

DIE SCHICKSALE DER TRANSFUSION IM LETZTEN DECENNIUM

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This paper titled 'The fates of transfusion in the last decade' is a transcript of a speech given by Ernst von Bergmann on the occasion of the Foundation Day of the Military-Medical Educational Institutions in Berlin on the 2nd August 1883. It is written in German and was published in 1883 by V.A. Hirschwald. A copy of this document is available to read or download from the following site:

https://www.deutschestextarchiv.de/book/view/bergmann_transfusion_1883?p=1

The author starts with questioning the actions of surgeons related to 'what we think we can do compared with what we actually know'. He expands this argument by examining in some detail what can be identified as historical missed opportunities for medical advancement and misunderstandings, especially regarding the perceived roles of blood, regarding its ability to prolong life, heal diseases, compared with what was recognised as the principle role of blood transfusion from the outset, which was to replace blood loss.

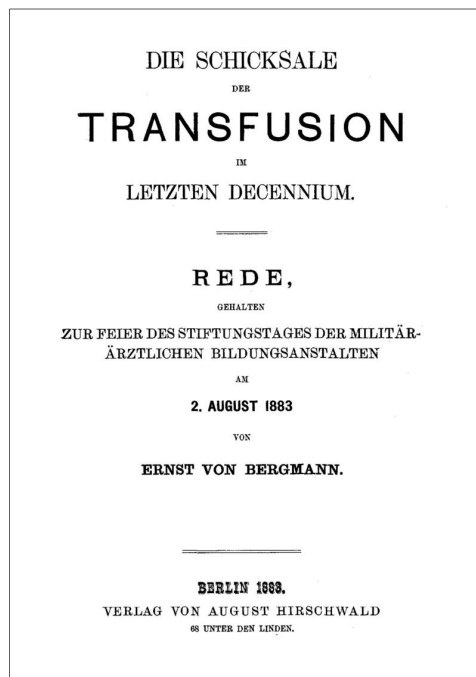
Bergmann then expands on this by discussing the ability of transfused blood to 'replenish the vascular system' and what is believed to happen to the red cells once transfused. He identifies that it is known that the haemoglobinuria, experienced after animal to human blood transfusions, is due to the 'dissolution of blood cells within the circulation' and uses such information to denounce such transfusions and the need to use human and not animal blood for transfusion purposes, during which he discusses the conflict of historical information and the denial of the significance of some results and outcomes of animal transfusions – picking up the threads of his opening comments.

He then concludes by discussing the misperceptions associated with and the dangers of transfusing defibrinated blood, based on what he identifies to be the recent evidence and increasing awareness of the 'coagulation ferment' (i.e. pathway), outlining the extreme dangers associated with its activation during defibrination as well as indirect transfusion procedures. He balances this however in identifying how different patients may be able to overcome some of these effects, especially if only small volumes of blood are transfused and therefore how it can produce differing clinical evidence that is based mainly on patient 'recovery'.

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

Although I have taken great care in accurately identifying the original text and producing a true representative translation of the author's original wording I cannot guarantee that this work does not contain 'translational errors' and the reader is recommended to check specific details against the original German text. I have maintained the original paragraph settings

and general layout of the text, as well as providing an English translation to the notes / references related to the content, that are within square brackets.



Title page of 'Die Schicksale der Transfusion im Letzten Decennium' (1883)
(Image credit: DTA – Akademie der Wissenschaften)

NOTE:

There is a great deal of biographical and professional information published about the author Ernst von Bergmann, who was the first physician to introduce heat sterilisation of surgical instruments and is known as a pioneer of aseptic surgery.



Ernst von Bergmann
(Image credit – Britannica)

Honoured Assembly!

At all times physicians have succumbed to the temptation to free and detach their actions from the foundations of their knowledge, or at least to raise them far above them. Remedies have been used without the slightest trace of the changes they have effected in the organism being known, and operations have been performed before anyone had the slightest idea of the anatomy of the organs into which they were cutting.

Since the deeds of the physician preceded medical knowledge, they turned out to be more magnificent than would have been granted or possible under the spell of what was known. It was not without reason that the achievements were surrounded by the aura of wonder. It is no different today.

Anyone who knows how difficult it is to protect the nutrient liquid in a test tube from contaminating yeast cells and bacteria falling into it will not admire the surgeon who thinks he can close the wounds of his patients to the pathogens of putrefaction and inflammation by means of cotton wool and bandages, so securely that he has no hesitation in attempting a probationary laparotomy or trepanation under the protection of his antisepsis to support his diagnosis?

No bandage has yet been conceived and made under which microorganisms from the group of pathogenic and infectious ones are not literally teeming, and yet a series of brilliant successes is the property of every surgeon of the present day.

In view of the everyday contradiction between what we think we can do and what we think we know, it is perhaps timely to remember that the art of surgery has not yet received any permanent support and has not retained any profit that has not flowed to it from the solid stock of biological knowledge. Whenever we reached beyond what we knew, we also made mistakes and went astray until we returned to the sources of our knowledge and used them to correct our errors.

Allow me to illustrate this experience today using the example of an operation which, only a few years ago, was praised as the most significant and important of modern surgery, which was intended to inaugurate a new era in the whole of medicine, and which seemed destined to be used in the medical field more than any other to preserve the fleeing life of the wounded man - it is the operation of transferring the blood into the vascular system of a sick person: the operation of transfusion.

