

OXFORD MEDICAL PUBLICATIONS

BLOOD TRANSFUSION

BY

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PREFACE

BLOOD transfusion is of rapidly growing importance in modern therapeutics, yet the subject has only been represented in the medical literature of this country hitherto by isolated communications concerning special points. The present work seeks to give a connected account of the whole subject and of the problems arising from it, together with practical instructions for performing transfusions by an efficient and simple method.

I am indebted for helpful criticisms and suggestions to Professor A. V. Hill, F.R.S., of Manchester University. Dr. J. H. Drysdale has kindly allowed me to use the records of three cases of pernicious anæmia treated in his wards at St. Bartholomew's Hospital. Dr. Joekes has permitted me to refer to some of his own observations concerning abnormal serum reactions. Dr. R. M. Janes has given me some account of the important work recently done by Dr. Bruce Robertson and himself at the Hospital for Sick Children, Toronto.

The Bibliography at the end of the book makes no pretence of being absolutely complete. It is, however, more extensive than any that has yet been printed, and I believe that it contains references to nearly all the contributions of present importance published up to the date of going to press. Numbers referring to the Bibliography have been inserted in the text only where no name is given to the authority quoted.

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BLOOD TRANSFUSION

CHAPTER I

HISTORICAL SKETCH

FROM the earliest times the vital importance of blood to the human system has been fully appreciated. It has been supposed to carry in it some of the virtues, such as the youth and health, of its possessor, and it has therefore been commonly regarded as a sacrifice acceptable to the gods. References to blood in the Old Testament, in classical authors, and, it is stated, in the writings of the ancient Egyptians, refer rather to these mystical attributes than to any definite transference of it from the veins of one animal to those of another. One of the earliest references to actual transfusion of blood that has been noticed is to be found in a work by Libavius of Halle, published in 1615. The passage has been translated as follows :

“Let there be present a robust healthy youth full of lively blood. Let there come one exhausted in strength, weak, enervated, scarcely breathing. Let the master of the art have little tubes that can be adapted one to the other; then let him open an artery of the healthy one, insert the tube and secure it. Next let him incise the artery of the patient and put into it the feminine tube. Now let him adapt the two tubes to each other and the arterial blood of the healthy one, warm and full of spirit, will leap into the sick one, and immediately will bring him to the fountain of life, and will drive away all languor.”

It may be assumed, however, that this was only an idea, and had not yet been carried into practice. It was, indeed, unlikely that any attempt to perform blood transfusion

- would be made until the conception of the circulation of the blood had been promulgated, and this in 1615 had not yet taken place.

William Harvey had been appointed physician to St. Bartholomew's Hospital in 1609, and already in 1616 as Lumleian lecturer had stated his theory of the circulation, but not until its publication twelve years later could it be generally known. His treatise entitled *Exercitatio Anatomica de Motu Cordis et Sanguinis in Animalibus*, which appeared in 1628, may therefore be regarded as the point from which blood transfusion first arose. It has often been stated in the literature of the subject that the first transfusion was performed in 1492, when the blood of three boys is supposed to have been transfused into the veins of the aged Pope Innocent VIII.¹ This, however, seems to have been a mis-statement of the facts. Actually a Jewish physician prepared a draught for the Pope from the blood of three boys, who were bled to death for the purpose.² The drinking of blood was not a new idea; this particular incident is of no special interest, and may now be allowed to sink into oblivion.

It is not until after the middle of the seventeenth century that authentic references to blood transfusion are to be found. The first is in the writings of Francesco Folli, a Florentine physician, who claims to have demonstrated the operation of transfusion of blood on August 13, 1654, to the Grand Duke Frederick II. There does not seem to be any confirmation of this in the writings of others. A few years later experimental work tending in the same direction was being done in England, and the inception of this was due to the ingenious Sir Christopher Wren, who in this connexion has not hitherto received the recognition that is his due. Dr. Wren, as he was designated at the time, was one of the most active members of the recently

¹ The first reference to this that I can find is in "Moines et Papes," by Emile Gebhardt, *La Chronique Médicale*, November 1912.

