, Jugleby, Nélaton, Soden, Marmonier, Bellasis, Malfen, Dutemps, etc., where they will see that this primitive instrument was the only one used.

It would be desirable that a well-made syringe, similar to the hydrocele syringe, be part of the obstetric kit. (It would not be a special instrument; a syringe is often needed in the practice of childbirth.) The pump body would be made of glass (nothing would prevent the use of this new variety called *unbreakable glass*) and the plunger piston, so as to make it capable of operating without grease. I am giving this idea to our skilful instrument makers: they may perhaps be able to take advantage of it. So far, let me tell them, they have only given us devices of an impossible or very limited practical application, very ingenious, in truth, but which they alone handle well; that is why I will not recommend them that poorly when I speak of them.

So the syringe is filled with blood and purged of air. All that remains is to empty its contents, *with an excessive slowness*, into the vein at the crease of the patient's elbow, either through the intermediary of a small trocar-cannula, which has been previously attached to it; or, better still, directly through a V-shaped opening made on the exposed vessel. The jet is directed towards the heart.

The quantity of blood to be injected should not be considerable; large restitutions are worth nothing, and we are entirely of the opinion of Desgranges and Devay, when they tell us that "transfusion is only a means of warding off immediate death, of giving the economy time to repair its losses ... the transfused blood is the drop of oil thrown into the empty lamp, the light fuel that raises the flame that is almost extinguished."

Another distinguished physician of Lyons, Diday, is also in favour of moderate doses; and with the exception of Dr. Soden, the greater number of transfusionists hold a similar opinion. For example, Higginson injects no more than 20 ounces (about 560 grams) and no less than 4 ounces (113 grams); Routh (1849), 16 ounces at most (454 grams), 6 at least (170 grams).

Here are some figures taken from the various observations of transfusions that we have examined: 1° *Haemorrhages during pregnancy*. – In cases followed by recovery, the maximum quantity was 660 grams (Wheatcroft), and the minimum 60 grams (Klett, 1828); most often only 120 to 320 grams of blood fluid were injected. 2° *Haemorrhages after childbirth*. – Maximum = 660 grams, minimum = 30 grams (Norman and Orman, 1849), most frequent doses = 90 to 360 grams.

In the unfortunate observations taken as a whole, I note the following figures: maximum = 755 grams (May), minimum = 60; the doses most often used are between 90 and 300 grams.

Once the blood has been infused, all that remains is to put the ordinary bloodletting bandage on the chosen arm. Some doctors then recommend artificial respiration. But I have no precise information to give on this complement of the operation; very rarely has it been used.

Phenomena observed after transfusion. I list the main symptoms observed. Some patients reported that they had felt a gentle warmth along their arm during the injection of blood, and a stimulation such that it seemed to them that life was restored to them with the infused liquid. This comparison is not very outrageous. The operator often witnesses a kind of resurrection: the patients seem to awaken from a deep sleep; they open their eyes, examine what is happening; their lips become coloured, the face becomes a little animated, speech returns, the pulse is more sensitive, the cooling is less; the haemorrhage stops or moderates, the vomiting ceases, in a word, there is a considerable improvement and a real return to life.

At other times things happen less simply: there is a sort of electric shock, with complaints, cries or groans, choking, convulsive accidents; but this storm quickly calms down and soon the condition is better. Quite often these disorders occur when the injection of blood has been too rushed.

In a few rare cases, the patients have been revived suddenly and entirely as if by an electric concussion (Klett); but more often than not, the gradual disappearance of sensory disturbances, the return of intelligence, and the disappearance of collapse or spasmodic accidents.

Quite frequently, when the transfusion is done too late, the operation fails, and the unfortunate women breathe their last while the liquid enters their veins.

Or we succeed in galvanizing their inanimate bodies for a few moments only, and life is extinguished immediately.

When the sick have to recover their general condition quickly becomes satisfactory, they tolerate drinks, are less agitated, feel stronger, and fall asleep. These signs have an excellent prognosis; unfortunately new disturbing symptoms may appear again, and the patients succumb, although a new transfusion has once again improved their situation. Finally, some die after a few hours or a few days, carried away by a new loss or serious puerperal accidents: metroperitonitis, metritis, etc.; or again, in the midst of sudden dyspnoeic disorders, analogous to those caused by thrombosis or embolism of the pulmonary artery (Carey).

I conclude by saying that it is not uncommon to see recovery take place slowly, when the collapse has been deep and the loss enormous. The body, stunned so to speak, has great difficulty in recovering from the shock it has suffered; it staggers for some time before regaining its equilibrium.

§ III. TRANSFUSION IN SUB-ACUTE ANAEMIA RESULTING FROM REPEATED BLOOD LOSS OR RAPID HYPHEMIA.

We have just shown the value of transfusion in acute anaemia following these lightning haemorrhages which throw the subjects into a state of apparent death; we must now inquire what services can be expected from this mode of treatment in the loss of blood, which is less abundant at the outset, but no less excessive and serious because of its repetition. We characterize the disturbing condition of patients suffering from such accidents by the expression of *sub-acute anaemia or hypphemia*.

It is clear that a host of causes can produce this special morbid state, they are as numerous as those of haemorrhages, and we will not attempt to enumerate them; but there are certain affections to which it stands out more particularly: metrorrhagia, haemophilia, ulcerated cancer, etc., and which it is essential to review. Before going into detail, I will give my general impression of the value of transfusion and the results it is able to procure in sub-acute anaemia. Well, this is no longer the sometimes heroic remedy that we have just appreciated in the lightning haemorrhages, where we have seen it resuscitate, so to speak, the dying; no, its action is not so wonderful. But, although it is less brilliant, it is not for that reason devoid of power. Transfusion supports weakened patients, first prevents them from declining further and, finally restores them.

I will add that unfortunately it fails in such cases more often perhaps than in sudden anaemia, because of the very conditions in which it is applied. The injected blood is in the presence of more or less altered organs, which it is powerless to restore to their functioning, precisely because of their degeneration. The tissues, badly nourished, as happens following abundant haemorrhages, deteriorate quite quickly, undergo fatty regressions that cannot be modified by the new blood: the body is worn out, so to speak, and its disorders are irreparable.

Ponfick (1873), after other observers, has insisted more particularly on the serious organic alterations which occur in subjects exhausted by haemorrhages; it especially points out fatty degenerations of the liver, kidneys and heart. On the other hand, Leopold Perl, of Berlin, noted these same regressive alterations in dogs that he exhausted by repeated bloodletting. It is therefore conceivable that transfusions made, as is most commonly the custom, on patients almost *in extremis*, have no chance of success. The infused blood is incapable of putting diseased organs back into motion; it's too late!

It should therefore not make the method always to blame for the failures with which it is sometimes willingly charged, it is better to inquire into the causes that make it to fail so as not to attempt a useless operation; and one should endeavour to apply it only when one is almost certain that the chances are in its favour. Unfortunately, we lack information capable of completely edifying us on the desperate situation of a subject exhausted by haemorrhages and consequently of providing us with the real contraindications to the operation; we may suspect imminent death, but not affirm it. Thus we are far from blaming the doctors who operate anyway, at the risk of a certain failure: *melius anceps, quam nullum*. As a general thesis, we will maintain that it is advisable to transfuse early, when the subjects are not quite exhausted, at the risk of incurring the anathema of those of our colleagues, very optimistic, who assure us that the subject would have been healed without the infusion of blood.

In short, we believe that we can affirm in advance that transfusion is an excellent mode of treatment in severe sub-acute anaemia; that it can provide real resurrections, applied in time to patients whose organs have not undergone fat regression; but that, unfortunately, we are not yet in a position, in the present state of science, to specify its formal indications or contraindications. By researching in animals, by the enumeration of globules, a method universally used at the present day, to what reduction in the number of globules corresponds to the organic degenerations after frequent haemorrhages, it would perhaps be possible to find terms of comparison for man.

Since, for example, the decrease of a million or more globules per cubic millimetre of blood already constitutes a serious state favouring fatty infiltration into certain tissues, it would be possible to infer some exact data applicable to our species. I do not know of any work carried out in the direction of this idea.

On the other hand, the globule count might perhaps furnish useful information by showing that a given decrease in the normal number of red blood cells (4,000,000 in man, on average) indicates the necessity of transfuse (Gubler).

Until further notice, we shall have to confine ourselves to deducing from the serious symptomatic set presented by the patients, as described later, the indications or contraindications to transfusion, and to asking the practitioner's art alone, his individual experience, if you will, what medical science is powerless to offer us at present.

But, before going any further in this question, I leave it to clinical observations to provide more solid arguments in favour of the efficiency of transfusion in sub-acute anaemia; and in order to better connect what follows with the considerations already presented, I begin this presentation by studying the applications of transfusion in anaemia, following uterine haemorrhages outside the puerperal state. The examples cited will, I hope, show once again how useful it is for gynaecologists to indulge in the infusion of blood into stubborn and abundant metrorrhagia.

I. *Non-puerperal metrorrhagia*. – The aetiology of these varieties of haemorrhage, taking into account only the most serious, includes very different causes. Among the most common, I will especially mention fibrous tumours, polyps, fungus of the uterine mucosa, degeneration of the uterine tissue resulting from chronic metritis, imperfect uterine involution, erosions and ulcerations of the body or cervix, etc., etc., and, finally, ulcerations of a bad nature: cancer or canceroid. I hesitated to speak of these latter diseases, because very few doctors will bring themselves to attempt a palliative transfusion in such serious circumstances; but, ultimately, as there are today some favourable observations in science, which excuse to a certain extent this audacious attempt, I thought it my duty not to abstain, and to classify, even carcinomatous affections of the uterus, among the causes of exhausting haemorrhages which may oblige the practitioner to have recourse to the infusion of blood.

Whatever may be the case with this questionable practice, we must say that it is mainly after the abundant losses caused by fibrous bodies, polyps, incomplete uterine involution, that transfusion has been applied as a treatment of consequent sub-acute anaemia. It is not uncommon, in these kinds of affections, to see the most energetic remedies fail; the patients, exhausted by repeated haemorrhages, soon become bloodless, and the doctor sees them fall into a state reminiscent of that of acute anaemia.

Their weakness is excessive, they can hardly stand upright, and at the slightest movement they are threatened with syncope; the appetite is nil, and often there is nausea or vomiting; then there is a deep discolouration of the mucous membranes, a waxy tint of the skin, cooling of the extremities, a very peculiar state of agitation, delirium, hallucinations, visual disturbances, lipothymia, hasty breathing, acceleration and considerable weakness of the pulse, analgesia, emaciation, oedema of the face or lower limbs, carotid murmur noises, etc. Needless to say, medications did not succeed in reviving these unfortunate exhausted and bloodless patients. Only one resource remains for them to escape certain death, and that is transfusion.

Here are, as I have announced, a few examples intended to show what it can do and how it has triumphed in the face of really desperate situations. I choose them from among the facts published at a time period close to us, or very recently, and I quote *three* of the most interesting, with some details, for they prove better by themselves than all the dissertations that could be made on the method. All three, I am happy, have been observed in France.

The oldest dates from 1866; it was reported by a distinguished provincial doctor, a practitioner no less skilful than an educated clinician, Dr. Gentilhomme, of Rheims.

Our colleague had to treat, around this time, a young woman aged 30, suffering from stubborn and serious metrorrhagia resulting from the presence of a fibroid implanted in the inner wall of the uterus. The losses began in February, 1865, and continued to increase in abundance and frequency, until the month of July, 1866, when they became continuous. The patient presented a serious general state of weakness at the slightest movement, a barely perceptible pulse, a dull voice, diplopia, transient delirium, deep discolouration of the tissues, extreme weakness. Fortunately, the blood then stops flowing. We just do a good

tamponade and prescribe tonics. It was in vain; the weakness was still increasing, and when, at the end of three weeks, it was decided to try the transfusion, the patient was very bad.

The injection of blood was made using the Moncoq apparatus, with a basin. Barely 125 grams had penetrated the vein, when the patient cried out "stop, I'm suffocating". The cheeks had suddenly become coloured; then there was trembling, a tumultuous beating of the heart, considerable anguish in the chest, coldness of the extremities, vomiting. This disquieting state lasted two and a half hours, and then gave place to a comparative calm: the heat returned, breathing was easier, and the pulse became stronger and more regular. The next day, this woman was still weak, retained her visual disturbances, complained of sharp pains in the kidneys and chest, but had recovered her appetite and speech. Little by little her strength was restored, and at the end of a fortnight the patient made her first outing in a carriage. She heals completely. However, her fibrous body remained and later gave rise to menorrhagia which she tolerated very well.

A successful observation of a transfusion carried out in Paris last year, by Professor Béhier, has become a medical event of great importance. The success of the operation, the beautiful lesson of the learned master, who had as his objective the transfused patient; the remarks of great value added to the clinical fact by Dr. Liouville, one of our young associates most devoted to science and serving it with the most conscientiousness and devotion: these are the causes of the great repercussions of the new case of transfusion. Here it is, summarized in a few lines.

A young woman of 21 years, vigorously constituted, who had been a nurse for 16 months, was suddenly seized with abundant metrorrhagia. The blood flowed freely, "as from a fountain", and did not cease to flow with more or less abundance for 15 days, the patient having submitted neither to rest nor to any kind of treatment. When she entered the Hôtel-Dieu (January 1874), she was bloodless, discoloured, had a small and soft pulse, suffered from frontal cephalalgia and presented all the classic signs of the most profound anaemia. Astringents, ice, are used in vain; the weakness is excessive, and we note: small pulse, at 132, axillary temperature 36.4°, nausea, obstinate vomiting, aphonia, refrigeration, syncope at the slightest movement, visual disturbances, quiet delirium, central temperature at 38°, complete insomnia.

A tamponade could not be endured for long, and the bloody discharge had reappeared. On the 17th day of the haemorrhage, 80 grams of non-defibrinated blood were infused, very slowly, into one of the veins of the elbow crease. Improvement is quite slow to occur; the patient experiences painful sensations in her limbs, cries, agitates, delirious, has panting breathing, is cyanotic in the face, presents a haggard appearance. These disorders persist quite intensely for two hours and the patient does not revive definitively until after four hours. Then we notice a clear voice, no more delirium and haggard appearance, a strong pulse, no more vomiting. The next night was good; and two days after the operation the patient was found at the visit talking with her neighbours. On the sixth day she could be considered saved.

Here is now one of the most interesting peculiarities of this observation, and which is pointed out to us by Liouville. The enumeration of the globules had given, before the transfusion, only 800,000 red blood cells per cubic millimetre, a figure, as we see, absolutely insignificant. Now, four hours after the injection, there were 1,110,000 globules; eight hours later, 1,143,000; fifteen days later, 1,850,000; finally, at the end of a month, 2,029,000. Another interesting remark a few hours after the transfusion was that Liouville saw in the blood studied under the microscope, among the normal corpuscles, very numerous red corpuscles which did not exist before; he does not know what their nature and origin might have been.

In the presence of such a complete result, it is perfectly understandable that the learned professor of the Hôtel-Dieu could say transfusion, "far from constituting one of those therapeutic boldness that success hardly justifies, deserves to pass definitively into practice in the same way as thoracentesis or tracheotomy."

I now come to the third observation, that of Féréol, reported on 28 May 1875, before the Society of Hospitals.

A woman, after a difficult delivery, ended by the version, had a profuse uterine haemorrhage, but which was finally stopped. This took place at sea, during a crossing from New York to Le Havre. The patient disembarked a little tired and anaemic, but healthy enough to be able to reach Paris. She had been delivered three weeks when she was seized with a frightful metrorrhagia which could not be stopped by tamponade, compression of the aorta, or ligation of the limbs. The general condition became very bad, enormous weakness, incessant syncopes. The transfusion of 135 grams of normal blood is performed by the cephalic median, using Mathieu's device. The patient complains of numbness in her arm, which she finds heavy, and her lips become cyanotic, but she tolerates the injection well. Her pulse drops immediately, from 120 to 112; her breathing, from 40 to 32; her temperature, from 38° to 37.6°. The haemorrhage, which had stopped spontaneously before the transfusion, did not reappear; but the patient recovered only quite slowly, frequent vomiting, easy tendencies to syncope, slight feverish movement. At the end of only eighteen days, the convalescence was frankly established. During this time, the number of blood cells increased. From 1 million (before the transfusion) it rose twenty-seven days later to 2,300,000 and, a little later, to 3,120,000.

