Blood products and the patients who need them: A biologics manufacturer's perspective

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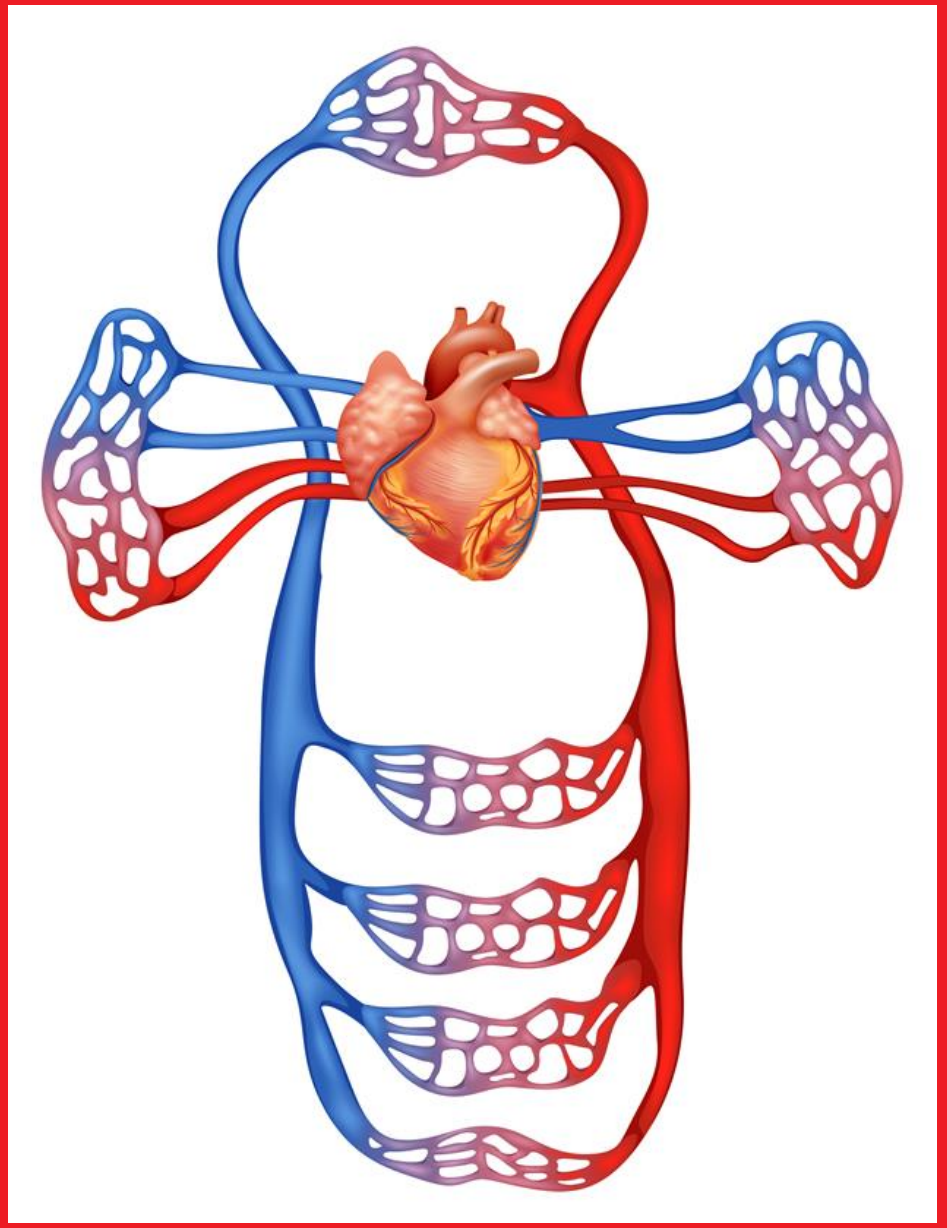
Canadian Blood Services
BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

Presentation objectives

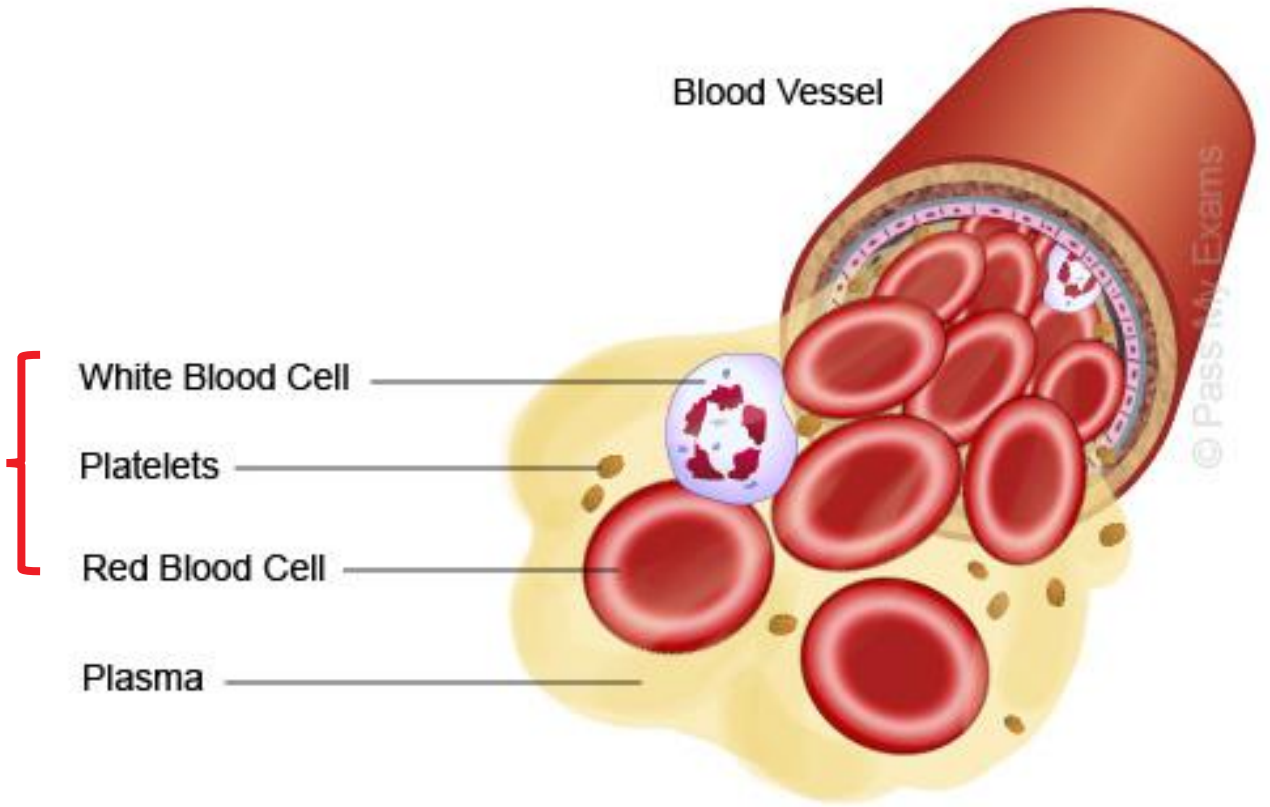
Provide an overview of blood products supplied by Canadian Blood Services, how they are manufactured and how they help patients.

