1. Using the blood of others

> 'No operation in the last two centuries has aroused such high expectations, nor experienced such periods of contempt and oblivion as the transfusion of blood. For more than a century, it virtually disappeared from medical attention and despite being revived fifty years ago, it did not gain ground in a steady march forward but rather followed an ascending and descending curve.'

These words, from 1874, belong to Friedrich Sander, chief physician at the city hospital of Barmen in northern Germany.[1] He was one of many doctors who, in the mid-1870s, shared what a later observer would call a 'widespread […] fanatical enthusiasm' for blood transfusion.[2] The therapy, Sander noted, had been previously met with both applause and critique, and now seemed to be in vogue again. In hospitals across the continent, hundreds of patients received blood from others and some from the arteries of lamb.

To Sander, the prospect of healing the sick with lamb blood was fascinating. So, too, was the history of blood transfusion. He, and many others, found it important to anchor their trials and tribulations in a dramatic past, and show the foresight and acumen of the pioneers. They traced the origin of transfusion in myths and magic, related the first practical experiences in the 1660s and the ensuing condemnation by medical and church authorities. They then discussed the revival of the therapy in the early 19th century. Many referred to Ovid's' play *Medea* – she withdrew blood from Jason's elderly father Eason's body, infused it with powerful herbs, and returned it to his veins, rejuvenating him. This was not strictly a blood transfusion, nor did Goethe hint

at this operation when he let Mephistopheles utter the famous words in *Faust,* 'Blut ist ein ganz besonderes Saft' – another often-used quote. Blood was indeed 'a very special fluid', symbolizing life and death, inclusion and exclusion.

I will follow the example of the enthusiastic doctors and give a historical backdrop to the events detailed in coming chapters. It will help situate the daring experiments with lamb blood transfusion and the acrimonious debates that followed.

The beginnings

The history of actual – not mythical – transfusion starts in the 17th century.[3] The intervention was not thinkable until the theory of blood circulation presented by William Harvey in 1628 had been understood and accepted. One could now imagine that blood introduced into the body's closed system would stay there rather than, as was thought before, be diffused out and destroyed. In principle, too, any artery or vein could function as a convenient entry into the blood stream. Animal experiments now got underway and blood transfusion to humans was the logical next step.

Interestingly, 19th century texts on transfusion sometimes present slightly different stories. Italian authors tend to underline what happened in Italy during the late 17th century. Harvey's work on the continuous circulation of blood had, in fact, been conducted in Padua, and the concept of blood transfusion was readily accepted by many 17th century Italian surgeons. In December 1667, Guglielmo Riva, chief physician to the pope, performed three public demonstrations of transfusion from sheep to very sick patients. At least two of them survived for a few months. He then made some further transfusions from sheep to men and several collaborators conducted animal transfusion experiments. A few years later, in 1680, the physician Francesco Folli published a detailed description of how to perform a human-to-human transfusion, but this was an operation that he himself never tried.[4] These Italian doctors believed that transfusion would bring nourishment and vitality to the body. They considered it more effective than bloodletting to restore the balance of the body's humours, and ideas circulated that the blood of a healthy young donor would induce vigour and strength into an older recipient.[5]

The 19th century German physicians doing historical overviews also often dwelled on the sheep-to-man transfusions performed in the 1680s by the Germans Balthasar Kaufmann and Matthäus Gottfried Purmann. These noted

Figure 1. Lower's blood transfusion, 1667. The tubes used to puncture the blood vessels and transfer the blood are at the top left. This illustration is from a 1692 work by the German surgeon Matthäus (Mattias) Gottfried Purmann (Wellcome Collection. CC BY, https://wellcomecollection.org/works/jj7nx24).

no improvement in two scorbutic soldiers but reportedly healed a leaper who, nevertheless, came to suffer from what Purmann called *Schafsmelancholie*, perhaps some sort of sheepish depression.[6]

All 19th century historical overviews, however, gave pride of place to events in France and England that happened somewhat earlier than the Italian and German attempts. In June 1667, the very first transfusion of blood into the

veins of a human being took place in Paris. The physician Jean-Baptiste Denis moved blood from a lamb into a young man suffering from anaemia. Some months later, in November 1667, a similar transfusion took place in London under the auspices of the Royal Society. In the presence of doctors and members of Parliament as well as a bishop, Richard Lower and Edmund King transfused blood from a lamb to a man suffering from mental weakness. Thus, the very first transfusions to humans used blood from a lamb and were considered successful. The experiments attracted awe and some ridicule, for instance when Samuel Pepys noted in his diary that they 'did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like'.[7]

