

From Blood Transfusion to Haemotherapy – the Anniversary of the German Society for Transfusion Medicine and Immunology (DGTI) from a Medicinal-Historical and Bioethical Perspective^a

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‘There will always be enough philosophers – but there will never be enough blood.’ This motto was part of a billboard campaign initiated by the German Red Cross in summer 2004 to motivate people to donate blood. Back in August, when I saw this advertisement for the first time, I was immediately reminded of the forthcoming 50th anniversary of the DGTI. Since the respective university professor for the history, theory and ethics in medicine is also somehow a ‘philosopher’ in his own right, I asked myself: What can I contribute to the 50th anniversary of a subject, whose task it is to dedicate all its efforts to help the seriously ill and not to reflect upon philosophical questions?

The formal reason for this 50th anniversary is the formation of the German Society for Blood Transfusion on October 30, 1954. In 1973 the name was changed to German Society for Blood Transfusion and Immunohaematology, and in 1986 the society received its current name German Society for Transfusion Medicine and Immunohaematology (DGTI) [1]. The two changes in the name alone imply how dynamically the tasks of this special medical subject have developed within a period of only five decades: Today, the scope reaches from blood transfusions via the production and application of plasma derivatives, for example for the treatment of blood coagulation disorders, to the therapeutic use of adult blood stem cells for life-threatening cancer diseases such as leukaemia.

Not only human beings have a life story. Even organisations such as a medical society reflect developments in which ac-

tions of participating protagonists, including all their pertinent aims, achievements and failures, as well as scientific, political and social conditions of their time are manifested. The task of the historian is to describe not only the straight forwardness of human actions but also the contingency, which means the unpredictability of events, processes and structures which are neither exclusively determined nor do they occur completely unmotivated. My intention is not to provide you with a short version of all written contributions for this publication but to raise some questions from the external, in some parts certainly ‘philosophical’, position of a medicinal historian and medicinal ethicist about the past and the present.

It is remarkable that blood transfusion has constantly been an issue between the mid 17th century and the end of the 19th century even though there has neither been sufficient scientific evidence nor considerable practical success until the discovery of the four classical blood groups at the beginning of the 20th century. Without doubt, this phenomenon is linked to the close interrelation between medicine and mythology. Since ancient times, common belief has considered blood to be the carrier of life as well as of physical and intellectual properties and close family bonds, the so called ‘blood relation’. It was believed that these individual characteristics could be transferred, together with the blood, from one person to another and even from an animal to a human being. The blood of a strong and brave animal would make oneself strong and courageous, the blood of animals with night vision could help to optimize one’s own capability to see at night, the blood of healthy human beings could cure the ill from epilepsy and leprosy. In most cases the blood was supposed to be drunk, either pure or mixed with wine, but some legends also say that it was enough to bath the body in the foreign blood.

These ideas also fired the fantasy of physicians in the early modern times with regard not only to biology but also to ethics. Thus, in 1489, Marsilio Ficino (1433–1499), a Renais-

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sance scholar from Florence, recommended to suck the blood of a young man's arm vein to revive the physical strength of aging men, he himself has been 56 years old at that time [2, 3], and the physician and mathematician Girolamo Cardano (1501–1576) argued in 1558 over the idea to improve the moral behaviour of an elderly gentleman by a direct transfusio sanguinis from 'a young man of good morals' [4]. After William Harvey published the blood circulation theory in 1628 and thus provided the relevant basis for a modern physiological understanding of blood movement in living beings [5], the symbolic characterisation of the possible effects of blood transfusions mingled with the idea of how to realise it technically. Thus, in 1652, Francesco Folli (1624–1685) illustrated a suggestion for a blood transfusion with, according to his opinion, the appropriate instruments. He then claimed to have been the first person to carry out a blood transfusion in Florence in 1654 [6, 7]. It is very likely that the first experiments with blood transfusions on animals originate from this time but not by a physician but by the English cleric Francis Potter (1594–1678). But the experiments failed miserably [3, 6, 8].

