Review of current alternatives to Blood Products

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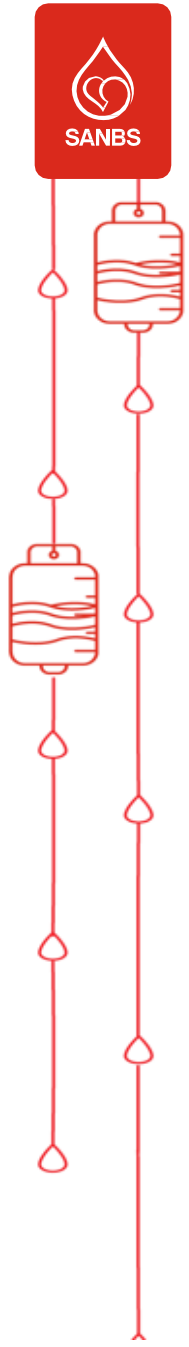
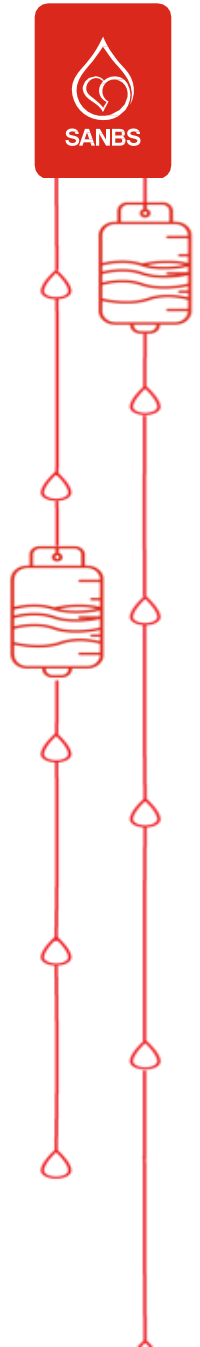
GPEXPO- Sandton Convention Center

Objectives

- Understand the history of blood
- Describe the reviewed literature on blood alternatives
- Describe the future outlook

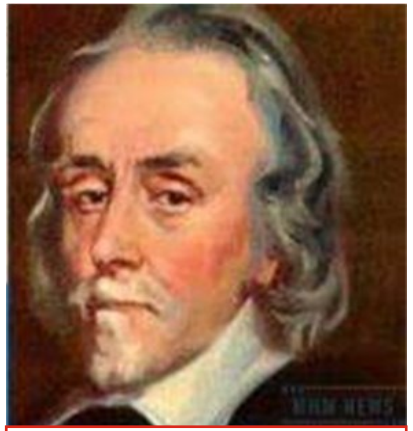


The history of blood



History of blood transfusion

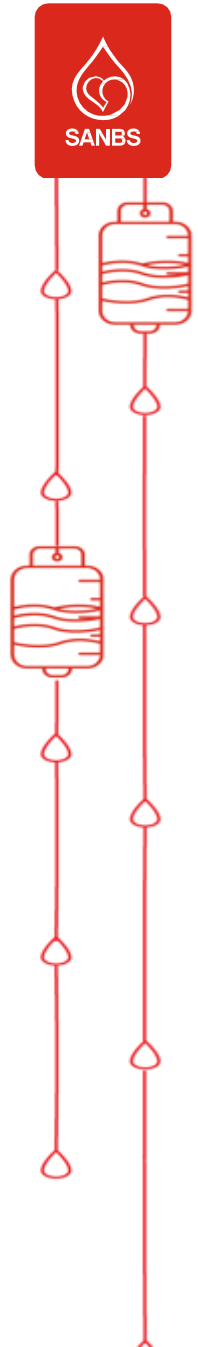
1492: Pope Innocent VIII Infused with / drank the blood of 3 Jewish boys.



