DIE TRANSFUSION DES BLUTES
NACH EIGENEN EXPERIMENTAL-UNTERSUCHUNGEN UND MIT RÜECKSICHT AUF DIE OPERATIVE PRAXIS.

By: A. EULENBURG and L. LANDOIS.

A TRANSLATION BY PHIL LEAROYD

A copy of this 72 page monograph titled 'The transfusion of blood according to our own experimental studies and with consideration of operational practice' by Albert Eulenburg (1840-1917) and Leonard Landois (1837-1902), published in 1866 in Berlin by A. Hirschwald, can be read or downloaded from the following sites:

https://wellcomecollection.org/works/w3yrpua3

https://books.google.co.uk/books/about/Die_Transfusion_des_Blutes.html?id=UaQLAQAAIAAJ&hl=en&output=html_text&redir_esc=y

CAUTIONARY NOTE: The reader of this translation should be aware that the nature of the animal experimental work described in this monograph must be viewed as being extremely and unacceptably cruel by today's standards which some people may find distressing.

As the title identifies this monograph contains a summary of the animal based experimental work performed by the authors to examine the recovery abilities of blood transfusion in different clinical situations, such as anaemia, poisoning, fasting, etc. A large part of the presented work involves what the authors call 'depletory transfusion', whereby the animal is first bled (to remove 'affected red cells' and reduce associated clinical effects) and then transfused with fresh defibrinated blood. The monograph however starts with a brief historical summary of blood transfusion, which mainly identifies the work of Panum in recognising that although the blood transfused from a different species may cause 'temporary resuscitation', it is subsequently soon destroyed, whereas blood from the same species remains in the circulation for longer.

In the first section, having stated that the role of blood transfusion in acute blood loss 'is now established', the authors describe their experimental work to investigate which of the blood constituents are involved in producing this 'restorative effect' in treating anaemia, looking at the effects of injecting fibrin and 'oxygenated serum' as well as defibrinated blood. The work also includes looking at the clinical 'anaemic paralysis' and convulsions seen in patients with acute anaemia caused by excessive blood loss, which the authors associate with its effect on the vital nerve centres.

The second section looks at the effects of acute poisoning by different chemicals in experimental animals (rabbits and dogs) and the responses to using blood transfusion to reduce their effects, especially when combined with bleeding the animal so as to 'flush-out the vascular system' containing the poison and then replacing it with normal blood, i.e. the so called 'depletory transfusion'. This part of the work is then divided into five sections that deal with poisoning by different chemicals, i.e. carbon dioxide, carbon monoxide, chloroform and ether vapours, morphine and opium, and finally strychnine.

The authors identify the poisoning effects of carbon dioxide and its association with a lack of oxygenated red cells, a situation where 'depletory transfusion' is argued to be potentially life-saving, having the duel action of reducing the clinical effects of the carbon dioxide with transfusing defibrinated oxygenated blood. The poisoning effects of the 'preferential binding effects of carbon monoxide within red cells' are discussed, again together with experimentally investigating the potential beneficial effects of ‘depletory transfusion’, stressing the need to repeat the procedure until a more normal red cell colour is seen in the drained blood. Chloroform and ether are identified to have been investigated due to their potential intoxication related to their use in anaesthesia. Although the authors state otherwise, the experimental results can however be interpreted to not conclusively show that resuscitation methods other than transfusion would have been equally successful, especially since they state that the degree of anaesthesia used in their animal experiments would never be used in humans.

Morphine is identified to be able to ‘immediately act on the central parts of the nervous system’ and therefore investigating the experimental effects of depletory transfusion in such cases is at best debatable. In addition, the results of their main experiment, performed on two dogs (from the same litter) who are both intravenously injected with morphine with one being given depletory transfusion and the other not, is open to interpretation, especially since both dogs recovered, though the transfused dog recovered quicker.

The section on the potential effects of transfusion on poisoning by strychnine is rather long and very detailed, in that it painstakingly describes the transfusion of 29 syringes of blood to a dog in a 60 minute period, resulting in it surviving for that time, instead of that of another un-transfused dog that survived for only 5 minutes. The author’s conclusion that ‘if the transfusions had continued the dog might have lived longer’ is to say the least somewhat controversial. The use of transfusion in such cases again appears controversial, especially since other alternative treatment options are available (e.g. stomach pumping).

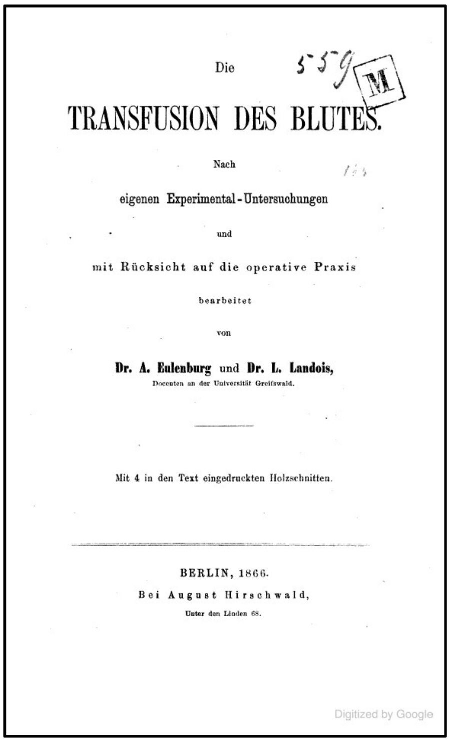
The section on ‘artificial inanition and lack of food’ involves attempts at trying to keep starving animals alive by giving them only blood transfusions as a ‘food substitute’, which reflect the beliefs of the earliest days of transfusion in which blood was believed to be able to ‘maintain life’. The authors are left to argue that the role of these ‘nourishing transfusions’ in humans who are for example unable to eat (e.g. as a result of carcinomas) would be at best only temporarily palliative.

Defibrinated blood of the same species is identified by the authors as being the most advantageous for transfusion, though they do comment that some adverse effects have been identified when used in humans and they discuss the possible benefits of transfusing non-defibrinated blood that would improve clotting potential in the patient who is bleeding. The section on the practical aspects of transfusion concentrates on the description and use of a glass injection syringe, the binding of the cannula into the vein using silk thread, together with an ‘air catcher’ attachment device to help avoid injecting air with the blood.

Finally, the ‘indications for transfusion’ section’ is somewhat repetitive in that it reiterates the beneficial use of transfusion in anaemia and use of ‘depletory transfusion’ in some cases of poisoning.

I have produced a translation of this monograph into English to enable its content to be read 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 each part of this paper has been maintained within the translation. The references in the original text are identified by asterisks and placed at the bottom of the relevant pages. I have sequentially numbered these and placed them at the end of the translated text, reproduced as originally printed – though I have also translated the reference titles and author's comments. The actual experimental results are presented as lists within the text, initially starting with the time that they were performed. This time is varyingly identified with the letters 'St, U and M'. I have standardised these with the single format of 'hr and m' to represent hour and minute. The word 'colirt' appears in the original text, which has no equivalent English translation, but is believed to indicate 'filtered' within the context of where it appears in the text and it is this word that has been included in the translation. In addition, haemoglobin is referred to as 'haematoglobulin' in the text - this has also been changed in the translation.



Die

TRANSFUSION DES BLUTES.

Nach

eigenen Experimental-Untersuchungen

und

mit Rücksicht auf die operative Praxis

bearbeitet

von

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Mit 4 in den Text eingedruckten Holzschnitten.

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Title Page - Die Transfusion des Blutes
(Image credit – Google Books)

Albert Eulenburg (1840-1917)
(Photo credit: en.wikipedia.org)

Leonard Landois (1837-1902)
(Photo credit: en.wikipedia.org)

ALBERT EULENBURG

Albert Eulenburg was born in Berlin on the 10th August 1840, the son of Moritz Michael Eulenburg (1811-1887), a prominent Jewish orthopaedist who converted to Christianity in 1847. He studied medicine at the Universities of Berlin, Bern and Zurich, earning his doctorate on the 31st May 1861. He later became professor of pharmacology at the University of Greifswald and in 1882, professor of neurology at the Humboldt University of Berlin. His most ambitious published work was the multi-volume *Real-Encyclopädie der gesammten Heilkunde*, which was published in four editions between 1880 and 1914. He died in Berlin on the 3rd July 1917.

LEONARD LANDOIS

Leonard Landois (1837-1902) was a German physiologist. He studied medicine at the University of Greifswald and later became a professor and director of the Institute of Physiology at Greifswald and a member of the German Academy of Sciences Leopoldina. Although his early work involved research in the field of parasitology, Landois was a pioneer in the study of blood transfusion. In 1874-5 he demonstrated inter-species incompatibility of blood by showing that the serum from one species of animal was capable of agglutinating or haemolysing the red cells of an animal of another species. He also linked this phenomenon with the appearance of black urine after a heterogeneous blood transfusion, establishing scientifically the dangers of transfusing blood of another species into humans. Extensive details of his in vitro inter-species experiments are included in a section of ‘Die Transfusion des Blutes’.

THE TRANSFUSION OF BLOOD ACCORDING TO OUR OWN EXPERIMENTAL STUDIES AND WITH CONSIDERATION OF OPERATIONAL PRACTICE

Dr. A. EULENBURG AND Dr. L. LANDOIS

PREFACE

This present monographic adaptation of the transfusion owes its origins to a series of experiments which were carried out jointly by the authors at the Anatomical Institute in Greifswald in the greater part of 1865. A preliminary report of the most important results, dated 17 September 1865, can already be found in the Centralblatt f. d. med. Wissensch 1865, No 46. It seems necessary to recall this explicitly because, owing to the long delay in printing, the work is only now being published in its final completed form and could therefore easily be criticised as if some recent investigations and publications in the field in question had not been due mention and consideration. This is especially true of the section on carbon dioxide poisoning, where, as is well known, Kühne was the first to pave the way for the therapeutic application of transfusion by his experiments, in a manner as original as it was fortunate. Friedberg’s monograph published in the meantime: "Poisoning by Coal Vapour", Berlin 1866, contains, in addition to the one also mentioned by us (described in the Wiener med. Presse) Sommerbrod's case, two observations on the execution of the transfusion in humans, one of which was made in the Charité in Berlin, the other by Prof. Möller in Königsberg. In addition, only recently, on 12 March 1866 in Berlin, there was a case of carbon dioxide poisoning in the practice of Dr. Badt, the transfusion performed by

Mr. Geh. Rath Martin with favourable success: as is evident from brief short notices in the daily papers and from that reported by Dr. Badt of the Berliner medicinischen Gesellschaft (meeting of 28 March 1866). The theoretical summary of the effect of carbon dioxide gas also requires investigations into this subject after the publication of the Traubeschen (in the proceedings of the Berliner med. Ges., issue I) of essential additions and modifications, which follow by themselves from the study of the aforementioned treatise.

Paris, 13 April 1866.

Dr. Albert Eulenburg.

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* Original monograph page numbers
** Page numbers in this translation

Nearly two centuries have now elapsed since Denis (on the 1st or, according to others, on 15th June 1667) carried out the transfusion on a living man for the first time, with happy success. Although not previously unknown as the subject of poetic fables or humorous-pathological speculations, it was only from then on that transfusion conquered the rank and validity of a physiologically based, rational-empirical method of healing, as which it is, of course, still far from being universally recognized and practiced today. A few years ago, on the occasion of his substantial studies on transfusion, Panum sought the reason why this operation, which has been so important and in many cases so beneficial, has been so difficult to gain acceptance and has hitherto received on the whole more theoretical approval than practical care and encouragement. We believe, however, that there is a second, quite heterogeneous motive that deters practitioners from transfusion: the (at least very exaggerated) idea of the technical difficulties and dangerous consequences of the operation – perhaps also the unfamiliarity with the details of its execution, since very few physicians are likely to have witnessed it even on animals, let alone on humans. However, it would be unreasonable to question the influence and, above all, the legitimacy of the moment highlighted by Panum. It is true that, in recent times, in different countries and at the same time efforts have been made to bring the numerous and partly complicated problems of transfusion closer to their conclusion by means of physiological experiments; nevertheless, as commendable as the combined forces of excellent researchers in this field have hitherto accomplished, it is of little consequence in comparison with the magnitude and scope of the task at hand. The previous experiments, most commendable in detail and in part extremely enlightening in regard to the operative technique, have neither in any exhaustive way appreciated the efficiency of transfusion in general, nor have given its effect in detail a thoroughly comprehensible and sufficient physiological basis. The natural consequence of this is that the question of the indications for transfusion, which is cardinal from a therapeutic point of view, is still the greatest obscurity on all sides, and we see the circle of its activity sometimes extended into the adventurous by vague and priori proposals, sometimes just as unmotivated, and even shrunk into nothingness.[1]

Let us try to briefly sketch the most significant advances that the theory of transfusion has made in recent times in the hands of the physiological experiment. With the sole exception of a recent publication, only the resuscitation of animals exhausted by blood loss has so far been the subject of experiments. The older experiments of Rosa (1783), Bichat and Portal (1800), Blundell (1818), Viborg, Hertwig and others do not yield any significant results. The first discovery of outstanding importance, which at the same time introduces a new phase in the theory and practice of transfusion, is that of the applicability of defibrinated blood by beating in place of fibrin, which was previously used alone. We owe this progress to the investigations of Dumas and Prévost[2] (1821), von Dieffenbach[3], Müllert[4] and Bischoff[5]. - Besides, Blundell, Dumas and Prévost, as well as Dieffenbach had already found that foreign blood also often carried out resuscitation, but as a rule causes serious coincidences and even subsequently precipitates death. Bischoff even believed from similar observations, which involved the transfer of mammalian blood to birds, that the blood of one animal was poisonous and therefore has a deadly effect on other animal species. He had used unbeaten blood (containing fibrin) for these experiments and blood obtained by the means of cutting through the cervical vessels. He later found that the fatal outcome occurred only when venous blood was used, but not when arterial blood was used. Older observers (e.g. Dieffenbach) had found the arterial blood more effective than venous blood, but without trying to explain this important fact[6]. Bischoff, too, at that time was not able to give one. Whereas he had previously blamed the fatal outcome essentially on account of the fibrous matter transferred with it, he now limits himself to conjecture that it might be the "animal dross" of the venous blood, whereby it had the same poisonous effect on animals of another species.

A solution to this riddle and a new, substantial enrichment of the theory of transfusion are only contained in the numerous, years-long experiments of Brown-Sequard[7]. The main result of these we may predict that the effectiveness of the blood used for transfusion depends on the gas content of it. Arterial and venous blood may therefore have a similar effect if they hold equal amounts of oxygen or carbonic acid. The sinister consequences of the transfer of venous blood are explained by the greater content of carbonic acid in it; they do not therefore occur when the venous blood is made oxygen-rich and bright red by beating or shaking before transfusion, as it were arterialised. Conversely, arterial blood can also be rendered toxic if carbonic acid is introduced into it, and blood saturated with carbonic acid is already life-threatening at an injection quantity that does not exceed $^{1}/_{500}$ of the body weight. Death occurs under asphyxial phenomena and convulsions, which Brown-Sequard attributes to the irritating influence of carbonic acid.

The statements of Brown-Sequard were confirmed in all essential respects by the classic investigations of Panum[8], which moreover provided valuable decisions on several questions raised by transfusion. - Panum first set himself the task of examining the objections recently raised by some (Schilz[9], Martin[10]) against the use of defibrinated blood, and to definitively establishing the superiority of fibrin-containing or fibrin-free blood for practice. We can now regard this question as being answered in the sense that the defibrination in itself has no disturbances in its wake and that defibrinated blood does exactly the same as fibrin-containing blood, and therefore necessarily merits the preference in view of its greater innocuity[11]. - In a second, no less important, experiment Panum demonstrated that the transfused blood of an animal of the same species not only causes temporary resuscitation, but also completely replaces the normal blood with respect to all its functions and remains viable as long as the latter - i.e. is formally "transplanted" or substituted in its place. The evidence of the ongoing preservation of transfused blood of the same animal species was provided by Panum by the fact that:

(a) The content of the red blood cells has not been subjected to abnormal fluctuations for a long time after the transfusion

(b) No abnormal excretory products occurred, and in particular the export of urea and the perspiratio insensibilis did not appear to be altered in any way.

A third and final series of experiments showed that the same is by no means the case when the blood of another species is used: this too is capable of causing a temporary restoration, but the introduced blood soon undergoes decomposition in the organism that is foreign to it, and is excreted again in a dissolved state by the secretary and excretory organs (especially through the urine and intestines).

While Panum expressly emphasizes at the end of his work that the use of transfusion seems to him to be primarily or exclusively limited to direct heavy bleeding, very recently Kühne[12] opened up new avenues for the therapeutic utilisation of the transfusion through his successful experiments in carbon dioxide poisoning, but on which no further observations are available at the present time[13].

