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The Development of Blood Transfusion: the Role of Albert Hustin and the Influence of World War I

Article in Acta Chirurgica Belgica · May 2015 D0I: 10.1080/00015458.2015.11681107 · Source: PubMed

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Acta Chir Belg, 2015, 115, 000-000

The development of blood transfusion : the role of Albert Hustin and the influence of World War I.

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Blood transfusion (¹) represents the opposite act to bloodletting and therefore could only come into practice after progressive decay of Galen s concepts of pathophysiology and treatment (²). It took approximately a hundred years after the epoch making publication in 1543 of Vesalius *Fabrica* to implement this decay (³).

Particularly the paradigm change from an ebb and flood movement of blood into a functional circulation induced the idea that blood should not be lost indefinitely but instead should be restored in case of massive loss (⁴).

It is therefore comprehensible that the first attempts of blood transfusion only started in the middle of the 17^{th} century (^s) (Fig. 1).

So did Richard Lower (1631-1691) In 1665 for the first time successfully try to keep dogs alive with blood, transfused from other dogs ($^{\circ}$).

In France Jean Baptiste Denis (1634-1704) in early 1667 performed analogous experiments (⁷) but later extended them to humans (⁸). He is credited to have performed the first lamb to man blood transfusion with success (⁹) (Fig. 2).



Figure 1. Blood transfusion from a dog to a man during simultaneous bloodletting. From : Johann Schultheiss (= Scultetus) (1595-1645) : *Armamentarii Chirurgici*. Amsterdam : J. van Someren, 1671.



Figure 2. Blood transfusion from a lamb to a man. From : Matthias Purmann (1648-1721) : *Chirurgischer Lorbeer-Krantz oder Wund-Artzney*. Halberstadt : Johann Erasmus Hynitzsch, 1684.

(1) A large number of publications on the history of blood transfusion have been issued in either medical journals or on the internet. A list of relevant historical publications is given by the British Blood Transfusion Society on their internet site. I refer here only to a small number of publications : Jennings 1884 ; Sturgis 1942 ; Farr 1980 ; Keynes 1992 ; Learoyd 2006 ; Kaadan & Angrini 2009. A special issue has recently been devoted to blood transfusion during the First World War : see Boulton & Roberts 2014.

(2) For Galenic pathophysiology and treatment, see Siegel 1968 and Debru 2008.

- (3) See Van Hee 2005.
- (4) See Keynes p.4. See also Hall 1830.
- (5) See Farr p.145.
- (6) See Lower 1666.
- (7) See Denis 1667 a.
- (8) See Denis 1667 b.

(9) His letter relating the first lamb to man transfusion, published in French in June 1667 in Paris (see Denis 1667 b), was sent to London, translated and published in the *Philosophical Transactions* in July 1667. Later the secretary of the *Transactions* Henry Oldenburg reissued the publication in another form, emphasizing Lower's invention ! See Denis 1667 c and Farr s comment pp.145-147. Mattheus Purmann (1649-1711) in 1668 in Germany followed his technique and later reproduced it with a relevant picture in 1684. See Purmann 1684.

Lower continued his research and published further results in 1669 (¹⁰).

It took however the whole 17th and 18th century to get rid of Galen's bloodletting practice, mainly because the ancient philosophical ideas concerning humoral treatment did not follow the new physiological discoveries (¹¹).

It lasted until 1818 before the British obstetrician James Blundell (1790-1877) (Fig. 3) resumed experiments with blood transfusion in dogs (¹²) and treated a patient with a postpartum haemorrhage with human blood transfusion (¹³).

He invented two devices which would be so innovative that their principle continued to be used into the 20^{th} century. For such veno-venous transfusion Blundell first used a so-called Impellor.

Later he used gravitation to increase the infusion pressure. It became the so-called Gravitator (¹⁴) (Fig. 4).

Nevertheless the pressure remained so low that coagulation swiftly occurred and hampered adequate and reproducible use.