These three observations carry with them their lessons and there is no need to comment on them at length.

Apart from the successes that they relate, and which no one can dispute, unless one denies the evidence, they show us the unforeseen facts of the operation: we are witnessed first of all (obs. by Gentilhomme and Béhier) moving scenes, disturbing to the highest degree, during which the operator trembles for the life of his patient; then calm comes, strength and health are gradually restored; in a few days or weeks all danger has disappeared, and the healing is complete. In the observations of Béhier and Féréol we have the mathematical proof of rapid repair, thanks to the enumeration of the blood cells, a valuable method, from now on inseparable from transfusion.

Shall I cite other happy facts? Yes, it is necessary, to be more or less complete. I am well aware that statistics prove nothing in medicine, as is repeated today ad nauseam; I do not disagree that they willingly say whatever they are asked to express, and I am on my guard against them as much as those who attack them most vehemently; but I still have the right to point them out at least by way of instruction, or perhaps even encouragement, leaving it to the reader to draw the consequences they entail. This well established and agreed upon once and for all, I come to my additions. To make them less arid, I add a few important details.

In 1874, Dr. Molinier, of Dreux, had the good fortune to save by transfusion a 45 year old lady, who had long been affected by symptomatic metrorrhagia of the fibrous body of the uterus. A more serious loss, which occurred at the beginning of April, threw her into a deep collapse. When the infusion of blood began, she was in agony; nevertheless 60 grams of blood could be passed into the vein, with the help of the Moncoq device. The patient slowly revived, and after 44 days she was able to go out by car.

On 3 February last, at the Society of Surgery, an observation of a happy transfusion was presented, under the patronage of an eminent scientist, Mr. H. Larrey, in the name of Dr. Martinez del Rio, of Mexico. I recall its principal titles: repeated metrorrhagia, in a 36 year old woman, produced by a uterine polyp; removal of the tumour by the crusher; consequential severe condition, although there was no bloodshed; transfusion of 300 grams of defibrinated blood, using the Belina device; fast healing.

Roussel (of Geneva), in his article being published today (*V. Archives gen. de Méd.*, 1875), reports the case which I summarize under the following title: excessive anaemia in a 37 year old woman, afflicted with uterine fibroids, as a result of repeated metrorrhagia and haemophilia; injection of 120 grams of blood, using the author's device; gradual improvement, healing.

Awater also recalled a cure, through transfusion, of a case of sub-acute anaemia in a 45-year-old woman with uterine polyps. After the operation of the polyp, a new loss made the

decision to proceed with the transfusion. 200 grams of defibrinated blood was injected and the cure was complete (1873).

Finally, I cite only, under the name of their authors, the favourable observations of Braun, 1863 metrorrhagia due to a fibrous polyp of the womb; Cristoforis, 1869, idem; Fabri, 1873, idem.

This represents a total of ten happy cases of transfusion in hyphemia following metrorrhagia not symptomatic of cancerous diseases of the uterus.

In these, I have already said that transfusion has sometimes took place in one way, we say happily. I will provide proof of this. Here are first two facts of some interest, according to J. Casse.

In a 51-year-old woman, suffering from uterine cancer and reaching the last degree of marasmus, this doctor determined a temporary improvement by transfusing her with 90 grams of defibrinated sheep's blood. The patient lived for another two months after the operation.

A similar result was obtained in another patient suffering from uterine encephaloid disease. Two transfusions of defibrinated human blood, one of 45 grams, the other of 35 grams, revived this woman and prolonged her existence for about fifteen days (1874).

Furthermore, last year Fisher (of Breslau) practiced with momentary success the infusion of defibrinated blood in a case of uterine cancer. The patient survived 48 hours.

And this year, a distinguished young surgeon of our hospitals, Dr. Nicaise, momentarily improved the serious condition of a 36-year-old woman suffering from epithelial cancer of the cervix and literally exhausted by repeated haemorrhages, by infusing her, with Colin's device, 10 grams of blood. Relief was immediate, but death occurred 4 days later, as a result of peritonitis, probably following the removal of the cervix.

To justify the conduct of doctors who transfuse diseases affected by cancerous affections of the uterus, I can see only the following reasons: the obligation placed on them by the family to try to prolong the life of a loved one; the possibility of a diagnostic error; the relative benignity of the condition (epithelial cancer); the existence of a pregnancy that can be carried to term or at a time when the child is viable. We know, in fact, that a woman with uterine cancer is still able to conceive and carry her pregnancy to term. The excellent work of Dr. G. Chantreuil, associate professor at the Faculty of Paris, fully edifies us in this regard. Out of 60 pregnant women affected by cancer of the womb, of which he reports the observation, 35 recovered and 25 died during labour or the aftermath of childbirth; 29 *gave birth to a living child*. (*On cancer of the uterus from the point of view of conception, pregnancy and childbirth; Paris, 1872.*) In such circumstances, therefore, we believe that the physician has not only the right but also the duty to transfuse the bloodless woman, in order to save her child, if there is still time.

I now come to the cases of unsuccessful transfusion in non-puerperal metrorrhagia. Only a few have been published, or at least I have found only a few negative facts reported in the collections I have consulted.

Must we conclude from this that the operation rarely fails, or rather is it not better to admit that the failures have been neglected to be disclosed? I adhere to this last opinion, and I admit, a priori, that there must be more unfortunate cases than those which have been reported. Anyway, here are still 4 facts I've gathered:

1° In 1857, Lever and Bryant performed transfusion in a woman rendered bloodless by metrorrhagia following the expulsion of a uterine myoma. She was revived, got better, but died of peritonitis on the fifth day.

2° In 1869, Huter attempted the infusion of 360 grams of blood into the veins of a woman who had been rendered bloodless by severe haemorrhages caused by a uterine fibroid. The immediate success was satisfactory, but the unfortunate patient passed away 12 hours later by a new metrorrhagia.

3° In the same year, Thaon reported to the Biological Society (20 February 1869) a case of unfortunate transfusion, observed in Lorain's service. It was a young woman of 19 years, who had given birth a month ago, and who by repeated blood loss and fairly severe diarrhoea had been thrown into a considerable state of anaemia. Six weeks after giving

birth, the situation of this patient seemed desperate, but it was nevertheless decided to try the infusion of blood at the very moment when the agony began: pulse at 120, temperature 40.8°, respiration 40. In 7 minutes, she was injected with the Mathieu device, 155 of normal blood. At first she seemed to be better, but at the end of an hour she succumbed.

4° The last fact is very recent. (See: *Union. med.*, p. 585, no. 47, 1875). We owe it to Dr. Filliette, of Boulogne-sur-Mer. A 43-year-old woman had had heavy discharge caused by a uterine polyp for 3 years. (She had never thought of seeking treatment.) When *she decided to consult*, she was excessively anaemic: discolouration of the tissues, puffiness of the face, oedema of the lower limbs, tendency to cold, easy syncope, drowsiness, anorexia, but no vomiting or diarrhoea. The polyp is removed, without resulting in any blood flow. In spite of this, the patient's condition is of the most serious kind, loss of intelligence, incessant syncope, complete insensitivity. With the Mathieu device, 100 grams of the husband's blood are injected. At the first waves the patient comes out of her torpor, straightens up, opens her eyes and asks for the basin. A few seconds later she collapses; she was dead!

It seems to me that at least two of these four failures bring us the best lessons. But let us say first that the first and the second cannot be attributed to the transfusion, since in the one case the patient died of peritonitis, and, in the other, of a new and sudden haemorrhage.

On the other hand, the observations of Thaon and Filliette show us that it is a great mistake to wait until the last moment to transfuse. Professor Lorain's patient was in agony and was unable to benefit from the blood that was returned to her. The autopsy showed that the organs were absolutely discoloured, but there is no question of microscopic research in the observation; it is regrettable, it is possible that the material proof of the uselessness of transfusion would have been demonstrated by the various fatty degenerations that would undoubtedly have been encountered in the viscera.

Certainly, such alterations would have been seen in the autopsy of Dr. Fillette's patient, if it had been possible to perform it. The author is therefore perfectly right in saying that the transfusion was made too late, and in adding that if it is indicated in *acute hyperemia*, it is contraindicated in *chronic hydremia* following losses lasting a long time.

Definitively, the very failures that we have just reported are not made to discourage the practitioner; they show him that in the presence of a rebellious and serious metrorrhagia he should not hesitate to try transfusion, as soon as signs of weakness present themselves and there is no longer any reason to rely on the ordinary resources of the *materia medica*. Some authors have attributed a double curative influence to the infusion of blood in cases of severe metrorrhagia. This liquid would act not only as a stimulant of the vital properties of the tissues and as a reconstituent, but also as a haemostatic. Klett had this idea a long time ago (1828), which he expresses by saying that: *by means of the transfused blood the centripetal force is awakened, and the circulatory current can be given a new direction towards the heart.* (See: *Gaz. med.*, 1834). I point it out, strange as it may seem, because it has just been taken up in Germany by Awater. Braune goes further, and he claims that after the transfusion he could have felt uterine contractions. Let us leave these hypotheses and refer to the facts. However, there is evidence that stubborn metrorrhagia stopped immediately after transfusion. Is this an effect of the syncopal state in which the operated generally find themselves, or is it to be attributed to the stimulating qualities of the blood? That is what I cannot say. It doesn't matter, the fact that haemostasis after transfusion is real, and it must be accepted as it is with its undeniable happy consequences.

PART 7

Operating Manual. – Transfusion is carried out in sub-acute anaemia in the same way as in the case of severe or sudden haemorrhage. There may be some nuances to report; for example, here the use of the devices is possible, the doctor has all the time necessary to bring them to where they are to work, to learn how to handle them well, and to ensure their regular play. Without recommending them completely, I do not think I should advise against their use. However, it should be noted that the best are far from perfect. I have designated

by the name of their inventor: Moncoq, Roussel, Mathieu, Colin, those who were used in the transfusions whose observation I have reported, and it was possible to see that they varied with each operator. A good syringe would still have its advantages in this case, as well as in more serious cases. For me, this is the ideal of transfusion machines.

It is clear that non-defibrinated human blood will be injected, in preference to any other defibrinated blood of man or arterial animal blood. The doses will be low: below 100 grams they give good results. This figure may be exceeded, but I believe that doses of 200 and 300 grams are very dangerous. The heart may be surprised by the arrival of such a large quantity of blood fluid and instantly stunned; the lungs would also become easily clogged, and one would have to fear their engorgement. It must not be forgotten that the transfused blood acts mainly by impression and that, if low doses excite, high doses can act too strongly and stun the organs, so to speak, far from stimulating their functioning. So we will only infuse 60, 80, 100 or 150 grams of blood at most. It is better to return to a new transfusion, while remaining below the necessary dose, than to exceed the goal by a too hasty a precipitation:

In vitium ducit culpæ fuga, si caret arte.

[The flight from guilt leads to vice, if it lacks art. – PL]

I am now continuing the study of transfusion in sub-acute anaemia following blood loss, following in my exposition a somewhat arbitrary but logical order, that of the frequency of its use in each of the main types of haemorrhage. In the absence of a natural classification, it may be useful to create an artificial one, especially when it has, like the following one that I am going to give here, has no other claim than to be simple, clear, and to facilitate descriptions. Besides, if I were to adopt the formulas of the pathologists, their divisions, I would find no advantage from the point of view of the special subject I am treating. It is only the abundance of the haemorrhage, its severity, which indicates the infusion of blood; and the practitioner, faced with an exhausted and bloodless subject, does not ask himself whether the haemorrhage is constitutional, diathetic, active or passive, he seeks to stop it and combat its disastrous effects. I shall therefore study transfusion successively in the *various varieties of haemorrhages* which have necessitated its use, beginning with those which have the greatest number of cases and ending with others which have much fewer. This is not to say that I will take no account of the general state of the subject; far from it, and on the contrary, I will be very concerned about it, taking great care to point out that the worse the background in a patient suffering from haemorrhage, the less chance the transfusion has of success. I will explain myself at greater length, however, when I come to the attempts at the infusion of blood attempted in certain dyscrasias.

Having said this, I enter the subject, taking the following general title of the new chapter, which has the advantage of only prejudging the simple classification of a group of similar facts:

II. *Various haemorrhages*. – The external blood loss or external haemorrhagia that most often required the use of transfusion are, in order of frequency, epistaxis, haematemesis; those of the injured or sick affected by wounds, haemoptysis, enterorrhagia, haemorrhoidal flow, etc.

a) *Epistaxis and haemophilia*. – Most of the patients transfused as a result of nasal haemorrhage were haemophiliacs, which is why I thought it necessary to bring together in the same paragraph the accident and its predisposing cause, the symptom and the disease. *Non-symptomatic* nosebleeds are never so abundant or incurable as to warrant the serious operation we are studying; when they succeed, by dint of persistence and violence, in endangering the lives of the sick, it is because they have as their origin a general cause, haemophilia most often, an infectious disease, leukocythemia, cirrhosis or other diseases of the liver, etc.

We shall say further what can be expected from the infusion of blood in certain constitutional diseases, in some special dyscrasias in which epistaxis is an ordinary

symptom without, however, being the dominant phenomenon; for the moment, we will only speak of the severe epistaxis of haemophiliacs.

A great number of works have been published on haemophilia or haemorrhagic diathesis since the beginning of this century, interesting, no doubt, for the many details they contain on the apparent causes, the symptoms, and the course of this strange affection, but which give us very little information as to its real aetiology and its nature. I recognize, with the authors, that it is in general a hereditary disease affecting men more frequently than women, and certain peoples more particularly; I again admit with the pathologists that the capillary vessels of haemophiliacs are thin-walled and friable; that they sometimes undergo fatty degeneration (probably secondary), and rupture with desperate ease; but I look in vain in the treatises for precise information on the composition of the blood before the haemorrhage and on the state of the tissues used for haematopoiesis in haemophiliacs who have succumbed to the progress of their disease. I nevertheless retain these two facts which interest us more particularly, namely, that epistaxis is very frequent in haemorrhagic diathesis, much more frequent even than the loss of blood from other regions of the body. Thus Grandidier informs us that it is reported 110 times in observations, while haemorrhages from the mouth or intestine are both represented in the statistics only by the number 32 and haemoptysis by that of 14. I also retain the following important remark, namely, that this special condition can be modified, improved, and cured, in other words, that it is sometimes curable, although most commonly it causes death by exhaustion.

Whether haemophilia is curable by ordinary restorative means; if, on the other hand, it does not originate from too profound organic alterations, and this is probable since no other tissue lesions are reported than fatty regressions, which are probably secondary, there is every reason to believe that patients who are affected by it can benefit from transfusion. The use of this treatment is therefore rational, and there is no reason to accuse the doctors who recommend or practice it as reckless, on the pretext that transfusing haemophiliacs is like pouring blood into a sort of Danaïeds barrel.

Practice, all in all, has come to vindicate the theory, as we shall see, and to justify their conduct, if it needed it needed justification.

I have already spoken of the remarkable fact of Dr. Lane, who succeeded in saving a young haemophiliac patient, who had rendered bloodless by a sudden haemorrhage during the strabismus operation, by restoring a little blood to him, and I added that the cure was complete in the sense that the strabismus and the haemorrhagic diathesis disappeared. This was a rather remarkable precedent and Lane had imitators.

Here are, for example, two cases which, although less fortunate, are no less interesting and curious.

In 1873, Mancini reports (quoted by J. Casse), a 32-year-old man became haemophilic after a miliary fever. He continually lost blood through his nose, in abundance, and grew visibly weaker. The astringents, the tonics, the tamponade acted only mediocly, the condition worsened more and more.

