THE HISTORY OF BLOOD TRANSFUSION*

By Dr. Cyrus C. Sturgis

IT MAY SOUND rather naïve to say this, but this is the first opportunity I ever had to talk to a group of medical librarians, and I want you to know how much we appreciate your essentialness to a medical institution. I don't know what we would do if you were to go on strike or suddenly desert us. We feel apologetic about rushing in and asking you to look up all sorts of material for us, but we always find you pleasant and courteous and helpful. I speak for the entire medical profession, I am sure, when I tell you how much you are appreciated. As far as our own medical librarian is concerned, we tell her every day how indispensable she is.

I recall one of our senior students was very much confused when asked how he would go about it to look up the literature on a certain condition, and I said to him, "I don't think you know how to find it." And he replied, "Yes, I do. I know exactly how I would." I said, "How?" He said, "I'd go down and ask Miss Biethan for it."

Some years ago in my spare time I became interested in the history of what is now common therapeutic proceeding—blood transfusion. I felt very much like an amateur, but I learned that the investigation of the history of blood transfusion was like the investigation of anything else. It entails first the careful accumulation of data, then the arrangement of data in an orderly manner, appraisal of authenticity, and finally, drawing conclusions. These methods are used in any type of research, and I employed them in trying to investigate the knowledge of blood transfusion.

Like many other subjects, it has been only superficially investigated. Too often, one man copies what another man wrote fifty years ago, without bothering to corroborate it, and publishes his findings as new information. This has been too true of both history and medicine. Often there is no sincere effort to delve into real facts concerning this particular therapeutic procedure.

I don't mean to say that my own investigation is completed. If I live to be a hundred years old and devote all my time to this study, I still wouldn't be able to get it all straight.

The history is fascinating. It involves every phase of medicine and

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surgery. It involves national and personal animosities concerning priority of discoveries and the jealousies that arise in almost every field of human endeavor.

I have divided history of blood transfusion arbitrarily into four periods. This is purely my own grouping, as it appears on the slide:

The first period is from ancient Greek and Egyptian civilization to the discovery of William Harvey in 1616 of the circulation of the blood. That is a period which I have not devoted much time to, and which is less adapted to investigation than the later years.

The second period, from 1656-70, is an extremely interesting one. During this time a remarkable group of men organized the Royal Society.

The third period begins with the works of James Blundell of London in 1818.

The fourth, or modern, period begins with the studies of Carl Landsteiner on the isoagglutinins of the human blood, in 1900.

Returning to the first period, it may be said that the ancients did not ever do a blood transfusion in the sense we speak of. They wrote about it and speculated about it, but never accomplished it. There appears in the literature the statement that Pope Innocent VIII was given a blood transfusion, and that the lives of three youths were sacrificed as donors to save the life of Pope Innocent VIII. I am convinced that he did not receive a transfusion. The most plausible explanation is that he drank the blood, which was not an uncommon form of treatment in those days.

This slide shows Pope Innocent VIII on his death-bed, and here is a youth who looks very frightened. The chief physician is standing at the bedside and he is incising the vein. According to the story, the blood was supposed to have been transfused into the Pope's vein, but I think we can dismiss that as hearsay. There is no proof that there was a transfusion.

The second incident of interest in this first period is the statement made by the chemist, Libavius, that he had performed a transfusion. He describes how blood was taken from the artery of one man and infused into the artery of another. This story is very much like that of Darius Green and his flying machine—he described it accurately and vividly enough, but he never transfused anyone. With that, we can close the first period.

The second period is extremely interesting. It begins with the story of William Harvey, who did not announce his theory of the circulation of the blood until 1616—a year after Shakespeare died. (I keep all my history straight by remembering the dates of blood transfusions.) The history of this period centers around the college of Oxford which developed later into the Royal Philosophical Society of England. In that group were some very remarkable persons. There was Christopher Wren,

the architect; Richard Lower; Robert Hooke, the first secretary of the Royal Society; Thomas Willis, an anatomist who published a book on the anatomy of the nervous system, the work of which was probably done by others, and with plates by Wren. The group also included Robert Boyle, the physicist and chemist; Sir William Petty; Thomas Sydenham; and Samuel Pepys, who recorded some of the work done in giving transfusions, and couldn't resist making a few wisecracks about it.