It was an English natural scientist who was the first to carry out a successful blood transfusion on animals in 1666: The physiologist Richard Lower (1631–1691) conducted the blood from the arteria cervicalis of one dog directly into the vena jugularis of another one [3, 8]. What started off as a basic experimental research on animals finally led to an attempt for a therapy of human beings in Paris, the Continental-European metropolis constantly competing with the British, one year later. In June 1667, the royal physician in ordinary Jean Denis (1640–1704) and the surgeon Paul Emmerez (†1690) transfused blood from the arteria cervicalis of a lamb into the vena cubitalis of a 15-year-old boy who had already been weakened by numerous therapeutic blood-lettings. The amazing thing happened: The patient survived the adventurous procedure unharmed.

Let us think which factors are to be held responsible for the success of the therapy? First of all there was the ambition, fanned by national pride, of the two French physicians to be ahead of the 'English'. In France we also did not encounter any legal obstacles against an experiment on a human being. Third, we had a patient suffering from a long lasting fever who had been treated wrongly for months – but nevertheless in accordance with the generally accepted humoral pathology concept of the time – by frequent blood-lettings which led to a further weakening of the patient. Fourth, Denis and Emmerez believed that the patient's blood was too thick and needed to be diluted. This rather poor theory justified finally the fifth reason for the blood transfusion with blood from a lamb because the animal was considered to be peaceful and physically and morally 'pure'. Sixth, they finally had the luck on their side when, by chance, no adverse reaction occurred at this premier.

Therefore one can say that the first successful transfusion on a human being happened – at least from a retrospective point of view – as a result of a wrong therapy of the underlying illness,

several misconceptions of physiological and pathophysiological models, lax criminal regulations, questionable national ambition and ethically hardly justifiable settings of priorities but also a great technical ability and good fortune. Fortune left Denis and Emmerez in December 1667 when they transfused the blood of a calf to the valet Antoine Mauroy (1633–1668), a man with reported psychiatric problems, to calm down the unpredictable patient. Mauroy died shortly after the third attempt to transfuse the blood. Denis was found not guilty because of the lack of evidence but the criminal court in Paris ordered in April 1668 that an approval of a physician who had to be a member of the medical faculty was needed before further blood transfusions were to be carried out [2, 8]. This decision made by the judges only implied to anticipate the function of an ethical committee as it is found in clinical research at the beginning of the 21st century since, de facto, no one dared to ask for a respective approval.

The physician Georg Abraham Mercklin (1644–1700) from Nuremberg published in 1679 a manuscript titled '*De ortu et occasu transfusionis sanguinis*' (English: 'About the Rise and Fall of Blood Transfusion') in which he demanded to terminate blood transfusions with animal blood and suggested the transfusion of blood from human beings for research purposes. However, until the end of the 18th century the moral verdict of Johann Sigismund Elsholtz (1623–1688), physician at the court of the grand elector of the king in Brandenburg, persisted which he set up back in 1667: According to Elsholtz, it might be considered as an act of barbarism to take the blood of one human being to save the life of another one. At the same time he speculated that it might be theoretically possible to reconcile hostile couples or brothers and sisters by a blood transfusion from one to the other [6, 10].

It was not before the end of the 18th century that new experiments on the transfusions of animal blood were to be carried out in Italy, France, England and Denmark using lambs, donkeys, horses, calves, bulls, dogs and even tortoises. Finally in 1825, James Blundell (1790–1877), an obstetrician from London, transfused human blood to a woman in childbirth, weakened by the acute loss of blood. The animal experiments prior to this now served a different purpose than in the mid of the 17th century: While in baroque times it was believed that a specific psychological character assigned to the donor animal used could be transferred to the human recipient of the animal blood, the animal experiments in Blundell's time had already developed into a scientific model, meaning a test run for a later application on human beings. It was no longer the supposed character that was transferred by the material substrate of an animal to a human individual but physiological reactions and technical methods, tested on animals, which were transferred to the human species by an epistemological conclusion of analogy.

