Historical Perspectives in Transfusion Medicine

Melanie Tokessy
Charge Technologist, Transfusion Medicine
Eastern Ontario Laboratory Association
The Ottawa Hospital
Objectives

• Review the historical landmarks in Transfusion Medicine
• Appreciate the strides the Transfusion Medicine community has made towards a safer blood system
THE ONLY TIME YOU SHOULD EVER LOOK BACK, IS TO SEE HOW FAR YOU'VE COME.
• No disclosures
Animal to Human Transfusions

- 1667 France
- Jean Baptiste Denys
- Transfused lamb blood into the carotid artery of a young woman
- The woman passed urine “black as soot” but she survived
Adverse Transfusion Event (AET)

- Fourth recipient
- Second transfusion
- “As soon as the blood began to enter into his veins, he felt...heat along his arm, and under his arm pits...His pulse rose presently and soon after we observ’d plentiful sweat over all his face. His pulse varied extremely at this instant, and complained of a great pain in his kidneys....he made a great glass full of urine, of a color as black...as soot”
ATE Reporting: Current

- TTISS-ON
- Contracted by MOH-LTC and PHAC
First Known Human to Human Blood Transfusion

• 1795 Philadelphia
• Physician Philip Syng Physick
• Known as the “Father of American Surgery”
• Never published his work in transfusion
First Reported Successful Human to Human Transfusion

- 1818 Britain
- Obstetrician James Blundell
- Used patient’s husband as donor
- 4 ounces through a syringe
- “By Jesus, I feel strong as a bull!”
OBSERVATIONS ON TRANSFUSION OF BLOOD.

By Dr. Blundell.

With a Description of his Gravitator.*

States of the body really requiring the infusion of blood into the veins are probably rare; yet we sometimes meet with cases in which the patient must die unless such operation can be performed; and still more frequently with cases which seem to require a supply of blood, in order to prevent the ill health which the belly suffers from large losses of the vital fluid, even when they do not prove fatal.

* The instrument is manufactured by Messrs. Maw, 55, Aldermanbury.

In the present state of our knowledge respecting the operation, although it has not been clearly shown to have proved fatal in any one instance, yet not to mention possible, though unknown risks, inflammation of the arm has certainly been produced by it on one or two occasions; and therefore it seems right, as the operation now stands, to confine transfusion to the first class of cases only, namely, those in which there seems to be no hope for the patient, unless blood can be thrown into the veins.

The object of the Gravitator is, to give help to this last extremity, by transmitting the blood in a regulated stream from one individual to another, with as little exposure as may be to air, cold, and inanimate surface; ordinary venesection being the only operation performed on the person who emits the blood; and the insertion of a small tube into the vein usually laid open in bleeding, being all the operation which it is necessary to execute on the person who receives it.

The following plate represents the whole apparatus connected for use and in action —
James Blundell

- Devised many transfusion instruments
- Blood transfused quickly would be successful with a syringe
- Discovered the importance of letting all the air out of a syringe prior to the transfusion
- Only 4 ounces will do!
Blood Transfusion 1980-1990

"...unquestionably the best Canadian book on the topic." - The Globe and Mail

THE GIFT
CONFRONTING CANADA'S
OF DEATH
TAINTED BLOOD TRAGEDY

ANDRÉ PICARD

WINNER OF THE CANADIAN SCIENCE WRITERS' ASSOCIATION SCIENCE IN SOCIETY JOURNALISM AWARD

Move to boost steps to battle HIV, help patients

A key focus will be on voluntary testing, to increase early detection.

By Jan Zanocius

HIV testing is still in its infancy, but the many people who have been tested have been reassured that the test is reliable. The test can be done in a few weeks and there is no waiting period.

Suspect blood: Red Cross faces scrutiny

Hepatitis C fears after suspect blood sent back into circulation

Blood disease victim welcomes inquiry

Campaigner hopes for answers over his brother’s death

Blood transfusion: The tragedy of tainted blood

Vic Parsons

BAD BLOOD

ORLA
Krever Inquiry

• Commissioned in 1993
• Published in 1997
• Guiding principles for managing a safe blood system:
  • Blood is a public resource
  • Donors should not be paid
  • Canada should have self-sufficiency in all blood and blood products
  • No part of the national blood operator’s duties should be contracted out to others
Transfusion – Current

- Highly regulated system in Canada
- CBS and HemaQuebec
- Evidence-based effective policies for donor selection, screening, product collection, testing and infusion
- Restrictive transfusion policies and effective blood conservation programs
- Blood coordinating networks
• Donor screening
• Sterilization and testing
• Production
• Storage
## Blood Safety – Donor Testing