The transfusion was made with Ruggi's device, and only 50 grams of blood were injected. Everything went well, except for a shudder after the operation, and the patient *remained six days without bleeding from the nose*. A new epistaxis having occurred quite strongly, 13 days later, two new transfusions of 50 grams each, one hour apart. The patient did not tolerate the operation well; he turned pale, broke out in a cold sweat, his vision was blurred, then his pulse weakened, then came a violent shiver, with accelerated and noisy breathing, and his lips became cyanotic. Fortunately these serious symptoms disappeared quite quickly and a notable improvement occurred afterwards in the patient's condition. A little later, unfortunately, the blood escaped again but in small quantities through the nose and through the wound of the arm. The Italian doctor nevertheless hoped to improve his patient's situation. I do not know whether his predictions have come true, for the observation has remained incomplete. As it is, however, it has its value, and I have willingly reported it because it shows us that the new blood prevented epistaxis or made it insignificant on two different occasions, during the 6 or 13 days that followed the transfusion; moreover, it is curious, as a striking example of those serious accidents which sometimes occur after the

injection of blood, and which we know from having seen them noted in other observations previously reported.

Here is a second fact of the same order, interesting for the excellent immediate result given by the transfusion, but which in reality represents only a relative success since the patient succumbed.

We owe it to two doctors from Paris, Messrs. Blondeau and Th. Anger.

A young woman of 24 years, who had been chloro-anaemic for a long time, was seized in the month of April 1874 with an excessively violent nasal haemorrhage; the blood flowed freely through the nostrils, came out through the mouth in abundance, and also entered the stomach by falling into the pharynx and oesophagus. Without too much delay a good tamponade was made and ordinary haemostats were prescribed; at the same time cognac and champagne were frequently swallowed. After 12 hours the condition is nevertheless more serious; the patient seems exhausted, she is livid, cold, covered with sweat, devastated, with a miserable pulse of 140; she is delirious, agitated to a very high degree, finally her pupils are insensible and enormously dilated. The bleeding continued despite the tampon, the blood *flowed through the lachrymal points*. Transfusion remained as a last resource to ward off an imminent danger of death. Therefore, 65 grams of normal blood were injected, using the Colin device, and through the basilic vein. The sick woman resurrected, so to speak; the pupils narrowed, the pulse fell to 100, the delirium ceased, and a perceptible improvement was pronounced by the woman herself.

But she was 4¹/₂ months pregnant, prone to miscarriages at precisely this period, and she had not felt any movement for 4 days; so everything raised fears of abortion. Indeed, an embryo was soon expelled, but the placenta remained in the uterus. The patient, although subject to metrorrhagia, *lost little blood*. For three days she was very well, on the sixth she gave up her deliverance and began to get worse: the fever flared up, fetid diarrhoea occurred, the lochia took on a foul odour, and on the seventh day she succumbed.

In summary, we see here again the transfusion acting marvellously, and almost, it may be said without exaggeration, as in a physiological experiment. The patient was revived immediately, as soon as the blood had penetrated her veins, and comes out of a serious condition in a few moments. What would have happened if this puerperal fever, the main symptoms of which we have just traced, had not come to take her away? This is a question that no one can resolve; however, what remains indisputable is that the epistaxis stopped, that the miscarriage was accomplished with an insignificant loss of blood, although the unfortunate woman had an annoying predisposition to metrorrhagia.

We therefore approve of the operation of Messrs. Blondeau and Anger and we can only congratulate our colleagues on their decision.

Assuming that the infusion of blood acted only as a haemostatic means, it would be permissible to practise it in a haemophiliac suffering from severe haemorrhages, thus saving time and perhaps having the right to hope for Lane's happy fortune, that of snatching from death and definitively curing his patient.

This surgeon found himself, it must be said, facing with relatively favourable conditions; the boy he operated on had not been slowly exhausted by blood loss, he was doing well. Usually, it is quite different, the subjects have been more or less hypemic for a long time when the transfusion becomes urgent, and the operation has but little chance of success in them, as I have pointed out previously, precisely because all the organs are diseased.

Conclusion: Transfusion is a rational operation in the serious haemorrhages of haemophilia, and the results it has given so far, although very unsatisfactory or non-existent if we consider only the definitive cure, are not bad enough to make us give up further attempts. It seems to me that it would be appropriate, to act early and not to wait for the exhaustion of the subjects before transfusing them.

Here are now other operations carried out to ward off accidents occurring as a result of nasal haemorrhages of ill-determined origin. Was it still haemophilia? It is possible, even probable, but the fact is not absolutely demonstrated. I summarize them in a few lines:

In 1851, Monneret received at the Saint-Antoine hospital a young woman of 28 years, suffering from epistaxis since childhood, and also affected by uterine haemorrhages for 6 or

7 years. She was then very ill, was covered with ecchymotic spots similar to those of scurvy, had swollen and fungal gums, and had fallen into such a state of weakness that she looked more like a corpse than a living person. Chassaignac injected 120 grams of defibrinated blood into her cephalic vein, without her experiencing any unpleasant sensations. The condition seemed at first to be better, but an hour later there came great agitation, cold, burning thirst, gradual weakening, and soon the patient succumbed.

It is this observation that leads Monneret to say that transfusion is an anti-physiological operation. Applied in this way, I agree that it has and cannot have any chance of success. When a subject has reached this degree of marasmus, the blood that is infused into him can have no effect on his altered organs; and it would be to fall into the error of the first transfusers, who believed in the renewing effects of a young man's blood infused into the veins of the old man, to think of a possible restoration of the vital forces, when the tissues of the economy have been completely altered by profound disorders of nutrition. Monneret's patient, most probably a haemophiliac, died because she had reached the last stage of cachexia. Transfusion could not save her and it had nothing to do with her death.

In 1863, Fenger gave the transfusion to a woman who had been rendered bloodless by repeated epistaxis. At first she was much better; but metrorrhagia prevailed after 24 hours.

In 1869, Buchser, in America, was happier. He saved from certain death a 28-year-old woman who had suffered, in the course of typhoid fever, abundant nosebleeds and metrorrhagia. The infusion of 100 grams of defibrinated blood with the addition of baking soda revived the patient and stopped the vomiting that tormented her relentlessly. The recovery followed, complete.

Finally, in 1873, Smith, finding himself in the presence of a little girl of 8 years old affected by severe sub-acute anaemia, as a result of frequent epistaxis, and converted to purpura spots, did not hesitate, in spite of the desperate state of this child, to attempt the infusion of blood: 350 grams of this defibrinated humor were injected. It was in vain, the dying girl recovered a little, but she succumbed two hours later. In summary: out of six transfusions performed in the case of nasal epistaxis, probably of a haemophilic nature, we note only one complete healing.

This statistic itself, although very mediocre, is therefore joined to the theoretical ideas we have put forward and to the favourable interpretations easy to deduce from observations, to induce practitioners to try this extreme resource.

I come now to the vomiting blood.

b) *Haematemesis*. – They may be of very diverse causes, which I shall not undertake to enumerate so as not to depart from my subject, and I am content to say that it is generally in those which are symptomatic of round ulcers of the stomach that transfusion has been attempted, and also sometimes perhaps in the case of cancer when the diagnosis was uncertain.

The abundance of the vomiting of blood is an important sign in the differential diagnosis of the simple ulcer, and on the other hand it is a factor of great power to bring about a state of serious sub-acute anaemia, especially since the haematemesis is repeated quite often and the general condition of the patients is poor because of the concomitant dyspeptic disorders. A stomach ulcer is a curable disease. Consequently, patients affected by it are entitled to be helped by infusion of blood when their situation has become worrying as a result of frequent blood loss.

A few facts will show us how useful this operation can be in such circumstances.

A 38-year-old man, treated by Anderson in 1869, had become bloodless as a result of enormous haematemesis caused by a round ulcer of the stomach. He was injected with 180 grams of defibrinated blood with immediate and definitive success: he got up and recovered completely.

In 1871, Ruggi was less happy in a 65 year old woman, who had suffered the same accidents. Four transfusions in low doses, made successively, simply moderated the haemorrhage and did not prevent the fatal termination.

Finally, I will summarize the interesting observation of Bernheim and Gross, reported in the *Revue médicale de l'Est* (May 1, 1874), and which, although negative as to the final result, nevertheless pleads in several of its interesting aspects in favour of transfusion.

It was a 52-year-old man, who had been suffering for two years from frequent and fairly abundant vomiting of blood, symptomatic of a simple ulcer. The anaemia being profound, it was decided that it was necessary to transfuse. Dr. Gross therefore injected, with the Dieulafoy device, 120 grams of defibrinated blood maintained at 35°. The operation was well tolerated; the temperature rose a little in the course of the day, then the general condition became very noticeably better during the ten days that followed. At that time, there were definite signs of "*nosocomial infection*" and the patient died four days later. The autopsy showed that it was indeed a simple ulcer. It was large and sat below the cardia, on the posterior surface of the stomach. The liver was *pale and pasty in consistency*; the heart *soft, pale and flabby*. I regret that a microscopic examination of these organs has not been carried out, we would probably have encountered fatty degenerations of the liver and heart, as *a priori* the particular consistency of these viscera seems to indicate, and we would be more authorised to exonerate transfusion from this relative failure.

The fact remains that the patient was revived by the injection of blood. It is to be feared, however, that the operation would have failed, all the same, in a more satisfactory environment than that of the hospital, because of the serious trophic alterations that the man's organs must have undergone, under the influence of a profound anaemia that had lasted for two years. Such is the power of the remedy, however, that for ten days the patient was actually and comparatively better.

I now list other observations of haematemesis which required transfusion, but in which the nature of the accident is no longer the same or is not mentioned.

These are, in chronological order, the following:

1° Uterhardt, 1860: repeated haematemesis, in a 60 year old man, poor general condition, beginning agony, transfusion of 120 grams of blood into the cephalic vein, no effect, death after 12 hours, cirrhosis of the liver noted at autopsy;

2° Seyfert, 1871: abundant haematemesis of unknown origin, in a 22-year-old woman, severe collapse, transfusion of 110 grams of defibrinated blood, recovery;

3° Seyfert, 1872: considerable haematemesis, of an unspecified nature, in a young man of 23 years, excessive weakness, convulsions, syncopes, etc., infusion of 150 grams of defibrinated blood, rapid improvement and recovery after one month.

In total: six cases of transfusion, three of which were due to symptomatic haematemesis of simple ulcers, three healings. If I were to point out that Uterhardt's patient, being afflicted with cirrhosis of the liver, could not be cured; that Bernheim's was transfused too late, and that finally Ruggi operated on a woman of 65 in pitiful conditions, I would almost be right in saying that transfusion is a means that almost certainly succeeds in haematemesis.

I will be very careful not to use these little tricks of calculation, which look like diverted dissimulations and which statisticians so readily abuse, and I prefer to blame three deaths out of six operations, which is an acceptable proportion. As for the three successes, they are well done to encourage new attempts in this direction. A subject suffering from severe haematemesis cannot be allowed to die of exhaustion from now on

c) *Traumatic haemorrhages*. Under this heading I am going to confuse blood losses of very different origins but having a common link, any lesion of the integuments producing the issue of the blood outside.

α) Sometimes transfusion has been attempted in subjects with *ulcers of a bad nature* and rendered bloodless by repeated blood loss. Such are the following cases:

1° Neudorfer, 1860: *epithelial cancer* in an 18-year-old boy, injection of 45 grams of defibrinated blood, died three hours later.

2° Tiersch, 1862: *sarcoma of the jaw*; transfusion of 40 grams of defibrinated blood following profuse haemorrhages, gradual improvement, recovery.

3° Thiersch, 1872: *cancer of the rectum*, in a 46 year old man, considerable haemorrhages, deep collapse; transfusion of 470 grams of defibrinated blood, in 2 times, instant improvement, died on the 8th day, as a result of a new loss.

β) Sometimes it was a question of *haemorrhages in operated patients*, as in the following cases:

1° Petersen, 1871: *ablation of the upper maxilla*, successive haemorrhages very abundant; transfusion of 600 grams of blood through the humeral, died during the operation. Such an end is not surprising: 600 grams of blood constitute a massive dose, more capable of annihilating the expiring vital forces than of awakening their energy.

2° Busch, 1872: *resection of the humeral head* in a case of complicated fracture, very abundant haemorrhages, ligation of the subclavian; transfusion of 180 grams of defibrinated blood, very obvious improvement, died after 6 days, of pleurisy.

3° Albert, 1873: operation for a strangulated hernia, in a 69 year old man, succession of serious blood loss; transfusion of 180 grams of defibrinated blood, improvement, death after two days, pulmonary oedema and asystole.

4° J. Casse, 1874: *ablation of a series of small cancerous tumours of the breast* in a woman; repeated haemorrhages, considerable weakness; injection of 85 grams of blood through the left saphenous vein, consecutive shivers, of short duration, sweating, more abundant urine, increased appetite, gradual improvement and complete recovery.

γ) From these facts we can compare without much effort of comment the transfusions made on individuals bled excessively and consequently fell into a serious state of anaemia.

Here are two examples:

1° Polli, 1852 excessive anaemia in a young woman of 23 years, bled more than three hundred times. The author, having previously determined *magnetic sleep*, infuses her four times in a row, at short intervals, with only 7 grams of defibrinated blood. The patient revived, ceased coughing, was able to walk and soon recovered.

Imagination *and willpower* have perhaps contributed as much as the transfusion to the healing of this young girl.

2° Bougard, 1847: a 26 year old woman, affected by haemoptysis, was treated by copious blood emissions and ended up falling into a real state of haemophilia and excessive anaemia; she had very strong metrorrhagia and loss of blood from all the orifices. Bougard, with the help of a device of his invention, infuses her with 80 grams of blood and thus reports the patient's sensation: "I feel," she says, "a warm liquid flowing into my body and particularly towards the heart; I feel an unusual heat." The improvement was considerable, and such that the patient, not yet feeling fully recovered, *demand*ed a new transfusion 7 days after the first. This time she was injected with 90 grams of blood. The condition is becoming very good. Unfortunately later on a periuterine phlegmon occurred and death was the end of it, 4¹/₂ months after the transfusion.

Ultimately, there are nine new cases of blood infusion, four of which were successful. When, moreover, I have made the following remarks on the subject of the five failures, which is only just, it will certainly be agreed that an operation which is so successful offers serious guarantees. These remarks are as follows: In the case of Petersen, the transfusion was made in too high a dose: 600 grams of blood, according to the opinion of a large number of transfusers, cannot be injected without danger; then I will add that in the observations of Thiersch, Busch and Albert the patients succumbed to accidents which had no connection with the transfusion: lightning haemorrhage, pleurisy, pulmonary oedema. The statistics, as we can see, are sufficient.

We therefore believe that we can once again call the attention of surgeons to the infusion of blood; it is capable, in our opinion, of rendering the best services to the exhausted wounded, whether it is a question of combating acute or sub-acute anaemia in them, or for preparing them to undergo in better conditions an operation recognized as urgent, and which one does not dare to undertake in view of their state of weakness.

Some doctors have, in fact, had the happy idea of transfusing the wounded weakened by blood loss before a serious operation, amputation, resection, etc., and have been able to make him easily bear the shock of the operation. This is how Higginson (1860), Simon (1851), etc., proceeded.

The first transfused 350 grams of blood into the veins of a 50-year-old man, suffering from gangrenous phlegmon of the forearm, exhausted by suppuration and haemorrhage,

and unable to undergo amputation. The improvement was such that the next day the operation could be carried out. The patient recovers. Same results, in Simon's observation; but the patient died of pneumonia on the 6th day.

All these interesting questions have led me, despite myself, further than I would have wished, and I am obliged to say, by simply stating the titles of the observations, that transfusion has still been practiced in the various cases of haemorrhage, of which here is the list:

1° *Enterorrhagia*. – Hüter, 1869, 36-year-old man, affected by abundant losses of unknown nature, state of severe anaemia, transfusion of 240 grams of blood; healing;

2° *Haemoptysis*. – Bliedung, 1839: according to Gesellius, an 83-year-old man, put in a state of excessive weakness by spitting blood, was cured by the transfusion of 120 to 150 grams of venous goat blood.

I cite this case for information, not as an example to be recommended;

3° *Haemorrhoidal flow*. – Albanese, 1869: 50-year-old woman, in a state of excessive anaemia, vomiting, having convulsions, etc.; transfusion of 95 grams of defibrinated blood into the left radial; healing.

These last three observations complete the series of known cases of haemorrhages requiring the operation of transfusion. This, as we see, has been practiced in all varieties of external blood loss. One author has proposed transfusion in the very case of rupture outside of aortic aneurysm.

