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Pathogen reduced red blood cells: a blood supply perspective

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Conflicts of interest

I have got no conflicts of interest related to this presentation

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Blood safety in Sweden



- Cold climate
  - No great fear of “warmer climate diseases” (malaria, zika, dengue etc…)*
- Generally reliable donors
  - Low prevalence of transfusion-transmittable infectious diseases (TTID)*
- 2–6°C storage, good hygiene routines and advanced, closed-system component processing technology
  - Not overly concerned about bacterial growth in red cell units*

➡ Pathogen inactivation systems for red cells have previously not been a top priority

What is Sweden concerned about?

***** I’m not saying we *shouldn’t* be more concerned about these parameters

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The Blood Supply

- The blood supply is facing some major challenges (and they're coming on fast)
  - Donor decrease and expected increase of patients
  - Migration, easier access to travel – growing donor/recipient blood type mismatch
  - Climate change, migration, easier access to travel – faster spread of pathogens
  - Oncoming ban of the blood bag plasticiser di(2-ethylhexyl) phthalate (DEHP)
  - Competition for donors – European plasma self-sufficiency and whole blood for trauma

- Expectations to increase contingency and emergency preparedness → requirements for a larger and more resilient blood supply
  - Regulatory (SoHO regulation)
  - Experience from recent challenging events

What is the answer – more donors?

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Yeah, more donors would be great but…

We also need to think smarter!

- Optimise what we already have got to balance the decreasing donor pool
- The shorter shelf life → the higher risk of outdating
- How can we reduce waste?
  - Avoid unnecessary cell damage
  - Find processing strategies that are “softer” yet as efficient to meet patient needs
- Ensuring component quality and safety is extra important when faced with an ongoing crisis situation

A red blood cell concentrate

Red cell concentrate

150-200 mL red blood cells
100 - 110 mL additive solution
10-15 mL plasma
<1 x 10^6 leukocytes

Contents

- Red blood cells
- Additive solution
  - Ensures adequate haematocrit
  - Provides nutrients and building blocks to support the metabolism
  - Protects the cell membrane
- Plasma – because whole blood separation not 100%
  - Provides some (limited) buffering
- Leucocytes – reduced via leucofiltration (or apheresis technology)
  - No benefit, just “garbage”



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A red blood cell concentrate

Red cell concentrate

150-200 mL red blood cells
100 - 110 mL additive solution
10-15 mL plasma
<1 x 10^6 leukocytes





With time, it also contains…

- Increasing levels of red cell debris
  - Free haemoglobin and iron ions
  - Free potassium ions
  - Pro-inflammatory membrane vesicles

It *could* also contain…

- Blood-borne pathogens (virus, bacteria, parasites)
  - If routines for donor selection, collection or processing were inaccurately followed

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Washed red cells

Red cell concentrate

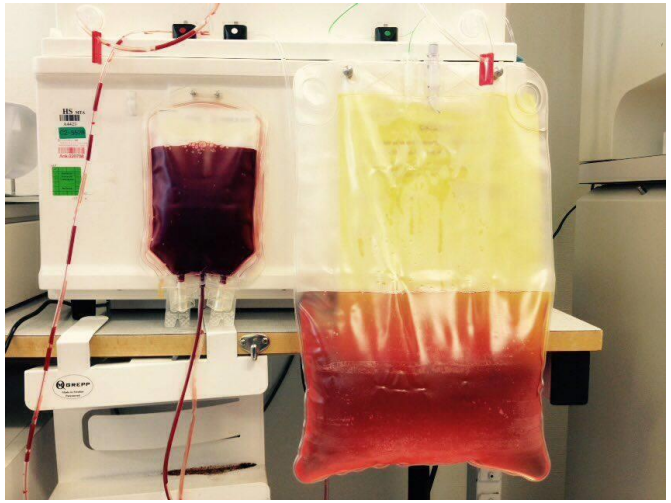
150-200 mL red blood cells
100 - 110 mL additive solution
10-15 mL plasma
<1 x 10^6 leukocytes

Why?

- Remove residual plasma
- Remove any accumulated debris

Who?

