EXPERIMENTELLE UNTERSUCHUNGEN ÜBER DIE TRANSFUSION, TRANSPLANTATION ODER SUBSTITUTION DES BLUTES IN THEORETISCHER UND PRACTISCHER BEZIEHUNG.

By: P. L. PANUM

A TRANSLATION BY PHIL LEAROYD

A copy of this two part lengthy paper (83 pages in total) titled 'Experimental studies on the transfusion, transplantation or substitution of blood in theoretical and practical terms' by Prof. Peter Ludvig Panum (1820-1885) was published in 1863 in the journal *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medicin*.

The first part (Ref: Vol. 27, No. 3, pages 240-295) can be read or downloaded from the following site: https://babel.hathitrust.org/cgi/pt?id=chi.77590115&seq=252
The second part (Ref: Vol. 27, No. 5, pages 433-459) can be read or downloaded from the following site: https://babel.hathitrust.org/cgi/pt?id=chi.77590115&seq=445

CAUTIONARY NOTE: The reader of this translation should be aware that it contains details of experimental work on animals, which will be viewed as being unacceptable and extremely cruel by today's standards and as such, some people may find this distressing. The vast majority of these experimental details are printed in the original paper in a smaller font size and I have reproduced this in my translation; therefore if the reader wishes to avoid these details they should not read the size 10 font text within this translation.

Panum essentially begins his paper by posing three questions, which relate essentially to the three sections of his paper. The first section deals with the question of introducing clots during a transfusion when using untreated blood and their possible effects. He looks at the difficulty in identifying whether the donor blood has actually clotted prior to transfusion by looking at clot formation times and the 'types of clot' that can be visually identified. This results in the author arguing for the use of defibrinated blood to avoid the potential problems associated by clot formation. Such blood is identified in the text by the terms whisked, whipped or beaten – these have been 'standardised' in the translation to be called 'whisked'. As well as the practical aspects of using defibrinated blood the author also looks at trying to experimentally identify the role of the 'fibrous matter' content that is removed from the transfused blood by defibrination and whether it has any detrimental effects in the recipient's blood clotting ability post-transfusion.

The second section of the paper attempts to look at whether transfused blood survives normally in the recipient's circulation or if it is removed more rapidly than normal. This section includes the greater part of the experimental work that is overly complex and essentially inconclusive in its outcomes as viewed with the benefit of later knowledge.

The third section essentially looks at the use of donor blood from a different species that is used for transfusion, relating to the 'historical' animal experimental transfusions performed mainly on dogs and sheep as well as the first transfusions to humans that used animal blood in the mid 17th century. As such, details of some of these early transfusions together with his own animal experiments leads the author to conclude that animal red cells do not survive normally in the human circulation and as such Panum strongly recommends that only human (defibrinated) blood should be used.

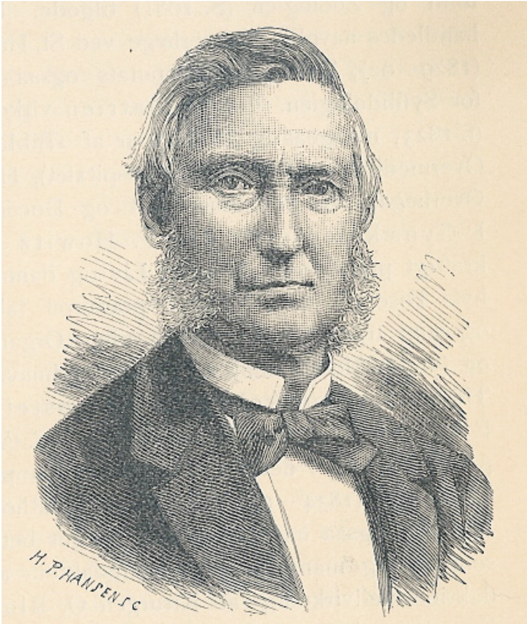
A large part of this paper relates to the author's experimental work and his interpretations of it, as well as commenting on other people's experimental work. As such it is mainly relevant to the authors own investigations and is debatably unrelated to the 'history of blood transfusion'. I have however translated the complete paper as some of the interpretations and conclusions the author provides are of historical interest, reflecting some of the beliefs of that time. However, detailed historical information relating to some of the original animal and human blood transfusion experimental work performed in the mid 17th century that is of more general interest is also included in the third part of this paper.

I have produced a translation of both parts of this paper into English to enable its content to be appreciated by a wider audience. Whilst I am aware that instantaneous computer generated translation is available, this process 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.

The paragraph settings and general layout of both parts of this paper have been maintained within the translation as near to the original as possible. The references in the original text are identified by asterisks and symbols placed at the bottom of the pages where they occur. I have sequentially numbered these for both parts of the paper and placed them together at the end of the translation of the second part. The references are reproduced as originally printed, though I have also translated the titles of the references where this information is provided, as well as those that are the author's comments. The actual (extensive) experimental results are presented in a smaller font in the original publications and I have reproduced this within the translation. These results include a number of 'shorthand' terms that vary in their presentation in the original text. I have where possible tried to standardise the presentation of these, though not all of them are easily understood and/or translated, especially in the somewhat overly-complex tables, which I have included, though their original format has been modified to accommodate the text format of the translation.

PETER LUDVIG PANUM – BIOGRAPHICAL INFORMATION

Peter Ludvig Panum was born on the 19th December 1820 on the island of Bornholm in Rønne, the son of Jens Severin Nathanael Panum (1792-1836) and Johanne Caroline Louise Charlotte Lande (1798-1844). The family moved to Eckernförde (Rendesburg) in 1829 where his father had assumed a position as regiment surgeon. After matriculating from Flensburg Learned School in 1840, Panum enrolled first at Kiel University before transferring in 1841 to the University of Copenhagen. After completing his medical studies in 1845, Panum took up a position at Almindelig Hospital in Copenhagen, undertaking research work on a measles epidemic in the Faroe Islands. In 1855 he became Professor of Physiology at the University of Kiel. In 1856 he published his research work into 'putrid poison', that was thought to be responsible for the symptoms seen in people with sepsis, what is now known as an endotoxin. He relocated to the University of Copenhagen in 1862, where he founded studies in exercise physiology. The Panum Institute in Copenhagen is named in his honour. He died on the 2nd May 1885



Peter Ludvig Panum (1820-1885)
(Image credit – Wikipedia)

PART ONE

EXPERIMENTAL STUDIES ON THE TRANSFUSION, TRANSPLANTATION OR SUBSTITUTION OF BLOOD IN THEORETICAL AND PRACTICAL TERMS

By: Prof. Dr. P. L. Panum in Kiel.

Transfusion, as the operation diametrically opposed to general blood extraction, seems to have come more to the fore in recent times, where one is stingy with blood, just as in 1665-1668 and about forty years ago, it can be understood as a protest against the excessive blood withdrawals that were common in the past. In more recent times, it has been used more often and has been recommended even more often, especially in the case of bleeding of newly delivered people. Martin has compiled 57 of these cases, of which 45 ended in complete healing[1]. Later, he himself performed this operation for the second time with happy success[2]. Transfusion has been used several times in older and more recent times and discussed even more often in cases of real or perceived lack of blood and in incorrect blood mixing. The older cases belonging to this category have been collected and compiled by Scheel[3] and Dieffenbach[4], the newer ones by Schilz[5] and Dreesen[6]. These cases, too, to which could be added several scattered in the journals and other unpublished cases have increased in a remarkable manner in the last 10 years. The fact that this operation, which undoubtedly has a greater future, has so far found more theoretical adherents among physicians than those who have carried it out in practice, is probably largely due to the fact that the preliminary physiological examinations on which it is based, have not yet progressed far enough.

The occasion for the following examinations came from two transfusions carried out here in the Friedrichs-hospital by Professor Esmarch, performed on people, in which he had the goodness to involve me. One of these experiments, which was used as a last resort, was actually carried out on a corpse. The patient, who had been caught in the gears of a mill, had had his thigh disarticulated, and had probably lost a great deal of blood before he was admitted to the hospital. He died suddenly during the preparations for the transfusion, before any other blood had been injected into him. The transfusion carried out on the fresh corpse and the other attempts at resuscitation were unsuccessful. The second attempt was published by Dreesen in the above-mentioned dissertation.

When I now examine the question of transfusion, with the practical question of the applicability of this operation with therapeutic purposes in mind, it became quite clear to me how much preliminary physiological examinations would be needed before the physician could carry it out on a larger scale with confidence. The questions that I have included in my research can be organised into 3 main groups:

I. The question of whether the transmission of clots should be feared when transfusing un-whisked blood, and of the consequences of such an introduction of fresh clots during transfusion seemed to require more detailed examination, and it was soon necessary to ascertain whether the removal of these dangers by the use of whisked blood is harmless, or whether the transfusion of the blood freed from fibrous matter by whisking perhaps entails other dangers which could render its application questionable? For the practitioner, this question coincides with that of whether pure blood or defibrinated blood deserves preference in transfusions?

II. What is the role of the foreign transfused blood of the same species of animal in the organism? Is it only able to have a temporary invigorating effect on the nervous system, which has been exhausted by previous severe loss of blood, and is it then excreted in some way - or can it function permanently, like one's own blood? In other words, can the blood and especially the blood cells, be transplanted into a foreign organism of the same species? The answer to these questions is directly related to several questions of the utmost importance for practical therapy: whether, in the case of blood loss, only a small amount of blood should be transfused in order to satisfy the indication vitalis, leaving the formation of the main mass of new blood to the patient's body? Or whether, under certain circumstances, by transfusion of a larger quantity of blood, it may be expected that the foreign blood, while continuing to function, will be able to take over the business of nourishment, and that consequently the convalescence may be substantially shortened by transfusion of a more abundant quantity of blood? And finally, whether it is conceivable under certain circumstances to improve a faulty blood mixture by removal of a large part of a person’s own diseased blood and replacing it with someone else’s healthy blood.

III. Furthermore, the question of the effect of the transfused blood of another animal species in larger or smaller quantities, e.g., the blood of calves, lambs, humans or cats in dogs, or the blood of cattle, lambs, etc., in humans, is by no means settled, and requires new investigations. For practical therapy, this question would be of particular interest in cases where human blood was not available or would not be available in sufficient quantity. This would then come into particular consideration if one were to think of substituting a larger portion of the blood volume of a human organism with new blood.

I.

In all older attempts at transfusion on humans and animals, the blood was used in its entirety. Dumas and Prevost[7] were probably the first to state that defibrinated blood, like un-whisked or liquid blood, was capable of reviving animals rendered lifeless by bleeding. They also stated that blood kept liquid by adding a little caustic soda had the same effect. Dieffenbach[8] confirmed the efficacy of the blood freed from fibrous matter by agitating and came to the conclusion that the blood cells contain the invigorating principle. Joh. Müller[9] soon expressed the thought: "that it will be of the utmost importance for the important operation of transfusion to be able to make use of blood that has been whisked and thereby freed of its fibrous material instead of the un-whisked blood." This idea was pursued experimentally by Bischoff[10] in his contributions to the Doctrine of Blood and Transfusion and in an addendum to his treatise[11]. Since, after injecting mammalian blood into birds, and vice versa, Bischoff observed dangerous symptoms and death, and then by Dumas-Prevost and Dieffenbach, only when he transfused fresh liquid venous blood, but not when he transfused whisked blood, he concluded that only the blood cells contained the invigorating principle, but that the fibrous material caused the principal danger in transfusion. In his later contribution, however, he stated that arterial blood was tolerated just as well as whisked blood, and that it was the venous nature of the blood on which the greatest danger depended. Among the practical physicians who later performed the transfusion, in spite of the recommendation of J. Müller and Bischoff, defibrinated blood was used much less frequently than pure blood. To the best of my knowledge, defibrinated blood has only been used in transfusion into humans in the following cases: first in an unpublished case of Larsen[12] in 1847, once by Monneret[13] in 1851, twice by Giovanni Polli[14] in 1851, once by Fenger[15] in 1853, six times by Neudörfer[16] in 1860 and twice by Esmarch[17] in 1860, a total of 13 times. In almost all of these cases, the operation was unsuccessful; but it would be very hasty to attribute this to the use of defibrinated blood; for, on closer consideration of the individual cases, one must admit that in each one of them, one was hardly justified in expecting a successful result from the transfusion with any degree of probability. On the other hand, in those cases where the operation was unquestionably indicated, in the case immediately preceding severe loss of blood, without any blood change other than that which was caused by the haemorrhage itself, as far as I know, defibrinated blood has never been used, but always pure blood. Martin[18], like Schilz before him, has recently spoken out against the use of defibrinated blood. Firstly, he claims, a lot of precious time is lost in defibrinating, and secondly, he thinks that the fibrous material does no harm. He tries to justify the latter by saying that the experiments on animals do not confirm Johannes Müller's opinion that fibrous material causes the main dangers in transfusion, since Bischoff's statement is refuted by his own later experiments and also by the experiments of Brown-Sequard, which showed that the excess of carbonic acid causes the poisonous effect[19]. He also further considers that there was no reliable evidence in the present experience of transfusion into humans for the concern that the fibrous matter of the blood could clot during transfer and thus the serious consequences of thrombosis and embolism could occur, and after examining some suspicious cases in this respect, he came to the conclusion that the dangers of blood clotting in transfusions of un-whisked human blood do not appear to be as great as was feared. Furthermore, against the fears of the formation of clots when using the still liquid non-whisked blood, an experiment by Blundel[20] was cited, in which, according to a fairly accurate calculation, 12 pints of blood had to have flowed out of a large dog in 24 minutes and had been injected back unbeaten, so that the entire blood mass of the dog had passed through the syringe more than once. However, in view of Magendie's[21] defibrination experiments, there have been special concerns about the use of defibrinated blood in human transfusions. It was stated that dogs from which blood was repeatedly withdrawn, and to which the same blood was then injected again after the fibrous material had been removed by stirring, suffered from bloody oedema of the lungs, bloody effusions into the intestines, and injection of the capillaries, especially those of the mucous membrane of the intestine, and he asserted, based on this, that the main function of fibrous matter and the only one which is known, consists precisely in the fact that it promotes the passage of the blood through the capillaries.

On closer examination of these reasons, which on a superficial inspection appear to be quite valid, against the use of defibrinated blood and for the retention of the old traditional unbeaten blood, they in fact lose their significance if we only take into account the experiences known to date, but they are likely to be rendered completely invalid by my experimental investigations.

1) The previous experience of physicians does not prejudge anything with regard to the question in question. This is because the statistical method presupposes comparable cases; up to now however, in cases where there was a fresh haemorrhage, without any other blood change other than that produced by the haemorrhage, and where the indication for the transfusion was therefore undoubtedly present, only un-whisked blood was used, and not in a single case defibrinated blood. In the experiments in which the latter was used, the prospect of success was always more or less clouded by complications which could not be eliminated by transfusion.

2) Martin's objection that a lot of precious time is lost in defibrinating is completely unfounded, if one is only clear about how one should behave in doing it. I let the blood destined for transfusion flow into a suitable cylinder glass. As it drains, I let the person who catches the blood whisk it. This does not need to be an expert assistant. For whisking, a rod is used which is round at the top and widened into a board at the bottom, which, while the board is immersed in the blood present in the cylinder glass, it is rotated as quickly as possible between the fingers of the free hand. After the fibrin has been separated within a few minutes, the blood is filtered through a linen cloth spread over a glass funnel into a vessel that is kept lukewarm if possible. It is not necessary to anxiously maintain the temperature of the heart of the blood to be injected. In this way, the defibrinated blood will certainly be able to be delivered by the assistant who provides the bloodletting as quickly as the surgeon, whose preparations will take at least as long even with the greatest fluency one could wish for. If, however, the surgeon were compelled to perform the transfusion without a competent assistant, he would first be able to produce the whisked blood and then perform the preparatory operation on the patient, without fear that the blood to be transfused would have become unsuitable for transfusion in the meantime.

3) The assertion that there is no danger to be feared from the coagulation of the blood during transfer is no more proved by Blundell's above-mentioned experiment than by Martin's statements.

Blundell emphasized that the danger of coagulation in transfusion of human blood is less great than in some animals, because healthy human blood does not coagulate as quickly as sheep, ox, and dog blood, and his above experiment with dogs was intended to show that even in this animal one does not have to worry much about coagulation during transfusion. It should be noted however, that the speed or slowness with which the coagulation of healthy human blood occurs, as well as the blood of healthy dogs, is extremely variable, and that the causes of these differences are still so little known that it is impossible to predict how early or late the coagulation will take place. Nasse[22] already noted that no observer agrees with the other with regard to the coagulation time, and says: "This is not only due to the possible difference in the coagulation time of the blood and the dependence of time on external conditions, but also the differences in the method of investigation of the observers, and finally to the fluctuating concept of coagulation itself. For it is possible to distinguish very different moments or degrees in it, and now the one, now the other, seems to have been envisaged when determining the time." These five moments are: 1) Formation of a membrane on the surface, which radiates from the edge towards the centre. 2) Formation of a skin that adheres to the walls of the vessel and encloses the liquid blood as if in a tube, and which can be removed from the vessel wall with a needle using careful movement. 3) Conversion of the blood to a jelly. 4) Coagulation forms into a solid cake, which can be moved around in the vessel without tearing it and at the same time the beginning of the sweating out of the serum. 5) Completion of this separation, which takes 10 to 48 hours. - I have observed the coagulation of the blood in 20 fairly healthy people, who were at most suffering from plethora or congestions or who had been prophylactically bled from the vein, in as many men as women. The table below gives the earliest and latest times for the first 4 moments, as well as the mean for the two sexes:

	The earliest	The latest	Mean for men	Mean for women
1)	1¾ min.	5 (at the most) 6 min.	3 min. 45 sec.	2 min. 50 sec.
2)	2 min.	6 (at the most) 7 min.	5 min. 22 sec.	5 min. 12 sec.
3)	4 min.	10 (at the most) 12 min.	9 min. 5 sec.	7 min. 40 sec.
4)	7 min.	13 (at the most) 16 min.	11 min. 45 sec.	9 min. 5 sec.

So much for Nasse. I myself have had ample opportunity in the past to make observations of these conditions, and although I have neglected to make such records as are available from Nasse, I can assure you that the differences in the coagulation time in humans tend to be greater rather than less than those stated by this author. In dogs I have noticed even greater differences, and in particular I have sometimes noticed a much greater speed at which coagulation occurs, so that I can assure you that the above-mentioned experiment by Blundell, in which 12 pints of blood passed through the syringe without coagulation occurring, will only rarely be feasible. He must have happened to have an animal in front of him whose blood coagulated unusually late. - However, the manner in which the blood flows during bloodletting also comes into consideration, over which, as is well known, the surgeon is by no means in control. If the blood flows out slowly, in many cases it will not be possible to carry out the transfusion with un-whisked blood without the transmission of clots. Even if it is possible to get the blood into the syringe while it is still liquid, the flow into and contact with the closer walls of the syringe, especially if it is made of metal, the contact of which accelerates coagulation, will very often cause the coagulation to begin earlier in the syringe than in the vessel in which the blood was first collected. However, since the first three degrees of coagulation, distinguished by Nasse, do not offer any serious resistance to expulsion from the syringe, which only arises when a solid cake is formed that can be removed without tearing, one can never be quite sure in the case of transfusion with un-whisked blood that one will not inject partially affected blood, even if it is only a matter of transferring small amounts of blood. However, the greater the amount of blood transferred, the greater the probability that clots will be transmitted, the greater the difficulties of execution and the greater the danger.