To cope with this low pressure, two methods were tried. On the one hand a pump system was inserted between donor and recipient. Alfred Higginson (1808-1884) in 1857 invented a rubber injection syringe with ball valves, inserted between the receptacle and the recipient s vein (¹⁵). In an article of 1864 James Hobson Aveling (1828-1892) used a tube, containing a balloon, that by manual pressure could induce such pump action (¹⁶).

The second method consisted of using a donor artery instead of a vein, using arterial pressure as the motor for



Figure 3. Picture of James Blundell (1790-1877).



Figure 4. Blundell s Gravitator .

transfusion. The Geneva physician Joseph-Antoine Roussel (1837-1901) realized such technique, which was presented at the *Acad mie des Sciences* in Paris in 1867, and made use of the afferent radial artery, a water filled glass tube and the efferent recipient forearm vein. Both other donor artery and recipient vein ends were ligated (¹⁷) (Fig. 5).

Roussel s technique proved so successful that between 1865 and 1882 sixty transfusions were performed in different countries (¹⁸), for instance during the Franco-Prussian War. Infections occurred in the early treatments but subsided after Lister s introduction of antisepsis in 1867.

Nevertheless, even with this higher arterial pressure blood coagulation often persisted partially or completely.

Therefore drugs were tested to counteract coagulation. Ignaz Josef Neudörfer (1825-1898) in 1860 used sodium bicarbonate (¹⁹). John Braxton Hicks (1823-1893) tried sodium phosphate (²⁰). However anticoagulation in both cases proved ineffective (²¹).

Charles-Edouard Brown-S quard (1817-1894) experimented with defibrillated blood, obtained after removing

- (16) See Aveling 1864.
- (17) See Roussel 1868. See also Jullien p.258.
- (18) See Jullien pp.258 ff.
- (19) See Neudörfer 1860.
- (20) See Hicks 1868.
- (21) See Giangrande 2000.

⁽¹⁰⁾ See Lower 1669.

⁽¹¹⁾ Some of the first antagonists of bloodletting were John Radcliffe (1652-1714) in England and Pierre Louis (1787-1872) in France. See Thomas p.74.

⁽¹²⁾ See Blundell 1818.

⁽¹³⁾ See Blundell 1819.

⁽¹⁴⁾ See Blundell 1828-1829.

⁽¹⁵⁾ See Higginson 1857.





Figure 5. Arteriovenous blood transfusion according to Roussel.

the coagulum from the blood containing flask $(^{22})$. Between 1875 and 1880 even bloodless infusions, such as with sodium chloride, were used instead of blood $(^{23})$.

Both latter methods deprived blood partly or totally from its red blood cells, and consequently proved equally inadequate.

However these experiments demonstrated that infusions could delay the appearance of hypovolemic shock. George W. Crile (1864-1943) (Fig. 6) unravelled the pathophysiology of shock (²⁴), and therefore used blood transfusion in case of haemorrhagic shock (²⁵), particularly when Crile joined the American troops at the end of the First World War.

As coagulation nevertheless could not be eliminated, even with the use of a donor arterial artery, researchers after the century switch again turned to other devices, able to improve veno-venous transfusion.



Figure 6. Picture of George W. Crile (1864-1943).



Figure 7. Representation of the Kimpton-Brown apparatus for blood transfusion.

This resulted in the so-called Kimpton-Brown apparatus (Fig. 7), which was used from 1913 onwards. It was devised by Arthur Ronald Kimpton (1881-?) and James Howard Brown (1884-1956), and consisted of a paraffin coated gradient glass cylinder with a horizontal side tube for suction to draw blood from the donor vein, and then pump it as fast as possible in the recipient vein (²⁶).

Notwithstanding the many failures it proved to be one of the most useful apparatus of the pre-WW I period.

This was the more so since Karl Landsteiner (1868-1943) in 1900 discovered the A, B and C (later renamed O) blood groups and the inborn presence of agglutinins against absent A/B genes in human blood (²⁷).

This led to the suggestion by the American Reuben Ottenberg (1882-1959) to test pre-transfusion compatibility between donor and recipient by cross-matching both individuals blood samples (²⁸).