I do not have to do justice to this exaggeration, there is no one who stops to listen to such propositions; and, without mentioning the *Operating Manual*, which does not differ from the one described above, I conclude by formulating some general conclusions which seem to me to follow from the facts studied in this long chapter.

Conclusions: Transfusion is a heroic remedy for acute anaemia resulting from rapid haemorrhage, when practised in time.

It can and has already rendered considerable services in traumatic haemorrhages and, even more, in puerperal metrorrhagia.

It is more rarely successful in uterine discharge, outside the puerperal state, because it is performed late, when there are probably already profound alterations in the tissues, but it has nevertheless quite often given good results.

If it has almost always failed in haemophilia, it must not be concluded that it is absolutely powerless against this formidable affection, and further attempts must be made, since some patients have benefited from the injection of blood, and an authentic example of complete recovery has been cited (Lane).

Finally, transfusion has been very useful in certain cases of haematemesis, in the repeated haemorrhages of the wounded, and as a preparation for major operations, and finally in various other enterorrhagial losses, haemorrhoidal flow.

In summary, in the presence of a serious uncontrollable haemorrhage, in the presence of a worrying state of acute or sub-acute anaemia, the doctor must have transfusion accepted, an extreme resource which is now imposed on practice by a large number of undeniable successes.

The operation will be carried out with normal blood, for although defibrinated blood has given rise to good results in a fairly large number of cases already, although it is convenient and harmless to use, we can recognize in its use various disadvantages: its relatively long and difficult preparation, the possible alteration of the globules by beating, the incorporation into its mass of the germs of the air, etc.

For the infusion of blood, transfusion devices are not essential; all you need is an ordinary syringe. At a pinch, when the urgency of the operation is not absolute, when one has time ahead of you, one can use a few simple transfusions which we will talk about later.

Finally, the doses will always be rather *small* than *massive*. I recall the opinion of Bérard, which a typographical error has led me to previously attribute to Professor Gubler, and I quote the complete passage relating to it, written by the eminent physiologist:

"It is not necessary," he says, "to give back to an animal or an individual, which a haemorrhage has rendered anaemic and plunged into a state of apparent death, as much

blood as it has lost. The urgent indication is to set in motion cogs that have ceased to function, so that the individual who has been subjected to transfusion can then form blood by his own activity."

As for the blood of animals, if physiology did not almost forbid its use, it would still have against it the material difficulties that would be found in obtaining it under good conditions.

In short, and this is my final conclusion, blood transfusion must henceforth be part of the treatment of profound anaemias following haemorrhages. This is even the best of all the applications of this remarkable operation.

PART 8

CHAPTER 2

TRANSFUSION IN SOME CONSTITUTIONAL DISEASES AND CERTAIN ANAEMIAS DUE TO DYSCRASIA

Among the constitutional affections sometimes called dyscratic or dystrophic, there are three, scurvy, purpura, and leukocythemia, in which the blood undergoes considerable alterations, and which frequently lead the subjects affected by them to severe rapid anaemia, cachexia, and death. This ending should surprise no one. To a first cause of anaemia, the proper affection of the blood, still unknown in its essence, which I recalled only a moment ago, is added another no less powerful, haemorrhage. Thus the sick are sometimes drawn very quickly towards the fatal outcome, without art having time to usefully intervene to stop their fall.

Transfusion was naturally to present itself to the minds of doctors, as a remedy, if not curative, at least a palliative remedy for this deep hyphemia into which patients struggling with these morbid states can be thrown. It has been proposed, in fact, either as an emergency treatment following an abundant loss of blood which has caused collapse, or as a suitable means of combating the anaemia and the weakening produced by these diseases, even without any accident of haemorrhage.

In short, in scurvy, purpura, and leukocythemia, the blood mass may decrease just as much as in the haemorrhages proper which we have just reviewed.

Consequently, it therefore seemed natural and logical to place, in our study of transfusion, these morbid affections following post-haemorrhagic anaemias, because both have a common pathological background, the enormous impoverishment of the blood. However, it must be said at once, the conditions are far from being the same in these two orders of accidents; and transfusion, which we have just seen so heroic in certain haemorrhages, will have only a mediocre influence here, because of the trophic alterations of the tissues, inseparable from a violent disturbance in nutrition.

§ I. TRANSFUSION IN PURPURA, SCURVY AND LEUKOCYTHEMIA.

a) *Purpura*. – If the so-called *simplex* variety is generally benign and easily curable by ordinary restorative means and a well-understood hygiene, that which is designated under the name of *haemorrhagica* is much less so and certainly kills $\frac{1}{3}$ of the patients who are affected by it; consequently it is absolutely essential to try to improve this rather not very brilliant statistic and to see if transfusion would not be a better resource than those provided by the *materia medica*. Evidently this is possible, for, on the whole, the alterations of the blood in Werlhof's disease are relatively benign and the lesions of the solids are not very advanced or absent when the affection is of recent date. It is therefore necessary, without hesitation, to transfuse in cases where the haemorrhages are abundant and threaten existence, it will be possible to prevent the immediate fatal outcome and *perhaps* definitively save the lives of the patients.

Unfortunately, the transfusion observations are not encouraging, and it is only on the foregoing theoretical considerations that I base my recommendation. In fact, in the four cases that I have collected from the authors, healing has not been obtained once.

Josenhaus, in 1832, transfusing a young girl plunged into collapse by a severe haemorrhage, could only galvanise her momentarily. Jurgensen, 1871, was no happier, after having injected 275 cubic centimetres of blood into a 6 year old child. But this was not a true Werlhof disease, since a caseous pneumonia was found at the autopsy.

Finally, Potempski, 1873, also failed in an 18-year-old girl; and Thomas Smith, in an 8-year-old child. The English doctor only decided to transfuse when the young patient was almost dying. He injected him with eleven ounces of defibrinated blood and passed through a horsehair sieve, with some immediate success. Nevertheless, 2¹/₂ hours later, the child succumbed. The author regrets, and in this, I am of his opinion, to have used defibrinated blood; he thinks that normal blood would probably have more healing properties in hemorrhagic purpura.

b) *Scurvy*. – This disease is rare in France, in its most serious degree; but in Russia and Germany it sometimes rages with great intensity and hits certain subjects harshly. It is in these two countries that transfusion has been opposed to almost desperate cases, and the treatment has been favourable, as evidenced by the particular observations of Roussel. The three patients he transfused healed easily. One of them, a young man of 25, had an ancient scurvy which had put him in the worst condition: anasarca, albuminuria, diarrhoea, excessive weakness, temperature at 36.8°. The infusion of 250 grams of blood revived him and, after nine days, he obtained a "complete healing, brilliant as well as unexpected."

A few years earlier (1868), Mader, with 200 grams of defibrinated blood, had also cured a subject affected by severe scurvy.

It is quite obvious that this disease of misery only very slowly produces visceral lesions beyond the resources of the art, and that, if we manage to stop the slow wasting, with the help of the infusion of rich blood, the patients, as Roussel says, will be able to wait for the action of the usually used means, the effectiveness of which, in the great majority of cases, is not doubted by anyone.

c) *Leukocythemia*. – Here the question completely changes its aspect; not only is the blood altered, but the organs are also diseased. If the red cells have decreased to a considerable extent, the white globules have increased enormously, also the spleen, the lymph nodes, and the lymphoid tissues in general have undergone serious changes, and it may be said that the whole body is under the influence of considerable and irreparable disorder.

When haemorrhages occur and add a cause of weakness and exhaustion to those already resulting from defective nutrition, it is clear that the severity is extreme and that the diseases are doomed to certain death. Under these conditions, therapeutic intervention has no chance of success and treatment can only be palliative. Transfusion is no more successful than the most recommended medications, it may well delay the fatal termination of the disease, but it cannot prevent it.

The three examples reported by Mosler (1866), Hüter (1868) and Heineke (1871) support what I am saying. The injection of blood no doubt improved the condition of the subjects, temporarily, but they died soon after.

Ultimately, despite transfusion, the prognosis of leukaemia remains absolutely fatal; and, as long as we are not better informed about the nature of this affection of the haematopoietic organs, we cannot hope to see its severity change.

I now come to another constitutional disease in which we can well suspect an alteration of the haematopoietic glands, but in which pathological anatomy is still powerless to edify us as to its nature, I want to talk about chlorosis.

§ II. TRANSFUSION IN CHLOROSIS AND CHLORO-ANAEMIA.

Although the microscope has not yet taught us anything about tissue lesions in chlorosis, we must nevertheless believe in the existence of special organic modifications which still escape our investigations, and consider that the alterations of the blood may well not be primary, but secondary. In any case, hypoglobulia [hypoglobulinaemia – PL] is until further notice the capital and indisputable fact in this disease, and it is this poverty of the blood that the transfusers have sought to make disappear by the method we are studying.

The idea is good; I would say excellent, if I were not obliged to reservations about tissue lesions. But, in short, since these escape us, it is because they are shallow. Consequently, *a priori*, it is permissible to base good hopes on the use of transfusion in chlorosis. Ultimately, it would only be a matter of raising the number of globules, which has often fallen so low that we find barely half the normal proportion. It was thought that transfusion could act in two ways to combat this shortage of globules. First of all directly, through the contribution of billions of red blood cells. The fact is beyond doubt, as demonstrated by the globular count in various transfusion observations, it is easy to count, a few moments after the injection, several hundred thousand more red blood cells in a cubic millimetre of the blood of the transfused person.

We then accepted the hypothesis of a particular stimulating action of the blood globules on the haematopoietic glands, by virtue of which these organs would function more actively and produce a greater number of red blood cells. Polli has especially supported this thesis and readily sees in the infusion of blood a sowing of globules which would become the origin of an abundant production of these histological elements. This opinion is admissible, but the preceding one is much less so. The contribution of globules is illusory and cannot be taken into account since all of them are destroyed very quickly and disappear from the economy shortly after their introduction; it is better to accept the idea of their exciting action on the organs of haematopoiesis.

How else can we understand their role, and, certainly, they have a very real and serious one, in the curation of chlorosis? I do not see any other satisfactory way to interpret it. It is now known that the blood globules of the chlorotics have not only diminished in number, but also that their very composition is altered, because their haemoglobin no longer has its normal qualities. Such elements, if modified, would not be able to provide the nervous system and the organs of haematopoiesis with the stimulus necessary for their regular functioning; on the contrary, healthy globules are able to awaken their numb energy.

But, let us put an end to hypotheses and seek convictions in clinical facts. Their number is quite limited. Chlorosis is a condition that is most often curable, and we possess today, apart from the thousand martial preparations in the pharmacopoeias, a good number of effective means of curing it; this is why doctors are rarely confronted with rebellious cases requiring transfusion. Sometimes, however, when gastric disorders become predominant, nutrition languishes, strength declines, and weakness is such that death may occur. We then decide on the transfusion: it is only time!

I have before my eyes various examples very capable of inspiring confidence in this mode of treatment, and I will summarize them in a few words.

Nussbaum, from 1861 to 1864, cured three patients by the injection of large doses of defibrinated blood: 360, 450, 350 grams.

Hasse, 1872, obtained two successes using much lower doses 30 and 90 grams of defibrinated blood.

Casse, 1873, reports three more favourable observations; he injected only small amounts of defibrinated blood: 80, 75 and 25 grams. He saw in his three patients the appetite rise noticeably after the transfusion, sleep return, the painful neuralgia disappear and the strength increase rapidly.

Roussel and Cristophoris were no less fortunate. The first had the satisfaction of seeing a 39 year old woman, who had been ill for 20 years, and in the most serious condition, cured in 1½ months, after the infusion of 250 grams of normal blood. The second succeeded, despite the infusion of 600 grams of blood, in saving his patient.

Finally, Heyfelder had the audacity, I would gladly say the imprudence and temerity, to open the humeral of a blood donor, who was really too benevolent, and to infuse seven ounces of arterial blood into the veins of a chlorotic. Both recovered; however, this is not an example to follow.

I find only 2 failures reported: Mader, 1868 the transfusion failed completely; M. Reynaud, 1868: insignificant improvement.

In summary, these are ten favourable cases out of twelve. Among the examples of healing, all of which are conclusive, there is a certain observation whose reading alone

would be enough to convince the most incredulous of the value of the method; so that the number and importance of the observations are added here to induce us to recommend transfusion in rebellious cases of severe chlorosis.

§ III. TRANSFUSION IN CERTAIN ANAEMIAS DUE TO DYSCRASIA.

A large number of long lasting acute diseases, and all chronic affections, it may be said, enjoy the sad privilege of altering the composition of the blood. At the end of a very short time, chemical or microscopic analysis often reveals in this mood various qualitative or quantitative changes in the principal components, not to mention other modifications which these very inadequate modes of investigation still leave us unaware of. Always, in the course of serious illnesses, the blood globules, the salts of the blood and its albumin decrease; that the water, on the contrary, increases, and that, in a word, the blood becomes sick. It is then that we pronounce the word anaemia, the terminology of which has often been attacked, and rightly so, but which is convenient and deserves to be preserved since everyone understands its meaning. The anaemia thus considered is therefore a defective state of the blood, characterized by qualitative or quantitative alterations of the elements which enter into the composition of this humor, and which may naturally occur under very diverse dyscratic influences; I call it dyscratic for this reason in order to distinguish it from the acute or sub-acute post-haemorrhagic anaemia of which I spoke previously. This distinction seems to me necessary from the clinical or therapeutic point of view. We conceive, in effect, that transfusion, which we have seen succeed wonderfully in hyphemias symptomatic of haemorrhages, has much less chance of success in dyscratic anaemias which, after all, reflects a more or less serious state of the economy and make one think of deep tissue changes.

A host of morbid states, I repeat, inevitably lead to dyscratic anaemia; but there are some which seem to possess a more effective and more rapid action to produce it, and which have given rise, for that very reason, to attempts at transfusion; I will study them successively under the following titles: prolonged suppurations, excessive breastfeeding, inanition, serious fevers, etc.

a) *Prolonged suppuration.* -- Like haemorrhages, prolonged and abundant suppurations weaken patients and exhaust them. The diapedesis of the white globules is to a certain extent comparable to the outcome outside the blood corpuscles; there is therefore no reason to be surprised that this purulent flow has been opposed, as to the blood flow, by the same treatment, that of the infusion of the blood. Unfortunately, the conditions are no longer the same; the patient who has just lost blood may be as debilitated and weakened as the one whose wound has let out streams of pus for a long time, but the tissues of the former have not suffered, while the organs of the latter are sometimes profoundly damaged. This is the capital difference which must be taken into account. After prolonged suppurations, the main viscera have frequently undergone extensive fatty or amyloid degeneration which renders them incapable of functioning regularly; there is therefore nothing to hope for from transfusion. It can only be palliative and cannot save the sick from certain death.

Does this mean that I recommend non-intervention, the pure and simple expectation, for the sole reason that the chances of recovery by transfusion are very limited? Not in the least. If we can foresee and suspect organic alterations in a wounded person exhausted by abundant suppurations, we have no characteristic signs that allow us to make a diagnosis; and I maintain that in the absence of a better remedy one should try this extreme resource, especially when one has the hope of being able to dry up the flow of pus. There is obviously no need to think of this operation in the case of vast detachments, enormous foci such as those sometimes observed after extensive diffuse phlegmons, complicated fractures of the thigh, vast burns, etc.; but in certain more localized affections, when the possibility exists of stopping the flow of pus by amputation, resection, removal of sequestration, good epidermal grafts, drug injections, etc., etc., I do not see why one should hesitate to raise the strength of the patient by the infusion of new blood, and thus to prepare him for an operation that could save him.

Roussel, in a case of excessive anaemia in a subject suffering from a cancerous thigh wound, made the transfusion after the removal of the epithelial tumour. Healing took place.

In two patients, one affected by pleurisy, the other by psoriasis, it still succeeds as desired. But in two other cases, the Geneva doctor obtained only a momentary improvement and could only prolong the life of the patients (suppurations in a scrofulous patient and in a tuberculosis patient).

Albanese (1869), Hasse (1869), Leisrink, 1872, have each reported a case of success, after the injection of defibrinated blood.

Unfortunately, alongside these happy results, what setbacks!

In 1859-60, at the San-Spirito hospital in Verona, Neudorfer failed 6 times, by transfusing wounded members of the Austrian army reduced to stagnation, and could only prolong their existence for a few days. Later, in 1870, he was no more successful in a similar circumstance.

