INTRODUCTORY NOTES

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This short review article does not include references to the information provided but does provide a short summary of some of the more important milestones in the history / development of blood transfusion from the first 'successful' transfusions of Denis and Lower. The article is noteworthy in that it mentions and quotes the work of Christian Zagado who is rarely identified in texts apart from providing the equivalent statement that in 1665 he demonstrated that a dog could be revived if given blood from another dog, i.e. equivalent to Lower's experiments a year later in 1666. It is also noteworthy in also mentioning the work of Alexander Bogdanov in Moscow, which led to the setting-up blood banks in the Soviet Union in the 1930s.

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HISTORY OF BLOOD TRANSFUSION

EARLY ATTEMPTS

The first historical attempt at blood transfusion was described by the 15th-century chronicler Stefano Infessura. Infessura relates that, in 1492, as Pope Innocent VIII sank into a coma, the blood of three boys was infused into the dying pontiff (through the mouth, as the concept of circulation and methods for intravenous access did not exist at that time) at the suggestion of a physician. The boys were ten years old, and had been promised a ducat each. However, not only did the pope die, but so did the three children. Some authors have discredited Infessura's account, accusing him of anti-papalism.

Beginning with Harvey's experiments with circulation of the blood, more sophisticated research into blood transfusion began in the 17th century, with successful experiments in transfusion between animals. However, successive attempts on humans continued to have fatal results.

The first fully documented human blood transfusion was administered by Dr. Jean-Baptiste Denys, eminent physician to King Louis XIV of France, on June 15, 1667. He transfused the blood of a sheep into a 15-year old boy, who survived the transfusion. Denys performed another transfusion into a labourer, who also survived. Both instances were likely due to the small amount of blood that was actually transfused into these people. This allowed them to withstand the allergic reaction. Denys' third patient to undergo a blood transfusion was Swedish Baron Bonde. He received two transfusions. After the second transfusion Bonde died. In the winter of 1667, Denys performed several transfusions on Antoine Mauroy with calf's blood, who on the third account died. Much controversy surrounded his death. Mauroy's wife asserted Denys was responsible for her husband's death. But Mauroy's wife was accused of causing his death. Though it was later determined that Mauroy actually died from arsenic poisoning, Denys' experiments with animal blood provoked

a heated controversy in France. Finally, in 1670 the procedure was banned. In time, the British Parliament and even the pope followed suit. Blood transfusions fell into obscurity for the next 150 years.

FIRST SUCCESSFUL TRANSFUSION

Christian Zagado examined the effects of changes in blood volume on circulatory function and developed methods for cross-circulatory study in animals, obviating clotting by closed arteriovenous connections. His newly devised instruments eventually led to actual transfusion of blood.

"Many of his colleagues were present towards the end of February 1665 he selected one dog of medium size, opened its jugular vein, and drew off blood, until ... its strength was nearly gone. Then, to make up for the great loss of this dog by the blood of a second, I introduced blood from the cervical artery of a fairly large mastiff, which had been fastened alongside the first, until this latter animal showed ... it was overfilled ... by the inflowing blood." After he "sewed up the jugular veins," the animal recovered "with no sign of discomfort or of displeasure."

Lower had performed the first blood transfusion between animals. He was then "requested by the Honorable Boyle … to acquaint the Royal Society with the procedure for the whole experiment," which he did in December of 1665 in the Society's Philosophical Transactions. On 15 June 1667 Denys, then a professor in Paris, carried out the first transfusion between humans and claimed credit for the technique, but Lower's priority cannot be challenged.

Six months later in London, Lower performed the first human transfusion in Britain, where he "superintended the introduction in a patient's arm at various times of some ounces of sheep's blood at a meeting of the Royal Society, and without any inconvenience to him." The recipient was Arthur Coga, "the subject of a harmless form of insanity." Sheep's blood was used because of speculation about the value of blood exchange between species; it had been suggested that blood from a gentle lamb might quiet the tempestuous spirit of an agitated person and that the shy might be made outgoing by blood from more sociable creatures. Lower wanted to treat Coga several times, but his patient refused. No more transfusions were performed. Shortly before, Lower had moved to London, where his growing practice soon led him to abandon research.

FIRST SUCCESSES

The science of blood transfusion dates to the first decade of the 19th century, with the discovery of distinct blood types leading to the practice of mixing some blood from the donor and the receiver before the transfusion (an early form of cross-matching).