More than a century before the discovery of the circulation, Pope Innocent VIII was dying. His life gradually faded away as he grew weaker and weaker day by day. Then his doctors came up with the same idea that Ovid inspires in Medea to rejuvenate Jason's aging father by having the sorceress say:

Veteremque haurite cruorem

Ut repleam vacuas juvenili sanguine venas!

Here, too, the empty veins of the exhausted old man were to be filled with youthful blood. Three Roman boys gave their fresh blood, which was unsuccessfully channelled into the veins of the high priest, for the sick man never awoke up from his lethargy. Even before they had any idea of how the blood runs and flows in the body, before they had learned where to direct its flow, they had tried by a bold act to force it into a new bed.

Just as language usage today still substitutes blood instead of body, life, spirit and soul, the less one knew about blood, the more one saw in it as the power that determines and creates all and every characteristic and expression of life. No wonder then, that as late as the 17th century, not individuals, but entire learned bodies and colleges were concerned with the question of whether a dog would gain wool and horns after the introduction of sheep's blood, whether the disposition of a light- and hot-blooded person, replaced by the pious and innocent blood of the lamb, could be reformed!

Transfusions were still being carried out for these fabulous purposes in the 18th century, so that from the time of Medea to the time of Frederick the Great, when Mackenzie (1) believed that the operation could prolong people's lives through its rejuvenating power, the theory of transfusion was not been essentially promoted. A definite healing purpose, a task achievable at the bedside, had not been set for her.

The transcendental ideas about the properties of blood had to be eliminated and the fear of demonic juice overcome before the operation of transfusion could be taken up again and, in a sense, invented for the second time in the course of our century. After Harvey's discovery, the animal experiment that it so brilliantly inaugurated contributed to this, and then the increase in surgical safety in operating, which was based solely on the control of bleeding, in housekeeping but also in the control and management of the blood.

The transfer of the blood of one animal into the vascular system of another was, so to speak, a test of the theory of circulation. Such an exchange, following the process of Lower (2), was carried out several times in the last century and established the fact that an animal which had almost bled to death by opening its arteries may be brought back to life by transferring the blood from the artery of another animal.

Judges like Hufeland claimed that the experience gained in animals was also true for humans and the Danish doctor Scheel (3) in the first years of this century tried to demonstrate this in a writing that reproduced all relevant experiences in rare detail and completeness. Since then, however, transfusions have been carried out everywhere and under a wide variety of indications, but always only rarely, here once and there once, until the frequency of the operation rose to an extraordinary height only in the second half of the century.

Since only one thing had emerged from the experiments of the physiologists at the time, the fact that the transfer of blood could save a life threatened by sudden blood loss, one would think that the operation would only have been used if there was a threat of bleeding to death. But the cases from the first half of our century alone relate much more to diseases of the most diverse organs, which were attempts made to be cured by transfusion, than to blood losses, which were supposed to be replaced by adding new blood to replace the lost blood. Cases of kidney, pulmonary, gastric diseases, pyaemia, typhoid, and especially cholera, significantly outweigh these. The doctors did not move within the circle of what was recognized, but preferred to go beyond it. Under such conditions, the failures increased until only then did the operation become more widespread and popular when, at the end of the 1850s, Martin (4) announced his resounding successes in the treatment of women who had recently given birth exhausted by blood loss. Now the happy cases followed one after the other, so that about 10 years ago transfusion reached its heyday and stood as a panacea that seemed destined to bring immortality to doctors and patients alike in almost all diseases, but especially surgical ones. One of its eulogists enthusiastically exclaims: "Animal blood transfusion has created a new era in medicine, the blood donation era" (5) and another sees it as the operation that the war surgeon should adopt above all, and has become almost more important than vascular ligation in the dressing stations! (6), indeed in the same year in which these confessions were written down, one lecture followed another at the Congress of German Surgeons on the benefits and splendour of transfusion. It was easy, as a frequently quoted author in the field of the interesting question of the day said, to be the prophet who predicted that this operation would have a triumphal procession through the hospitals like no other and an unshakably lasting civil rights in surgery. (7)

How little has this prophecy been fulfilled and come true! Not yet 10 years have passed and in Germany, as in England, the enthusiasm has faded, the transfusion machines are at a standstill and the ranks of undoubted indications have been thinned out one after the other. One begins to recover from the exaggerated expectations and reflect on how little land one really had for the construction of one's bold designs.

The knowledge about the significance of blood loss and the events and life in the blood has increased in the last decade, but with it increased the insight into the errors that had served as the basis for transfusion.

It was assumed that with every haemorrhage the danger arose from the loss of red blood cells, the carriers of oxygen, so that, logically, these had to be supplied to the threatened organism as its animating principle.

Initially, this assumption proved to be incorrect. In the case of death due to bleeding to death as a result of injury to a large blood vessel, which is the primary concern of the field doctor, death occurs at a time when the body still has a sufficient supply of red blood cells

for life. This was only proven in the last decade through an animal experiment that can hardly be disputed, an experiment the repetition of which is not difficult and thus makes the important fact accessible to our own view (8). If there is severe and sudden blood loss, the arterial blood pressure always drops so low after a certain time that the movement of the vessel contents is stopped. The heart still works, but its work is ineffective; it resembles an empty pump; it no longer raises or drives the blood column, whose tension differences in the various sections of the vascular system have ceased. If the quantity of blood still contained in the vascular tube were set in motion again, it would be sufficient to provide nutrition for the organs and the maintenance of the organism. Therefore, in such cases, as Kronecker first concluded and demonstrated, a simple infusion of a saline solution is sufficient to preserve and save life. The vascular contents are increased by it, an increase that increases the intravascular pressure and restores success and effectiveness to the work of the heart. We now understand why transfusion has become life-saving in so many cases, why Lower and Boyle's fundamental experiment in transferring blood into the veins of an exsanguinated dog brought him back to life. The filling of the elastic tubes of the vascular system to a certain level of tension was necessary for this and was carried out by the transferred blood just as it would have been achieved by any other relatively indifferent liquid injected in the same way.