- (24) See Crile 1907.
- (25) See Crile 1909.
- (26) See Kimpton & Brown 1913.
- (27) See Landsteiner 1900.
- (28) See Ottenberg 1911.

⁽²²⁾ See Brown-S quard 1869.

⁽²³⁾ See Bull 1884.

After proof of its positive results in 128 transfusions, Ludvig Hektoen (1863-1951) (²⁹) of Chicago reiterated this advice (³⁰).

Nevertheless the problem of coagulation remained as actual as ever, and continued to hamper the use of blood transfusion, not the least during the Balkan War of 1912 (³¹).

The discovery of Albert Hustin

The most potent and efficient anticoagulation was introduced by the Belgian surgeon Albert Hustin (1882-1967) (32) (Fig. 8).

Hustin, born in Ethe near Virton in the South of Belgium in 1882, became medical doctor at the Brussels Free University ULB in 1906.

In his last study year he was able to go to the USA, where he visited hospital units in Philadelphia (³³).

After his studies and supported by his mentor Antoine Depage (1862-1925) (³⁴), he went to Paris and Heidelberg during one year.

He started his surgical career in the department of surgery of the St. Jean hospital in Brussels, led by his previous professor Antoine Depage.

The scientific minded Hustin produced more than 39 publications, bound in a 428 pages volume in 1922 (³⁵).



Figure 8. Picture of the young Albert Hustin.



Figure 9. Albert Hustin in his laboratory.

His discovery of sodium citrate as prevention method against coagulation, dates from 1913 (Fig. 9). Looking for an anticoagulant to perfuse a canine pancreas, he tried sodium citrate which was known to stabilize solutions of mastic (³⁶). He reiterated his first positive results on animals in the physiology department of the Solvay Institute.

His first human transfusion with citrated blood dates from March 27th, 1914 (Fig. 10), when he drew 150 ml of blood of a hypertensive patient, added a glucose solution of sodium citrate, and in the Brussels' St. Jean hospital

(31) Be it, that also fear for racial factors played a role in blood transfusion during this eugenically charged research period of the Balkan War. Blood of white European races would be considered pure instead of the impurity of blood of dark-skinned races ! Such research was performed by the German Ludwik Hirszfeld, nota bene a Jew who later escaped the Warsaw Ghetto in 1941 ! See Frank Thadeusz s.d.

(32) For biographies of Hustin, see Dor 1993, pp.78-81, and Dupont 2000.

(33) For a description of his experiences, see Hustin 1906.

(34) For a biography of Depage, see Van Hee 2002 and Van Hee 2007.

(35) See Bouch & Hustin 1922.

(36) These experiments were the basis of Hustin s PhD. thesis. See Hustin 1913.

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⁽²⁹⁾ For a biography of Hektoen, see Cannon 1954.

⁽³⁰⁾ See Hektoen 1907.

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Figure 10. Hustin's report, written on March 27th 1914 in his laboratory notebook, concerning the worldwide first blood transfusion with citrated blood in man.



Figure 11. The apparatus used by Albert Hustin.

infused it in an extremely anaemic patient with the use of a flask and pump system (Fig. 11).

He published the positive outcome one month later in the *Bulletin des Sciences m dicales et naturelles de Bruxelles* (³⁷).

Followers of Albert Hustin

The Argentine physician Luis Agote (1868-1954) probably got informed about Hustin's publications (³⁸) and

performed analogous research. He was probably the second on November 9th 1914 to perform blood transfusion with citrated blood in the Rawson hospital of Buenos Aires (³⁹).

His report in the leading newspaper of Buenos Aires *Las Presna* was soon followed by two human blood transfusions by the German Richard Lewisohn (1875-1961) working at the Mt Sinai Hospital in patients in January 23th, 1915 (40).

The several trials of human blood transfusion proved however not always successful.

Vigorous reactions in the recipient were thought to be the effect of pyrogens or poisonous ingredients.

