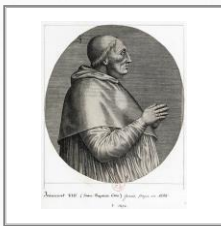


Great Achievements in Transfusion Medicine

Kristin Butler, MLS (ASCP)^{CM}
CLPC
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Objectives

1. Recall major discoveries in the field of transfusion medicine.
2. Describe the evolution of blood banking procedures.
3. Discuss the future of transfusion medicine testing.



First recorded blood transfusion attempt

- Pope Innocent VIII in 1492
- Was given the blood of 10 year old boys
- No one survived

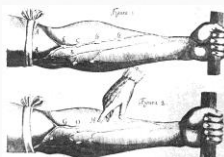


The circulation of blood

- William Harvey in 1628
- Experimentation on animals
- Book, "On the Motion of the Heart and Blood in Animals"

Harvey's experiments on circulation

- Initially on serpents and fish
- Tied off the veins and arteries in separate periods of time
- Later on humans using tight ligature on upper arm
 - Changes to arm above and below
 - Noticed valves in veins



First successful blood transfusion

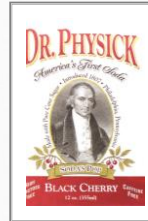
- Richard Lower in 1665
- Transfused blood from one dog to another
- Many transfusions were successful





From animal to human

- Jean-Baptiste Denis and Richard Lower in 1667
- Successful transfusions from lambs to humans
- After 10 years, this practice was prohibited
- No further studies for 150 years



1st successful human transfusion, unpublished

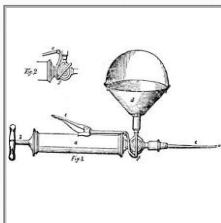
- Dr. Phillip Syng Physick in 1795
- “Father of American Surgery”
- Introduced carbonated water for medicinal use in 1807

1st successful transfusion, recorded

- James Blundell, obstetrician in 1818
- For treatment of postpartum hemorrhage
- Used patient's husband as donor
- Took 4 ounces from the husband using a syringe and injected into wife

Blundell's post-partum transfusions, 1825 – 1830

- Dr. Blundell performed 10 more transfusions
- 5 were unsuccessful
 - Issues with clotting
 - Fatal reactions



St. George's Hospital Medical School, London 1840

- Samuel Armstrong Lane and Dr. Blundell
- First successful whole blood transfusion to treat hemophilia
 - 11-year old George Firmin, post eye surgery
 - 6th day post-op, transfused blood from healthy young woman

1867



Joseph Lister and antiseptics

- Promoted using sterile techniques during surgery
- Used carbolic acid (coal – tar derivative) to sterilize
- Control infections during transfusions

Milk transfusion in late 1800s

- 1873 – mid-1880s
- Physicians transfusing milk from cows, goats, and humans
- “blood substitute”
- Saline infusions replace milk in 1884



Karl Landsteiner, 1901

- Austrian scientist
- Determined 3 basic blood groups: A, B, C
- C later changed to O (German for Ohne, meaning nothing)
- Experiments with blood from students
- Won Nobel Prize in 1930

Landsteiner's students, 1902

- DeCastello and Sturli
- Determined the AB group
- These 4 groups what we now know as the ABO blood group system

Blood transfusions in surgery

Routinely performed by 1903

1907: Hektoen suggests improving safety by crossmatching

Rueben Ottenberg, NYC: performs first transfusion using type and crossmatch

Ottenberg observes Medelian inheritance and describes “universal” utility of group O donors

1908

Alexis Carrel, France

- Develops vein-to-vein method of transfusion to prevent clotting
- Adopted by J.B. Murphy in Chicago
- Adopted by George Crile in Cleveland
- Nobel prize in 1912

Carlo Moreschi, Italy

- Forgotten pioneer
- Interest in hematology and immunology
- First to understand C' fixation
- First describes the antiglobulin reaction

Universal donor Universal recipient



- Defined by Roger Lee in 1912
- Demonstrated that group O blood could be given to all 4 types
- Demonstrated that group AB could receive all 4 types