Dr. William Harvey "De motu Cordis" **1628:**The correct description of blood circulation

Anthea Jeffrey; From Myths to Modernity- The Story of Blood Transfusion in South Africa; 2012

Alternatives to Blood



Definition of Alternatives

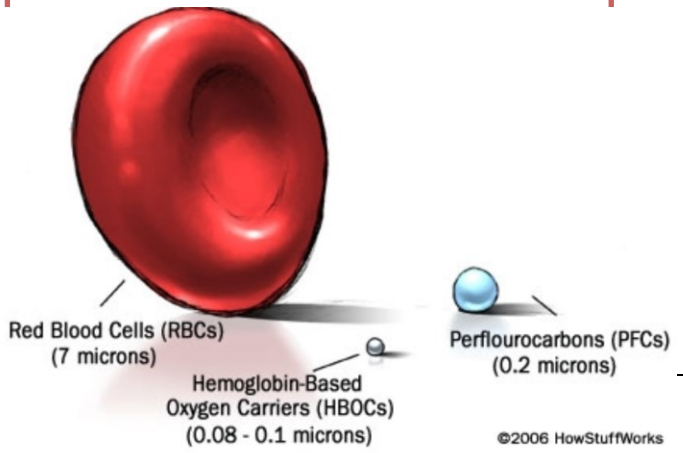
- **Alternatives are A.K.A. "blood substitutes" or "artificial blood".**

- Any product that may be used to **stimulate production**, **fulfil or mimic the function** or **replace**, the contents of biological blood in part or fully.
- Alternatives to red blood cells, plasma, and platelets, using the 3 headings below:

Red blood cells	Plasma	Platelets
• Stimulate production • Fulfil or Mimic fxn • Replace	• Fulfil • Mimic • Replace	• Stimulate production • Mimic the function of allogeneic platelets

A. Red blood cells substitutes

a. Stimulate	b. Fulfil/mimic	c. Replace
• Erythropoietin • Iron replacement	• Haemglobin based Oxygen carriers(HBOC) • Perfluorocarbon (PFC)	



Both HBOCs and PFCs are considerably smaller than red blood cells. [1]

A. Red blood cells substitutes

a. Stimulate

- **The recombinant human erythropoietin (rHuEPO)** drugs are called Erythropoiesis Stimulating Agents (ESA)
- Eprex® (Epoetin alpha) and Recormon® (EPO Beta)

- Used for patients with end-stage renal failure and anaemia
- Poor patient outcomes Food and Drug Administration (FDA)" black box warning"

A. Red blood cells substitutes

a. Stimulate

- **Iron replacement**

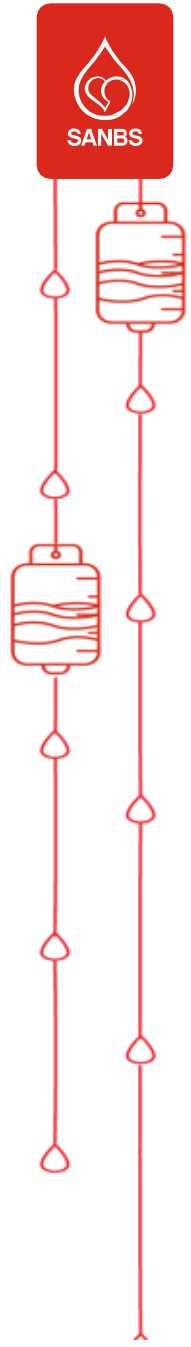
i. WHO policy brief:

- 1.95- 2,36 billion people living with anaemia, of which 1.2 -1.46 billion are iron deficient
- Global health problem.

ii. Patient Blood Management (PBM)

A. Red blood cells substitutes

b. Fulfil/Mimic	Developed over four (4) decades ago, with 1st trial in 1978	Hemopure
• **Haemoglobin-based Oxygen Carriers (HBOC)** • Hemopure® (bovine), Hemospan® (human), and Polyheme® (human)	• Early HBOC faced challenges related to their short half-life, vasoconstriction, and oxidative toxicity (Hb used for HBOCs is no longer inside red blood cells) • Clinical trials abandoned prematurely • Newer generation are bovine- & human-derived	

