HISTORICAL VIGNETTES IN VASCULAR SURGERY

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Direct blood transfusions

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Blood-letting was practiced for a wide variety of conditions from the 5th century BC, but infusing blood from one human being into another was not documented until December 22, 1818.1 Therapeutic bleeding was based on Hippocrates’ precept that illness was caused by imbalances among the four humors, phlegm, blood, yellow bile, and black bile that comprised all living matter. In the absence of illness, lust and arrogance were attributed to a preponderance of blood, so bleedings were also performed for behavioral adjustment and paradoxically, to restore vigor that had lapsed with aging. Similar rationales prompted many early transfusions, anticipating replacement of bad blood with good blood would be reinvigorating and that a donor’s demeanor and temperament would gain expression in the recipient.

James Blundell (1790-1878), an obstetrician and physiologist at Guy’s Hospital, performed his seminal human-to-human transfusion on September 25, 1818. He had extensive experience with homologous and heterologous (human) canine transfusions, showing the latter to be eventually lethal. Blundell intended to revitalize a 40-year-old man suffering inanition. He began by having a surgeon insert and maintain a cannula in the patient’s cephalic vein. Blundell then serially lanced the arm veins of several willing observers, allowing approximately 45 mL to drip into a cup to be aspirated with paraffin lined syringes for injection into the indwelling cannula. Ten such transfers were made over a period of 40 minutes. The patient seemed to gain strength for 2 days but withered on the third to die 56 hours after the injections. Necropsy revealed an obstructing distal gas-tic cancer. Blundell subsequently achieved good results with his multiple syringe technique, particularly for postpartum hemorrhage, typically using cannulae in both the donor and recipient veins.

Direct transfusion requires donor-recipient proximity and relies on quick transfusion to mitigate clotting. Transfusion from a donor artery to a recipient vein occurs spontaneously upon connection, whereas, vein-to-vein direct transfusion requires energizing, which can be accomplished by gravity, pumping, or withdrawal into a delivery device for prompt infusion (Fig 1).2 Authors have occasionally labeled the last as indirect transfusing, but “indirect” should be reserved for procedures that do not require immediate donor presence and include physical (defibrination) or chemical coagulation control for storage, no matter how brief.

Nobel Suydam Rustum Maluf’s3 History of Blood Transfusion, written in 1954, as a J. Bently Squire urology resident in New York, portrays the muddling allusions and uncertainties that preceded 50-year-old William Harvey’s 1628 publication of “Exercito Anatomica de Motu Cordis et Sanguinis in Animalibus.” These ranged from Ovid (43BC-18CE) relating a story of exsanguination and repletion with a “rich elixir,” to Saxon, physician-chemist Andreas Libavius’s vivid 1615 description of an artery-to-artery transfusion from a healthy person into a cachectic old man through connecting silver cannulae that imparted the “fountain of life” and drove away “all faintness.” Libavius had not actually performed the procedure, but his artery-to-artery connection reflected the prevailing belief that blood sloshed back and forth in arteries fortified by pulses of air, accounting both for their emptiness after death and a more temperate to-and-fro movement in veins.

Scientific Inquiry in the Face of Plague and Fire

Richard Lower (1631-1691) was admitted to Christ Church, Oxford in 1649 where he received several degrees and worked as a research assistant with neuroanatomist Thomas Willis (1621-1675).4 Astronomer and architect Christopher Wren (1632-1723), who drew the first illustrations of Willis’ Circle, used an animal bladder and quills to perform intravenous injections, which produced almost instantaneous effects, ranging from intoxication to death. Lower adopted Wren’s technique, for repeated broth injections to study how long a dog might live without meat.
The logical next step was to infuse blood, which Lower initiated in February 1665, just months before the beginning of London’s Great Plague. He transected a dog’s carotid artery, delaying ligation until the dog was near death, and revived it with a direct transfusion from a donor dog’s carotid into its jugular vein. Lower used silver tubes for cannulating blood vessels and horse or ox arteries as conduits. Quills were slick and too easily compressed for secure fixation. Silver was malleable, so cannulae could be fashioned with ligature-accommodating rims to ensure stable connections. He gradually morphed the silver tube and its connecting elements into a needle mounted on a plunger-activated syringe.5

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Lower followed Willis to London after the city’s devastating fire in 1666, which also ended its plague epidemic. He established a private surgical practice but continued his research activities, questioning Willis’ theory that the venous-to-arterial color transition occurred in the heart. Lower and mathematician Robert Hooke (1635-1703), whose law still defines spring constants, used a bellows to ventilate a dog’s lungs while the chest was open, showing that the transition took place in the lungs. Wren also moved to London where his architectural skills attracted many commissions, including redesigning St Paul’s fire-damaged Cathedral.

Lower became a member of the Royal Society of London in October 1667 and infused several ounces of sheep blood into the veins of Arthur Coga, at its November 23 meeting (Fig 2). Coga has been variously described as a deranged curate or a Cambridge University student who was “a little cracked in the head.” He suffered no ill consequences and agreed to a second treatment in December. Lower anticipated modulating Coga’s temperament toward a lamb’s gentle nature and proposed a third infusion, which Coga declined.

