UEBER DIE WANDLUNGEN DES LAMMBLUTES INNERHALB DES MENSCHLICHEN ORGANISMUS:
EIN BEITRAG ZUR LEHRE VON DER TRANSFUSION

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A TRANSLATION BY PHIL LEAROYD

A copy of this paper titled 'About the changes of lamb's blood within the human body: A contribution to the study of transfusion' by Emil Ponfick (1844-1913), published in 1874 in the journal *Berliner Klinische Wochenschrift* (Vol. 11, No. 28, Pages 333-336) can be read or downloaded from the following site:

https://babel.hathitrust.org/cgi/pt?id=mdp.39015049764577&view=1up&seq=343

This short paper is essentially a discussion based around a scientific investigation regarding the possible fate of lamb red blood cells following their transfusion to a human (though the exact details of the transfusion are not provided). The patient, a 36-year-old woman admitted to hospital several days after a 'secret birth', had a number of complicating clinical problems (as well as a retained placenta, severe endometritis and anaemia). Immediately after the transfusion the patient 'fell into a deeply comatose state and died just 20 minutes later'. Following the autopsy, Ponfick microscopically examined blood cell samples from different parts of the body, though the exact details of this are also not provided (i.e. stated only as being 'a drop of it, viewed without any additives').

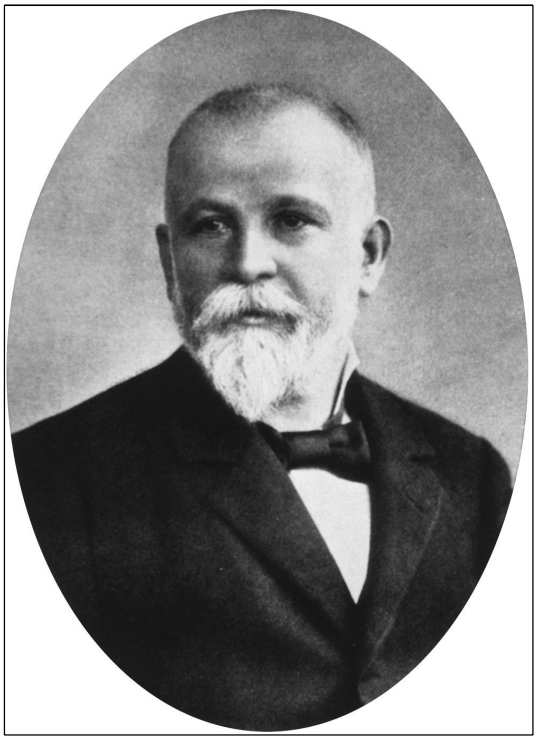
Ponfick states that he is able to identify what he believes to be red cell fragments in the patient's blood samples, some within the blood stream and others within white cells, and raises the question as to whether these are the transfused lamb red cells that have been rapidly destroyed following the transfusion, and as such therefore, whether lamb red cells transfused into a human patient react differently to those in experimental cross-species animal blood transfusions.

Although based on empirical evidence of a single case, this is an important paper in that it is the first publication that attempts to scientifically investigate the potential fate of the red cells used in an animal-to-human blood transfusion - even though it was James Blundell as early as 1818 who was the first to clearly state that only human blood should be used for human transfusions. Leonard Landois subsequently confirmed Ponfick's findings with his own statistical data, presented in his book 'Die transfusion des Blutes' (Leipzig: Verlag S.C.W. Vogel) published a year later in 1875.

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

original wording I cannot guarantee that this work does not contain 'translational errors' and the reader is recommended to check specific details against the original text.

The paragraph settings and general layout of this paper have 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 as well as those that are the author's comments.



Emil Ponfick (1844-1913)
(Image credit – Wikipedia)

EMIL PONFICK (1844-1913)

Emil Ponfick was born on 3rd November 1844 in Frankfurt. He obtained his degree at the University of Tübingen and his medical doctorate from the University of Heidelberg in 1867; and later became assistant to Friedrich Daniel von Recklinghausen at Würzburg and to Rudolf Virchow in Berlin. In 1873 he became professor of pathology at Rostock, followed by professorships at Göttingen (from 1876) and Breslau (from 1878), where he became director of the pathological institute, where he remained until his death on the 3rd November 1913. His research in 1874 into the dangers of animal to human blood transfusions led him to warn the Association of Baltic Physicians against zenotransfusion.