In the centuries to follow, transfusions with animal and human blood were predominantly used in cases of acute blood losses after birth and – what was to become relevant for the future

scientific, organisational and economical development of transfusion medicine – in a military context after severe injuries of soldiers in the theatres of war; both with changing results. These were caused by technical problems, the only partially understood and not yet completely mastered coagulation of the blood in its pathophysiological complexity as well as immunological reactions, not yet understood as such, which occurred in cases of blood group incompatibility [11]. A statistics published in 1875 reported results that 48% of more than one 100 transfusions, mainly with blood from lambs, ended fatally. The transfusion of human blood was even less successful since 52% of the almost 359 transfusions had taken a ‘less fortunate ending’ [12]. Also the use of defibrinated blood, as demanded by several scientists, did not help; it even had an opposite effect. For this reason, the surgeon Ernst von Bergman from Berlin warned his students: ‘We have to be modest in the things we do as long as our knowledge is still inadequate’ [13, 14]. With this, he referred to a dilemma still present in today’s medical research, namely the tension between reflection and empiricism, between experimental recognition and clinical use.

The discovery of the blood groups O, A, B and AB at the beginning of the 20th century was not only the ingenious achievement of the Viennese pathologist and later Nobel Prize winner (1930) Karl Landsteiner (1868–1943) but rather a process of at least one decade and of the participation of several scientists – many of them working independently from one another. Apart from Landsteiner [15, 16], the Viennese specialist for internal diseases Alfred von Decastello-Rechtwehr (1872–1960) and his co-author Adriano Sturli (1873–1964) have to be mentioned here (both described in 1902 the blood group later referred to as AB [17]), the neurologist Jan Janský (1873–1921) from Prague who reported in 1906 about the existence of four human blood groups, a Czech publication that was hardly noticed [18], as well as the two immunologists Emil von Dungern (1867–1961) and Ludwik Hirsfeld (1884–1954), who investigated the hereditary side of the blood groups in 1910 and who also suggested the ABO nomenclature which then was not to be established as internationally binding until 1928 [14, 19]. Due to this research, the long-term prospects for a fruitful expansion of blood donation and blood transfusion in clinical applications were very positive.

The further development during the 20th century may not be seen as a linear process of a successful story, resulting exclusively in combining the results of straightforward biomedical research. Large contributions to this – without doubt impressive – scientific point of view came from physiology and pathology, hygiene, immunology and serology, surgery, internal medicine and anaesthesiology, and in recent times to an increasing extent from cell biology, adult stem cell research, biotechnology and gene therapy [20]. Also the effective and influential factors of the political and social circumstances of the time need to be considered. In this context, especially, the two world wars have to be mentioned with numerous severely injured victims – soldiers and civilians alike. Many of them

needed blood transfusions to save their lives, and this led to a fast development of scientific and technical innovations, contributing largely to the improvements in the treatment of the casualties. Dramatic effects were also caused between 1933 and 1945 by the era of National Socialism susceptible for technical innovations but disrespectful of human beings. Thus, only persons of a ‘pure Arian descent’ were accepted as blood donors by the NS state. In 1940, a circular order by the Ministry of the Interior of the Deutsche Reich demanded the following consent: ‘I herewith confirm that I am of German or German similar descent and that I do not have any – not more than one – non-Arian grandparents’ [14, 21]. The delusion of the purity of the ‘Arian race’ and the ‘Arian blood’ was not only considered to be metaphorical but was concretely evident in an almost frightening material way since it continued to believe in concepts of the Early Modern Times which were believed to be long since extinct.