Finally, other surgeons, Nussbaum (1862, 1870, and 1871), Huter (1869-1871), Busch (1871), Leisrink (1872), Kuster, of Berlin (1874), and Roussel, were no more favoured in the ten or twelve cases they published.

We can therefore contrast the six favourable attempts that I have just indicated, followed by an excellent result, with more than 20 failures.

However, this mediocre statistic must be accepted as relatively good and offered to the meditations of surgeons. This is what we are doing, adding to them the reservations we made at the beginning of this paragraph; the question deserves to be studied again, experimentally, if I dare so say.

b) *Prolonged breastfeeding.* – Three cases of transfusion in the anaemia of wet nurses have been reported by Higginson (1855), Cristophoris (1867), el Moutard-Martin (1875, - Society of Hospitals). The first succeeded alone in saving his patient.

c) *Inanition.* – When the body receives less than it expends, when the assimilation of food materials is very imperfect, nutrition languishes, the strength weakens, and the organism falls into that state of debility and prostration which has been so well described by Chossat under the name of inanition. It is clear that the blood is profoundly altered in such cases, and that dyscratic anaemia is again one of the dominant symptoms of this organic decline. In a few rare circumstances, inanition recognises as causes, in man, certain curable affections or lesions, and it is against the effect, against anaemia, that recourse is had to transfusion, to support the patient and put him in a position to await the cure of his disease.

We already know, and I need not dwell at length on the point I mentioned previously, that in *starvation* properly so-called, caused by absolute deprivation of food, methodical transfusion is powerless to prevent the death of animals, and that it would even seem, whatever may have been said, to make it quicker.

The blood, considered by Denis to be the "ultimate and most perfect result of digestion," is incapable of feeding animals put on a complete diet; therefore there is no hope to be found on its methodical introduction into the veins of inanimate subjects; the authors who believed in its restorative effects were perfectly deceived. Blood is only a stimulant of vital properties and cannot serve as food, for this reason it is eliminated quickly and completely after being injected.

In 1819 Blundell gave his first transfusion to a man named Brazier, suffering from stomach cancer and exhausted by starvation. He injected 12 to 14 ounces of blood, in 30 or 40 minutes. The patient immediately assured that he felt "better, much better and less weak", he had a spontaneous bowel movement, which had not happened to him for a long time, regained some appetite, but nevertheless succumbed, 56 hours later.

This was a transfusion *in extremis*, which could not have any definitive favourable result since the patient had cancer of the pylorus, but the benefit was real; and this observation distorts the advantage that a physician can derive from the infusion of blood, to make a dying man live a few days longer.

Under similar circumstances, Mayer, 1860, and Potemski, 1873, were the first to succeed in relieving a 40-year-old woman suffering from stomach cancer, and in prolonging her life by 2 months; the second, to give a patient, in the same situation, 15 days of survival.

On the other hand, Higginson, 1857, and Brouardel, 1873, obtained only insignificant results from the transfusion of blood in inanition. Higginson transfused a melancholy woman who refused to eat, and Bronardel an 18-year-old boy who, after an ingestion of sulphuric acid, had fallen into marasmus as a result of complete apepsy. It seems to me that it is useless to attempt transfusion in poisoning by sulphuric acid, except as a palliative; secondary lesions of the liver and kidneys (fatty degeneration) do not allow us to count on complete success, unless, however, the dose of the poison was weak.

Transfusion, in starvation, has not always failed. In 1843, Pritchard and Clarke published a remarkable observation of excessive anaemia in a dyspeptic man, cured by this operation, and Roussel cited another, no less curious, more recently.

The case was a 28-year-old man with a nasopharyngeal polyp obstructing the pharynx and preventing feeding; 200 grams of blood revived him and restored his strength.

d) *Severe fevers. Intestinal disorders.* – In severe fevers: typhus, typhoid fever, etc.; in some phlegmasias, malnutrition is excessive and, in addition, assimilation and repair are almost nil.

Thus the weakness may become considerable and the anaemia profound. Quite often, the patients, after having successfully struggled against acute accidents, are exhausted when they retrocede, they touch the port without being able to enter it. Under these conditions, the infusion of blood comes to their aid, supports them in this fight which no longer turns to their advantage and they end up triumphing.

Here again, however, there arises that insurmountable obstacle which I have so often indicated, the fatty degeneration of the tissues, the inevitable consequence of the rapid malnutrition which is commonly observed in all continuous febrile states with high temperature. Need I recall in this regard the granulo-fatty alterations of the kidneys, the liver, the waxy or fatty degenerations of the striated muscles (Zenker) and of the heart, in subjects who died of typhoid fever. Everyone recognizes them today in this pyrexia, and pathological anatomy still reveals them in many other febrile affections.

This is a cause of failure for transfusion. At any case, this operation has already rendered great service in the anaemia consequent to serious febrile states, and science has recorded some of its successes.

Roussel saw it succeed completely in three patients suffering from typhus or dothientery, out of five whom he subjected to the infusion of blood with the help of his device. The other two were, however, improved; one died of cholera and the second of intestinal perforation.

More recently Liouville, Channel and Voisin raised the strength of a young man suffering from typhoid fever by injecting him with a few grams of blood. However, he died of intestinal haemorrhage.

Professor Béhier considers that typhoid fever is one of the diseases in which transfusion has the best chance of success; he wants it to be depleted, that is to say, preceded by a small bleeding "so as not to overload the circulatory system and to act only by the quality of the blood, which is more apt to fight against general debility.

In this way it might be hoped to revive the nervous system, and through it the digestive and absorbent system, to restore to the blood its qualities necessary to continue the vital movement."

Of typhoid fever I compare gastroenteritis, which has some affinities with it and which disturbs nutrition by a similar mechanism, I content myself with saying that in two cases of serious anaemia, symptomatic of this alteration of the digestive tract, reported by Hasse, in 1871, and observed in children of 1¹/₂ and 12 years of age, the injection of 30 grams of defibrinated blood was successful once: it was in the case of a 1-year-old patient. And I add that Mr. Reynaud, in a case of uncontrollable diarrhoea in a pregnant woman, was not able, after childbirth, to prevent death by infusing her with 200 grams of defibrinated blood. It is true to say that the patient had imminence of metro-peritonitis.

e) *Purulent fever, septicaemia.* – It was intended to counter by transfusion the profound alterations of the blood in purulent infection and septicaemia, at the same time as an attempt was made to raise the strength of the subjects by providing them with blood of good quality.

Some of de Belina's experiments, made on dogs made sick by the injection of septic matter into their veins, were quite successful, and the animals eventually recovered. Absolutely nothing can be concluded from these imperfect tests; and it is to be feared that another experimenter, Berns, who has also transfused dogs made septicaemic without succeeding in curing them, is right against de Belina, when he says that transfusion is useless or dangerous in septicaemia.

The clinical facts are so far absolutely unfavourable to de Belina's view.

Albanese (1868-69) reported 4 unsuccessful attempts in diseases showing signs of pyhoemia; Hüter (1869-71) cites two others; Busch (1869-73), also two; König and Hasse (1869), one each. In short, out of ten transfusions performed in subjects suffering from septicaemia or pyohemia, there was not a single case of recovery and quite rarely was a small improvement noted. Several times the blood was infused after a bloodletting.

§ IV. TRANSFUSION IN SOME CACHECTIC STATES.

I have already spoken of transfusion in cancerous cachexia, to say that it can only be palliative, and I have added that it should only be performed in special circumstances, to preserve a loved one a little longer and to ensure a survival dictated by family reasons. The state of pregnancy in a woman would still be a condition to be invoked, as I mentioned in connection with metrorrhagia. Apart from these circumstances, it must be recognized that the operation should never be performed for cancerous cachexia.

In tuberculous cachexia, reasons of the same extra-medical nature could be invoked to justify the practice of transfusion; in fact, this method cannot be proposed as a serious mode of treatment to improve the condition of phthisis in the final period.

Prejalmini (1852), Neudorfer (1862), Hasse (1869), obtained only zero results or temporary improvements in the six cases they published.

Potemski (1873) speaks of a considerable improvement in a 23 year old woman suffering from caseous pneumonia, after the infusion of 200 grams of blood, and Dr. Heyfelder would have seen a similar result in a woman with 3rd degree tuberculosis, after she had received 12 ounces of *human arterial* blood, introduced into a vein by direct transfusion. Success, if it exists in Heyfelder's observation, cannot once again excuse the audacity of this surgeon, who did not hesitate to plunge a cannula into the *humeral* of a subject who offered to give blood.

Today, in Germany and Russia, some doctors, convinced of the value of arterio-venous transfusion as a treatment for pulmonary phthisis, are content to borrow the carotid blood of the sheep. We will return to this new method later.

By way of conclusion, we will say that in cancerous and tuberculous cachexia transfusion is and can only be a purely palliative operation.

PART 9

CHAPTER 3 TRANSFUSION IN POISONINGS

When a poison, morbid or chemical, has entered the body, its obligatory vehicle is the blood. This is the first tissue that it encounters, that it alters, transforms in its own way, without us being able to realize most of the lesions he inflicts on it.

In spite of this, we almost affirm, without fear of hazarding an adventurous hypothesis, that in contact with toxic agents, miasmas, contagions, effluvia, poisonous chemical compounds, etc., the blood loses more or less of its physiological qualities, that it becomes poorer, if not in quantity, at least in quality, and this *because its composition has been modified*.

So, ordinarily, we suppose the lesion of this humor, but without being able to demonstrate it, in the great majority of cases, except as a result of certain poisonings by chemical bodies.

This abnormal state of the blood, in intoxications of various kinds, naturally attracted the attention of transfusion doctors; and there will be no need for long developments to make clear the idea which dominated them when they proposed and applied their method in serious cases of toxic diseases.

Their goal was to remove the tainted blood and replace it with healthy blood.

Theoretically, transfusion applied to poisonings seems to me to be a good operation, especially when it is depletive, that is to say, preceded by bloodletting. It is a fortunate way of ridding the organism of useless blood, since it has lost its physiological properties, and a fatal one, because it may still contain a part of the absorbed poison.

It is also an excellent means of stimulating the economy, of strengthening it temporarily, of enabling it to await the elimination of the toxic agent, and of supporting it in this unequal struggle in which the violence of the poison threatens to carry the day.

Unfortunately, I repeat, these are only theoretical considerations, subject to many objections, and I can say in advance, which seems to me more serious, that rather rarely has transfusion succeeded in serious poisonings. Is it because it was done too late, when the tissue lesions were already too advanced, or is it because of real impotence? - that is what I cannot say.

I will set forth the facts as they have been reported, as a historian rather than as a judge, leaving it to the reader to draw the rigorous consequences which they entail. I classify them in various paragraphs, ranging from simple to compound. In a logical order, I begin this study with the vulgar poisonings best known to all, those which result from the absorption of chemical bodies, and I will end it with infectious diseases, the nature of which is still so ill-defined, in spite of the manifold efforts of pathologists.

§ I. POISONING BY VARIOUS TOXIC SUBSTANCES OF A CHEMICAL NATURE.

The number of compounds borrowed from chemistry and capable of producing toxic effects is considerable.

But there are some which cause more particularly frequent accidents, whether man voluntarily exposes himself to their disastrous influence, or he suffers it involuntarily. Among the latter, the usual poisons, if I may so say, still very numerous, I have only to mention those whose effects have been combated by means of transfusion; thus my task is much simplified.

This operation has been *practiced* especially in asphyxiation by coal vapour, carbonic acid, carbon monoxide, etc.; in poisoning by phosphorus, opium, belladonna, etc.; then it was *proposed* in poisoning by lighting gas, hydrogen sulphide, chloroform, etc.

In all these cases, obviously, in spite of the diversity of toxic symptoms, the two dominant phenomena are the asphyxial state and the chemical alteration of the blood: this internal environment has lost its oxygen and it contains harmful substances; hence the indication to modify it by transfusion.

Let us come to the facts and try to learn from them.

a) *Poisoning by coal vapour*: If I give the first place to this variety of poisoning, it is because the number of examples of transfusion here is very considerable, relatively at least, and which, moreover, we know today very well, I should say completely and better than in any other circumstance, thanks to the remarkable work of Cl. Bernard, the effects on the blood of coal vapours.

The first idea of the use of transfusion in the asphyxia produced by coal vapour seems to me to have been put forward by Polli, in 1852. At that time, the Italian doctor proposed this operation to combat asphyxia in general: that of drowned people, newborns, people who have breathed carbonic acid, carbon monoxide, or those who have been struck by thunder.

Later, in 1864, Kühne also proposed it and it was tried the same year by Traube.

Coal vapours have, as we know, a complex composition (carbon monoxide, carbonic acid, carbonaceous hydrogen), but they are especially dangerous because of the carbon monoxide they contain in large proportions. This gas gives them their pernicious influence; That is why we make no distinction here and consider the asphyxiation produced by the vapours of coal as synonymous with poisoning by carbon monoxide

I would like to remind you of the main features of this poisoning. It has been well understood, especially since 1855, when Cl. Bernard demonstrated the mode of action of this gas on the blood. He then taught us that carbon monoxide drives oxygen out of the globules, substitutes itself for it, volume by volume, to form a stable combination with haemoglobin. From now on the red blood cells are, so to speak, paralyzed and incapable of serving vital actions.

The physiological proof of this inertia of the globules which have been influenced by carbon monoxide has been given by Cl. Bernard in the following very pretty experiment: if a certain quantity of normal defibrinated blood is injected into the artery of one of the hind limbs of a dog which has just been bled white, all the properties of tissues are awakened; but if the same blood is infused into the other limb, after contact with carbon monoxide, the return of these properties will never be observed; the muscles and nerves remain insensitive to stimulants.

Thus carbon monoxide has a considerable affinity for haemoglobin, and it satisfies it by displacing oxygen from the blood globules.

So that it is permissible to compare the animal poisoned by the vapours of coal to the subject made bloodless by haemorrhage: both are, in the end, deprived of the stimulating elements of their blood.

Must we admit that the combination of carbon monoxide with haemoglobin is absolutely stable and cannot be destroyed? It's unlikely. Cl. Bernard is inclined to think that gas is eliminated from the body in a form that he cannot designate; perhaps, in part, under that of carbonic acid, and partly in nature. What is certain is that it disappears, since many asphyxiated animals survive.

This proves that transfusion is a rational operation in poisoning by coal vapours; it can provide man with the means to wait for the elimination of the poison. Cl. Bernard says that it has a double purpose: *to return oxygen to the blood and to promote the transformation of intoxicated blood into normal blood.*

This is also the opinion of Landois and Eulenburg (*Ac. sc.* 23 October 1865) whose conclusions are as follows: "Depletive transfusion, as perfect as possible, has shown itself to be the safest and most effective remedy, even in serious cases where there was asphyxiation and absolute paralysis, cases entirely resistant to treatment either by bloodletting alone, or by the most energetic artificial respiration (faradisation of the phrenic nerves, insufflation into the open trachea)."

Other physiological experiments, undertaken in animals (rabbits), by Maurice Raynaud, confirm this way of seeing.

Let us now see what the clinical facts tell us. Here is a brief analysis of two observations that seemed interesting to me.

In 1870, reports Hüter, of Greifswald, a young man of 26 years remained exposed for five hours to the action of carbon monoxide. When they came to his aid, he was completely anesthetised and almost in a state of apparent death, intermittent breathing, very weak; pulse very small, frequent; pupils and corneas insensitive. Artificial respiration and the electrification of the phrenic give no results. Hüter, seeing the breath almost suspended, opened the vein. Barely a few drops of blood flow. So he no longer hesitates to inject 500 grams of blood through the radial artery. After half an hour, the pulse is fuller, slowed down, the breathing is natural, the pupils sensitive and voluntary movements possible in an arm. Five days later, the recovery was complete.

In the same year, Jürgensen, in a case of asphyxiation by carbon monoxide, in a 28-year-old pilot, exposed for a day in a toxic atmosphere, also transfused 375 cubic centimetres of defibrinated blood, taken from three different people, and this treatment was a complete success. The patient, who was unconscious, had been bled (400 grams) beforehand. After the operation, he was put in a deep bath and given cold showers. Three hours later, intelligence had returned. The improvement was gradual and the healing fairly rapid, despite the appearance of gangrenous patches on different areas of the skin.