ABOUT THE CHANGES OF LAMB'S BLOOD WITHIN THE HUMAN BODY
A CONTRIBUTION TO THE STUDY OF TRANSFUSION

PROFESSOR DR. PONFICK IN ROSTOCK [1]

Once again, as more than two centuries ago, the promising idea of giving sick people new strength through the supply of the blood of a healthy animal, of restoring life, perhaps full health, has proven its full power in a restlessly moving forward of medical science: this is evidenced by the rapidly increasing series of bold, it would seem, lamb's blood transfusions, accompanied by astonishing successes, in which it has once again found an active expression.

As a result of the expanded version that must now be given to the much-discussed question in view of the favourable experiences of Oscar Hasse[2], it is no longer just the surgeon and the obstetrician who have an urgent interest in its impartial answer. Today, the all too often helpless counsellor of the colourful group of internally ill "incurables" is involved in their solution to an at least equal extent, for who the new healing method seems to open up an unexpectedly wide field of beneficial activity.

But whatever the final decision may be, the verdict on the value or worthlessness of the animal blood transfusion has already undergone too many changes, according to the changing opinions of the day, for it not to be necessary to call upon all the resources of our more advanced science, in order to bring the burning question to a well-founded solution in all directions. It is precisely this fluctuating favour or disfavour that the operation has encountered over time that can, I think, lead us to the conclusion that from an observation at the bedside alone, no matter how cautious, no matter how conscientious, even how sceptical, can be a complete benefit if one cannot hope for a full understanding of its healing effects and thus also a resounding long term satisfactory verdict. Rather, it will be a matter of carefully examining the experience gained from the carefully examined patient and comparing it with the results that experimental research, which works with simpler and easier to estimate factors, gives us, and then trying it on the human being himself to test the animal blood introduced into his body to follow the long path from step to step in order to gradually penetrate into the secret of its wonderful effectiveness. In this sense, I believe we cannot be content with adding a number of other cases to the considerable number of cases with more or less blatantly favourable results from lamb blood transfusion. Rather, every fact that is capable of forming a solid link in the long chain between cause and effect and thus establishing a genetic connection between the intervention on the one hand and the healing miracle on the other, which we still lack, must be sought out and used for the purpose of a justification that is no longer purely empirical, but at the same time strictly scientific, for the method that is greeted with fresh hope.

The transfused human being itself is of course an absolutely conclusive object, and therefore the most fruitful one for promoting such an endeavour, and so in the abstract we must certainly prefer any information that can be obtained from it to any evidence that can be obtained experimentally on animals. But in concrete terms, the solution of a whole series of special questions is faced with not inconsiderable difficulties, which even the most scientific zeal will hardly be able to overcome in their entirety, and even among the many consequences of the operation that can be observed without too much difficulty, only a few individual series of symptoms have so far become the subject of more detailed consideration. From the very beginning, there have been those quoad vitam of the most significant importance, which can be traced back to an alteration of the nervous system, be it the cerebrum, the respiratory or the circulatory centres. Furthermore, another group of symptoms is reported in the illness histories shared by Hasse, which definitely indicate significant anomalies in urinary secretion[3]. And Sander has recently turned his attention to the latter, especially the most obvious of them, "haematuria", in fair appreciation of their decisive influence on a recommending or warning judgment: this is evidenced by several

undesirably complicated cases in this direction, which he has recently communicated to us from his observations[4].

Even before Sander's adverse experiences in humans had come to my knowledge, I had had a very similar experience on the occasion of an experimental investigation that was actually carried out with a different end goal. During transfusion experiments on dogs that I carried out together with my assistant Dr. Bamberg, explained that the blood of an individual from another order of mammals, even in very small doses, experienced a completely different fate than the blood of an individual belonging to the same species, insofar as that (the foreign one) was destroyed to a certain extent and is excreted again through the urine.