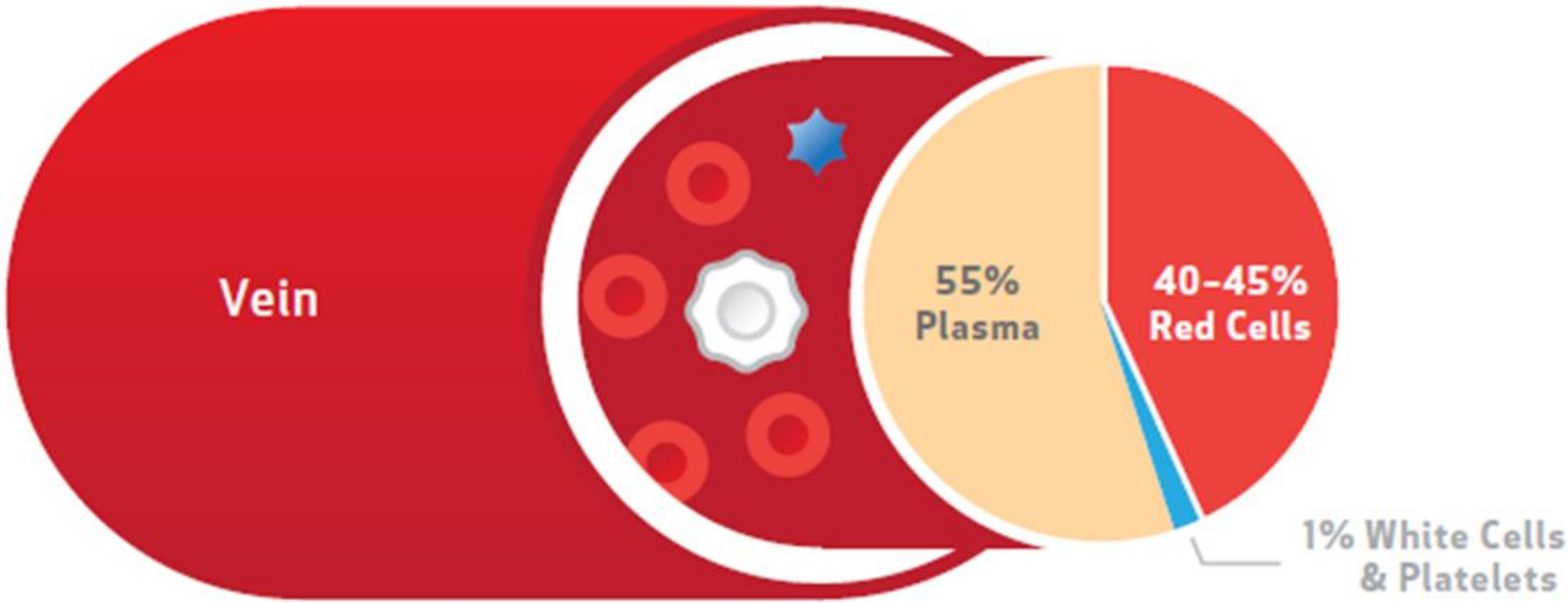
Blood overview



There are 3 types of cells in our blood.

Transported by plasma.




Vein
55%
Plasma
40-45%
Red Cells
1% White Cells
& Platelets

Blood products manufactured from blood

Red blood cells

Plasma

Platelets

Blood stem cells

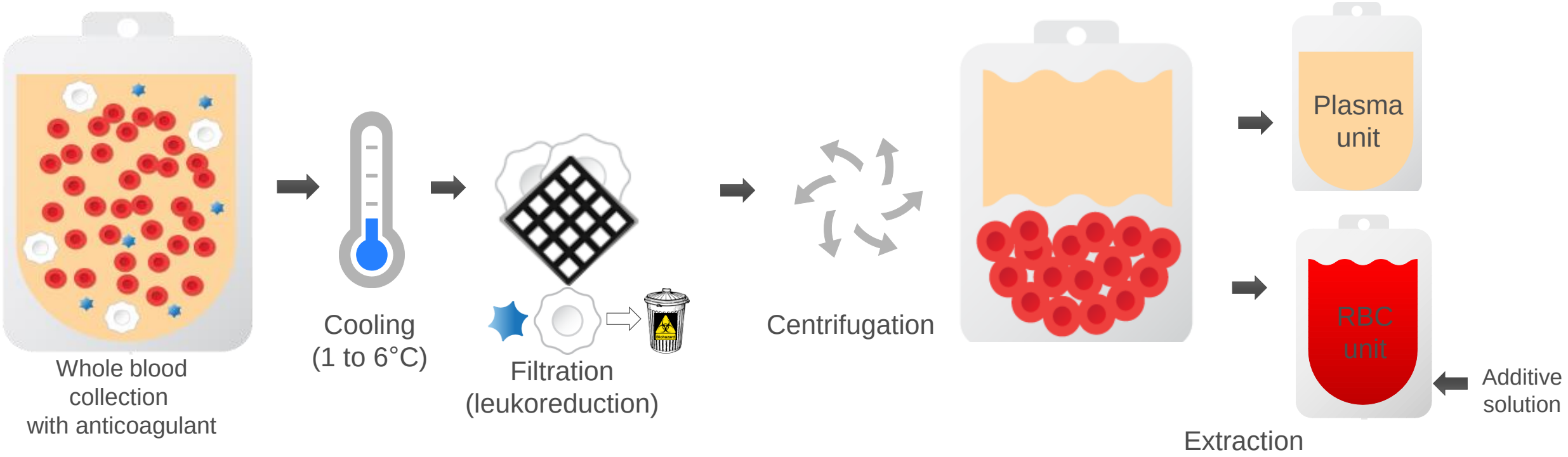
Plasma protein products

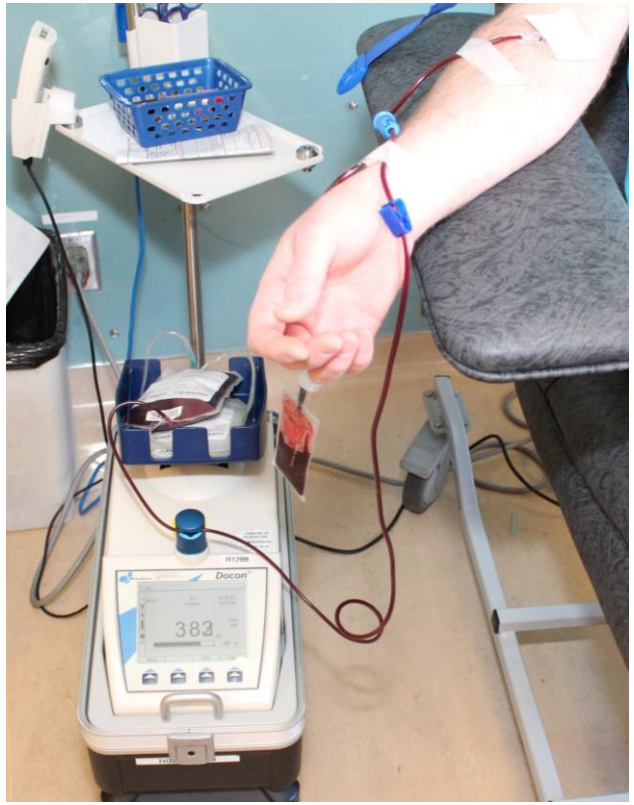
Blood collection

Donor screening: all prospective donors are screened using a questionnaire to ensure donor health and product safety