² *Life and Times of Rodrigo Borgia*, A. H. Mathew, D.D., 1912, p. 66.

formed Royal Society, and was responsible for many new experiments in several sciences. It is clear from references in the *Philosophical Transactions* that his first experiments were done in 1659, and the following statement is made by Dr. Thomas Sprat in his *History of the Royal Society*, published in 1667 :

“ He was the first author of the Noble Anatomical Experiment of Injecting Liquors into the Veins of Animals. An Experiment now vulgarly known ; but long since exhibited to the Meetings at Oxford, and thence carried by some Germans, and published abroad. By this Operation divers Creatures were immediately purg’d, vomited, intoxicated, kill’d, or reviv’d according to the quality of the Liquor injected : Hence arose many new Experiments, and chiefly that of Transfusing Blood, which the Society has prosecuted in sundry Instances, that will probably end in extraordinary Success ” (p. 317).

Sir Christopher Wren did not actually carry out any transfusion experiments on his own account. This was done by his friend, Richard Lower, well known for his work on the anatomy of the heart, who worked in the laboratory of Thomas Willis at Oxford. In these experiments, some account of which was published in 1666, he used a silver cannula for obtaining continuity between the artery of one animal and the vein of another. Lower must therefore receive the credit for having done the first transfusion actually performed in England. In the following year other experiments were done by Dr. Edmund King and Thomas Cox, both of whom recorded their experiences in the *Philosophical Transactions*.

Meanwhile Wren’s work had become known in other countries, and it is said that transfusion was performed in 1664 by Daniel of Leipsic, who thus anticipated the work of Lower. However this may be, the first transfusion done upon a human being was certainly carried out in France by Jean Denys of Montpellier, physician to Louis XIV. This is admitted in the *Philosophical Transactions*, but the

following statement in extenuation of English hesitancy is made :

“ We readily grant, They were the first, we know off, that actually thus improved the Experiment ; but then they must give us leave to inform them of this Truth, that the Philosophers in England had practised it long agoe upon Man, if they had not been so tender in hazarding the Life of Man (which they take so much pains for to preserve and relieve), nor so scrupulous to incurre the Penalties of the Law, which in England, is more strict and nice in case of this concernment, than those of many other Nations are.”

Dr. Edmund King further asserts that “ We have been ready for this Experiment these six Months,” that is to say, since March, 1667. Moral precedence must, however, give way to the actual, and it is clear that Denys had snatched the laurels. A translation of a full and interesting account of his earlier experiment upon animals and his first two transfusions done upon men was published in the *Philosophical Transactions* for July 22, 1667. Of the first of these he wrote as follows :

“ On the 15 of this Moneth, we hapned upon a Youth aged between 15 and 16 years, who had for above two moneths bin tormented with a contumacious and violent fever, which obliged his Physitians to bleed him 20 times, in order to assuage the excessive heat.

“ Before this disease, he was not observed to be of a lumpish dull spirit, his memory was happy enough, and he seem'd chearful and nimble enough in body ; but since the violence of his fever, his wit seem'd wholly sunk, his memory perfectly lost, and his body so heavy and drowsie that he was not fit for any thing. I beheld him fall asleep as he sate at dinner, as he was eating his Breakfast, and in all occurrences where men seem most unlikely to sleep. If he went to bed at nine of the clock in the Evening, he needed to be wakened several times before he could be got to rise by nine the next morning, and pass'd the rest of the day in an incredible stupidity.