- From this condensed overview, which hardly passes over anything essential, it will not be difficult to see the present experimental standpoint of the theory of transfusion. It seemed to us that it was urgently necessary to rework and expand it in various directions. - Even in the field hitherto cultivated almost alone (effect of transfusion in exhausting bleeding) there are wide, gaping gaps, and in particular the theoretical question of the mode of action of the transfusion, the origin of its anabiotic influence on the nervous system, is still waiting to be decidedly explained. We believed that we had to submit this question to an attempt to answer it, especially since it is directly connected with interesting points of contention in physiological research, which are often voiced today. We still consider these investigations to be scientifically worthwhile even if a significant gain can no longer be made for the practice of transfusion in the case of exhaustive blood losses according to the productive achievements of the previously mentioned authors.

We have also included acute poisoning by various substances with a lethal effect into our circle of experimental investigation. The points of view which have guided us in this connection, and the results, some of which are highly surprising, which we have arrived at by means of a combined process (transfusion with simultaneous depletion), will find their further communication in the following.

Finally, we have studied the effects of transfusion on disturbed nutrition (by artificially maintained, continuous inanition).

So let us deal with it in order:

I. Transfusion in acute anaemia (due to exhaustive blood loss);

II. Transfusion with simultaneous depletion in acute poisoning;

III. Transfusion in inanition, followed by:

IV. Comments on the practical execution of the transfusion and its indications

I. Transfusion in acute anaemia.

The experiments in this series were aimed in particular at answering the following questions:

1. Is the peculiar restorative effect of transfusion in anaemic animals connected with certain constituents of the form and mixture of the injected blood, and what are these constituent parts?
2. In what way does the effect of transfusion manifest itself on the vital nerve centres, and by which nerve pathways are these influences mediated?

As far as the first question is concerned, in addition to the older ones, Panum's experiments in particular have sufficiently demonstrated that fibrous matter is a completely unnecessary stock substance during transfusion, indifferent to the functional effect and can easily be disregarded. There are several reasons, however, to believe that the invigorating influence of transfused blood is linked to the presence of the red blood cells in it - an assumption that has already been advanced here and there by older authors, but which has only received significant factual support in the experiments of Brown-Sequard quoted above. Since these experiments showed that oxygen-rich blood has an invigorating effect, whilst carbonated blood does not, it was most obvious to regard oxygen as the condicio sine qua non for the success of the transfusion: and since we know precisely that the red cells are the preferred carriers of blood oxygen, the assumption seemed quite justified that these latter, or rather the haemoglobin compound of oxygen contained in them, constituted the effective agent of the transfusion which could actually be considered.

However, a second hypothesis is conceivable to explain the transfusion effect in the case of sudden anaemia, to which Goltz first drew attention to in his meritorious treatise on the vascular tone[14]. - According to Goltz, the main value of transfusion in cases of bleeding is not the "increase of the nutritional substance", but the improvement of mechanical circulatory conditions, which are directly produced by the greater filling of the empty vessels. "The sudden fatal outcome after blood loss is not so much caused by the cessation of nourishment, but by the fact that the movement of the blood stops, and the latter stops because the heart can no longer work successfully after the sudden reduction of the vascular contents. The remnants of blood still present in the vessels in such cases would be able to eke out a living for a while, at least in a makeshift way, if they were only set in motion, if the mechanical movements for the circulation were established." - The manner in which Goltz interprets the beneficial influence of the transfusion on the mechanics of blood circulation is not explicitly stated, but we may well conclude from the immediately preceding passage (p. 30) that he imagines this effect as follows: by the increased tension of the vascular contents, the vascular tone is first stimulated in a powerful manner; therefore a tonic contraction of all contractile vessels takes place, whereby the blood movement and as a result, the secondary action of the heart is also restored. - If this hypothesis were correct, it would depend only on the increased filling of the vascular system, not the specific effect of certain parts of the blood during transfusion; therefore a favourable effect would possibly be conceivable even if not blood, but an indifferent (and of course harmless) fluid were used for injection. For this purpose, Goltz himself proposes an air-shaken protein solution from the concentration of the blood, and is "firmly convinced" of the (temporary or permanent) effectiveness of such an injection. According to this hypothesis, the ineffectiveness of the transfusion when using venous or carbonic acid saturated blood would have to be derived less from the lack of oxygen deficiency than from the direct lethal influence of the former gas. -

The difficulties which oppose the Goltz hypothesis from the outset cannot be overlooked, in particular, inasmuch as the phenomena observed in the death of anaemic animals (see below) indicate that their death occurs from asphyxia through the sudden oxygen deficiency (and perhaps at the same time by carbonic acid poisoning), and thus primarily caused by respiratory paralysis, and that the disturbances of the blood movement, the cardiac action, only reach their culmination point some time after the cessation of breathing. On the other hand, a direct confirmation of the conjecture expressed by Goltz would be of the upmost importance for the practice of transfusion, since an easy-to-present and store protein solution could be used instead of the hard to obtain, in any case fresh, blood. We therefore experimentally tested Goltz's hypothesis by using other (non-lethal) fluids for injection into the circulatory system instead of defibrinated blood. - However, before describing these experiments in detail, it is necessary to make some comments on the procedure required to be followed and the methods of transfusion in anaemic animals in general.

All experiments in this series were carried out on rabbits. As a rule, one type of blood deprivation was usually used to draw blood, the common carotid artery, and the bleeding from it was maintained for as long as anything flowed off at all; in addition, in some cases the external jugular vein was opened, so that the total quantity of the drained blood probably reached the maximum of what could be extracted from the animals by experimental means. - It was always a waiting for this condition which may be most appropriately described as "anaemic paralysis" and which, left to its own devices, immediately precedes death. This stage of paralysis follows a primary stage of irritation, which is eminently characterized by dyspnoeic phenomena and by the convulsions usually referred to as "anaemic" (the interpretation of which is still doubtful). When the central impulse of active movement to the latter has expired, the animal falls into complete motor and sensory paralysis; the cornea no longer reacts, and even in the rest of the body every trace of excitability is completely extinguished; respiration is at a standstill, and finally after a long period of time, the heart stops, so that a needle inserted into it no longer shows pulsations. - By a sufficient series of experiments, we became convinced that at this stage of anaemia spontaneous resuscitation was impossible - that on the other hand by the transfusion of oxygenated, defibrinated blood, in almost all cases, respiration was restored and life was preserved without other functional disturbances. In these experiments, either the blood drained from the experimental animal itself was used for transfusion, or the blood of another rabbit, which was obtained by venesection from the external jugular vein, or previously collected by cutting the cervical vessels and prepared in an appropriate manner. As soon as it flowed out of the vein, the blood was carefully stirred with a glass rod in the porcelain bowl used for collection and completely freed from its fibres, so that it was an even, vividly bright red liquid; then it was collated and maintained continuously until use in the water bath at a temperature of almost 30°R. For the execution of the transfusion, a syringe containing 16 cc of liquid (= 15.4 grams of defibrinated rabbit blood) was used with a precisely closing attachable cannula, which was inserted into the latter after prior peripheral ligation of the vein and was quickly connected to the syringe.

The following experiment may serve as an example.

I. A strong rabbit of 891½ grams body weight was deprived of 31 grams of blood by cutting the right carotid artery, and since nothing flowed out, the vessel was closed with tweezers. The animal breathed very weakly, but had not yet had any convulsions. The right jugular vein was now also opened, and about 10 grams of blood was emptied from it by stroking and pressing with central compression, whereupon the discharge stopped, the animal fell into convulsions, became respiration-less and lay there as if dead, with completely abolished reflex excitability and no longer externally perceptible heart pulsation. From the first drained (arterial) blood, which in the meantime had been prepared in the manner described above, the contents of a syringe (i.e. 15.4 grams) were now placed into the right external jugular vein. During the injection itself, the respiration was initially weak and irregular, but gradually intensified and restarted in a rhythmic way. The vein was cut off and the skin wound was stitched; the animal, now untied, was able to walk at once, was still dull and sluggish, but otherwise showed a complete return of all its functions. - Body weight after the experiment 866½ gm. - Other liquids were substituted for the defibrinated blood for the purpose of transfusion, with otherwise the same repetition of the experiment, namely:

(a) Solution of albumin (egg white and distilled water in equal parts);

(b) Serum shaken with air or oxygen, obtained from the blood of rabbits[15].

II. A rabbit weighing 912 grams was deprived of almost 40 grams of blood by opening the left carotid artery and the external jugular vein, whereupon the above described state of paralysis and lack of respiration occurred after previous convulsions. 16 cc of albumin solution was injected into the left external jugular vein. At the very beginning of the injection, isolated breathing movements were apparent; however, the animal did not recover, and the initiation of artificial respiration was no longer successful. Convulsions did not occur during and after injection. (The immediately performed dissection showed significant bloodlessness of all organs of the thoracic and abdominal cavities, as well as the brain, and a peculiarly bright, watery serous quality of the blood contained in the pulmonary vessels; the heart already unexcitable, contained no air bubbles.)

III. A rabbit weighing 904 grams had 36 grams of blood taken in the same way as the previous one. As soon as the paralytic stage had occurred, 16 cc of serum (from fresh rabbit blood) was injected into the right external jugular vein, but without any effect; convulsions did not occur during injection. The subsequent transfusion of defibrinated blood came too late and, although it still produced sporadic, deeper breathing movements, did not cause a permanent resuscitation; injections into the open trachea were also unsuccessful. At the time of the dissection, the various organs were still found to be quite rich in blood; the heart is in-excitable, not airy. - The same result was obtained by experiments in which the serum used for injection was previously shaken with atmospheric air or oxygen (as Brown-Sequard had already done, also with negative success).

Blood was also used for the transfusion, which was defibrinated by beating and made bright red, but was subsequently shaken with carbonic acid until it assumed a blackish venous colour. In these cases, too, the effect in terms of resuscitation was quite negative; but there was a striking difference between the experiments first described, in that the injection of carbonic saturated blood almost regularly produced dyspnoeic breathing movements and frequently caused general convulsions, whereas these phenomena never occurred with the injection of blood serum or albumin solution. - We shall return to this circumstance, which is not at all unimportant for the theory of transfusion and anaemia, below. - First of all, from the experiments quoted so far, a refutation of Goltz's hypothesis emerged, and a confirmation of the previously asserted view, that the presence of red blood cells and oxygen in the transfused fluid is of particular importance in the transfusion undertaken for acute anaemia.

Indifferent fluids that contained neither oxygen nor blood cells (protein solution, serum) - fluids that contained free oxygen but no blood cells (oxygen-shaken serum) - and blood containing red blood cells but little or no oxygen, were equally inadequate. It can therefore be asserted that under the conditions indicated, transfusion cannot have a significant effect and in any event, cannot act exclusively by increasing the filling of the vascular spaces and thus improving the mechanical circulatory conditions. Preferably, however, the influence of the above mentioned parts of the blood of those animals may be taken into consideration on those parts of the nervous apparatus which are of the most intervening importance for the undisturbed continuation of the vital functions, namely the central heap of the respiration in the medulla oblongata, must be considered. - The favourable effect of the transfusion is always characterized first by the recurrence of the extinguished breathing, or by the intensification of the rhythmic movements of the breath reduced to a minimum. The first question arises as to whether this phenomenon is due to a direct action of the defibrinated, oxygen-rich blood on the medullary respiratory centre - or whether the blood reaching the lungs exerts a primarily influence on the peripheral vagus endings, whereby a production of the respiratory movements are produced in a reflexive way. In order to decide this question, the experiments with the transfusion of defibrinated, oxygen-rich blood were modified in such a way that immediately before the injection both vagus nerves were cut at the neck.

IV. A rabbit weighing 820 grams, first had its left vagus cut, followed by a blood removal of about 24 grams from the left carotid artery. Convulsions, stage paralyticum, and only sporadic respiration. Now the right vagus was cut, and immediately a transfusion from a syringe (= 15.4 grams) into the left exterior jugular vein made. During this time, the animal visibly recovered and began to breathe deeply and regularly; but this favourable change was only of very short duration, in that after only 5 minutes violent dyspnoea with facial breathing, etc. occurred and death occurred after 7 minutes with asphyxial phenomena.

A second experiment yielded the same result: the animal recovered noticeably during the transfusion, but died after barely 10 minutes under the signs of asphyxia.

V. For comparison, a rabbit weighing 844 grams had about 29 grams removed from the right carotid artery and both vagus nerves were cut without performing a transfusion. Immediately after cutting the second vagus, the most severe dyspnoea arose, and the animal died from asphyxia in less than a minute. - It seems evident from the latter experiment that in the case of animals that are made anaemic by a significant depletion, the cutting of the vagus nerve causes death in a very accelerated manner, among the usual manifestations of dyspnoea and asphyxia. This outcome can be somewhat delayed by the transfusion and respiration can be temporarily established if oxygen-rich blood is injected immediately after the second vagus has been cut. Transfusion is therefore still able to induce respiratory movements even after bilateral vagus cutting; this therefore does not happen by acting on the peripheral endings of the vagus nerve.

Let us try to make use of the facts described above for a theory of the transfusion effect in acute anaemia caused by bleeding.

It is probable that the oxygen supplied with the transfused blood acts directly as an excitatory agent on various parts of the central nervous system - perhaps also on the automatic motor ganglia of the heart. (In the former respect, the recently published experiments of Setshenov[16] are of great interest, insofar as here the wetting of spinal cord or brain cross-sections with defibrinated, oxygen-rich blood produced direct excitation of the affected centres of reflex action, or rather the inhibition centre of the same, and thus produced a significant reflex increase or reflex depression.) However, these possibilities do not yet explain the effect of transfusion on respiration, which is so conspicuous and can be observed in the first place during transfusion, the restoration or normalization of which can be regarded as a measure for the success achieved. In earlier times it was very easy to explain this effect, since oxygen was also thought to be the excitatory agent of respiration, the lack of which therefore resulted in stagnation, and the renewed supply of which resulted in the return of the respiratory movements. At the moment, thanks to Traube's investigations, we know that oxygen does not exert such a function - but rather that breathing in a pure oxygen atmosphere produces apnoea, and in an oxygen-poor and carbonic acid-rich atmosphere, according to circumstances, sometimes normal, sometimes causing dyspnoeic breathing. It is therefore either the carbonic acid, or (about which, as we know, there are still differences of opinion) the lack of oxygen, which must be regarded as the usual stimulus for the medullar respiratory centre and as the cause of rhythmic respiration movements. (We will have to return to this question in more detail in the following section, but at this point we cannot refrain from declaring that we are inclined towards the mediating view, which attributes a direct influence on the respiratory movements to both the lack of oxygen as well as to carbonic acid). How then can it be explained in both cases that the supply of oxygen-rich blood causes the recurrence of the respiratory movements when respiration has already stopped, while the supply of carbonated blood does not restore the same? - The most obvious conjecture seems to us to be the following: if a sudden and significant depletion, such as was carried out on the experimental animals, and moreover from the largest arteries, the total and relative amount of oxygen contained in the blood is reduced to a certain minimum, then the excessive lack of oxygen (and perhaps also the simultaneous accumulation of carbonic acid in the blood) must first cause a significant overstimulation of the respiratory centre of the medullar oblongata to take place. This overstimulation, if it persists, passes into paralysis and thus, left to its own devices, into permanent stagnation of the respiratory movements, as we regularly observe in the case of anaemic animals in the second stage. If at this time a blood saturated with carbonic acid is injected in large quantities at once, the already existing causes of excessive irritation and paralysis of the respiratory centre are in any case significantly increased, by both the relative oxygen content of the circulating blood, and significantly increasing the relative and absolute carbonic acid content of it. - If, on the other hand, a sufficient quantity of oxygen-rich blood is thrown into the circulation in time, the overstimulation leading to paralysis is not completely eliminated (which would give rise to apnoea), but it is reduced to the stage of normal stimulus, so that respiratory movements occur anew. According to the most recent experiments, the transfused blood exerts this influence by direct action on the medullar oblongata, not reflexively from the vagus endings, with which, as we know, the other results of Rosenthal and other researchers, also correspond for the most part.

Although it is possible to some extent to explain the effect of oxygen in transfusion, it is still not yet proved what role the red blood cells play in this, the presence of which it seems, is just as necessary as that of oxygen, since according to Brown-Sequard's and our experiments, even oxygen-rich serum does not resuscitate. For the time being, it would be an idle gimmick to pursue the hypotheses conceivable here (e.g. the necessary organization of oxygen by the red blood cells!).