In 1818, Dr. James Blundell, a British obstetrician, performed the first successful blood transfusion of human blood, for the treatment of postpartum hemorrhage. He used the patient's husband as a donor, and extracted four ounces of blood from his arm to transfuse into his wife. During the years 1825 and 1830, Dr. Blundell performed 10 transfusions, five of which were beneficial, and published his results. He also invented many instruments for the transfusion of blood. He made a substantial amount of money from this endeavour, roughly $50 million (about $2 million in 1827) real dollars (adjusted for inflation).

In 1840, at St George's Hospital Medical School in London, Samuel Armstrong Lane, aided by Dr. Blundell, performed the first successful whole blood transfusion to treat hemophilia.

George Washington Crile is credited with performing the first surgery using a direct blood transfusion at the Cleveland Clinic.

Many patients had died and it was not until 1901, when the Austrian Karl Landsteiner discovered human blood groups, that blood transfusions became safer. Mixing blood from two individuals can lead to blood clumping or agglutination. The clumped red cells can crack and cause toxic reactions, which can have fatal consequences. Karl Landsteiner discovered that blood clumping was an immunological reaction which occurs when the receiver of a blood transfusion has antibodies (A, B, both A & B, or neither) against the donor blood cells. Karl Landsteiner's work made it possible to determine blood groups (A, B, AB, O) and thus paved the way for blood transfusions to be carried out safely. For this discovery he was awarded the Nobel Prize in Physiology or Medicine in 1930.

DEVELOPMENT OF BLOOD BANKING

While the first transfusions had to be made directly from donor to receiver before coagulation, in the 1910s it was discovered that by adding anticoagulant and refrigerating the blood it was possible to store it for some days, thus opening the way for blood banks. The first non-direct transfusion was performed on March 27, 1914 by the Belgian doctor Albert Hustin, who used sodium citrate as an anticoagulant. The first blood transfusion using blood that had been stored and cooled was performed on January 1, 1916. Oswald Hope Robertson, a medical researcher and U.S. Army officer, is generally credited with establishing the first blood bank while serving in France during World War 1.

The first academic institution devoted to the science of blood transfusion was founded by Alexander Bogdanov in Moscow in 1925. Bogdanov was motivated, at least in part, by a search for eternal youth, and remarked with satisfaction on the improvement of his eyesight, suspension of balding, and other positive symptoms after receiving 11 transfusions of whole blood.

In fact, following the death of Vladimir Lenin, Bogdanov was entrusted with the study of Lenin's brain, with a view toward resuscitating the deceased Bolshevik leader. Tragically, but perhaps not unforeseeably, Bogdanov lost his life in 1928 as a result of one of his experiments, when the blood of a student suffering from malaria and tuberculosis was given to him in a transfusion. Some scholars (e.g. Loren Graham) have speculated that his death may have been a suicide, while others attribute it to blood type incompatibility, which was still incompletely understood at the time.

THE MODERN ERA

Following Bogdanov's lead, the Soviet Union set up a national system of blood banks in the 1930s. News of the Soviet experience traveled to America, where in 1937 Bernard Fantus, director of therapeutics at the Cook County Hospital in Chicago, established the first hospital blood bank in the United States. In creating a hospital laboratory that preserved and stored donor blood, Fantus originated the term "blood bank". Within a few years, hospital and community blood banks were established across the United States.

In the late 1930s and early 1940s, Dr. Charles R. Drew's research led to the discovery that blood could be separated into blood plasma and red blood cells, and

that the plasma could be frozen separately. Blood stored in this way lasted longer and was less likely to become contaminated.

Another important breakthrough came in 1939-40 when Karl Landsteiner, Alex Wiener, Philip Levine, and R.E. Stetson discovered the Rhesus blood group system, which was found to be the cause of the majority of transfusion reactions up to that time. Three years later, the introduction by J.F. Loutit and Patrick L. Mollison of acid-citrate-dextrose (ACD) solution, which reduces the volume of anticoagulant, permitted transfusions of greater volumes of blood and allowed longer term storage.

Carl Walter and W.P. Murphy, Jr., introduced the plastic bag for blood collection in 1950. Replacing breakable glass bottles with durable plastic bags allowed for the evolution of a collection system capable of safe and easy preparation of multiple blood components from a single unit of whole blood. Further extending the shelf life of stored blood was an anticoagulant preservative, CPDA-1, introduced in 1979, which increased the blood supply and facilitated resource-sharing among blood banks.