Donor testing: Canadian Blood Services tests every donation for known pathogens to prevent transfusion-transmitted infectious diseases (HIV I and II, hepatitis B and hepatitis C, human T-lymphotropic viruses I and II, and syphilis)

Manufacturing blood products: Whole blood (B2) method



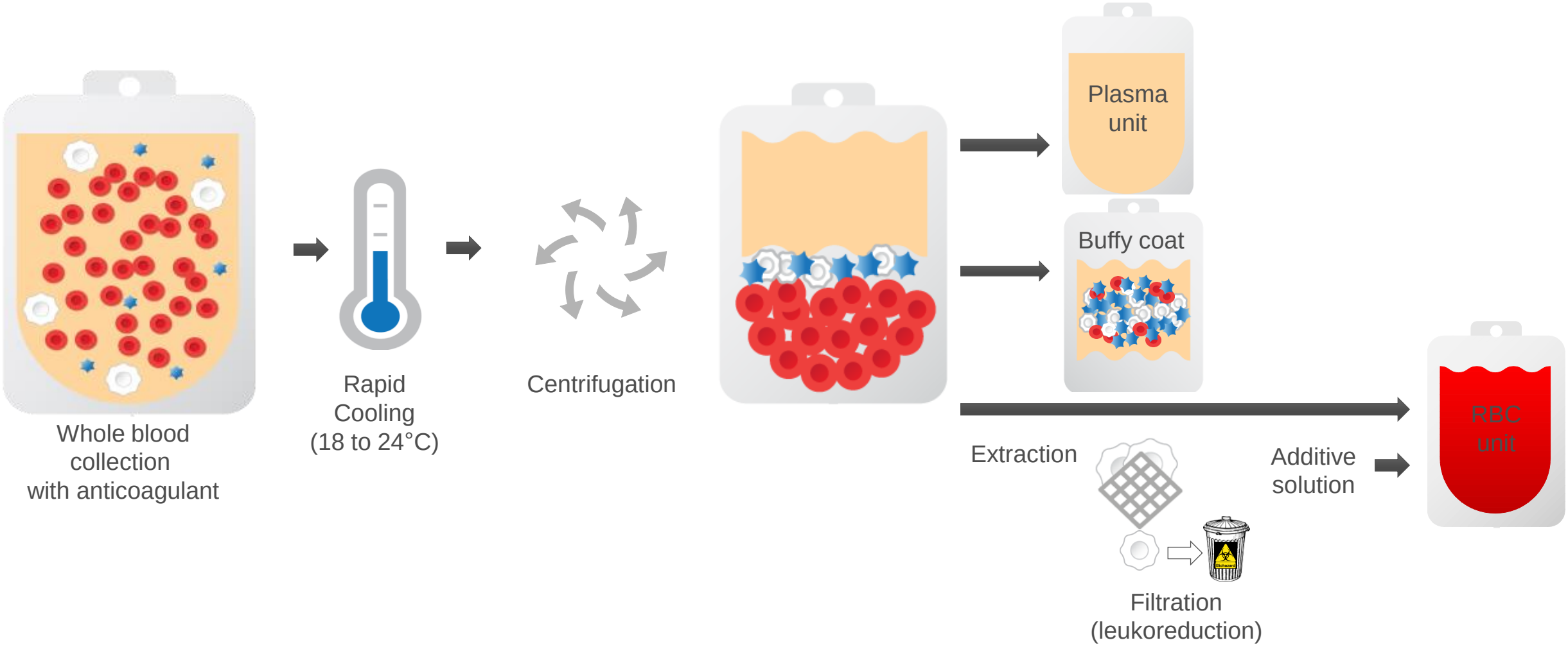


Whole blood
Collection
with anticoagulant

Filtration
(leukoreduction)