<table>
<thead>
<tr>
<th>Implementation Date</th>
<th>Donor Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>1949</td>
<td>Syphilis Ab</td>
</tr>
<tr>
<td>1972</td>
<td>HBV HBsAg</td>
</tr>
<tr>
<td>1984</td>
<td>CMV Ab (selected units)</td>
</tr>
<tr>
<td>1985</td>
<td>HIV1/2 Ab</td>
</tr>
<tr>
<td>1990</td>
<td>HCV Ab</td>
</tr>
<tr>
<td>1990</td>
<td>HTLV 1</td>
</tr>
<tr>
<td>1998</td>
<td>HTLV1/2 Ab</td>
</tr>
<tr>
<td>1999</td>
<td>HCV NAT</td>
</tr>
<tr>
<td>2001</td>
<td>HIV NAT</td>
</tr>
<tr>
<td>2003</td>
<td>WNV NAT (seasonal 2015)</td>
</tr>
<tr>
<td>2010</td>
<td>HBV NAT</td>
</tr>
<tr>
<td>2010</td>
<td>Chagas (selective donor testing)</td>
</tr>
</tbody>
</table>
Autologous Donations – 1990s

• Use of perioperative autologous blood donation promoted in response to HIV epidemic in 1980s
Autologous Donations – Current

**Total Autologous Collections**

<table>
<thead>
<tr>
<th>Year</th>
<th># Units (Transfused)</th>
<th># Units (Discarded)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>2,050</td>
<td>2,379</td>
</tr>
<tr>
<td>2007</td>
<td>1,979</td>
<td>3,537</td>
</tr>
<tr>
<td>2008</td>
<td>1,222</td>
<td>1,501</td>
</tr>
<tr>
<td>2009</td>
<td>815</td>
<td>1,181</td>
</tr>
<tr>
<td>2010</td>
<td>668</td>
<td>1,030</td>
</tr>
<tr>
<td>2011</td>
<td>491</td>
<td>716</td>
</tr>
<tr>
<td>2012</td>
<td>208</td>
<td>432</td>
</tr>
<tr>
<td>2013</td>
<td>104</td>
<td>250</td>
</tr>
<tr>
<td>2014</td>
<td>148</td>
<td>152</td>
</tr>
<tr>
<td>2015</td>
<td>81</td>
<td>89</td>
</tr>
<tr>
<td>2016</td>
<td>87</td>
<td>68</td>
</tr>
</tbody>
</table>

*Figure 1: Total autologous collections (red cells) at Canadian Blood Services by year*
Autologous Donations – Future

- Risks of TACO, bacterial contamination
- Risk of receiving wrong unit
- Preoperative anemia
- Cost-effectiveness?
- 60-80% discard rate
- Patient time and health care resources
- Exceeding low risk of TT infection with allogeneic donation
- “No role for routine autologous donation except in rare cases” (Choosing Wisely Canada)
“To the extent that we have indeed learned the lessons from the tragedy of the 1980s and reform the system as recommended in this Report, the likelihood that the tragedy will happen again will be markedly reduced. When it does, the few members of our society to whom the risk accrues and to whom the harm results must be treated more compassionately than their predecessors were, and they must be given suitable compensation without the necessity of proving fault”
Father of Transfusion Medicine

• Karl Landsteiner (1868-1943)
• Credited for discovering ABO blood group in 1901 (groups A, B, O)
• Nobel prize in 1930

<table>
<thead>
<tr>
<th>Antigen (on RBC)</th>
<th>ABO Blood Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen A</td>
<td>Anti-B Antibody</td>
</tr>
<tr>
<td>Antigen B</td>
<td>Anti-A Antibody</td>
</tr>
<tr>
<td>Antigens A + B</td>
<td>Neither Antibody</td>
</tr>
<tr>
<td>Neither A or B</td>
<td>Both Antibodies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antibody (in plasma)</th>
<th>Type A</th>
<th>Type B</th>
<th>Type AB</th>
<th>Type O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-B Antibody</td>
<td>Cannot have B or AB blood</td>
<td>Cannot have A or AB blood</td>
<td>Can have any type of blood</td>
<td>Can only have O blood</td>
</tr>
<tr>
<td>Anti-A Antibody</td>
<td>Can have A or O blood</td>
<td>Can have B or O blood</td>
<td>Is the universal recipient</td>
<td>Is the universal donor</td>
</tr>
</tbody>
</table>
• Karl Landsteiner (1868-1943)
• Credited for discovering ABO blood group in 1901 (groups A, B, O)
• Nobel prize in 1930
ABO Testing - Current

• Tube agglutination
  • Gold standard – tried and true!
  • Easy
  • Inexpensive
• Gel/Column agglutination
  • Stable reactions
  • $$
  • Can be automated
• Liquid microplate
  • Inexpensive
  • Can be automated
Molecular Testing ABO: Future?