In my experimental contributions to the doctrine of embolism[23], to which I must refer here since I have shown that the transfer of fresh blood clots into the veins can produce the following different effects: 1) If the mass of the clot is large enough to cut off the blood supply to the left heart and from there to the arteries of the brain, medulla oblongata and spinal cord by blocking the branches of the pulmonary artery, sudden death occurs during or immediately after the transfusion. This sudden death, which occurs independently of the cessation of the movements of the heart, which usually persist for some time, and independently of the interruption of the respiratory process, depends solely on the interruption of the supply of blood to the large nerve centres, is initiated by symptoms of irritation which soon give place to the cessation of all phenomena of life, and which cease all the more quickly and are all the more limited the more completely the blood supply is cut off. 2) However, the absence of such a death in the case of a transfusion with un-whisked blood in no way proves that blood clots have not been transmitted nevertheless; for if the mass of the introduced clots was smaller, either only deep respiratory movements with transient breathlessness occur immediately and initially, or no symptoms of circulatory disturbance occur at all. 3) Secondary sudden death occurring over the course of the next few days or weeks may be caused by secondary clot deposits on the embolic clots, whereby the initially insufficient blockage of the pulmonary artery becomes sufficient to interrupt the blood supply necessary for the maintenance of the functions of the large nerve centres, either by blockage of the large branches directly by the secondary clot deposits, or by obturation of the small branches, in which smaller clots are flushed or torn loose from the large secondary clot. 4) The local nutritional disorders of the lung tissue, which may result from embolism of the pulmonary artery, are partly lobular infarctions, partly tubercle-like fibroid nodules and the transitions between them. Lobular infarctions are, of course, by no means a constant consequence of the penetration of fresh blood clots into the pulmonary artery, but they are only produced by it under certain conditions, some of which are not known in detail; nor are they usually of such a magnitude that they could become dangerous due to the impairment of respiration that they cause, however, they are nevertheless very questionable, especially probably due to the formation of clots in the pulmonary veins. The small tubercle-like nodules of the lung tissue will not of course significantly impair respiration either, but it is to be feared that they may develop into true pulmonary tuberculosis under certain circumstances. 5) The circulatory and nutritional disorders of the lung tissue most likely often lead to the formation of clots in the pulmonary veins, which are very easily torn loose by the constant movements of the lungs during respiration and would then enter the large circulation. In this case, they would then act as arterial emboli, causing sudden death after the course of several days or weeks, partly by blockage of the arteries of the large nerve centre, and partly causing the very diverse symptoms of disease and pathological findings which depend on the arterial embolism. - With regard to the more specific explanation of these dangers, I must, as I said, refer to the detailed treatise cited above.

With these facts in mind, it must be admitted that the transfusion of un-whisked blood is certainly a very dangerous operation, and the greater the quantity of blood to be transfused, the more precarious. For if, as has been discussed above, the surgeon can never be quite sure that blood which has already partially coagulated is not transferred during the transfusion, he must be prepared for all the various possible consequences which may be produced by it, although these consequences do not always actually occur. In view of the variety of these consequences, and of the dissection findings, which are almost always not very conspicuous in providing evidence for the dependence of death on clot injection, even a negative result of a carefully performed dissection with the above possibilities in mind will not, as a rule, be able to reassure a conscientious surgeon as to the harmlessness of his procedure, although it must be readily admitted that in most cases other unfortunate circumstances, namely the patient's previous condition, can hypothetically be used to explain an unfortunate outcome. Such an unfortunate outcome, as the cases collected by Martin show, is by no means a rare occurrence in the case of transfusion of un-whisked blood, under circumstances that would otherwise really be indicative of the operation, and the number of unfortunate cases would doubtless have been far greater if they were not frequently withheld from publication, which has hardly ever happened in the case of fortunate cases. The rule, strongly recommended by all those who have used whisked blood for transfusion, to use only small quantities of blood (in the case of patients who had lost the greater part of their blood through bleeding, they were usually satisfied with the transfusion of an ounce or less, and even with two drachms), is probably due to the fact that the dangers of the transmission of clots must increase in a very enormous proportion with the increase in the amount of blood. If Martin had studied the consequences of the transfer of blood clots in more detail, he would certainly not have attempted to prove that they were innocent of the unfortunate results which had occurred in the transfusions with un-whisked blood, which had hitherto existed, for the proof of this cannot be adduced at all, least of all from the findings of dissections, in which the points of view obtained by more detailed studies were ignored. Even in the cases that seem to have been quite successful, it remains to be seen whether the patients in question did not later suffer from the consequences of a possible clot transmission. Under these circumstances, it would be very desirable for the surgeon and for the patients who require a transfusion if he could avoid all these partly revealing, partly hidden, insidious, possible dangers of clot transmission by removing the fibrous material which causes all these dangers, provided that the operation does not thereby lose its effectiveness, nor be associated with other perhaps as great or even greater dangers.

4. However, based partly on theoretical objections and partly on Magendie's defibrination experiments, it was feared that the absence of fibrous material might have other, particularly secondary, harmful consequences. The bloody oedema of the lungs, the bloody effusions into the intestines, the injection of the capillaries, especially of the intestinal mucosa, observed in the stomach, could certainly be explained in different ways. However, as already noted above, Magendie concluded from his experiments that the fibrous material facilitated the passage of the blood through the capillaries. If Magendie's observations were really confirmed to the effect that it was the deficiency of fibrous matter, and not other overlooked circumstances, that caused these bloody exudations and circulatory obstructions, one might well deduce from this the apprehension that the transfused, defibrinated blood was exposed to an abnormal decay and subsequent excretion, which might not be expected, or not in the same way, in the case of the transfusion of un-whisked blood. In which case, however, it might be feared that the abnormal products of decomposition, as well as the directly perceived pathological transudations and blood stagnation, might perhaps be even more dangerous than the sum of the dangers caused by embolism when using un-whisked blood.

However, the experiments, which will be communicated in detail below, resolutely reject these fears. In fact, in dogs, by alternately withdrawing blood and injecting the whisked blood of other dogs, almost all of the fibrous blood originally present in them can be replaced by fibrous-free foreign blood, so that the fibrous content of the circulating blood is reduced to a minimum without any significant disturbances occurring, and in particular without the pathological transudations and blood stagnations mentioned by Magendie coming to light. For example, on 18th, 20th and 23rd August, a very young dog, weighing about 2500 grams, was able to successively have 863.5 grams of blood withdrawn and replaced with a similar quantity of whisked blood from other dogs, without any significant loss of vivacity, appetite or weight, and without any symptom having occurred that would have indicated decomposition of the blood or capillary circulatory disorders. Even urinary secretion can remain qualitatively and quantitatively unchanged in these experiments, and the normal fibrous content of the blood is restored from one day to the next after such defibrination. However, in order for this to succeed, the following precautions must not be neglected: a) The whisked blood to be used for transfusion must be properly protected from decomposition, to which it is exposed if for a long time to dry or impure air, especially at a temperature approaching the heat of the blood. If this is neglected, the symptoms of putrid intoxication can occur. b) The whisked blood to be injected must first be filtered through a dense canvas wall so that fibrous clots are not injected, which could under certain circumstances cause pathological changes in the lungs. c) Care must be taken to ensure that the amount of the injected blood is not greater than that of the blood that has just been withdrawn, otherwise the overcrowding of the vascular system will easily cause bleeding and many other disorders. d) It is necessary to be aware of the strong convulsions of the nervous system which occur when too large a quantity of blood is withdrawn at once. e) Only whisked blood of healthy animals of the same species may be used. f) One must not inject too quickly, otherwise the overcrowding and tension of the heart brings with it the greatest danger. It is probably difficult or impossible, but also unimportant, to decide which of these circumstances misled Magendie in his experiments. But that the absence of fibrous matter in the whisked blood used for transfusion, even if the fibrous content of the circulating blood is reduced to a minimum by an initiated exchange of blood, does not cause any disturbances, namely, neither pathological transudations, nor local circulatory disorders, nor any sign of decomposition of the blood, and that the normal fibrous content restores itself in about 24 hours, is, according to my experiments, which shall be set forth in more detail below, an established fact.

5. In a further respect, however, the use of whisked blood deserves a decided preference over un-whisked venous blood in transfusion. For by whisking the blood, it is saturated with oxygen and freed from a large part of the carbonic acid contained in the venous blood. However, according to the investigations of Dieffenbach, Bischoff, and Brown-Sequard, the oxygen bound to the blood cells is definitely the invigorating principle by which the transfusion becomes a salutary operation; while a blood too rich in carbonic acid can, according to the experiments of Bischoff and Brown-Sequard, kill on the spot. In this respect it may be appropriate to recall here in particular Brown-Sequard's investigation, which appears in the Comptes rendus[24] of the Academie of Paris and the Soc. de biologie[25], as well as in the Journal de physiol.[26]. In his first memoirs, Brown-Sequard showed that oxygenated blood, whether removed from an artery or a vein, can restore the lost vital phenomena of contractile and nervous tissues when injected into the arteries after the lapse of not too long a time. By interrupting the arterial blood supply to the brain, very sudden death occurs; but resuscitation is effected by a new influx of oxygen-rich blood, if this occurs early enough. However, if you wait 3 minutes, resuscitation rarely occurs. Even in the case of severed heads, it was possible in this way to produce respiratory movements of the face and nostrils, movements of the eyes, etc. Defibrinated blood worked just as well and vigorously as arterial blood; serum did not have this effect, even if it was saturated with oxygen as much as possible. The more blood cells and the more oxygen the blood contained, the greater its ability to restore the forces of life. The blood cells alone do not have this ability, because black blood has no effect. Oxygen-saturated mixtures of blood and serum are less invigorating; 2 parts of blood to 10 parts of serum were sometimes able to restore the respiratory function of the medulla oblongata, but not the brain activities; this required at least 3-4 parts of blood per 10 parts of serum. As stated above, Prevost-Dumas,

Dieffenbach, and Bischoff had already arrived at quite similar results, with regard to the excellent efficacy of arterial or whisked blood over venous blood. Brown-Sequard, however, established the excellent ability of oxygen-saturated blood to produce and maintain the phenomena of life, and furthermore through the experience that the reflex movements, as well as the irritability of the muscles and nerves, are much more lively in those animals in which very strong artificial respiration had been employed, which lowered the animal heat, but coloured the venous blood bright red, and that, like the movements of the heart, they persist much longer than usual, whereas these vital phenomena disappear very rapidly in asphyxia, especially if it had been less complete, but long-lasting. But he also found that all blood, when it is so far saturated with carbonic acid that it has assumed a blackish colour, causes the greatest danger to life when injected into the veins of any vertebrate animal, even of the same species; even an amount of blood corresponding to $^{1}/_{500}$ of the body weight, blackened by carbonic acid, had a life-threatening effect if injected reasonably quickly. Even 50 grams of carbonated blood from an animal of the same species would kill a dog or other mammal on the spot, as well as a bird, if it was rapidly injected into the jugular vein; with a very slow injection, during which the carbonic acid could be removed through the lungs, it was still possible to keep the animals alive. He further confirmed the statement made by Bischoff in his last communication[27] that the immediate danger to life which arises from the injection of the venous blood of a vertebrate animal into the veins of an animal of another species can be avoided by the use of arterial or agitated blood[28].

All the circumstances that have been mentioned so far therefore speak decidedly in favour of the use of whisked blood and against the use of fresh, still liquid blood containing fibrous matter in the transfusion. For by the use of the blood freed from fibrous substances, not only are the numerous and malignant dangers of embolism eliminated, the great importance of which has by no means been refuted by previous medical experience, but also those dangers which depend on those volatile substances which, like carbonic acid, are removed during the process of whisking at the same time, a stronger more invigorating effect is achieved by the oxygen-saturated whisked blood, while the lack of fibrous material has no harmful effect, neither on the blood mixture nor on the local circulation and transudation conditions, and is replaced within a short time by newly formed fibrous material. Not only is no time lost in defibrinating, but the whole execution of the operation is greatly simplified by it, and secured against all eventualities that may otherwise occur due to the occurrence of coagulation. These technical advantages would become particularly important if it turns out that it is not always necessary to confine oneself to transfusion of minimal quantities of blood in order to satisfy the immediate indication vitalis, but that it may be advisable under certain circumstances to use larger quantities of blood, and if by using blood preserved in ice in field hospitals or by the use of freshly whisked blood on the battlefield, it should be possible to make this operation as useful for military surgery as it is for bleeding of newly delivered patients. While these advantages are so great that, in my opinion, they make it almost obligatory for a physician who wishes to perform a transfusion to have the blood to be used stirred, in my opinion nothing else other than old sloppiness stands in the way. For it has already been shown above that the experience of the physicians who have hitherto performed this operation does not prejudice anything in this question. But if, however, it should be confirmed, as stated by Brown-Sequard (Journal de physiol. I. p. 671), that defibrinated blood may also be dangerous in that it could cause a sudden coagulation of the blood of the animal into which it is transfused, it is certainly not probable that the deficiency of the fibrous matter of the blood used for transfusion should have this effect and this misfortune would be at least as much to be feared if un-whisked blood were used. To what extent it should be advisable to counter this supposed danger by adding $^{1}/_{1000}$ to $^{1}/_{1500}$ caustic ammonia to the blood to be transfused, as Brown-Sequard, relying on Richardson, recommends; that may be left open for the time being, as the fact itself still appears quite doubtful, since all further data which might be suitable to support such an assertion are concealed by Brown-Sequard, who, moreover, always uses defibrinated blood in his experiments, and unconditionally recommends it before un-whisked blood.

II.

The question of whether the blood of one animal transferred during transfusion can really be transplanted into the circulation of another animal of the same species (or from human to human), e.g. can continue to function normally in the new organism, or whether the foreign blood will soon be decomposed and excreted, is still the subject of controversy. Nevertheless, the resolution of this question would not only be of great theoretical interest, but would also have a very significant impact on practice. For if the foreign blood were soon to be decomposed and excreted, one could only think of fulfilling the immediate indication vitalis through the transfusion, and it would be advisable to use only as small amounts of blood as would be sufficient to effect the revival or to prevent the extinction of the last signs of life by fearing that the decomposition products of the foreign blood might become dangerous to the organism before or during their excretion, and indeed all the more dangerous the greater the quantity would have been. If, on the other hand, the foreign blood continues to function normally and can be used for respiration and nourishment like one's own blood, then it will obviously be indicated to produce the normal amount of blood and blood cells as completely as possible during the transfusion by the use of larger quantities of blood in order to thereby shorten the protracted convalescence, with its dangerous chances, as far as possible, and it could be questioned whether it might not be indicated, under certain circumstances, to improve a faulty blood mixture by a partial blood exchange. Marfels and Moleschott[29] recognized sheep blood cells in the circulating blood of frogs for months after they had introduced sheep blood into the intestines of the frogs, and they concluded from this that the blood cells had a long lifespan. Brown-Sequard[30] also detected the blood cells of dogs, rabbits and guinea pigs transferred into the circulation of geese, roosters and chickens for one month after the transfusion. On the other hand however, the latter confirmed Magendie's statement that the blood cells of birds disappear in the mammalian circulation. After only an hour, the blood cells of chickens and pigeons were no longer to be found in the blood of dogs, cats, and rabbits, and he concluded that they must have dissolved, since they were found everywhere ¼ hour after the transfusion, so they had been able to pass through the capillaries. - However, one objection to the evidentiary value of these experiments, apart from the difficulty of recognizing the foreign blood corpuscles with certainty given the large variation in the size of the animals' own blood corpuscles, is that there is no evidence that the blood corpuscles preserved for such a long time are actually functioning normally. In every blood there are individual blood cells which resist dissolution by water and other reagents much more strongly than others, and it is not probable that these blood cells which are more difficult to destroy should function particularly well. It is well known, as Hanover has shown, that by drying the blood in very thin sections, the blood cells can be dried in such a way that they retain their shape fairly well and to a large extent become difficult to dissolve, and it is quite possible that a certain number of blood cells, through the action of air during transfusion or in the intestinal canal of the frogs, would have attained such insolubility at the expense of their functional capability. Finally, however, these experiments have the very unfortunate fact that they only take into account the behaviour of the blood cells of another animal species. In order to tackle the question of the functional capacity of transfused blood, I also initially carried out experiments which followed those of Marfels-Moleschott and Brown-Sequard. But it soon became clear to me that a final decision could not be reached in this way, partly because of the difficulty or impossibility of distinguishing, for example, the smallest blood cells of a dog from the largest of sheep or cattle, and partly because it soon became apparent that the blood of one species of animal in another species of animal, at least in so far as it is not very closely related, does not continue to function normally, but is in fact decomposed and excreted. Even if it should really be confirmed that some of the foreign blood cells escape this fate, it does not follow that they have really continued to function and with benefit to the animal, but only that, favoured by special circumstances, they have preserved themselves in their external form and structure, just as a fish lens may be preserved for months in the pulmonary artery of a living dog.

Far more significant are some of the older experiments, by which the question in question has in fact been tackled by means of an exchange of blood, carried as far as possible between animals of the same species. Lower[31], in the presence of Doctors Wallis, Thomas Millington, and other physicians (1666), opened the jugular vein of a dog of moderate size, and allowed the blood to flow out until it became faint and was on the point of falling into convulsions; he then directed blood to glow from the crural artery of a large Great Dane that had been tied up next to it into its open vein until one could see from its restlessness and anxiety that it was overflowing with blood. He then stopped the flow of foreign blood and allowed blood to flow out of the vein again. He repeated this reciprocal tapping and draining of the blood, until two large mastiffs had gradually given all their blood to the smaller dog, and bled to death, and Lower's intention of exchanging the whole mass of blood was accomplished. Then the wound of the smaller dog was bandaged with the basting needle and it was untied. Although he had gradually lost and regained as much blood as he himself was heavy (?), he immediately jumped down from the table, flattered his master, and rolled in the grass to cleanse himself of the blood, as if he had only been thrown into the water. The experiment did not have the slightest adverse effect on his well-being.

The Philosophical Society of London, at Robert Boyle's instigation, took up Lower's experiments, and the commission appointed by him, consisting of D. and Th. Coxe, Dr. King, and Hook, made the following experiments in 1666 and 1667[32]: they drew blood from the jugular vein of a sheep, and at the same time let the blood of another sheep flow from the carotid artery into the lower part of the jugular vein. After about four of five jugs (pints) of blood had drained from the vein, the sheep, whose blood was allowed to flow into the other, began to grow weak. It was untied and its owner slaughtered it in the usual way. It contained no more than half a jug of blood. The other sheep seemed to be as well as before, and behaved as if no such attempt had been made upon it. When it was slaughtered, the usual amount of blood was found in it.

As in the previous experiment, they transferred the blood of a small bull dog into a Spanish dog (spaniel) and, while the foreign blood flowed over, let the spaniel’s own blood flow out. The latter shed about 64 ounces of blood, until the bull dog bled to death, without any harm to its health. It was very well and cheerful the next morning, and remained so from that time. A week later this dog was presented to the Philosophical Society, which confirmed his complete well-being[33].

The experiments carried out by Denis in 1667, partly in connection with Emmerez, are much less trustworthy. Two experiments are described in detail, in which 9 and 12 ounces respectively of dog blood were transfused with appropriate blood withdrawal, whereby the animals that received the blood remained well both during the experiment and afterwards[34]. On 25th June 1667, Denis had performed the transfusion on 19 dogs, of which not a single one is said to have died, although sometimes from an artery to a vein, sometimes from a vein to a vein, and although in not a few cases the blood of other animals was also used for the transfusion. It is reported, for example, that a dog which had previously been deprived of so much blood that it could hardly move, received more strength and vitality from the transfused calf's blood than it had before the loss of blood! Another time he tells of a 12-year-old, very decrepit female dog, that quickly became stronger and livelier than before, and that, 8 days later she even came into heat. Analogous is the story of an old 26-year-old horse who, by the transfusion of the blood of 4 rams, regained much more strength and an unusual appetite[35]. These experiments, carried out in the presence of various distinguished (!) persons do not bear the objective character of the English researchers, and the personal ambition of Denis, as well as the passion developed by the dispute with Lamy, Moreau, and other opponents of the transfusion, raise great doubts as to the reliability of his information.