The life-saving effect of the transfusion was explained not in this way, but in a completely different way, as we have just seen. By assuming that the only thing that mattered was to supply new respiratory substances, new carriers of oxygen in the form of infused red blood cells to the endangered organism, it was immediately assumed that the blood cells of one individual would continue to exist in the vascular tracts of another in other words, their transplantation was taken as a foregone conclusion

However, the revival of transfusion coincides with the experiments by transplanting a piece of tissue into tissues of the same or different kind to bring about the healing and replacement of losses of all kinds.

In particular, the results of Reverdin's skin transplants supported the idea of bringing living tissue that had been separated from its base for many minutes, even hours, and separated from all connection with the rest of the organism to continue to exist and heal in a foreign location.

Why shouldn't the red blood cells in the blood recipient's circulation behave like the epithelial cells in the Reverdin skin pieces? To make such a suggestion, one only had to forget that the epithelial cells in the Rete Malpighii are endowed with a remarkably high level of life energy, which allows them to maintain their existence for days, while the red blood cells represent an extraordinarily frail structure - one only had to ignore the fact that when the epithelial cells adhere, special preparation of the base onto which they were to be grafted was required, namely its transformation into a vascular-rich granulation layer, whereas when the red blood cells were transplanted, the nutrient base, i.e. the rest of the blood in the vessels of the exhausted and sick person had experienced a reduction rather than an increase in its production capacity. All of this was simply neglected and all these concerns about the success of the revival were suppressed. The success, of course only this, guaranteed the continued existence and continued functioning of the transferred blood cells. They were satisfied with the success; it was so sufficient and so certain that scientific control by counting the blood cells before and after the operation seemed useless. However, the counts in the past decades have also been unfortunate; it was only 10 years ago that Malassez's method made this control possible because it only required a minimal amount of blood to determine the number of blood cells. When people began counting barely two years ago with the improved apparatus from Thoma and Zeiss, the result turned out to be completely different from what was expected. After every major blood loss, the numbers of red blood cells initially present decreases even further, and over a certain period of time by a not insignificant amount (9). So the loss continues even further even though the bleeding has stopped, apparently due to influences that are now taking effect within the bloodstream. However, after the transfusions of such large amounts of blood as Worm-Müller and Lesser used in their experiments, the blood cells appeared in increased numbers, but only for a very short time, and soon their number fell and quickly, while the urea and

potassium content of the urine decreased and the depth of its colouring increased, a sign of the destruction of the elements supplied in excess.

However, the theory of transfusion experienced its first shock not through these counts, but through the results of the direct transfusions of animal blood, which, based on the astonishing cures of Hasse, had become a favourite remedy of doctors and were repeated everywhere. It is hard to believe how stubbornly people still clung to them until the end of the last decade, even though the first cases in which they were used should have convinced us of their danger and harmfulness. Each time these transfusions with lamb or dog blood were followed, the patients experienced chills with an increase in temperature that lasted for many hours and the evacuation of urine containing blood pigment. (10) We now know about both phenomena, which were only known at the time about haemoglobinuria, that they are the consequences of the dissolution of blood cells within the circulating blood.

Today, after so few years have passed, we are hardly able to understand how one could ignore the observation of such serious disorders and the experiences already brought by Panum about the dangers of transfusion with foreign blood because one and the other lamb's blood transfusions seemed to be successful, or to put it more correctly and precisely, they had not killed the patient subjected to them. From the history of these transfusions one can learn how little value a medical success has when it stands there suddenly, unrecognized, and not understood in its conditions and context, unsupported by the only secure foundations of our physiological knowledge!

The harmful effects of a dissimilar blood, i.e. taken from another animal species during transfusion, which Prevost and Dumas had already shown, was only related to the unequal size of the blood cells of different animal genera. Since the blood cells of sheep were smaller than those of humans, sheep blood was considered harmless. It is Ponfick's achievement to have shown the incorrectness of this assumption. (11) It is not mechanical factors, such as the different size of the blood cells, that make the dissimilar blood so harmful, but other and more important things, chemical effects, which, at a certain dose size, turn the sheep's blood into a deadly poison for the dog and vice versa that of the dog for the sheep. Something of the old speculative manner of natural-philosophical medicine resounds in the final words: "Foreign blood is harmful, strange blood is not." One would simply have had to continue to ask, what is the malignancy of foreign blood? When the answer to this question was finally found, transfusion disappeared from the treasure trove of surgical remedies. The ground had been taken away from it.

Long before Panum made the transfusion of defibrinated blood mandatory for doctors, Magendie (12) found in his animal experiments that injections with the filtrate of beaten blood resulted in very specific, pathological disorders: accelerated breathing, diarrhoea with tenesmus, bloody exudations into the peritoneal cavity, the pericardium and the pleural sacs. As a result, he warned against using defibrinated blood and considered the fibre, which he thought was pre-formed and dissolved in the blood, to be necessary for a successful transfusion. It is understandable that the doctors did not follow him, because the formation of clots in the syringes and cannulas was always the main danger of a direct transfusion and over time Virchow's fundamental work on thrombosis and embolism no longer overlooked, or even just underestimated, this danger. At the moment it is still the main reason against the only permissible form of transfusion, that with whole, untouched human blood.