Extraction

Manufacturing blood products: Buffy coat (B1) method



Manufacturing platelets

Buffy coat (B1) manufacturing process

Donor 1

Plasma unit

Buffy coat

Donor 1

Buffy coat

Donor 2

Buffy coat

Donor 3

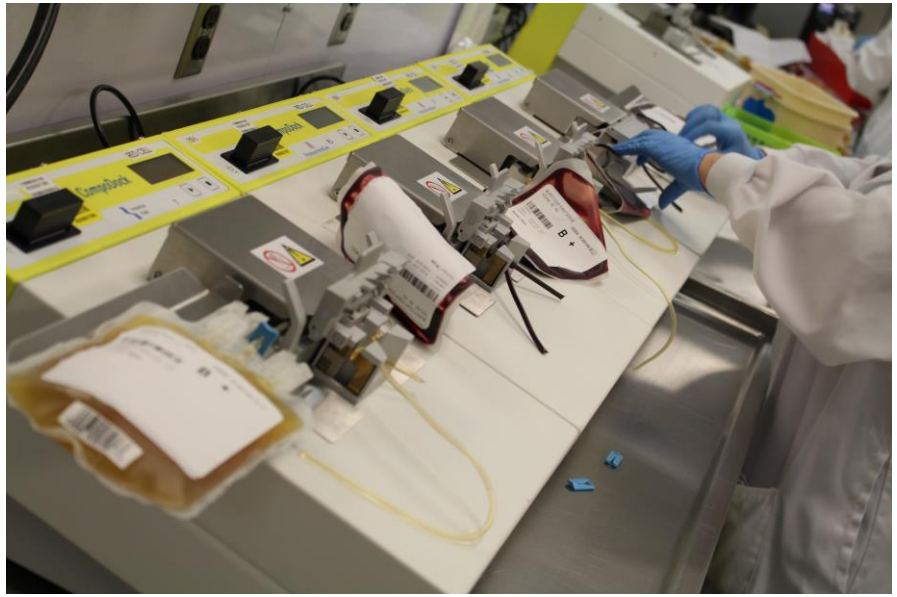
Buffy coat

Donor 4

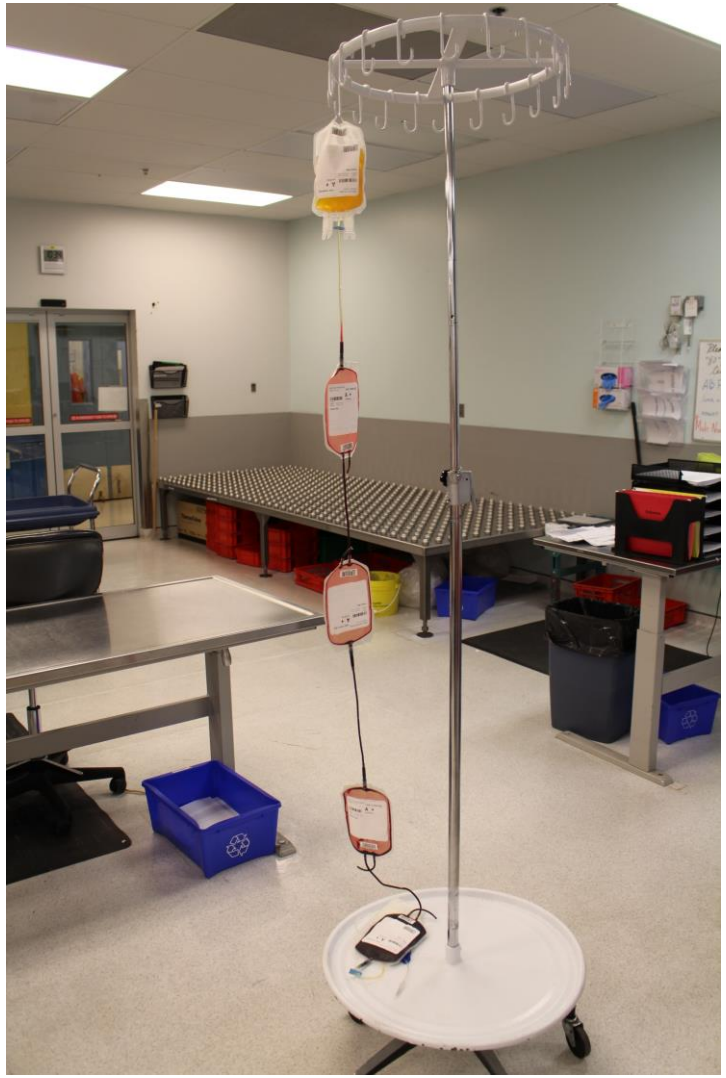
Pooled platelets unit

Apheresis Process

Apheresis platelets unit

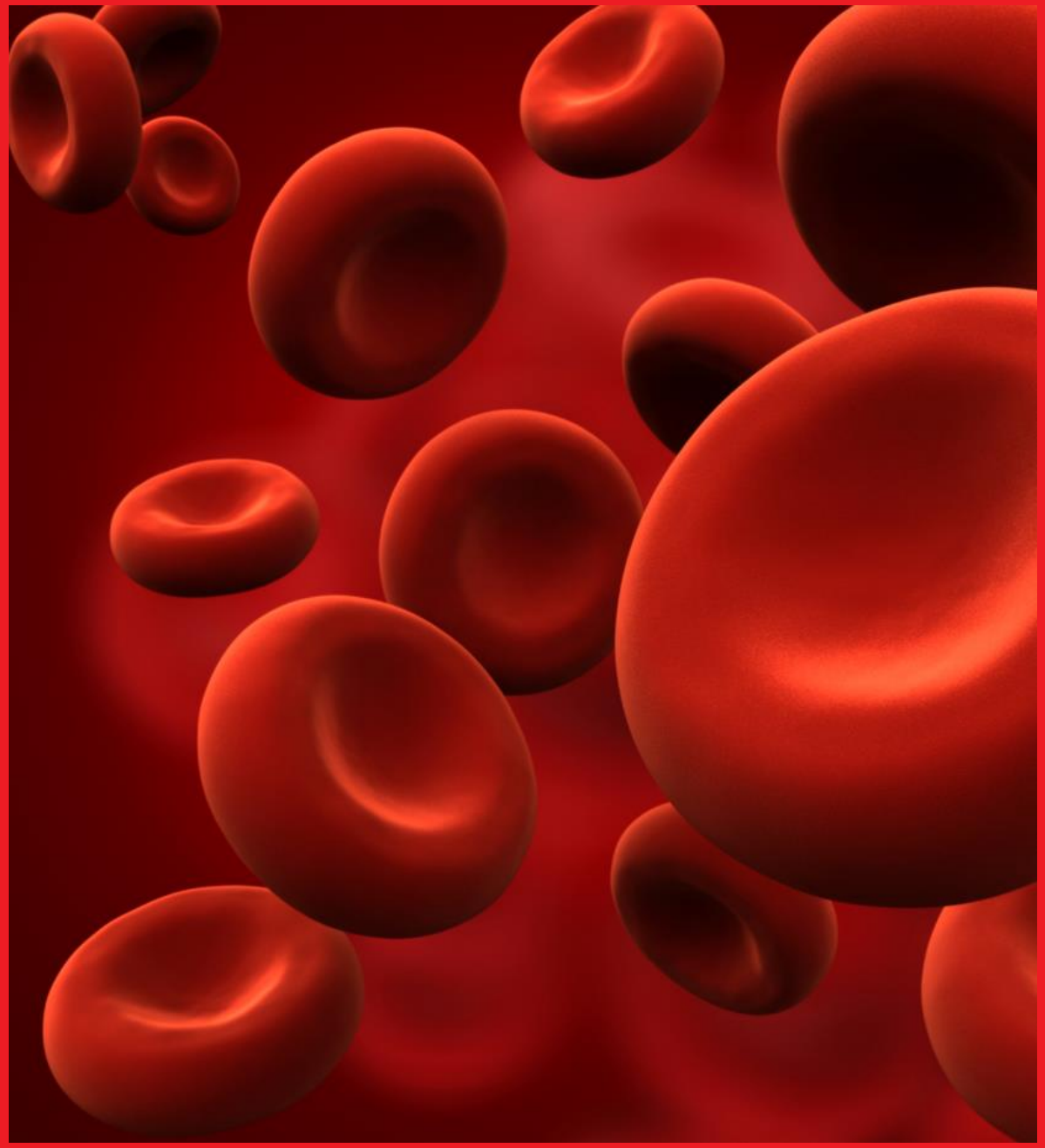


Sealing the plasma and buffy coat bags together



Pooling of buffy coats and plasma

Red blood cells

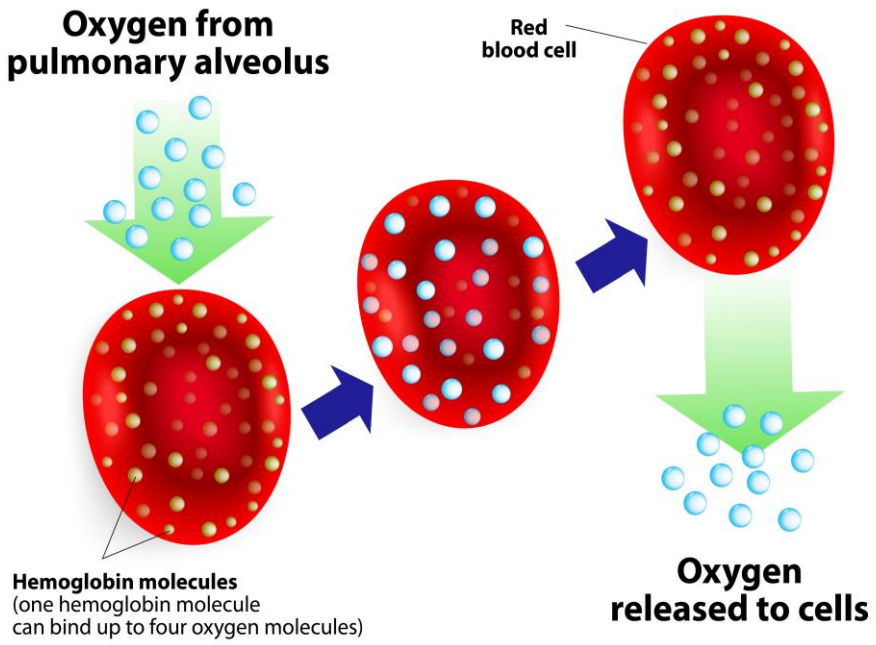


Basic facts

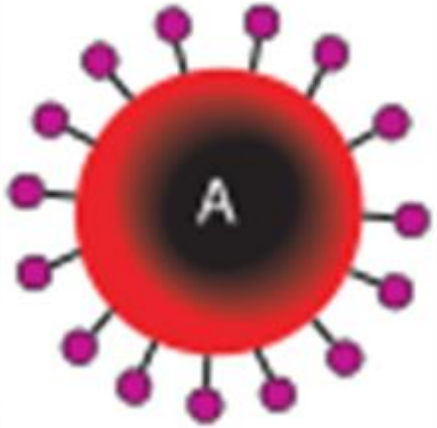
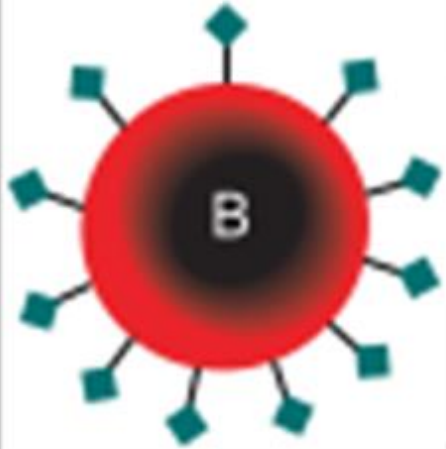
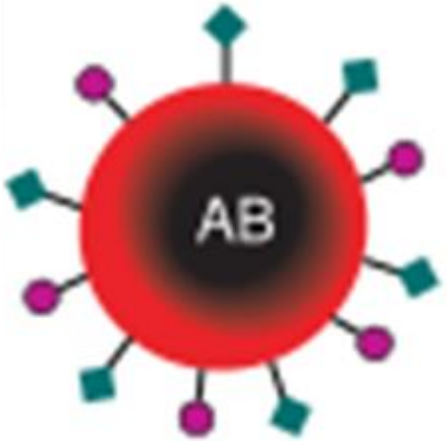
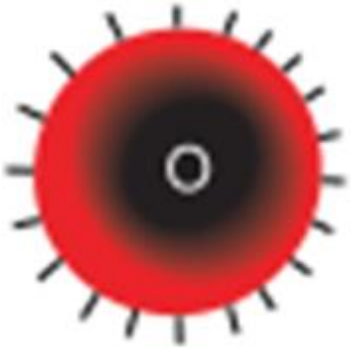
Red blood cells use their hemoglobin to carry oxygen from the lungs to the rest of the body and return carbon dioxide to the lungs.

When red blood cells are damaged and their content is released into the blood, we say the blood is hemolysed.

Red blood cells that are damaged can no longer carry oxygen and the released cellular content is toxic to the body.



All red blood cells are not the same

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies present	 Anti-B	 Anti-A	None	 Anti-A and Anti-B

Red blood cell unit

Prevent red blood cell damage, maximize product quality and ensure patient safety:

- ✓ Handle with care
- ✓ Prevent clotting
- ✓ Provide nutrients and preservatives
- ✓ Store the product at 1-6°C for a maximum of 42 days
- ✓ Test and label the product correctly

Tess*

Tess has leukemia, a cancer of the blood cells.

Doctors are transfusing Tess with red blood cells because she can not make her own during her chemotherapy.

Tess may receive up to 20 red blood cell units during the course of her treatment.

Tess relies on the units to be identified properly or she may develop dangerous transfusion reactions.

**Patient cases are hypothetical cases based on current transfusion practice.*

Jane

Jane was critically injured in a car accident and is losing a lot of blood.

Jane was transfused with red blood cell units immediately on arrival in the emergency department and then went straight to the operating room.

During this time, Jane was transfused with 10 red blood cell units.

Because time was an issue, the units were not cross-matched and Jane received universal blood or O-neg.

