A Note from History:
Blood Transfusion from Antiquity to the Discovery of the Rh Factor

Steven I. Hajdu

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Use of blood as a therapeutic agent by drinking it as “Elixir Vitae” goes back before Biblical time. Despite the opposition of Celsus (25 BC – AD 50), drinking blood continued; it was routine to drink the blood of fallen gladiators as a remedy for various ailments, including epilepsy.

Rational thinking about blood transfusion was prevented by the beliefs of Aristotle (384–322 BC) and Galen (130–200 AD), who taught that the blood was made in the heart or the liver and flowed until it was used up. These views remained undisputed for >1400 years, until the discovery in 1616 of the blood circulation by William Harvey (1578–1657). Harvey’s discovery gave a sudden impetus to transfer blood from animals to humans and from one person to another. The first blood transfusion was carried out in 1628 by an Italian physician, Giovanni Francisco Colle (1558–1631) [1]. In 1665, Richard Lower (1631–1691) in England successfully transfused dogs with blood [2].

In 1666, blood transfusion into a human was performed in Paris by the mathematician, philosopher, and teacher, Jean Baptiste Denis (1625–1704) [3]. He transfused lamb’s blood into 3 men with great success to cure their diseases, but the fourth patient died as the result of the transfusion. Denis, a target of opposition and jealousy of the medical and religious communities, was sued for wrongful death by the widow. Although Denis was found not negligent, the Paris court ordered him to stop further transfusions. Subsequently, the Medical Faculty of Paris petitioned the Parliament to outlaw blood transfusion throughout France. The Parliament agreed with the petitioners; transfusions fell into disrepute until the early 1800s. Exceptions were
a German army surgeon, Matthäus Gottfried Purmann (1649 – 1711) and his associates [4,5] (Fig. 1). It is of interest that, among Purmann’s long list of reasons for transfusion, acute blood loss was not included.

The revival of blood transfusion in England in 1796 came from Erasmus Darwin (1731–1802), the grandfather of Charles Darwin (1809–1882). Erasmus Darwin advocated blood transfusion in conditions with inadequate nutrition. To transfer the blood from one person to another, he endorsed an earlier suggestion [5] to use goose-quills tied together by a piece of chicken gut.

James Blundell (1790–1877) (Fig. 2) was an eccentric obstetrician at Guy’s Hospital and St. Thomas’s Hospital in London. After he had performed blood transfusion in dogs, he introduced human to human transfusion in acute hemorrhage following child birth. Blundell understood the incompatibility of interspecies transfusion and he developed a method of indirect transfusion [6]. He replaced arterial blood with venous blood and described a three-way valve with an “impellor” and a “gravitator” for indirect transfusion. The “impellor” assured continuous supply of blood under pressure to the recipient and the “gravitator” was an apparatus to achieve uninterrupted flow of blood by gravity [7]. Blundell’s instrument was well received because once the transfusion begun, the operator had little to do, except as he wrote [6] to guard against an overcharge of the recipient heart.

As a practicing obstetrician, Blundell wrote two influential textbooks of obstetrics and he was the first to recommend transecting the Fallopian tubes on delivery by Caesarian section to prevent further pregnancy. He discontinued hospital practice in 1836, because of irreconcilable differences with the hospital administration, but he continued in private practice and was elected a Fellow of the Royal College of Physicians. He retired in his late fifties and devoted himself to studying literature and perfecting his Greek.

In the mid-1800s, transfusion was abandoned once again, when the infusion of physiologic salt solution was introduced as a blood substitute. Work in bacteriology of Jules Jean Baptiste Vincent Bordet...
(1870–1961) of Belgium showed that 2 substances (sensitizing antibody and complement) are involved in bacteriolysis, which established the basis for complement fixation [8]. Shortly after this discovery, Bordet observed that the injection of red blood cells of an animal of another species induced the creation of antibodies in the serum and hemolyzed the red blood cells [9]. For his contributions to immunology Bordet received the Nobel Prize in 1919 and an Institute was named after him in Brussels.

From the initial experiments with blood transfusion in the 1600s to the introduction of safe transfusions in the 1900s, the road was a long one. It took approximately two and a half centuries from the origins of transfusion to the discovery of the blood groups in 1900 by Karl Landsteiner (1868–1943) (Fig. 3). Landsteiner was an assistant in pathology at the University of Vienna when he discovered iso-agglutinins in the human blood and identified 3 specific blood groups [10]. The fourth group was added 2 years later [11]. The discoveries that sodium citrate prevents the coagulation of blood and that the blood groups are inherited according to Mendelian laws [12,13] were also crucial to the development of safe blood transfusion.

Landsteiner is credited with introducing darkfield microscopy for the diagnosis of Treponema pallidum and he was the first person to transmit poliomyelitis to monkeys, in an attempt to develop a vaccine. He received the Nobel Prize in 1930. In 1933, Landsteiner published the first monograph on specific antigen–antibody interactions [14] and he emigrated to the United States. He became an esteemed research professor at the Rockefeller Institute in New York City, where he discovered the Rh factor [15]. In 1942, the year before Landsteiner died, he described the crucial role of mononuclear cells in cellular immunity.

References
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