It is with more confidence that we read the report of Dominicus Cassini at Bologna[36], who in May 1667 let as much blood flow out of the jugular vein of a lamb as the vein would give, and then let the blood flow from the carotid of another lamb into it. Then he tied the vein of the lamb that had received the blood at both ends and cut it. The animal, as it was released, followed the surgeons without betraying weakness, and the wound subsequently healed quickly, and it continued to grow like the other lambs. When it died suddenly 6 months later, it was dissected. The stomach was found full of rotten food. The severed jugular vein was found to be fused and a small lateral branch mediated the connection of the upper part with the lower.

The fact that these experiments have not received the consideration they well deserve may be due in part to the fact that they date from so early a period, from a time when the question of transfusion was so adventurous, and when truth and deception were so mixed in this matter that it is not an easy critical task to separate the true from the false. Also, as a rule, there was no information about the behaviour of the individual functions. In part, they may have fallen into oblivion because the ratio of the quantity of blood transfused and that previously extracted was not given due consideration, and because they were lumped together with those experiments in which the blood of other kinds of animals was transfused. For when, too large a quantity of blood was transfused, or when the blood of one animal is transfused into the veins of a very different species, then as we shall see later, very alarming symptoms occur, which seem to have led to the general assumption that the foreign blood, even of animals of the same species, can only function and have an invigorating effect very temporarily, but then perishes and is excreted. Thus, Nasse[37] declared it very likely that the "foreign" blood would soon decompose and be expelled, and therefore advises only small amounts of blood to be used. The same thought has also guided, at least in part, the practitioners. The possibly well founded fear of overcrowding of the vascular system by too large a quantity of blood, cannot possibly be the reason why in half of the cases where the transfusion was performed on account of profuse bleeding in newly delivered patients, only 4 ounces of blood or less were used. Practical experience has not decided the matter; for although the result was successful in about 17 out of 20 cases when 4 ounces or less were applied, and only in 7 out of 10 cases when 1 to 2 pounds were applied, on the one hand these figures are still too small for a statistical justification, and on the other hand it should be considered that in all these cases un-whisked venous blood was used, whereby the dangers of embolism and intoxication due to the venous nature of the blood increase in an extraordinarily strong proportion with the amount of blood used. Finally, in the cases that have been successful, no consideration has been given to the duration of convalescence.

If, as seems to be evident from the experiment of Lower and his successors (assuming their full credibility), it is really possible that the functions of an animal may continue to exist normally for a long time, after a great part, if not the greater part, of its blood has been exchanged for the blood of another animal of the same species, no other conclusion is possible than that the foreign blood does not perish and is expelled in an abnormal way, but that it can continue to function just as well as the blood prepared by one's own organism. It seemed to me, therefore, above all, necessary to resume these old experiments with a more precise consideration of the quantities of blood transfused and withdrawn, and of the individual functions, and in doing so, instead of the direct transfusion from an artery into a vein, to use whisked blood.

1. On 4th May 1861, a dog weighing 7370 gm. before eating was placed in an observation box lined with zinc sheet, from which the urine flowed into a bottle placed underneath, with continuous plentiful feeding of bread and intestines. The bladder had been emptied immediately beforehand. In 24 hours, until 5th May, he emptied 260 cc. of urine of 1046 spec. wt. According to Liebig's method, taking into account the correction for table salt, it contained 23.16 gm. of urea. On the morning of 6th May he also had 555 cc. of urine of 1037 spec. wt. and 46.287 gm. of urea were found in it. On the 6th May at noon he emptied 260 cc. of urine of 1035 spec. wt. and with 15,548 gm. urea. In 48 hours, therefore, the dog had emptied 84.995 gm. of urea after being fed with copious amounts of bread and intestines, or 42.497 gm. in 24 hours. The animal now weighed 7470 gm. From then on, he was deprived of all solid and liquid food. At 3.30 pm in the afternoon of 7th May, he had not yet urinated. His bladder was now emptied through the catheter and 160 cc. of urine was obtained, of 1049 spec. wt. and with 14.63 gm. urea. This quantity referred to the 26 hours after the last meal. For 24 hours there are 13.5 gm.

In the following 24 hours, during which the complete inanition was continued, 75 cc. of urine of 1055 spec. wt. were collected (by means of 2 catheterizations); it contained 7.5 gm. of urea. After a little more than 2 days of starvation, the dog weighed 6900 gm. at 7.30 pm in the evening on 8th May. On 9th May at 10.30 am, the bladder emptied at 7.30 pm the previous evening contained 20 cc. of urine and the dog weighed 6800 gm. He had thus lost 80 gm. in 15 hours through perspiratio insensibilis, i.e. calculated on 24 hours c. 130 gm.

100 cc. of blood was now taken from him and 64 cc. of whisked blood from another dog was transfused through the jugular vein. With continued complete inanition, he delivered 148 cc. of urine of 1055 spec. by weight by catheterization in the following 48 hours, with 14.652 gm. urea. For every 24 hours after the transfusion, i.e. 7.326 gm. of urea with continued inanition. The urine was of the same quality as that previously emptied and contained neither blood nor protein, but, as in the previous 48 hours, it was so concentrated that nitric urea was precipitated in quantities simply by the addition of nitric acid. He weighed 6370 gm. on the 11th (48 hours after the transfusion). So he had lost 430 gm., of which 148 were urine. This leaves 282 gm. in 48 hours or 141 gm. in 24 hours for perspiratio insensibilis.

Now the dog was given food again, first 470 gm. of lungs and 8 hours later 200 cc. of water and 150 gm. of lungs. In the following 24 hours he secreted 270 cc. of urine of 1057 spec. wt., containing 37.120 gm. of urea. The perspiratio insensibilis during these 24 hours was 144.6 gm. Already on the evening of 11th May, after the second meal, he weighed 7130 gm. and on the 20th May he weighed more than before the experiment, namely 7480 gm. So, the substitution of a quantity of blood corresponding to about $^1/_{100}$ of the body weight was not only endured without harm, but also the urea separation, urine volume and perspiration, which had been made as uniform as possible by inanition driven to the emptiness of the intestine, was not noticeably altered in any way by this blood exchange. The quality of the urine and other secretions, so far as they could be examined, had remained unchanged, and the proportions of weight of the animal were entirely in accordance with the rules applicable to healthy animals, which are first subjected to inanition and then fed again. In particular, when the inanition was interrupted, the food was eaten with the greatest appetite and digested so well that the former weight was regained in a short time (9 days). The dependence of the amount of urea excretion on food was also shown to be completely normal. As I have said, this amounted to 42.497 gm. before the inanition, 13.5 gm. on the first day of the inanition, and 7.5 gm. on the second. Previous experiments had shown me that from the second day of inanition onwards, the amount of urea excreted remains fairly constant for several days and with continued inanition, decreases only slightly. Accordingly, in the 48 hours following the exchange of blood, the starving animal emptied 14.652 gm. or 7.326 gm. for each 24 hours. When abundant food was served, the amount of urea in the following 24 hours immediately rose to 37.120 gm. The amount of blood in question would be equivalent to 1-1$^1/_2$ pounds in humans.

2. The same dog weighed 7250 gm. on the 25th May, after the urine had been removed by catheterization. He had always been very lively and healthy, and the slight weight loss was only due to the fact that he had eaten less, having been accustomed to meat food, but now fed with bread. 205 cc. of blood was taken from him and 80 cc. of whisked blood from another dog was injected into the jugular vein. He was a bit faint and shivering because of the blood loss (125 cc) that had taken place despite the transfusion. 6 hours later he had fully recovered and was jumping around cheerfully. He now weighed 7070 gm.; since neither urine nor excrement had been emptied, he had lost 55 gm. through perspiration in these 6 hours. On 26th May at 11.00 am he weighed 6990 gm. In the meantime, 68.4 gm. of urine had been withdrawn from him by means of the catheter. (This urine was acidic, dark-coloured, with a spec. wt. of 1053, and contained neither protein nor blood.) In the last 16$^1/_2$ hours the perspiration had been only 12.6 gm., as he had passed no excrement and, apart for that withdrawn by catheterization, no urine. The amount of urea emptied in the 24 hours following the transfusion was 7.501 gm. This quantity corresponded to the state of inanition which began 24 hours after the last meal in the earlier experiment. Of course, he had only eaten a little black bread and drank water before and after the transfusion. Nevertheless, the significant blood loss seems to have contributed significantly to the fact that the amount was so small. He was now offered raw ox spleen, together with milk and bread, and he ate 430 gm. of it, so that his weight rose to 7420 gm. In the evening he ate again 400 cc. of thin rice groats and weighed 7750 gm. From 7 o'clock in the evening until 10.30 o'clock on the morning of 27th May, he had secreted more than 272 cc. of urine. This quantity was withdrawn from him on the morning of the 27th, after his bladder had been emptied by catheterization at 7 o'clock in the evening on the 26th. In addition, however, two small portions had been lost, which had to be disregarded. The urine emptied by catheterization was bright, clear, acidic, non-proteinaceous, of 1030 spec. wt. The 272 cc. secreted from 7 p.m. to 10.30 a.m. contained 15.29 gm. urea. This would correspond to 23.67 gm. for 24 hours, but this amount would

be a little too small because of the loss that has taken place. The amount of urea secreted had thus increased in proportion to the amount of nitrogen-rich food; however, it was again lower than might have been expected from the earlier experiments with the same dog, which is probably to be attributed to the rather considerable loss of blood of the animal 205 - 80 = 125 cc. Apart from the consequences of the loss of blood caused by the fact that much more blood had been withdrawn from the dog than had been restored, the transfusion had had no noticeable consequences, and no phenomenon had indicated a decomposition and expulsion of the foreign dog blood that had been infused into it. In the days that followed he was perfectly well, until he was sacrificed to another experiment.

3. A small, short-haired, male dog, which weighed 4080 gm. on 20th May, was placed in the observation box on 23rd May 1861, without solid or liquid food. 24 hours later, on 24th May, he weighed 3860 gm. and had 220 cc. of urine with a spec. wt. of 1045. It contained 19.58 gm. of urea. On 25th May, 24 hours later, the dog weighed 3700 gm. after urinary extraction. The amount of urine was 55 cc. with a spec. wt. of 1046. In addition, he had emptied 20 gm. of solid excrements. Of the 160 gm. he had lost in weight, 57.5 + 20 = 77.5 gm. were due to urine and excrements, and 82.5 gm. to perspiratio insensibilis. In the 55 cc. urine there were found 4.776 gm. of urea.

140 cc. of blood was taken from his carotid artery and 96 cc. of whisked blood from another dog was injected into the jugular vein. Due to the severe blood withdrawal, he first became very restless, then fainted and emptied a few drops of urine. Immediately afterwards there followed bilious vomiting and violent peristaltic movements with rumbles in the body; the pulse had become very weak and counted 100 beats per minute. Respiration occurred 16 times per minute. After injection of the whisked blood about 32°C, he remained very faint for some time, but the temperature, which had dropped considerably, soon recovered, and six hours later he had recovered so completely that when the observation box was opened, he sprang out of it vigorously, barking violently, and resisted when he was again shut up in it with solid and liquid food. The body temperature had returned to normal. He now weighed 3650 gm. Since he had not emptied urine or excrements, but had lost 44 gm. more than the blood he had received, the amount of the loss due to perspiratio insensibilis during the first 6 hours after the transfusion was only 6 gm. and this loss, calculated over 24 hours, was therefore 24 gm.

On 26th May, the dog was as lively as before the operation. He now weighed 3530 gm., so he had lost 120 gm. in the 24 hours immediately after the transfusion. During this time there were 65 cc. of urine, of 1048 spec. wt. = 67.4 gm.[38]. Thus, from 6.30 pm to 10.30 am, or in 16 hours, he had lost 52.8 gm. through perspiration, considerably more than immediately after the transfusion. The urine was pale yellow, slightly alkaline, somewhat clouded by triple phosphate crystals and phosphoric acid lime, but free of protein. The amount of urea found in it was 6.090 gm[39], even a little more than during the inanition before the transfusion. He was now offered food and ate 70 gm. of white bread with butter, 90 gm. of raw ox spleen and 130 gm. of milk. He now weighed 3820 gm. and was again placed in the observation box with solid and liquid food. At 5.30 pm in the evening he had passed neither urine nor excrement and now weighed 3800 gm. In the $6^1/_2$ hours he had lost 20 gm. to perspiration. At 10.30 am on the morning of the 27th, he weighed 3650 gm. He had not emptied any excrement, but secreted 92 cc. of urine of 1050 spec. wt. It was bright, cloudy and slightly alkaline. So since yesterday evening at 5.30 pm he had lost 150 gm., of which 96.6 gm. urine and 53.4 gm. by perspiration (in 17 hours). In the last 24 hours, he had lost 73.4 gm. to perspiratio insensibilis. In the 24-hour urine, 10.405 gm. of urea were found.

He was then left to his own devices for a few days, and was quite well.

4. On the 30th May, 130 cc. of blood were first drawn from the carotid artery of the same dog; after this he had become very weak. After 70 cc. had been extracted from both carotids, he appeared to be dead. Cornea and conjunctiva were quite insensible, as everywhere the whole body; lifted by the hind legs, hung limply without the slightest movement; only individual spasmodic contractions of the diaphragm, occurring with long pauses, were still noticed. By means of a 32 cc. syringe, in 5 portions, 148 cc. blood of another dog was injected into the jugular vein. He then recovered completely and was able to walk around immediately after the transfusion was completed, although of course he was very weak. In the evening he was still faint when he was taken out of the observation box; he immediately went to his usual bed, and resisted, when they made a gesture to put him back into the observation box. On the 31st May, the dog was running around the room, but was very shy and did not want to eat. He weighed 3500 gm., while he had weighed 3610 gm. after the transfusion was finished. The urine extracted from him by catheterization (30 cc.) was, as before, slightly alkaline and somewhat cloudy, but contained neither blood nor protein. The spec. wt. of it was 1043. On the 1st June, the animal seemed to be alert. He had emptied acidic and clear urine along with solid excrements. His weight had dropped to 3350 gm. In the afternoon he ate meat and boiled fish and

drank with it. In the evening, the condition was unchanged. On the morning of 2nd June, the condition had become quite different. The dog was very restless and ran like mad around the room. The foam came to his mouth and he had his tail between his legs. Then he fell into convulsions. These continued into the night of 3 to 4 June. The animal lay on one side, and kept the three extremities stiffly stretched, the head strongly bent and the tail raised, while the right hind limb was always moving as if it were running. The temperature dropped more and more and the respiration became more and more difficult. In this state, about 55 cc. of urine was secreted, which had a spec. wt. of 1055, was alkaline, dark and rich in protein. He died on the morning of 4th June.

In the dissection performed on 5th June, the heart and the large vessels contained large and very firm fibrous clots, which, however, were arranged in both the left and right hearts in such a way that the discoloured parts occupied the highest place. Since the animal had been lying on its left side, the two vena cava vessels were filled to the brim and felt firm to the touch due to clots that had formed post-mortem. Those parts of the heart and the large vessels, which had been at the bottom (left) side contained very dark, almost liquid, dark red blood. By the way, the heart and lungs were completely healthy. The lungs were nice and bright red and did not show any condensed areas anywhere. The pulmonary artery did not contain any clots that could have formed during life. The stomach and intestines were pale and contained a lot of mucus strongly coloured by bile. The mucous membrane of the small intestine and large intestine was pale and healthy everywhere, as was the peritoneum. On the gastric mucosa there were some round, very pale places, where the mucous membrane, as if knocked out by a punch, seemed to be missing. The liver, kidneys, and spleen were of perfectly healthy appearance; as well as the mesenteric glands. The pancreas was slightly reddened. The spinal cord, along with its membranes, was normal down to the area of the medulla oblongata. Here, however, the skins were very strongly injected, especially the pia mater, and stretched with blood-stained serum. The membranes of the brain were also heavily injected, especially at the mesencephalon. The wound on the neck was filled with a white, crumbly, cheese-like mass; the Nn. vagi were wrapped up in it, and their trunks were quite dark red in the region of the ligation sites of the two carotids. It can be inferred from these dissection results that it was not a decomposition of the blood, but disease of the nervous system that had caused the symptoms and death. This could depend partly on the inhibition of both carotids, partly on the disease of the ends of the vagus nerves adjoining the ligatures.

5. An old long-legged black dog, weighing 9020 gm., had 190 cc. of blood taken on 8th June 1861 and 200 cc. on 9th June. He was very faint and sad after this second bloodletting. An hour later, 120 cc. of the blood of another dog, heated to 36°C., was injected into him through the jugular vein. He obviously became much stronger and more alert afterwards. On the morning of the 10th June, he was perfectly well and ate with great appetite.

He had 140 gm. of blood taken from him again and 120 cc. of whisked blood from another dog were injected through the other jugular vein. The fatigue caused by the bloodletting was immediately and completely lost by the transfusion. Immediately afterwards he ate bread and drank water with great appetite. Immediately afterwards he took pleasure of snapping at the flies that flew around the room. He now weighed only 8520 gm., so he had lost 500 gm. since the 8th June; but there were also 290 gm. more blood drawn from him than transfused. Until the 30th June he remained perfectly healthy and cheerful; the condition of the urine remained normal and he maintained his weight. Before eating he weighed 8230 gm. on the 11th; 8250 gm. on the 13th; 8150 gm. on the 14th; 8320 gm. on the 15th; 8250 gm. on the 30th after eating; he weighed 8550 gm. on the 11th; 8650 on the 26th and 8700 gm. on the 29th.

6. A young female dog of large breed, which weighed 9020 gm. on 8th June before eating and 9950 gm. on 9th June after eating, was deprived of 200 cc. of blood on 9 June and in return was injected with 128 cc. of whisked blood from the previous dog. This blood had already been withdrawn from the other dog twenty-four hours before (on 8 June), but immediately afterwards had been kept cooled to 0° in ice with the cylinder in which it was collected; immediately before the injection, this blood had been heated to 36°C. Immediately after the operation, the dog was as lively as before, after the bloodletting had previously weakened her greatly. She was placed in the observation box after she had eaten very heavily before the operation. The next morning she was also perfectly well, and ate with great appetite. During the night, she emptied 220 cc. of urine, which reacted somewhat alkaline and was quite dark in colour, but did not contain blood or protein. The spec. wt. of it was 1037.

On 10th June, 160 cc of blood were taken from her again. For this she was given 152 cc. of whisked blood of the black dog discussed in the previous experiment was injected into the right jugular vein, which had been kept in ice from the day before, but which had now been heated to 36°C. She was perfectly well afterwards and ate and drank immediately afterwards with great appetite. She then weighed 10450 gm., so had gained a considerable weight. Before eating, she weighed 10520 gm. on the 11th; 10670 gm. on the 13th; 10350 gm. on the 14th; 10700 gm. on the 15th; 12430 gm. on the 30th; after eating she weighed 11200 gm. on the 11th; 13170 gm. on the 26th, and 14300 gm. on the 29th. So she had steadily and significantly gained weight, and had always been very lively and healthy.