Consequently the controversy flared up between the protagonists of fresh blood arterio-venous or veno-venous transfusion and transfusion with modified citrated blood.

But by then the First World War had broken out in August 1914.

Blood transfusion during World War I

Military medical officers now also heard about this new tool, which could help them in treating soldiers with acute haemorrhagic shock.

However, while intravenous infusions with saline or glucose were by then fully implemented (Fig. 12), this proved not the case for blood transfusion.

This had greatly to do with the organizational problems that medical commanders had to cope with in the first years of the War. Belgian troops had retreated after the front line of the river IJzer in October 1914, but the medical institutions, particularly the Océan Hospital (⁴¹),



Figure 12. Use of intravenous solutions during World War I.

(40) See Lewisohn pp.141-142.

(41) The Red Cross Oc an Hospital in De Panne opened on December 20th, 1914.

⁽³⁷⁾ See Hustin 1914a.

⁽³⁸⁾ A second report of Hustin's blood transfusion results got published in August 1914. See Hustin 1914b.

⁽³⁹⁾ See Agote 1915.



Figure 13. The Red Cross Hospital L Oc an with its annex buildings in the later years of the War.



Figure 14. Direct blood transfusion as performed during World War I.

were only fully operational in early 1915 (Fig. 13). Then the surgical department of Dr. Antoine Depage was in full activity. Already the same year 1915, Dr. Georges Debaisieux (1882-1956) and Dr. Carl Janssen made use of citrated blood transfusion to counteract severe blood loss in wounded soldiers. Nevertheless most transfusions still were performed directly between the veins of donor and recipient, using a modified Aveling tube system (Fig. 14).

Richard Weil (1876-1947) in 1915 got the idea to refrigerate the citrated blood, what permitted him to store such blood for 2 to 3 days (42).

When in 1916 medical staffs of the Allied troops got the reports of Francis Peyton Rous (1879-1970) and Joseph R. Turner that addition of glucose to the citrated blood improved red blood cell preservation, storage of refrigerated blood was increased to 2-3 weeks (⁴³) (**Fig. 15**).

Dilution of blood through addition of glucose solution however necessitated removal of up to 50% of the solution just before transfusion !



Figure 15. The young Francis Peyton Rous in his laboratory.

Use of stored citrated blood during World War I

Nevertheless the method was revolutionary and was implemented for the first time during the battle of Cambrai in November 1917, where a first rudimentary blood storage centre was set up.

The Kimpton-Brown apparatus was then the mostly used tool for effective transfusion, especially in the British hospitals.

In general there was no problem in finding blood donors during the war. For direct transfusion, whether arterio-venous or veno-venous, soldiers and officers, chaplains and nurses presented themselves to help their wounded compatriots or allied friends. Many stories have been recorded of such generous acts (⁴⁴), which however included a real operation of donor artery denudation and distal artery ligation. Moreover such arteriotomy often occurred without narcosis or under insufficient local novocaine anaesthesia (⁴⁵).

To use stored blood volunteers had to be selected. Such organisation was first implemented by Canadian and later American surgeons, who favoured this type of citrated blood stored transfusion.

In 1918 Oswald Hope Robertson (1886-1966) of the 3rd British Army (Fig. 16) realized a completely worked

⁽⁴²⁾ See Weil 1915.

⁽⁴³⁾ See Rous & Turner 1916.

⁽⁴⁴⁾ For numerous such reports (in French), see Patrick Loodts, s.d.

⁽⁴⁵⁾ Ibidem.

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Figure 16. Portrait of the military doctor Oswald H. Robertson (1886-1966).

out storing centre with blood, refrigerated and stored for up to 3 weeks (⁴⁶).

It also allowed stored blood to be transported, as was for instance the case with a refrigerated blood flask, carried from the battle field in Arras up to London by Captain Kenneth Walker !

The Oc an Hospital in De Panne was not only one of the leading transfusion laboratories, it also performed continuous research on the subject (⁴⁷). Results of the performed transfusions were published by Dr. Paul Govaerts (1889-1927) in 1918 (Fig. 17) (⁴⁸).