Here are, however, other less u observations, of which I give only the titles, for the sake of brevity.

1864. Traube. – Severe poisoning by coal vapour; double transfusion of 240 grams of defibrinated blood; slight improvement; died after 13 hours.

1864. – Müller and Wagner. – Transfusion of 180 grams, during the agony. – Complete failure.

1864. – Sommerbrodt. – Transfusion of 120 grams, in a 20-year-old girl, in a state of complete asphyxia; improvement; died on the 3rd day of pulmonary oedema.

1865. – Mosler. – The same failure occurred in two similar cases.

Finally, I quote again the negative results reported by Uterhardt (1867) (1869), Fischer, of Breslau, six in number. So, we can count eleven failures.

But to the two very convincing observations which I have analysed above, I must add four other facts no less fortunate, which I enumerate under the names of the authors who published them: Badt and Martin Geheimerath, of Berlin (1866); König (1870); Martin, of Berlin (1870); Lehmann (1870). And I contrast these six observations of recovery with the eleven negative cases, to point out that this statistic is sufficient and worthy of encouraging new attempts.

Several operators were unable, moreover, to act in time, they transfused the dying; others have lost their patients as a result of oedema or pulmonary congestion, septicaemia. So that transfusion should be accused of insufficiency only quite rarely.

Consequently, it seems to me appropriate to recommend it in cases of asphyxiation by coal vapours. It should be used preferably when the means used in such cases: artificial respiration, electrification of the phrenic, cold showers, hot baths, and whose effectiveness has often been recognized, have failed. It will obviously be depletive, not very abundant and performed either with defibrinated blood or with normal blood; we do not establish any difference between the two, in terms of effectiveness.

b) *Poisoning by mephitic gases or vapours.* It is theoretically, or after some experiments on animals, that transfusion has been proposed in the asphyxia produced by *lighting gas* (Eulenburg and Landois), *hydrogen sulphide*, pure *carbonic acid*, and *gases from cesspits*. This operation has not, as far as I know, been performed on humans. It could, it seems to me, succeed as well as in asphyxiation by carbon monoxide. The lesions in the blood are comparable on both sides to a certain point. A distinction should perhaps be made with regard to hydrogen sulphide, which combines (Liebig) with the iron in the globules, and the vapours in cesspits, which are really toxic, while the lighting gas and carbonic acid are only unbreathable environments. Physiologists could doubtless prepare the way for doctors and indicate to them whether they have a right to expect some favourable results from transfusion. This is a very vast field of experiments, and one that has hardly been explored.

c) *Poisoning by phosphorus.* In 1872, Jürgensen rescued from death, with the help of a transfusion, a young man of 28 years, who, after swallowing a maceration of chemical matches, had gradually fallen into a most worrying state. He first drew 500 cubic centimetres of blood from him and, two months after the suicide attempt, injected him with 580 grams of defibrinated blood.

This boy had had jaundice, abundant epistaxis, and his life seemed very compromised at the time of the operation.

This successful attempt, crowned with complete success, cannot in itself bring conviction in the minds of practitioners of the value of transfusion in phosphorus poisoning. This metalloid does not inevitably cause death, and the proof here is that Jürgensen's patient survived two months. At the time of the transfusion, he was mainly anaemic, and it was his anaemia that gave way to the infusion of blood.

New experiments on animals and new clinical observations are essential at the present time to enable a judgment to be made on this question, which has just been asked.

We already possess, in the essence of turpentine (Andant, Sorbets, Personne, etc.), an excellent remedy against acute phosphorism, but of limited efficacy. It is a counter-poison which ensures diseases against the toxic influence of phosphorus by neutralizing the poison or its deleterious derivatives; however, it remains powerless against the lesions that this agent has already produced, it cannot repair the impaired blood and tissues. I believe that the infusion of normal blood could perhaps come to the aid of turpentine oil and happily

combine its benefits with the physical effects of this drug. I doubt, however, that it will always succeed and that, moreover, the association of which I speak will have infallible effects. In acute phosphorism, steatosis invades the liver, heart, or other tissues with surprising rapidity, and in many cases the disorganization of the body is, after a few days, beyond the resources of art.

d) *Various poisonings.* Attempts at transfusion are still in the trial period, in poisonings other than those due to coal vapour and carbon monoxide. From the experiments of Eulenburg and Landois (1865), it would appear that in poisoning with non-lethal doses of *opium*, the infusion of the blood reduces the duration and severity of the accidents; that in more serious cases, with lethal doses, this operation, combined with artificial respiration, is capable of saving the lives of animals. However, Fischer is said to have failed twice in humans.

There is one case of transfusion in *nitrobenzine* poisoning. 60 grams of defibrinated blood improved the condition of the patient, but death occurred after 4 hours (Robert and Bahrtdt, 1872).

Finally, transfusion has been proposed in poisoning by the *cobra venom*, the famous spectacled snake that claims thousands of victims in India (Cockle, Branton and Fayrer). The idea does not seem to me to be a happy one, because the operation will never be practicable in time.

J. Casse still thinks that transfusion could be useful in serious chloroformisation accidents. He was able to save 2 out of 4 dogs, which he had plunged into a state of deep collapse by inhaling chloroform, by injecting them, after depletive bleeding, with a few grams of defibrinated blood. These experiments deserve to be continued.

e) *Asphyxia of newborns.* I compare it to poisoning, for the reason that it constitutes a real intoxication by carbonic acid. It was Dieffenbach who first gave a transfusion to a newborn. He injected 60 grams of defibrinated blood into its umbilical vein, but without any success.

De Belina is a great advocate of this method, probably because it was successful in one case, the following: a child came into the world with several turns of cord on his neck and in a state of complete asphyxiation. 30 grams of blood *from the mother's placenta* is immediately defibrinated and injected through the umbilical vein. Immediately the heart began to beat again, the breathing begins, the child was saved (1870). Unfortunately, this is the only favourable fact. In 1868 this doctor had failed, and in 1869 Beneke was no more fortunate.

Eulenburg and Landois thus explain the efficacy of transfusion in asphyxia: the injected blood excites in the lungs the peripheral ends of the vagus nerve, which transmits the influence to the centre, and the latter reacts in its turn to restore the respiratory function.

I cannot linger to discuss this theory, and I cannot dwell at length on questions of practice; I am anxious to finish the study I have undertaken, for I have already exceeded the limits I had set for myself. Consequently, I shall confine myself in the following pages to the simple enumeration of the data acquired by science relating to the use of transfusion in some infectious diseases.

§ II. MORBID POISONINGS.

Three major diseases have given rise to transfusion attempts: cholera, diphtheria, malaria infection.

a) *Cholera.* It would be rather difficult to indicate the real motive which led the doctors to transfuse cholera. Did they wish to combat the simple poisoning of the blood by the cholericogenous miasma, the asphyxia of the algid period, the thickening of the blood; or have they simply tried to apply this extreme resource to a serious disease, considered in a third of cases to be completely incurable? The answer to these questions is impossible. I consider that all these causes together may have influenced the determination of the transfusion doctors. In any case, is the operation rational? I don't believe it. The blood globules are relatively in excess in cholera patients; they already obstruct the general capillaries, so the addition of new red blood cells may be more harmful than helpful. If it is as vehicles of

oxygen that the blood globules are infused, it will be agreed that the means offers only mediocre guarantees, because the supply introduced by the transfusion will soon be exhausted.

Theoretically, what should be injected into the vessels of patients would be blood plasma loaded with oxygen; these are the two elements that are lacking in the blood of these unfortunates. The transfusion of blood can produce in them only one advantageous result, the stimulation of the circulation. Oxygenated globules are very capable of exciting the heart and vessels and restoring their functioning.

Such an effect is, however, very random, and when it does occur it is fleeting. There is a risk, moreover, of clogging the pulmonary vessels and of stopping the gas exchanges which are already taking place in the lungs with the greatest difficulty, as is well known: patients suffering from cholera exhale almost normal air in the advanced periods of the disease.

Clinical observations are not, moreover, very favourable and plead only very poorly in favour of blood transfusion. In 1831-32, Dieffenbach, Walton, and South obtained only short remissions in two patients; in 1866-67, Kwasnicki, Schiltz, and Fischer were no more fortunate in six others.

Gustave Kaslischer (Berlin, 1873) collected all the cases of transfusion in cholera and counted 17, three of which were successful.

I summarise the favourable observation of Stadthagen, of Berlin. A woman of 29 years was stricken in 1873 with epidemic cholera and soon fell into a state close to death: excessive cold, small pulse, cyanosis, insensitivity, flaccid skin, anuria. She was injected with 180 grams of defibrinated blood. She revived after an hour, and recovered without a long lived reaction.

The same doctor failed completely in another case, in a 34 year old patient. I know of only three favourable observations: the previous one and two others, published by Professor Fischer. In short, the method is far from perfect and could well be abandoned. If we compare it with another of a simpler practice, that of intravenous injections of water or saline solutions, we see again that it certainly does not have the advantage of efficacy. In fact, during the epidemic of 1832, some doctors in Edinburgh practiced this mode of treatment, first proposed in France by Magendie (in rabies), and they sometimes had reason to praise it. Lata, Lewins, Lizars, infused into the veins of cholera patients really enormous quantities (several kilograms) of an aqueous solution of soda ash. They obtained 5 healings out of 15 patients, considered to be in a desperate state, who were thus treated. Lorain, whose recent loss is deplored by science, also cures a cholera patient by the simple injection of water. It is therefore not surprising that the question has been taken up again recently (1873) by two distinguished hospital doctors, Messrs. Dujardin-Beaumetz and Hérard. By infusing the veins of cholera patients with an artificial serum (a solution of the following salts: phosphate of soda, sodium chloride, potassium chloride, carbonate of soda) they obtained enviable results. "The dying patient," says Beaumetz, "is reborn to life, he regains consciousness, he speaks, he sees and recognizes his own; its circulation reappears, its temperature rises..." Ultimately, the improvement is remarkable, but the affection often takes over and the patient is carried away.

Transfusion does not work any better, perhaps not even as well; so that it will doubtless give way, in the treatment of cholera, to the intravenous infusion of water or artificial serum. These liquids certainly have the serious disadvantage of destroying or altering red blood cells; it is to be hoped, however, that the progress of science will place in our hands these weapons, made more harmless but no less powerful.

b) *Diphtheria*. It is not the infectious principle of this disease that has led to the use of transfusion, but rather the mechanical asphyxia that is observed in the course of [angines couenneuses] or croup. Three attempts by Hüter, 1869, Demme, 1867, and Czerny, 1871, have been absolutely unsuccessful. In Demme's case, it was infectious diphtheria; the patient succumbed to intestinal haemorrhage; in the observations of Hüter and Czerny, croup and [angines couenneuses], not improved by tracheotomy.

c) *Maremmatic fevers*. In malarial cachexia, says Luigi Tassinari, the formal indication is to repeat the transfusion several times. Under the influence of the operation, the crass of

the blood is perfected, the digestion improved, the pigments disappear from the blood, and the healing gradually appears.

It is in Italy, in particular, that serious cases of malaria have been combated by the infusion of blood.

Luigi Tassinari, 1874, found this in a 28-year-old subject, who had arrived at the last period of malarial cachexia. Five successive transfusions of defibrinated blood enabled him to obtain a radical cure in the space of a few months. – Paolo Postempski (1874) also attributes to a direct transfusion, from arm to arm, the merit of the radical cure of a rebellious intermittent fever.

A few years earlier, in 1869, Concato had improved the serious condition of a subject affected by advanced malarial cachexia, by means of several transfusions of 20, 35 and 44 cubic centimetres of blood, performed a few days apart. Nevertheless, the patient had a violent attack of fever, which won.

I conclude this study of transfusion in infectious diseases with some indications on the use of this method in certain diseases which are part of the nature of the latter and may be close to them, I am talking about virulent diseases.

§ III. VIRULENT DISEASES.

a) *Rabies*. – The idea of transfusion in rabies is reported by Riva. In any case, Russell, in 1792, once transfused a young boy who had become rabid. After a huge bleeding, he injected him with lamb's blood and thus healed him.

We must always be wary of examples of healing in rabies; most, if not all, are questionable; so I am far from vouching for the reality of the success reported by the English doctor.

Nowadays, Dieffenbach (1831) is not successful. Transfusion, in rabies, improves the condition of patients, in the same way as injections of water (Magendie - Sanson), but it is only palliative; death inevitably occurs.

b) *Smallpox*. – It is easy to understand the practice of transfusion in haemorrhagic smallpox. The blood is so altered in this disease that it seems natural to replace it with a healthier humor.

Heinemann and Zuelzer (1871) tried this mode of treatment in vain in four patients.

c) *Syphilis*. – I do not understand at all the use of transfusion in serious syphilis. A young doctor, Emile Masson, speculated that this mode of treatment "could exhaust the violence of the virus by the successive subtraction of certain quantities of tainted blood, at the same time as it would restore to the diathetic a purer blood which would enable him to fight the infection with advantage." This hypothesis is not tenable. Fortunately, today, cases of rebellious and fatal syphilis are very rare and our so-called specific treatments are generally sufficient to improve the condition of the patients, if not to cure them radically.

CHAPTER 4 TRANSFUSION IN NERVOUS DISEASES

Some doctors, perhaps basing themselves on the well-known aphorism, *sanguis moderator nervorum*, have thought that the transfusion of blood would have its advantage in the neuroses of intelligence and movement. Let us see if they reasoned rightly; and for that let us simply refer to the clinical observations.

§ I. CONVULSIVE NEUROSES. – ECLAMPSIA, HYSTERIA, EPILEPSY, TETANUS.

a) *Eclampsia*. – Professor Lange, of Heidelberg, treated with complete success by the infusion of blood, a young woman suffering from puerperal eclampsia. She was infiltrated, had albuminuria. In vain they bled her, they made her breathe chloroform; in vain they delivered her with forceps, she was getting worse and worse. Dr. de Belina then injected her with 220 grams of defibrinated blood, with a remarkable result: the cyanosis disappeared,

consciousness returned, the attacks stopped. Gradually, the woman's condition improved and she recovered quite quickly.

This observation also supports what I said earlier, of the necessity for obstetricians to study this great question of blood transfusion, which is of particular interest to them. Doubtless this isolated clinical fact has only a limited value; but, as it has now been demonstrated that puerperal eclampsia fatally kills many women, in spite of the best directed treatments, it is still necessary to make some new attempts to perfect our therapeutic methods. The one I am reporting is already a good omen.

Beside the observation of Lange and Belina there is a fact of the same order, related by Brown.

Uremic eclampsia has also sometimes been treated by transfusion. Three cases which we owe to Stöhr, of Würzburg, have given only doubtful results; they were albuminuric, in a serious condition. The infusion of blood no doubt came to their aid, in the sense that it diminished the severity of the attacks, but death came soon after the injection. In such circumstances, transfusion can only be purely palliative, because of the advanced alterations that are known to the kidneys and other viscera.

b) *Hysteria*. – Profound anaemia, in certain hysterics, contributes to aggravating the neurosis. In such cases, the infusion of blood can become a precious resource. Hasse put it to good use twice, with advantage.

c) *Epilepsy*. – In an epileptic exhausted by a series of attacks, Nussbaum, according to Belina, obtained a complete cure by the venous infusion of 720 grams of defibrinated blood. The remedy should be tried in the state of *epileptic disorder*, so often fatal to the individuals who are affected by it.

d) *Tetanus*. – Roussel, of Geneva, observed the following fact: a 30-year-old man was taken, after a resection of the knee, with generalized tetanus. He was injected with 120 grams of blood and immediately the convulsions ceased completely, only to reappear seven hours later. It is important to add that the patient had been bled and that he soon succumbed, in spite of this complete remission in convulsive accidents.

§ II. NEUROSES OF THE INTELLECT.

Blood transfusion was first practiced on the insane. Two of them have their names recorded in the annals of science: Mauroy, transfused by Denis, and Arthur Coga by Lower and King (1667), because they represent the first two proven cases of transfusion in man. We need not recall in this connection the ideas of the first transfusions, relating to the treatment of furious madness by infusion of the blood of animals renowned for their gentleness: calves and sheep. These bizarre conceptions do not surprise us on the part of the doctors of Molière's time. However, we like to point out this historical curiosity, for we shall see later that the method of Denis is now very much in honour in Italy.