Richard Lower was the first person to give a blood transfusion to animals successfully. He did this early in February of 1665. The Royal Society was chartered in 1662, and the Proceedings for the first year, issued in 1665 contained the recital of the experiment whereby Richard Lower bled one dog almost to the point of death. Then he tied the artery, and transfused this dying dog from a larger dog—a mastiff—and revived the bled dog. He did this three times, exhausting the donor each time, but he had very clearly saved the animal from dying by the performance of blood transfusion.

Now it occurs to us, where did Lower get the idea for blood transfusions? He states that he got it from those who had injected other liquids into the veins of dogs previously. Christopher Wren had performed intravenous injections using wine and beer, and Lower said if wine and beer could be injected into the veins, blood could be used just as well. This he did, and this was the first successful animal transfusion. Richard Lower must be given the credit for that. Later he attempted to transfuse a human being, a demented curate by the name of Arthur Coga. The excuse for performing a transfusion was that it was believed that it might improve his mind. Arthur Coga was a little cracked in the head, and the idea was that a transfusion might cure him. Lamb's blood was used for the transfusion, and Arthur Coga got a very severe reaction, as you might imagine. In this experiment, Richard Lower was assisted by Edmund King, a member of the Royal Society. Thus, in 1666, Edmund King and Richard Lower for the first time transfused a human being in England.

This was not, however, the first time a human being was transfused. There has been much controversy about this, and it is not settled yet. Probably the first person to transfuse a human being was Jean Baptiste Denis, a Frenchman from Montpellier, who was a very remarkable man. He began by transfusing dogs, just as Lower did, but he transfused a human being several months before Richard Lower and Edmund King performed the transfusion on Coga. Denis' experiment was upon a manic-depressive type suffering from a psychosis. His wife thought that a transfusion would restore his sanity. Lamb's blood was used for the transfusion, and the man had a violent reaction, the horrible

symptoms being chills and fever and black urine. Denis described it as a reaction to incompatible blood. In his description he stated that the urine became as black as if soot had been dissolved in it.

Dennis and Lower got into a controversy over who was the first to perform a transfusion. I think that Richard Lower was the first to transfuse animals, but I am confident that Denis was the first to transfuse a human being.

One can't help wondering just why lamb's blood was chosen for these early transfusions, but about that time people all over Europe were beginning to use lamb's blood for transfusions. This was a rather premature affair, resulting in the death of one man, and Denis was tried but acquitted. In 1670 an act of Parliament was passed forbidding transfusions. There is a story that in 1675 the Pope issued an edict likewise to stop transfusions. That is not true. I have devoted much time and study to investigating this story, and there is no evidence that there was such an edict. It probably would have been a good idea if he had, because there was no reason on earth why lamb's blood should be used in transfusions and undoubtedly some lives were lost on this account.

This put a stop to Denis' work for the time, and no more work was done on blood transfusions for 150 years.

Now let us turn our attention to Sir Christopher Wren. We know him well as an architect, but we are now recognizing him rather tardily for his contributions to medicine. He conducted experiments of intravenous injections in 1656-57, with the assistance of Timothy Clerk, and it was doubtless the work of Wren which brought about Richard Lower's attempt at blood transfusion. About the time of this first blood transfusion, London was in part destroyed. Lower gave his transfusion in 1665, the same year of the Great Plague in London, and the following year, 1666, was the great fire of London, which burned sixteen thousand homes and left countless people homeless. It is interesting to think of the fact that now the famous St. Paul's Cathedral is being bombed, and at the same time blood transfusions are being used to treat the injured people in London. Thus Christopher Wren, the architect of St. Paul's Cathedral, is playing an important part in today's drama from two different angles.

This slide shows St. Paul's Cathedral, of which Wren was the architect, and which is now being destroyed. It may be completely destroyed by this time.

Here is the great fire of London in 1666, the year after the first blood transfusion.

This is the only picture of Richard Lower in existence which I am sure is authentic. Richard Lower made this one great contribution to medicine, and shortly afterwards he gave up research and went to

London, where he became a fashionable physician. Here is the title page of his book, taken from my own copy. This was published in 1669. It contains, in addition to material on the structure of the heart, one chapter on blood transfusions.

Here is a sample of the Latin, which I hope you can read better than I can. I had to ask Professor Arthur Boak, the head of our History Department, to read this for me. He reads Latin like we read the morning paper, and I impose upon him regularly to translate for me. I find him always willing to give help in matters of this sort.