After establishing this fact for dog and sheep blood, I had to look, returning to humans, to decide the obvious question of whether the relationship that prevailed there should also apply in the same way to lamb and human blood, in other words: whether lamb's blood does not also represent an adequate medium for man. With this in mind, I endeavoured to demonstrate any intermediate steps between the perceived “haematuria” by those transfusors and the introduced lamb's blood.

However, given the great willingness of the local population to act as blood donors for a small fee, however, lamb blood transfusions are a great rarity in our clinics, and so I have not yet had the opportunity to gain living experience of the fate of the foreign blood species. On the other hand, I recently had the privilege of carrying out a detailed post-mortem examination of a woman who had recently given birth and died quickly after the injection. - If I report on the results to a wider circle today, without having acquired any new observational material, especially those collected from the living, it is essentially in the hope that more fortunately situated colleagues will be encouraged to check my findings intra vitam in their cases. However, this can only be achieved through the not effortless method of a methodical examination of the patient's blood in the various periods after the operation.

The case in question involved a 36-year-old maid who was brought to the maternity hospital several days after the secret birth (1st May this year), extremely exhausted by repeated heavy bleeding. The retained placenta, which the internal examination proved to be the cause of this significant blood loss, was immediately removed. But severe endometritis had already developed, accompanied by extremely discoloured discharge, chills had appeared, and the patient's steadily worsening condition gave rise to the urgent suspicion that the destructive process had now spread from the inner surface of the uterus to the other pelvic organs. In addition to these puerperal symptoms in the narrower sense, the symptoms of severe fatty degeneration of the heart gradually emerged in a way that could not be misunderstood. The only thing that remained doubtful for the time being was whether this was to be viewed as a pre-existing ailment or as a direct consequence of the acute anaemia, in accordance with the view I developed on the basis of anatomical-clinical observations[5], which has since been confirmed by the subsequent experimental investigations by Perl[6].

With so many severe and complicated changes, such as the puerperal local affection, severe anaemia and fatty heart disease, transfusion could only be considered a last attempt, and so it was undertaken only with extremely low expectations. It therefore hardly needs to be particularly emphasized that the present case is by no means suitable to be taken into account in the solution of the general question of the value or unworthiness of transfusion, and nothing is further from my mind than, by communicating this, than wanting to make a contribution to the statistics of the method.

The operation was carried out by my esteemed colleague, Professor Schatz, on the 12th day after the birth in the usual manner and took about 1-2 minutes. The indication to close the cannula resulted in a paroxysmal increase in the previously weaker symptoms of oppression. Otherwise, the patient's behaviour during the act of the injection presented nothing unusual; but while it was being aborted she fell into a deeply comatose state and died just 20 minutes later.

The dissection, which I carried out a few hours post-mortem, revealed the main finding to be a diphtheritic-slurry endometritis, which was most pronounced at the placental site. This was followed by an analogous metrophlebitis, which in turn continued into the spermatic

venae, but was already separated from the central bloodstream by a wall of well-preserved thrombi. Apparently in connection with this venous affection, there was a solitary, partially excreted abscess of small size in the upper lobe of the left lung and, above it, partly rejuvenated, a circumscribed pleurisy. The degree of fatty degeneration of the heart exceeded expectations. There was an extraordinary pallor in all the internal organs, most notably in the kidneys, which however, otherwise appeared to be completely unchanged, even microscopically.

Given the peculiar course of this case, great interest had to be devoted to the findings of the heart, the large vessels and the blood. The heart appears significantly enlarged due to excessive expansion with blood, and is wilted and flaccid. The right atrium and ventricle contain a copious amount of mostly blubber-skinned dirty gray-red clots, along with a little cruor and liquid blood. In the left half there is also a considerable, but much smaller amount of largely congealed dark cruor. The cardiac cavities are all somewhat dilated, especially on the right side, and the walls are relatively thin; the musculature dirty grey-brown, very pale. Within this discoloured, very brittle tissue mass, numerous yellowish spots and stripes, mostly arranged in groups, can be seen in certain places, which are most densely located in the conus pulmonalis on the right, on the outer circumference of the ventricle on the left, and in the papillary muscles. The valve apparatus is completely normal. - In the pulmonary artery, trunk as well as branches, very abundant loose filling masses of the same appearance as those in the right heart. - The large veins of the thoracic aperture and neck, as well as the right axillary, brachial and cephalic veins (the right elbow was chosen for injection) contain delicate grey-red clots, apparently of very recent date.