Plasma and plasma proteins

Water

Sugar

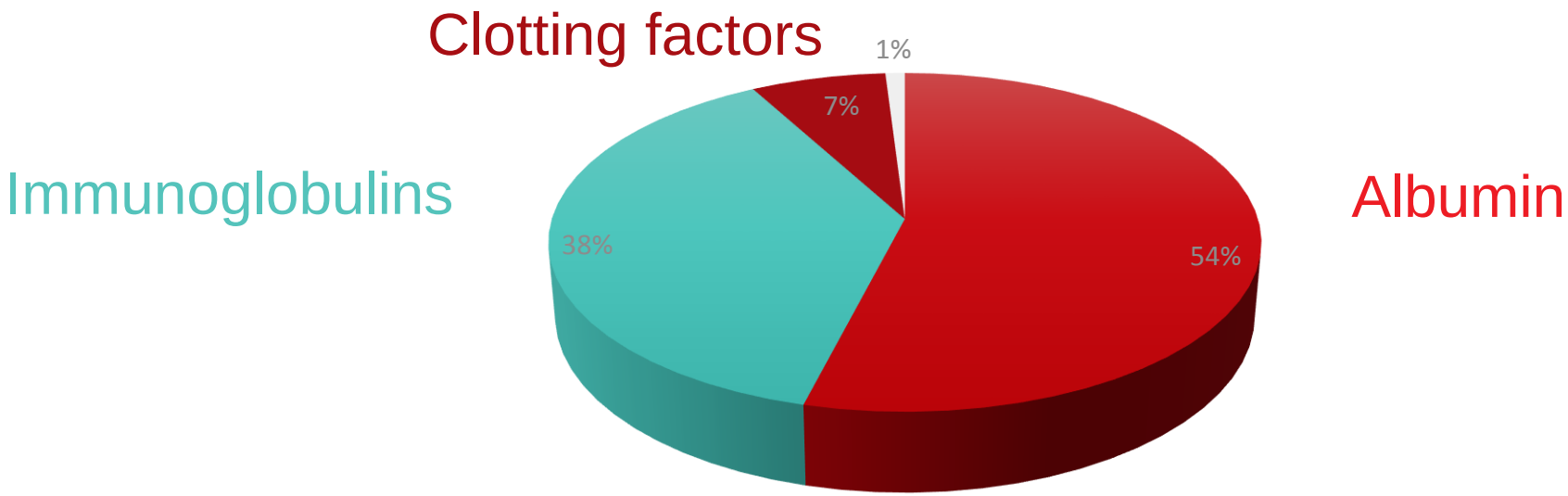
Proteins

Minerals

Vitamins

Hormones

Three main types of plasma proteins



Proportion of proteins in plasma

Albumin

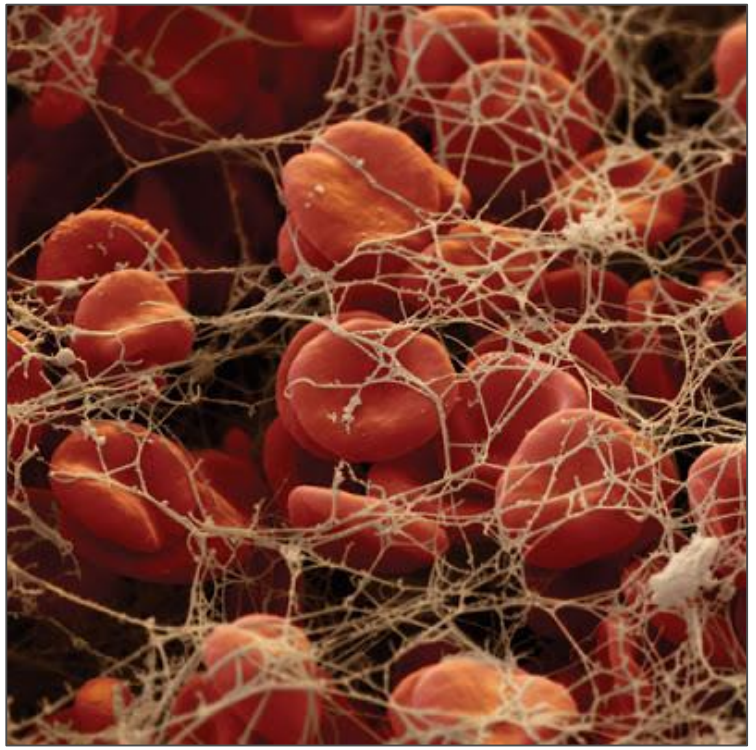
- ✓Keeps proper balance of fluids in the body.
- ✓Carries minerals, hormones and other substances through the blood.
- ✓Transfused to help restore fluid balance in critically ill patients, for instance those with burns.

Immunoglobulin or antibodies

- ✓Produced by white blood cells.
- ✓Part of the immune system and help us fight diseases.
- ✓The most common type of immunoglobulin is Immunoglobulin G or IgG.

Clotting factors

- ✓Include fibrinogen, factors II, V, VII, VIII, IX, X, XI, XII, and XIII.
- ✓Interact in complex ways to convert fibrinogen to fibrin, the meshwork in a blood clot.



Manufacturing plasma

Whole blood (B2) manufacturing process

Buffy coat (B1) manufacturing process

Apheresis process

Plasma unit

Freezing

Store below -18°C for up to 12 months

Manufacturing plasma protein products

Plasma is used directly for transfusions into patients.

Plasma can also be further manufactured into specialized and purified proteins (a.k.a. plasma protein products).

This process is called fractionation.

Fractionation

Plasma protein products

Plasma fractionation

¾ of Canadian Blood Services plasma goes to fractionation.

The fractionation process is performed outside of Canadian Blood Services.

The fractionation process is used to make plasma protein products including IgG and albumin.

GRIFOLS

CSL Behring
Biotherapies for Life™

Jane

Jane was critically injured in a car accident and is losing a lot of blood.

Doctors have transfused red blood cells.

Doctors are also transfusing plasma to replace the coagulation factors Jane has lost and to help her to stop bleeding.

Victoria

Victoria was born with an immune disorder where her body does not make enough antibodies. Victoria is vulnerable to infections.

Victoria receives IVIG (intravenous immunoglobulin G) every four weeks to reduce her risk of infections.

She must take it for the rest of her life.

Brian

Brian was born with a clotting disorder known as hemophilia A. He is missing clotting Factor VIII.

Without Factor VIII, Brian is susceptible to repeated bleedings, or hemorrhages.

Brian is treated by replacing the missing Factor VIII three to four times a week.

Nowadays, most of the Factor VIII Brian receives is called recombinant factor VIII. It is made in the laboratory; it is no longer manufactured from donor plasma.

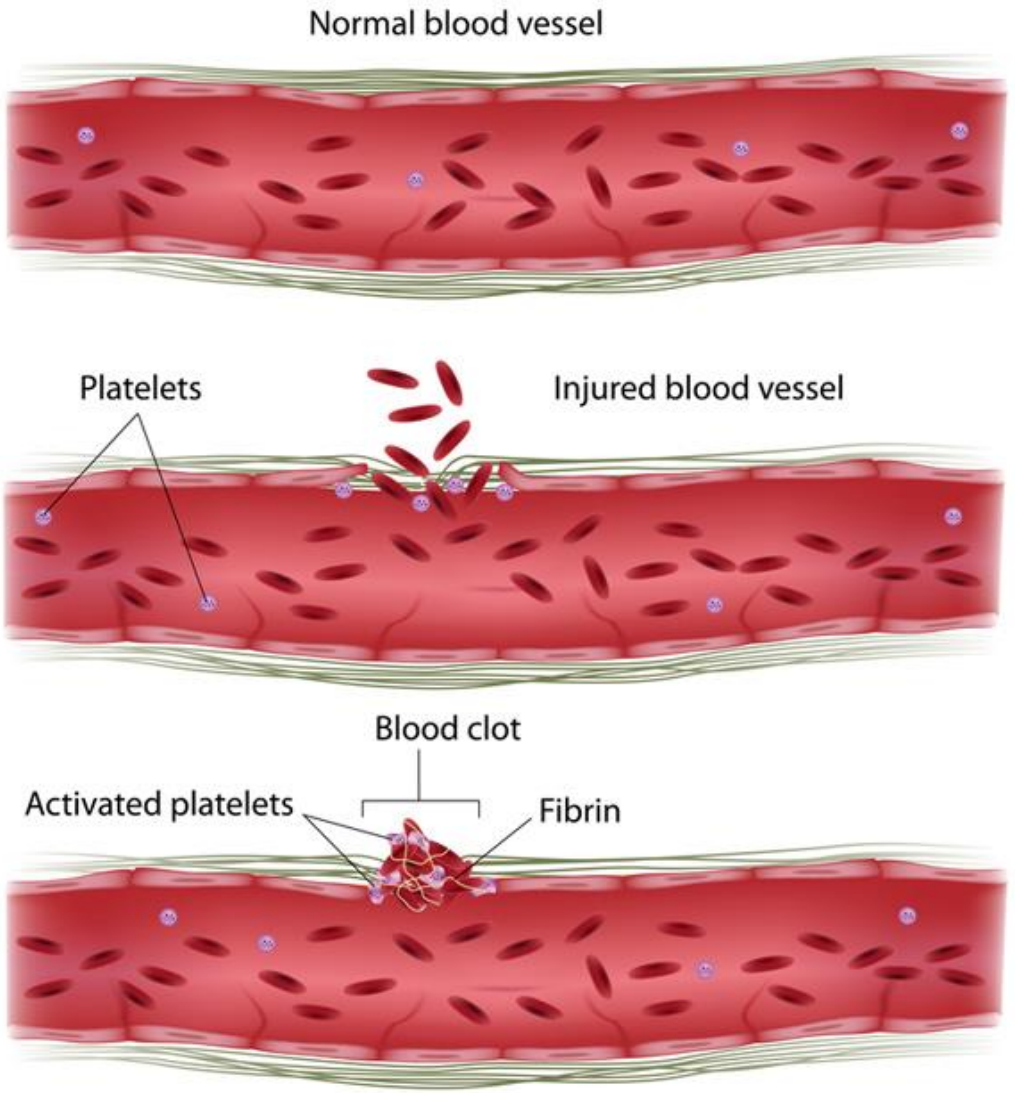
Platelets

Plug formation

When damage to the wall of a blood vessel is detected, platelets are “activated”.