This page from Richard Lower's book, with its very nice engravings, shows his simple method of transfusion.

Here is Samuel Pepys, whose writings I have enjoyed reading. He covered a large variety of topics, and didn't miss the opportunity to comment about Richard Lower's blood transfusions. Here is a reproduction from the original manuscript of his shorthand. He said he wrote in shorthand because he didn't want his wife to read what he had written —which was probably a good idea, considering some of the things he wrote about.

During those times, people associated blood with the soul, and there originated such expressions as "bad blood," "blood and tell," "blue blood," and such sayings, which are common yet today. Interestingly enough, all early transfusions were given in the hope that they would help improve mental conditions. One person in 1666 made the recommendation that if a man and wife did not get along well, each should have a transfusion from the other, and by thus mixing their blood, they would be made compatible.

From 1675, for a period of 143 years, nothing was done in the way of blood transfusions. Then along came a very remarkable man by the name of James Blundell, of London. His maternal uncle was Dr. Haighton, a pupil of John Hunter. He was a professor of physiology and obstetrics at St. Thomas and Guy's Hospital. James Blundell trained under him for two years. Then he was sent to Edinburgh, where he graduated in 1813. James Blundell was well trained to promote the idea of blood transfusion. As a physiologist, he knew of Richard Lower, and as an obstetrician he saw the terrors of bleeding to death in the third stage of labor. He became a lecturer in surgery at St. Thomas, and to him goes the credit of being the first person to transfuse human blood into a human being.

He became interested in blood transfusions when he attended a woman patient who bled to death. Returning from the house where she had died, he reflected on this sorrowful scene, and he could not help thinking that a blood transfusion might have saved her. A year later —or eleven months, to be exact—on September 26, 1818, a very historic date, James Blundell visited a patient named Brazier, who had

carcinoma of the stomach. He was at the point of death, and James Blundell tried to revive him with blood transfusions. Several members of the family gave twelve to fourteen ounces of blood to the patient. Unfortunately, this was a poor case to try it on. He was almost dead then, and he died within twenty-four hours after the transfusion—not because of the transfusion, but nevertheless, he died. James Blundell tried transfusions on others, and out of ten patients transfused, five died and five lived. Blundell was a very proud and arrogant man, and had little respect for other people's ideas. He was not very well liked. Later he went to Paris, and when he came back his hospital appointments had been taken away. But the last word was his. He declared that some day the world would realize that blood transfusions are useful. He had a considerable amount of money, so he retired in a home near London, where he had a huge library. He became a recluse and nothing more was heard of him in the field of research.

Where did Blundell get the idea for transfusions? He said he got it from seeing the poor woman dying of hemorrhage. But it seems probable that he got his idea from John Henry Leacock, for in his writings there is a brief reference to Leacock, who graduated three years ahead of Blundell at Edinburgh. Dr. Crosby, of the University of Michigan, went to Aberdeen last year as visiting professor, and I asked her if she would try to find John Henry Leacock's inaugural dissertation for me while she was over there. She located it through the librarian at Edinburgh, and got a photostatic copy, which she sent to me. It is on hemorrhage, and it is very likely that this gave James Blundell his idea. Leacock evidently got the idea of transfusions from a Dr. Jones from the Barbadoes, who had performed all his experiments on dogs. And where did he get his idea? That is as far as I got. I know that Dr. Jones was supposed to have written a book on hemorrhage, so let me know if you ever find such a book by Dr. Jones.

The two major problems in blood transfusion are how to prevent clotting, and how to know if one blood is compatible with another. Great difficulties were often encountered because blood used for transfusion was not compatible with that of the patient.

Here is the apparatus which Blundell used for transfusions, which is very formidable looking, but is fairly simple and worked fairly well. The apparatus was attached to the back of the chair, and the blood passed through a tube into the recipient's arm.

This is the dissertation of John Henry Leacock—a very famous piece of work, but no one paid any attention to it at the time, although Blundell says he does owe his inspiration to this particular man.

This is another type of blood transfusion apparatus called the "impeller," introduced by an American named Aveling. In this process, blood was pumped by a valve through the tube.