7. On the 30th June, since the dog discussed under 5 weighed 8250 gm., the dog discussed under 6 weighed 12430 gm. (before eating), an exchange of blood of both animals was effected in the following manner: namely, both dogs alternately had their own blood taken from the crural artery and injected with the blood of the other dog into the crural vein. This was carried out in 4 repetitions from 12.30 a.m. to 4.15 a.m. in such a way that the black, male, 8,250 gm. dog received 3 x 32 = 96 cc., 5 x 32 = 160 cc., 5 x 32 = 160 cc., $5^1/_2$ x 32 = 176 cc., together 592 cc. of whipped blood of the brown, young, female dog, while the latter received 2 x 32 = 64 cc., $4^1/_2$ x 32 = 144 cc., 4 x 32 = 128 cc., $5^3/_4$ x 32 = 184 cc., together 520 cc. of whipped blood from the first-named older, black, male dog.

Both dogs had lost a little more blood than was used for the transfusion into the veins of the other animal; 22.5 gm. of the black dog's blood remained and 35 gm. of the brown dog's blood after the transfusion was completed. So the black dog had lost at least 542.5 cc. of blood, i.e. 47.5 cc. less than he received; the brown dog 627 cc., i.e. 107 cc. more than it had received.

At the end of the operation, both animals were weak and stiff in their movements, which could very well be due to the prolonged tying in a forced position, the wounding and the fear, but otherwise showed no noticeable symptoms. Even during the injections, only slight phenomena were perceived, namely, sometimes alternating contraction and dilation of the pupils, restlessness of the respiratory movements when the injection was rapid, and when the blood had become cold, shivering. In fact, during these experiments no precautions were taken to keep the blood warm. Immediately after the operation the animals did not want to eat, but by 8 o'clock in the evening they had not only eaten the food they had previously been given, but they also ate a large quantity of meat offered to them (from the rumen of an ox) and seemed to be perfectly well. They were also very well on the following days and ate with great appetite, especially the young dog. The urine they secreted was consistently clear after the operation, acidic, without a trace of blood or protein, and generally of a normal nature. The weight ratios were as follows: the old black dog, which had weighed 8250 gm. before the operation, weighed 8170 gm. immediately after it; on the 1 July after eating 8020 gm., on the 2nd before eating 7720 gm., on the 3rd before eating 7775 gm., on the 4th before eating 7774 gm., after the same 8190 gm., on the 7th, after 36 hours of starvation 7850 gm. The young brown dog, who weighed 12430 gm. before the transfusion, weighed 12200 gm. immediately after the transfusion; on the following day (1 July) after eating 14450 gm.; on the 2nd July before eating 12760 gm., on the 3rd July before eating 13120 gm., after the same 14000 gm.; on the 4th July before eating 12650 gm., after the same 14200 gm.; on 7th July, after 36 hours of starvation, 12150 gm. Therefore, the exchange of blood had not disturbed the well-being of both dogs, and not even the steady weight gain of the young dog had been impaired by growth. Even later on, her well-being remained undisturbed and on the 13th August the young brown female dog weighed 16480 gm. after eating and on the 15th before the meal 15640 gm. The old black dog weighed 8820 gm. after eating on 13th August and 8490 gm. on 15th August. So both of them had gained weight.

But even if the blood of two dogs of about the same size were completely exchanged, it can only be achieved by about half of the blood of each dog would be substituted by the blood of the other, while it would retain at least half of its own blood. Therefore, I decided to modify the experiment so that the blood of a smaller dog would be replaced by the blood of another or several other larger dogs. At the same time, however, in order to better assess the role of foreign blood, it seemed very desirable that analyses of the various types of blood should be carried out in addition to transfusions. This happened in the following experiments. The fibrous content was determined in the following way: the blood collected in a weighed glass was shaken vigorously and persistently after the glass had been securely sealed, then weighed with the glass and filtered through a white satin filter. The collected pulp was then washed out with water until it was white, pressed on the satin filter between blotting paper until the paper was no longer wet, and then boiled with a mixture of alcohol and ether, completely dried and weighed. As it was only necessary to know the relative ratio of the water and blood cell content of the different types of blood, I could confine myself for the purpose of these determinations to determining the specific weight of the whisked blood and the serum, and to using the difference in the specific weights of these fluids as a relative expression of the richness of the blood cells in blood. To determine the specific weight of the serum and the whisked blood, I use very small picnometers, which only hold about 4 gm. of blood, and which are always cleaned very carefully to prevent the adherence of air bubbles. According to Brücke's instructions, I rinse them out first with concentrated sulphuric acid and then with alcohol until it no longer reacts acidically; then the glass is dried and now the blood or serum lies quite smoothly on the glass. It goes without saying that when pouring in the whisked blood, one must on the one hand ensure that the blood cells are evenly distributed by shaking, but on the other hand also that foam is not formed by shaking too strongly. The air bubbles, which are at least suspended in the whisked blood by the shaking, are removed by over filling the picnometer during the pouring and by brushing away the air bubbles that rise upwards before putting on the stopper. By careful repetition of experiments with the same blood, results are obtained which, except for slight variations in the decimal places, and show no greater inconsistency than repeated analyses of the same blood by other methods. With the exception of the counting method, which is too laborious and slow for a series of experiments, and thus impracticable for such experiments because of lack of time, all the other methods provide only relative expressions for the amount of blood cells. I have made the following comparisons among them: 1) The method of determining blood cells from the difference between the solid residue of the serum and the whisked blood; 2) from the difference between the amount of proteins in the serum and in the whisked blood; 3) from a certain colouring of a certain quantity of water by different quantities of blood; 4) from the difference between the specific weights of the serum and the whisked blood. All these methods, carefully executed, give useful results, if one only intends to compare several blood samples with each other as to their abundance in blood cells; for it has never occurred to me that the one method would have given a plus, the other a minus, if the differences went beyond the decimal places, that is, were large enough to even be taken into account. Since, as I have said, the determination of the absolute quantity of blood cells must be dispensed with, one may well refrain from the well-known calculations, which nevertheless aim in vain at such an absolute determination, since these only cloud the relative standard without attaining the absolute one. I shall return to this point later on, on the occasion of the studies of the quantity of blood and of the changes in the blood during inanition, and I shall here give only one example of the comparability of the three main methods of relative blood cell determination, which concerns the blood of three young dogs whose nutritional conditions had been different. I will refer to them as A, B and C and tabulate the results:

	A	B	C
Specific weight of the serum	1021.8	1020.08	1017.8
Specific weight of the whisked blood	1033.06	1045	1035.4
Solid residue in 1000 p. serum	63.061	55.39	48.26
Solid residue in 1000 p. of collected blood	109.7	152.97	113.82
Difference in the specific weight of the serum and the whisked blood	11.26	24.92	17.6
Difference of solid residues in 1000 parts of serum and 1000 parts of purified blood	46.64	97.58	65.56
To achieve the same colour from the same amounts of water, the amount of blood used in gm.	0.3525	0.1625	0.237
Ratio of the amount of blood cells in blood types A, B and C, calculated from the difference in the specific weights	46.9	100	73.3
Ratio of the amount of blood cells in blood types A, B and C, calculated from the difference in solid residues	47.8	100	67.2
Ratio of the amount of blood cells in blood types A, B and C, calculated from the difference in the blood quantities used for the same colouring of the same amounts of water	47.7	100	73.9

It should therefore be obvious that the determinations of the specific weights of the serum and the whisked blood are sufficient for our purpose here.

The experiments, which were now carried out with the above considerations, were as follows:

8. A small, long-haired, female dog, only 2-3 months old, which weighed 2620 gm. on 13th August 1861, had been locked up in the observation box, raged and made a lot of noise and worked itself out tremendously. On 15th August it weighed only 2460 gm. I now intended to replace the blood of this little dog with the blood of the two large dogs used in the previous experiment. To this end, 122.4 cc. of blood was drawn from the carotid artery. After this bleeding, which was very strong for the small dog, no more blood flowed from the opened carotid artery, the animal developed convulsions and was very weak. But when 3 x 32 = 96 cc. of whisked blood from the black male dog (experiment 7) was injected into it through the jugular vein, it recovered completely. - Immediately afterwards the little dog was again deprived of 100 cc. of blood, after which it was even more affected than before after the withdrawal of the 122.4 cc. During the preparations for the injection of the foreign blood, which lasted 5 to 10 minutes, the breathing movements suddenly ceased completely, and before the injection could be carried out, the sensation and voluntary movement, as well as any trace of reflex movements, especially when touching both the cornea and the conjunctiva, had completely disappeared. The dead dog was nevertheless brought back to life by the transfusion of whisked blood from the black dog. After the injection of the first 32 cc, there were at first some slow and deep breaths, but these soon became more frequent; during the injection of the following 32 cc. the breaths became regular, but at first they remained very deep, so long as the contact of the cornea and conjunctiva did not cause any movements of the eyelids; but then, towards the end of the injection of these 32 cc, the reflex movements of the eyelids and the sensation returned, and at the same time the breaths were greatly accelerated, while maintaining the regular rhythm. The dog was now injected with 16 cc. of warmed whisked blood of the black dog into the jugular vein, and then voluntary movements took place again. (The first injected 32 + 32 = 64 cc. had not been heated.) For the 122.4 + 100 = 222.4 cc. of blood taken from it, the dog had regained 96 + 80 = 176 cc., i.e. lost a total of 46.4 cc. In the process, however, the dog had hardly lost any solid parts of blood, for the blood which had been withdrawn first, and which had originally been its own, had, after it had been whisked, only had a spec. wt. of 1041.7 and the spec. wt. of its serum was only 1019, while the spec. wt. of the whisked blood of the black dog instilled in her amounted to 1062.8. Nevertheless, the little dog was very sick after the transfusion. It was so weak that it couldn't stand on its feet and after some time it started choking (but without vomiting), with a dark, bloody, foamy liquid coming to the mouth. It had now been about 2 hours since the beginning of the experiment. $^{3}/_{4}$ hour after the last transfusion, 40 cc. of blood was taken from the carotid artery and 32 cc. of whisked blood from the large, brown female dog, which had been warmed beforehand and whose spec. wt. 1052, was injected through the jugular vein. During the injection, the respiration was very accelerated and a brown-red liquid flowed out of his mouth afterwards. Mucus tinged with blood was also emptied from the anus. In consideration of the poor condition of the animal, which lay quite still, respiring rather rapidly, further operations were temporarily suspended. At 1.30 pm she vomited a considerable amount of a blood-stained liquid. By 2.30 pm the condition had improved perceptibly, although the voluntary movements were still very dull. Once again (for the 4th time), 63.4 cc. of blood were drawn from the carotid artery and 32 cc. of whisked blood were injected. After that, however, vomiting of black bloody masses occurred, respiration became slow and irregular, the cornea became insensitive, the movements of the heart very weak, and death occurred at 3 o'clock.

The blood of the little dog had undergone the following changes in composition as a result of the operations: the original blood contained 151.5 pr. m. solid parts and 2666 pr. m. fibrin. The spec. wt. of the whisked blood was 1041.7, that of the serum 1019, and the difference in the specific weights of the whisked blood and the serum due to the blood cells was therefore 22.7. The blood taken from her at the 2nd blood draw contained 212 pr. m. solid parts and 0.108 pr. m. fibrin; the specific weight of the whisked blood was 1057.6. In the last portion of blood extracted from it were 222 pr. m. solid parts and it contained 0.71 pr. m. fibrin. The specific weight of the whisked blood was 1059.5.

Taking into account previous experience, it now seemed to me very likely that the most alarming phenomena ending in death, including the emptying of bloody fluids from the muzzle, mouth, and anus, had occurred only in consequence of the extraordinarily violent convulsions of the nervous system, the functions of which had repeatedly been wholly or almost wholly suspended by the withdrawal of blood and restored by the transfusions. These convulsions must have been all the more violent, as the animal was very young, and had worked itself out a great deal by romping while it was confined in the box. The bleeding could then be explained by a higher tension of the blood in the venous system as a result of the disturbances of cardiac activity. If the blood pressure in the arteries decreases due to the weakness of the heart's activity, then it must rise in the veins as it spreads more evenly over the whole vascular system (as the pressure of the stationary blood), and if now and then the activity of the heart becomes temporarily more energetic, the pressure in the capillaries must also rise above the usual level, since then almost the usual amount of blood flows into them from the arteries, while the increased venous pressure is an obstacle to the outflow.

These considerations induced me to modify the experiment in such a way as to avoid the strong convulsions of the nervous system caused by the excessive withdrawal of blood, and to try to accomplish the blood rush by frequently repeated smaller doses.

9. On 18th August 1861, a female puppy of 2-3 months old, by the same mother, which was exactly the same as the one in the previous experiment who had sat in the observation box for 24 hours and romped around a lot, was used for the experiment. Blood was withdrawn from one carotid artery in moderate quantities five times in succession, and each time immediately afterwards the blood of another dog was injected into the jugular vein. The numerical results of this experiment are summarized in the following table, which at the same time gives an overview of the changes in the composition of the blood:

	Found weight of the animal in gm.	Supplied weight of the intestinally clean animal.	Calc. Blood m., apart from v. d. changes due to endosmosis during d. experiment and assuming v. one $^{1}/_{13}$ d. weight d. Thiers corresponds normal blood m.	Emptied blood volumes in gm.	Amount of injected foreign, whisked blood in gm.	Calculated quantity d. remaining original blood, under d. mentioned earlier – requirement in gm.	The same expressed in percent.	Specific weight of the whisked blood.	Specific weight of the serum.	Difference in specific weight d. serum and the whisked blood.	Amount of fibrin per mille.	Absolute amount of fibrin removed.	Remaining amount of fibrin, calculated by subtraction, the original amount = 2.4 p.m. in 182 gm. blood = 0.436 gm.	Amount of fibrin, calculated according to the ratio of the remaining original blood as 2.4 p.m.	Residual amount of fibrin, calculated from the percentages found and the calculated amounts remaining after each bleeding. Whole blood.	Fibrin before each blood withdrawal, calculate. a. d. total d. emptied and in the restir. blood returned fibr.
On 18th August 1861	2420v 2550n d. Fress	2366	182	-	-	-	-	-	-	-	-	-	0.436	0.436	0.436	0.436
10.30 am																
1st Portion	-	-	} 183.99	64.95	-	117.05	64.3	1041	1019.2	21.8	2.4	0.156	0.280	0.280 in 117.05 u. Bl	0.280 in 117.05 g. Bl	0.436
In return	-	-		-	66.94	-		(1045.9*)								
11.00 am																
2nd Portion	-	-	} 190.3	60.9	-	77.22	42.3	1042.2	1019.9	22.3	1.7	0.103	0.177	0.185 in 77.22 u. Bl	0.209 in 123.09 g. Bl	0.312
In return	-	-		-	66.94	-		(1045.9*)								
11.40 am																
3rd Portion	-	-	} 173.07	83.9	-	43.12	23.1	1042.4	1020.1	22.3	0.827	0.069	0.108	0.103 in 43.12 u. Bl	0.088 in 106.4 g. Bl	0.157
In return	-	-		-	66.94	-		(1045.9*)								
12.30 pm																
4th Portion	-	-	} 153.36	86.65	-	21.6	11.8	1039.8	1020.4	19.4	0.745	0.064	0.044	0.052 in 21.6 u. Bl	0.064 in 86.46 g. Bl	0.128
In return	-	-		-	66.94	-		(1045.9*)								
1.00 pm																
5th Portion	-	-	} 152.77	34	-	16.82	9.24	-	1020.4	-	-	0.0205				
In return	-	-		-	33.47	-		(1045.9*)								
End result	2460	-	152.77	330.8	301.3	16.82	9.24	-	-	-	-	0.4125				

* The foreign defibrinated blood came from the large, young, female dog discussed in Experiments 6 and 7.

There was no noticeable disturbance of the dog's well-being during these operations. After the third transfusion, however, she had a semi-liquid defecation coloured brown by bile. The latter was repeated after the entire completion of the experiment, and the emptied excrement was not only liquid, but also bloody coloured. Apart from this, however, she remained perfectly cheerful all the time, and seemed to be at ease in every respect. When she was placed in the observation box she behaved rather rudely, as long as it was daytime; in the evenings she drank milk, and during the night she made a noise and raged, as she had done the night before, before anything had happened to her, in order to be freed from the box. The next day she was also quite cheerful. During her nocturnal stay in the box, she had emptied 117 cc. of urine and 17 gm. of fairly liquid excrements. The urine was dark in colour, contained a little blood and had an alkaline reaction. It was rich in urea and had a spec. wt. of 1048. The urine emptied immediately afterwards, on the morning of 19 August, was acidic, clear and contained no trace of blood or protein.

Our conjecture that the unfortunate result observed in the preceding experiment was not caused by some decomposition of the mass of defibrinated blood of another dog, but was only caused by the fact that too much blood was withdrawn at once, thereby the nutrition of the nervous system was so disturbed that it could not recover later, in spite of the presence of a plentiful quantity of functional blood, had been brilliantly confirmed by this experiment. For this time even more blood had been gradually extracted from an equally small dog, and replaced by whisked blood from another dog, without any alarming symptoms having occurred. Only insignificant irregularities in the blood pressure conditions were present during the operations, and to them, as in the previous case, I think I must ascribe the quite temporary bloody condition of the excrement and urine. A closer look at the numerical results summarized in the preceding table reveals several remarkable conditions. During the $2^1/_2$ hours duration of the experiment, the dog had lost 90 gm. in weight, of which 29.23 gm. was due to more blood being withdrawn from it than transfused, the rest to perspiration, excrement and urination. After the 2nd transfusion, the amount of blood had increased by about 8 gm. above the norm and after the 5th injection it had fallen by more than 29 gm. below the norm. After the respective blood withdrawals, however, the remaining amount of blood had dropped even lower for a short time, lowest after the 4th, where, according to our above assumption, only 86.42 gm. of blood remained until the new blood was added. These fluctuations in the amount of blood and the fluctuations in blood pressure which occurred as a result of them, could not remain without an effect on the supply of fluid to the blood, which was dependent on the absorption and lymphatic flow. An expression of this can be found in the fibrin determinations, on the one hand when one calculates the quantities of fibrin which are calculated with the original 2.4 pr. m. containing blood, and, on the other hand, compares with it the amounts of this substance that was actually emptied and those that remained. The 1st blood withdrawal resulted in 0.156 gm. of fibrin being removed, from the probably originally existing 0.436 gm., so 0.280 gm. remained in 117.05 gm. of blood. This amount of blood was then brought to 183.99 gm. by the transfusion of whisked blood and these should now also contain 0.280 gm. of fibrin. As a result of the 2nd blood withdrawal, 60.9 gm. of the 183.99 gm. of blood was emptied with 0.103 gm. fibrin remaining in the 123.09 gm. of blood, therefore, 0.209 gm. of fibrin would have remained behind, and in total the blood would have contained 0.312 instead of 0.280 gm. of fibrin before the second blood withdrawal. So, between the 1st and 2nd blood withdrawal, 0.032 gm. of fibrin would have been added to the blood via the lymphatic stream or would have been formed in the blood. As a result of the 3rd blood withdrawal, 83.9 gm. of the 190.3 gm. of blood available there were raised with 0.069 gm. of fibrin emptied. Of the 0.209 gm. of fibrin present after the 2nd blood withdrawal, 0.140 gm. of fibrin should therefore be removed after the 3rd blood withdrawal or before the 4th; but since of those 190.3 gm., 106.4 gm. with 0.088 gm. fibrin must have remained, thus 0.157 instead of 0.140 gm. fibrin was present, and consequently 0.017 gm. fibrin must have been added to the blood between the 2nd and 3rd blood withdrawals. If, before the 4th blood withdrawal, 0.157 gm. fibrin was present in 173.07 of blood and 0.064 gm. was emptied into 86.65 gm. of blood, then 0.093 gm. fibrin should remain. But since in the remaining 86.46 gm. of blood there must have been 0.064 gm. of fibrin remaining, 0.128 instead of 0.093 gm. of fibrin would really have been present after the

4th blood withdrawal, i.e., 0.035 gm. of fibrin would have been added to the blood between the 3rd and 4th blood withdrawal. The fact that less fibrin had been added to the blood between the 2nd and 3rd blood withdrawal than between the 1st and 2nd and between the 3rd and 4th blood withdrawal could be explained by the fact that the amount of blood after the 2nd transfusion was higher (190 gm.) and dropped lower (to 123) by the 2nd blood withdrawal than in the other experiments, since it can be assumed that the lower the blood pressure, the more lymph will have become poured into the blood.