The microscopic examination of the blood in different parts of the body consistently led to an unexpected result. A drop of it, viewed without any additives, showed, even on superficial inspection, such a number of small yellowish coloured elements within the plasma that, apart from the normally present cellular components, it resembled a dense emulsion. The most extensive of these bodies reached two-thirds the size of the surrounding red blood cells and they were followed in the most varied gradations but in a completely continuous sequence by a long series of smaller and smaller granules, down to the finest ones that were just visible. Some of the latter, due to their small size and therefore in connection with the lively (Brownian) movement phenomena that can be perceived in them, would perhaps have been viewed under other circumstances as particles of fatty detritus or as some form of coco shape. Here, of course, their distinctly yellowish colouring, and then the immediate chain of ever larger shapes of exactly the same nature, showed that they all belonged closely together and represented something very strange. - Just as in terms of colour, the large and small ones are essentially the same in terms of shape: they both reproduce the image of red blood cells on a smaller scale. Most of them are round, only a small part elliptical or irregularly shaped, and from the lively motion into which they may be set by a slight dislocation of the medium which supports them, it may be plainly seen that the larger ones are distinctly disc-shaped, and that the more they diminish in circumference, the nearer they approach the type of a sphere or ellipse. - If, on the basis of these characteristics, it must have been regarded as quite probable that these structures, which are coloured and shaped quite like red blood cells, represented fragments of these very cells, this assumption was raised to full certainty by their chemical behaviour. For they proved to be quite equal to all agents which act upon the red blood cells in a well-known characteristic manner; I only mention here their rapid disappearance on the addition of well water, as well as their gradual lightening, further dissolution after the addition of a few drops of a solution of acetic acid 10 per cent.

But now it was necessary to investigate whether the elements in question floating in the plasma of the woman who had recently given birth came from the pre-existing human blood cells or from the introduced lamb blood cells. This made it necessary to decide the preliminary question: Is it really possible to differentiate between the cells belonging to the two varieties in individual cases? I have to admit that, given the not insignificant variation in the size of normal human blood cells, I originally had only limited confidence in the general validity of the observation that the two types of blood could be distinguished everywhere.

And the measurements given to us in histology textbooks seemed to justify such doubts to a certain extent. However, it is not difficult to convince yourself, by looking at a drop of human blood that has been intimately mixed with lamb's blood outside the body, of such a striking difference between the cells of one type and the other that one can at least recognize the vast majority without further ado and will be able to classify then into this or that group. The results of repeated measurements, according to which the size ratio of lamb to human blood cells turned out to be 0.6:1.0 to 0.7:1.0, was completely in line with this general impression

After this, I believe there can no longer be any doubt about the possibility of a distinction within the bloodstream in general. Especially for the present case, a comparison and measurement carried out in flagrante of the largest of those coloured structures in the plasma of the woman who had recently given birth on the one hand and fresh lamb blood cells on the other hand confirmed that they were exactly the same in every respect, especially with regard to size. Therefore, not only for internal reasons, but also with regard to their special properties, one would be justified in referring to them as lamb's blood cells. As far as the analogous smaller forms are concerned, it would be very difficult to provide conclusive proof that they arose from the decay of human or lamb blood cells. However, the fact that no intermediate stages could be found between the intact human elements and the largest coloured elements, which are understood to be lamb's blood cells, seems to me to speak most decisively against any more extensive dissolution of the former. And these certainly shouldn't be missing if continuity in the sequence of the decay products is to be maintained.