In 1852, Polli, whose interesting work we have mentioned several times, said the following: "Since the conditions of the blood modify more or less profoundly and rapidly the mode of operation of the nerves, we dare to propose, following the example of the first transfusers, and as Schneider and Hufeland did later, to try blood injections in certain cases of mental alienation or insanity, which are not connected with any obvious organic alteration of the sensory apparatus or of the viscera which may awaken its sympathies." The Italian doctor's call was heard and his idea accepted and executed. Various observations have been published, which demonstrate, unfortunately, that one cannot rely much on the infusion of blood to improve the mental state of the insane.

Let us cite the examples given by Stricker (1874): melancholic woman; by Meynert (1874): young man affected by melancholy and in a cataleptic state; by Roussel (1873): melancholy in a 23-year-old male, dementia and idiocy in a 23-year-old female, general paralysis in a 40-year-old man.

Only the melancholic of Roussel benefited completely from the transfusion. The day after the operation, says this doctor, "this man is no longer cataleptic or melancholic." Meynert had obtained exactly the same result as Roussel: considerable improvement of the mental state, disappearance of stupor, etc.; but nine days later the accidents reappeared.

Roussel's patient, of whom he gives us no news, will probably not have been more favoured than the previous one.

In summary, I think that transfusion can only be palliative in madness. The doctor should ask himself only one thing, the improvement of the general condition, so often compromised in melancholic alienated people. We will return to this interesting question a little later, in connection with animal transfusion.

Here ends the considerations which I had to present on the therapeutic applications of transfusion practiced in man with human blood. They have been very long, and I cannot apologize too much to the reader for having allowed myself to be led so far in this direction. My only excuse is the importance of my subject.

Generally poorly understood and poorly appreciated in our country, blood transfusion is considered by many French doctors as a dangerous operation, difficult to perform, useless or not very effective. I wanted to react a little against these ideas, against this denial of justice, and I lingered to plead a cause that seemed good to me.

In finishing this study, it seems useful to me to produce some figures, to show that this operation is now being practiced more and more and to remind us that it already has a considerable number of successes.

Dr. Peet, in 1842, reported 35 cases of transfusion, including 13 deaths and 22 cures.

In 1869, Marmonier gathered together 199 in his thesis, of which 103 were successful and 96 were unsuccessful. The progress was considerable; but, since 1869, the number of cases has increased in very notable proportions, as my own statistics indicate. I warn the reader in advance that it is very incomplete; I have purposely or unintentionally omitted many facts, and consequently it is far from giving an exact idea of the present state of science on this question of numbers. In any case, it offers a certain interest and that is why I will produce it. I estimate that transfusion may have been practiced in man, with human blood, more than 450 times, from the end of the 17th century to 1875. In this review, I alluded to more than 360 observations that provide the following statistical details:

Haemorrhages.

Severe trauma.	22	13 healings	9 deaths
Puerperal.	104	70 -	34 -
Non-puerperal metrorrhagia.	18	10 -	8 -
Epistaxis.	6	1 -	5 -
Haematemesis.	6	3 -	3 -
Repeated trauma.	9	4 -	5 -
Miscellaneous.	3	3 -	0 -

Constitutional diseases.

Purpura.	4	0 healings	4 deaths
Scurvy.	4	4 -	0 -
Leukocythemia.	3	0 -	3 -
Prolonged suppurations.	22	6 -	16 -
Anaemia.	9	2 -	7 -
Severe fevers.	9	4 -	5 -
Sepsis.	10	0 -	10 -
Cachexia.	8	2 -	6 -

Poisonings.

Coal vapour.	17	6 healings	11 deaths
Phosphorus.	1	1 -	0 -
Nitrobenzine.	1	0 -	1 -
Asphyxia of newborns.	3	1 -	2 -

Infectious and virulent diseases.

Cholera.	17	3 healings	14 deaths
Diphtheria.	3	0 -	3 -
Malaria.	3	2 -	1 -
Rabies.	1	0 -	1 -
Haemorrhagic smallpox.	4	0 -	4 -

Nervous diseases.

Eclampsia.	2	2 healings	0 deaths
Uremia.	3	0 -	3 -
Hysteria.	2	2 -	0 -
Epilepsy.	1	1 -	0 -
Tetanus.	1	0 -	1 -

Mental illnesses. - Momentary improvement in some melancholics.

Adding up the cases of complete success, I find that of the 358 facts reported in this work, their number is equal to 140.

This, I hope, is a proof which adds to all those I have already given, of the real value of transfusion and its efficacy in many serious conditions.

PART 10

THIRD PART: TRANSFUSION IN MAN WITH THE BLOOD OF ANIMALS.

After two hundred years of almost complete oblivion, the attempts of the first transfusers have just been resumed, and the question raised by them is again discussed, studied with the same ardent convictions that we saw occur at the end of the 17th century, during the abortive experiments of Denis, R. Lower, King, etc. Will we be completely enlightened this time, and will this old therapeutic method finally be able to be definitively judged?

Maybe! The struggle is today, as in the past, quite vigorously engaged between transfusionists and anti-transfusers, and it is to be hoped that in the near future the impartial writer will be put in possession of all the documents of the trial and that he will have every facility to draw from the arguments for or against provided by both parties, the reasoned judgment for which medical practice awaits with some impatience.

The problem is this: can animals supply us with their blood, as a remedy for different morbid states, and will the infusion of this humor into our vessels become an effective and first-rate mode of treatment, leaving behind the best drugs or restorative means that we prescribe or implement to regenerate an exhausted body?

Already certain species of animals provide us with the protection against smallpox; others, epidermal flaps to be grafted onto wounds to hasten their healing; and it is now being asked whether new tributes could not be levied by man on animals, to enable him to fight advantageously against certain serious diseases.

Research in this direction is very laudable and deserves to be encouraged. Unfortunately, we must fear that they will not lead to serious results. *A priori*, based on some physiological data reported at the beginning of this study, we dare to say that they are opposed by theory and are not based on any solid scientific basis.

Let us, however, see to it that the facts are set forth as they have been published, to better show the present state of this controversial question.

It was in Russia, Germany, and Italy that they were chiefly provoked, under the impetus given by Gesellius, of St. Petersburg, Hasse, of Nordhausen, and various alienist doctors of northern Italy.

CHAPTER 1

The transfusion of lamb's blood in various anaemias and cachexias

All the anaemias or dyscrasias that we have just seen combated with more or less real or complete success by the infusion of human blood have been treated by the transfusion of lamb's blood. The advantages attributed to this method are as follows: this humor has excellent restorative and reviving qualities; it comes from a source that is always available; finally, its use saves man a sacrifice that can have serious inconveniences for him.

I cannot linger to discuss these various reasons, for the time I have devoted to this Review is already very long, and I would not finish it if I did not limit myself to the pure and simple enumeration of the facts. These facts are here summarised as succinctly as possible.

§ I. ACUTE ANAEMIA, CHRONIC ANAEMIA.

In a case of *severe metrorrhagia*, in a woman who had a vicious insertion of the placenta, Dr. Hasse gave a transfusion of 200 grams of carotid lamb's blood through the median vein after delivery, and obtained a rapid cure (1872).

This is the only case reported, and its value is mediocre. It proves, however, that 200 grams of lamb's blood can be injected into the veins of an almost bloodless patient, without great inconvenience. The patient experienced chest anxiety, dyspnoea, and spinal pain; she had shivers, sweats, but these phenomena dissipated very quickly, and recovery was easy.

The same German doctor reported an observation of a cure of a profound chloro-anaemia in a 31 year old woman, hysterical and ill for five years. The infusion of lamb's blood lasted 90 seconds and was fairly well tolerated (1873).

Finally, I would indicate that other attempts also made by Hasse, in patients affected by anaemia due to dyscrasia, succeeded in improving their situation, without, however, curing them. Once, however, he succeeded in saving from death a young girl of 13 years old, very anaemic and weakened by severe diphtheria, by infusing her vein with 150 grams of lamb's blood.

For his part, Heyfelder reported another favourable observation, in a case of anaemia following prolonged suppuration, in a 44 year old woman, who had previously had an attack of typhus. Sixteen days after the operation, the recovery was complete.

But in similar cases of weakening as a result of prolonged suppuration, Paul Schliep (1874) and Küster were unable to prevent the death of the patients, in spite of the transfusion of lamb's blood.

I continue my presentation hastily, and although it is urgent to hurry a great deal, I still yield to the temptation to dwell a little longer on the use of lamb's blood transfusion as a mode of treatment for pulmonary phthisis and mental alienation, for these are the two most important indications for this therapeutic method.

§ II. PULMONARY PHTHISIS.

Gesellius, of St. Petersburg, and Hasse, of Nordhausen, have promoted the infusion of lamb's blood in pulmonary phthisis. For these doctors, it is no longer the operation we know, intended to raise the depressed vital forces, to revive a weakened body; no, it is a new treatment for tuberculosis. I confess that I do not share the enthusiasm of these two observers with regard to their method. Not only does it seem to me to be ineffective, but it is often dangerous and useless. A few facts analysed very quickly will show that I am not wrong in making this severe judgment.

Here is a summary of an observation published by Hasse and given as a conclusive example of the value of treatment. Dr. Redtel, who was suffering from pulmonary and laryngeal tuberculosis, was transfused in the following manner: a tube connected his basilic vein with the carotid artery of a lamb, and the animal's blood stream entered the human vessel for 55 seconds.

The patient experienced, among other symptoms, the following: a sensation of warmth in the arm and formication, redness of the face, very intense dyspnoea, sharp pains in the

lower back, pulsatile and offering a perfect synchronism with the pulse; general rigidity, cyanosis; then reaction with profuse sweat, pulse at 140, breathing at 32, fairly frequent cough, drowsiness. On the fifth day, nettle fever. Finally, on the eighth day, the appetite returned; but the tuberculosis, the local signs of which had seemed to improve for a moment, was in no way improved.

The author claims that in other patients he was happier and that after the operation he saw the cough diminish as well as the expectoration, the hectic fever disappear, the appetite return, and the local condition improve (1873).

I do not dispute the improvement indicated by the German doctor, but I fear that it was only temporary. This supposition on my part is based on the observations of Ernest Küster (1874).

In 4 phthisics, he saw the general condition improve during the few days following the transfusion, but the disease soon resumed a progressive course, which could not be stopped by new injections of lamb's blood.

I have said that this mode of treatment offered dangers; I will give as proof of this the following fact, related by Gesellius himself. Performing a transfusion on a man of 35 years of age, very weakened by pulmonary tuberculosis, by connecting the carotid artery of a lamb to the median basilic vein of the patient with a tube, he determined in the latter an extreme agitation with asphyxial symptoms, coughing up blood, cyanosis, excessive acceleration of the pulse, then of haematuria, albuminuria, etc. The patient died on the third day.

Fiedler and Birch-Hirschfeld (1874), applying the methods of Gesellius and Hasse to six phthisics, made them very ill at first and later noted a worsening of the morbid symptoms.

Heyfelder was no more favoured. He improved, he says, slightly, the condition of a young woman afflicted with phthisis in the third degree, by the infusion of lamb's blood; nevertheless, death occurred 4 weeks after the operation.

Ultimately, in spite of the overfly enthusiastic assertions of Gesellius, Hasse, Brügelmann, the transfusion of lamb's blood in pulmonary phthisis can only be considered, until further notice, only as a means at most palliative, against the serious accidents of this dreaded disease; still less is it a remedy capable of delaying or definitively hindering its progress.

§ III. MENTAL ALIENATION.

At the congress of Italian alienist doctors, held at Imola this year (See: *Arch. Ital. per le malattie nervose*, Milano, 1875), various very long communications of real interest were made on the use of lamb's blood in intravenous infusion in certain insane people. I cannot, in the small space I still have here, give an analysis of this work; I limit myself to reporting some of their most important conclusions and to citing titles of observations.

Antonio Michetti observed a very noticeable improvement after a transfusion of 15 grams in a woman affected by pellagra and who had become manic.

In a subject aged 30, melancholy, 40 grams of lamb's blood initially caused some alarming asphyxial symptoms, fortunately averted by bloodletting, but produced a notable improvement in this man's condition. His appetite returned, he ate alone, was less sad, spoke. Then after a few days he fell back into his melancholy.

Finally, in a third case of melancholy with a cataleptic state, the transfusion of 20 grams of blood led to a considerable drop in temperature (34°), a slowing of the pulse and a favourable but temporary change in the mental state.

Similar results have been reported by Carlo Livi (2 cases), of Modena, in two lypemaniacs, by Blessich, Fabri and Frigerio, in melancholic lunatics or pellagra patients.

Here are some conclusions indicated by Dr. Ponza, at the Imola Congress, and which result from his observations at the manicomio of Alexandria.

1° Direct arterial transfusion of lamb's blood is an easy, safe, not very painful operation, and very capable of producing excellent reconstituting effects in some cases of pellagrous madness;

2° It is an advantageous operation to stimulate certain lypemaniacs. It acts like a real diffusible stimulant;

3° It can combat hypoglobulia in some cases of mental alienation. But it would be unwise to practice it in advanced pellagrous cachexia and in the stage of manic excitement.

In short, the transfusion of lamb's blood has so far given only imperfect results. If, in truth, it temporarily stimulates melancholics, this effect does not last, and the affection soon regains the upper hand.

To date, however, there has been no case in science of a proven cure of madness by the infusion of lamb's blood; and it is absolutely necessary to come to the despairing conclusion that in this neurosis the advantages of the operation are doubtful, limited, or non-existent.

In summary, this new mode of transfusion has neither the reasoning, based on the theoretical considerations already presented, nor the clinical facts. There is therefore every reason to fear that it will not meet the hopes that certain doctors have based on it. Let us nevertheless wait for further unfavourable observations to condemn it definitively.

To complete the description that I have undertaken, it remains for me to give some details on the effects of the transfusion of lamb's blood and on the manner in which this operation is performed.

§ IV. SYMPTOMS OBSERVED AFTER THE INFUSION OF LAMB'S BLOOD.

Most commonly they are very worrying, as is shown by the following observation, reported by Hasse: a young girl of 22 years, suffering from agitating paralysis, experienced immediately after the injection of the blood dyspnoea, lumbar pain; she had an involuntary bowel movement, shivers, vomited. Then her pulse became very frequent, threadlike, uncountable, her breathing became embarrassed, her temperature reached 42.8°, and the unfortunate woman died after 4¹/₂ hours.

Usually patients are seized with more or less violent dyspnoea, asphyxia, back pain; they become agitated, complain of tingling, heat in the injected limb, become cyanotic, have chills, a tendency to syncope, a small, irregular pulse; then after an hour their temperature rises, profuse sweating appears, their pulse slows down, their temperature falls below normal, there is a marked subsidence or collapse. Later, some have an exaggerated appetite, haematuria, albuminuria, urticaria, haemaphilic jaundice; others weaken, lose their weight.

Various explanations have been proposed for these various accidents. Küster attributes them to the excess of carbonic acid in sheep's blood; Hueter, to the too rapid eruption of arterial blood into the right chambers of the heart, when it is a question of *immediate arteriovenous* transfusion; Landois supposes that the foreign globules, destroyed in the human body, will accumulate in the capillaries of the organs, in the form of embolic masses, and produce their obstruction. There are capillary embolisms in the lungs, kidneys, intestine and skin, which are thought to cause dyspnoea, albuminuria, diarrhoea, and urticaria (1874).

It is conceivable that such accidents have frightened many doctors, and one is not very surprised at the violent attacks directed against transfusion with lamb's blood.

Panum, above all, considers it more harmful than useful and he sharply rebukes those who advocate it.

I have little to say about the *Operating Manual*, because previously, in the physiological part of this study, I spoke of it. I will limit myself to pointing out the following particularities:

We usually choose a lamb of 3 to 4 months, because its globules are then quite numerous and above all relatively small. It is fixed firmly in a sort of wooden box, so as to obtain absolute immobility; then, the carotid artery (sometimes the crural) exposed receives a glass or metal cannula, connected by a rubber tube a few centimetres (10 to 20) in length, sometimes filled with a saline solution, to another cannula immersed in one of the veins of the patient's elbow crease.