- Patients with previous allergic reactions, IgA deficiency, or sensitive to for instance high levels of potassium ions



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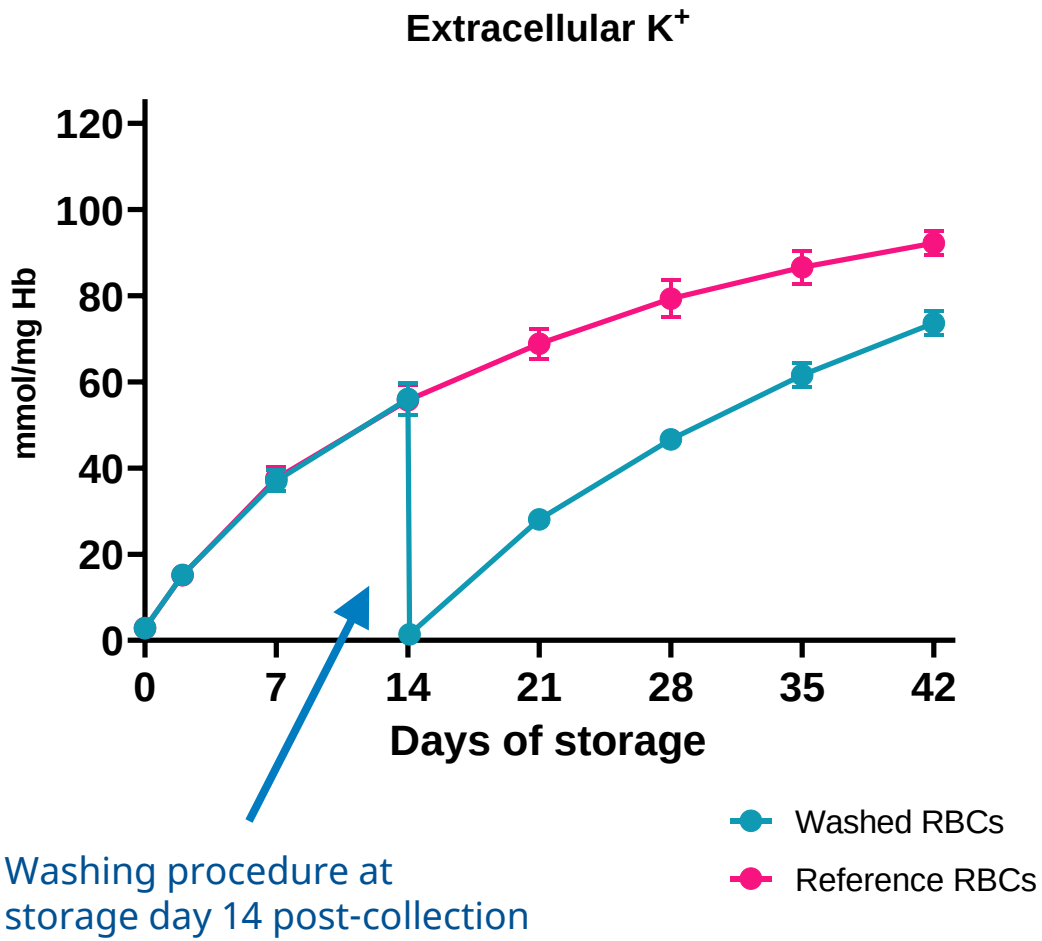
Washing procedure

Pros

- Very efficient removal of plasma and debris

Cons

- Mechanical stress – membrane damage and/or cell breakage (+ no plasma left)
  - Therefore, shortened shelf life (up to 28 days reduction)



Larsson et al, Pathogen reduced red blood cells as an alternative to irradiated and washed components with potential for up to 42 days storage. Blood Transfus. 2024 Mar;22(2):130-139. doi: 10.2450/BloodTransfus.479. Epub 2023 Jul 14.

Irradiated red cells

Red cell concentrate

150-200 mL red blood cells
100 - 110 mL additive solution
10-15 mL plasma
<1 x 10^6 leukocytes

Why?

- Prevent the residual leucocytes from proliferating → reduce the risk of transfusion-associated graft-versus-host disease (TA-GvHD)

Who?