People tried to deny the significance of Magendie's bad experiences with defibrinated blood by initially claiming that he had chosen for transfusion the blood of animals whose blood cells were larger than those of his blood-receiving animals, and when this allegation could not be maintained, said that the quantities he transferred were so large that he created a plethora universalis, which was the cause of the diarrhoea and watery excretions. Now we know, but only for barely 10 years, through Worm-Müller's and other measurements of blood pressure in experimentally produced plethora that the dreaded increase in blood pressure, the alarmingly increased tension in the aortic system, does not occur at all. Within wide limits, the vascular system accommodates itself to its increased contents and adapts sufficiently to an enormous filling without an increase in pressure and therefore also without its consequences.

Once again we have reached a point which forces us to remember how willing people have always been to advance their knowledge on the transfusion question. The construction of a plethora vera with enormously increased blood pressure after transfusions gave reason to precede the operation in certain diseases with depletoric bloodletting. Indeed, the aim was to cure septicaemia by drawing a large amount of blood from the septic patient in order to replace it with new blood from a healthy blood donating individual. Today we can prove that this type of operation causes double damage to the patient, namely through bloodletting and through transfusion. Almost immediately after this unfortunate suggestion, which significantly hastened the fatal outcome in a number of cases of septicaemia, the non-existence of a blood pressure-increasing plethora artificialis was demonstrated!

The febrile movements, the haematuria, the diarrhoea and transudates in those subjected to the animal blood transfusion were neither dependent on the globular embolism and stasis that was to follow the injection of voluminous and agglomerated blood cells, nor on the increased blood pressure. One had to have taken a step forward in the knowledge of the coagulation processes within the circulating blood in order to find out the cause of these disorders. I can attribute the credit for this to one of my best students, Armin Köhler, who unfortunately died very young. Köhler (13) first showed with rabbits that not only foreign blood, but also strange blood, which was first removed from the rabbit through bloodletting, then defibrinated and returned to the vessels, was disturbing, harmful and poisonous in the same sense as the foreign blood. The animal was killed by its own blood. The experiment, which was initially disputed, has now been repeated so often that Cohnheim said of it: "Everyone who has seen it will from now on have serious reservations about considering the infusion of blood in which coagulation has already taken place to be an innocent procedure. (14) All you have to do is take 10-12 cc of blood from a carotid artery in a rabbit, let it clot and squeeze the clot out between canvases. If the squeezed out material is filtered and about 5-6 cc of it is slowly brought back into the same animal's jugular vein or, even better, as an arterial transfusion into the femoral artery, the animal dies during the operation or very soon after the experiment. It ends in extensive coagulation in its small circulatory system. If you open the chest immediately after death, you will find the heart full of tough, matted clots and the entire branch of the pulmonary artery bulging and brimming with red thrombi, which can be traced down to the smallest branches of the vessels.

The result of this experiment is the consequence of Schmidt's coagulation theory. In the defibrinated blood, the fibrinoplastic substance and the fibrin enzyme are released; if they are brought into the blood in this state, they also cause coagulation within the bloodstream, in the still circulating contents of the vessels. The organism therefore has what appears to be a very effective series of devices which prevent this intra vital coagulation in the vascular tree. However, like every such facility, this one only proves to be effective within certain limits. If the quantity of injection fluid whose influence on the blood is to be eliminated becomes too large, despite the organism's counter-work coagulation occurs intra vitam and the blood solidifies in the veins.

But Köhler's experiments and their continuation revealed even more. Everything that destroys the blood cells in the bloodstream, especially the white ones, releases the fibrin generators, creates a vital ferment content in the blood and also causes two things: with massive and extremely acute dissolution of the blood cells - coagulation in the circulation, with less, less intensive and extensive destruction - just a blood decomposition with which the organism can still cope, which it overcomes, but only with the manifestation of a specific clinical picture, the complex of symptoms that Magendie already described as typical for transfusions with defibrinated blood, Panum for those with foreign blood and which Köhler rightly calls, with good justification, "ferment intoxication".

You only need to inject Schmidt's blood enzyme, (15) or, as I have done with Angerser (16), pure pepsin and pancreatin into the artery or vein of an animal in large doses in order to bring about the dissolution of the blood cells in them and then precisely according to the dose of ferment used, symptoms of the disease are sometimes mild, quickly temporary, sometimes severe, long-lasting, sometimes fatal. Now it becomes understandable why, of all types of blood, defibrinated bovine blood has the worst effect and results in the most

severe disorders after its transfusion, because, as Schmidt has shown, its serum has the relatively highest ferment content. (17) This ferment is not missing in any blood in which coagulation and defibrination has occurred outside the body; it is present in every blood. For this reason, with every transfusion of defibrinated blood, a poison that affects and destroys the blood cells is introduced into the bloodstream. The person subjected to such an operation is made ill by it, and if he was already ill before, the operation added a second and new illness to the already existing one. Fortunately, the organism has the possibility and ability to cope with the noxious substance that has been introduced to it. But the fever from which he suffers as a result of the disturbance caused to his blood and which, as the enthusiasts of transfusion assure (10), regularly manifests itself in the feeling of increased heat and chills; this fever is the organism's inevitable response to the intervention, through which people have tried to cure him, and yes, how often even to get rid of the fever. (18)

We surgeons these days are used to attributing all wound diseases to harmful substances and germs that arose outside the sick patient; i.e. have come to it from outside. In ferment intoxication, however, we are dealing with the effect of a substance that was formed within the organism in question, in the midst of its blood, supplied solely by the products of the dissolution of its own constituent parts, its blood cells.