On the other hand, it may be possible to draw a somewhat more definite conclusion about the effect of carbonic acid from the experiments carried out so far. Brown-Sequard already mentions that convulsions occur when carbonated blood is injected, and is inclined to attribute the same to the direct irritating effect. Panum rejects this explanation: according to him, the "irritations" observed by Brown-Sequard are not caused by the positive stimulus of carbonic acid, but by the lack of a blood supply suitable for the maintenance of the functions, i.e. in a purely negative way. According to Panum, carbonic acid does not act as a stimulus, neither on nerve nor muscle, nor on the heart; it does not cause twitching, but paralyzes the muscles in a very short time, without any prior irritation. - If Panum's view were correct, convulsions would have to occur after the injection of albumin solution or serum just as well as after the transfusion of venous or carbonated blood. However, as our experiments show, this is never the case: after the first "anaemic" convulsions have expired and the animals fall into respiratory listlessness and paralysis, convulsions are no longer induced by injection of serum or albumin solution, while they are almost certain to occur during the transfusion of carbonised blood. The isolated exceptions to this rule can be explained very easily by the irritability of the nerve centre that has already been reduced far too much. It therefore seems, according to the above experiments, that it is the carbonic acid which by direct or reflective excitation of the motor nerve centres, brings about the convulsions which occur under the described circumstances. We would like to suggest that the convulsions associated with the earlier stage, which are usually referred to as "anaemic" and are derived from a reduced blood supply to the basal parts of the brain, are also due to a direct irritation by carbonic acid accumulating in the blood and must therefore be interpreted as "dyspnoeic". In these cases the content of carbonic acid in the blood is not only relatively increased by the significant depletion of arterial blood, but it is also relatively increased over time inasmuch as the arteries remain empty on account of the reduced blood circulation, the veins remaining relatively full, and with the reduced movement of blood in the lungs, the removal of carbonic acid by them can only take place very imperfectly. But we give the opinion expressed, as far as the anaemic convulsions are concerned, only as a conjecture, which for the time being still lacks experimental confirmation.

II. Transfusion with simultaneous depletion in acute poisoning, or the substitution of normal blood in place of that impregnated with toxic substances.

The basic idea that led us to apply transfusion on a large scale as a cure in the field of acute intoxication is as follows. The toxic substances that exert their detrimental influences on the body, act in such a way that they are first absorbed into the blood and are carried with the blood to those places to which they primarily assert their lethal influences. It does not matter whether the poisonous substance is immediately injected directly into the vessels, or whether it comes from the stomach, intestines, lungs, wound surfaces, or after the subcutaneous injection to adsorption. Once the poison has passed into the blood mass, it is usually no longer possible to effectively resist the harmful effects. However, we will be able to eliminate the harmful effects of the poison if we remove from the body the mass of blood to which the poison is added and introduce normal blood into the vessels in its place. If, as is often the case, the poison gradually comes to adsorption, a repeated substitution of a normal blood will be necessary, namely, as often as the threatening symptoms seem to reach their climax. What is necessary here, as it were, is to repeatedly flush out the vascular system by the means of normal blood. From this point of view, transfusion with simultaneous depletion must be regarded as a summum remedium and it deserves to be fully introduced into practice, especially since in the vast majority of cases of poisoning, in which a transition into the blood has already taken place, the physician had to put his hands in his lap, since in fact there is no longer any means of rescue from the disease.

We have therefore thought it worthwhile to use our so-called method in a number of the most varied types of poisonings in order to test the beneficial effects of it.

1. Poisoning by carbon dioxide and lack of oxygen.

As the first intoxication, we chose poisoning as a result of the disturbed normal gas content of the blood, which is either derived from the overloading of the blood with CO_2 or is believed to arise as a result of lack of O. The same is very often the subject of the medical treatment as asphyxia, caused by a variety of causes; it confronts the physician in the case of the simply suffocated, in the drowned, in the hanged and strangled, and finally in the case of apparently dead newborns. The manifestations of asphyxia are sufficiently well known to make it unnecessary to develop them here, but the question of what is the actual cause of asphyxia, the CO_2 overload, or the O deficiency, is different. Practitioners have not bothered themselves with this theoretical question; they generally speak of carbonic acid intoxication, while the physiologists, especially in recent times, have often occupied themselves with the solution of this problem. The many attempts carried out by the researchers have led to different results and, as things stand now, no decision can so far be made with absolute certainty. Traube was the first to claim that CO_2 was the effective agent in asphyxial death. He tried to prove this by allowing animals to breathe H-gas and he claims to have observed here that in this gas, which is absolutely poor in O, respiration remained for a time completely undisturbed. He used this fact to prove that the cause of asphyxial death was not O-deficiency, but the overloading of the blood with CO_2. The experiments of Krause, Thiry, Rosenthal and Dohmen, on the other hand, have shown that when animals breathe pure H, violent dyspnoea always sets in, and finally asphyxia occurs. We have repeated these attempts and can vouch for the correctness of the result. For these experiments we used small rabbits, which were placed under a glass bell filled with H and sealed off with water. Here are a few examples. - In the first rabbit used, convulsions and complete cardiac arrest occurred after just 15 seconds after previous vivid dyspnoea[17]. After 50 seconds, breathing stopped; after 2 minutes, 14 weak pulses were counted, no respirations; after 3 minutes 15 pulses and 1 respiration; after 4 minutes 13 pulses and 2 highly superficial respirations. From then on, the respiration stopped completely, after 19 minutes the heart made only 3 extremely weak atrial contractions.

In a second animal, half a minute after the onset, the respiration and the activity of the heart ceased; convulsions occurred and the newly rekindled heart activity was short lived.

In a third animal, respiration ceased after 1¾ minutes, after a few dyspnoeal breaths, after the transient cardiac arrest had previously been observed. Complete death occurred after 5 minutes.

In a fourth animal, death occurred within just one minute after previous dyspnoea, convulsions and cardiac arrest. Extremely weak heartbeats, 13 in number, were observed 24 minutes after insertion.

A fifth rabbit experienced dyspnoea, convulsions and a brief-onset cardiac arrest after one minute. After 2 minutes 1 breath for 6 weak cardiac contractions; complete death after 9½ minutes with 9 barely noticeable heartbeats.

It will not be necessary to increase the number of these experiments, especially since they are in line with the experiments of the above mentioned researchers. So the manifestations of asphyxia appear very rapidly in pure H, the respiratory movements become dyspnoeal and soon cease and the cardiac contractions decrease in number in a short time to the point of complete cardiac arrest, just as with suffocated animals, in which one of us first described this phenomenon before Thiry[18]. Some researchers have now concluded from these experiments that the symptoms of asphyxia are caused by the lack of oxygen. This interpretation of the H experiment has been opposed by Thiry[19]. Even if, as this researcher claims, dyspnoea develops during H-breathing, this is explained by the fact that the H is not able to expel the CO_2 accumulating in the blood during the breathing process. He relies on the experiments of Schöffer, Holmgren and Preyer and claims that it is the CO_2 that evokes the asphyxia phenomena. We could oppose these statements in our experiments with carbon dioxide gas. When animals are placed in a CO-rich atmosphere that is poor at O, the signs of dyspnoea very soon arise. However, the CO is very well able to expel the CO_2 from the blood during the process of breathing and one could therefore assume here that in fact the O deficiency causes the dyspnoeal phenomena here. But again, we do not know whether the CO absorbed into the blood does not act directly on the central parts of the nerves in such a way that the manifestations of asphyxia become apparent. Finally Dohmen[20] has tried to solve the question. He found that when mixtures of CO_2 and O, which contained more O than atmospheric air, were breathed, the size and depth of respiration increased to twice normal. Later it drops below the normal value, but the animal remains alive for a very long time. Now, as the animal always received enough O, it is necessary to increase both and the subsequent decrease must be the effect of the CO_2. Dohmen therefore concludes that the CO_2 in these experiments excites the respiratory centre and finally has a paralysing effect. Since he now also saw dyspnoeal phenomena occurring in H-breathing, he explains himself by saying that both CO_2 and O deficiency can cause asphyxia. Although we agree with the latter view, we believe that the files on this subject have not yet come to a definitive conclusion.

Assuming, therefore, that asphyxial death is brought about by the overloading of the blood with CO_2 and by the lack of O in it, the treatment of asphyxial patients will have to be directed to impregnating the blood of the body again with O, to getting rid of its excessive CO_2. So far, we have tried to satisfy this indication in three different ways:

1) Attempts have been made to produce respiratory movement reflexively by stimulating the emotional nerves of the body, and especially directly stimulating the respiratory nerves;
2) Passive artificial respirations were performed, either by alternating compression and relaxation of the chest, or by blowing air directly into the lungs;
3) Severe blood withdrawals were made, so that a quantity of CO_2 and the O-poor blood were partially diverted from the central nerve parts.

All these experiments are quite rational and have had good results, but it is evident that we meet the indicatio causalis much more quickly, more directly and perfectly if we partially drain the blood, which is poisonous because of its abnormal gaseous content, from the body, and inject O rich again into the veins. The introduction of artificial respiratory movements, hitherto the most excellent and reliable means of resuscitation of asphyxia, works in such a way that, during the respiratory movements of the O, atmospheric air enters into the lungs and decarbonises and arterialises the blood in them. However, artificial respiration can only be effective if cardiac activity has not already been reduced to a minimum, if the heart still possesses the ability to extract the bright red blood from the lungs to the central nerve centres, whose overstimulation has caused stagnation in the vital processes. But if however, bright red blood is injected directly into the heart from the veins, it is able to revive the heart's activity, which itself has already declined. It can be seen that if we treat asphyxia with artificial respiration and with injections of O-containing blood, we are one big step ahead of the latter treatment. In desperate cases, therefore, the latter treatment deserves unconditional preference.

We have tried to confirm what has been developed here by means of very simple experiments. Rabbits, which had previously had their external jugular vein exposed, were simply killed by suffocation and then resuscitation attempts were made on them. It was shown that the resuscitation by injection of arterialised blood after abundant bloodletting was still successful in all cases in which artificial respirations, initiated in various ways, could no longer have an invigorating effect.

The importance for practice is self-evident. We strongly recommend our new method of treatment in the most urgent way for all the more severe forms of asphyxia, especially the obstetrician to save the seemingly dead newborns. First of all, give the asphyxiant a plentiful bloodletting and proceed immediately to the transfusion. It is self-evident that in these experiments one must above all have quite bright red blood. In addition, i.e. before and after the operation, the other resuscitation agents should also be used: skin irritation, faradization of the dwarf phrenic nerves, artificial respiration, removal of fluids, mucus, blood, etc. from the airways. For it is not a question of discussing at the hospital bedside which means of salvation is the most suitable, as we are to test it in the physiological laboratory, but only by striving to save life by using all the aids, the best of all. But do not wait too long with the transfusion, because from second to second the vital centres without O fall into ever greater lack of irritability.

Special attention is also to be paid to the apparent death of the newborn. It is to the credit of Pernice[21], following Schwartz's views on the manner of death of newborns, to have provided incontrovertible proof that "when a child is born apparently dead, the reason lies in the cause which prevents the free circulation and gas exchange in the placenta. Either the mother's blood quantity is too insignificant and the strength of the heart too small to supply the placenta properly, or respiratory abnormalities of the mother do not sufficiently induce oxidation in her lungs (eclampsia); or by the continued contraction of the uterus, the detachment of the placenta to a greater extent, reduction of the uterus behind the foetus, inhibits the entry of the blood to the foetal vessels, or finally, as in the case of compression, intestinal entanglement and rupture of the umbilical cord makes the access of the oxygenated blood to the child more difficult or impossible. These are the causes of apparent death."

The practitioner thus faces the same indications in the treatment of apparently dead newborns as with other asphyxias. The most excellent methods of imparting the O of the air to the blood are considered, after prior removal of mucus masses from mouth and nose, are the following: one either tries to induce reflexive breathing movements by irritation of the sensitive nerves, or one electrically stimulates the phrenic nerve and its companions at the neck (Pernice), or one blows air directly into the lungs (Guardian), or alternate compression of the thorax is effected, either directly with your hands, or by one's own body weight when rolling the body back and forth (Marshall Hall, Spiegelberg). But in the deepest forms of apparent death, where this treatment proves inadequate, transfusion remains as the last important remedy. The irritability of the medulla oblongata is much longer in young animals and probably also in humans, than in adults, as many observations have shown us. As a result, rescue is still to be expected among the seemingly dead newborns, where there may be no hope left in adults. Nevertheless, we believe that it will be good, when a seemingly dead child is born, to necessarily think as soon as possible about the preparation of bright red blood and the arrangements for transfusion. Here, too, there is a "too late", which we believe can be averted by a transfusion that can be done here without much trouble. Make an injection of half an ounce of fairly light-coloured blood into the umbilical vein and drain a corresponding amount of blood from the umbilical arteries (if there is no anaemia present). This procedure can be performed several times in succession, while other aids can be used during the breaks, as well as before and after the transfusion. We have no evidence to support the beneficial effects of this treatment of apparently dead newborns, but it would be very desirable if this remedy were first subjected to examination by the maternity institutions. For the syringe and cannula that are necessary for this purpose, see the practical part of this work.

2. Poisoning by carbon monoxide.

In our experiments, we used carbon monoxide gas (CO) as a second representative of the gaseous toxins. Before proceeding to the description of our experiments themselves, it seems necessary to discuss the effect of CO on the blood, because only after taking note of these will it be possible to clearly state the guiding aspects that our overall therapeutic interventions had in mind. - After Lothar Meyer[22] had demonstrated that the oxygen contained in the blood was not for the most part "absorbed" in the true sense of the word, but chemically bound, albeit only very loosely, F. Hoppe[23] had made it very probable by his experiments that the behaviour of CO in the blood was quite similar; this circumstance led L. Meyer[24] to subject the effect of CO on the blood to another series of investigations, and he sought, by means of the absorptiometer, to determine the amount of CO absorbed by the blood, the dependence on this quantity on the pressure of the free gas and finally the behaviour of the blood against a mixture of CO and O. In this series of experiments he came to the following very important results: he found that the amount of CO absorbed by the blood is independent of pressure, in a similar way as O, and that the CO is retained in the blood by chemical forces, just like that of O. It also emerged that the same blood shaken with CO or with O absorbs equal volumes of these gases, so that the quantities of O and CO taken up by the blood are in a simple atomic ratio, according to which it is probable that both gases are bound by one and the same constituent part of the blood. Furthermore, it turned out that the chemically bound O in the blood can be completely expelled by CO and replaced by an equal volume of this gas, so that a substance is contained in the blood, which has the curious property of connecting with both CO and O directly. The deadly effect of CO is thus explained in a very simple way by the fact that every particle of CO that comes into contact with the blood in the lungs displaces an equal volume O from the blood until the remaining amount O is no longer sufficient to sustain life. Cl. Bernard, in his experiments, found that a blood completely saturated with CO can absorb only a fifth part of O, which it is able to bind under normal conditions. As regards the ratio of the blood cell to the toxic gases, F. Hoppe has shown that outside the body they do not change their shape or colour for weeks at a time, that blood retains its bright red colour even when treated with CO_2 and O, and well as under the air pump, that even putrefaction does not immediately make it darker. Finally, Cl. Bernard has found, by observations of animals that have been intoxicated but brought back to life, that the bright cherry-red colour of the blood, which always occurs at the same time as the poisoning, eventually disappears at the same time as the toxic phenomena diminish, from which it must be concluded that either in the living body the blood cells can nevertheless gradually get rid of the CO, or that they are meanwhile perishing and newly formed ones are taking their place. Pokrowsky[25] found that, in those animals who had recovered from poisoning, the CO is indeed eliminated from the blood, but not as CO, as Cl. Bernard claimed, but is oxidised to CO_2. An animal is able, within a certain time, to burn a certain amount of CO in its blood and thus eliminate it. The danger of CO therefore depends on the content of the CO in the inhaled air, which the organism is no longer able to process beyond a certain extent. Therefore, death is more likely to occur in an animal that breathes air rich in CO than in another which absorbs a low percentage of the poisonous gas, even if the former has on the whole breathed a smaller quantity of CO than the latter.

According to these observations, CO is a poison, which adheres with great tenacity to the blood cells, which the organism may be able to gradually get rid of to a small extent, but of which we have no means of removing it from the blood. This view is of course of the greatest importance for the determination of therapeutic interventions. But it is no less important to investigate on which organs and systems of the body that the poison exerts its lethal effects. The CO does not affect the peripheral extensions of the motor and sensory nerves, as Pokrowsky has demonstrated to Ozanam for the latter, nor is the muscles themselves deprived of their ability to contract. On the other hand, the nerve centres of the cerebrospinal axis are severely prostrate and with progressive intoxication complete paralysis of the nerve centre gradually occurs. Unconsciousness and coma occur; the voluntary movements are impossible. The reflex action is impaired and later abolished, the respiration becomes less frequent and finally ceases completely as soon as the medulla oblongata is drawn into the paralysis, the cardiac contractions are indeed slowed down, but they are relatively little disturbed, as long as the general paralysis does not occur with death. But a phenomenon in the realm of circulatory processes is of importance; it is the extraordinary drop of the pressure in the arterial system, the low filling of the left heart and the arteries in general. Pokrowsky assumes that the reason for these phenomena, which he has studied in more detail, is the paralysis of the cerebrospinal centre of the heart. However, since such a cardiac nervous system does not exist, we are referred to another explanation. This is apparently the paralysis of the spinal centre of all vascular vessels. Goltz has provided proof that this is due to the phenomena here described: the blood pressure decreases as the tone is abolished, the blood accumulates in the veins, there is a lack of the tonic tension of the vessels that it is supposed to supply the heart, and as a consequence the heart works laboriously, slowly, like a pumping mechanism lacking an object for its removal. It is evident that with such impaired circulatory activity the onset of paralysis must be promoted and we will see how efforts have been made to counteract CO poisoning therapeutically from this side.