PARISIAN ALACRITY AND PURPORTED PRESCIENCE

Reports of Lower’s animal transfusions reached Paris near the end of 1666, prompting both the Académie des
Sciences and Habert de Montmort's philosophic group to designate specific members to verify the English experiments. The Montmort group chose Jean Baptiste Denis, who described himself as a Professor of Philosophy and Mathematics and Paul Emmerez, a St Quentin surgeon. Denis performed two direct transfusions in dogs, three in calves, and then asked for Emmerez's assistance to infuse a human patient on June 15, 1667. The recipient was a teenage boy who had undergone 20 bleedings for a "contumacious and virulent fever" to assuage the excessive heat, which left him exhausted and listless. Approximately 250 mL flowed from a cannula in a lamb's carotid artery into the boy's cephalic vein, causing only a localized sensation of warmth. He "rapidly recovered from his lethargy, grew fatter, and was an object of surprise and astonishment to all who knew him."6 A robust 45-year-old sedan chair bearer was chosen to be Denis' second recipient, perhaps as "a negative control." He received sheep blood and returned to work the next day with no ill effects.

His third patient was a Swedish nobleman who became deathly ill in Paris while on a grand tour of Europe. His family prevailed upon Denis to try transfusion after his case was judged hopeless by his physicians. Denis infused him with calf blood, which briefly awakened his vigor, but he died while receiving a second transfusion.

Denis' fourth case was his most scandalous. The patient was a 34-year-old house servant named Antoine Mauroy who would intermittently disappear from his suburban home to indulge in Paris' sensual pleasures. On December 19, 1667, Denis and Emmerez withdrew 290 mL of Mauroy's blood and then connected a calf's femoral artery to a vein in Mauroy's arm, transfusing approximately 175 mL. This seemed to quiet his disposition, so the procedure was repeated several days later when several physicians had requested to be present. As the infusion was nearing completion, Mauroy complained of lumbar pain and an oppressive sensation in his chest, which coincided with an irregular pulse. The next day, his nose bled and his urine was dark and bloody. Mauroy behaved as his wife wished for 2 months but became truculent again, prompting her to insist on another transfusion. Mauroy refused to cooperate and received no blood, but died that evening, and his wife, perhaps with encouragement from some physician critics, accused Denis of killing her husband. Denis was tried for manslaughter but exonerated when it was discovered that Mrs Mauroy was poisoning her husband with arsenic.

Denis wrote to Henry Oldenberger, the Secretary of the Royal Society of London, claiming precedence for the first animal-to-human transfusion, adding that "the project of causing blood of a healthy animal to pass into one diseased" was conceived 10 years ago [1657] at an “illustrious Society of Virtuosi” meeting in de Montmort’s home.7 Oldenberger countered that “The English might well have been first, if they had not been so tender in hazarding the Life of a Man.” By 1678, British and French Parliaments had both banned all transfusions involving humans putting the issue to rest for 140 years.

DIRECT TRANSFUSION’S MAGICAL MOMENT

Two contemporaneous but very different surgical careers intertwined to achieve a momentous result on Sunday, March 8, 1908 (Fig 3). Adrian Van Sinderin Lambert (1872-1952) was a prominent native New York surgeon who followed his uncle and two brothers into medicine. He studied anatomy and pathology in Europe and was now an attending surgeon at New York’s Presbyterian and Bellevue hospitals with lauded expertise in neuro, trauma, and thoracic surgery.

Alexis Carrel (1873-1944) was born in Ste-Foy-les-Lyon. His education and training were at the University of
Lyon and enhanced by renowned embroideress, Mme. Leroudier’s coaching in fine needlework. His interest in vascular surgery began as an intern in 1894, when he observed his teachers being unable to repair French President Sadi Carnot’s portal vein that had been severed by a Lyon assassin’s knife. Carrel pursued research in vascular and organ grafts in Lyon until 1904 when he emigrated to Chicago where he had 2 productive years with Charles C. Guthrie before joining the Rockefeller Institute in 1906.

The object of their attention was Dr Lambert’s 5-day-old, nearly comatose daughter, Mary, who had been bleeding since birth from her respiratory and gastrointestinal tracts as well as into a large periorbital hematoma. The Lambert brothers awakened Carrel early on Sunday morning, asking if he could give Mary some of their blood. He agreed to try using his triangulation anastomotic technique. Adrian Lambert would be the donor and his partner, George Brewer would assist. The Lambert dining room at 29 W. 56th Street was the venue. It had a south facing window, providing relatively good lighting. Dr Lambert lay supine on the dining table with his left arm extended at a right angle on an ironing board where Mary was secured by loose strapping. No local anesthesia or systemic analgesic was used. Moments after the anastomosis had been completed, Mary began to stir and cry, as her pallid color gave way to a healthy pink, and bleeding from her incision and nose ceased. Eldest brother, Samuel Lambert, an internist and College of Physicians and Surgeons dean thought she might burst and asked Carrel to stop the transfusion. The vessels were not repaired, and Adrian Lambert never experienced hand ischemia. Carrel became the first surgeon to receive the Nobel Prize in Physiology or Medicine in 1912 and was an honored guest at Mary’s 21st birthday party.