In the liquid tissue that circulates as blood in our veins, the cells are also the "centres of its activity" and their change is what the disease represents, a real blood disease, but such a condition cannot be without influence on the condition of all organs and all other tissues of the body. The great mobility, diversity, variability and frailty of the blood cells make them easily diseased and in a certain sense at least restore haematopathology. But the thought takes me too far. My intention was simply to show in what sense every transfusion with defibrinated blood, even that of the same animal species, and especially with defibrinated human blood, becomes harmful and must become harmful every time. As often as a transfusion has saved a person bleeding to death, this happened because the injected fluid caused the stagnant blood column to move again by tensioning the vessel walls, but not because new blood cells were brought into the circulation to resume the endangered respiratory activity of the blood. On the contrary, their existence was actually shaken by the operation that was intended to increase them. We always used a very questionable remedy and it was only because we usually used it in very small doses that our patients, who were still resistant, were able to endure it and overcome the new damage that we had caused them with the old one.

Where the gifts were larger, where we had to deal with feverish illnesses, e.g. for septicaemia, we poured oil on the fire. The depletoric bloodletting mentioned above already increased the vital content of the blood in fibrin ferment, (19) which is present in every person with fever, (20) but especially in those with septic infections. (21) If the transfusion then followed, the amount of ferment newly added to the transfused blood led to such a significant increase and accumulation of the latter in the circulating blood that only in exceptional cases could the lethal end be averted. In fact, almost nineteen percent of those subjected to transfusion because of septicaemia died a few hours after the operation. The others died later.

As already mentioned, we have two circumstances to thank for the fact that the transfusion has so often passed safely and has even been tolerated by our patients without any noticeable disturbances. In the first place, the small quantities of blood chosen for transfusion, 20-30 grams, with which one tried to cure phthisis, chlorosis and chronic intestinal catarrh, and then the great resistance with which the organism is usually equipped against the effects of the fibrin enzyme. In this case, it will depend on how great this resistance, i.e. the performance of excretion and replacement in the blood-receiving individual is and then how high the ferment content of the transfused defibrinated blood turned out to be. The latter fluctuates within wide limits.

But if transfusion has the dangers that we have gradually learned about, then our advanced and better knowledge will force us to admit that we have exceeded our abilities in the worst possible way, in particular over estimated the operation. With this more than doubtful, even dangerous remedy, we achieved nothing other than restoring the activity of

the heart in cases of acute anaemia by filling the elastic vascular tube. But we are able to do this by choosing a few different means, such as we have been offered, for example in the saline infusion. It has already been confirmed through multiple experiences, including cases in my clinic, that saline infusion in humans does the same thing as transfusion: it awakens the person who is bleeding from unconsciousness and causes their impalpable pulses to beat again. It is conceivable that one day one could revive someone who is starving with a poisoned drink, but if the dangerous gift can be replaced by a better and harmless one, we welcome this turn of events with joy.

Only one transfusion could perhaps be justified: the transfer of blood from one person's artery directly into the vein of another person in need of help. I will leave it open to question whether a procedure that demands so much sacrifice from a fellow human being would ever become widespread; I also want to say nothing about the fact that the same difficulties that gave rise to fears of clot formation in the connecting cannulas at the beginning of the century still exist today - it is enough that the continued existence of the red and white blood cells transferred through the operation in the blood recipient's circulation can, indeed must, be questioned. At least where whole animal blood is supplied to a human or another animal species, it can be demonstrated and proven with certainty that both types of blood cells perish in large quantities.

The infusion of a concentrated solution of the blood enzyme into the vessels of an animal causes first and foremost the dissolution of the white blood cells, and probably only of a certain part and of a certain type of them. How this dissolution works has become the subject of studies by Köhler, Edelberg, (22) Angerer (23) and others. Only in the transfused blood are destructive factors other than Schmidt's ferment present. It has already been repeatedly mentioned that the passage of foreign blood, in addition to fever, dyspnoea, jaundice, vomiting and tenesmus, is very usually followed - according to Hasse's reports, it seems always - by the evacuation of blood-tinged urine. This haemoglobinuria is caused by the dissolution of the red blood cells. The mixture of heterogeneous blood types causes the added coloured cells to perish rapidly, almost instantly. But their decay produces a poison which could not be produced in any medicine as effectively and as perniciously as in the body of the animal subjected to the transfusion. The haemoglobin, released through the aforementioned dissolution process, enters the circulation freely and now energetically attacks the existence of the recipient's blood cells. Thus, instead of supplying blood cells, the direct animal blood transfusion also destroys the existing oxygen carriers. The disintegration of the red blood cells is followed and preceded by that of the white ones. As a result, the ferment is released in large quantities and the highest degrees of ferment intoxication now attacks the life of the person being operated on.

The foreign haemoglobin works in this direction just like your own. There is no difference here. The most severe cases of fermentation intoxication are always those which are associated with haemoglobinuria.

Although the toxic effects of haemoglobin had already become known through Naunyn, it was only Alexander Schmidt's and his students' studies that made clear the relationship of this body to the coagulation process and especially to intravascular coagulation.