Since, as can be seen from the above discussions, the harmful effect of CO is the fact that it forms a chemical bond with the haemoglobin of the red blood cells, thus making it impossible to absorb O into the blood, since we still have no means of removing the toxic gas from the blood, the indicatio causalis of this intoxication is obviously met in a direct manner if we substitute a new O-containing blood in place of the CO-containing blood. For this purpose, blood was alternatively drained from animals poisoned by us and new O-containing blood was transfused from the same animal species. The results were very favourable, in that animals which had fallen into the deepest intoxication were completely restored by this treatment in the shortest possible time.

The experiments were carried out in such a way that the animals (rabbits) were placed under a glass bell jar, which had a capacity of about 10,000 cc and which was filled with a mixture of air and $^1/_{12}$ - $^1/_6$ CO. A still more abundant content of CO was avoided because the animals succumbed to death too rapidly in such an atmosphere. The CO itself was made from oxalic acid with sulphuric acid and carefully washed out with acetic potassium. The animals remained under the bell jar, under which a potash vessel was kept ready to absorb the excreted CO_2 until they fell over under the sign of general paralysis, often after previous convulsions and urinary and faecal passages, when they became respiration-less, which was usually the case after 2-8 minutes. They were then taken out and resuscitation attempts were made. In all these cases, we were able to directly demonstrate the intensive absorption of CO by the exquisitely light cherry-red colour of the blood flowing from the veins. None of the animals recovered of their own accord in the open air, or with the application of abundant venesection, or by initiating artificial respiration, either by direct injection of air into the trachea, cut and connected to a bladder bellows, or by faradic irritation of “the phrenic nerve and its comrades" in the neck. The following experiments may serve as evidence:

Experiment 1: A small grey female rabbit is placed under the glass bell jar, which is filled with a mixture of atmospheric air and CO to equal parts. Almost immediately after being placed into the cylinder, the animal collapses, but at first it still respires as normal. After barely 2 minutes, violent dyspnoeal breathing movements occurred, the pupils dilated, individual twitches. After 3½ minutes, the animal is removed, has respiration-less and has weak decreased heartbeats. It is taken out to the open air, but does not recover. The dissection showed a strikingly bright cherry-red colouration of the organs (liver, lungs, heart and muscles) and the blood in the right heart and the large veins, which could not be distinguished in their colouration from the vascular arteries.

Experiment 2: A small black rabbit is placed under the aforementioned glass cylinder, which is filled with CO for $^1/_6$ of its space, and with atmospheric air for the rest.

(9hr 55m) After ½ minute, the animal falls onto its side, gets individual convulsions, shows diminished respiration activity, initially dilated, later narrower pupils.

(9hr 59m) The animal, which has breathed only rarely and superficially, is taken out. The same shows (on the acupuncture needle) diminished activity. Immediately the faradization of the phrenic nerve and its comrades in the neck is carried out.

(10hr 3m) Since the faradization is without influence, the trachea is cut crosswise, and a tube connected with a bellows is inserted and thus direct air injection is made. No visible success; the animal no longer able to make spontaneous respirations, although the heart continues to pulsate.

(10hr 15m) At the time of the animal's death, which was already in an incipient rigor mortis, very bright cherry-red blood was found in the right heart and in all the vessels and organs.

If, on the other hand, the animals that had been poisoned in a similar way were injected with new O-containing blood after the CO infected blood had previously been partially removed by bloodletting, the best result was shown. Of our four rabbits, three recovered completely, the fourth also revived, but died about 20 minutes after recovery (which, among other things, was also recognizable by a normal blood colour) from quite unclear causes.

In these cases, the transfusion was combined with a significant depletion, and was carried out in a manner that can best be described as a flushing out of the blood, or with Panum as a substitution of the blood. We did so in the following manner: before the animal was placed under the glass bell jar filled with the poisonous gas mixture, we had exposed the external jugular vein on one side and placed two loops of thread at a distance of about 10 mm. When the animal placed under the bell jar had been subjected to a sufficiently deep anaesthesia, it was brought out, placed on its back, the central thread loop tightened and the bristling vein between the two loops was opened. After a plentiful bloodletting had been made, the central noose was loosened again whilst the peripheral one was tightened, so that the bleeding stopped naturally. The cannula of the filled syringe was quickly inserted through the opening of the bloodletting and an injection was performed against the heart. The injected blood had previously been drained from another healthy rabbit, defibrinated and arterialized by beating, as well as filtered by a fine linen cloth and heated to 30°R. After a short interval, a new depletion with a subsequent transfusion was performed, indeed at several intervals again and again, until the animal had fully recovered, until the venous blood, which had previously been light cherry-red, had regained its normal dark blue colour, in other words, until the poisoned blood was completely replaced by a more normal, arterial one. Once this was achieved, both loops of thread were each tied into a ligature and the small skin wound was united by means of sutures. The amount of blood injected was 24 to 31 grams, which is about $^{1}/_{30}$ to $^{1}/_{40}$ of the body weight; - the quantity emptied by the venesection was at least as much, and usually a little more, since a little blood loss is endured without harm. We chose the same jugular vein for bloodletting and transfusion, not one side for bloodletting, and that of the other side for injection, which might seem expedient, because the necessary connection of these two largest jugular veins would lead to significant circulation disorders in the brain, since, as it is well known that the internal jugular veins and the vertebral veins are significantly less developed in rabbits and dogs, than the external jugular veins. It can be assumed, however, that in the case of the one rabbit which died suddenly after the operation had been performed, and in which both external jugular veins had been tackled in the manner just indicated, death was partly caused by the disturbed circulation in the brain. As evidence of the above arguments a few experiments may be given:

Experiment 3: The right external jugular vein of a large white female albino rabbit is exposed and a double noose is pulled underneath. A large black rabbit is then subjected to a copious bloodletting from the left external jugular vein, the blood is defibrinated, arterialised, filtered and stored at 30°R. (4hr 7m) The white rabbit is placed under the glass bell jar, which is filled with 1 part CO and 6 parts of atmospheric air. At first the animal sits quite comfortably, after ¾ of a minute, violent convulsions occur; the animal then falls limp on the right side and becomes asphyxial. (4hr 9m) The rabbit is removed and the vein between the two loops is opened wide for bloodletting. The syringe is then immediately inserted and gradually, with repeated interruptions, with almost two syringes full of blood (i.e. about 31 grams) are infused, in the meanwhile blood has been alternatively drained, which at first presents a very bright red, then gradually an all round darker colour.

After the transfusion is completed, double ligation of the vein and suture of the skin sore. The animal has fully recovered, immediately walks around, sits on its hind legs, cleans and licks away the bloody spots, shows good appetite and complete well-being for several days afterwards.

Experiment 4: In a large male albino rabbit the right external jugular vein is exposed, provided with two loops, and then the animal is placed under the bell, which has been filled with 1 volume CO and 11 volumes of atmospheric air.

(3hr 43m) After insertion, the animal initially sits upright, breaths well; gradually the respiration becomes superficial and accelerated; the initially constricted pupil is greatly dilated. After 5 minutes, the animal is very apathetic, but still excitable under pressure; then convulsions occur, the respiration becomes most weak and imperfect and the animal falls over onto its side.

(3hr 51m) The vein of the removed animal is opened and 1½ syringes of well prepared blood are introduced in batches, with alternate depletion. The animal recovers completely, and after the ligatures and sutures have been applied, runs around quire cheerfully.

In addition to these two successful attempts, which we do not want to multiply, there should also be found a place for the unsuccessful one.

Experiment 5: The above mentioned bell jar is filled with a gas mixture of 1 volume CO and 7 volumes of atmospheric air. Both external jugular veins are exposed and a noose is threaded under each one. Then blood is extracted in plentiful quantity from a large female white rabbit taken from the opened right outer jugular vein and prepared for transfusion. –

(3hr 41m) The experimental animal was put under the bell, sat quite still at first, gradually began to sway everywhere, then developed severe clonic convulsions and fell over after two minutes.

(3hr 43m) The animal is removed and immediately injected with 2½ syringes into the left jugular vein, while shortly before and at the same time blood was drained from the opened jugular vein. The blood was drained three times at short intervals and also infused three times; the drained blood was initially light cherry red at first, gradually darker in colour. The two veins were then cut and the neck wounds were united by sutures. The animal initially recovered, breathing strongly as normal; suddenly (4hr) it became restless, got clonic convulsions and died (4hr 5m). The dissection showed the veins of a normal colour, containing a lot of dark coloured and remarkably frothy blood, as well as the heart. Brain moderately bloody.

In the light of the studies communicated, there can no longer be any doubt that in CO poisoning the substitution of a normal arterialized blood in place of the infected blood should be regarded as a first-rate remedy. Particular emphasis should be placed on the fact that the substitution should be as comprehensive as possible. In the more severe cases, therefore, a one-off bloodletting and subsequent transfusion will not be enough, but this procedure will have to be carried out repeatedly, as our severe cases of poisoning show. Only for milder cases can such a one-time treatment suffice. - In dogs that can generally withstand much more than rabbits in such experiments, Kühne has already achieved very good results of resuscitation after the single transfusion with simultaneous depletion, and indeed in cases where bloodletting and artificial respiration were no longer successful, and in which breathing itself had been interrupted for up to seven minutes. (Centralblatt für die medizinische Wissenschaften. 1864. No. 9)

However, the experience with experimental animals now allows an unconditional transfer to humans. Since the transfusion with the necessary cautel is a completely relatively safe and harmless operation, the substitution, the flushing out of the blood in CO-poisoned people, should be applied in the first place. In our opinion, substitution should be taken immediately in all poisonings by CO or luminous gas in which the sensorium has already been dazed or even in a coma. The longer the wait, the more abundantly the CO, which adheres tenaciously to the blood cells, will be able to exert its pernicious influences on the central nerves. Too often, slowly but surely, in the course of apparently not at all serious cases, the paralysis of the nerve centres occurs, and when pulmonary oedema and unproductive irregular breathing have occurred, then often enough the transfusion will certainly come too late. It will therefore be important to ensure that the greatest possible amount of blood is obtained immediately and, once it has been prepared, to proceed towards early substitution as soon as possible. If we were able to deprive the blood of its CO as it left the vein, a lot would be gained in practice by infusing the purified blood again. Unfortunately, we do not have a means to do this, because of the intimate chemical consolidation of CO with the haemoglobin, as F. Hoppe has taught us, and as Kühne recently confirmed against Eulenburg, since the CO-containing blood still retains its red colour even until it is rotten. However, we should continue with the procedure of substitution until physiological and chemical indications show us an energetic reduction in CO in the blood. We have no doubt, from our experiments with heavily poisoned animals that substitution will soon become documented by an improvement of the vital processes. On the other hand, we can also conduct a very practical chemical control. A blood in the veins that is bright red warns us to continue the substitution. In addition, it is possible, from time to time, to chemically test of the drained blood by means of caustic soda. If normal defibrinated blood is mixed with an equal amount of caustic sodium hydroxide, a dirty greenish mucilaginous mass is created, whereas a blood rich in CO treated in the same way provides a thick mass of a light red colour. If the gradually drained blood is treated in this way and, in addition to normal blood, is held and compared in test tubes next to each other, signs can be obtained from this for the continuation or cessation of the operation. We repeat: a simple transfusion after previous bloodletting will be insufficient in many cases. Last year, the daily press gave a brief report of a case of the latter kind, which is said to have been carried out by Messrs Drs. Sommerbrodt and Schiffer with initially apparent success. However, the patient after the unmistakable initial improvement, as we have learned from private communications, died soon afterwards.

In addition to substitution, which is therefore to be applied in the first place, the use of irritants as an adjuvant finds a legitimate position: cold waterings in a warm bath, rubbing with irritating substances, furthermore the faradization of the phrenic nerve and its comrades, as was used by Ziemssen with such fine success. In addition, the therapeutic procedure may extend to another side. Klebs and Pokrowsky have pointed out the strong dilation of the vessels in CO poisoning, which, as we discussed above, may encourage the occurrence of paralysis of the nerve centres due to the impairment of normal circulatory conditions. From this point of view, ergotin can be used, probably preferably subcutaneously, from which it can be assumed that it brings the vascular walls to contraction. Electrical irritation of the skin and application of cold will not be without success in this direction. But it should be noted that all these means are to be regarded only as adjuvants, as the principle remedy we recognize is substitution.

3. Poisoning by chloroform and ether vapours.

In view of the extraordinary frequency with which chloroform is used, especially in the fields of surgery, obstetrics and internal medicine, it is not surprising that occasionally accidents are observed with abundant administration of the anaesthetic: sudden death under anaesthesia. The examinations of the blood by animals killed by ether or chloroform have taught that both narcotic substances can be detected as such in the blood and it is therefore most likely that these substances, apart from other decompositions, which may also occur in the blood, have a fatal effect by the fact that the blood is too abundantly impregnated with them, as a result of which a paralysis of the vital centres must set in. In addition, it has been repeatedly observed that in humans and animals recovering from anaesthesia, not inconsiderable amounts of ether and chloroform vapours are exhaled from the lungs until the intoxication symptoms disappear. At the instigation of Privy Councillor Bardeleben, we have included ether and chloroform poisoning into the circle of our investigations. Dogs and rabbits were anaesthetised as deeply as possible by inhaling chloroform and ether vapours until only isolated superficial breaths were performed; then the poisoned blood was drained from the vein and new O-rich was injected again. It turned out that the anaesthesia was lifted in the shortest possible time and the regulation of the vital processes was restored. Some examples may serve as an illustration.

Experiment 1: A medium-sized brown and white male dog (who had previously served Professor Budge in his experiments on the bladder movement to show contractions of the bladder as a result of irritation of the pedunculi cerebri by means of needle electrodes inserted through the skullcap, and had fully recovered), had the left external jugular vein exposed. It was then anaesthetised by chloroform inhalations: 5hr 12 m.

(5hr 45m) Complete anaesthesia, cornea insensitive; respirations deep, 44 per minute, a little irregular.

(5hr 46m) Respiration 80, snoring and very superficial.

(5hr 47m) Respiratory movements only sporadic, superficial and rattling; - a plentiful bloodletting is made from the external jugular vein and after that a syringe of fresh bright red blood is injected against the heart as quickly as possible. Even during the injection, the breaths become deeper.

(5hr 48m) For the second time blood is drained and a second syringe of blood transfused.

(5hr 49m) Repeated bloodletting; third transfusion of a full syringe.

(5hr 50m) The fourth syringe is injected after previous blood drainage. The animal is again completely restored to its senses, twitching and whimpering during the injection.

(5hr 51m) Blood is drained again and the fifth syringe full of blood is injected. Ligation of the vein; suture of the skin wound. The animal is untied and laid on the ground, tries to get up and run around, but is hindered by the weakness of his hind limbs and makes only lateral rotational movements. The animal is perfectly sane, shakes its head and scratches the wound with its hind paws.

(5hr 55m) The animal, now fully recovered, runs around the room.

This experiment proves that the transfusion of O-rich blood with simultaneous depletion in a deeply anaesthetised animal can revive the respiratory movements close to extinction in the shortest possible time and can make the complete anaesthesia disappear in less than four minutes.

A second experiment will be reported below, in which anaesthesia was removed from a rabbit deeply anaesthetised by ether, by means of dog blood drained from the carotid artery.

Experiment 2: A large white female rabbit. Carotid blood of a large strong dog kept in readiness.

(6hr 4m) The exposed left jugular vein is cut; the transfusion cannula is tied into the central end, the peripheral is kept closed by a clamping tweezers: inhalation of ether.

(6hr 12m) Respiration very frequent, stertorous, with deep whistling tone during inspiration. With strong pinching of the mouth, the animal still shows reaction, screams and makes convulsive movements.

(6hr 15m) Likewise, respiration very frequent and superficial.

(6hr 17m) Respiration extremely weak and superficial, partially suspended; the animal is absolutely insensitive. Removal of the ether cloth, bloodletting; transfusion 1 syringe of dog blood; new bloodletting of corresponding size.

(6hr 19m) Second syringe transfused. During the injection, sensation is already shown again; the respiratory movements are much more productive and less frequent.

(6hr 20m) After another blood drain, the third syringe is emptied into the vein, with a hissing sound announcing the entry of air into the veins.

(6hr 21m) Another half syringe is infused. Ligature; suture. Respiration good; normal sensation, reaction to stimulus.

(6hr 24m) The animal is laid on the ground, but makes no movement; respiration weaker.

(6hr 28m) The respiration stops for about 30 seconds, then returns, but only sporadically, weakly and irregularly.

(6hr 30m) Death of the animal.

When the immediately employed dissection was carried out, the heart was still vividly pulsating, in the right atrium there are some air bubbles and adjacent to them in the ventricle abundant coherent blood deposits. –

This experiment is interesting in that it shows that the blood of an alien species is also able to eliminate very deep ether anaesthesia with impairment of the respiratory movements in a very short time. It was produced despite the entry of air into the veins, to which the animal had to succumb soon afterwards.