But even if I had to refrain from an immediate decision on the question of the latter, special origin, at any rate the fact was established that the structures in question were fragments of red blood cells, and therein lay the urgent invitation to also turn my attention to the colourless elements. For, through von Recklinghausen's well-known investigations we have learned that small foreign bodies (cinnabar granules, etc.) introduced into the plasma from the outside are immediately taken up by the white blood cells[7]. Moreover, in the course of experimental work following the individual phases and modalities of this process[8], I was able to convince myself often enough how quickly this transition takes place, how it follows the introduction of those granules into the bloodstream almost immediately. The same result could then also be expected for small particles that, having become free for some reason within the bloodstream, were floating around in the stream as a bonne prise.

In fact, clearly yellowish coloured bodies were found in the blood of the most diverse regions, completely identical to the fragments described floating freely in the plasma, enclosed in white cells; sometimes they were solitary, more often in groups of 2, 3 or more, and in the latter case in a different varying size ratio. Individual cells contained noticeably large such structures, so much so that I had to ask myself whether they were not intracellular lamb blood cells (they would have been much too small for human ones). However, in view of the physiological variations in size and the difficulty of making an exact determination of the various dimensions of intracellular components, I do not dare to make a quick affirmative decision. No matter how this point may be interpreted, there is no doubt that within the general bloodstream we have before us colourless bodies in which red bodies are enclosed, either whole or in fragments, a finding that, as far as I can see, is still today completely isolated in the physiological as well as in the pathological field.

If, in conclusion, we summarize the findings obtained in this case with the aim of bringing them into an internal connection with the symptoms observed intra vitam mentioned at the beginning of this article, we can already see 3 actual indications for the assumption that blood cells are destroyed as a result of the lamb blood transfusion. "Haematuria", strictly speaking haemoglobinuria, already known enough to the older experimental researchers and no less to the first as well as the latest transfusors, represents the final link in the series of phenomena, which lies beyond the blood circulation, in which this process of dissolution finds expression[9]. Within the bloodstream there are two findings that are evidently directly related to the introduced medication: namely, firstly the crumbling or disintegration of red blood cells into a multitude of larger and smaller fragments and then secondly the absorption of some of the resulting cell debris, perhaps even intact undamaged cells, into the body of

the colourless elements. It seems to me that these last two phenomena can hardly be interpreted as anything other than a sign that a certain group of red blood cells as such, i.e. as mediators of gas exchange, are in the process of disappearing in order to be used solely as metabolic food.

What, in my opinion, cannot yet be answered with certainty is the question of whether the fragments can be traced back to crumbling lamb or human blood cells. However, perhaps while reading these lines, the interested reader himself may have made certain assumptions that will hopefully point him in the right direction in his efforts to further advance our knowledge of the individual phases of this complicated process of transformation and regression. In any case, I think we must remain clear that, in accordance with the assertion made by Hasse in the course of his theoretical discussions, the decrepit blood cells of the sick patient were the ones that perished; that they provided the material for “haematuria”, while the lamb blood cells would take on the role of mediator of gas exchange in their place - so far no anatomical or experimental fact has been adduced as support it.

REFERENCES

1. Nach einem am 28. Mai d.J. vor der Versammlung baltischer Aerzte zu Rostock gehaltenen Vortrage. [According to a report on 28th May this year Lectures given before the meeting of Baltic physicians in Rostock]
2. Die Lammbluttransfusion beim Menschen. Petersburg 1874.
3. a. a. O. p. 43. etc.
4. Berlin. klin. Wochenschrift. 1874. Nr. 15 und 16, p. 191.
5. Berliner klin. Wochenschrift. 1873. Nr. 1 u. 2.
6. Virchow's Archiv, Bd. LIX, p. 39.
7. Die Lymphgefässe etc. p. 22 fgde. Ueber Eiter- und Bindege-webskörperchen. [The lymphatic vessels etc. p. 22 fgde. About pus and connective tissue bodies], Virchow's Archiv Bd. 28. p. 184.
8. Studien über die Schicksale körniger Farbstoffe im Organismus. [Studies on the fate of granular pigments in the organism.] Virchow's Archiv, Bd. 48, p. 37 fgde.
9. Im vorliegenden Falle war der Tod erfolgt, noch ehe es dazu hatte kommen können. [In the present case, death occurred before it could have happened.]