The quantity of blood injected is set approximately according to the flow time. It is known in advance that the flow rate in the air through the venous cannula is so much per quarter of a minute.

Hasse recommends stopping the introduction of blood as soon as dyspnoea begins.

Need I point out the practical difficulties of this process and the serious dangers to which it exposes patients? The reader will have recognized them very quickly by reflecting on them for a moment, and it seems pointless for me to list them.

A young French physiologist, F. Glénard, has at least the merit of proposing a much more convenient method. He would like to see the injection of blood by means of *vascular segments*, which, as we have said, allow the blood to be kept in full fluidity for several hours.

Here is the method of preparation that it indicates:

The animal (ox or sheep) having been slaughtered by the section of the bulb, the jugular is discovered, with the help of a long incision. A ligature is immediately placed in the lower part of it, which closes the vein on the side of the heart. The vessel fills up, inflates more and more. Then a second ligature is placed at the top of the incision. The bag thus circumscribed will contain significant quantities of blood (200 or 300 grams). It is detached from the animal, fixed on a trocar cannula introduced into the vein of the transfused, and gentle pressure empties the contents into this vessel. This new type of transfusion device is, as we can see, very simple. The author is careful to inform us that the blood of the segments remains *completely unaltered*, even after several hours, and that its plasma retains its fluidity entirely. Glénard has only tried this mode of transfusion in animals. All of his experiences have been satisfactory so far.

FOURTH PART: TRANSFUSION DEVICES – OPERATING MANUAL.

I have had the opportunity on several occasions in the course of this study to indicate the devices used by certain doctors to transfuse their patients. I have also said a few words in the operating manual on the subject of haemorrhages. Therefore I will be very brief in the description that follows. The lack of space forces me to abbreviate again.

§ I. DEVICES.

They are of three kinds: 1° those which are used in immediate transfusion; 2° those used in mediate transfusion with whole blood; 3° finally those intended for the injection of defibrinated blood. We will talk about the former a little later, in connection with arterio-arterial transfusion. Of the others we will say only a few words.

I have made my opinion known about them. Almost all of them are complicated, rather difficult to handle, subject to alteration, of a high price, and they are hardly convenient to use except in large centres, where their inventor undertakes to operate them.

There is not a year when a new device is not proposed, the least advantage, according to its author, is that it does not offer any of the defects of those already known.

Be that as it may, the most commonly used in France are those of Moncoq (1874), Mathieu and Collin (1874). In England, various models have been described by Walton and Routh (1849), Beatty (1870), Hewit, B. Richardson (1871), which appear neither superior nor inferior to the preceding ones. In Italy, Giuseppe Albini imagined and described, in 1874, a rather complicated transfusion machine, because of the play of its valves, which does not seem to me to be endowed with greater merits than its predecessors.

In my opinion, I repeat, all these instruments, very ingenious, no doubt, can be placed on the same level and cannot be recommended to the exclusion of each other. Will it be necessary to make an exception to this somewhat rigorous assessment in favour of the Roussel transfusion machine, which, in a competition for transfusion machines, has prevailed over all its rivals? I can't say. According to Neudörfer, he attains the ideal of a practical instrument; according to O. Heyfelder, "it responds better than any other to the physical laws and physiological requirements of transfusion"; finally, according to its inventor, it has succeeded in a very large number of cases. These are excellent recommendations, well calculated to draw the attention of French doctors to him. This transfuser draws venous blood from the transfuser and immediately injects it into the patient's vein; it allows, as we see, a kind of immediate transfusion. Thanks to him, Roussel

was able to practice without inconvenience, in one case, the infusion of venous *blood* from animals to man.

Nevertheless, until the absolute proof of the excellence of this transfuser is perfectly established, I will continue to place in the first line the ordinary syringe, which everyone has at hand and knows how to operate. Many times it has been put into use in serious circumstances, and the operators have only had to praise it.

To carry out the transfusion with defibrinated blood, there is no need for very complicated devices, and I am surprised that it has been thought of proposing special instruments. Drs. de Belina, J. Casse, have had special devices built which, although very simple, have no chance of being adopted by practice; they are very good in laboratories for physiological experiments, but they cannot impose themselves on the doctor as indispensable.

The same remarks can be made about cannulas intended to be introduced into the veins of transfused patients. A large number of models have been manufactured, which can be very convenient when operating in particular conditions; they only apply, however, only to very limited cases, and we can easily do without them.

§ II. OPERATING MANUAL.

I would like to remind you that transfusion is generally divided into *mediate* and *immediate*.

a) *Immediate transfusion*. – It is carried out, either directly from one artery to another artery, and it is called arterio-arterial; or from one vein to another vein, and it is called veno-venous.

The first was advocated mainly by Küster. To establish communication between the two circulations, he joins the radial artery of the transfused to the radial artery of the transfuser by means of a tube equipped at its ends with trocar cannulas. The operation was executed 2 times, one of which was successful. This example is obviously not to be imitated. Arterio-arterial transfusion has only theoretical advantages, and its disadvantages are obvious to everyone.

Mr. Parinaud, a hospital intern, thought that we could take advantage of the artificial tension given to venous blood by muscular contraction, to pass a blood current directly from one vein to another, from the vein of the giver into that of the taker. In a woman suffering from haemophilia, he put his idea into practice and succeeded perfectly in performing an infusion of blood. The patient was revived, regained consciousness, felt better, but she succumbed six hours later. (*Jullien's aggreg. thesis.*)

This procedure requires excessive skill and does not seem to me very practical. He had already been advised by Morel, in 1856, and this experimenter confessed that he had only been able to put it into execution very imperfectly in animals.

I can also place in this class of immediate transfusions, the method of A. Guérin, which he designates by the name of *reciprocal transfusion*. The author presented it at the Congress of Bordeaux, on 6 September 1872.

"The central end of the artery of the subject that supplies is in direct communication with the peripheral end of the subject that is to receive... The balance is soon established between the two circulatory torrents." To avoid overflow, we connect "the peripheral end of the artery belonging to the healthy subject to the central end of the artery of the sick subject. The two circulations are now one."

Thanks to his great skill, A. Guérin succeeded in establishing this *community of circulation* on heifers and dogs; but I doubt very much whether he will ever be called upon to perform the same operation in man.

At the time of Denis' success, more than two centuries ago, Tardy had already imagined and recommended this variety of transfusion. The author of the article *Transfusion* in the *Encyclopaedia Diderot*, who informs us of this fact, is careful to add that "this cruel operation has never taken place except in his imagination."

In conclusion, I would add that several years ago an attempt was made to draw blood from the donor's veins with the help of special devices (Oré, Moncoq, etc.) and to launch it

immediately into the circulation of the transfused. We have generally given up on this method today, which is hardly used any more other than in laboratories.

b) *Mediate transfusion*. – It includes several sub-varieties. Sometimes it is *veno-venous*, sometimes *veno-arterial*. The first is the most commonly used: it is the one we have already spoken of several times, and to which it is unnecessary to return. It is moreover classical; and his description is found everywhere. I will say only a few words about the second.

To avoid the dangers of introducing air or clots into the heart, Hueter recommends veno-arterial transfusion, which he performs in the following way: he exposes the radial artery, at the wrist, or the posterior tibial below the medial malleolus, he isolates it, passes under it four ligation wires: the upper one intended to prevent the flow of blood from the heart during the operation, the lower one to securely fix the cannula, and the intermediaries to serve as a waiting ligature; then, the vessel being cut at an angle and the cannula in place, he injects defibrinated venous blood into the peripheral arterial end. The patient's hand swells, reddens, becomes covered with sweat and becomes painful. These phenomena do not last. Naturally the artery is bound after the injection, and it is simply bandaged. In 1870, Hueter had applied his process at least 12 times, and Albanese, of Palermo, cited 7 personal observations.

The author claims that this method is simple and harmless. But this is not the opinion of some of his imitators. They found that blood had difficulty entering the radial artery; and sometimes it has been necessary, on the spot, to have recourse to ordinary transfusion.

It was de Græfe, in 1866, who first had the idea of this method; he applied it to a choleric. Hueter, who made it his own by popularizing it, saw it succeed wonderfully in two cases of freezing of the feet. He injected defibrinated venous blood into the posterior tibial and saw the general condition improve and the sphacele immediately restricted. Albanese and Wilks attribute antipyretic effects to it.

Artery ligations are not always harmless operations, which is why I do not believe in the future of this transfusion procedure. Its advantages, if indeed it offers any real ones, are certainly not compensated by its disadvantages.

Finally, there is a last mode of transfusion, very mediated this time, recently proposed by two German physicians, Karst, of Kreusnach, Landenberger, of Stuttgart, and of which I should perhaps not speak, because it seems to me outside the rules of the most vulgar scientific common sense. I am referring to the *transfusion of blood through the subcutaneous cellular tissue*. These authors recommend hypodermic injections of defibrinated blood and delivery of this fluid for simple interstitial absorption.

Sad enough to say, this method has been applied in Vienna, without any success, I need not mention, but with a result that will surprise no one: the formation of abscesses or phlegmon.

It is claimed that the blood injected under the skin is absorbed and passes into the circulatory torrent. No doubt the fact is real, and it is almost naïve to state it because it is so banal; but is it admissible that the haematic debris on which absorption is exerted in the cellular tissue can be used by the body, and for its benefit? I don't believe any of it.

So that the ordinary transfusion, *veno-venous*, still rightly remains the most used and practical procedure.

Without going into the details of the operating manual concerning it, I think it useful to report here some interesting particularities on the *choice of blood*, *the quantity* that must be injected and the *temperature* that this humor must have at the time of injection.

c) *Choice of blood*. – I have already hinted several times at my preferences with regard to the use of whole blood. With the majority of transfusion doctors, I consider it capable of rendering greater services than defibrinated blood, particularly in haemorrhages. However, I must say that Polli, Neudörfer, Belina, Demme, Brown-Séguard, J. Casse, attribute to the latter excellent reviving properties, besides that it is more convenient to infuse and protects against embolisms.

Gesellius, who is cited several times in this work, has, however, strongly attacked the practice of transfusion of defibrinated blood, using the following arguments: defibrination wastes time, diminishes the revivifying action of the blood; it does not arterialize, as seems

to be believed, this liquid, because it is only charged with oxygen in the lungs, but it deprives it of an important part of its constituent elements, and probably modifies its red blood cells, which, according to the expression of the Russian physician, are *beaten to death*. Gesellius adds more serious objections, the following: defibrinated blood becomes toxic to animals of different species, while whole blood is well tolerated or rarely harmful (this proposition is far from being demonstrated and the reverse would be more accurate); it exposes to infarctions, promotes haemorrhages from the intestine, wounds, etc., very different in this respect from normal blood which, by its plasticity, becomes an occasion for haemostasis.

Finally, he points out that out of 115 transfusions performed with defibrinated blood, there are only 36 successes compared to 79 failures.

I could say, in support of this last argument, that for my part, looking at 74 cases of transfusions made in this way, I found only 20 cures. However, recognizing that such reasoning based on such few statistics is of no value, I refrain from any conclusion. Moreover, these figures themselves do not indicate anything serious against defibrination.

Without stopping to discuss with the authors who have fought this practice, I will say that none of the reasons given by them against it seems to me to be of capital importance. Theory guides them above all in establishing their contradictory opinion.

I therefore believe that I can declare here that if the transfusion of normal blood seems rational and is above all imposed on common sense, we are not entitled to affirm that the infusion of defibrinated blood is a bad operation that must be proscribed from practice. The question of pre-eminence between the two methods is obviously pending.

To finish this paragraph, concerning the choice of blood, I will simply state the following proposition: the venous blood of a young and healthy man should be taken, because it is richer in globules and poorer in water than that of a woman.

d) *Quantities to inject*. – An English doctor, Routh, said in 1849 that the greater the quantity of blood infused, within certain limits, the more patients survive. Studying 48 cases of transfusion, he had drawn up the following table, which had led him to state the opinion I report.

In transfusions of less than 4 ounces of blood	1 death in 0.7.
In those with doses included: between 4 and 8 ounces of blood	1 death for 2.3
In those with doses included: between 8 and 12 ounces of blood	1 death in 2.5
In those with doses included: between 12 and 16 ounces of blood	1 death in 5
In those with doses included: between 16 and above:	1 death to 1

It would be imprudent to draw from this little statistic the conclusion that it seems to include. It is now generally agreed that small quantities of blood are more successful than large ones: 50, 100, 150, 200 grams, these are the recommended doses. I do not insist on this question, which I have already dealt with previously.

It would be wrong to fear the plethora, which is supposed to be produced by high doses; that is not the danger. Thus, it is possible to increase the blood mass of a dog by half its presumed weight without causing accidents (breakage).

The whole question is to proceed very slowly in the infusion of the blood, so as not to stupefy the heart, not to distend the right cavities of this organ, which would inevitably cause the cessation of its contractions. Massive injections are capable of bringing about this result.

e) *Temperature*. – It will be as close to normal as possible, for defibrinated blood; but it can be injected without inconvenience at 20° or below.

§ III. TRANSFUSION ACCIDENTS.

a) *Entry of air into the veins*. – Only three observations are cited, those of Jewel, Scott, and Ritgen. It would therefore be wrong to fear this serious accident excessively, especially if one chooses one of the veins of the elbow fold or the short saphenous vein. Several experimenters have shown that it is possible to push slowly into the veins of the limbs in dogs up to 50 and 60 cubic centimetres of air, without producing fatal effects (Blundell (1818), Restelli, Strambio, Qualigno, Manzolini, Uterhardt, Lowenthal, Oré (1862). It is

unlikely, however, that bloodless patients can easily tolerate even small proportions of air, for, according to the remark of Amussat (1859), bled animals perish very quickly when minimal quantities of air are introduced into their veins; so that it will be wise to expel the air from the apparatus when infusing the blood.

In the event that air has penetrated in a toxic proportion during the transfusion, Oré recommends, in order to prevent the fatal outcome, to electrify the vagus nerve in the neck. "Electricity," he says, "acts on the lungs, whose particular sensitivity, when brought into play, determines by reflex action the extreme dilation of the chest walls."

b) *Embolisms*. – We can imagine the possibility of launching small fibrinous clots into the right heart when whole blood is infused. But, it must be said, very fortunately cases of embolism have been very rare. We cite barely two doubtful cases, in which the possibility of thrombosis of the pulmonary artery was admitted rather than demonstrated, because an autopsy was not carried out.

c) *Phlebitis*. – Also inflammation of the vein in the transfused person was rarely observed and most often, when it occurred, healing took place. This accident would perhaps be more often avoided if a cannula was simply introduced into the undiscovered vessel and the vein was not tied.

d) *Accidents and various phenomena following transfusion*. – Among the most frequent I will mention the following: agitation of the patient, convulsive state, symptoms of pulmonary congestion, all phenomena noted especially when the transfusion has been made too quickly. We have also seen delirium, collapse, a more or less violent shivering, an increase in temperature ($\frac{1}{2}$ to 1°), the acceleration and then slowing of the pulse, sweating, the urgent need to urinate or defecate, polyuria, vomiting, palpitations, dyspnoea, colouring of the face. Quite rarely has albumin been found in the urine, or the presence in this secretion of the colouring matter of the blood: 2 times out of 17 cases (Christoforis).

It goes without saying that these effects don't always occur. Roussel goes so far as to claim that a well-done transfusion, with human blood, goes unnoticed by the patient.

I think it unnecessary to go further in the study of transfusion, and I end this much too long *Review* here, by giving it the following general conclusion:

The transfusion of blood is an operation whose importance is demonstrated by the clinic as well as by experimental medicine. It is easy to practice, very harmless when it is well done, and of an effectiveness that cannot be doubted by impartial minds. If its capital indications, admitted by the generality of doctors, are mainly found in post-haemorrhagic anaemias, it must also be recognized that it also succeeds in certain anaemias by dyscrasia and in some poisonings.

We hope that the history of this beautiful therapeutic method will be completed in the near future by the provision of new improvements. The art of healing will then, we have no doubt, be put in possession of one of its most heroic means. In any case, we can already say, with Professor Gubler: Honour to the method that has saved more than 150 lives!