Thus, since the transfusion of a normal O-rich blood with simultaneous depletion of the poisoned blood has a decisively revitalizing influence in the case of intoxication with chloroform and ether vapours, by quickly reversing sensitivity, as well as rekindling the disturbed respiratory activity, we do not hesitate to propose the procedure of depletory transfusion in the event of an accident during chloroform or ether anaesthesia. Here too, it is also the means which most fully corresponds to the indicatio causalis (just as in the case of intoxication by carbonic acid and the lack of oxygen) - and which is one weighty step ahead of the irritation of the nerves and the artificial respiration. Therefore, one does not want to lose a long time in the threatening cases of asphyxia in chloroform or ether anaesthesia due to the above-mentioned treatment methods. It is best to immediately prepare everything for transfusion, to perform artificial respiration during the preparation, to clean the mouth of mucus, to pull out the tongue, to apply skin stimuli, to make (if the patient does not already begin to recover) a strong bloodletting and conclude the immediate transfusion. The procedure must be repeated depending on the circumstances. Before and after the operation, as in the breaks, of course, other resuscitation agents find their deserved application.

However, the rescue of chloroform and ether poisonings by the depletory transfusion even to a certain extent finds the limit of its revitalizing effectiveness. If a dog continuously breathed chloroform vapours for more than a quarter of an hour, with limited access to atmospheric air, even when during the last few minutes only sparse sobbing, extremely superficial diaphragm convulsions occurred, until finally the respiration movements, always taking place in larger intervals, stopped completely, even a copious and often repeated depletory transfusion had no more success. But it can be assumed that in humans, to such a degree, the administration of the anaesthetic will never continue to such a degree.

4. Poisoning by morphine and opium.

Morphine appeared to us to be a very suitable poison, in which to observe the favourable results of the substitution of a normal blood for one mixed with the poison because of its concise symptoms of poisoning. We chose the most acute form of poisoning, the direct infusion of a morphine solution into the venous system. This form of poisoning is evidently by far the most dangerous, all other things being equal, since the entire mass of the toxic substance is able to act immediately on the central parts of the nervous system. The situation is different with the subcutaneous application or with the administration from the primary routes. Here, only a portion of the total dose is able to gradually entre the circulation by absorption, the effect will develop much slower, gradually and with increasing vehemence, and the physician will gain time. If, therefore, we succeed in providing assistance by our measures in the most acute and violent forms of poisoning, we can assume that a favourable success can be expected in the slower forms, which are much more frequent in practice. There is only one self-evident difference here: whereas with the direct transfer of the poison into the bloodstream it is necessary to substitute a new normal quantity of blood as quickly as possible in place of the blood mixed with the toxic fluid, in the case of the gradual absorption of the poison, one will proceed to substitution only temporarily and intermittently, and always when more threatening phenomena suggest to us that a considerable amount of poison is again accumulated in the blood. It is precisely these slower poisonings that require special attention from the doctor and one will also have to have a fairly significant amount of blood available at ones disposal.

In order to be able to arrive at a correct judgement by experiments on animals about the beneficial effect of substitution, the flushing out of the bloodstream with normal blood, it is of course necessary to apply such high doses that they either already have a lethal effect, or that they at least lead to severe, concise intoxication symptoms. And indeed it has been shown that in the most acute form of morphine poisoning, the effect of substitution is quite favourable, as subsequent experiments will show us.

Two 1-year-old yellow-grey female butcher dogs, which are of the same litter, size and same good diet, are taken for the experiment.

To the first of these dogs (a) the right external jugular vein is exposed and a noose is placed under it, opened, and then 60 drops of a solution of morphine hydrochloride (gr. j ad 3j) is injected into it towards the heart. This vessel is then stopped. The injection is finished at 3hr 39m; after lively cries and some twitching, the animal falls into deep sopor half a minute later. After it has been untied it falls comatose onto its side and remains motionless on the floor of the room in the deepest anaesthesia.

Twelve minutes later, the second dog (b) is given the same infusion (3hr 35m). After barely a minute it was also in a deep sopor. Blood is then drained from the peripheral end of the vein and then a syringe full of normal blood is transfused towards the heart. The blood used for this had previously been drained from the carotid artery of a strong dog, beaten, filtered and kept warm. Draining of blood from the peripheral end of the vein and injecting it anew into the central piece is then repeated alternately at short intervals.

(4hr) Even after three syringes have been given, and as much poisonous blood has been drained, a very noticeable difference between the two animals appears.

Dog (a) seems to be lying there as if dead, with weak and rare respirations (12 in 1 minute), but shows the characteristic excitability for sounds, as specified by Cl. Bernard, by accompanying every louder noise, stronger appearance and the like with a shrug of the body and then sinking quietly down again.

Dog (b), which was just as anaesthetised at first, has its eyes open, often spontaneously moves the eyelids as well as the head, and has stronger and more frequent respirations (33 in 1 minute).

(4hr 6m) A total of 6½ syringes of normal blood have been infused into dog (b) and a corresponding amount of blood has been drained from it. The vein is now stopped above and below the opening, the wound at the neck is united by means of sutures and the animal is released.

(4hr 10m) It immediately walks around the room at a strong rate and apparently quite normally. The resulting noise startles dog (a), which until then had been lying on the right side with outstretched legs deeply stunned for more than 21 minutes. It straightens up and tries to escape as well. It clearly shows the hyena-like gait described by Bernard (clear paresis of the hind limbs and the whole posterior body) and generally displays a tumbling, uncoordinated action. A further difference can be seen when the pupils of both dogs are examined, they are a very constricted in dog (a), but quite dilated in (b), as under normal circumstances. Released again, dog (a) falls powerless on its side in the middle of the room after a short staggering run and remains in this position in the deepest stupor, - the dog (b) on the other hand crawls under a locker, sits there upright with open, straight-directed, anxious lurking eyes, pricked ears etc., and seems only somewhat offended, but without disturbances of intelligence, without paralysis and without anaesthesia.

(5hr) The dog (a) still much more deeply stunned than dog (b); pupils as above.

(5hr 30m) Dog (a) is still lying on its side; shaken up, he walks restlessly around the room with a pitiful howl and finally collapses again after running back and forth several times. Dog (b) sits under the locker, but as soon as the room door is opened, he runs out of it; his gait shows nothing abnormal; in progress, the animal is also somewhat sluggish and powerless, because on the whole, a little more blood was withdrawn than was injected again. There is no trace of the instability, the restlessness, the howling in this animal; it behaves quite similar to a healthy one.

The following morning both dogs show the same and normal behaviour.

The experiment presented is such a striking one that we feel presumptuous to report further experiments of this kind.

In addition to morphine, we have also done experiments with opium of a very similar type as the above, namely on rabbits with the tinct. Opii simplex. The method of substitution also showed itself in a favourable light, in comparison with different chosen doses of this poison, which was also injected into the veins, in that it was able to moderate the duration and intensity of the intoxication phenomena, as could be seen from comparatively equally poisoned animals, to which the substitution was not made. It will not be necessary therefore to present in detail experiments of the kind, which in their entirety, bear a great similarity to the morphine experiment.

However, at a dose of 60-90 drops (of the freshly prepared opium tincture), the transfusion with bloodletting, which was carried out as quickly as possible after the infusion, no longer provided any saving help in our rabbits. Almost immediately after the injection of the poison, or a few seconds after it, tonic convulsions of the whole muscles of the body occurred, so violently that there was a loud audible muscular sound, and the animals, even if fresh blood was injected during the convulsions and the poisonous blood was drained, a rapid asphyxiate death occurred. Here we have just crossed the border of the still possible rescue from death by poisoning.

5. Poisoning by strychnine.

In the case of strychnine poisoning we have also tried to investigate the effect of depletory transfusion in a series of experiments. All experiments were carried out on dogs and the poison was administered subcutaneously in an aqueous solution (different strength doses of a solution Strychnii nitrici gr. ij ad Aq. distill. 3ij). Strychnine has to very violent effect on dogs: after only $^{1}/_{96}$ grain a 10-day-old dog of a vigorous breed developed pronounced convulsions, which reached their climax after a ¼ hour, but gradually died out over the course of an hour, without the animal succumbing to death.

When an 8-week-old large strong butcher dog was given $^{1}/_{32}$ grain, we saw the dog fall down after only 2 minutes under the most violent tonic convulsions and died after only 5½ minutes after a previous urinary outflow.

Experiment with transfusion: A double dose was then administered subcutaneously to an adult dog of the same type, $^{1}/_{16}$ grain, after it had been untied and the femoral vein prepared for transfusion.

(3hr 25m) Injection of the poison.

(3hr 27m) After a depletion transfusion of a syringe of fresh dog blood. Stiffness of the extremities, incipient extensor convulsions.

(3hr 29m) Reflex action is significantly increased, after each touch tetanic stretching of the whole body; - second syringe injection after a precious corresponding depletion.

(3hr 30m) Third syringe.

(3hr 30½m) Fourth syringe. The twitches have increased in intensity.

(3hr 32m) Fifth syringe. Extremely violent general convulsions.

(3hr 33m) The convulsions persist, urine is excreted. The venous blood squirts in a strong stream during depletion. – Sixth syringe.

(3hr 34m) Seventh syringe.

(3 hr 35 m) Eighth syringe.

(3hr 36m) Ninth syringe. The convulsions appear to subside during the continuous depletory transfusion.

(3hr 38m) Tenth syringe.

(3hr 40m) Eleventh syringe. Only a few individual twitches. Respiration good.

(3hr 41m) Twelfth syringe.

(3hr 43m) As the convulsions increase again, two more syringes are transfused after a more plentiful depletion.

(3hr 45m) Fifteenth syringe.

(3hr 45½m) Sixteenth syringe.

(3hr 46½m) Seventeenth syringe. As a result of the more frequent transfusions, the twitches, even with direct irritation, are only weak.

(3hr 48m) Eighteenth syringe.

(3hr 50m) Nineteenth syringe. The dog lays very still, the respiration quite undisturbed.

(3hr 52m) Twentieth syringe. Reflex excitable is only slightly increased.

(3hr 56m) Twenty-first syringe. Only isolated twitches on stimulus.

(3hr 58m) Twenty-second syringe.

(4hr 2m) Twenty-third syringe.

(4hr 3½m) Twenty-fourth syringe. No change in well-being.

(4hr 6m) Twenty-fifth syringe.

(4hr 7½m) Twenty-sixth syringe.

(4hr 10m) Twenty-seventh syringe. Only single twitches on direct irritation. Respiration good.

(4hr 12½m) Twenty-eighth and twenty-ninth syringes.

(4hr 17½m) Another slight depletion.

(4hr 20m) Since the animal does not present any frightening phenomena, the vein is stopped, the skin wound is stitched and the animal untied. As soon as the animal is released, the most severe general convulsions occur almost suddenly, urine is sprayed out in a stream and the death occurs with great rapidity at 4hr 25m.

The favourable effects of depletory transfusion are undeniably evident in this case, in that not only are the convulsions repeatedly reducing and alleviated, but life could also be maintaining for a whole hour at a decidedly lethal dose. In the case of the aforementioned dog, death occurred after only 5 minutes and the dose was only half as strong. Furthermore, there is no direct reason not to assume that the dog would have escaped with life if the transfusion had continued in the manner in it had begun.

In another medium-sized strong dog, we succeeded in keeping the animal alive for 25 minutes with the use of depletory transfusion, despite the subcutaneous injection of ¼ grain of strychnine. Christison, on the other hand, claims to have poisoned a dog within 2 minutes with $^{1}/_{6}$ grain. (Re-adsorption from the thoracic cavity.)

In another medium-sized strong dog, we succeeded in keeping the animal alive for 25 minutes with the use of depletory transfusion, despite the subcutaneous injection of 1/4 grain of strychnine. Christison, on the other hand, claims to have poisoned a dog with 1/6 grain within 2 minutes. (Absorption from the thoracic cavity.)

However, there is one more point that deserves special attention in strychnine poisoning. The amount of strychnine that is required to produce general convulsions and death has certain definite limits in humans and animals, but within these there are not insignificant fluctuations depending on the individuality of the poisoned person, as Christison has already pointed out, and as we can confirm after our experiments. Thus, for example, according to Christison, it is beyond doubt that ½ grain of strychnine, placed into a wound, can kill a man in less than an hour. Often, however, on the other hand, much larger doses are tolerated (internally) and one has even dared to give the strychnine up to 2 grains, without in some cases having caused more than the milder degrees of poisoning. In addition, it should be noted that with strychnine, just as in the case of digitalin, there is a habituation that takes place to this poison in the body. Therefore, in experiments on animals, it is appropriate to take absolutely lethal doses and then to study the effect of depletory transfusion on them. If, therefore in the aforementioned experiment, Christison states that dogs die within 2 minutes after subcutaneous application of the poison in a dose of $^{1}/_{6}$ grain, which was made at an even stronger dose ($^{1}/_{4}$ grain), must certainly show the depletory transfusion in favourable light.

We therefore believe that we are justified in proposing depletory transfusion in cases of strychnine poisoning. It will have to be continued according to the degree and severity of the phenomena until it can assumed that the adsorbed poison has decomposed or has been excreted in the body, or until the symptoms of poisoning have been reduced to modest limits. The fact that one should also make use of the antispasmodic antidotes: morphine, atropine, aconite, hyoscyamus, namely worrara (subcutaneous in strong doses) and under certain circumstances one may also have to resort to the gastric pump and other aids, probably does not require any special elaboration.

III. Transfusion in artificial inanition and lack of food.

Warm-blooded animals, which are subjected to a persistent inanition, are known to show a steadily progressive reduction in body weight from day to day, and die when the total weight loss (the "relative integral loss" according to Chossat) exceeds an aliquot part of the original body weight. The experiments that Chossat[26] and after him especially Bidder and Schmidt[27], on the metabolism of starving animals are well known. Death generally occurs at $^{2}/_{5}$ (Chossat) or slightly above ½ (Bidder) of the original body weight; however, the ratio is however highly variable not only for different animal species, but also for animals of the same species according to individuality and age.

The weight loss of starving animals is due to the decomposition of their tissues, which are burned in place of food to meet the animal's constant functional needs. If the starving animal is injected with a quantity of blood capable of functioning and at the same time capable of being preserved (i.e. O-rich blood of the same animal species), then the ratio in some respects is apparently analogous to that in the case of renewed importation of food, in that the transfused blood is directly taken up by the parts capable of being consumed, and therefore the measure of the body substance to be burned is likely to be proportional to the amount of combustion substrates imported from outside. This reduction can only be temporary in the case of a single transfusion; however, it may become permanent if, by frequent repetition of transfusion at certain intervals, analogous to regular food intake, the body is supplied with a sufficiently combustible substance in sufficient quantity. It therefore does not seem impossible to reduce the daily (absolute and relative) weight loss in starving animals through repeated transfusion, and to maintain life for a longer period of time.

On the basis of these premises, we undertook a number of experiments on starving mammals, using transfusion in the manner just defined, as it were, as food. We made the first series of experiments on rabbits - but discovered very soon that these animals are not suitable for the intended purpose, because apart from the inanition - they seldom survive three or four transfusions, especially performed via the jugular veins, but as a rule soon perish through diffuse phlegmons, pus reductions and feverish general suffering. Accordingly, most of the rabbits we used for the inanition experiments died on the 6th or 8th day after the start of the experiment. A better result was obtained in a dog, on which the regular repetition of the transfusion could be continued for a longer period of time.