The point in which I am interested is when was the first blood transfusion in the United States. I am not sure. In the *Philadelphia Journal of Medicine and Physical Sciences* published in 1825, there is an abstract of Blundell's work which was published in 1818, and at the bottom of this abstract is a note by the editors stating that this same procedure had been carried out thirty years earlier by Philip Syng Physick, a Philadelphia surgeon. That would make the date of the first American blood transfusion 1795. However, there is no evidence that he ever did such a transfusion. He had been called the father of American surgery, but although he did a lot of talking he did practically no writing.

Three years later in 1828 the *American Journal of Medical Science* published a statement referring to this and saying that if Philip Syng Physick ever transfused anyone, no record was made of it, and as far as the editor knew, no transfusion had been performed in America prior to 1828 and he knew of none at that time. However, a little later several people in the United States were interested in this problem. At a meeting of the New York Academy of Medicine which occurred in 1874, Austin Flint presided, and Benjamin Fordyce Barker presented six cases of blood transfusions.

There were three main difficulties encountered in giving transfusions: first, they didn't know how to prevent clotting; second, they did not know how to select proper donors; and third, they didn't know the proper indications for blood transfusions.

What about knowledge of anti-coagulants? The first persons who ever tried any experiments along this line were Prevost and Dumas, who used caustic soda. This wasn't particularly successful, but it was a step in the right direction.

That brings us to the introduction of defibrated blood. Dr. J. B. Hicks, an English physician and obstetrician, made the best attempts in this direction and found that sodium phosphates had been used in 1839. He did not follow this up, however; I don't know why.

No headway was made in finding effective anti-coagulants until suddenly in 1915 several persons discovered the effect of sodium citrate at the same time. Everyone was claiming the credit, and it was the worst mess imaginable.

In 1914 sodium citrate was used to prevent clotting. Louis Agote reported a transfusion on November 14, 1914, in which sodium citrate was used. This was published in January, 1915. Richard Lewisohn of New York reported his discovery in a paper which appeared in the *Medical* Record on January 23, 1915. Richard Weil of New York gave a report on his findings before the New York Academy of Medicine on December 17, 1914, which was later published in the *Journal of the American Medical Association* in January, 1915. But none of these men should have the credit. It was a man by the name of Albert Hustin who was re-

ally the first to use sodium citrate so that clotting was prevented. He told of this in a paper presented before the Royal Society of Medicine and Natural Science of Brussels on April 6, 1914, which was published in May, 1914.

There is one other thing to be settled. From the very beginning, it was noticed that even human blood sometimes gave the recipient a reaction, with chills, fever, and dark-colored urine. Some thought this was due to air bubbles which were permitted to enter the veins during transfusion, but this theory has been disproven. A lot of air in the veins is not to be recommended, but it doesn't do much harm.

In 1900 an article by Carl Landsteiner contained a footnote indicating that individuals could be divided into three types as far as blood is concerned, and he named the first three types. He said that donors must be selected according to the type of blood. The fourth group was discovered by two students, De Castello and Sturli, in 1902.

So today blood transfusion is reduced to a very safe procedure. We have an average of 2,300 transfusions a year at University Hospital, and only three or four per cent reactions, which may be caused by various circumstances. These successful transfusions were in a large measure made possible by the discovery of Carl Landsteiner, who was a member of the staff of the Rockefeller Institute. I saw him last year, and though he is quite old, he is hale and hearty, and his eyes are as bright as ever. He is now retired.

It is a strange thing that after waiting two and a half centuries to learn how to make blood transfusion safe, men in clinical medicine paid no attention to Landsteiner when he told of his discovery in 1900. It was not until thirty years later that he was awarded the Nobel prize. It is a regrettable fact that we frequently pay no attention to valuable information. Ludwig Haktoen emphasized the idea later on, in 1907, but not until 1908 was any use made of this knowledge.

That problem was then solved. Recent developments I can pass over. You have all heard of the development of blood banks. It is possible to keep blood stored for thirty days. This is used entirely in University Hospital at the present time. Oswald H. Robinson of the University of Chicago was the first to use stored blood in 1918. The first blood bank was established at Chicago in 1934, at the Cook County Hospital. There are many of those in this country now.

Wangensteen of Minnesota tried using beef plasma for human injection in treatment of shock. This brought about very severe reactions, but it had promise. Edwin Cohn of Harvard divided beef plasma, removing the globulin and using the albumen to give intravenous injections as treatment in case of shock. During the war, wounds may be treated by using beef plasma entirely.