More experiments followed in England but in several cases the recipient died. The Royal Society finally saw little value in the procedure. Denis, too, tried some more transfusions, including one with calf's blood to a Swedish nobleman. The Swede was close to the then abdicated Swedish queen Christina. In a letter to her physician she clearly found the idea of a transfusion alluring:

> I think the invention of injecting blood is all very fine, but I should not like to try it myself, for fear that I might turn into a sheep. If I were to experience a metamorphosis, I should prefer to become a female lion so that no one could devour me.[8]

The Swedish nobleman did not make it, however. When another patient died Denis was put to trial but was acquitted. Suspicious colleagues at the Medical Collegium of Paris soon prohibited transfusions, followed by a ban from the Catholic Church. To move blood into humans was to set oneself up as an equal to God with unknown consequences. 'Opponents warned of the risk of transferring the beastly spirit of the donor, which would transform the very nature of man, acquiring the instincts and behaviour of the animal', later historians note.[9]

During the next 150 years, there would be very few attempts to move blood into humans but many animal experiments. These led to advances in the understanding of the components of blood and the role of oxygen in respiration.

One may wonder: How did the physicians writing overviews in the 1860s and -70s know about this early history? Had they read Denis' accounts of his struggles or the *Proceedings of the Royal Society*? No, more likely they had perused the very thorough history of blood transfusion published in German in 1802 by the Danish doctor Paul Scheel, or read the equally detailed follow-

up by J. F. Dieffenbach in 1828.[10] They may also have consulted the overviews published in the 1850s and -60s about more recent transfusions.[11] The procedure had, as Sander alluded to above, returned some fifty years earlier to make a certain, though uneven, progress through the hospital wards.

The return

The 19th century revival of blood transfusion was primarily the work of a young doctor in London, James Blundell. He came to think of this remedy after the experience of standing helpless beside a woman bleeding to death from post-partum haemorrhage. His teacher in Edinburgh, John Leacock, had made experiments with transfusion between dogs, so Blundell now proceeded to do some animal-to-animal transfusions himself. Their success encouraged him, in 1818, to make the very first blood transfusion ever to a human using human blood. The patient died but Blundell's later attempts would be more positive. From the mid-1820s onwards, he and others performed several successful human-to-human transfusions. Patients who seemed close to death, mostly women suffering from severe post-partum bleedings, were thus miraculously saved. An 1834 article in *The Lancet* captured the wonder inspired by this recovery: 'Life seemed to be immediately revived as by an electric spark'.[12]

Blundell's daring endeavour – to use the blood of others to bring very sick patients back to life – meant a break with contemporary medical orthodoxy. The prevailing norm was to *bleed* patients rather than to supply them with new blood. He may have been inspired by the romantic notions of contemporary scientists and physicians bringing the nearly-dead back to life.[13] The borderline between life and death was then conceptualized as unclear, shifting and difficult to ascertain. Horror stories were told of people buried alive but rescued in the last instance from the grave, and of drowned and seemingly dead persons awakened by medical men. The step to experimenting with blood, the body's own life-giving substance, was perhaps not difficult to take for a romantically-inclined physician. The very same year, 1818, that Blundell made his first transfusion, Mary Shelley published her book, *Frankenstein: Or The Modern Prometheus*. It built on a similar idea of science giving life to the dead. The scientist, Victor Frankenstein, applied the electrical spark of a lightning bolt to a body whose parts were assembled from local graveyards, and so the live 'monster' was created. The next year, 1819, the first vampire study was published to great public acclaim. It used the same theme, now with the

Figure 2. A transfusion with Blundell's 'Gravitator' 1828/29 (Blundell 1828/29, 321).

vampire surviving through blood harvested from other living beings. Its author, John Polidori, was, like Blundell, an Edinburgh-trained doctor. He was physician to Lord Byron and a friend of the Shelleys' and was possibly present at the famous gathering when Mary Shelley's ideas were first aired.[14]

Thus, transfusion had by the late 1920s been performed by some daring English physicians in cases of severe post-partum haemorrhage. The quite complicated operation may be seen as yet another way for educated male surgeons to wrestle power over childbirth from female midwives.[15] More generally, it was part of a revolution in medical epistemology that started in the 17th century and had been refined from the 18th century onwards. As summarized by later historians, the 'infusion of pharmacological liquors in the veins in general, and transfusion in particular, represented a shift to a new therapeutic concept of care: that of rapid intervention to immediately restore the natural state of the body when traditional long-term therapy has not been effective'.[16]

How to most effectively perform this life-giving intervention was, however, a matter of dispute. There is one very concrete inconvenience with blood: it will rapidly coagulate once outside the donor's body. So, how to avoid introducing life-threatening blood clots into the bloodstream of the recipient? This problem was not easily resolved.