- Has ABO genotyping become a victim of its own ABO serology success?
- Traditional ABO testing is inexpensive
- Can be performed within 10 min, 24/7
- The principle of the test remains unchanged in the last 90 years
Discovery of RH – 1939

- Group O woman transfused with husband’s group O blood has severe reaction (Levine and Stetson)
- Her serum reacted with 80% group O RBC
- They suggested that the mother had been immunized by a fetal antigen of paternal origin
RH Testing – Current

• Tube – Gel – Microplate
• Monoclonal antisera (late 1990s)
• BUT! Rh is very complex

Diagram:

- No Rh antigen
- Rh antigen
- Rh -ve red blood cell
- Rh +ve red blood cell
- Rh antibody
RH Testing – Current

- 51 antigens, more than 200 alleles
- Partial D
- Weak D (Formerly D^u)
- How to handle pregnant women?
RH Testing – Current/Future

• Prenatal patients with discrepant, weak or inconclusive serological RhD test results should be further investigated with RHD genotyping to determine RhIg candidacy and optimal Rh type for transfusion

• This improvement in practice is unlikely to result in a significant cost increment in terms of RHD testing for the provinces since it is already an established practice in some provinces
RH: The Future is Now!

- Confirm D status by molecular testing
  - Distinguish partial D from weak D
- Fetal *RHD* Typing
  - Cell free fetal DNA (cffDNA)
Coombs Test

- Robin Coombs (1921-2006)
- Over coffee with colleagues Drs. Race and Mourant, incomplete Rh antibodies (1945)
- Further bridging of the antibody would agglutinate the cells
Antibody Screen/Identification

- Shortly after the Coombs test (direct and indirect) was adopted world-wide
- Immediate spin: IgM antibodies
- 37C incubation: IgG complete antibodies
- Wash x4: remove unbound proteins
- AHG: IgG antibodies
- Auto control: auto antibodies
Antibody Screen/Identification: Current

- Most performed by “novel” methods
- Gel or Solid Phase
- Enhancement media
- Peg or LISS
- No longer perform IS or 37C reading
- Don’t look for something you don’t care about!
- No auto control
Immunoglobulin Crossmatch

• To provide blood that is fully compatible with the patient’s plasma
• Immediate spin: IgM antibodies (ABO)
• 37°C incubation: IgG complete antibodies
• Wash x4: remove unbound proteins
• AHG: IgG antibodies
Crossmatching – Current

• Immediate Spin Crossmatch
  • Patient plasma + donor RBC
  • Confirms ABO compatibility
• Electronic/Computer Crossmatch
  • Negative antibody screen
  • Confirm ABO on donor units
  • Computer validated
• Two ABO records on patient
Blood Prejudice WWII

• U.S Army and Navy would only accept blood from white donors

• Scientific studies had proven no racial differences existed in the chemical makeup of blood

• “For reasons not biologically convincing but which are commonly recognized as psychologically important in America, it is not deemed advisable to collect and mix caucasian and [N]egro blood indiscriminately”
Dr. Charles Richard Drew

• Blood storage and preservation
• Established first American Red Cross, Bloodmobiles
• Resigned in 1942: African American donations would be accepted but would have to be stored separately from that of white donors
• American Red Cross stopped segregation of blood in 1950
Blood Prejudice 1960s - 1970s

- Some southern states such as Arkansas and Louisiana continued blood segregation
- Blood prejudice in pop culture
Alloimmunization is common in sickle cell disease patients.
Recipient phenotyping and prophylactic matching reduces alloimmunization.
Use of Rh neg units to match recipients that are D+C-E- (Ror)
O Negative Red Cells to Non-O Negative Sickle Patients

<table>
<thead>
<tr>
<th>Year</th>
<th># Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td></td>
</tr>
</tbody>
</table>
Who can participate?

You can take part in the program if you meet the following criteria:

- You are a Black woman;
- You meet Héma-Québec’s eligibility criteria for giving blood.

Why participate?

To help optimize the collective blood supply. You will be helping people who have genetic characteristics similar to yours and who regularly need blood transfusions.

Sickle Cell Disease Program

Volunteer donors help people affected by Sickle Cell Disease. Sickle Cell is an inherited blood disorder that affects more than 50,000 people in the U.S., 98 percent of whom are African American. People with sickle cell disease may need frequent blood transfusions throughout their lives and other African-Americans can often provide blood which may more closely match the blood of these patients in need. While African-Americans represent 12 to 14 percent of the total U.S. population, only about 1 percent of the African-American community donates blood.

Under the program, blood donors who identify themselves as being African-American or Black, can have a “blue tag” attached to their blood collection bag. This indicates that the donated unit of blood may be matched to a patient with sickle cell disease. If a patient with sickle cell disease does not need the blood within 21 days, or if there is not a match, the donated blood will be available for any patient in need.

- Learn more about Sickle Cell Disease
- The Importance of African-American Blood Donors

Blue Tie Tag blood donations are accepted at all Red Cross blood drives and centers as well as at specific Blue Tie Tag blood drives in the Bay Area. Businesses, schools, churches, social or community groups interested in sponsoring a Blue Tie Tag blood drive, are encouraged to call 1-800-RED CROSS.
Full Speed Ahead!

- Molecular and more molecular!
- Stem cell therapies
- Blood substitutes and replacements
Thank you!

MY BLOOD TYPE

IS BE NEGATIVE