Another consequence of National Socialism was the expulsion of Jewish scientists and university teachers. Many of them first had to face the taking away of the possibility to work and later on were forced to emigrate. Representatives are Fritz Schiff (1889–1940), Otto Neubauer (1874–1957), Ernst Witebsky (1901–1969), Ludwik Hirsfeld (1884–1954) and Ernst Unger (1875–1938) who, after his professional career had been ruined, was only saved from further prosecution by his own death in an accident. The haematologist and neurologist Hans Hirschfeld (1873–1944) who was head of the policlinic and of the department of haematology and histology at the institute for cancer research of the Friedrich-Wilhelms-Universität in Berlin, was killed in the concentration camp of Theresienstadt in 1944 [14, 22].

After the Second World War the effects of almost 45 years of political separation of Europe, and especially of Germany, still took considerable influence on the development of transfusion medicine. In the Federal Republic of Germany and in the rather centralistic German Democratic Republic we faced the rise of different organisational structures within the blood donation service on a communal, state, civilian and military level and under the responsibilities of the German Red Cross which had to be joined together in a very short time after the reunion of both states [1, 23, 27]. The development of transfusion medicine in Austria [28] and Switzerland [29] took place independently from one another.

The complex disciplinary structures in which transfusion medicine and immunohaematology present themselves today are also the consequence of an exorbitant increase in the tasks the subject sets for itself in the meantime. The focus is no longer mainly on blood transfusions as the program of the 37th annual meeting of the DGTI shows. Thus, in particular, the safety aspects of haemotherapy play an important role, e.g. the protection of blood components from bacterial contamination, and also questions such as computer-aided logistic planning or accreditation and certification have gained considerable relevance for the quality management of the subject. Further-

more, especially the field of adult stem cell research and adult stem cell therapy moved into the focus of professional interest. Thus, the transplantations of autologous and allogeneic haematopoietic stem cells have contributed greatly to the therapeutic success in the treatment of cancer diseases of the blood during the last two decades.

Far more than the work with adult stem cells which fortunately is meanwhile established in science and in practice, another sector of stem cell therapy, i.e. the research on embryonic stem cells, has moved into the centre of political and journalistic attention. Considering the highly successful and for many patients life-saving therapy with adult stem cells, with transfusion medicine and immunohaematology playing the leading role in the collection and supply, one almost has to regret that stem cell research is associated and even identified by the public with experiments on human embryonic stem cells. At present, the bio-political discourse is about whether human embryonic stem cells can be produced for biomedical research purposes, misleadingly called 'therapeutic' cloning at the moment, in Germany in the future [30]. In this case we do not only have a scientific debate but an ethically, legally and politically highly explosive dispute: From a basic right and normative aspect, when shall human life and its legal protection ensured by the state begin?

The main ethical argument against the moral approval of research on human embryonic stem cells is based on the fact that such a research uses and makes use of human embryos. Precisely in this, the ethical discourse in the German-speaking countries sees a violation of the dignity of man. This violation of dignity depends greatly on the moral status assigned to these formations similar to blastocytes originating from a transfer of cell nuclei. Within the scope of future experiments, could the formation of new cell clusters be possible with the ability for biological-developmental totipotency in the sense that they bear the potential to mature to a new organism, and could this organism initiate an independent development?

Current basic research in biology shows that fast and often unexpected innovations are possible. Further investigations about germ cells derived from embryonic stem cells and their ability for development are to be expected. With regard to the expected therapeutic applications in medicine, it is nevertheless important to keep the clinical reality, including the complex pathophysiological connections, in mind in a matter-of-fact kind of way. Currently, the use of embryonic stem cells as substitute for tissue is being discussed, but a clinical realisation is still out of reach. Specifically, the grave problem of the formation of tumours after transplantation of embryonic stem cells with unrestricted growth potential needs to be solved [31, 32]. Furthermore, the anatomical observation of ingrown tissue does not ensure its proper physiological function [33].