Direct or indirect transfusion?

Blundell's transfusions were of, what he called, the 'mediate' kind. His apparatuses – the Impellor and the Gravitator – were brass implements constructed to gather the blood from the donor and then force it, either mechanically or with the help of gravity, into the patient's body. The idea was to simulate how blood circulates naturally in the body. Blundell's purpose was not primarily to avoid blood clots but to retain what he saw as the 'natural vitality' of the blood. Thus, he thought that rather small quantities of blood would suffice.[17]

Physicians in Great Britain also experimented with techniques of *direct* transfusion. By imitating as closely as possible the heart's natural pumping of blood and thus avoid losing the blood's 'living force', they wanted to move it very quickly from donor to recipient. One influential promoter of this idea was the obstetrician James Hobson Aveling. His transfusion instrument made of rubber tubing and some metal connections had by the 1870s become quite widely used in Anglo-Saxon countries. It was then challenged by the more complex instrument for direct transfusion invented by the Swiss physician, Joseph-Antoine Roussel. We will meet both him and his apparatus quite frequently in coming chapters. For now, we may note that Aveling in 1874 was the first, and ultimately almost the only, doctor to perform a lamb blood transfusion in England.

On the European continent, other transfusion methods were tried out. As early as in 1821, the scientists Dumas and Prévost argued in favour of the *indirect* method. To avoid getting partial or total blockage of the blood stream, one should first bleed the donor of a certain amount of blood. Then, through whipping and filtering the blood to be administered one would remove the fibrin that caused coagulation. Finally, the defibrinated liquid could be introduced into the recipient's vein. Nobody dared to test the method on a human patient until 1847. That time it did not work, but some fifteen years later it had evolved into a rather established procedure and was backed up by clinical experience and physiological research. Most influential were the experiments

undertaken by the German-trained Danish professor, Peter L. Panum, whom we also will meet again later in this book.[18] He, and others, bled and transfused large numbers of different animals. They argued for the utility of the indirect method and promoted it as a more reliable operation than the direct variant. But not everyone agreed. Many questioned the medical correctness of whipping and filtering the blood, meaning, they feared, killing its vital, life-giving elements![19]

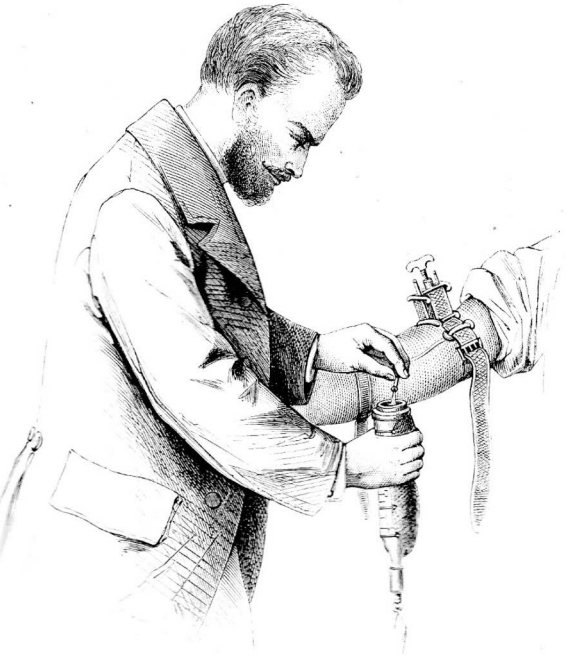

Figure 3. Tapping a donor for blood using the indirect method (Gesellius 1873, 23).

Gaining acceptance

By the early 1870s, enough transfusions, with direct or indirect methods, had been successful for an ever-growing number of physicians wanting to try it. Hundreds of transfusions were made across Europe and several, more or less well-functioning, instruments were devised (including using an English stomach pump, or, in an emergency, a common beer pump, of the kind found in every German village).[20] To some physicians, such as the Belgian doctor, Joseph Casse, this meant that the turbulence of earlier attempts was now a thing of the past: A therapy that had once been 'madly advocated by some, excessively criticized by others, condemned and praised in turn, forgotten for a very long time' was now, he argued, seen as a fairly harmless operation, if properly conducted.[21] The German physician, Heinrich Leisrink, was even more enthusiastic:

> There are not many operations which in such an eminent sense deserve to be called lifesaving as transfusion […] so simple in its technique, so safe in its execution.
>
> Hit by a sudden, enormous loss of blood, a human being lies on a bed, breathing only laboriously, with wax pale face, and a barely noticeable pulse. Around are relatives frightened to death, expecting the end in any second. Finally, the long-awaited physician arrives and explains, after a short examination, that the patient can be saved by this operation. Everyone volunteers to provide the blood. [Soon] new life runs through the veins of the almost-dead beloved. The face reddens anew, the pulse rises, the central organs are supplied with fresh blood; as if touched with a magic wand, the scene is changed, the person is saved.[22]

Others, however, still saw transfusion as a daring intervention, to be attempted only when no other remedy had worked. But there were problems. How long could you wait until it was *too* late? And if there was no willing donor present, should the doctor offer his own blood – though might he not then himself lose consciousness and control?[23]

Scientific knowledge of the physiology of blood was expanding but still uncertain. Crucially, it would take nearly a half-century before knowledge of the existence of different blood groups would effectively influence transfusion practices.[24] Still, the danger of transfusing incompatible blood was not as great as one may expect. Many 19th century patients got blood from near relatives. Later calculations, based on the prevalence of different blood

groups in Western/European populations, show that nearly two-thirds of the mid-19th century transfusions would have passed as compatible.[25] Why some transfusions failed was at the time attributed to air bubbles having entered the blood stream, doctors performing the transfusion too rapidly or with too much blood, or the fact that the patient was on the verge of dying anyway.

Figure 4. A blood transfusion at the Hôpital de la Pitié, Paris, in 1874. The presence of a nun may indicate that the intervention was no longer prohibited by the Catholic Church (Harpers Weekly, June 4, 1874, 570).

Indications for a transfusion varied. Many physicians, especially in Great Britain, followed Blundell's instruction to transfuse only in cases of acute anaemia, most notably for post-partum haemorrhage and gynaecological afflictions. On the continent, doctors were more audacious. Blood transfusion was tried for conditions such as rabies and cholera, asphyxia, intestinal diseases, carbon-monoxide poisoning, sepsis and leukaemia. Here, too, however, obstetrical and gynaecological problems and cases of acute or prolonged anaemia were the most common indications.[26] This prudence was lauded in 1869 by French physician Charles Marmonnier:

> We are far from the time when we claimed to heal everything by transfusing blood: madness, phthisis, cancer, skin diseases, paralysis, fever, without any discrimination, without any solid physiological principles; when we hoped to modify the morale of a deranged individual by injecting him with lamb's blood, to make a pusillanimous man brave by injecting him with the blood of a lion, to restore to an old man the vigour of his youth by injecting him with blood taken from a robust young man. Fortunately, reason and experience soon diminished the exaggerated expectations produced by the enthusiasm generated by the discovery of transfusion.[27]

As we shall see in coming chapters, this verdict would be reversed only a few years later.

Those who in the late 1860s and early 1870s advocated blood transfusion may have fought over what exact method or instrument to use. Still, they all agreed on one thing: *only human blood* could be used for transfusions to humans. Blundell set the tone in the 1820s when he jokingly told his midwifery students why he preferred a human blood donor. In a sick-bed emergency, he said, '[a] dog, it is true, might have come when you whistled, but the animal is small; a calf or sheep might to some have appeared fitter for the purpose; but, then, it had not been taught to walk promptly up the stairs.'[28]

Around the same time, the scientists Dumas and Prévost used animal experiments to show the danger of species-alien blood. Dieffenbach, Magendie, Panum and other physiologists followed suit. Their experimental animals were starved for days, emptied of blood, then transfused with alternately species-similar and species-alien blood. The physiologists injected horses with blood from dogs, transfused sheep blood to ducks, cow blood to cats, bird blood to frogs, and so forth.[29] Their reactions were recorded and the animals, if not already dead, were killed, then dissected, and their urine, liver and blood components studied in detail under the microscope. By late 1860s, the physiologists had established what to them was an indubitable truth: only species-similar blood could be used for transfusion – all else was poison! Science had spoken and the issue was closed.

Or, maybe not?