The changes in the specific weight of the whisked blood also deserve attention in this regard. One would have to expect that the same would become higher and higher in the following portions, since the transfused whisked blood of the other dog had a specific weight of 1045.9, while the original blood of our dog had shown only 1041. In fact, however, the whisked blood obtained at the second blood withdrawal was slightly heavier (1042.2), and the blood obtained at the 3rd blood withdrawal had become somewhat heavier (1042.4), but these increases were evidently less than they would have been if the blood had not been diluted in some other way. Quite evident, however, was this other dilution during the 4th blood withdrawal, in which the specific weight of the whisked blood, instead of being higher, was found to be noticeably lower than in the preceding blood withdrawal, and even lower than in the original blood. The supply of the diluting fluid between the 3rd and 4th blood withdrawal was obviously greater than before, and it is evident from the above that, in addition to this dilution, 0.035 gm. of fibrous matter had also been supplied to the blood. From this it follows that, in fact, that during the $2^1/_2$ hours of the experiment, a considerable quantity of fibrous lymph had poured into the blood vessels, more than had been removed from them by exosmosis in the same time. From this, however, it follows that the changes in the quantities of blood given in the table are not entirely correct, but that the fluctuations were in fact probably less than they appear in the overview. Nevertheless, this does not materially alter the validity of the calculations about the reduction in the quantity of the original blood; because if we assume that the normal amount of blood of 182 gm. would have been completely restored each time before the new blood was withdrawn, the figures are quite corresponding, namely, 77.9 instead of 77.22, 42 instead of 43.12, 22 instead of 21.6, and 18 instead of 16.82 gm. Accordingly, at any rate, there is only a little more than 9 per cent of the original blood remaining in the animal after the end of the experiment, always assuming that the amount of blood was equal to the original body weight.

10. On the 20th August, the experiment just described was repeated with the same dog. He had not presented any abnormal symptoms since then, and was as lively as before the first attempt. On the 19th he weighed 2350 gm. before eating, 2450 gm. after eating. On the 20th before eating 2210 gm., after the same 2400 gm. The blood was now withdrawn from him, in similar portions as in the previous experiment, bled from the carotid artery and each time immediately afterwards injected the whisked blood of another dog through the crural vein. The numerical results of this experiment are shown in the following table:

During the whole experiment, which this time was completed in about $1^1/_2$ hours, there were no morbid phenomena at all, and immediately afterwards the dog ran very nimbly and cheerfully around the room, drinking milk and eating old lungs. He had just become a little shy and didn't make the same noise as before. The next day he was quite well, except that the wounds on his neck and groin naturally embarrassed him a little. On the next day, the 22nd, his health was unchanged; but the wound in his groin evidently embarrassed him more than the wound on his neck. His weight, which had decreased somewhat from the 18th to the 20th August, probably because of the confinement in the observation box, as usual with dogs, had reduced his appetite, increased rather than decreased in the following days, weighing 2290 gm. on the morning of the 21st August, and 2470 gm. after dinner. The urine he had passed this time after the experiment had always remained clear and had (not even temporarily) contained neither blood nor protein. The excrement also remained of normal colour, but the consumption of the milk made it thin again. On the afternoon of the 21st he weighed 2600 gm. after eating, on the 22nd after eating 2480 gm., and on the 23rd before eating 2300 gm., and 2520 gm. after eating. He had not lost any weight and his well-being had remained completely undisturbed; the wounds also healed well.

	Weight of the dog. Gm.	A. Blutm. obne consideration of their changes through endosmosis since the 18th and during d. Verse.	B. Blutm., assuming that they are at the beginning of d. Vers. the norm. height v. 182 gm. had reached again, while d. Vers. was not changed by endosmosis and exosmosis	Amount of blood withdrawn. Gm.	Amount of blood injected. Gm.	Amount of original blood assuming A. Gm.	Amount of original blood assuming B. Gm.	Specific weight of the whisked blood	Specific weight of the serum	Difference	Amount of fibrin etc.
20th August	2210 before eating										
	2400 after eating	152.77	182	-	-	16.82	20.4				
1st Portion	-	} 161.15	} 190.38	59.1	-	10.32	13.533	1036.5	1017.1	19.4	2.538
In return	-			-	67.48	-	-	(1054.39*)			
2nd Portion	-	} 170.43	} 199.66	58.2	-	6.60	9.403	1040	1019.2	20.8	0.56
In return	-			-	67.48	-	-	(1054.39*)			
3rd Portion	-	} 166.09	} 196.32	70.82	-	3.86	6.069	1044.7	1020.4	24.3	0.51
In return	-			-	67.48	-	-	(1054.39*)			
4th Portion	-	} 140.75	} 169.92	76.95	-	2.09	3.439	1046.4	1020.2	26.2	0.34
In return	-			-	50.61	-	-				
End result	-	140.75	169.92	265.07	253.05	2.09 or 1.14%	3.433 or 1.88%				

* The whisked blood used for the transfusion had been taken from the old black male dog used in the 5th and 7th experiments. He had been perfectly well since the last exchange of blood on the 30th June. After injection of the 3rd portion, the blood that had been first taken from the black dog had been consumed and a second blood sample had to be taken from the crural artery. Only 60 cc. could be extracted if you didn't want to kill him. Afterwards he was so weak that he could only stand with difficulty and staggered badly when walking. The large brown dog used on 18th August was so weak after losing blood that it could not give blood again.

If we take into account that by this experiment the blood originally peculiar to the dog had been removed to within 2 or at least up to $3^1/_2$ gm. and replaced by the blood of another dog[40], it is clear, in view of the unchanged manner in which all functions were nevertheless carried out, that the foreign blood had to function in his body as if it were his own; for no one would think that an animal which had only 1.14 to 1.88 per cent of functional blood could continue to live in the normal way as if nothing at all had happened to it. - Regarding the perceived changes in the blood during the experiment, only the very strong decrease in the fibre content from the 1st to the 2nd blood withdrawal is striking. If the animal contained 0.460 gm. of fibrin in 182 gm. of blood, then after withdrawal of 59.1 gm. of blood, 0.320 gm. should remain, which was then distributed to 190 gm. of blood, and at the second bloodletting a fibre content of 1.68 pr. m. could be expected, instead of the found 0.56 pr. m. It appears, therefore, that in the meantime fibrous matter has disappeared from the blood, or that the defibrinated blood has not yet completely mixed with the rest of the blood. In the following blood withdrawals, on the other hand, the same slow decrease in the fibre content is observed, which in the previous experiment forced us to assume that significant quantities of fibrin had been added to the blood by the lymph during the experiment. The strong increase in the specific weight of the whisked blood, the weaker increase in the specific weight of the serum, and the strong increase in the blood cells recognizable from the difference, are fully explained by the high specific weight of the whisked blood of the old dog used for transfusion.

But this experiment is of particular interest because it shows the changes which the blood had undergone from the 18th to the 20th of August. These concerned (1) the fibre content, (2) the water and solid contents of the serum, and (3) the blood cell content.

On 18th August, the fibrin content of the blood was reduced to 0.745 pr. m. during the 4th blood withdrawal. On the 20th, the first portion of the drained blood contained 2.528 pr. m., i.e. even a little more than in the first portion of the blood emptied on the 18th (2.4 pr. m.). Therefore, the normal fibrin content had been completely restored over the course of two days, without any disturbance to the animal's well-being. The absence of fibrous matter in the whisked blood when it is used in transfusion for healing purposes appears to be quite harmless.

As far as the composition of the serum is concerned, we have a somewhat imperfect expression in the specific weight of the serum. For the assessment of the water content of the serum, however, this expression should be quite sufficient, as has been shown by experiments on the subject by Nasse and by myself. In the last portion of the blood withdrawn on the 18th, the serum had a specific weight of 1020.4, in the 1st portion of the blood withdrawn on the 20th, the serum showed a specific weight of 1017.1. Accordingly, the content of solid particles would have decreased considerably, or, as may also be said, the content of water would have increased. This is easily explained by the fact that, on the 18th a greater quantity of blood was withdrawn from the animal than was injected; for it had lost 330.8 gm. and regained only 301.3 gm. back, or its blood quantity of 182 gm. taken as the original quantity, had fallen to 152.77 gm.

The difference between the specific weights of the whisked blood and the serum, which served as an expression of the amount of blood cells, was 19.4 in the 4th portion of the drained blood on 18th August and also 19.4 in the 1st portion of the blood drained on 20th August. Accordingly, the blood cell content would not have changed at all over the course of the two days. The change in the blood, which is recognized by the fact that the specific weight of the serum on the 18th in the 4th and 5th portions of the drained blood was 1020.4, on the 20th, in the 1st portion was 1017.1, while the specific weight of the whisked blood in the 4th portion of the blood emptied on the 18th was 1039.8, in the 1st portion of the blood emptied on the 20th was only 1036.5, so it would therefore depend only on a dilution of the serum. It should of course be noted here that the composition of the blood was changed on the 18th by the fact that the 4th portion of whisked blood was injected, the 5th portion was withdrawn from it and the 5th portion of whisked blood was injected into it again. This circumstance, however, cannot significantly alter the conclusion that from the 18th to the 20th there was no remarkable decomposition of the transplanted foreign blood cells. For the whisked blood used on the 18th for the transfusion in the 4th and 5th portions was the same as that used for the transfusion of the 1st, 2nd and 3rd portions, and by which the specific weight of the serum increased from 1019.2 to 1019.9, 1020.1, and 1020.4, while the specific weight of the whisked blood rose first from 1041 to 1042.2, and then to 1042.4, then dropped again to 1039.8. The difference between the specific weights of the serum and the whisked blood had risen from 21.8 to 22.3 and then decreased to 19.4. From this it follows that the whisked blood used for transfusion had a somewhat more concentrated serum, and was a little richer in blood cells than the original blood of the animal, but that these differences were only slight, and therefore that any mass destruction of the transplanted blood cells could not have taken place from the 18th to the 20th August. This becomes particularly remarkable when one considers that at the end of the experiment the animal had only 2.09 to 3.439 gm. or 1.14-1.88 percent of its original blood, and thus essentially connected its own budget with the foreign blood transfused in a whisked state, of which at the end of the experiment about 166.481 gm. circulated in his body.

11. On 23rd August, the operations performed on the 18th and 20th August were repeated with the same small dog, which in the meantime had been quite well, as has already been remarked above, using the arterial and crural vein of the other side. The numerical results of this third series of transfusions are shown in the following table:

This time the operation was very painful and the animal had become a bit weak after the 3rd transfusion. The reason for this was that a branch of the crural nerve had been accidentally caught in the ligature; for when he was removed from it, these phenomena immediately ceased. Incidentally, no alarming symptoms occurred during the operation, and immediately after the end of the whole experiment, the dog ran merrily about the room and drank milk when it was offered to him. On the following day too, the animal showed nothing remarkable, only its appetite was somewhat less than before. On the 25th there was a fever and the wound was very painful; the weight had dropped slightly, but not significantly. On the 26th, the thigh was very painful and was lifted up while walking around. The appetite was small, and the animal preferred to lie down. On the 27th, the whole thigh and foot was very swollen and extremely painful. At the bottom end of the lower leg, a solutio continuitatis and friction of two ends of the bone against each other was noticed during movement. A lot of pus was emptied through an incision in the lower leg and a bare bone was felt in depth by means of the probe. The limb was amputated in the middle of the lower leg, with very little blood lost. Before the amputation the animal weighed 2160 gm., after the amputation 2050 gm. The amputated leg weighed 44.5 gm.; the remaining 65.5 gm. was almost entirely due to the outflow of pus. On examination, it was found that the ankle joint was destroyed and that the lower halves of the tibia and fibula, exposed by the periosteum, were surrounded by pus. Thus, widespread necrosis of the lower leg bones with inflammation of the surrounding parts had been the cause of the phenomena. After the amputation, the dog seemed to be much better than before and he ate 100 gm. of meat and milk. - On the following day, 28th August, the wound had a good appearance, and the dog ran about merrily on his three legs. After passing normal urine, he weighed 2104 gm. As I had to abandon the experiment on account of a long journey, I killed the animal by letting the blood drain out of the carotid artery and the jugular vein. When the blood stopped flowing, the remainder was collected by stroking the extremities and trunk and then after opening the abdomen and thorax and incising the heart. The washing out of the still remaining blood had to be omitted due to lack of time. Although not all the blood was obtained, this determination is not entirely worthless, since the amount of blood obtained was 153.2 gm., i.e. $^{1532}/_{19580}$ or $^{10}/_{127}$ of the body weight. This amount, however, as will be shown later in a subsequent paper, corresponds approximately to the normal amount of blood of a healthy young dog; but since not all the blood was obtained in this case, the amount of blood in it appears to be increased rather than diminished.

This experiment shows, on the one hand, the changes which the blood underwent from the 20th to the 23rd August, between the 2nd and 3rd series of transfusions, and, on the other hand, the changes in the blood after the 3rd series of transfusions from 23 August until death on the 28th.

	Weight of the dog. Gm.	A. Blood quantity without regard to its change by endosmosis since 18 and 20 August and during the experiment.	B. Blood quantity, assuming that it is normal at the beginning of the experiment. Height of 182 gm. reached again, but was not changed by endosmosis and exosmosis during the experiment.	Amount of blood withdrawn.	Amount of blood injected. Gm.	Amount of original blood assuming A. Gm.	Amount of original blood assuming B. Gm.	Specific weight of the whisked blood.	Specific weight of the serum.	Difference of the specific weights as an expression of the relative amount of blood cells	Amount of fibrin p.m.
21st August	2290 before 2470 after eating Later 2600										
22nd August	2480 after eating										
23rd August	2300 before 2520 after eating	140.75	182	-	-	2.09	3.68				
1st Portion	-	141.21	182.46	66.1	-	-	-	1043.8	1019.9	23.9	2.57
In return	-			-	66.56	-	-	(1040*)	(1023.6*)	(16.4*)	
2nd Portion	-	127.57	168.82	80.2	-	-	-	1043.2	1021.4	21.8	1.869
In return	-			-	66.56	-	-	(1040*)	(1023.6*)	(16.4*)	
3rd Portion	-	129.33	170.58	64.8	-	-	-	1040.9	1021.3	19.6	1.179
In return	-			-	66.40	-	-	(1037.5**)	(1023.4**)	(14.1**)	
4th Portion	-	139.09	180.34	56.6	-	-	-	1037.5	1021.1	16.4	0.17
In return	-			-	66.40	-	-	(1037.5)	(1023.4)	(14.1)	
End result	-	-	-	267.7	265.92	0.139 gm. or 0.076%	0.548 gm. or 0.3%				

On 24th August the dog weighed 2250 gm before eating and 2320 gm after eating
On 25th August the dog weighed 2200 gm before eating and 2290 gm after eating
On 26th August the dog weighed 2170 gm before eating and 2290 gm after eating
On 27th August the dog weighed 2060 gm before eating
(Ablation) the dog weighed 2050 gm before eating and 2150 gm after eating
The leg weighed 44.50 gm.
On 28th August the dog weighed 2104 gm.; after deducting the intestinal contents 1958 gm.; the leg with 44.5 gm gives 2002.5 gm. 153.2 gm of blood was obtained by flowing out and smearing without washing out. $^{153.2}/_{1958.0} = ^{10}/_{127}$ of body weight. The whisked blood had a spec. wt. of 1028.2; the spec. wt. of the serum was = 1020.8, so the difference was only 7.4. The amount of fibrin was 4.53 p.m. - 1000 parts of the whisked blood left 101.2 parts of solid residue; 1000 parts serum 67.5 parts of solid residue.

*) The whisked blood used in the first two transfusions had been withdrawn from the large, young, brown dog, which was already discussed in experiments 6 and 7 and which on 18 August had produced over 300 gm. of blood, the specific weight of which was 1045.9 after whisking.

**) The blood used in the last transfusions was later withdrawn from the same dog because he could no longer tolerate losing so much blood at once. The number of blood cells in the last blood withdrawal was noticeably lower than in the first, while the serum had pretty much maintained its specific weight.

With regard to the fibre content, the phenomenon which had already been perceived on the 20th was repeated on the 23rd, namely, that the amount of fibre which had been reduced to a minimum during transfusion had risen again to the normal level. On 20th August, the amount of fibre in the 4th portion of the drained blood had fallen to 0.34 pr. m., and the subsequent injection of whisked blood must have lowered it still further. Nevertheless, in the 1st portion of the blood drained on 23rd August there was 2.57 pr. m. fibrin, which was almost the same as the amount found in the 1st portion on the 20th (2.528 pr. m.) and with that which was present in the original blood, in the 1st portion drained on the 18th (2.4 pr. m.). After the fibre content in the 4th portion of the blood drained on the 23rd had been reduced to 0.47 p.m., and must have fallen still further by the quantity of whisked blood injected into it, it was found to be 4.53 pr. m. on the 28th. This time, therefore, the fibre content had risen above the norm, which is fully explained by the added inflammation in the extent of the necrotic parts of the bones, and then by the amputation wounds, since the blood tests of Andral-Gavarret and Becquerel-Rodier have shown the increase of the fibre of the blood in all inflammations of any extent. - This experiment, therefore, has once again shown that the fibre of the blood is a substance, the absence of which entails no more perceptible disturbance than an increase of it seems to do, and which, in any case, is so rapidly reproduced that the use of whisked blood in transfusion would appear harmless, even if one were inclined to attribute to it a greater significance than it appears to us to have according to our experiments and from some other observations.