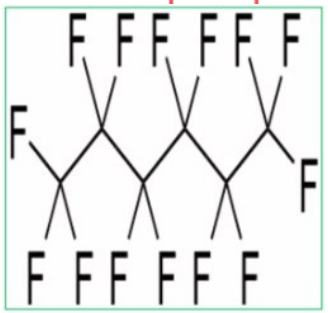


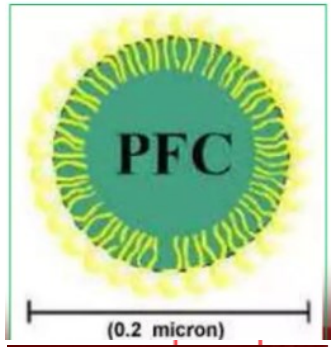
A. Red blood cells substitutes

b. Fulfil/Mimic

- **Perfluorocarbons (PFC) emulsion**

- High gas-carrying capacity and can dissolve large amounts of oxygen, offering potential as oxygen carriers
- However, unable to deliver large quantities of oxygen (30% of WB)





A. Red blood cells substitutes

c. Replacement product or technology

- **Autologous:**
- The collection, storage, and re-infusion of patients' own blood

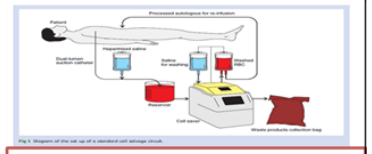
- Indications:
- 1) patients with rare blood groups or multiple blood group antibodies where compatible allogeneic (donor) blood is difficult to obtain;
- 2) at serious psychiatric risk because of anxiety about exposure to donor blood

- 3) who refuse to consent to donor blood transfusion but will accept pre-deposit autologous donation (PAD)
- 4) in children undergoing scoliosis surgery (in practice, most specialist units now use other blood conservation measures)

c. Replacement product or technology

- **Intraoperative Cell salvage (ICS)**

- Defined as the method of harvesting red cells during surgery for later reinfusion as autologous T/F (during /post surgery.)



- Indication: estimated blood loss >500ml where allogeneic T/F nor preferred.
- Three phases involved in cell salvage:
  - collection,
  - washing, and
  - re-infusion.

c. Replacement product or technology

- **Acute Normovolaemic dilution (ANH)**

- Used since the 60's
- Aim: to reduce or even avoid the need for perioperative transfusion of allogeneic blood.

- How it works?
- withdraw a percentage blood volume from the patient and simultaneous infusion of acellular fluids in order to maintain the volume.
- At end of surgery, then replace with fresh autologous blood.

B. Plasma substitutes

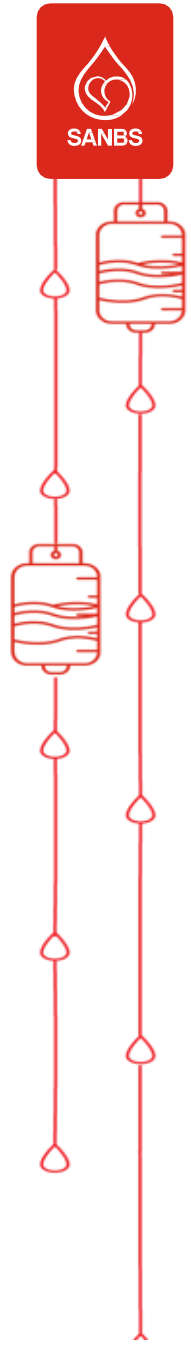
Stimulate

- **Coagulation factor concentrates**
- produced from **donated plasma and used as alternatives to plasma components for specific conditions.**

Recombinant coagulation factor concentrates:

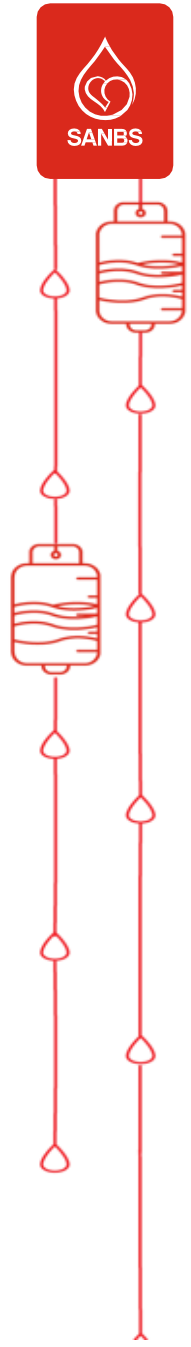
- Factor VIII, and IX used in haemophilia A and B
- Factor VIIa in congenital factor VII deficiency

Human-derived factor/factor complex concentrates:

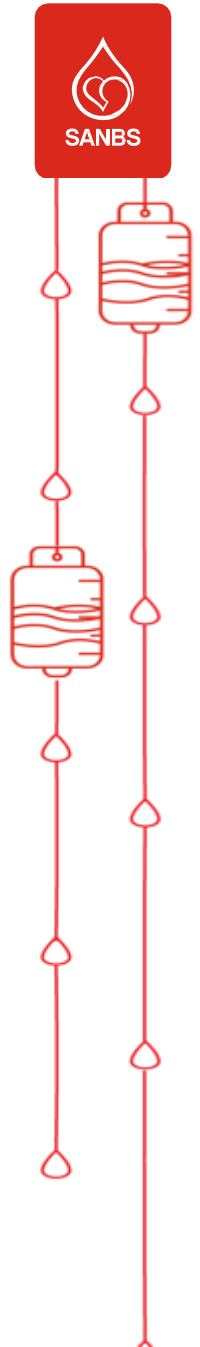


B. Platelet substitutes

a. Stimulate	b. Fulfil/mimic	c. Replace
• Endogenous platelet production drugs called (**thrombopoietin mimetic,or thrombopoietin-receptor agonists):** • E.g. eltrombopag and Amgen Megakaryopoiesis Protein 531 (AMG531), **stimulate megakaryocyte division in the bone marrow ↑Platelet counts**		