Production of anticoagulants

- **Late 1800s:** European experiments
 - Discovery of Ca^{2+} role in clotting
 - Oxalate used in dogs
 - Ammonium citrate used in dogs
 - Understanding Ca^{2+} affinity for citrate
- **Beginning 1914:** development of sodium citrate for human blood transfusion

Production of anticoagulants

- **1915:** Richard Lewisohn uses sodium citrate blood
 - Changes procedure from direct to indirect
- **1915:** Richard Weil shows feasibility of refrigerated storage of sodium citrate stored blood
- **1916:** Francis Rous and J.R. Turner introduced a citrate-glucose solution
 - Allowed refrigerated storage for several days
 - Facilitates indirect procedure
 - Allows for establishment of first blood depots

World War I: Western Front 1917



- US Army officer Dr. Oswald Robertson
- First blood depot established
- Using blood stored with sodium citrate

Establishing hospital and community blood banks

- 1926: British Red Cross – first human blood transfusion service
- 1932: Leningrad, Russia – first hospital blood depot
- 1937: Bernard Fantus, Cook County Hospital in Chicago
 - First hospital blood bank in the United States
 - Originates the term “blood bank”
 - San Francisco, New York, Miami, Cincinnati....

The 1940s

- Philip Levine and R. E. Stetson described the Rh system in 1939
 - Mother to stillborn child receives husband's blood and suffers severe reaction
- Karl Landsteiner and Alex Wiener named the Rh system in 1940
 - Studies using Rhesus monkey
 - Obtained anti-Rh factor
 - Samples from NYC population

The 1940s

- Edwin Cohn, Harvard Chem professor
- Cold ethanol fractionation
 - Albumin, gamma globulin, and fibrinogen now available for use
 - Pearl Harbor victims treated with Cohn's albumin for shock
- Army Blood Transfusion Service and Depot established
 - Blood type every member
 - Donations in the field

The 1940s

- US Govt establishes nationwide program for blood collection
- “Plasma for Britain” program started
- American Red Cross collects 13 million units of blood by the end of WWI



Charles Richard Drew

- 1st African American to earn doctor of medical science degree
- 1st African American to be elected to serve on the American Board of Surgery
- Medical Director of the “Blood for Britain” program
- Started “bloodmobiles” and localized donation centers
- 15,000 whole blood units collected; 5,500 units of plasma

The 1940s

- Acid citrate dextrose (ACD) developed
- J.F. Loutit and Patrick Mollison, 1943
 - Reduce amt of anticoagulant
 - Store greater volumes
 - Longer term storage
- Paul Beeson publishes first description of transfusion-transmitted hepatitis, 1943
 - Development of jaundice months later

The 1940s

- Coombs, Mourant, and Race use **AHG** to identify “incomplete antibodies”, 1945



- American Association of Blood Banks (AABB) is formed in 1947
 - Promote common goals
 - Blood banking practitioners
 - Blood donors

United States, 1950

1500 hospital blood banks

46 community blood centers

31 American Red Cross regional blood centers

Worldwide establishment

Single most influential technical development: **PLASTIC COLLECTION BAGS**

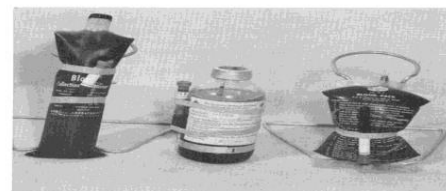


FIGURE 180.—Plastic equipment, standardized as replacement for glass bottles during Korean War. In center is collecting bottle formerly used.