However, the amount of blood cells had decreased somewhat from the 20th to the 23rd August, but the decrease was so small that the blood in the 1st portion on 23rd August was still richer in this component than it had been in the 1st portion of blood on the 20th and in the 1st blood portion on the 18th, i.e. in the original blood. The difference between the specific weight of the whisked blood and the serum, which serves us here as a relative expression of the abundance of blood cells, was 21.8 on the 18th in the 1st portion and 19.4 on the 20th in the 1st portion. Through the use of a very rich blood, it rose during the experiment on the 20th to such an extent that it was 26.2 in the fourth portion of the blood drained on that day, and by the subsequent 4th transfusion of the same blood, which was so rich in blood cells, the whisked amount will probably have risen a little higher at the end of the experiment. So, while in the 4th portion of the blood drained on the 20th, the specific weight was found to be 1046.4 for the whisked blood, and 1020.2 for the serum, i.e. a difference of 26.2; the blood of the 1st portion, which was drained on the 23rd showed a specific weight of 1043.8 for the whisked blood and 1019.9 for the serum, i.e. a difference of 23.9. The serum had therefore been diluted only slightly by water absorption, which corresponds to the assumption that the amount of blood, which had been reduced to 169.92 gm. by the test on the 20th, would have risen again to the norm (182) by water absorption, which means that only about 12 gm. of water would have been absorbed. The not very significant loss of blood cells from 26.2 to 23.9, i.e., by 8-9 percent, is probably explained by the fact that blood so rich in blood cells did not correspond to the individuality of the animal, since originally, on the 18th, the blood cell content was still around 8-9 percent lower than on the 23rd, i.e. about 17 percent less than in the 4th portion of the blood drained on the 20th. For, I have made several observations in the case of the black and brown dogs, which served as blood donors in these experiments, and which were formerly used for various transfusion experiments, that the original specific weight of the blood, which is peculiar to the animals, and the original content of blood cells, tend to be more or less restored after a certain, usually longer, time period. How the blood cells, which are too abundant, perish, and what becomes of them, is still unknown to me; however, the fact that they are not simply dissolved and pass through the urine un-decomposed, is evident from the fact that the urine does not contain protein or blood. In the present case, too, the condition of the urine remained normal from 20th to 23rd August. - However, the fact that the foreign blood cells as such do not perish and are excreted within a short period of time was already evident from the fact that the number of blood cells remained unchanged from 18th to 20th August, although more than 90 percent of the blood circulating in the animal at this period was foreign and belonged to other dogs. This, however, is made still more evident by the present experiment, in that on 20th August only 2-3$^1/_2$ grams of the original blood remained, while in 166$^1/_2$-168 grams of foreign blood circulated in it. Now, as the ratio of the original blood cells to the foreign or transplanted blood cells was most likely even weaker, because the transfused blood was considerably richer in blood cells than the original, the circumstance proves that the blood cell richness of the blood from the 20th to the 23rd increased by only 8-9 percent, at least the vast majority of the transplanted foreign blood cells were still circulating in the animal and functioning normally.

On the other hand, however, the blood cell content decreased greatly from the 23rd until death on 28th August; but this is entirely explained, on the one hand, by the fact that the blood used for the transfusion on 23rd August was so poor in blood cells, and on the other hand, by the extensive periostitis that had developed, and by the amputation of the thigh which had thus become necessary. For if 23.9 was the relative expression for the blood cell content of our dog's blood in the 1st portion of blood drained on 23rd August, the corresponding expression for the blood cell content of the transfused foreign blood (from the large red dog) was only 14.1; so the ratio was like 100:59. As a result, the blood cell content of our little dog's blood decreased during the experiment to such an extent that the difference between the specific weights of the whisked blood and the serum in the 4th portion of the drained blood was only 16.4. This was already a decrease of 31.4 percent. A further sinking had to result from the fact that the 4th portion of the thin whisked blood was injected. Since, however, at the time of death on the 28th the difference had been reduced to 7.4, there must have been another cause by which the blood cell content had significantly reduced. As to the cause, however, we immediately encounter the severe inflammation in the whole circumference of the large necrotic parts of the bones, amputation and the suppuration that follows it; because it has long been known, through the investigations of Andral-Gavarret and her successors, that the amount of blood cells is greatly reduced by inflammation and suppuration. How this happens, and what becomes of the red blood cells in the process, is as unknown in such simple cases as in our more complicated case. The increased excretion of urea, the decrease in body weight, the reduction in food intake and the formation of pus are likely to be important factors in this respect, but it is not possible at present to give a more specific relationship. This much is certain, however, that neither the decrease in the blood cell content in our case from 23rd to 28th August, nor in the decrease in other cases of simple inflammation and suppuration, did the decomposition of the blood cells take place in such a way that they were in a simply dissolved state, as proteins, excreted through the urine. Furthermore, it is also clear that the significant decrease in the blood cell content observed from 23rd to 28th August is sufficiently explained by the circumstances cited, and that there is absolutely no reason to believe that their status as "foreign" or transplanted blood cells facilitated or accelerated their destruction. On the contrary, it is also proved by the symptoms of the animal's vital signs from 23rd to 28th August, and by the findings at death, that the foreign, transplanted blood cells must have remained permanent and functioned like the blood cells originally belonging to the animal, since the animal had only about $^1/_2$ gm., or 3 pr. m. of its original blood remained after the end of the operation on the 23rd. Another question is how the bone necrosis and the extent of the inflammation in the necrotised parts were related to the transfusion? As neither this nor any analogous phenomenon had been observed in the preceding cases, one will certainly be inclined like me to regard it as purely accidental, brought about by incidental circumstances. This is also very decidedly supported by the fact that the affection developed on the leg, whose vein and crural artery was last used in transfusion. It is possible that too much pressure in holding the limb during the experiment on the 23rd may have caused the local disease; it is also possible that the initial entrapment of the nerve in the ligature had a part in this. It is most likely however, that the necrosis was of embolic origin, and that the inflammation of the surrounding parts occurred secondarily. By amending the crural artery it is easy to understand that, from the site of the ligature, there was the formation of grafts, which, by pressure or movement, were removed from the place of their formation, and which were discharged with the bloodstream into the artery nutritia. However, the fact that the artery nutritia of the bones can cause their necrosis is evident from earlier experiments directed directly at this point, including those by Hartmann.

PART TWO

III.

In the older experiments on transfusion, which were eagerly pursued, especially in the 17th century, the question of the influence of the use of the blood of the same or any other species of animal was not made the subject of experimental investigations. Sometimes the blood of the same species of animal, sometimes of different species, and other, was used for the experiments, without any difference in effect being noticed by the observers. In the communications of Denis and his companions, it is certainly not at all strange to read that in the presence of a duke and other distinguished persons he gave an old horse new strength and an excellent appetite by transfusing ram's blood, in short, rejuvenated it, etc. On the other hand, it is very striking and remarkable that the experiments made by Lower, Thomas Coxe, King, and Hook, with the assistance of Robert Boyle, some of which have been excellently observed before the Faculty of Philosophy in London, got over this important point with such astonishing ease. Their experiments were carried out without distinction with the blood of animals of the same or of any other species, and it is only striking that the reports of those cases in which the blood of distant animals were used are, for the most part, very incomplete. It is reported, for example, that a bull biter dog was infused with the blood of a sheep and that it was quite well afterwards[41]. It is further said that a sheepdog was given sheep's blood in the same way, but that the coagulation of the blood made this experiment not as easy as the previous ones[42]. There is no further information about the final fate of these two dogs. Also there is no further information about the result of an experiment in which King drew 15 ounces of blood from a Spanish dog, and then gave it at least 17 ounces of blood from the crural artery of a sheep[43]. However, the fact that they did not want to intentionally conceal unfavourable results, seems to be evident from the more detailed accounts of the fate of a fox that was transfused with lamb's blood, of a sheep with dog's blood, and of another sheep with calf's blood. Since these reports are interesting in several respects, I think I may reproduce them here according to Scheel.

"King[44] drained blood from the vein of a very small and lean fox, which had been prepared for transfusion, but only 5 ounces because of its leanness. He then poured the blood of a lamb into him until he became very short of breath, whereupon King, fearing that he should suffocate, stopped the flow of blood from the lamb. As he remained just as short of breath, King allowed 4 ounces more blood to drain from him, which was now much brighter red than before it had been mixed with the sheep's blood. The fox, however, seemed even weaker after this loss of blood than before; blood of the lamb was therefore poured into him again until it was believed that he was incapable of receiving more without danger. Nevertheless, he continued to be very ill, was more shy than before, and left his usual food and drink, but he barked and snapped with great fury at a stick held in front of him. After 24 hours, a tremor came over him, he weakened, and died. After his death, some blood flowed from his nose. His chest and abdomen were found half full of bloody water, or rather blood; all the vessels were very dilated and the intestines seemed to be inflamed."

"King[45] drew blood from a sheep until it became weak, and then passed the blood of a dog into it until it had, according to his reckoning, received as much blood and more than had been drained from it, and until it appeared to be extremely sick. Then he set her on her feet, but she would not stand, but lay down, and was in such agony that it was feared that she would die. As it was inferred from the violent sobbing (clapping of the diaphragm) that she had received too much blood from the dog, ten or twelve ounces were allowed to flow from her, whereupon the sobs subsided, and the breathing became much freer; but the animal was still ill for 2-3 hours. The next morning she was tolerably well and ate hay. When it was sent out to pasture, it ate and seemed to be well for 6-7 days, but it did not keep to the rest of the herd; 3 or 4 days later it died. The wound on the neck, because it had been neglected, was found very badly damaged by the heat of the weather and by the injuries of the flies. The transfused blood had at first been taken from the jugular vein of the dog, but when it would no longer flow from it, it had been necessary to remove the blood from the carotid artery. The autopsy findings are missing except for the information regarding the neck wound."

"King had extracted 49 ounces of blood from the jugular vein of a sheep[46] and injected it with a supposedly corresponding quantity of calf's blood from the jugular vein of a calf. After this the sheep had the same strength as before, and walked around when it was placed on the ground. Immediately afterwards it was slaughtered and died after 65 ounces had flowed out. This experiment was repeated in accordance with the wishes of the Society[47] in such a way that an attempt was made to keep the animal alive afterwards. A smaller sheep had more than 45 ounces of blood drawn from it, which left it in a state of extreme weakness and seemed to be lost without rescue. King then passed the blood from the vein of a large calf into the sheep for seven minutes, so that, according to his calculations, it received more blood than it had lost. When it was untied after the experiment, it was so courageous that it immediately attacked a dog that happened to be there, that Dr. King had infused with sheep's blood. Then it was sent to the pasture on the grass; it was perfectly well for 3 weeks, but then it fell ill, became wasted, and died."

The above-mentioned researchers, whose complete love of truth cannot be doubted, had convinced themselves in their numerous experiments of the dangers arising from the coagulation of the blood, from injecting too quickly, and from the transfusion of too large a quantity of blood, and they therefore wrote about the unfortunate cases which they perceived when using different kinds of blood which they attributed to these circumstances, but not to the strangeness of the blood. This idea was so far removed from them, as well as from all other experimenters of the time, that they had no hesitation in giving decisive preference to lamb's blood, mutton's blood, or calf's blood over human blood in the transfusion of humans. In fact, several of these cases are so interesting and curious that they may be placed here in brief excerpts.

A foolish, by the way, physically healthy baccalaureate of theology, Arthur Coga, had 6-7 ounces of blood taken from him by Lower and King[48] for one guinea (!) and in return about 10-11 ounces of blood were infused from the carotid of a lamb. When he was asked why he preferred to have the blood of a lamb poured into him, he replied in Latin with comic seriousness: Quia sanguis agni habet symbolicam quandam facultatem cum sanguine Christi. Christus enim est ovis Dei. He then smoked tobacco and drank wine. As a result, he sweated for a couple of hours, had 3 to 4 bowel movements during the day, but was so comfortable that he offered to have the operation done on him again, which happened about 3 weeks later. In this second attempt, 8 ounces of blood were removed from him and 14 ounces of lamb's blood were transfused in return. Afterwards he suffered from a temporary feverish state, which, however, was attributed to the wine he had enjoyed. By the way, he was still physically well, but remained as foolish as before. For the third time, however, he had no desire to have the operation performed on him, and he used to call himself the martyr of the philosophical faculty.

Even in the transfusion experiments carried out in France and Italy during this period, no one thought to pursue the question whether the blood of the same or any other animal species would be better tolerated in transfusion, and the blood of ruminants was always used for transfusion in humans. In Italy, for example, the transfusion was carried out 3 times by Riva and once by Manfred, by allowing the blood from the carotid of a sheep or a ram to flow into the arm vein of sick people. There was hardly any talk of diagnosis and indication, and the only thing that appears to be certain with regard to success is that the patients in question neither died nor had any noticeable damage from the operation. Nevertheless, it was formally forbidden by Rome in 1668, but apparently for spiritual, not medical reasons. Among the experiments carried out on animals in Italy about this time, some by Ippolito Magnani[49] deserve to be mentioned here, because a symptom was noted in them, which subsequently appears to be important. A dog into which he had transfused mutton's blood emptied bloody urine and died. After death, the veins were found to be very full with blood and the urinary bladder full of blood. Magnani therefore suspected that too much blood was transfused and warned strongly against this. - A second (scabies and dull-witted) dog, which walked about immediately after the operation, seemed much more lively than before, and shook himself several times, urinated blood, and died by bleeding to death, as it was thought, because he had unexpectedly torn his vein with his paws. How much blood was extracted from and re-injected into these two dogs is not specified. A third dog, whose blood had previously been transfused into another, was given so much blood from a sheep that he regained his strength after the operation, but behaved strangely by running around in circles and lying down in a corner of the room. During the night and the whole of the following day he emptied a great deal of bloody urine; he trotted round and round in circles with rapid steps, and then a sound was heard in his intestines, as when water is shaken in a vessel. He died the next morning. The abdomen was then found to be filled with a dark red serous liquid; a similar but darker, somewhat greenish matter was found in the stomach; the intestines and kidneys also contained a blood-like serous fluid. In the heart, bladder, and left half of the cranium was a similar bloody, but thicker fluid. In this case too, Magnani explained the phenomena as being due to the excessive amount of blood injected. Lastly, an experiment is cited in which mutton's blood was infused in the usual way into an old, very meagre greyhound, without any of the above accidents occurring; on the contrary, it is said, it received new strength, and was constantly well. Magnani attributed this to the fact that they had been wary of overflowing with blood. However, it is not specified how much blood was introduced. The numerous experiments on animals communicated by Denis, Carassini, Harwood and others, are as worthless as those of King in this matter. Attempts were made by the Society of Paris, not so much for the purpose of scientific research as for the apparent support of preconceived or alleged opinions, and dictated by personal ambition, avarice, and animosity. Under such circumstances, therefore, it is not surprising that not only are no harmful consequences reported by these experimenters from the transfer of the blood of ruminants into dogs, or vice versa, but even cures of the most miraculous kind were invented. Only in 2 out of more than 50 experiments which Denis carried out on animals, mostly dogs, and in which mostly calf or lamb blood was transfused, is blood urination mentioned, but as a symptom which could be prevented with certainty by proper preparation[50]. With regard to this symptom, on the other hand, the attempts of an unnamed person cited by Gurye deserve to be noted, stating that "the dogs always pissed blood after a more abundant transfusion[51]." However, it is not noted whether blood of the same or a foreign species was transfused. More remarkable than his experiments on animals are the transfusion experiments carried out by Denis on humans, always with lamb or calf blood, because these could not be removed from the control of his jealous colleagues. This, of course, is less true of his first two attempts. The first was carried out on a person he had taken into his service, who was sleep-addicted as a result of severe anaemia, and the second on a man who had been hired for money, and who, by the way, was healthy. In both cases blood was extracted directly from the carotid artery of a lamb into a vein in the arm. In the former case, 3 ounces of blood were withdrawn from the person concerned, and about 9 ounces of lamb's blood were given in return; in the latter case, 10 ounces of blood were withdrawn from the man, and the same amount was instilled. Both subjects are said to have been very well immediately after the operation and do not seem to have suffered any damage from it afterwards. However, the servant lost a few drops of blood from his nose a few hours after the operation. Both seem to have been a little restless after the operation, but this was interpreted as an improvement, especially in the case of the sleep-addicted servant. Denis undertook his third transfusion on a distinguished stranger, a Baron Bond from Sweden. The prognosis was very unfavourable and Denis only reluctantly decided to have the operation at the urging of other doctors and the relatives of the patient, who had given up. The transfusion, which was performed with about 6 ounces of calf's blood, seemed to temporarily improve the patient's condition. When he deteriorated again, the transfusion was repeated the following day, but 12 hours later the sick man died. Regarding the diagnosis, it is said that the patient suffered from "fluxus hepaticus and lientericus with bilious diarrhoea and violent fever". After the transfusion, there is also repeated talk of emptying the intestinal tract. When the body was opened, an intussusception of the ileum was found, along with hardening and enlargement of the pancreas, spleen and liver. - Far more important than these 3 cases seems to us to be the 4th. It concerned a valet Mauroy, who had been insane several times, and who, in the last attack, had been wandering about in the open air for a few months, and had endured much hunger and cold. Supposedly to cure him, 10 ounces of blood were taken from him and 5-6 ounces of blood of the crural artery of a calf into a vein in the arm. The operation was interrupted because the patient cried out that he was fainting. Afterwards he ate and drank, but he was as mad as before. However, since Denis found him a little less crazy than usual, the operation was repeated the following day, this time taking only 2 or 3 ounces of blood from him, and injecting at least 1 lb. of calf's blood. At this his pulse rose; then a heavy sweat broke out on his face, the pulse became irregular, and the patient complained of pain in the kidney region, as well as a severe shortness of breath. During bandaging, vomiting, the urge to urinate and defecation occurred. He vomited for two hours and then fell asleep. When he awoke, he complained of pain and fatigue in all his limbs, and emptied a large amount of urine, which was as black as if soot had been mixed with it. By the way, he had become calm and sensible (!?). He slept a lot the following day and night. The next day he again emptied a large quantity of urine, which was almost as black as the previous one. He was also bleeding profusely from his nose. A little bloodletting was done to him. The urine now gradually took on a brighter appearance, his condition improved, and he had become as sensible again as he had been in the free periods. The patient did not live cautiously for the next 2 months. His wife, who was tired of him, tried several times to poison him with arsenic, and finally, by much pleading and urging, induced Denis to perform the transfusion for the third time. However, during the preparations for the operation, M. died, most likely from the poison given to him by his wife, before the artery of the calf he had brought with him had been opened[52]. According to Lamy's report, on the other hand, M. is said to have died during the transfusion and his statements about the success of the operation differ significantly from those of Denis. As a result of this death, Denis was involved in a lawsuit. As he had meanwhile become a doctor of the Faculty and personal physician to the King, he later did not continue with the transfusion, and this operation lost all its credit in France, although, according to Scheel's investigations, a proper prohibition against it does not seem to have been enacted there.

The idea that it is important for the failure of the operation to take into account the relationship of the animals whose blood is being experimented on seems to have first appeared through the experiments which Rova carried out with Scarpa in 1783-1785, and which bear the character of scientific and credible investigations. What is remarkable here is that the blood of calves proved perfectly useful to lambs, and that neither blood urine nor other serious symptoms occurred in these animals, although large quantities of blood were withdrawn and transfused (20 to 28 ounces in lambs weighing 40 to 50 pounds, and 61 ounces to 3 pounds in muttons). The growth of the lambs was not affected and they became exceedingly fat and strong. Incidentally, these researchers also strongly emphasize the dangers of transfusion of a greater amount of blood than that which was previously withdrawn from the animals. - This result agrees well with a recent experiment by Milne Edwards, who revived a donkey killed by bleeding by transfusion of horse's blood.

But it was not until Prevost and Dumas, in accordance with their experiments, that the assertion was made with full force that the blood of a vertebrate animal might be truly poisonous to a vertebrate animal of a different order and family, and that favourable results could only be expected from the use of the blood of the same species. The blood of birds was particularly dangerous in the circulation of mammals.