In the early 1900s, Hemorrhagica Neonatorum described bleeding from multiple sites, commencing shortly after birth, which may have been due to vitamin K deficiency. Mary was the first reported case to be cured by a single transfusion, but by 1914, five cures could be compiled, including another baby transfused by Carrel. Most surgeons could not match Carrel’s dexterity with straight needles and used George Washington Crile’s device, which Crile used clinically to perform 32 direct transfusions (Fig 4). A similar device was described by Rueben Ottenberg in 1908, while an intern at the New York’s German (Lenox Hill after 1914) Hospital, who suggested pretransfusion cross-matching by Carrel. Most surgeons could not match Carrel’s dexterity with straight needles and used George Washington Crile’s device, which Crile used clinically to perform 32 direct transfusions (Fig 4). A similar device was described by Rueben Ottenberg in 1908, while an intern at the New York’s German (Lenox Hill after 1914) Hospital, who suggested pretransfusion cross-matching in the same paper. The exigencies of World War I prompted both Lieutenant Colonel Alfred J. Hull of the Royal Army Medical Corps and Ferdinand Sauerbruch to develop an artery-to-slit vein pull through (independently, of course).

WERE THEY JUST LUCKY?

Karl Landsteiner (1868-1943) published Ueber Agglutinationserscheinungen normalen menschlichen Blutes in Vienna’s 1901 klinische Wochenschrift (14:1132-34), describing A, B, and C (later O) blood groups, which were largely ignored on both sides of the Atlantic for more than a decade. Several factors contributed to the apparent safety of unknowingly indiscriminate transfusion. The amounts transfused were even smaller than estimated or intended from restrictive clotting in conduits, syringes, and stopcocks. Related donor use increased the chance of compatibility through Mendelian inheritance, but under-reporting and attributing deaths to the original illness or condition were the principal illusionists.

In 1913, Ottenberg, now an attending physician at Mount Sinai Hospital, confirmed the importance of pretransfusion cross-matching and the relative unimportance of donor antibodies. Within the next 2 years, Hustin in Brussels, Agote in Buenos Aires, and Richard Lewisohn (1875-1961) at Mount Sinai showed that sodium citrate in low concentrations was a safe and effective anticoagulant, superseding swirling with glass beads, and opening the prospect for indirect transfusion just as World War I began. U.S. Army Capt Oswald Robertson administered 22 transfusions of cross-matched, sodium citrate treated, cold stored blood (up to 26 days) to 20 injured soldiers, noting in a preceding article about immediate citrated blood transfusions that “The immediate effect of the transfused blood and subsequent progress of the cases were fully as good as that seen following ordinary transfusion.”

The American and British armies’ success with wartime transfusion emphasized the importance of Landsteiner’s original observations. He was recruited to a senior position at The Rockefeller Institute in 1923 where he continued his work with isoagglutinins in collaboration with Philip Levine and was awarded a Nobel Prize in 1930.
A MID-20th CENTURY REPRISE

C. Walton Lillehei (1918-1999) viewed J. H. Gibbon, Jr’s 1953 heart-lung machine and systemic hypothermia as being unnecessarily cumbersome and too time- and vision-limiting to perform complex intracardiac surgery. He and his colleagues demonstrated that a relatively low <40 mL/recipient kg “Azygos flow” cross circulation system would allow one dog to provide sufficient oxygenated blood to permit total heart bypass in another to complete complex repairs in a bloodless field. The circuit involved donor and recipient aortic and caval catheters, with two pumps driven by a single motor shaft to equalize inflow and outflow exchanges. This system was used clinically for 32 patients with high ventricular septal defects and Fallot’s Tetralogy with total cardiac bypass times up to 40 minutes, 15 successful outcomes, seven patient deaths, and no donor mortality. One donor required a thoracotomy and cardiac massage from a cumulatively disproportionate exchange that caused profound hypotension, harkening back to Samuel Lambert’s concern about too much blood flowing into the baby.

TRANSFUSION IN 21st CENTURY ASYMMETRIC WAR

Direct transfusions and the prominence of New York institutions in transfusion’s early 20th century maturation were significant events in the development of civilian blood banking, which led, in turn, to modern military’s forward availability of blood components. Freedom fighters and guerilla insurgents represent the other extreme. They depend on unfettered nimbleness to challenge goliaths with surprise attacks and rapid withdrawals to safe houses, where their wounded can expect only minimalist medical care. In Syria, where the movement is coalescing, this often includes freshly drawn O or type specific indirect transfusion–direct transfusion’s enduring step-child.

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