- Patients with suppressed or inadequate immune system



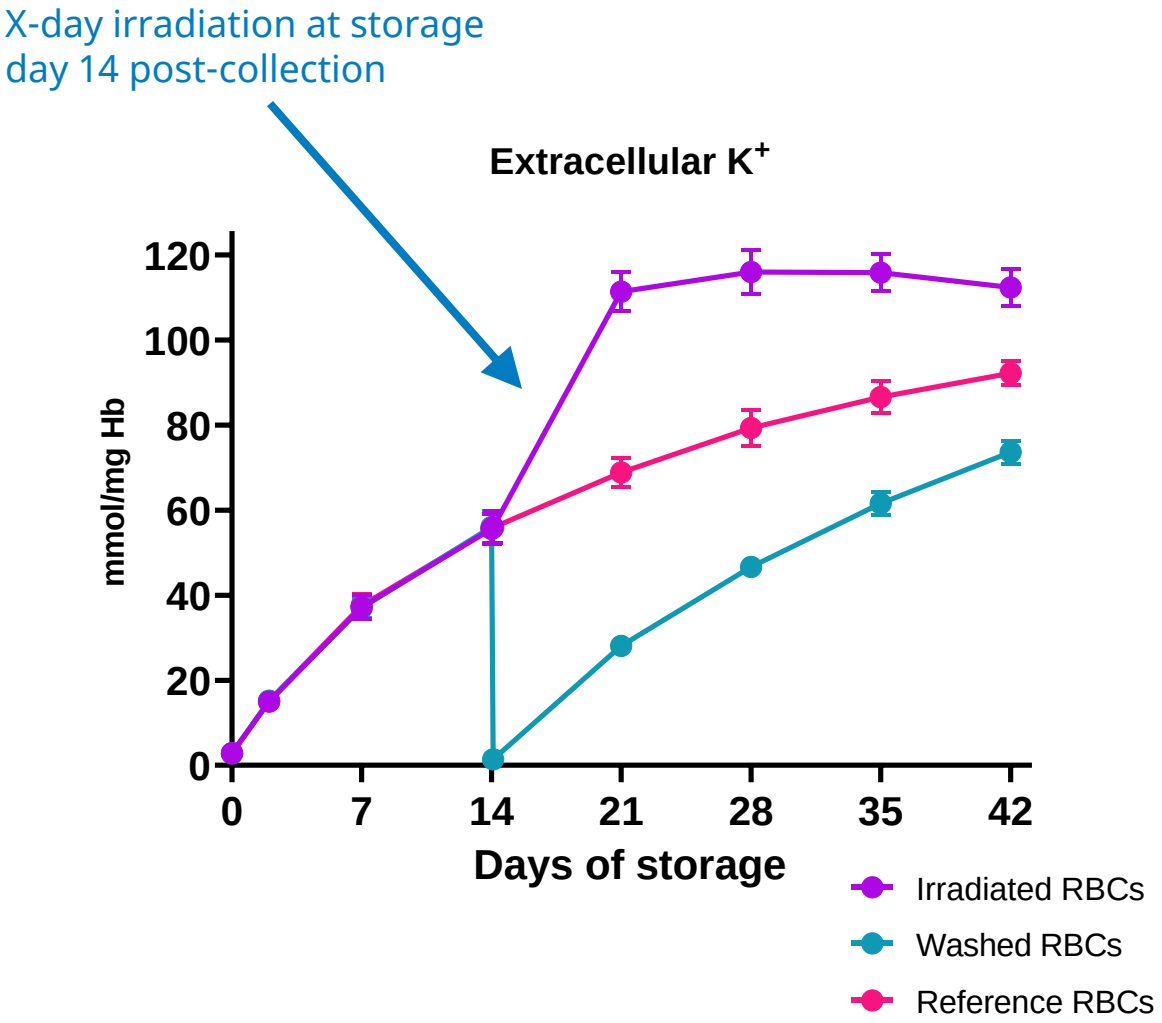
Irradiation procedure

Pros 👍

- Significant reduction of TA-GvHD risk

Cons 👎

- Stress from irradiation – membrane damage (even more than washed cells)
  - Therefore, shortened shelf life (up to 28 days reduction)



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Irradiated and washed red cells: supply challenges

- Because of the shortened shelf life, irradiation and washing is often only done on demand or to a limited part of the stock
  - **On demand: if no stock** at a hospital blood bank – risk that patients may have to wait for proper blood
  - **Limited part: if stock-keeping** at a hospital blood bank – risk of outdating or issuing to patients not in need of irradiated/washed red cells

Is there a smarter way? *

* Leading question, considering the topic of this presentation

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Pathogen inactivation of red cells

Red cell concentrate

150-200 mL red blood cells
100 - 110 mL additive solution
10-15 mL plasma
<1 x 10^6 leukocytes