“ I attributed all these changes to the great evacuations of blood, the Physitians had been oblig’d to make for saving his life, and I perswaded myself that the little they had left him was extreemly incrustated [? incrassated] by the ardour of the fever. . . . Accordingly my conjecture was confirmed by our opening one of his Veins, for we beheld a blood so black and thick issue forth, that it could hardly form itself into a thread to fall into the porringer. We took about three ounces at five of the Clock in the morning, and at the same time we brought a Lamb, whose Carotis Artery we had prepar’d, out of which we immitted into the young man’s Vein, about three times as much of its Arterial blood as he had emitted into the Dish, and then having stopt the orifice of the Vein with a little bolster, as is usual in other phlebotomies, we caus’d him to lie down on his Bed, expecting the event ; and as I askt him now and then how he found himself, he told me that during the operation he had felt a very great heat along his Arm, and since perceiv’d himself much eased of a pain in his side, which he had gotten the evening before by falling down a pair of staires of ten steps ; about ten of the clock he was minded to rise, and being I observed him cheerful enough, I did not oppose it ; and for the rest of the day, he spent it with much more liveliness than ordinary ; eat his Meals very well, and shewed a clear and smiling countenance. . . . He grows fat visibly, and in brief, is a subject of amazement to all those that know him, and dwell with him.”

This boy had been transfused for therapeutic purposes ; the second transfusion performed by Denys was done upon an older man “ having no considerable indisposition,” and was purely experimental. About twenty ounces of lamb’s blood are stated to have been transfused, but the procedure was without any ill effect, and it may be doubted whether the man received as much as this.

In the succeeding number of the *Philosophical Transactions*, October 21, 1667, the remarks of another French

experimenter, Gaspar de Gurye, are quoted. These are of considerable interest, as they contain the first warning of the dangers attending the administration of incompatible blood. De Gurye affirms "that an expert Acquaintance of his, transfusing a great quantity of blood into several Doggs, observed alwayes, that the Receiving Doggs pissed Blood."

Other cases were subsequently recorded by Denys. In one he claims to have cured a patient suffering from "an inveterate Phrenzy." His account of it is too long to be quoted here in full, but it is of special interest in that it contains the first account of hæmolysis and the attendant symptoms in man which follow the transfusion of incompatible blood. The blood of a calf was used in this instance and on two occasions; at the first transfusion only a small amount was given, but at the second,

"the Patient must have received more than one whole pound. As this second Transfusion was larger, so were the effects of it quicker and more considerable. As soon as the blood began to enter into his veins, he felt the like heat along his Arm and under his Arm-pits which he had felt before. His pulse rose presently, and soon after we observed a plentiful sweat all over his face. His pulse varied extremely at this instant, and he complained of great pain in his Kidneys, and that he was not well in his stomach, and that he was ready to choak unless they gave him his liberty.

"Presently the Pipe was taken out that conveyed the blood into his veins, and whilst we were closing the wound, he vomited store of Bacon and Fat he had eaten half an hour before. He found himself urged to Urine, and asked to go to stool. He was soon made to lie down, and after two good hours strainings to void divers liquors, which disturbed his stomach, he fell asleep about 10 a Clock, and slept all that night without awakening till next morning, was Thursday, about 8 a Clock. When he awakened, he shewed a surprising calmness, and a great presence of

mind, in expressing all the pains and a general lassitude he felt in all his limbs. He made a great glass full of Urine, of a colour as black, as if it had been mixed with the soot of Chimneys."

The hæmoglobinuria, which was not at that time attributed to its true cause, cleared up in the course of a few days, and the patient appeared to be greatly benefited.

Although the first transfusion performed upon a human being was done in France, similar experiments were shortly afterwards carried out in England. The passage already quoted concerning the "sundry instances" mentioned in Sprat's *History of the Royal Society* is amplified by the diarist, Samuel Pepys, who witnessed the experiments on at least one occasion. His first reference to the subject is under the date November 14, 1666 :

"Here [at the Pope's Head] Dr. Croone told me, that, at the meeting at Gresham College to-night, . . . there was a pretty experiment of the blood of one dogg let out, till he died, into the body of another on one side, while all his own run out on the other side. The first died upon the place, and the other very well, and likely to do well. This did give occasion to many pretty wishes, as of the blood of a Quaker to be let into an Archbishop, and such like ; but, as Dr. Croone says, may, if it takes, be of mighty use to man's health, for the amending of bad blood by borrowing from a better body." (*Diary*, ed. Wheatley, vi. p. 60.)