The revival of lamb blood transfusion

It is the 15th of May 1871 in Wilmington, North Carolina. The local newspaper reports about 'a singular operation to save a man's life – that of the transfusion of blood to his body' having just taken place at the city hospital. The most singular aspect of this event was the identity of the blood donor: a six-month-old lamb.[30]

The patient was a man with a gangrene-infected amputated leg. He was now in a comatose state and rapidly sinking. In the presence of the city's mayor, several other gentlemen and assistants, doctors King and Winants transfused the patient with about six ounces of blood from a lamb's severed artery. He felt much better, got some milk-punch and soon fell into a quiet sleep. He continued to improve for about ten days – but then got rapidly worse. The plan was to transfuse him again but the doctors 'failed to get either a human or an animal in time' and the patient died.[31] The transfusion was nevertheless considered successful, Dr Winants concluded, 'as it was very evident the patient would not have survived through the night if the operation had not been performed'.[32]

The event was covered in US and European media. It was greeted with some amazement but soon forgotten. After all, it was not a lasting success. A year and a half later, another such singular event occurred, this time in Naples, Italy. On the 15th of November 1872, Giuseppe Albini, professor of physiology, transfused a thirty-year-old woman exhausted by severe menorrhagia. The thought of using animal blood was not new to him but this was the first time he tried it. The procedure was reported by, among others, the *Obstetrical Journal of Great Britain and Ireland*:

> A gum elastic tube about half a metre in length was inserted into the artery of a lamb and placed in communication with the vein opened in the lady patient. [Albini renounced the use of a syringe and preferred instead] to use the natural pump, the heart of the animal itself, which with vigorous contractions is able to impel a liberal supply of blood into the arm of the patient.[33]

The patient seemed to improve, but then a new haemorrhage occurred. A second transfusion was performed but this time without much benefit, and the patient died shortly thereafter.

The story about the revival of lamb blood transfusion could have ended there – but the next doctor to seize upon the idea that human lives could be saved by animal blood was more resolute. His energetic promotion of the

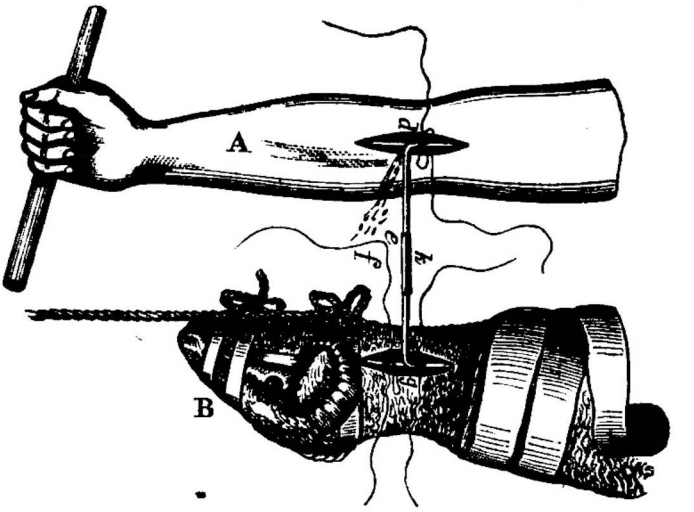

Figure 5. Lamb blood transfusion according to Albini (Albini 1872, 264). Interestingly, he almost exactly reproduces an image published by Paolo Manfredi in 1668.

intervention would, from the autumn of 1873, start an international 'epidemic' of lamb blood transfusion. Was Oscar Hasse aware of the events taken place in North Carolina and Italy? That is not evident.

Hasse's main inspiration was instead a thick volume sent to him by his bookseller who knew of Hasse's transfusion experience with defibrinated human blood. The book, *Die Transfusion des Blutes. Eine historische, kritische und physiologische Studie,* was published in 1873 by Franz Gesellius, a German doctor in St. Petersburg. It was an ambitious, though erratic and polemical, overview of the literature and experience of transfusion since the 17th century. It contained an attack on transfusions with defibrinated blood and ended with a plea for the direct transfusion of blood from the artery of a lamb: it was oxygen-rich, alive, and life-giving! Gesellius' concluding prophecy, *Die Lammblut-Transfusion wird in der Medicin eine neue Aera die – blutspendende – inaugurieren!*, did not fail to make an impression on Hasse. The idea that 'lamb blood transfusion would inaugurate a new era within medicine' was encouraging. And so, on May 26, 1873, Hasse made his first attempt on the young girl, Hermine

Krüger, in Schwenda. Since it was a success, he followed it up with another fourteen lamb blood transfusions, soon to be reported to the world.[34]

The scene was set for the widespread return of a 17th century medical innovation. But who were the main actors behind the 'avalanche' of transfusion that would soon occur? They were many, and not always in agreement. Yet some stand out. I will focus on three central protagonists who personify the experimental, controversial and sometimes successful experience of the 1870s' transfusions. They inspired followers, irritated opponents, and influenced medical practices across Europe and the USA. So, onto the scene I now call Oscar Hasse, Franz Gesellius and Joseph-Antoine Roussel.