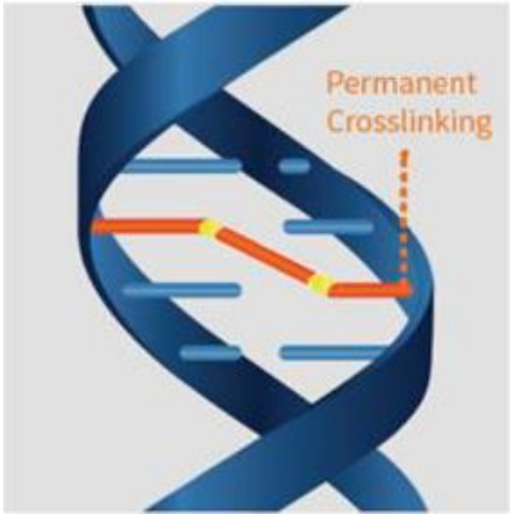
Why?

- Prevent any present pathogens and residual leucocytes from proliferating

What else?*

- Contains a washing step (centrifugation) that can remove plasma and debris

* INTERCEPT pathogen inactivation technology, Cerus Corp.



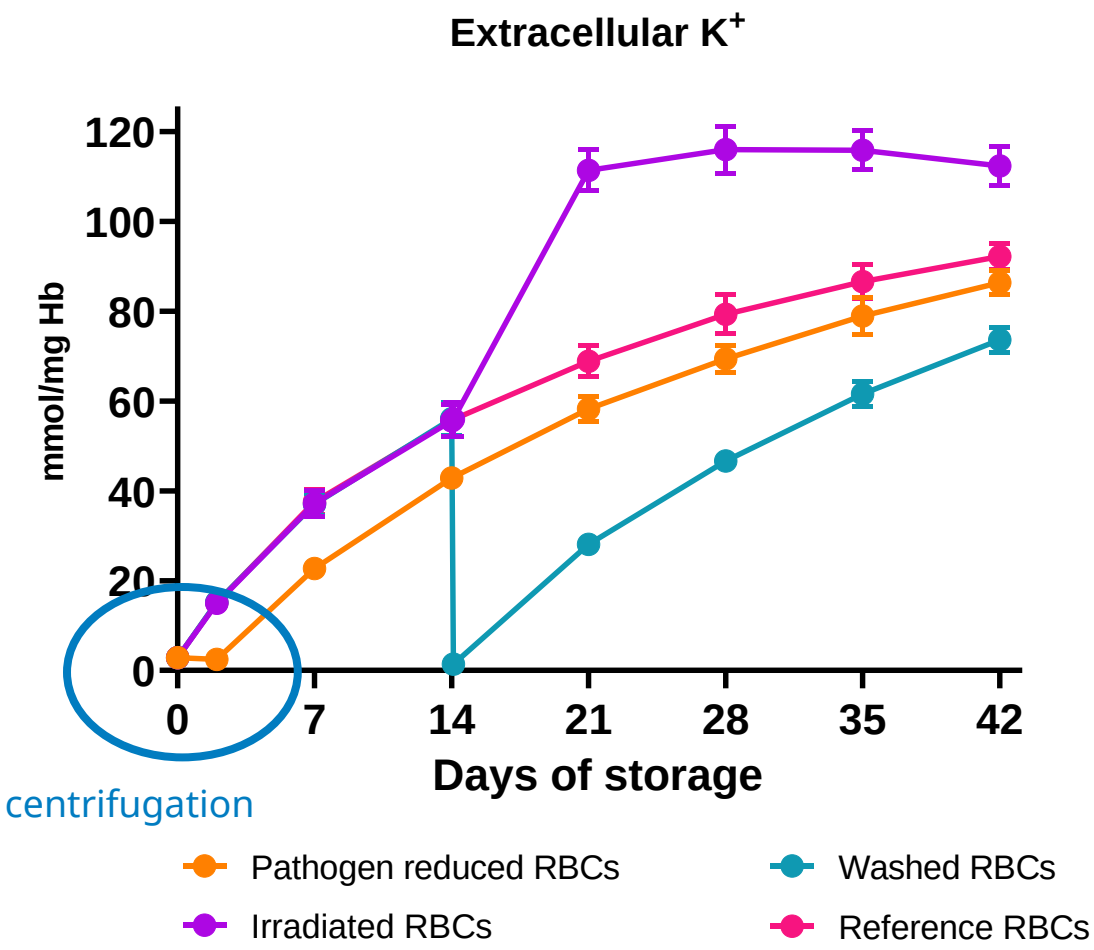
Picture: Cerus Inc.