This result was confirmed by Rayer, Leecock, and others, but was made doubtful again by the later investigations of Bischoff and Brown-Sequard. Bischoff, of course, first came to the conclusion that the foreign fibrous material was the carrier of the poison, since the whisked blood did not produce the same harmful effects[53]. But when he later became convinced that arterial blood, in a direct transfusion, although it contained the fibrous material, was no more harmful than whisked blood, while venous blood produced the phenomena and death observed by Prevost-Dumas, Dieffenbach and himself, he abandoned this idea and ascribed the poisonous effect to the venous nature of the foreign blood. He raised the question of whether it was perhaps the "animal dross" of the venous blood that was so deadly?[54]

However, Brown-Sequard[55] has dealt most intensively with experiments belonging to this category. He came to the conclusion, as already remarked above, that it was the richness of the carbonic acid of the venous blood which caused its poisonous effects. He found that dogs, cats, rabbits, guinea pigs and birds are also killed by injecting their own blood when it is heavily impregnated with carbonic acid. The fatal effect occurred when the quantity of carbonic acid saturated blood was more than $^{1}/_{300}$ of the body weight, whether it came from the same animal, from another animal of the same species, or from an animal of a different species. The convulsions in asphyxia, which also occurred in the hind body even after the spinal cord had been cut, were derived by Brown-Sequard from the carbonic acid content of the blood. He also explained those convulsions which he produced in certain parts of the body by injecting carbonated blood into the arteries concerned. When, for example, he opened the abdomen of a living animal and injected black blood into the aorta, above the outlet of the renal vein, convulsions of the hind body occurred, which disappeared again by injection of red, arterial, or whisked blood shaken with air. The richer the blood was in carbonic acid, the more severe the convulsions became, and the richer it was in oxygen, the faster they stopped. Further, if he injected venous blood into the aorta of a pregnant bitch or rabbit shortly before giving birth, after all connections with the nervous system had been severed, the uterus contracted, and often one or more fetuses were expelled. The uterine contractions stopped instantly when he injected arterial blood. The muscles of animal life behaved in the same way when they were paralyzed by the cutting of their motor nerves, but their contractions were less vigorous. Brown-Sequard adds that all contractions produced by black (high-carbonated) blood are intermittent, often with regular intervals. The faster the carbonic acid-rich blood was injected, the more violent and deadly was the effect, and with very slow injection, in which the carbonic acid could be removed through the lungs, the injection sometimes succeeded without death. Animals killed in this way could sometimes be revived by artificial respiration. From this he concludes that the black, carbonated, or venous blood gives a very strong stimulus to the nerve centres, and a weaker stimulus to the nerves and contractile structures, and that it is incapable of preserving the vital qualities, and still more incapable of recalling them. For the reasons already mentioned on a previous occasion, I cannot agree with the conclusions drawn by Brown-Sequard from his experiments on the irritating properties of carbonic acid. On the other hand, it is certainly true that the black, carbonated or venous blood is incapable of maintaining and recalling the vital qualities.

Moreover, Brown-Sequard came to the conclusion that the blood of a vertebrate animal, as long as it was not impregnated with carbonic acid, was not poisonous to another vertebrate animal, and that it was even perfectly capable of re-evoking the vital forces extinguished by haemorrhage, and that the more it was saturated with oxygen, the more suitable it was. According to Brown-Sequard, the blood of any vertebrate animal, made bright red by shaking it with atmospheric air, can be safely injected into the veins of any vertebrate, provided that not too much is injected. Whisked blood from rabbits, guinea-pigs, roosters, pigeons, ducks, turtles, frogs, and eels was injected into dogs through the jugular vein, without any disturbance other than a momentary effect on respiration and circulation, which also occurs when the blood of the same animal species is used, probably by the expansion of the right atrium. 20-40 grams of foreign blood were injected into dogs without prior blood withdrawal without significant harm to their health. If, however, as much blood was taken before the transfusion as was injected again, 100, even 150 grams of bird blood could be injected into the dogs without harm. In the same way, Brown-Sequard was able to transfuse chicken and pigeon blood into rabbits with impunity, and chickens, roosters, and pigeons tolerated it very well when an equal quantity of dog, guinea pig, or rabbit blood was injected into them after extracting 10 to 20 grams of blood. Only when whisked blood was injected too quickly or too much that severe and even fatal disturbances of circulation and respiration occurred, especially in birds; but the same phenomena appeared when their own blood or someone else's blood was injected. Using the microscope, he claims to have found the blood cells of dogs and rabbits in birds for a month after the injection; on the other hand, he could not find the blood cells of the birds, after they had been brought into the circulation of the mammals, after 1 hour had elapsed, whereas they were everywhere $^1/_4$ hour after the injection. He concluded that the blood cells of birds dissolve rapidly in the mammalian circulation. I do not think this conclusion is justified, since the gradual disappearance in the course of an hour could depend on the fact that the larger oval blood cells of the birds can pass through some capillaries but get stuck in others. A certain amount of time must elapse before all the blood cells of the bird's blood get stuck in the narrow capillary networks. Especially from the lack of conspicuous phenomena caused by the embolism, he seems to have concluded, like Magéndie before him that they could not have been stuck in the capillaries, but must have been dissolved. This argument, however, is by no means valid in comparison with the experiences given in Virchow's and my studies on embolism, since such small plugs, if they do not clog entire vascular areas very often do not produce any noticeable disturbances. Moreover, the dissolution of the blood cells of birds in the circulation of mammals would be remarkable, if it be true that the blood-cells of mammals preserve themselves so well in the circulation of birds, as Brown-Sequard states, and as Marfels and Moleschot[56] also confirm. However, in my experience the recognition of the blood cells of one animal in the circulation of another is by no means as easy and certain as one might theoretically expect. The oval blood cells of birds and frogs are, of course, easily recognizable in comparison with the round ones of mammals, but even the blood cells of dogs on the one hand, and of sheep or calves on the other, although considerably different in their mean sizes, cannot always be recognized with any degree of certainty, since smaller blood cells occur in the dog's blood, which are surpassed in size by the largest specimens of the blood cells of those ruminants.

Be that as it may, it would be of theoretical as well as practical interest if the blood cells of one animal species could function and continue to exist in another, provided that their size did not present an obstacle. People in many places, and not without good reason, are now so little inclined to give their blood for the good of others, that it would be quite pleasant if animal blood could be safely used for transfusions, and according to Brown-Sequard's account there seems to be no further objection to this use, provided that it is properly impregnated with oxygen by agitation. Finally, if one were to think of substituting a large part of the blood of an individual by other blood, as it is possible, according to the above experiments, to displace and substitute the blood of one dog by the whisked blood of another dog, it would in most cases be quite impossible to procure the necessary quantity of human blood. However, there are two serious objections to such a conclusion, which can be used in practice. On the one hand, Brown-Sequard, assuming the full reliability of his statements, has so strongly emphasized the necessity of impregnating the blood with oxygen, and the harmfulness of impregnating it with carbonic acid, that his further assertion that the blood of one vertebrate animal is by no means poisonous to another, but only acquires the same poisonous properties through lack of oxygen and an abundance of carbonic acid, assumes the same poisonous properties that would also be perceptible in the blood of the same species under the same conditions, is perhaps not to be understood so strictly, but is only intended to strengthen those statements to a certain extent. On the other hand, the older reports, according to which arterial blood of an animal, when brought into the circulation of an animal of another species, had a harmful effect, and was found unsuitable for resuscitation by transfusion, the animals recovering at first, but dying soon afterwards of violent illness, are by no means invalidated by this. Even a case reported by Brown-Sequard seems very suspicious, in that a sick horse, which had been injected with 120 grams of bird blood, died after 5 days with an accelerated pulse and respiration. However, the horse's pre-existing illness could be to blame for this, and it is possible that the overcrowding of the vascular system in other cases, where the foreign blood had had a harmful effect, without the carbonic acid content or the lack of oxygen of the same being blamed, could have caused the unfortunate outcome. Nevertheless, it seems to me that further experiments are necessary in order to decide the questions whether the foreign blood had a harmful effect independently of its content of carbonic acid and oxygen, and whether the blood of one species of animal could be used with lasting success for the revival of animals of another species which had been brought close to death by the loss of blood, can use it or not?

The following experiments, which I have made on these questions, give an unfavourable result to the opinion advanced by Brown-Sequard, at least for the utilization of the blood of calves and lambs in the circulation of dogs:

1. A healthy dog weighing 7800 grams was deprived of 100 cc. of blood from the jugular vein and 64 cc. of newly emptied, still warm, defibrinated calf's blood was injected into it. The injection was carried out slowly and there were no notable symptoms. After that, however, a great dejection and loss of appetite of the otherwise lively and voracious animal was noticeable. In addition, there was a very persistent and difficult to stop bleeding from the small skin vessels of the neck wound, which usually never bleed after such an operation, even in animals that were almost entirely defibrinated. He also emptied strongly blood coloured urine, which also contained preserved blood cells, along with a lot of protein, and had a strong alkaline reaction. This condition of the urine remained unchanged on the following day, except that blood cells were no longer to be found in it with certainty. Over the course of 4 days after the injection of the whisked calf's blood, the urine gradually became lighter with less protein content until it had returned to its normal condition at the end of the 4th day. In the process, the bloody colouration disappeared earlier than the protein content. In the same proportion as the urine returned to normal, the appetite and former cheerfulness returned. On the 5th day he seemed to have recovered, except for a rather considerable emaciation; during the experiment he had lost 750 grams of weight.

2. The same dog has now been fed abundantly for 2 months and its 24-hour amount of urea has been determined from time to time. In order to completely collect the 24-hour amount of urine, he was placed in the observation box, which, lined with zinc sheet and by means of an elastic catheter, immediately allowed the urine, which had been emptied in the meantime, to flow immediately into a bottle placed underneath. At the end of the 24-hour period, the urine still in the bladder was emptied through the catheter and combined with the amount that had flowed into the bottle. So, the dog, with a mixed diet in any quantity, secreted an average of 42.5 gm. of urea in 300-400 cc. urine in 24 hours. In the 24 hours following such an abundant feeding period, during which he received no food, he secreted 13-14 gm. of urea, and in the following 24 hours of starvation of the animal, which can be regarded as devoid of intestines, an average of 7.5 gm. of urea. On 26th May 1861 after 48 hours of starvation, he weighed 6990 gm, on 27th May after eating, 7650 gm. On 28th May, 400 cc of blood was taken from his carotid artery until all signs of life had disappeared. The surface of the cornea and the conjunctiva became insensitive before the respiratory movements had stopped. Then, 320 cc. of freshly drained, still warm, whisked lamb's blood, was gradually injected into his jugular vein. With the 2nd syringe, each of which held 32 cc, spasmodic diaphragmatic twitches occurred. With the 3rd injection, the respiratory movements became regular. At the 4th the eyes became sensitive, and gradually the sensation as well as the voluntary movement returned, and the sensitivity itself seemed to have become greater than normal. After the injection was finished, the dog barked in a very strong voice, but without any external cause. He looked wild and moved his head and neck with great force, while his extremities were so weak that he could not stand on his feet. Soon after, extraordinarily heavy bleeding occurred from very small vessels of the cut, and it was only after more than an hour that the bleeding could be stopped by button sutures and tamponade. Furthermore, the cerebrospinal aqueous fluid of both eyes was heavily bloodied, which gave the eyes a very peculiar appearance. The temperature, which had dropped significantly after the bleeding and initially after the injection, had risen very noticeably, so that the groin area felt very warm. The pulse was very strong, quite accelerated and the respiration seemed to be normal. Two hours after the operation he was still barking incessantly, with a peculiar but very strong and as it were, courageous tone, and looked very wild. Then his strength sank more and more, the pulse became weak, and at 8.30 am, $3^1/_2$ hours after the operation, he died. - The dissection revealed the following: In one lung there was a small area infiltrated with blackish blood. In the stomach there were strong sugillations of the muscular membrane and 3-4 ounces of mucus of acidic reaction and of a very dark, blackish, chocolate-like colour. Bloody mucus was also found in the intestine with injection and imbibition of the mucous membrane. Many small petechiae-like ecchymoses were seen in the liver. The gallbladder was full of dark bile. The pancreas was pale. The kidneys had taken on an almost completely black appearance due to enormous injection. The urinary bladder was contracted; the mucous membrane

was lifted off to a large extent by bruising in the sub-mucosal connective tissue. The appearance of the spleen was normal. The brain was bloody and soft everywhere. The gray mass was, especially in places, very much reddened and softened, and showed many small extravasations. The cerebrospinal fluid was bloody. The greater part of the blood at the dissection was quite thin, dark, and hardly reddened in the air, but subsequently coagulated. Only individual blood cells of such size could be found that they could be unequivocally recognized as belonging to the dog's blood. The muscles were unusually dark in colour. Fat was quite abundant in the subcutaneous connective tissue and omentum. - There were no blood cells in the bloody stomach contents. A few could be found in the urine, but in the main the dark colouring of it was due to dissolved blood-redness; it contained a lot of protein, but only trace amounts of urea. - The cerebrospinal aqueous fluid of the eye was strongly bloody in colour, but there were no blood cells to be found in it.

3. A fat dog weighing 15130 gm. had been subjected to 200 cc of blood 10 days before, and which had been fed only bread and water, was then subjected to inanition for several days in order to determine the extent of his urea secretion during complete inanition. After starving for 24 hours, he yielded 7.227 gm. of urea in the following 24 hours; in the following 7.42 gm. and in the following 24 hours 7.3535 gm. His perspiration loss amounted to 225 gm., 195 gm. and 175 gm. respectively. On 21st May he weighed 13710 gm. At 5.00 pm in the afternoon, after emptying the urinary bladder by means of the catheter, 200 cc of blood was withdrawn from him and 160 cc. of defibrinated calf's blood, which had just been emptied, still warm, was injected into the jugular vein. During the injection, there were no symptoms at all. Later, secondary bleeding occurred from the small skin vessels of the wound. In consequence of this, the observation box in which the animal had been confined was stained with blood on the inside the following day. The jar placed under the box for the collection of the urine contained about 30 cc. of a rather thick, bloody liquid, which, however, did not contain clots or coagulate in the air. The chemical examination revealed a lot of protein and blood-red, but no urea. The animal was very weak the day after the operation, and could only stand on its feet with difficulty. The pupil was dilated, the pulse slightly accelerated, the respiration natural. The bladder contained only about 10 cc. of a very bloody fluid, in which no urea could be detected. The temperature in the rectum was 36°C. The lips, skin and extremities were cold to the touch. The old wound on the neck was completely bluish in colour. In the evening he was still alive, but he lay quite still and was very weak. He died during the night, about 30 hours after the injection of the calf's blood. Neither the glass nor the bladder contained any liquid. Thus, in the last 30 hours of the animal's life, no urea had been secreted.

On dissection the lungs were normal, except for a somewhat darker colouration of the left lung, which was explained by the position of the animal on the left side. There was a lot of liquid blood in the vessels, especially in the left ventricle. The stomach contained 100 cc. of an acidic, yellowish liquid mixed with brown flakes. The gastric mucosa was infiltrated red at the folds, otherwise pale. In the small intestine, which was otherwise pale, there were some pale red streaks and spots, and very dark sugillations were visible on the folds of the transition point from the small intestine to the large intestine, as well as on the longitudinal folds of the large intestine. The colon was empty, as was the strongly contracted urinary bladder. The kidneys were very hyperemic. The spleen appeared normal, the pancreas pale. The liver was spotted yellow in places. The gallbladder was filled with dark bile. There was still a lot of fat in the subcutaneous connective tissue and in the ometum. The muscles were remarkably dark.

From the above experiments it is evident that the blood of ruminants (sheep and calf) can, by transfusion into the veins of a dog, recall the life extinguished by haemorrhage, revive the nervous and muscular activity, as well as the respiration and heat production - but only for a short time. The injected foreign blood does not excite any particular symptoms when injected, but is expelled again, partly by haemorrhage, partly by dissolution of the blood cells. The decomposition products, which do not include urea, produce serious disorders, which can be survived with the use of small quantities of foreign blood and with a sufficient amount of one's own, but which soon lead to death with larger amounts of someone else's blood and with greater deficiency of one's own blood, sometimes with appearances of silent death, sometimes with those of brain irritation. Replacement of about $^1/_6$ - $^1/_7$ of the blood mass caused death after about 30 hours, the substitution of about $^3/_5$ of the blood mass led to death in just $3^1/_2$ hours, $^1/_9$ - $^1/_{16}$ of the blood mass caused serious illness without causing a fatal outcome. Neither the abundance of carbonic acid and the lack of oxygen (the venous nature of the blood), nor the overcrowding of the vascular system, nor the fibre content, nor any other abnormal condition of the blood, other than it came from another species of animal, could be considered in these experiments as the cause of the morbid symptoms and the fatal outcome.

The results obtained by the above investigation can be divided into two classes, namely, those which are important for physiology and those which are of practical interest.

From a physiological point of view, the most important results of this series of studies are likely to be the following:

1. The removal of fibrous material or the defibrination of the blood does not, in and of itself, result in any noticeable disturbances, even if the original fibrous blood is substituted by the whisked blood of another individual of the same species. In particular, defibrination in and of itself does not cause the blood stagnation and exudation reported by Magendie, which led this researcher to conclude that the fibrous material promotes the passage of blood through the capillaries. There must therefore have been special circumstances in Magendie's experiments that led to this erroneous result.

2. The removal of a large part of the fibrous material normally present in the blood has no appreciable effect on the amount of urea excretion. So the hypothesis that the fibrous material of the blood provides the material for the urea is unfounded.

3. The fibrous material is soon completely reproduced, and at least 48 hours after the greatest quantity of this substance has been removed from the blood, the normal amount of it is present again; however, in the case of accidental inflammation, a quantity is formed at the same time that far exceeds the normal measure. This reproduction of the fibrous material is not impaired by the substitution of the greater part of the original blood of the animal by whisked blood of another individual of the same species.

4. Since the blood, deprived of its fibrous material is not only capable of completely and permanently restoring and preserving the vital properties of the nervous system which have been lost through loss of blood, but it is able to completely replace the original fibrous blood (with regard to the nourishment of the tissues, even of growth in young animals, as well as with regard to digestion, respiration, heat formation, and secretions), therefore the fibrous material cannot play an essential role in these functions. The view expressed by me in 1851 and later emphasised in particular by Virchow, that fibrous material is only a by-product of cell formation and tissue nutrition, which enters the blood secondarily, but is not, as Vogel, for example wanted, the material from which the tissues are formed, seems to be essentially supported by this whole series of experiments.

5. The oxygen-saturated blood cells contained in the whisked blood, even if they come from another individual of the same species, are capable of completely restoring the vital qualities of the nervous system that were lost by loss of blood, if only a short time after the extinction of the vital symptoms has elapsed through the loss of blood.

6. Since it is possible to remove and replace the whole blood mass of one animal, at least up to about 3 pr. m. with the whisked blood of another animal, without thereby abolishing the normal functions of the organism, even without being substantially disturbed, the red blood cells, which are at any rate very important for these functions, can also be transplanted into another animal organism of the same species, i.e., they are transferred into them in such a way that they continue to function in a normal manner, like the animal's own original blood cells.

7. The transplanted foreign blood is not only able to completely substitute the blood originally belonging to the animal with regard to all functions, the maintenance of nervous and muscular activity, nutrition, digestion, respiration, heat formation, and secretions, but it also seems to be able to be preserved viable for as long as normal blood, and finally to decompose in the same normal manner as the normal blood. This may be inferred from the circumstance that no abnormal excretory products interfere with the normal continuation of ordinary secretions and other functions, and, with regard to red blood cells, also from the circumstance that the red blood cell content of the transplanted blood does not appear to be

subject to greater fluctuations than when the animal continues to function with its original blood cells, indeed, after the greater part of the blood has been substituted by foreign whisked blood, this content may be maintained unchanged for several days.

8. The reduction of the original, normal amount of blood caused by taking blood or by exchanging blood, in which more blood is emptied than re-injected, is very soon compensated for, partly by the lymphatic flow, partly by the absorption of water from the intestines.