A small female dog, about 1 year old, of 3970.2 grams body weight (weighed in the morning before eating), got neither food nor drink since the morning of 20 August. It lost 63 grams on the first day, 82 on the second, 95 on the third, 107 on the fourth, 99 grams on the fifth, and after a little over five days (total 126 hours in all) of fasting weighed 3502.7 grams, i.e. 467.5 grams less than at the beginning of the experiment. - On 25 August, at 3 o'clock in the afternoon, 30 cc of defibrinated (light red) and warmed blood of another dog were transfused in the dividing branch of the right jugular vein (V. facialis comm.). We deliberately chose this high-placed location in order to be able to continue to use the central part of the jugular vein for the operation. The vein was cut off, the skin wound was stitched. The animal was apparently livelier after the transfusion than before, and moved around the room with great cheerfulness. Weight loss in the following 48 hours totalled 135.5 grams (i.e. an average of 67½ grams per day). On both days, repeated emptying of faeces. On 27 August (at the same time of day) a second transfusion was given, with the same dose, at the left common facial vein. - Weight loss in the following 48 hours 131 grams (average 65½ grams). On 29 August a third transfusion of 45 cc of blood into the right jugular vein as high as possible, just below the confluence of the common facial vein. - Weight loss in 48 hours = 205 grams (average 102½ grams). 31 August: fourth transfusion (45 cc) into the left jugular vein, at the same height. The neck wound on the right is suppurated. Weight loss in 48 hours = 143.6 grams (average 71.8 grams). - 2 September: fifth transfusion (66 cc), which, since both neck wounds are festering, is performed on the left femoral vein. The wound, as usual, is sutured. In 48 hours, weight loss is only 77.6 grams (average 38.8 grams). - 4 September: sixth transfusion (45 cc). The operation was first attempted on the right epigastric vein, but failed because the introduction of the cannula presented difficulties and the lumen of the very fine cannula, which was finally brought in, became blocked, so that the blood flowed only partly by. It was therefore necessary to return to the external jugular vein, in the granular wound and used in its lowest part (near the upper thoracic aperture) for the transfusion. Weight loss in the following 48 hours = 94 grams (average = 47 grams). - 6 September: seventh transfusion (90 cc) at the central end of the jugular vein. - Weight loss in 48 hours 172.4 grams (average 86.2 grams). The animal is relatively cheerful, especially immediately after each transfusion; the neck wounds on both sides fester abundantly. - 8 September: eighth transfusion (83 cc) at the right femoral vein. Weight loss in 48 hours = 164 grams (average 82 grams). - 10 September: ninth transfusion at the left femoral vein (105 cc). The right thigh wound is festering. Weight loss in 48 hours = 98.5 grams (average 49¼ grams). - 12 September: tenth transfusion at the right femoral vein near the trunk (60 cc). - The left thigh wound also in suppuration; the animal is already very feeble before the transfusion and does not recover after the transfusion and dies in the evening at 7 o'clock, i.e. within the 24th day after the start of the experiment. - The dissection performed the following morning revealed relatively abundant blood in all organs, nowhere the manifestations of phlebitis, embolism or metastatic herds; intestinal canal completely empty, in the stomach a lot of brown, mucous bile; liver of normal colour and consistency, without a trace of fat metamorphosis; in the gallbladder a lot of bile of the same quality. Nothing abnormal in the heart and lungs either.

So the dog starved for 24 days; during this time (from the 6th day onwards) a transfusion was carried out regularly at 48 hour intervals, ten times in total; the weight of the blood introduced in this way was 606 grams in total, i.e. an average 60.6 grams = about $^{1}/_{5}$ of the (original) body weight of the animal. The absolute integral weight loss was 1744.6 grams, i.e. 39 percent of the total weight. If we calculate the average value for one day, we get 72.7 grams (= 1.8 percent of the total weight) for the absolute daily loss. However, the above figures revealed very significant fluctuations in the absolute daily loss and in relation of the same to the total weight. In the first five days, when no transfusion was performed, the dog lost an average of 93½ grams = 2.4 percent per day of total weight; in the next 19 days, when transfusions were carried out at regular intervals, the daily loss fluctuated between 47 and 102½ grams, and averaged 66⅔ grams per day, = 1.6 percent per day of the total weight.

There is therefore a significant decrease in weight loss in favour of the time when combustion substrates were supplied from the outside by the transfusion. The cause of the difference cannot be found in the food residues emptied during the first days, since the dog repeatedly emptied faecal masses even after the initiation of the transfusions (beyond the 6th day); neither can the direct increase in weight due to the injected blood be considered, since the total weight of it, distributed over the day, by no means compensates for the differences in absolute daily looses, and moreover, was almost compensated for by the (albeit small) blood loss associated with the operation and the subsequent suppuration of the transfusion wounds.

We would like to place less emphasis on the minimum losses observed between the 5th and 7th transfusion, since Chossat also saw the lowest relative loss values during the middle of the fasting, whilst the strongest were at the beginning and end of fasting.

The fact that the dog lived without any solid and liquid food is in itself, if not unheard-of, is at least within the circumstances of the experiment highly noteworthy and also speaks very strongly for the good effect of the transfusions. Magendie however, reports that he received dogs up to the 30th day; but they were 6 year old dogs, whilst ours was still a young animal, only one year old. How much depends on the age of the animals is shown by the fact that, according to Magendie, very young dogs succumb after only two days. - In the case of medium-age and medium-sized dogs, an average of 12-14 days, calculated from the beginning of fasting can be assumed to be the maximum.

In order to make a direct comparison, we also subjected a dog of the same breed, same age and nearly the same body condition (only a little larger and stronger, like the above experimental dog) to the continuous inanition, without using the transfusion on it. At the beginning of the experiment (on the morning of 27 November), it weighed 5324 grams - i.e. slightly more than ⅓ of the first. On 29 November it weighed 4147 grams; on 1 December 3825, on 3 December 3539, on 5 December 3128 grams. - Death took place on the morning of 6 December, i.e. only nine days after the start of the experiment. The body weight of the animal immediately after the death was 2863 grams, - so that during the fast it lost 2461 grams or just over 46 percent lost weight. - These figures speak most clearly when compared with the corresponding values of the first attempt. The first dog died on the 24th day, the second (even bigger and stronger) after a completed ninth day. The second lost 46 percent of its body weight at a time when the weight loss of the first (see above) did not yet exceed 18 percent of the original body weight. The second lost an average of 273.4 grams = 5.1 percent each day, whereas the first lost only 72.7 grams = 1.8 percent of the original weight.

Although this parallel experiment leaves little doubt that the relatively long lifespan of the first animal is due to the favourable influence of the repeated transfusions, we must still discuss the question of why this influence was so limited and what circumstances, despite its existence, led to the death of the animal on the 24th day. - As mentioned, the dog had 39 percent weight loss at its death. This is a loss that starving animals often outlast for a long time, as the dog of the second experiment showed a relatively higher weight loss (46 percent) at its death. We believe that the cause of the eventual failure is mainly due to certain purely accidental complications of the attempt. The frequent repetition of the transfusion requires that a larger number of veins as superficial as possible are available and can be used in turn. In a dog the size of our experimental animal however, most veins (especially the superficial skin veins) are quite unsuitable for this because of their fineness. We were therefore limited to a very small selection (except for the jugular veins, only the two femoral veins); and in the need to repeatedly expose the same veins and to reopen the still inflamed wounds, it was impossible to prevent the occurrence of diffuse suppurations in different parts of the body, which undoubtedly caused fever and an even greater loss of animal's strength.

If the experiment were repeated on an older and larger dog, the evils described could be excluded to a certain extent, and therefore an effect of even greater duration and stability could probably be expected; however, it has its difficulties in obtaining the quantities of blood required for frequent transfusions for such an animal, in which the food requirement is correspondingly greater. In this case, the blood of another species is of course completely unusable, according to the information given by Panum about the behaviour of foreign blood in the organism, since it is not intended to have a temporary effect, but to ensure that function of the injected blood is as long-lasting as possible, in accordance with normal conditions.

In addition to these incidents of the experiment, it must not however be overlooked that the replacement by transfusion of the foods normally ingested was, after all, very imperfect in the present case. Therefore, as the daily weight losses revealed, there was still a certain amount of body weight to be burned to meet the functional needs of the animal; and the ever-increasing dissolution of the tissues alone had to cause the death of the animal sooner or later - albeit significantly faster than without the help of the transfusion. - However, even if the compensation by the latter would have been as perfect as possible, it is nevertheless conceivable that the permanent deprivation of food itself leads to certain functional disturbances, which, despite that compensation in the long run, present a lethal element that cannot be excluded. This includes the suppression of the activity of the entire digestive system, and the disturbances which the secretory activity of the liver must necessarily suffer by the alternation of the blood flowing in the portal vein; perhaps also the altered mixture of the chyle and lymphatic flow, and the resulting decomposition of the blood coming into the right heart and lungs. Incidentally, it should be remembered here that in the dog we examined, the liver showed no conspicuous macroscopic changes, namely no signs of fattening or atrophy.

According to what has been discussed so far, there may a possible prospect for the therapeutic use of transfusion in humans in those cases of general nutritional disorder, where the mechanical conditions either prevent food intake altogether, or the assimilation and absorption of that ingested is more or less completely excluded. We only remember the cases of carcinomatous or scarring strictures of the oesophagus, cardia and pylorus, where the sick so often starve to death in the most literal sense of the word; and tetanus, where so often every attempt to ingest food so often produces the most threatening reactions, and where, moreover, transfusion might also satisfy a more causal indication by feeding the central parts, and especially the medulla oblongata, with a less irritating and oxygen-rich blood. Certainly, the idea of feeding the patient by transfusion in such desperate cases is more rational and promising than the sad expedient of nourishing baths and clystiers, and far less problematic than the "gastrotomy", to which the admirable audacity of individual surgeons has repeatedly ascended. Let it not be objected that we are trying to extend the field of therapy to conditions which, by their very nature, are often incurable and inaccessible to therapeutic endeavours; for even if the effect of transfusion were only a palliative one, it would still prove to be beneficial in such cases, and it would certainly be the most misguided policy to dispense with such a palliative treatment or to reject it as "useless" in view of the incurability of the underlying condition. - In addition, it is quite conceivable that there may be cases in which the disturbances are of a more temporary and repairable nature and where the “nourishing transfusion" could provide the most essential services. Apart from tetanus, we only recall those diseases in which it is important to strictly prevent any change in the position of the organs located in the abdominal cavity, and above all any intestinal movement. Penetrating abdominal wounds, especially intestinal injuries, diffuse or circumscriptive peritonitis and inflammation of the intestinal serosa, stomach or intestinal ulcers with impending perforation, as well as certain forms of internal entrapment, are included in this subheading; and here it would perhaps be able to carry out with help from the nourishing transfusion, the absolute immobilization of the abdominal organs for a longer time period, without simultaneously endangering life directly by the consequences of the strictly observed inanition.

When alluding to these possibilities, it should not be forgotten that the chances of prolonged preservation by transfusion are far more favourable in starving people than in animals. The superficial location and the elongated course of numerous large vein branches are likely to allow a very frequent repetition of the operation without the need to recourse to the same or a nearby site and therefore without the dangers of subsequent suppuration; indeed, the probability of the latter would even be zero if the "subcutaneous" version of the transfusion, which will be discussed below, proved itself in practice.

When performing the "nourishing transfusion" in humans, it may seem particularly advisable to take the blood from a strong, normally nourished individual and, where possible, a few hours after a plentiful and appropriately mixed meal. It is easy to see that the blood obtained under these circumstances must have a greater nutritional value than in a fasting state or immediately after food intake. Although complete comparative analyses of the (venous) blood before and during digestion are not available, we do know that, on the one hand during digestion the brimming thoracic duct empties its contents into the area of the superior vena cava under greater pressure - on the one hand, the chyle contained in the duct at this time is richer in protein, extractives and especially in fat, on the other hand, it is poorer in water than in fasting animals. It can therefore also be assumed that in the veins of the larger circulation the substances mentioned will be more strongly represented during digestion, and that the content of these veins represents, as it were, a more concentrated nutrient material. - The question of how much and how often one has to transfuse with a depressed diet in order to maintain a normal metabolism and at least prevent large losses of body weight cannot be answered exactly at the present time. Even if, according to the exact examinations of Valentin[28], Barral[29], Hildesheim[30] and others, we can approximate the daily food requirements in the adult human being, it is certainly very different according to individuality, body weight, etc., and similarly, the nutritional value of a particular quantity of blood, i.e. its content of proteins, fat, extractives and salts, is probably no less variable according to the conditions just discussed. Moreover, we know that, in the ordinary mode of nutrition, a not inconsiderable portion of the absorbed material is directly employed to maintain the secretory activity of the intestinal glands and the function of the large glandular ancillary organs of the digestion apparatus. Since these expenditures are eliminated in the case of dormant intestinal absorption, there is probably a considerable saving of food material in the case of nutrition by transfusion, the absolute value of which and relative distribution of individual nutrients we are certainly not able to determine. - Incidentally, this much can be inferred from our experiments for the time being, that the introduction of a quantity of blood, which amounts to about $^1/_{130}$ of the (original) body weight per day is not sufficient for complete nutrition - at the completion of all other sources of help.

Practical execution of the transfusion and its indications.

The first task of the doctor who has decided to perform the transfusion is to obtain as quickly as possible a sufficient quantity of fresh, healthy human blood. The solution to this problem is certainly in some cases connected with not inconsiderable difficulties, since here only the willingness to sacrifice of those persons who either happen by chance to be present with the patient or can be quickly called to the patient – the willingness to give their own blood in order to save the life of another. Where one has the choice, one takes a perfectly healthy strong person, free of dyscrasia (especially without syphilis), where this is not acceptable, the use of any human blood still deserves preference over animal blood, the use of which should only be resorted to in the extreme emergency. It is true that Bliedung has successfully used goat's blood in one case. He transfused four ounces to a man exhausted by a pulmonary haemorrhage and claims to having made a full recovery. Here, however, Panum's careful experiments advise great caution. The latter, as is well known, found that the blood infused from another species was not able to be maintained, but must immediately be the subject of decay and excretion in the body of the operated animal. - The blood obtained by bloodletting is collected in a bowl and immediately defibrinated and arterialised by beating (by the means of a rod or a fork). The use of defibrinated blood necessarily deserves preference over non-defibrinated blood. The experiences already made by Müller, Bischoff and Panum with regard to defibrinated blood, and with which ours agree, make this advantage seem unquestionable. Nevertheless, it might seem that the human experience did not speak in favour of defibrinated blood, because in the thirteen cases reported by Larsen, Monneret, Polli, Fenger, Neudörfer, Esmarch, the transfusion of defibrinated blood was not followed by a rescue, but always by death; - however, a detailed critical analysis of these cases suggests that they were among the most desperate, and that death would have followed the use of the blood anyway. The great advantage of defibrinated blood is that it is free of clots and therefore the injection cannot give rise to the development of embolism. If one takes non-defibrinated blood, it is by no means certain that one does not transport partially coagulated blood into the circulation. Panum has emphatically pointed out these great dangers. He found that in the case of larger clots, death can occur during or immediately after the transfusion due to blockage of the pulmonary arteries; moreover, that the absence of clots does not prove that death in the course of the next days and weeks cannot still occur, as a result of a secondary embolism.

On the other hand, it can be assumed that the absence of the fibrous material is not without a danger to life. Although Magendie believed that while experiments on dogs with fibrous-free blood had led to a certain conclusion that the fibrous material could promote the passage of the injected blood through the narrow pulmonary capillaries and that the absence of it can even give rise to serous and sanguinolent transsudates in the lungs and intestinal tracts, but it was already clear from Panum's experiments that in dogs the fibrous matter of the circling blood was kept to a minimum without any significant disturbances. We, too, can also confirm exactly the same thing in our experiments on rabbits and dogs. In addition, if one wanted to ascribe to the fibrin-containing blood the favourable property that in cases of profuse bleeding, which are not accessible to direct manual or instrumental interventions, such as the lung, stomach, intestinal and uterine bleeding, the fibrous matter added to the injected blood can prove to be beneficial by clotting in the bleeding vessels, then this influence must not be exaggerated. This is especially true of the often colossal uterine bleeding. If here, the gaping vessels are not closed by independent contractions of the uterus, then a blockage of them by fibrin droplets of the transfused blood would probably also be counted among the pious desires. Finally, the objection was made that too much time is wasted due to defibrinating the blood. However, it should be borne in mind that the injection of venous blood is often completely inadmissible, as it can result in immediate death. This applies to the cases where the respiration has either already been completely extinguished or must already appear to be insufficient. Here one would have to use arterial blood for transfusion. But, quite apart from the possible unpleasant consequences, no one is so easily willing to give himself up to an arteriotomy as to a bloodletting; and besides, it is still very much the question whether arteriotomy with the exposure and ligation of the artery or a bloodletting with defibrination of the blood takes more time. We must therefore state that the use of blood defibrinated and arterialised by agitation must be preferred to the use of fresh blood still containing liquid fibrous matter in a transfusion.

Once the defibrination has taken place, the blood is filtered through a thick linen cloth and, if there is enough time, heated to body temperature in a water bath. The latter can be improvised anywhere in the easiest way by placing the blood-containing vessel in a washbasin filled with warm water. It is only when danger is imminent that one can refrain from the previous warming, since after injection of a blood cooled below 16°R a shaking sensation occurs, but this apparently proceeds without threatening consequences. - During the warming in the water bath, the blood is still continuously stirred in order to bring as large a number the blood cells as possible into contact with the oxygen of the atmospheric air.

If, as is often the case, the transfusion is accompanied by a depletion of the blood, as is the case with poisoning, the drained blood, after it has been defibrinated and arterialized by agitation, may be used again for transfusion. This is especially true of the drained blood of the suffocated. It will probably also be possible to use the blood of those asphyxiated by chloroform and ether, when the poisonous gases which easily escape from the blood have been expelled by prolonged heating and beating in wide open shallow vessels. Unfortunately, the blood of those poisoned by CO cannot be made usable again in this way. It is self evident that the use of drained blood, especially in cases where the procurement of foreign blood is difficult, is of the utmost practical importance.

After the transfusing blood has been prepared, the operation itself can be performed.

The operation can either be performed on the previously exposed vein, or it can be carried out subcutaneously. Both methods are to be described in turn and their indications developed. However, since a good transfusion syringe is necessary for both, we shall fist describe one, which in our opinion should be recommended.