Who?

- To reduce the risk of TTID for any patient
- But also:
  - Patients that need irradiated components
  - Patients that need washed components

Extracellular K^+

Pathogen reduced red cells



- Accumulated extracellular K^+ is efficiently washed away by the pathogen inactivation (PI) process
- Similar increase rate in PI and reference units
- Slower increase rate compared to after washing (ACP215, Haemonetics Inc.)
- Significantly lower levels than after irradiation

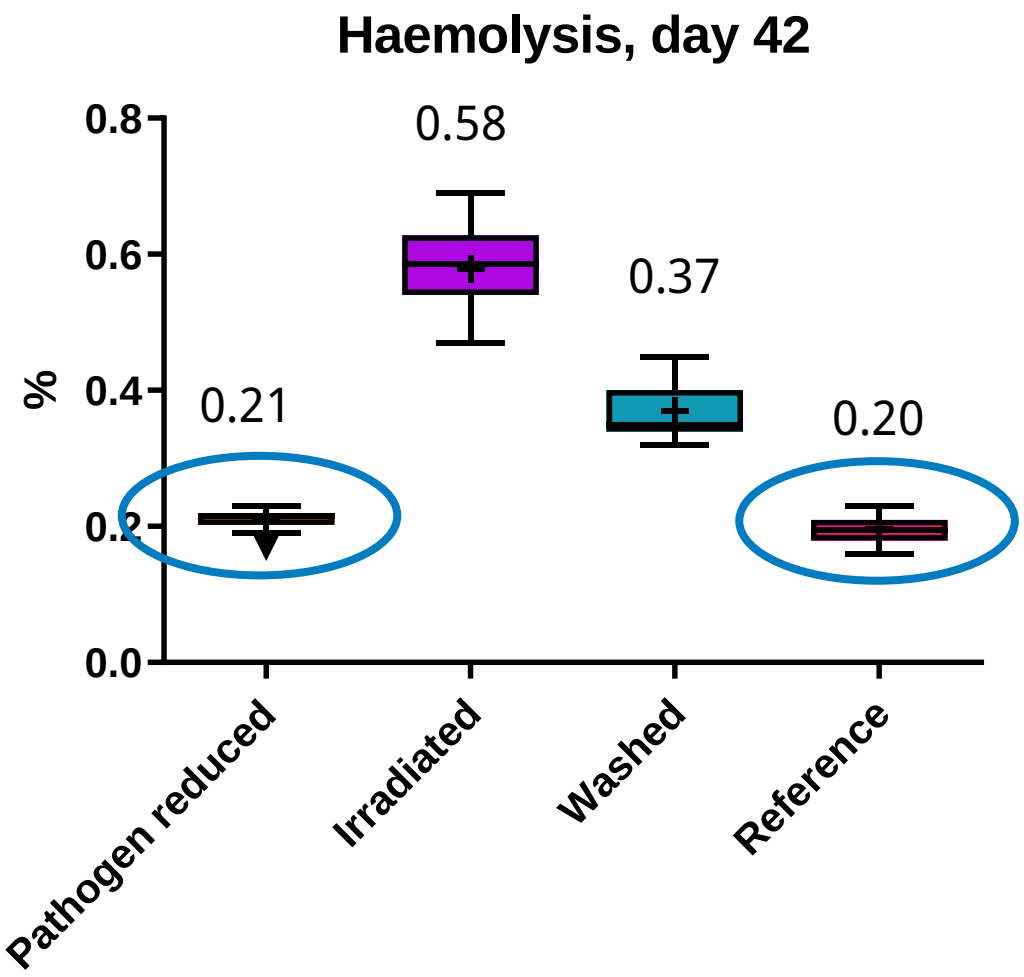
→ Suggests better membrane and/or ATP preservation after PI than after washing or irradiation