9. The extent of urea secretion, which has been reduced to a fairly constant level by prolonged inanition for several days, is not changed by the substitution of a large, indeed the greater part, of the original blood of an animal of the same species by the whisked blood, and the changes in urea excretion dependent on the diet occur in the same manner and to the same extent after the greater part of the blood has been removed and replaced by foreign whisked blood of an animal of the same species, as before.

10. Nor does the degree of perspiratio insensibilis seem to be altered by the substitution of a large part of the blood by foreign whisked blood of an animal of the same species, but investigations should be directed more specifically to this point.

11. By means of the whisked blood of ruminants (sheep or calf) it is possible to restore in dogs the functions of the nervous system, respiration and the formation of heat, which have been suspended by bleeding, but only temporarily, since the transplanted foreign blood breaks down in the organism of the other animal species, and is excreted in a dissolved state through the urine and intestines, as well as into the parenchyma and the serous cavities of the body.

12. Urea is not one of the decomposition products of the blood of ruminants in the circulation of a carnivore, but urea secretion is completely suppressed by them. Bischoff's opinion that urea is not formed directly from the blood, but from the tissues of the body, seems to be substantially supported by this whole series of experiments.

For the practical application of transfusion as a remedy in humans, I believe that I can derive the following results from the present study:

1. Whisked blood definitely deserves preference in transfusion over un-whisked venous blood, a) because it avoids the obvious and hidden dangers of the transmission of clots during transfusion, b) because whisked blood is more effective than venous blood due to its greater oxygen content, c) because the dangers caused by the greater carbonic acid richness of venous blood are avoided, (d) because if the blood is used without causing any loss of time in the execution of the operation, the completion of the operation is never frustrated by too early coagulation of the blood, even if larger quantities of blood are to be used, and finally (e) because the use of the whisked blood does not involve any specific dangers due to the absence of the fibre, such as those that can be avoided by the use of venous blood.

2. Only healthy human blood is permissible for transfusion in humans. For although older experiments seem to show that the blood of closely allied animal species may be successfully transplanted, and may continue to function permanently in the new organism, e.g., calf's blood in the lamb (Rosa) and horse's blood in the ass (Edwards), and although the vital characteristics of one mammal extinguished by haemorrhage may also be recalled by transfusion of the whisked blood of another species of mammal at a distance from it, it is very much to be feared that this success, as in the case of dogs by the blood of lambs or calves, would be only very temporary, and that the decomposition and excretion of the foreign blood would again bring secondary danger and result in death.

3. Whisked blood cooled and kept cold by ice immediately after emptying, which was warmed back to body temperature immediately before application, also proved to be perfectly useful for transfusion. In military surgery, for example, it might perhaps be worth considering whether this method of conservation could not be considered, although of course one would give preference to freshly emptied, whisked blood.

4. When time is of the essence and there is danger of delay, one need not be anxious about warming the blood to be used for transfusion completely to body temperature, as the whisked blood, even at moderately warm air temperature, restores the animals just as well

without any harmful after-effect. It is only when the temperature of the blood has dropped below about 16°R (20°C) that chills occur during the transfusion, but this soon passes and, as it seems, without harmful consequences.

5. In the case of transfusions carried out on account of severe loss of blood, it is not always necessary to confine oneself to fulfilling the indication vitalis by transfusing only such small quantities of blood that the vital forces only just return, but in most cases it is possible to considerably shorten the convalescence, with its dangers, by the use of a larger quantity of blood. For the extinguished, or nearly extinguished forces increase in proportion as the quantity of blood and the abundance of blood cells approach the norm; furthermore, the transfused blood is actually transplanted, and functions in the new organism of the same species, and for as long as the original blood, without yielding abnormal products of decomposition, the consequences of which would be feared; however, there is no obstacle to the transfer of an arbitrarily large quantity of blood (if it is available) in the case of the use of whisked blood.

6. If, however, one endeavours to return the measure and richness of the blood as far as possible to the norm by the application of a larger quantity of blood, and thereby to restore the strength of the patient as completely as possible, one must be very careful a) that one does not fill the vascular system beyond the norm, and b) that one does not disturb the activity of the heart by injecting it too quickly. The overcrowding of the vascular system, the dangers of which were already recognized by the most ancient observers, is especially noticeable in the venous system and in the capillaries, when at the same time the activity of the heart is disturbed. Overcrowding and expansion of the right atrium can easily lead to cardiac paralysis and death, and the increase in blood pressure in the veins can lead to bleeding in the internal organs in the case of impaired cardiac activity, even if the arterial pressure (due to weakening or irregularity of the heart's activity) has fallen sharply, or is subject to strong fluctuations. In order to protect oneself against this as much as possible, one must inject very slowly, whilst closely observing the pulse, especially with regard to its tension, and it is also advisable to open a vein on the other arm from which the blood can flow freely as the tension in the venous system increases. This is especially important if the transfusion is carried out because of more chronic bleeding, because then the amount of blood will have become almost normal again through the lymphatic flow and through water absorption, and because the transfusion will then not so much have the indication of restoring the normal quantity of the blood with regard to its volume, but rather the extremely reduced content of red blood cells in the blood due to the bleeding. Thus, in the case of chronic, slow-proceeding bleeding, one must not simply increase the quantity of blood by injecting new whisked blood from another human being, but rather make a substitution of the blood by allowing one's own blood, which has become far too poor in blood cells due to the bleeding, to flow out in the same proportion as the new whisked blood, which is rich and normal in terms of its blood cell content, to flow into the body. Only in the case of very acute bleeding is the simple injection without simultaneous blood withdrawal indicated, because only then is the amount of blood really reduced and not, as in the case of slow bleeding, only the amount of blood cells. Even in the case of very acute bleeding, however, it may be advisable to protect oneself against overfilling of the veins by opening a vein on the other arm, because the refilling of the vascular system with an aqueous fluid is so extremely rapid due to the absorption and the lymphatic flow.

7. One must not wait for the last moment to carry out the transfusion, because the shock caused by the disturbance of the nutrition of the nervous system in the case of fainting and convulsions causes the greatest dangers. While the substitution of foreign blood is in itself safe, and can be carried out gradually, in smaller recapitulations, down to the last remnants of blood in animals, without any disturbance, the production becomes more and more doubtful in the case of too strong blood withdrawals and losses of blood which have taken place at once, the further they go and the more often they recur. Every fainting and every convulsion of the nervous system greatly diminishes the hope of a favourable outcome.

8. The dangers of transfusion or substitution of fresh, healthy, whisked blood of an individual of the same species, instead of the lost blood, and especially instead of the lost

blood cells, depend only on incidental circumstances, not on the substitution of the foreign blood in and of itself, and on the disintegration of it in the new organism, which was previously so dreaded; however, this operation is by no means entirely without danger, precisely because of the numerous questionable incidental circumstances. The main dangers, which depend on too rapid an injection, on overfilling and tension of the vascular system, especially of the right atrium, the veins and capillaries, and on the too strong vibrations of the nervous system caused by excessive withdrawal of blood all at once, can be avoided, at least for the most part; likewise, the injection of air is not to be concerned if the operation is carried out carefully; but there are still not only the dangers of phlebitis, which are probably not very great, but also other, hitherto unknown circumstances, which can bring about an unfortunate outcome. Therefore, the substitution of the blood is not to be used without hesitation even in those cases where the cause of the deficiency of red blood cells lies in some defect in the preparation of the blood, and still less in those cases where the blood has become abnormal due to some pathogenic substance which is reproduced again and again, e.g., from the tissues and which would therefore contaminate the new, substituted blood again within a short time. However, the fact that neither the transfusion alone (without blood withdrawal) nor the substitution of it (with blood withdrawal) is used in those cases where an apparent lack of blood and blood cells has arisen from inanition, is sufficiently evident from the following series of investigations. In the event of a great impoverishment of the blood by suppuration, a simple injection of new blood would result in a dangerous overcrowding of the vascular system, if at the same time a corresponding part of the blood, which had become much too poor in blood cells, were not withdrawn, but the great and prolonged weakening and exhaustion of the nervous system would certainly always render the success in these cases very doubtful. It seems to me therefore that the use of this operation should preferably or exclusively be limited to direct heavy bleeding. It is only in the case of very acute bleeding, such as occurs during childbirth and military surgery, that one can be sure that the quantity of blood quoad spatium is really diminished, and only in these cases can one be content with simply injecting the new blood. In the case of slower bleeding and chronic loss of blood, it is definitely indicated to carry out a transfusion at the same time as a proportion of one’s own blood, which has become unsuitable for the maintenance of the functions due to dilution and especially due to the enormous loss of blood cells, is drained that corresponds to the amount of blood injected. Since, therefore, one must never transfuse blood without the intentional or, as is usually the case, the unintentional emptying of at least as large a quantity of one's own blood, it would actually be most correct to call the operation in question the substitution of the blood, instead of as before, speaking only of the transfusion.

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4. Paul Scheel, Die Transfusion des Blutes u. s. w., fortgesetzt von J. F. Dieffenbach. [Paul Scheel, The transfusion of blood, &c., continued by J. F. Dieffenbach] Berlin, bei Enslin. 1828.
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8. Paul Scheel, Die Transfusion des Blutes etc., fortgesetzt von Dieffenbach. [The transfusion of blood etc., continued by Dieffenbach]
9. Handbuch der Physiologie. 1. Bd.
10. J. Müller's Archiv für Anatomie u. Physiol. 1835. S. 347-377.
11. J. Müller's Archiv für Anat. u. Physiol. 1838. S. 357.

12. Dieser Fall betraf einen alten Officier, dem während der Aethernarcose die Zunge wegen eines Cancroïds exstirpirt worden war. Es entwickelten sich nach dieser Operation Erscheinungen von Zersetzung des Blutes und Professor Larsen wollte nun die Blutmischung des hoffnungslosen Kranken verbessern, indem er durch Transfusion einen Theil des kranken Blutes durch gesundes ersetzen wollte. Ich war bei der Operation als Assistent zugegen und veranlasste, dass gequirltes Blut transfundirt wurde, anstatt, wie anfangs beabsichtigt war, das Blut in toto. Das zu transfundirende Blut wurde einem plethorischen übrigens gesunden Frauenzimmer entzogen. Der Zustand des Kranken schien sich anfangs etwas zu bessern; bald kehrte aber der frühere hoffnungslose Zustand zurück und er starb, wenn ich nicht irre, am 2ten Tage unter den Erscheinungen der Pyämie. Doch wurden keine lobulären Prozesse in den Lungen oder der Leber gefunden. [This case concerned an old officer whose tongue had been extirpated due to a cancroid during ether anaesthesia. After this operation, symptoms of decomposition of the blood developed and Professor Larsen now wanted to improve the blood mixture of the hopeless patient by replacing part of the diseased blood with healthy blood through transfusion. I was present at the operation as an assistant and arranged for agitated blood to be transfused instead of pure blood, as was initially intended. The blood to be transfused was taken from a plethoric, otherwise healthy woman. The patient's condition initially seemed to improve somewhat; but soon the previous hopeless condition returned and, if I am not mistaken, he died on the second day under symptoms of pyemia. However, no lobular processes were found in the lungs or liver.]
13. Gaz. méd. de Paris 1851. Lancet 1851. No. 14. Vol. 2.
14. Schmidt's Jahrbücher. Bd. 75 S. 88. 1852.
15. Hospitalstidende Bd. VI. 1853. Schmidt's Jahrbücher 1854. S. 207.
16. Oesterreichische Zeitschrift für praktische Heilkunde. VI. Jahrg. No. 8.
17. Jobannes Dreesen, Dissert. inaug. de transfusione sanguinis. Kiliae, 1861. und oben.
18. Ueber die Transfusion bei Blutungen Neuentbundener' [About transfusion for bleeding in newly born babies] S. 66.
19. Martin vergisst hier freilich, dass es gerade das venöse Blut ist, das sich vor dem defibrinirten durch dieses Uebermaass an Kohlensäure auszeichnet. [Martin, of course, forgets here that it is precisely the venous blood that is distinguished from the defibrinated blood by this excess of carbonic acid]
20. Dieffenbach, Paul Scheel, Die Transfusion des Blutes u. s. w. Bd. 3. p. 197.
21. Leçons sur le sang et les alterations de ce liquide (Phénomènes physiques de la vie. Tom. IV. Paris, 1838.).
22. Artikel: Blut, in Rud. Wagner's Handwörterbuch der Physiologie. 1. Bd. 1842. S. 102.
23. Virchow's Archiv Bd. XXV. Hft. 3, 4, 5 u. 6.
24. Comptes rendus 1851. T. 32. p. 855 u. 897.; 1855. T. 41. p. 629.; 1857. T. 45. p. 562. 925.
25. Comptes rendus de la soc. de biol. 1. Série. Vol. I. 1849. p. 105 u. 158.; Vol. II. 1850. p. 271.; Vol. III. 1851. p. 100, 147.
26. Journal de physiol. I. p. 95-122. 173-175. 666-672.
27. J. Müller's Archiv 1838.
28. In den angeführten Beziehungen kann ich Brown-Sequard's Angaben nur bestätigen. Wenn er aber zugleich die Meinung zu begründen sucht, dass die Kohlensäure des Blutes eine incitirende Wirkung habe, so kann ich diese Angabe nicht constatiren. Die von Brown-Sequard bei Injection kohlensäurereichen Blutes beobachteten Reizungserscheinungen finden ihre Erklärung durch die in meinen Untersuchungen über Embolie mitgetheilten Erfahrungen, denen zufolge eine jede Unterbrechung der arteriellen Blutzufuhr zu den Nervencentren zunächst Reizungserscheinungen hervorruft, denen sehr bald gänzliches Aufhören der Lebenseigenschaften folgt. Sie sind nicht, wie Brown-Sequard meint, durch den positiven Reiz der Kohlensäure, sondern durch den Mangel der zur Unterhaltung der Functionen geeigneten Blutzufuhr, also auf rein negative Weise, hervorgerufen (s. Virchow's Archiv Bd. XXV. S. 320). Die Kohlensäure wirkt, meinen speciell auf diese Frage gerichteten Untersuchungen zufolge, nicht als Reiz, weder auf Muskel noch auf Nerv, auch nicht auf das Herz; sie ruft keine Zuckung hervor, sondern lähmt in sehr kurzer Zeit, ohne vorhergehende Reizung, die Muskeln. Ein Herz in Kohlensäure gebracht pulsirt langsamer, und steht sehr bald, nachdem die Bewegungen immer langsamer und schwächer geworden sind, in der Diastole still. Es ist das Herz dann auch nicht durch galvanische oder elektrische Reizung zur Contraction zu bringen, an die Luft gebracht erholt es sich aber wieder und kann alsdann, nachdem es wieder zu pulsiren anfing, erst durch eine viel länger dauernde Einwirkung der Kohlensäure wieder zum diastolischen Stillstand gebracht werden. Ebensowenig kann ich die Behauptung Brown-Sequard's bestätigen, dass das Blut eines Wirbelthieres kein Gift für eine andere Wirbelthierart sei (bei Injection in die Venen) und dass die toxische Wirkung, wenn sie

eintrâte, wesentlich vom Kohlensäuregehalt des injicirten Blutes abhinge. Die von Bischoff, Prevost-Dumas und Anderen beobachtete unmittelbare Todesgefahr ist nämlich allerdings wesentlich von der Kohlensäure abhängig und kann daher durch Quirlen des Blutes beseitigt werden, aber später, nach Verlauf von Stunden und Tagen, entfaltet das fremde Blut durch seine Zersetzung und Ausscheidung in der That toxische Wirkungen, die um so intensiver sind, je grössere Mengen des fremden Blutes injicirt wurden. Wir werden auf diesen Punkt noch im Verlaufe dieser Untersuchung ausführlich zurückkommen. [I can only confirm Brown-Sequard's statements in the relationships stated. But if at the same time he tries to justify the opinion that the carbonic acid in the blood has an inciting effect, I cannot confirm this statement. The irritation symptoms observed by Brown-Sequard when injecting carbonated blood are explained by the experiences reported in my studies on embolism, according to which any interruption of the arterial blood supply to the nerve centres initially causes irritation symptoms, which are very soon followed by a complete cessation of vital functions. They are not, as Brown-Sequard thinks, caused by the positive stimulus of carbonic acid, but by the lack of blood supply suitable for maintaining the functions, i.e. in a purely negative way (see Virchow's Archives, Vol. XXV, p. 320). According to my research specifically aimed at this question, carbonic acid does not act as a stimulus, neither on the muscles nor on the nerves, nor on the heart; it does not cause twitching, but rather paralyzes the muscles in a very short time, without prior irritation. A heart in carbonic acid pulses more slowly and very soon stands still in diastole after the movements have become increasingly slower and weaker. The heart cannot then be brought into contraction by galvanic or electrical stimulation, but when exposed to air it recovers again and can then, after it begins to pulsate again, only be brought to a diastolic standstill after a much longer period of exposure to carbonic acid. Nor can I confirm Brown-Sequard's assertion that the blood of one vertebrate animal is not a poison for another species of vertebrate animal (when injected into the veins) and that the toxic effect, if it were to occur, depended essentially on the carbonic acid content of the injected blood. The immediate danger of death observed by Bischoff, Prevost-Dumas and others is essentially dependent on carbonic acid and can therefore be eliminated by stirring the blood, but later, after hours and days, the foreign blood develops toxic effects through its decomposition and excretion which become more intense the larger the quantity of foreign blood that is injected. We will return to this point in detail later in this study.]

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31. Rich. Loweri tractatus de corde. Lond., 1669. 8°. p. 191. Scheel Bd. I. S. 47-49.
32. Birch, History of the Royal philos. Society 4. Vol. II. 1757. p. 117, 118, 125. Bayles Works V. p. 363. Scheel 1. c. p. 56-57.
33. Birch I. c. II. p. 123, 125. Scheel I. c. p. 57-58.
34. Scheel I. p. 87-88.
35. Ibid. I. p. 104.
36. Gjornale de' Literati per il Tinassi 1668. No. 7. Scheel II. 9..
37. Rudolph Wagner's Handwörterbuch. Artikel “Blut“.
38. Vor der Transfusion war die Blase durch Katheterismus entleert worden und dasselbe geschah am 26 Mai 10½ Uhr Vormittags. [Prior to the transfusion, the bladder had been emptied by catheterization and the same thing happened on 26th May at 10.30 am.]
39. In allen Versuchen ist die Correction für Kochsalz vorgenommen worden. [In all experiments, the correction for table salt was made]
40. Ich bin hierbei, wie gesagt, immer von der Voraussetzung ausgegangen, dass die Blutmenge normal $^{1}/_{13}$ des Körpergewichts ausmacht. Dass diese Voraussetzung nicht weit von der Wahrheit abweichen kann, geht aus der folgenden Untersuchung über die Mengenverhältnisse des Blutes hervor. [As I said, I have always proceeded from the premise that the amount of blood normally amounts to $^{1}/_{13}$ of the body weight. The fact that this assumption cannot deviate far from the truth, is evident from the following study of the proportions of the blood.]
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42. Birch 1. c. II. S. 133. Scheel I. c. S. 59.
43. Scheel 1. c. S. 62.
44. Birch 1. c. II. S. 190. Scheel I. c. S. 67-69.
45. Birch 1. c. S. 166, 167. Scheel 1. c. S. 66, 67.
46. Birch 1. c. S. 164. Philos. Trans. No. 25. Scheel 1. c. S. 63, 64.
47. Birch 1. c. II. S. 166-169. Scheel 1. c. S. 65.
48. Scheel 1. c. I. 170-177.
49. Scheel 1. c. II. S. 10-14.

50. Scheel 1. c. I. S. 131.
51. Scheel 1. c. I. S. 119.
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