Haemoglobinaemia also plays an important role in areas other than transfusion. Just as I have tried to group the symptoms of ferment intoxication at the sickbed and in their relationship to intoxication with putrefactive alkaloids, Ponfick has also just done the same with those cases in which free haemoglobin is present in the circulating blood, cases which he first summarized as haemoglobinaemia. The analogy in both series of diseases is obvious; the justification for the difference requires further investigation. It also remains to be determined why the haemoglobin of individual animals has a stronger dissolving effect on the same blood corpuscles than that of others, a relationship which may well explain the disintegration of the red cells when heterogeneous types of blood are mixed. First of all, the only thing that is certain is that the haemoglobin of very closely related animal species can behave chemically in very different ways. (26)

But these questions are also beyond my presentation and my conclusions, as I just want to establish one thing, an animal blood transfusion, both direct and indirect, one with whole

blood as well as one with defibrinated blood, never donates blood, but always only just takes and steals blood. The new, blood-donating era in medicine, which was prophesied not ten years ago, has already been nipped in the bud and quickly buried, insofar as it began with lamb's blood transfusion. We just have to be modest in our ability as long as we are still lagging behind in knowledge.

There will be no lack of attempts to add what the infusion cannot do to the blood through other means, and there is already no lack of them. But they are all premature and misguided. When it became known that fluids were absorbed extraordinarily easily, completely and quickly from the peritoneal cavity, attempts were made to fill it with defibrinated blood and to substitute these infusions for the usual transfusions. In experimental animals you can certainly see the lymphatic vessels of the diaphragm filling with red blood cells, but you can also observe the most beautiful haematogenous jaundice and you will hardly miss the urobilin in the urine, which comes from the absorption of large extravasates and indicates the dangers associated with them. Angerer's and Edelberg's clinical and experimental studies on these dangers also break the bar on intraperitoneal transfusion.

As true as it is that giving is more blessed than receiving, it may also bring more joy and satisfaction to increase medical skills through new healing methods than to shake up existing ones and contribute to the axe being laid on them.

But the aspiring doctor should not only be trained in art and science, but should also be encouraged, through the discipline of his school, to strictly criticize and judge each of his actions. His duty requires him to examine these only in the light of what he has discovered and to always remember the limitations that the current state of medical knowledge imposes on him.

However, duty as such does not give us any creative ability, because it is merely a means of discipline for our spirit. But without discipline towards oneself, without dutiful coercion, there is no sustainable energy and no loyalty in one's profession.

This is precisely what the medical officer should be trained to do in this educational institution, so that one day the full range of medical work and the duty of the responsible leader can be entrusted to him.

This is the sublime will of our German warlord, which we also consider it a special honour to fulfil through obedience and sacrifice.

God protected, God preserve, God bless His Majesty the Emperor!

NOTES / REFERENCES

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3. Scheel: Die Transfusion des Blutes und Einspritzung der Arzneien in die Adern. Kopenhagen 1802–1803. [Transfusion of blood and injection of drugs into the veins. Copenhagen, 1802-1803.]
4. Martin: Ueber die Transfusion bei Blutungen Neuentbundener. Berlin, 1859. [About transfusion for bleeding in newly born babies. Berlin, 1859.]
5. Gesellius. Zur Thierblut-Transfusion beim Menschen. Leipzig 1874. S. 17. [To animal blood transfusion in humans. Leipzig 1874. p. 17]
6. Malachia de Cristoforis: La trasfusione del sangue. Annali univ. di Med. e. Chir. 1876. Ottbr. [The transfusion of blood.]
7. Hüter: Langenbeck's Archiv für klinische Chirurgie. Bd. XII. S. I. [Langenbeck's Archive of Clinical Surgery Vol. XII, p. 1.]
8. U. Kronecker und J. Sander: Berliner klinische Wochenschrift. 1879, No.52. - E. Schwarz: Ueber den Werth der Infusion alkalischer Kochsalzlösung in das Gefäßsystem bei acuter Anämie. Habilitationsschrift. Halle 1881. – v. Ott: Virchow's Archiv für pathologische Anatomie. Bd. 93. 1883. [On the value of infusion of alkaline saline solution into the vascular system in acute anaemia. Habilitation thesis. Hall 1881. – v. Ott: Virchow's archive for pathological anatomy. Vol. 93. 1883.]