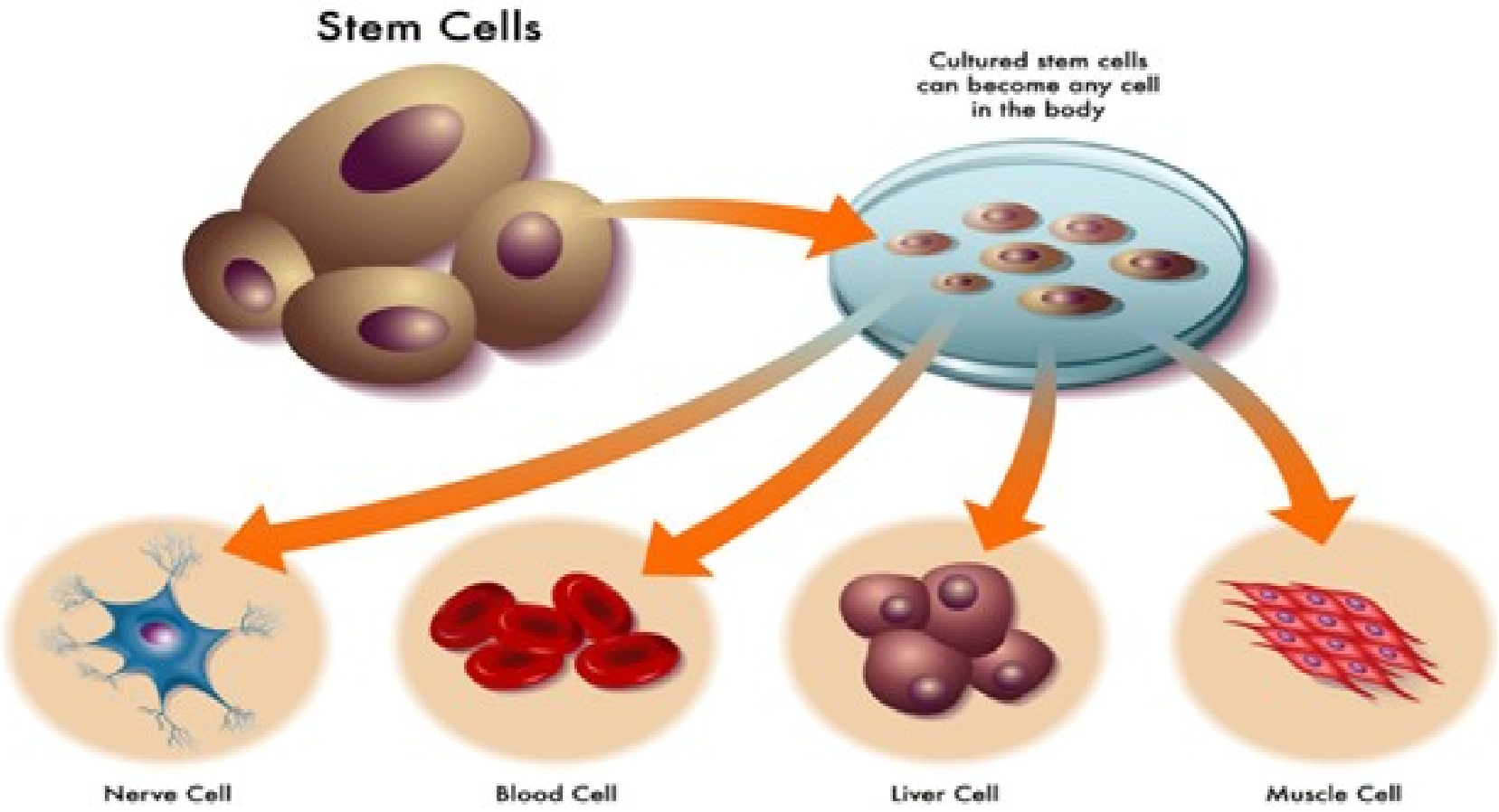


Future outlook



Stem cells

- Techniques to reprogram adult cells, such as skin cells, into induced pluripotent stem cells, which have the potential to differentiate into various cell types, including blood cells.



https://bioinformant.com/allogeneic-versus-autologous/

Artificially produced/grown red cells

History and clinical trials of Induced Pluripotent Stem Cells (iPSCs):

- **The limitation** is the **higher costs** to manufacture the cells as compared to donated allogeneic blood.
- England's National Health Service (NHS), to produce a unit from stem cells costs **over 200 times more than the cost of a standard unit of a red cell concentrate.**
- More studies are needed using larger quantities of blood to assess the safety and effectiveness of the laboratory-grown red cells

2017: Consortium

allogeneic transfused , then 6 months later manufactured rbc.

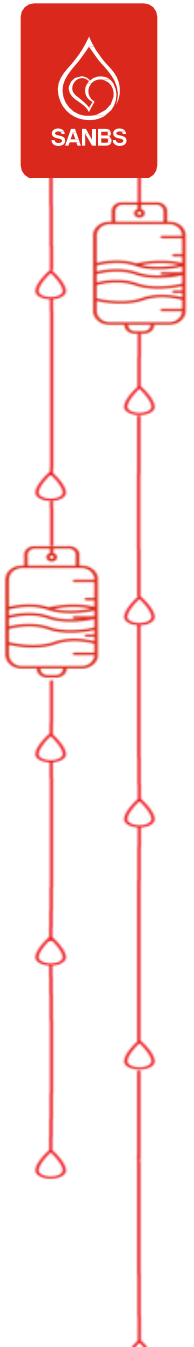
Conclusion

No true alternatives to blood and blood products that could replace allogeneic blood donation in the near future.

- Current methods to reduce allogeneic blood transfusion:
  - Patient blood management principles
  - Technology to replace – ANH,Cell salvage
  - Drugs to stimulate the production(RBC & Platelets)

- Future directions include the use of :
  - Stem cells and artificially grown red cells
  - Synthetic biology, nanotechnology, and bioengineering →gene editing

- Research in blood substitutes needs to address the limitations of previous approaches.



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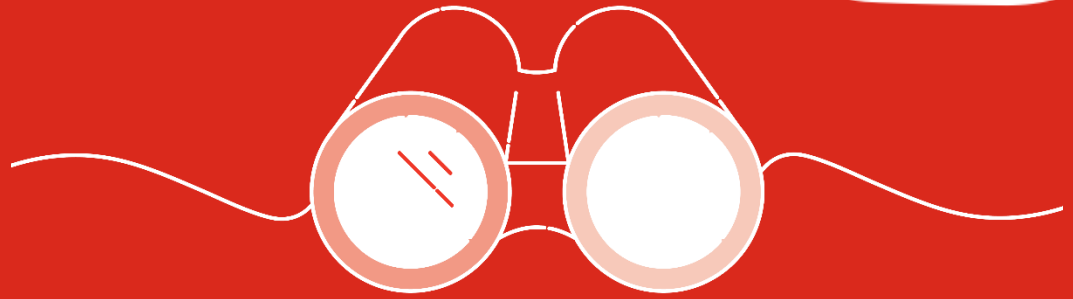
Thank you



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