Govaerts reported on 14 patients with transfusions in the Oc an Hospital. Three patients died from gas gangrene infection, three others had a complicated follow up and eight recovered. One of the three complications included a blood incompatibility reaction with haemoglobinuria and fatal uraemia.

Registration of mortality as recorded by Govaerts was not really in favour of transfusion : this resulted more from the fact that mostly moribund patients were transfused, when no other therapeutic options proved possible (⁴⁹). A study of Fullerton *et al*. stated that in the Boulogne base in 1916, 19 patients had been transfused, and 15 deaths were recorded (⁵⁰). Results progressively improved, since a statistical report of June 1918 recorded a mortality of 9 out of the 20 patients treated with 22 transfusions.

These reports were the reason why from 1918 onwards transfusions were not only performed in the back stage 'clearing stations', but also in the front line 'advanced dressing stations . It certainly improved the results



Figure 17. Paul Govaerts (1889-1927) at work.

obtained with transfusion as one of the treatment adjuncts to the wounded victims.

Blood transfusion after World War I

One can say that the development of blood transfusion techniques during the First World War was one of the most impressive medical advances, that shed their shadow far into the 20^{th} century.

Not the least was the role of Albert Hustin preponderant, also in the interbellum period. In those years Hustin worked in the surgical department of Robert Danis (**Fig. 18**). In 1934 he participated in the opening of the first blood transfusion centre in Belgium (Fig. 19), after the establishment of analogous centres in Great Britain in 1921 (⁵¹) and in the Netherlands and Spain in 1930.

It was Queen Elisabeth of Belgium who inaugurated the Brussels transfusion centre of Hustin in the Brugmann Hospital in 1934 (⁵²). The recruitment of volunteers for

⁽⁴⁶⁾ See Robertson 1918.

⁽⁴⁷⁾ Research performed in 1915-1916 by Hustin and Bouch also centered around immunology and anaphylactic shock. See Bouch & Hustin 1922.

⁽⁴⁸⁾ See Govaerts 1918.

⁽⁴⁹⁾ Even though a series of new operative procedures had become possible during the First World War. See Van Hee 2014.

⁽⁵⁰⁾ See Fullerton et al. 1917.

⁽⁵¹⁾ This centre was opened by Percy Lane Oliver (1878-1944).

⁽⁵²⁾ The same year Hustin was elected 2nd vice-President of the Royal Belgian Society of Surgery, to become its President in 1936. See Mendes da Costa & Van Hee p. 180.



Figure 18. Albert Hustin, at the right hand side of Robert Danis, with colleages and nurses of the Surgical Department of Prof. Danis in Brussels in 1929.



Figure 19. Portrait of Albert Hustin in the 1930 s.

blood donation helped change the then still mostly used direct blood transfusion technique !

That every new invention takes long to be implemented routinely, proved also to be the case for indirect blood transfusion with citrated stored blood !

Certainly during the War, but even many years after the War ended, direct blood transfusion was the preferred method. In particular the syringe of the Frenchman Louis Jubé, developed in 1923, and the handy apparatus of his compatriots L. Henry and P. Jouvelet introduced in 1934 (Fig. 20), was used during decades to realize a direct donor-recipient transfusion (⁵³).

Nevertheless when the Spanish War and later World War II broke out, the method of storage of Hustin's



Figure 20. Apparatus of Henry and Joulivet (Coll. Museum Lambotte, Antwerp, Belgium).

citrated blood became definitively the method of choice (⁵⁴).

Blood transfusion is one of the so many examples where war conditions unintentionally have given a boost to scientific research and successful medical practice.

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(53) See Gosset et al. 1939.

(54) This is witnessed by the reports, given in the references, of Balachowski & Guinsbourg in 1934 and of Bagdassarov in 1937 in Russia; of Tzanck & Dreyfuss in 1937 in France; of Goodall *et al.* in 1938 in the United States; of Elliott *et al.* in 1939 in Great Britain; and of Duran Jorda in 1939 in Spain.

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