Activated platelets become sticky and develop long thread-like structures that extend and make contact with the torn vessel or other platelets.

Activated platelets clump together and secrete proteins required to create a firm seal.



Platelets for transfusion

Prevent aggregation to maintain product effectiveness:

- ✓ Store in gas permeable' bag to provide oxygen and remove carbon dioxide
- ✓ with continuous gentle agitation to keep platelets apart and facilitate gas exchange
- ✓ at room temperature for a maximum of 7 days

Bacterial contamination

Unfortunately, this storage environment is favorable to the growth of bacteria.

Transfused to a patient, platelets containing bacteria can have terrible consequences.

To mitigate this risk, the arm of the donor is disinfected (a.k.a. arm scrub) and the first few mL of the blood collection are diverted (a.k.a. diversion pouch). Platelet units are also tested for bacterial contamination.

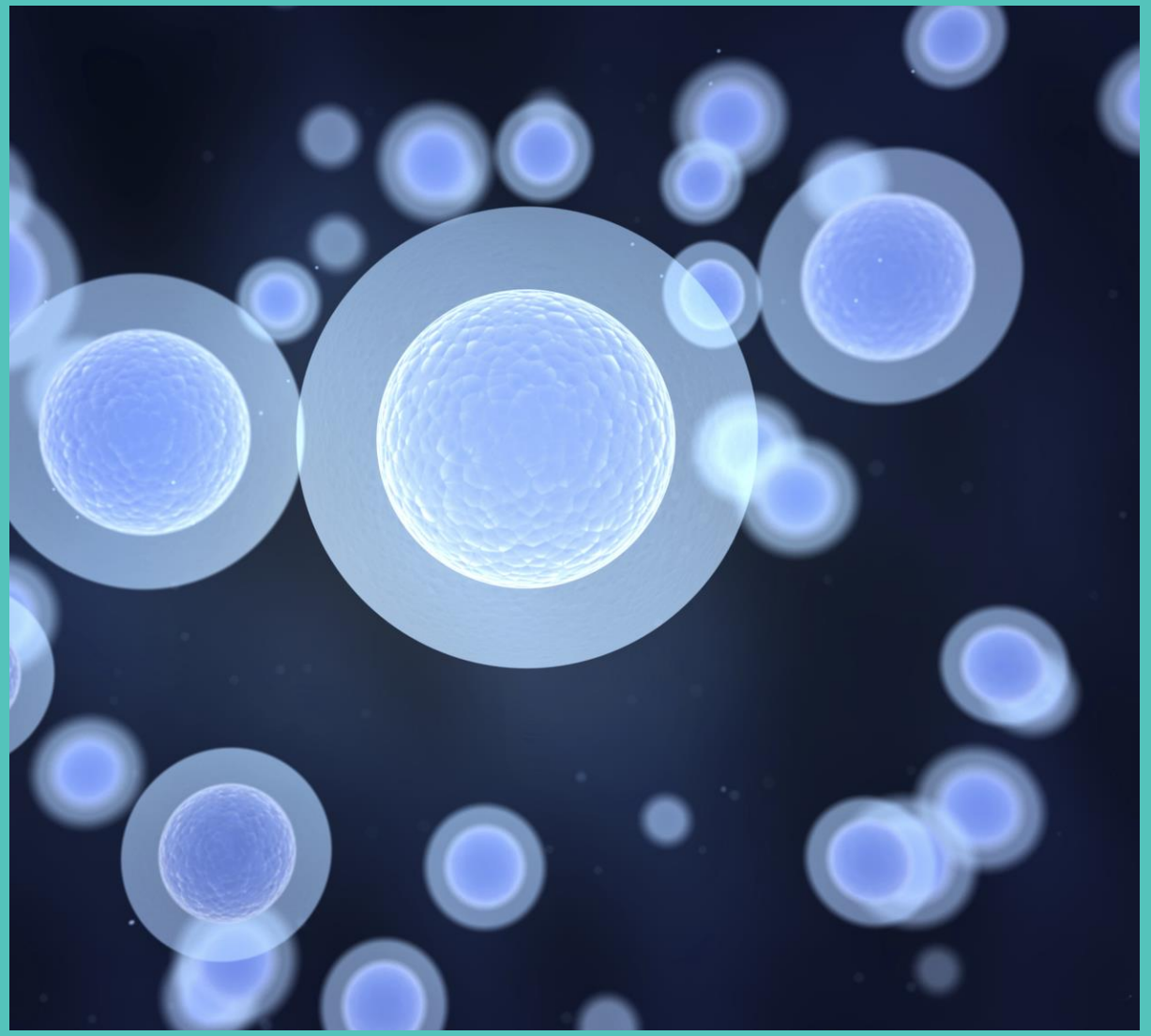
Jane

Jane was critically injured in a car accident and is losing a lot of blood.

Doctors have transfused red blood cells to treat her low red blood cell level and plasma to restore her coagulation factors.

Doctors also transfused platelets to help her body form coagulation plugs that will stop her bleeding together with the coagulation factors.