Two days later he reports :

"This noon I met with Mr. Hooke, and he tells me the dog which was filled with another dog's blood, at the College the other day, is very well, and like to be so as ever, and doubts not its being found of great use to men,—and so do Dr. Whistler, who dined with us at the tavern." (*Ibid.*, p. 63.)

On November 28 there was further conversation at Gresham College to the same effect (*ibid.*, p. 79). In the following year the experiments were taken a stage further,

and Pepys refers again to them under the date November 21, 1667 :

“ Among the rest they discourse of a man that is a little frantic, that hath been a kind of minister, Dr. Wilkins saying that he hath read for him in his church, that is poor and a debauched man, that the College have hired for 20s. to have some of the blood of a sheep let into his body ; and it is to be done on Saturday next. They purpose to let in about twelve ounces ; which they compute, is what will be let in in a minute’s time by a watch. They differ in the opinion they have of the effects of it ; some think it may have a good effect upon him as a frantic man by cooling his blood, others that it will not have any effect at all. But the man is a healthy man, and by this means will be able to give an account what alteration, if any, he do find in himself, and so may be usefull.” (*Diary*, vii. p. 195.)

On November 29 Pepys dined at a house of entertainment, and enjoyed good company.

“ But here, above all, I was pleased to see the person who had his blood taken out. He speaks well, and did this day give the Society a relation thereof in Latin, saying that he finds himself much better since, and as a new man, but he is cracked a little in his head, though he speaks very reasonably, and very well. He had but 20s. for his suffering it, and is to have the same again tried upon him : the first sound man that ever had it tried on him in England, and but one that we hear of in France, which was a porter hired by the virtuosos.”¹ (*Ibid.*, p. 205.)

The subject of this experiment was Arthur Coga, an indigent Bachelor of Divinity of Cambridge, aged about thirty-two. It is recorded in the *Philosophical Transactions* that the experiment was performed by Richard Lower and Edmund King at Arundel House on November 23, 1667, in the presence of many spectators, including several physicians. Coga, when asked why he had not the blood of some other creature transfused into him, rather

¹ This refers to the experiment of Denys, mentioned above.

than that of a sheep, replied: "Sanguis ovis symbolicam quandam facultatem habet cum sanguine Christi, quia Christus est agnus Dei."¹ It was estimated that Coga received eight or nine ounces of blood, but he seems to have felt no effects, good or ill, and it is probable that he did not actually receive as much as this.

These beginnings in England and France led to the more frequent use of blood transfusion, but soon afterwards the operation fell into disrepute. Disasters followed the transfusions, and the practice also met with violent opposition on the ground that terrible results, such as the growth of horns, would follow the transfusion of an animal's blood into a human being. In consequence of this they were actually forbidden in France by the Supreme Court until the Faculté of Paris should signify its approval, but the necessary permission was not given. The "extraordinary success" predicted by Sprat and the sanguine expectations of Pepys and his friends were destined not to be fulfilled until a later age.

For more than a hundred years the possibilities of blood transfusion were almost entirely neglected. There are some isolated references to it in medical writings towards the end of the eighteenth century, but of these it is only necessary to notice two. In 1792, at Eye in Suffolk, blood from two lambs was transfused by a Dr. Russell into a boy suffering from hydrophobia, and he claimed that the patient's recovery was to be attributed to the treatment. Soon afterwards in 1796 Erasmus Darwin recommended transfusion for putrid fever, cancer of the œsophagus, and in other cases of impaired nutrition. He suggested that the blood should be transferred from donor to recipient through goose quills connected by a short length of chicken's gut, which could be alternately allowed to fill from the donor and emptied by pressure into the patient. This operation he never actually performed.