The boot and top should be made of glass under all circumstances, so that it can be seen at all times whether there are air bubbles in the syringe chamber in addition to the blood. Martin and Moncoq have already rightly spoken out in favour of the glass syringe. Performing the transfusion on a person with a metal syringe must always keep alive the feeling of insecurity and the thought of the danger to life. Because no matter how well the syringe closes, even if you have carefully sucked in the blood and injected a little of it with the outflow tube turned upwards, it will never be possible to say with certainty whether an air bubble has not adhered to the wall of the syringe boot or on the plunger, the injection of which can lead to instant death. The risk of air ingress into the veins cannot be overstated. The case of Devay and Degranges, which passed happily despite the penetration of small amounts of air into the vein, must not lead to indifference in the filling and application of the syringe, which must be carried out with the most meticulous care. In contrast to them, there is the case of Rittgen, in which death was caused by air entering into the vein. Perhaps it was similar in the case reported by Jewels, in which death occurred half an hour after the injection, and in which the autopsy showed air in the right heart. In these experiments, as well as in others, we have been convinced of the great danger of air ingress. In a case of poisoning of a canine with ether fumes, the animal at first regained its senses completely after the substitution of a normal blood, but soon died because some air penetrated into the vein during the injection, which we were able to detect at the dissection in the right heart next to coagulated blood masses. If the syringe is made of glass, you can convince yourself beforehand that only blood is present in the syringe chamber. - A scale in ounces and cubic centimetres may be appropriately etched onto the syringe boot, so that one can see at any time how much blood has already been used, which may seem desirable for comparison with the amount of the amount that may have flowed out.

The syringe itself is provided with hard caucus attachments at the top and bottom, one of which carries the 1-inch-long conical outflow tube to the attachment of the infusion cannula, the other guides the metal punch rod at the central point of penetration. The latter, as well as the punch rod, are equipped with rings on which the syringe can be held with the fingers of one hand when in use. The interior of the syringe must be able to hold a liquid quantity of 5 - 6 ounces.

If the operation is to be performed with the exposure of the venous vessel, the skin is incised over the vein in the longitudinal direction of its course after the fold has been raised and the vein is exposed for a short distance on its upper surface. It is very convenient to choose the median basilica vein. The vein is then opened by a 3-4 millimetre long oblique incision on the anterior wall and the cannula is inserted in a central direction. The tube of the cannula attached to the outflow tube of the syringe has a diameter of 1 millimetre in the lumen and has a rounded button at its end. The cannula is never inserted individually, but is always connected to the filled syringe beforehand and filled with blood by pushing the punch forward. The infusion is now carried out by uniform, not too stormy pushing of the syringe punch with the right hand, while the surgeon presses the vein wall against the walls of the cannula with the thumb and index finger of the left, after he has previously convinced himself that even when inserting the cannula into the vein, an air bubble has not slipped into the vascular tube at the same time. During injection, it may be necessary to compress the peripheral end of the vein. If several syringes full of blood are to be administered, the cannula is always removed together with the syringe, because the leaving the cannula and then attaching the syringe can cause air to enter too easily.

If, as is the case with poisonings, depletion is to be combined with transfusion, the same exposed vein can first be used for an abundant bloodletting. However, one may choose the median basilica vein of the other arm just as well for this purpose.

Since it is very important during the operation that the vein wall fits the wall of the cannula as close as possible, on the one hand so that blood does not to flow out at the same time, on the other hand in order to safely prevent entry of air into the vein, one can use the following method, which we have proven to be very useful in our experiments on animals. Towards the centre of the incision in the vein, a grown silk thread is drawn under the vessel through the connecting tissue surrounding the vein. After the cannula is inserted, the ends of this thread are simply crossed at the front surface and kept moderately taut. (Compare Figure 1.D, in which the noose has not yet been tightened.) This makes it possible to apply the vein wall to the infusion tube more precisely than can be achieved by pressing of the thumb and index finger. Such an under-laid thread, especially if it lies in the connective and adipose tissue of the venous area, will certainly not increase the dangers of subsequent phlebitis, especially since it is carefully removed again after injection.

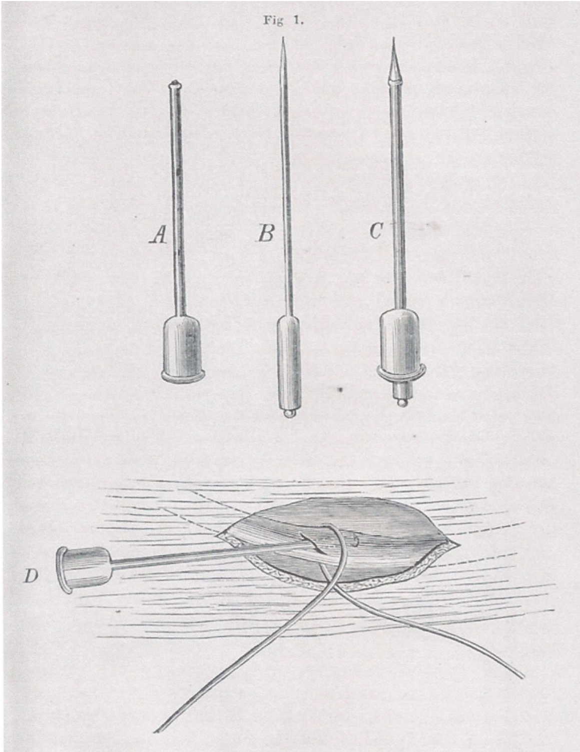
In the case of acute intoxications, as can be seen from the description of our experiments, it will sometimes be necessary to combine the transfusion alternately with depletion, for the execution of which more detailed technical instruction will be required.

In the case of apparently dead newborns, the cannula is inserted into the umbilical vein of the cross-cut umbilical cord, which can be done without any particular difficulties. The simultaneous necessary depletion takes place from the umbilical arteries. The extent of the injected and drained blood must be weighed against each other more precisely than it needs to be in the case of adults.

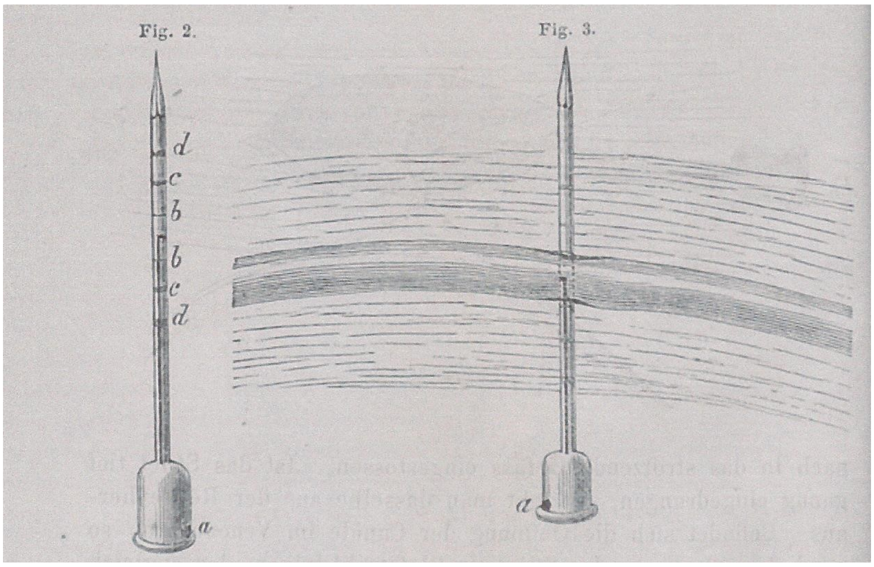
After completion of the operation, the first thing to do is to check whether there is still spontaneous bleeding from the venous wound. If this is not the case, the skin wound is united with a few button sutures and treated like a simple cut wound. If the bleeding persists, try to see if it does not stop by compression of the peripheral part of the vein, in which case one then proceeds to join the skin together. It is only in the most extreme cases that it is permissible to stop the peripheral, or similarly even the central part of the vein, because of the phlebitis that may occur afterward with all its ominous consequences. - In newborns, the umbilical cord is simply tied tightly after the end of the operation.

The second method by which transfusion can be carried out is the subcutaneous type, but about which we have no experience ourselves. This operation requires specially made cannulas that can be connected to the syringe.

For this purpose, a cannula (Fig. 1.A) with rounded buttons at the end is used, into which a thin troicart can be inserted, which is shown isolated in Fig. 1.B, and inserted into the cannula as shown in Fig. 1.C. The introduction of the latter is carried out in the following way. First the median basilica vein is made to swell and the troicart cannula is placed in an oblique direction into the length of the bulging vessel. When the stylet has penetrated deep enough, it is drawn out of the tube. If the opening of the cannula is in the venous tube, the out-flowing stylet will be followed by a stream of blood, which at the same time fills the cannula with blood and expels the air from it. The cannula can now be pushed forward a little, depending on the need, whereby, because of the rounded button, there is no risk of injuries to the vein walls. If the cannula is in a good position and you have satisfied yourself once again that there is no more air in it, the well-filled syringe is inserted and the transfusion can begin after the central-facing compression device has been removed from the vein.

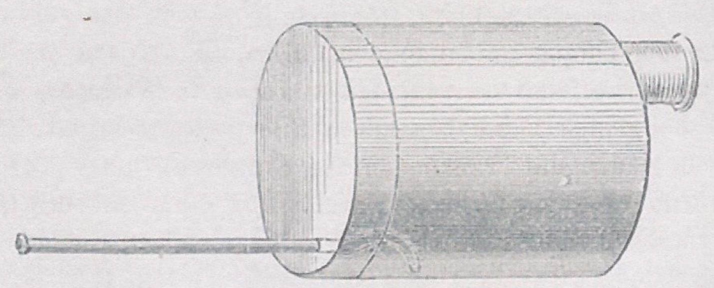


The subcutaneous application of the transfusion can still be carried out in a second and different way, requiring a different stylet needle, which is shown Fig. 2. This (modified by us according to Moncoq's information [L'Onion 1863]) is a cannula that ends at the front into an un-pierced troicart tip. The canal of the cannula tube opens laterally in the middle of it. The execution is now done in such a way that the stylet is pushed transversely through the swelling vein, so that the lateral opening lies in the middle of the venous tube, directed towards the centre. Whether the latter is actually the case will be seen from the stream of blood which pours out of the cannula when in its correct position. Fig. 3 shows the stylet cannula in its correct position. The mark a. (Fig. 2) on the edge shown side on which the lateral opening is located on the tube, the corresponding marks bb, cc, dd, affixed at equal intervals from the latter opening provide guidance on the position of the opening when the stylet cannula is introduced within the vein. The connection of the syringe with the cannula and the transfusion take place in the same way as with the first subcutaneous method.



Finally, we will describe a special cannula, which is equipped with its own device to prevent the passage of air bubbles, which may still be in the syringe, into the veins. This is shown in Fig. 4. The device, by means of which this cannula provides safety against air penetration into the vein is called the "air catcher". The air catcher represents a 1¼ inch long metal drum of elliptical cross-section. The height of the ellipse is 1 inch, its width ¾ of an inch. The syringe attachment and the outflow tube are attached to the two elliptical end surfaces in such a way that the former opens into the metal drum hard at the upper edge of the ellipse on one end surface and the latter on the other end surface hard at the lower edge of the ellipse. The outflow tube extends a distance into the interior of the drum, and there it is directed downwards in a concave curve so that the inlet opening looks straight downwards. Before use, the whole cannula is filled with blood, and after it has been inserted into the vein opening, the syringe attachment piece is always held facing upwards. It is now clear that if air bubbles enter the air catcher through the syringe attachment with the injected blood they immediately pass under the upper ceiling of the air catcher. In this way, the opening of the outflow tube will always lie and remain under the blood, even if larger air bubbles have entered the air catcher. It goes without saying that the syringe contents must not be emptied too quickly, but this rule applies not only when using the air-catcher cannula, but also with any other in general. One end plate of the air catcher can be removed and put on by means of a simple, well-closing box closure so that the interior can be cleaned[31].

Fig. 4.



In fact, the air-catcher provides a great deal of security against the penetration of air into the veins, which is rightly feared, and its use should therefore be advisable when relatively abundant masses of blood are to be transfused with the greatest possible speed, i.e. especially in threatening cases of acute intoxication.

Finally, it should be noted that the air catcher is constructed according to the principle of Schuh's troikartcénüle for the draining of effusions from body cavities into which the penetration of air is to be prevented. But here the instrument works in exactly the opposite sense.

For the transfusion into the umbilical cord of apparently dead newborns, only a smaller, otherwise very similar syringe of about 2-3 ounces content and a simple cannula such as that shown in Fig. 1.A are required.

If, after this description of the instruments and their application, we are now to decide which method is to be preferred, the following must be considered: the subcutaneous method will have to be completely abandoned in all those cases where a swelling of the venous vessel can no longer be achieved, either because of the significant anaemia, or as a result of the excessively reduced circulation activity. On the other hand, preference will be given to the subcutaneous method in cases where transfusion is repeatedly envisaged on different days and where no particular haste is necessary, i.e. in cases where transfusion is supposed to maintain nourishment. In this case, repeated exposure of the vein would greatly increase the risk of thrombosis and phlebitis and phlegmonous inflammation of the surrounding tissue, as was sometimes the case with our experimental dog. In the remaining cases, the greater manual skill in one way or another may be the decisive factor; the inexperienced, however, will do well to perform the transfusion with the vein exposed, though perhaps with a little more chance of subsequent phlebitis.

As far as the devices proposed by other authors is concerned, we cannot approve the use of the metal syringes by Major, Graefe, Dieffenbach and others for the reasons given above, which Martin has already rightly pointed out. The other syringes, usually of the kind that are connected to devices, through which blood is constantly being directed into the syringe chamber in a special way, as indicated by Blundell, Sotteau, Bougard, Demme, Moncoq and others, are not at all recommendable on account of their complicated design. Here, too, as with so many surgical instruments and devices, the simplest are at the same time the safest and best

As far as the dangers of the operation are concerned, we have already spoken of the entry of the air into the veins and the prevention of it by caution and by our 'air catcher'. Apart from these dangers, which can almost certainly be avoided by the use of good instruments, the performance of the operation itself is exceedingly easy and simple, and still, in spite of this, at the meeting of the Society de Chirurgie in Paris (5 August 1863), Liégard calls the operation a heroic and deceptive one, so one must assume that he never performed it himself and that he probably has no real idea of how it is performed. -

However, there is one more point that deserves special consideration: this is phlebitis that may occur after the operation with its nasty consequences. Cruveilhiers, in "La phlebite domine toute la pathologie", calls for careful unbiased discussions about this danger in this area as well. However, subsequent inflammation of the vein used for surgery may be experienced and in some cases it has actually been observed. However, the dangers of this inflammation have often been exaggerated by the opponents of the operation and have been painted into a frightening spectre. Martin, in his critical assessment of this point, has already limited the fear of the dangers of phlebitis to its appropriate level. In the cases of Blundell, Uwins, Soden and Masfen, the inflammation that occurred went away without any nasty after-effects, as we often see inflammation developing in simple bloodletting wounds, which usually resolves without any further relief when treated with aqua plumbi and ice. In the case treated by Turner, the death was caused by a carbuncle on the posterior surface of the arm on the 10th day, but this most likely had nothing to do with phlebitis as a result of the operation. Furthermore, in the cases in which the transfusion occurred the only thing that can be expected is saving help, and any discussion about the onset of phlebitis goes away by itself.

Indications for transfusion.

I. Transfusion in acute anaemia, chlorosis, hydremia and leukaemia.

Until now, it is almost entirely acute anaemia in which transfusion has been used, and it is especially the bleeding of newly delivered persons that caused it. Martin in his writing: On the Transfusion in Bleeding of Newly Delivered Persons, Berlin, 1859, specifies that the indications for these special cases in the following way: "If, in the presence of signs of higher-degree anaemia - general pallor of the skin, coldness of the extremities, small, barely distinguishable pulse, fainting spells, the impossibility of restoration by means of the mouth and stomach, is made apparent by the recurrence of the corresponding nutrients or medicines, I consider the time for transfusion has come and advise you not to delay any longer with this almost risk free operation." (L c. p. 77.) Above all, he warns against indecisive delays, otherwise it could easily be "too late". Martin's statistics show that out of 57 newly delivered persons treated in this way, 45 recovered completely, and to these cases (since 1859) can still be supplemented by newer favourable ones, e.g. those of Simon Thomas[32]. Such favourable results should prompt the doctor to perform this simple operation in cases that arise and in the face of such a favourable operation, the opposing omissions of Depaul, Morel-Lavallée, and others, must be silenced.

However, transfusion is also indicated in the case of severe haemorrhages of a different kind under the same conditions: in the case of bleeding as a result of injury, in the case of severe exhausting haemoptosis, in the case of haemorrhages of the stomach, intestines and genital organs, as well as in the case of bleeding of haemophiliacs. Chlorosis and severe hydraemia may also indicate transfusion under certain circumstances, especially when persistent vomiting (especially with simultaneous ventricle ulcers) and pathological affections of the alimentary canal increasingly impair the general diet more and more and strong foods, iron preparations and roborants are not tolerated. .