Blood stem cells

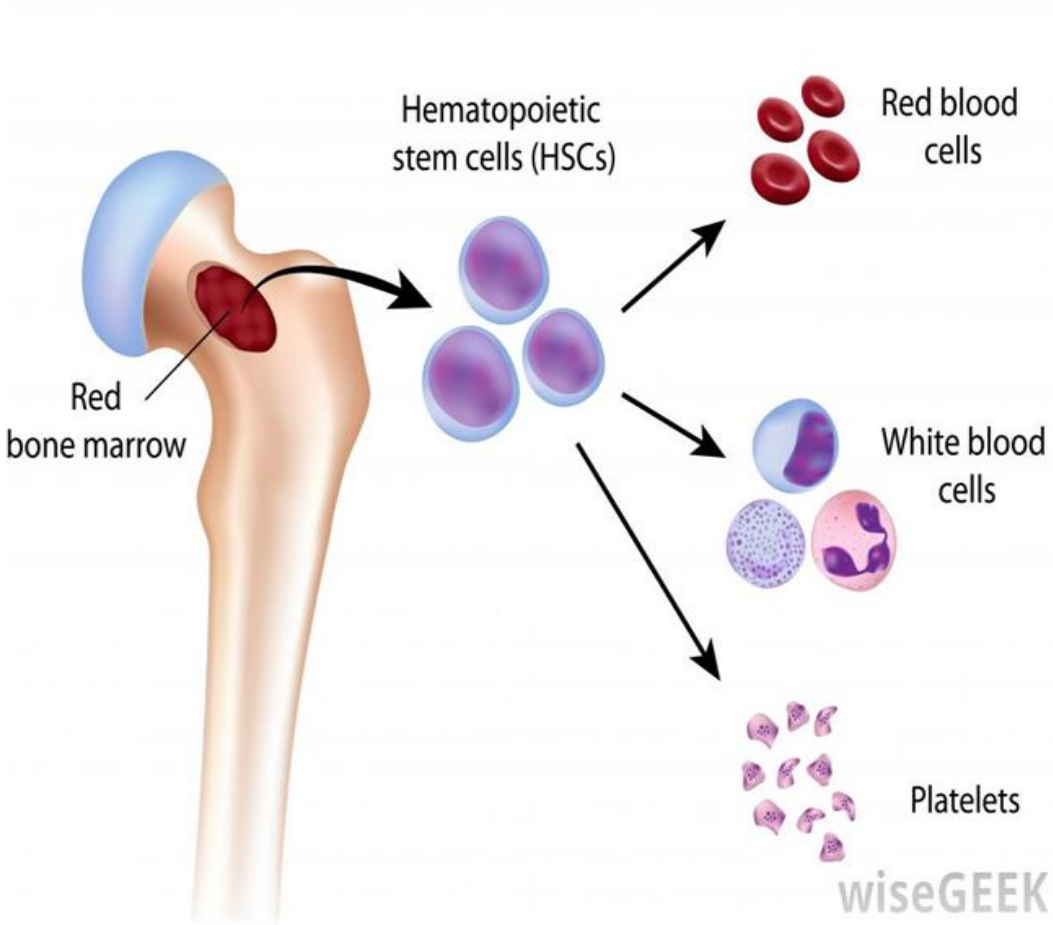


Basic facts

Blood stem cells reside in the bone marrow of long bones.

Like all stem cells, blood stem cells can :

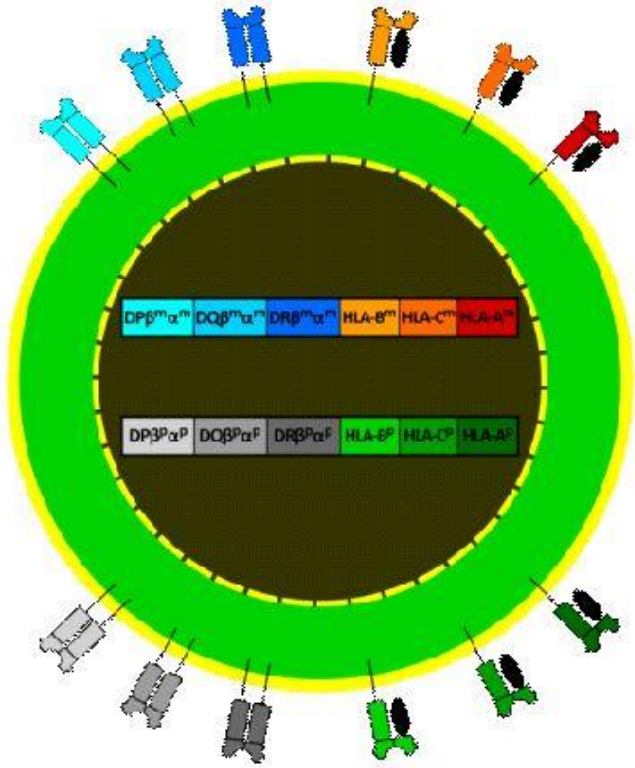
- ✓ self-renew to make more blood stem cells
- ✓ specialize to generate new blood cells.



All blood stem cells are not the same

Special proteins present on the surface of blood stem cells determine their tissue type.

For a successful transplant, donor and patient stem cells have to be tissue typed matched.



Stem Cell Registry (OneMatch)

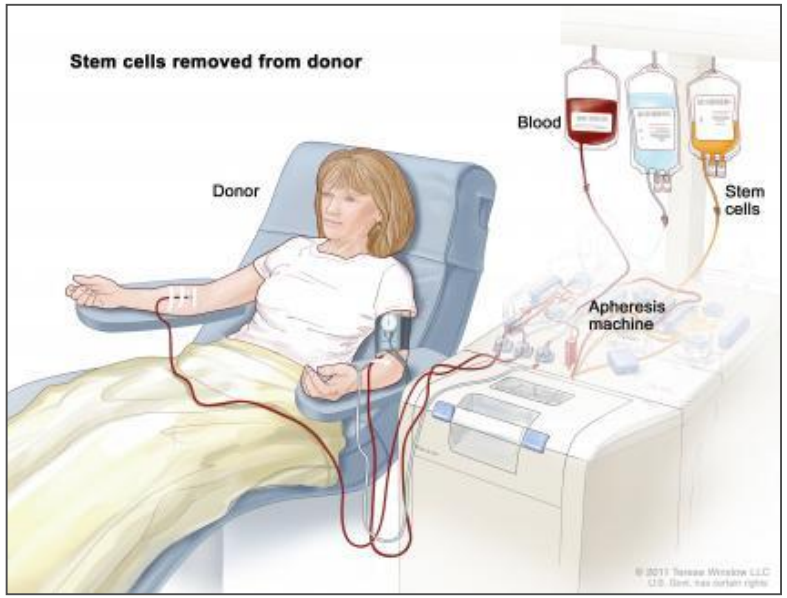
More than 75% of patients who need stem cell transplants rely on a stem cell donation from a stranger.

The registry is a service that matches volunteer donors to patients who require stem cell transplants. It is connected to an international network of 50 registries.

As of July 2018 there are over 430,000 Canadian registrants, over 30,000,000 registrants worldwide and over 1,400 patients looking for a match.

Collection process

Bone marrow



Peripheral blood (Apheresis)

Umbilical cord blood

Production process (cord blood)

Cord blood unit

To prevent blood stem cells damage, maximize product quality and ensure patient safety we

- ✓ Isolate and store the cells within 48 hours of collection
- ✓ Freeze or thaw at appropriate rate
- ✓ Add a cryo-protectant
- ✓ Store the cells in liquid nitrogen (–196°C)
- ✓ Test and label the product correctly

Philip

Philip was diagnosed with aplastic anemia. Stem cells in his bone marrow are damaged so he is not able to make enough new blood cells.

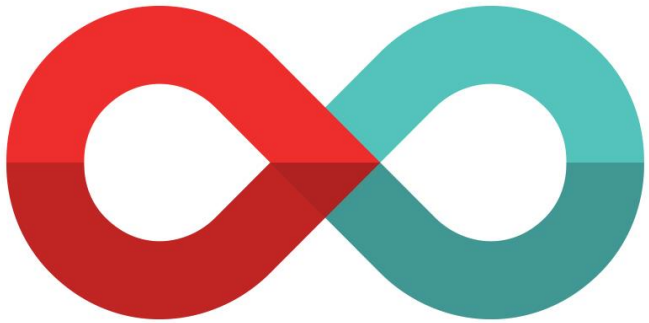
He is anemic (low red blood cells), susceptible to infections (low white blood cells) and bruises easily (low platelets).

Philip’s treatment

Doctors transfuse Philip with red blood cells and platelets.

Philip has developed iron overload as a result of the many red blood cell transfusions. This can seriously damage his heart and liver, and he remains susceptible to infections.

Philip will receive a blood stem cell transplant. The blood stem cells from the donor will replace his damaged stem cells and make the blood cells he needs.



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