For the ethical assessment of all scientific work with human embryonic stem cells, it will be relevant also in the future whether it is human life that will be terminated within the scope of research and therapy. The human dignity must not

be touched by the fact that human life that is worth being protected is constantly defined anew according to current research priorities [34]. Further scientific studying of adult stem cells, being not only the field of intensive occupation of physicians specialised in transfusion medicine and immunologists, can support the breakthrough of therapeutic alternatives which are at the same time beneficial for medicine and ethically unproblematic. This might be a goal worth setting.

Ethical questions play a decisive role in more than one way in our subject, may it be in the field of cryo-preservation of umbilical cord blood, may it be in the difficult and problematic field of handling the, for economical reasons, limited financial resources within the health service, or may it be in the case of a 'reciprocal altruism' of a recently as a mere sequence of evolutionary selection mechanisms declared driving force for the decision of human beings to donate blood for other human beings [35]. On the other hand side, if we understand the altruistic blood donation – different from the belief of the sociobiologists – not as a determined phenomenon but as an expression of a, by no means, natural idealism or even as a sign of an active charity, even would interpret it as a conscious acting of responsible citizens, then the blood donor as a person will be in the focus of all transfusion processes.

Whoever donates blood for someone else without financial motives, must not be considered as a human deliverer for natural resources since the human body including all its relevant components is not suitable for being treated as a merchandise (statement of the Federal Government on the transfusion law (Transfusionsgesetz), § 10) [36]. The blood donor can be seen as a person with a pertinent personal history full of individual motives for his/her actions and personal aims, gifted with emotions such as happiness and hope but also hit by insecurity and fear. It is in particular this decision-forming process to donate blood for the first time that proves to be difficult: The will to do something good for the ill, but, first of all to do so, the lay person is lacking some important basic medical information. Furthermore, a personal network of friends and relatives is needed to establish the first contact with a blood donation service. Finally, thinking about a possibly painful and maybe critical blood donation for one's own health may also cause fear. In the year 2004, even an optimally informed donor invisibly carries the historical burden of a traditionally mythological idea about blood and its miraculous properties. 'Won't I be lacking something after the blood donation?' This fearful question is left unasked. Taking all this into account, it is understandable that only about 3% of the population actually donate blood while more than 90% of all Germans confirm their good will to become active for the good deed.

But does the active action of 'donating' blood receive an adequate appreciation apart from the festive rhetoric? Sometimes language itself gives us a hint. Thus, I personally believe that the term used in § 2 of the transfusion law passed in 1998 is irritating, it says: 'In the true sense of the law, blood donation is a collection of blood or blood components from a human

being which serves as a medicament or is used for the production of a medicament' [36]. And in a statement about the law, the former Federal Government determines: 'This refers to the 'product', not the collection process'. With this statement, two meanings, a legal and a political meaning, of the word 'donation' were specified: 'Product' and 'collection process'. In one case, the donor only serves as a supplier of a product, in the other, as a passive object in a medical procedure through which material is collected from him/her. The third and very decisive meaning of the word 'donation', namely, as an active altruistic giving of a vital part of one's own body to help other human beings, is left out completely in the technical, legal word of the law. The transfusion law aims therefore – according to its own definition (§ 1) – mainly at 'winning' blood and blood components and at the 'application' of blood products. It thus remains a substantial medical responsibility in the daily routine of the physicians specialised in transfusion medicine not to be content with the mere execution of seemingly per-

fect laws, but, for one and for always, to respect and to protect the dignity of all human beings who volunteer to donate blood. The physicians specialised in transfusion medicine are aware of this.

By referring to ethics, I have touched the field of practical philosophy. Philosophy is indeed present everywhere, even in transfusion medicine and in immunohaematology! I wish the DGTI good luck in the next few years to cope with all the scientific, economical and ethical questions, and all of you a continuation of the persistent behaviour which made the subject such a beneficial field within clinical medicine and an independent academic discipline.

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