In the case of leukaemia too, transfusion deserves attention, and it has already been carried out here by Blasius[33] on advice of Th. Weber, in a man suffering from lienal leukaemia. About 4 ounces of venous blood from a strong man were injected in total. The patient was then more comfortable than before and was even able go out again. On the 9th day, suppurative phlebitis appeared at the surgical site. Although there was no pyemia, the leukaemia worsened and death occurred on the 16th day after the operation. However, transfusion in leukaemia will always only be of a palliative effect; but since we know from the experiments of Marfels and Brown-Sequard that the injected red blood cells can be preserved in the body for a long period of time, the physician is certainly right in making use of the (subcutaneous) transfusion carried out from time to time as the only one to which he is entitled, to directly counteract the severe disorders caused by the preponderance of most blood cells in the body.

Since the injection is likely to have to be repeated, the subcutaneous method of application deserves preference.

II. Transfusion with simultaneous depletion in acute poisoning, or the substitution of blood

By the above experiments, we have endeavoured to bring the depletory transfusion into medical practice in the field of acute poisoning in a comprehensive manner. As an indication, we can simply state that if a toxic substance has been absorbed into the blood, the presence of which causes life-threatening disturbances, an attempt should be made to substitute a normal blood in place of the blood mixed with the toxic substance. It will depend essentially on the way in which the toxic substances are absorbed into the blood, whether a single or repeated depletory transfusion must be used: it is always indicated, as often as the threatening accidents have increased to an alarming level. Since we have no antidotes for a large number of poisonings in which the poison has already passed into the circulation, the depletory transfusion does indeed deserve the full attention of the therapists and the relatively minor dangers of the operation itself can hardly be considered in view of the imminent danger to life. The fact that, in addition to, before and after the surgical treatment, one should also try the more tried-and-tested antidotes and apply other helpful treatment methods hardly requires a special recommendation. But do not delay the transfusion until the last moment. Among the gaseous toxins, we would like to cite above all the luminous gas and the hydrogen sulphide gas, against which one should have more opportunity to intervene with the transfusion in practice. With regard to the latter poison, this applies in particular to the accidents that occur in the cleaning out of cloaken and cesspools.

According to Liebig's opinions, hydrogen sulphide gas has a poisonous effect in such a way that it combines in the blood with the iron of the red blood cells to form sulphurous iron. On the other hand, we also know from theoretical discussions from the same researcher that the living respiratory activity of the red blood cells can only exist if the iron found in them is an oxide, or as an oxoide in the arterial and venous blood. So the respiratory activity of the blood mass is directly destroyed by the hydrogen sulphide. Since we have no means at hand to remove the sulphur compound in this type of poisoning, the depletory transfusion will of use here; the blood, which is incapable of respiration due to the sulphurous iron compound, will be replaced by a normal blood.

In addition to the poisons introduced into the body from the outside, there are still two conditions against which the depletory transfusion deserves to be recommended: the so-called uremia and cholemia, although the effect here will certainly often be only a palliative one. As far as uremic intoxication is concerned - it is irrelevant to the question in question whether it consists in a collection of urea or carbonated ammonium in the blood, or whether the manifestations of it are derived from acute anaemia of the brain: – transfusion will prove to be beneficial in both cases. In the case of the intoxication phenomena, such as occurs in the severe forms of icterus, the depletory transfusion is likely to have a life-saving effect in those cases where the causes of the icterus are only transitory; temporary blockage of the choledochus ductus, etc. - Transfusion has also been proposed in pyemia and Neudörffer[34] claims to have observed in five cases during the Italian campaign that the condition of the patient was noticeably improved immediately after the transfusion. Lücke (War Surgeon, Aphorisms) believes that it can be recommended for theoretical reasons, especially in certain forms of acute septicaemia, such as those that occur after penetrating joint gunshot wounds. We refrain from giving our consent to this proposal and must leave it to the surgeons mentioned to prove the proposed procedure to be worthy of imitation through practical evidence or experimental investigations.

We do not consider the depletory transfusion to be indicated in chronic poisoning.

III. Transfusion in conditions of inanition.

With regard to the indications on this subject, we refer to what was already been noted in the third section. Since the transfusion has to be carried out repeatedly, the subcutaneous method of application definitely deserves preference.

If, after these remarks on the practical side of transfusion, we review the conclusions that we have arrived at through the experimental investigations that we have undertaken, we can summarize them in the following:

1) The transfusion of oxygen-rich, defibrinated blood of the same species brings about the restoration of life and all functions in acute anaemia caused by exhaustive loss of blood, even if it is carried out at the stage of "anaemic paralysis", i.e. after respiratory paralysis, motor and sensory paralysis has occurred, and in the event of imminent or pre-existing cardiac arrest.

2) The transfusion of such blood cannot be replaced in these circumstances by the injection of albumin solution, or serum (shaken with air or oxygen), or finally by defibrinated blood but subsequently carbonated. In all these cases, resuscitation does not occur; but in the injection of a blood saturated with carbonic acid, the animal dies of convulsions, while in the injection of serum or albumin solution the latter is absent.

3) The effect of transfusion in anaemic animals is manifested first by a restoration or amplification of the rhythmic respiratory movements. This effect still occurs even after double-sided vagus cutting - but only in a very temporary way.

4) Theoretically, these experiments show that the efficacy of the transfusion in acute anaemia caused by bleeding is based on the presence of oxygen bound to the blood cells in the transfused blood. The anaemic animals die of asphyxia, caused by oxygen deficiency as a result of the sudden decrease in the amount of red blood cells, resulting in an over-stimulation and partial paralysis of the respiratory centre of the medulla oblongata. By the renewed supply of oxygen bound to the blood cells, the over-stimulation can be reduced to the stage of normal stimulus, and the respiration (direct, from the medulla oblongata, non reflective, from the vagus ends) are aroused again.

The accumulation of carbonic acid in the still remaining blood is probably the cause of convulsions that occur in acute anaemia – as evidenced by the facts mentioned within section 2.

5) In the case of acute poisoning, where the toxic substance is absorbed into the blood or enters directly into it, and from there has a lethal effect on the nervous system, transfusion proves to be the most powerful remedy at our disposal, in a form which we call "combined" or "depletory" transfusion ("substitution" according to Panum). This consists in the alternating application of transfusion and depletion until the blood impregnated with poison is completely "flushed out" or replaced by a normal, non-toxic blood - and this continues until the absorption has ceased or the amount of absorbable poison is too much reduced to still produce dangerous symptoms through accumulation in the blood.

6) The nature of the toxic substance is in itself inherently to the principle on which this method is based; the only thing that seems of greater importance appears the timing of operation and the manner of its execution. However, the experiments carried out on animals have specifically confirmed the effectiveness of "combined transfusion" in the following cases:

(a) In cases of poisoning by carbonic acid (and concomitant oxygen deficiency);
(b) In cases of poisoning by carbon dioxide, in cases of the most intense poisoning, where depletory blood withdrawals alone or artificial respiration in the most energetic form (faradic irritation of the phrenici - injections into the opened trachea) no longer had any effect;
(c) In cases of poisoning by chloroform and ether vapours;
(d) In cases of poisoning by various alkaloids (morphine, opium, strychnine). - In these cases, where the poisoning was brought about partly by infusion into the veins, partly by hypodermic application of the poisoning substance, the possibility arose by means of a transfusion combined in the above manner, as soon as it was carried out in good time, to considerably shorten the duration of the poisoning period and the intensity of the symptoms of poisoning at a non-lethal dose, - nay, even to ensure the preservation of life and the integrity of all functions at otherwise lethal doses.

7) In the case of artificially induced lack of food due to prolonged, complete inanition, it is possible to prolong life for a relatively long time by supplying the animal at appropriate intervals with sufficient quantities of defibrinated blood of the same animal species made bright red by beating, as a substitute for food and the bodily substance burned during fasting. Death occurs much later, even with only an incomplete nutrition by transfusion, and the daily absolute and relative weight losses are much lower than is usually the case with starving animals.

REFERENCES

1. Vergl. die Debatte in der Pariser soc. de chir. vom 5. August 1863, wobei Depaul, Morel-Lavallée und Liégard (von Caen) als absolute Gegner der Transfusion auftraten und selbst die Berechtigung derselben bei erschöpfenden Blutverlusten in Abrede stellten - freilich aus keinem besseren Grunde, als weil auch zuwelen in derartigen Fällen eine spontane Wiedergenesung stattfinde! [*Compare the debate in the Parisian Society of Surgeons of 5 August 1863, with Depaul, Morel-Lavallée and Liégard (of Caen) appearing as absolute opponents of transfusion and even denying the justification of it in the event of exhaustive blood loss - of course for no better reason than because it occurs in such cases that spontaneous recovery sometimes takes place!*]
2. Bibliotèque universelle de Gen. t. 17. Ann. de chémie, t. 18, pag. 294.
3. Die Transfusion (Berlin 1828). - Vergl. operative Chirurgie, Band I, pag. 110.
4. Handbuch der Physiologie, Band I.
5. Müller's Archiv 1835 pag. 347. - 1838 pag. 357.
6. Dagegen behauptete Blundell nach seinen sorgfältigen Experimenten, Arterienblut scheine nicht mehr zu beleben als venöses. - Wahrscheinlich erklären sich diese widersprechenden Resultate älterer Autoren durch die Beobachtung von Brown-Sequard, dass, wenn man kohlensäurereiches Blut so langsam injircirt, dass das Uebermaass von Kohlensäure durch die Lungen ausgeschieden werden kann, die giftige Wirkung ausbleibt. [*On the other hand, Blundell claimed after his careful experiments that arterial blood did not seem to be more stimulating than venous. - These contradictory results of older authors are probably explained by the observation of Brown-Sequard that if blood rich in carbonated blood is injected so slowly that the excess of carbonic acid can be excreted through the lungs, the toxic effect does not occur.*]
7. Comptes rendus der soc. de biologie 1849, 1850, 1851; der acad. des sc. 1851, 1855, 1857; journ. de phys. I. p. 95, 173, 666.

8. Experimentelle Untersuchungen über die Transfusion, Transplantation oder Substitution des Blutes in theoretischer und praktischer Beziehung. [*Experimental investigations on the transfusion, transplantation or substitution of blood in theoretical and practical terms*.] Virchow's Archiv, Band 27, p. 240.
9. Diss. inaug. de transfusione sanguinis. Bonae, 1852.
10. Ueber die Transfusion bei Blutungen Neuentbundener. [About transfusion for bleeding of newly born babies] Berlin 1859.
11. Dennoch hat die Defibrination noch vor Kurzem wieder einen Gegner gefunden in Graily Hewitt (British med. journal, 29 Aug. 1863 p. 232). Die von ihm geltend gemechten Gründe sind jedoch grösstentheils schon von Panum hineichend widerlegt: so namentlich die angeblich minder belebende Eigenschaft defibrinirten Blutes und das Eintreten plötzlicher Todesfälle nach Injectionen desselben. Der ausserdem hervorgehobene Zeitverlust ist, zumal da das Blut gleich während des Ausfliessens geschlkagen warden kann, jedenfalls so minimal, das er den anderweitigen Vortheilen der Defibrination gegenüber nicht in Betracht kommt. - Wir warden auf diese wichtige Frage unten in dem practischen Theile unserer Arbeit noch einmal zurückkommen. [*Nevertheless, defibrination has recently found another opponent in Graily Hewitt (British Medical Journal, 29 Aug. 1863 p. 232). However, most of the reasons he put forward have already been sufficiently refuted by Panum: especially the supposedly less invigorating properties of defibrinated blood and the occurrence of sudden deaths after injections of the same. The loss of time, also highlighted, especially as the blood can be beaten as it flows out, is in any case so minimal that it cannot be taken into account compared to the other advantages of defibrination. - We will return to this important question in the practical part of our work below*.]
12. Centralblatt 1864, No. 9.
13. Die Therapie hat bisher der Transfusion gegenuber im Allgemeinen den Standpunkt von Panum auch zu dem gemacht, wie dies die Statistiken von Blasius (Deutsche Klinik 1863, 11), Oré (Gaz. des hop. 1863, 96) und Anderen beweisen. Allerdings hat man in neuester Zeit in Einzelnen Fallen von Pyämie (Neudörfer), von lienaler Leukämie (Weber-Blasius und von Kohlenoxydvergiftung die Transfusion versuchsweise angewandt, und zum Theil nicht ohne Erfolg; doch scheute man im Grossen und Ganzen davor zurück, das Gebiet derselben über die engen Grenzen der durch plötzlichen Blutverlust herbeigeführten, erschopfenden Anämie hinaus zu erweitern. [*Therapy to date has generally made Panum's point of view towards transfusion, as the statistics of Blasius (Deutsche Klinik 1863, 11), Oré (Gaz. des hop. 1863, 96) and others prove. However, transfusion has recently been used experimentally in individual cases of pyaemia (Neudörfer), lienal leukaemia (Weber-Blasius) and carbon oxide poisoning, and in some cases not without success; but on the whole people have shied away from the subject to expand beyond the narrow limits of exhausting anaemia caused by sudden blood loss*.]
14. Ueber den Tonus der Gefässe und seine Bedeutung für die Blutbewegung. [*About the tone of the vessels and its significance for the movement of blood*] Virchow's Archiv XXIX. (Separatadruck p. 31)
15. Versuche der Art sind - ohne die hier vorliegende Frage zu berücksichtigen - mit Serum und überdies mit Wasser schon von Dumas und Prevost, Dieffenbach und Bischoff angestellt worden. Abgesehen davon, dass reines Wasser (wegen seiner Einwirkung auf die noch vorhandenen Blutkörperchen) nicht als eine indifferente Substanz zu betrachten ist, geben auch die Versuche mit Serum, welche negativ ausfielen, keinen schlagenden Beweis, da das hierzu verwandte Serum möglicherweise reich an Kohlensäure gewesen sein kann. Dagegen erhielt Brown-Sequard (s. u) auch durch Einspritzung von mit Sauerstoff geschütteltem Serum keine Wiederbelebung. [*Experiments of this kind have already been carried out - without taking the present question into account - with serum and, moreover, with water, by Dumas and Prevost, Dieffenbach and Bischoff. Apart from the fact that pure water is not to be regarded as an indifferent substance (due to its effect on the remaining blood cells), the experiments*

with serum, which were negative, do not provide conclusive evidence either, since the serum used for this purpose may have been rich in carbonic acid. On the other hand, Brown-Sequard (see below) did not receive resuscitation even after injecting serum shaken with oxygen.]
16. Ueber die erregende Wirkung des Blutes auf die cerebrospinalen Nervencentra des Frosches. [*On the excitatory effect of blood on the cerebrospinal nerve centres of the frog*.] Centralbl. 1865, Nr. 17.
17. Vergl. über den bei Asphyktischen eintretenden, von Landois entdeckten, Herzstillstand. [*Compare about the cardiac arrest that occurs in asphyxial patients and was discovered by Landois*.] Berliner klinische Wochenschrift 1864 Nr. 10.
18. Vergl. Landois, Allgem. medicin. Centralzeitung, 7. November 1863.
19. Cfr. Centralblatt f. d. medicin. Wissenschaften 1865, No. 39.
20. Unters. aus dem physiol. Laborat zu Bonn 1865.
21. Greifswalder medic. Beiträge II. 1863.
22. Zeitschrift f. ration. Medicin. Neue Folge. Bd. VIII. p. 256.
23. Virchow's Archiv Bd. XI. u XIII.
24. Zeitschrift f. rat Med. 3. Reihe Bd. 5. 1859.
25. Virchow's Archiv. Bd. 50. 1864.
26. Recherches expérimentales sur l'inanition. Paris 1843.
27. Die Verdauungssäfte und der Stoffwechsel. [*Digestive juices and metabolism*.] Mitau u. Leipzig 1852, pag. 292-413.
28. Lehrbuch der Physiologie, Band 1, p. 723.
29. Ann. de chim. et de phys. III. Sér. t. XXV.
30. Die Normaldiät, Berlin 1856.
31. Transfusionsapparate nach der im Vorstehenden gelieferten Beschreibung (Glasspritze mit Hartkaoutschoukansätzen, Canüle 1. und 2., und Luftfänger-Canüle in einem Besteck) werden von dem Berliner Instrumentenmacher Herrn Goldschmidt verfertigt. [*Transfusion devices according to the description provided above (glass syringe with hard rubber attachments, cannulas 1 and 2, and air-catching cannula in one set) are manufactured by the Berlin instrument maker Mr. Goldschmidt*.]
32. Nederlandsch Tydschrift von Geneesk 1865.
33. Monatsbl. f. medicin Statistik. Beilage der Dentsch. Klinik. II. 1863.
34. Oesterr. Zeitschrift für practische Heilkunde 1860, No. 8, 9.