A more general interest in the subject was revived in

¹ Birch's *History of the Royal Society*, 1756, ii. p. 216.

England by the work of James Blundell, lecturer on physiology and midwifery at St. Thomas's and Guy's Hospitals. He published in 1818 his earliest paper on experimental



Fig. 1.—BLUNDELL'S IMPELLOR

From *Researches Physiological and Pathological*, 1824

transfusion with a special form of syringe invented by himself. His first apparatus consisted of a funnel-shaped receptacle for the blood, connected by a two-way tap with a syringe from which the blood was injected through a tube and cannula into the recipient. His experiments were

performed upon dogs, and he began by drawing blood from the femoral artery and re-injecting it into the same animal through the femoral vein. He then conducted a long series of investigations into the properties of blood, the effects of its withdrawal, and the resuscitation of an exsanguinated animal. Soon he had opportunities of transfusing patients with human blood, and the results are recorded in his paper of 1824. His apparatus had by then been elaborated, and an engraving of his *Impellor*, as he termed it, is reproduced here. It consisted as before of a funnel-shaped receptacle for the blood, but the syringe was now incorporated in one side of the funnel, and contained a complicated system of spring valves, which caused the blood to travel along the delivery tube when the piston was pushed down. The *Impellor* was fixed to the back of a chair in order to give it stability.

All the patients transfused by Blundell were either exceedingly ill, or, judging from his description, already dead, so that his results, considered statistically, were not favourable! Nevertheless, he was not discouraged, and stated his "own persuasion to be that transfusion by the syringe is a very feasible and useful operation, and that, after undergoing the usual ordeal of neglect, opposition, and ridicule, it will, hereafter, be admitted into general practice. Whether mankind are to receive the first benefit of it, in this or any future age, from British surgery, or that of foreign countries, time, the discoverer of truth and falsehood, must determine." Blundell's work has been described in some detail because, after the experimental work of the seventeenth century, the year 1818 may be taken to mark the real beginning of the clinical application of blood transfusion.

The chief difficulty in the way of successful transfusion was, of course, the obstacle introduced by the coagulation of the blood. Bischoff in 1835 sought to overcome this by injecting defibrinated blood, and that solution of the difficulty was adopted by many operators, including Sir

•Thomas Smith, who, in 1873, used defibrinated blood for transfusing a case of *melæna neonatorum* at St. Bartholomew's Hospital. The apparatus on this occasion consisted of "a wire egg-beater, a hair sieve, a three-ounce glass aspirator syringe, a fine blunt-ended aspirator cannula, a short piece of india-rubber tubing with a brass nozzle at either end connecting the syringe with the cannula, a tall narrow vessel standing in warm water for defibrinating the blood, and a suitable vessel floated in warm water to contain the defibrinated blood." Others, too numerous to be individually named, used the same method throughout the nineteenth century and during the first ten years of the twentieth. Even in 1914 a method of using defibrinated blood was described by Moss. An objection was raised in 1877 that it was dangerous to do this, owing to the excess of fibrin ferment introduced with blood thus treated, but this did not greatly discourage its use. Then, as now, one of the chief uses of blood transfusion was found to be in the practice of obstetrics. A series of 57 cases of this kind were reported by Martin of Berlin in 1859, 43 of these having been successful. A further series of cases was collected by Blasius in 1863. He was able to report that of 116 transfusions performed during the previous forty years, in 56 the results were satisfactory. These statistics did not indicate a remarkable degree of success. Fatalities due to the transfusion had occurred, attended by the symptoms which we have now learned to associate with incompatibility of the transfused blood. At that time, however, the deaths were believed to be due chiefly to the introduction of air bubbles into the circulation, although it had been shown experimentally by Blundell in 1818, and again by Oré in 1868, that small quantities, such as might be accidentally introduced during a transfusion, produced no ill effects. Some explanation, however, was required, and so air bubbles for a long time received the blame.

Although some of the early experiments on blood transfusion had been done in England, and although its revival