9. Sörensen: Undersøgelser om Awtallet ot rode og huide Blodlegemer under fors kjellige physiologiske og pathologiske Tilstande. Diss. Kjöbenhavn 1876. – Lion: Virchow's Archiv. Bd. 84, 1881. – Hünerfauth: Virchow's Archiv. Vol. 76, 1879, p. 327. [Studies on the number of red and white blood cells under different physiological and pathological conditions. Diss. Kjöbenhavn 1876. – Lion: Virchow's Archive. Vol. 84, 1881. – Hünerfauth: Virchow's Archive. Vol. 76, 1879. p. 327.]
10. Hasse: Die Lammblood-Transfusion beim Menschen. St. Petersburg 1874. "Dann beginnt Dyspnoe, gefolgt von einem Gefühle von Vollsein des Leibes, von Uebelkeit, Brechneigung, ja selbst von unwiderstehlichem Stuhldrang." Auch Kopfschmerz, Schwindel und kurze Bewusstlosigkeit werden beobachtet. "Zehn Minuten bis eine Stunde nach der Transfusion stellte sich Frost ein, oft zum heftigen Schüttelfrost gesteigert, dann ein Hitzestadium mit Erhöhung der Körpertemperatur um mehrere Grade." "Der schon einige Stunden oder erst am nächsten Morgen nach der Operation gelassene Urin war von schwärzlich rother Farbe, enthielt Eiweiss und Blutfarbstoff." – Ueber denselben Frost ½-2 Stunden nach der Operation in fast allen seinen Fällen von Transfusion defibrinirten Menschenblutes berichtet Heyfelder: Deutsche Zeitschrift für Chirurgie, 1874. Bd. IV. S. 496. Auch Neudörfer: Deutsche Zeitschrift für Chirurgie, 1876. Bd. VI. S. 76 bezieht den nach einer Stunde eintretenden Schüttelfrost auf seine Transfusionen mit defibrinirtem Blute. [Lamb blood transfusion in humans. St. Petersburg 1874. "Then dyspnoea begins, followed by a feeling of fullness of the body, nausea, a tendency to vomit, and even an irresistible urge to defecate." Headache, dizziness and brief loss of consciousness are also observed. "Ten minutes to an hour after the transfusion, chills set in, often progressing to severe chills, then a heat stage with an increase in body temperature by several degrees." "The urine, which had been passed a few hours or the next morning after the operation, was blackish-red in colour and contained protein and blood pigment." – Heyfelder reports on the same chill ½-2 hours after the operation in almost all of his cases of transfusion of defibrinated human blood: German Journal of Surgery, 1874. Vol. IV, p. 496. Also Neudörfer: German Journal of Surgery 1876. Vol. VI, p. 76 relates the chills that occurred after an hour to his transfusions with defibrinated blood.]
11. Ponfick: Virchow's Archiv. Bd. 62. S. L [Virchow's Archive. Vol. 62, p. 1.]
12. Magendie: Lecons sur le sang et les alterations de ce liquide. Phenomènes physiques de la vie. Paris 1838. t. IV. [Lessons on blood and the alterations of this liquid. Physical phenomena of life. Paris 1838. t. IV.]
13. Armin Köhler: Ueber Thrombose und Transfusion, Eiter und septische Infection und deren Beziehungen zum Fibrinferment. Dorpat 1877. [On thrombosis and transfusion, pus and septic infection and their relations to the fibrin ferment. Dorpat 1877.]
14. Cohnheim: Vorlesungen über allgemeine Pathologie. 1877. Bd. I. S. 346. [Lectures on General Pathology. 1877. Vol. I. p. 346.]
15. Köhler I. c. Birk: Das Fibrinferment im lebenden Organismus. Dorpat. Dissert. 1880. [The fibrin ferment in the living organism. Dorpat. Dissertation. 1880.]
16. v. Bergmann und Angerer: Festschrift der medicinischen Facultät zum 300j. Jubiläum der Univers. Würzburg. 1882. [Commemorative publication of the medical faculty on the occasion of the 300th anniversary of the University. Würzburg. 1882.]
17. A. Schmidt: Pflüger's Archiv. Bd. VI, 1872. [Pflüger's Archiv. Vol. VI, 1872.]
18. Hüter: Allgemeine Chirurgie. 1873. S. 644. [General Surgery. 1873. p. 644.]
19. Bojanus: Experimentelle Beiträge zu Physiologie und Pathologie des Blutes der Säugethiere. Dorpat 1881. Der vitale d. h. im circulirenden Blute vorhandene Fermentgehalt des Blutes steigerte sich bei einem Schaaf nach einem Aderlasse von 1,4 auf 2,7, bei einem Hunde von 7,1 auf 28,5. [Experimental contributions to the physiology and pathology of mammalian blood. Dorpat 1881. The vital fermentation content of the blood, i.e., present in the circulating blood, increased from 1.4 to 2.7 in a sheep after bloodletting, and from 7.1 to 28.5 in a dog.]
20. Edelberg: Deutsche Zeitschrift für Chirurgie. 1880. Bd. 13 S. 111. [German Journal of Surgery. 1880. Vol. 13, p. 111.]
21. Bojanus I. c. S. 53. Bei einem Schaafsbocke, dem faulendes Fleischwasser in eine Vene injicirt worden war und der nach 6½ Stunden der putriden Intoxication erlag, war der vitale Fermentgehalt von 1,0 auf 20,0 gestiegen, bei einem Lamme (Exp. 12) von 8,3 auf 35,3, bei einem Kalbe (Exp. 13) von 8,7 auf 100,0. Im Fieber nimmt nach Maissuriaz (Experimentelle Studien über die quantitativen Veränderungen der rothen blutkörperchen im Fieber. Dorpat 1882. S. 37) der Gehalt des Blutes an farblosen Blutkörperchen ab, nicht selten auf einen Rest von 5–10%. [p. 53. In a ram that had been injected with rotting meat water into a vein and succumbed to putrid intoxication after 6½ hours, the vital ferment content had risen from 1.0 to 20.0 in a lamb

(Exp. 12) from 8.3 to 35.3 in a calf (Exp. 13) from 8.7 to 100.0. According to Maissurianz (Experimental studies on the quantitative changes in red blood cells in fever. Dorpat 1882, p. 37) during fever the content of colourless blood cells in the blood decreases, often to a remainder of 5–10%.]