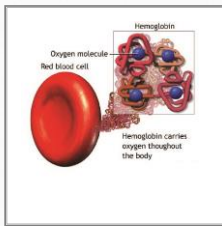


Wartime blood shipment



AABB Clearinghouse

- Established in 1953
- Centralized system for exchanging blood among blood banks
- Now called the National Blood Exchange



Explosive growth in blood use during the 1950s

- Open heart surgery and trauma care
- AABB forms Inspection and Accreditation committee
- 1st Edition of AABB Standards published
- Max Perutz of Cambridge University deciphers the molecular structure of hemoglobin

United States,
1962

4400 hospital blood banks

123 community blood centers

55 American Red Cross regional blood centers

5 to 6 million units of blood collected per year

Component therapy in the 1960s

- Therapeutic plasmapheresis procedure introduced
- Platelet concentrates for cancer patients
- Antihemophilic factor (AHF) concentrates for hemophiliacs
- Cryoprecipitated AHF methods introduced
- Rh immune globulin commercially introduced to give Rh(=) women
- Feasibility of storing platelets at room temp

All-volunteer blood donor systems began in 1970

- Careful donor selection and infectious disease testing
- Hepatitis B surface antigen (HBsAg) testing began in 1971
 - Dr. Baruch Blumberg at National Institute of Health (NIH)
 - Developed first test for HBV in 1967
 - Developed first vaccine for HBV in 1969
 - Won Nobel Prize in 1976 for these contributions



Increasing demand and blood shortages

- Apheresis being used frequently
- Increasing demand plus volunteer system
- CPDA-1 saves the day!



The Era of Transfusion Medicine

- Begins in early 1980s
- Packed RBCs
- Plasma exchange
- Coagulation products
- Doctors specifically trained in blood transfusion

Infectious disease testing in the 1980s

- **1981**: first AIDS case reported
- **1984**: HIV identified as cause of AIDS
- **1985**: first HIV screening test licensed and implemented to protect blood supply
- **1987**: hepatitis B core antibody (anti-HBc) and ALT tests implemented
- **1989**: Hepatitis C identified; Human T-Lymphotropic Virus I antibody testing begins

Infectious disease testing in the 1990s

- **1990**: first specific test for HCV
- **1992**: HIV-1 and HIV-2 antibody testing
- **1996**: HIV p24 antigen testing; vCJD identified
- **1997**: US Govt reports on blood safety – National Blood Data Resource Center founded by AABB
- **1992**: HCV lookback campaign
- **1999**: nucleic acid amplification testing (NAT)



Where are we now?

- >7,000 hospital blood banks and blood centers
- >13 million whole blood units collected per year

Blood demand in the U.S today

- 36,000 units of RBC
- 10,000 units of plasma
- 7,000 units of platelets



Source: American Red Cross

Today's technology: AUTOMATION!

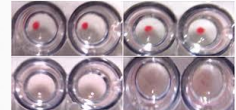


Today's technology: Replacing tube testing

Gel technology



Solid Phase technology 6A Sample number 293



Increasing demands for blood systems and safety

- West Nile
- Zika
- Ebola
- Chagas
- Bacterial contamination
- Maintaining the blood supply

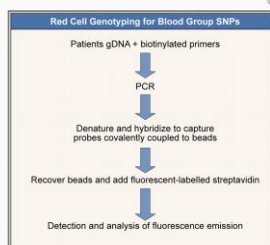


Molecular testing in the Blood Bank

- RBC genotyping, an alternative to serological typing
- Expression of many clinically significant antigens is determined by single nucleotide polymorphisms (SNPs)
- Detecting these SNPs can predict the red cell phenotype
- Using donor or patient DNA

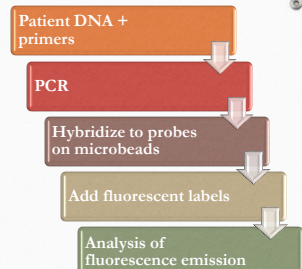
RBC genotyping

- Mass screening of donors
- When antisera not reliable or available
- Detecting weak or variant Ag
- Pregnancy



RBC genotyping

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Artificial blood substitutes

RBC substitutes

- Perfluorocarbons (PFCs)
- Dissolve O₂
- Must be mixed with lipid emulsion
- Short half life

Synthetic O₂ carriers

- Hemoglobin-based O₂ carriers (HBOCs)
- Recombinant, polymerized Hb products
- Derived from humans and animals

Artificial blood substitutes

- And the (re)search continues...

- Marine worms in Romania
- RBCs from stem cells in UK and Scotland
- Human trials are near

The only thing that never changed throughout the years is the importance of blood.

Thanks to these many researchers, we have reached the safe standards that we have today.