22. Edelberg: Archiv für Pharmacologie und experimentelle Pathologie. Bd. 12. 1880. S. 283. [Archives of Pharmacology and Experimental Pathology. Vol. 12, 1880, p. 283.]
23. Angerer: Klinische und experimentelle Studien über die Resorption grosser Blutextravasate. Würzburg 1879. [Clinical and experimental studies on the absorption of large blood extravasates. Würzburg 1879.]
24. Sachsendahl: Ueber gelöstes Hämoglobin im circulirenden Blute. Dorpat. Dissert. 1880. und Maissurianz l. c. S. 40 "Das mächtigste Mittel zur Herbeiführung eines explosionsartigen Zerfalls der farblosen Blutkörperchen und einer plötzlichen, hochgradigen Accumulation des Fibrinferments im circulirenden Blute ist das Hämoglobin im gelösten Zustande. – Es ist dabei gleichgiltig, ob die Hämoglobinlösung aus dem Blute des Versuchstieres selbst oder einer fremden Thierspecies genommen worden ist. Je frischer die Hämoglobinlösung, desto gefährlicher wirkt sie. Krystallisirtes Hämoglobin ist unwirksam. Auch Injection von destillirtem Wasser führt die geschilderten Blutveränderungen nebst fieberhaften Körpertemperaturen herbei, doch sind dazu grosse Wassermengen erforderlich und der Effect ist verhältnissmässig gering, wie das schon v. Bergmann hervorhebt, welcher Autor zuerst auf die fiebererregende Wirkung des Wassers aufmerksam gemacht hat. Das Auftreten von Hämoglobin im Harn nach Wasserinjectionen, sowie der Nachweis desselben in der Blutflüssigkeit der betreffenden Versuchsthiere führt zur Annahme, dass die schädlichen Folgen der Wasserinjectionen wesentlich auf die, durch die blutkörperchenlösende Wirkung des Wassers bedingte Gegenwart von gelöstem Hämoglobin im Blute beruhen." Nicht bloss nach Injection von Wasser und von Fermentlösungen, sondern auch nach Injection klar filtrirter, faulender Flüssigkeiten tritt nicht selten Hämoglobin im Harn auf. Es scheint hierfür wesentlich die Quantität der injicirten Jauche oder Fermente massgebend. Wenn defibrinirtes Blut in der indirecten Transfusion gleichartigen Blutes für gewöhnlich keine Hämoglobinurie macht, so ist der Grund hierfür der, dass es seine Wirkung auf die Auflösung der weissen Blutkörperchen beschränkt Umgekehrt werden wir dort, wo nach direkter Transfusion von Thierblut beim Menschen Hämoglobinurie auftritt, eine hochgradige Zerstörung weisser sowol als rother Blutkörperchen annehmen dürfen, eine Zerstörung, die höhere und höchste Grade der Fermentintoxication zur Folge haben kann. In der Wirkung der verschiedenen Transfusionen werden wir eine gleiche Scala der Gefahr wie nach den Injectionen von Pepsin und Pancreatin (v. Bergmann und Angerer l. c. S. 13) zusammenstellen können: geringere Wirkungsgrade, die sich nur im Fieber äussern, Repräsentanten der schweren Fermentintoxication Köhler's, wo zum Fieber Dyspnoe, Erbrechen, Diarrhoeen, Hämoglobinurie treten und schwerste Fälle, die schnell durch ausgedehnte Gerinnungen in den grösseren Gefässen oder dem Capillarraume der Lungen tödten. [About dissolved haemoglobin in circulating blood. Dorpat. Dissertation. 1880. and Maissurianz l. c. p. 40, "The most powerful means of bringing about an explosive disintegration of the colourless blood cells and a sudden, high-level accumulation of the fibrin enzyme in the circulating blood is the haemoglobin in a dissolved state. - It does not matter whether the haemoglobin solution comes from the blood of the experimental animal itself or from one taken from foreign animal species. The fresher the haemoglobin solution, the more dangerous it is. Crystallized haemoglobin is ineffective. Injection of distilled water also causes the described blood changes in addition to feverish body temperatures, but this requires large quantities of water and the effect is comparatively small, as already emphasized by von Bergmann, who first drew attention to the fever-inducing effect of water. The occurrence of haemoglobin in the urine after water injections, as well as the detection of haemoglobin in the blood fluid of the experimental animals concerned, leads to the assumption that the harmful effects of the water injections are essentially due to the presence of dissolved haemoglobin in the blood due to the blood-dissolving effect of the water." Haemoglobin often appears in the urine not only after the injection of water and ferment solutions, but also after the injection of clearly filtered, putrefying liquids. The quantity of the injected liquid manure or ferments seems to be crucial for this. If defibrinated blood does not usually cause haemoglobinuria in the indirect transfusion of similar blood, the reason for this is that it limits its effect to the dissolution of the white blood cells. Conversely, where haemoglobinuria occurs after direct transfusion of animal blood in humans, we will find a high degree of destruction of white blood cells as well as red blood cells, a destruction that can result in higher and highest degrees of ferment intoxication. In the effect of the various transfusions, we will be able to compile the similar scale of danger as after the injections of pepsin and pancreatin (v. Bergmann and Angerer

l. c. p. 13): lower levels of effectiveness, which manifest themselves only in fever, representatives of Köhler's severe ferment intoxication, where the fever is accompanied by dyspnoea, vomiting, diarrhoea, haemoglobinuria and the most severe cases, which are rapidly killed by extensive coagulation in the larger vessels or the capillary space of the lungs.]

25. Ponfick: Ueber Hämoglobinämie und ihre Folgen bin der Berliner klinischen Wochenschrift 1883. No. 26. [On haemoglobinaemia and its consequences in the Berlin Clinical Weekly 1883. No. 26.]
26. Körber: Ueber Differenzen des Blutfarbstoffes. Dissert. Dorpat 1866. [On Differences of the Blood Pigment. Dissert. Dorpat 1866.]