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Pathogen reduced red cells



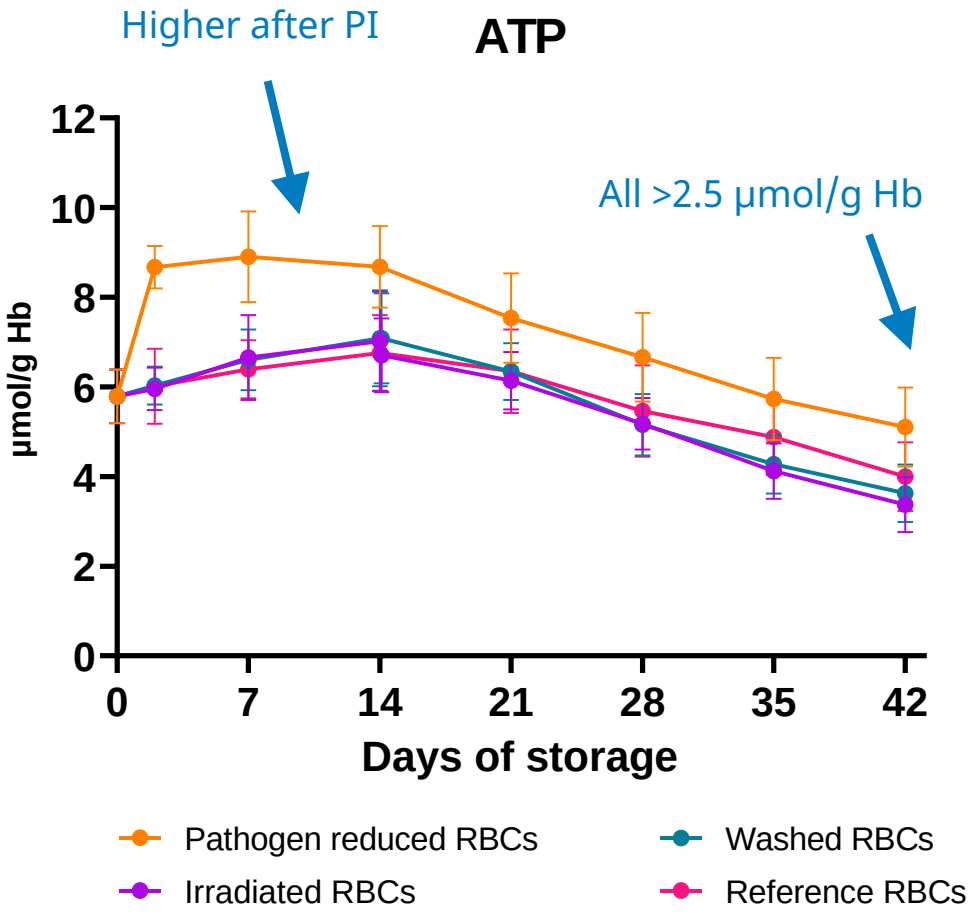
- PI and reference units: similar haemolysis at storage end (ns)
- Significantly lower haemolysis than after irradiation and washing
- ¼ of the European limit 0.8% at storage end

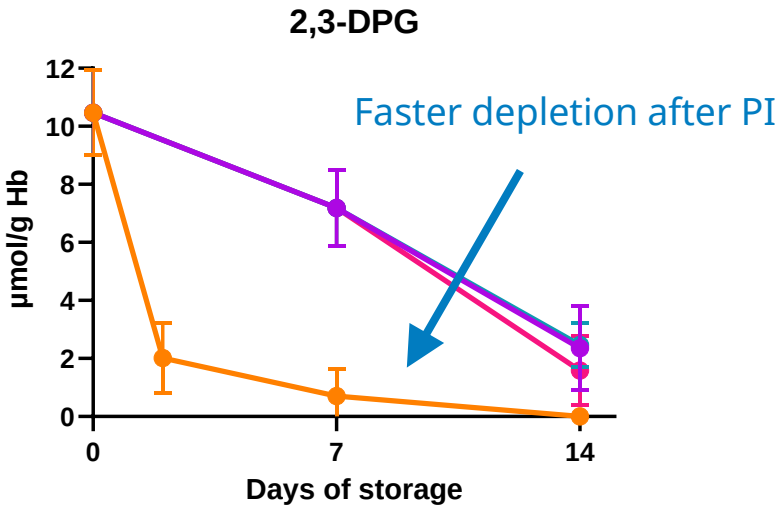
→ Suggests better membrane preservation after PI than after washing or irradiation

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Pathogen reduced red cells





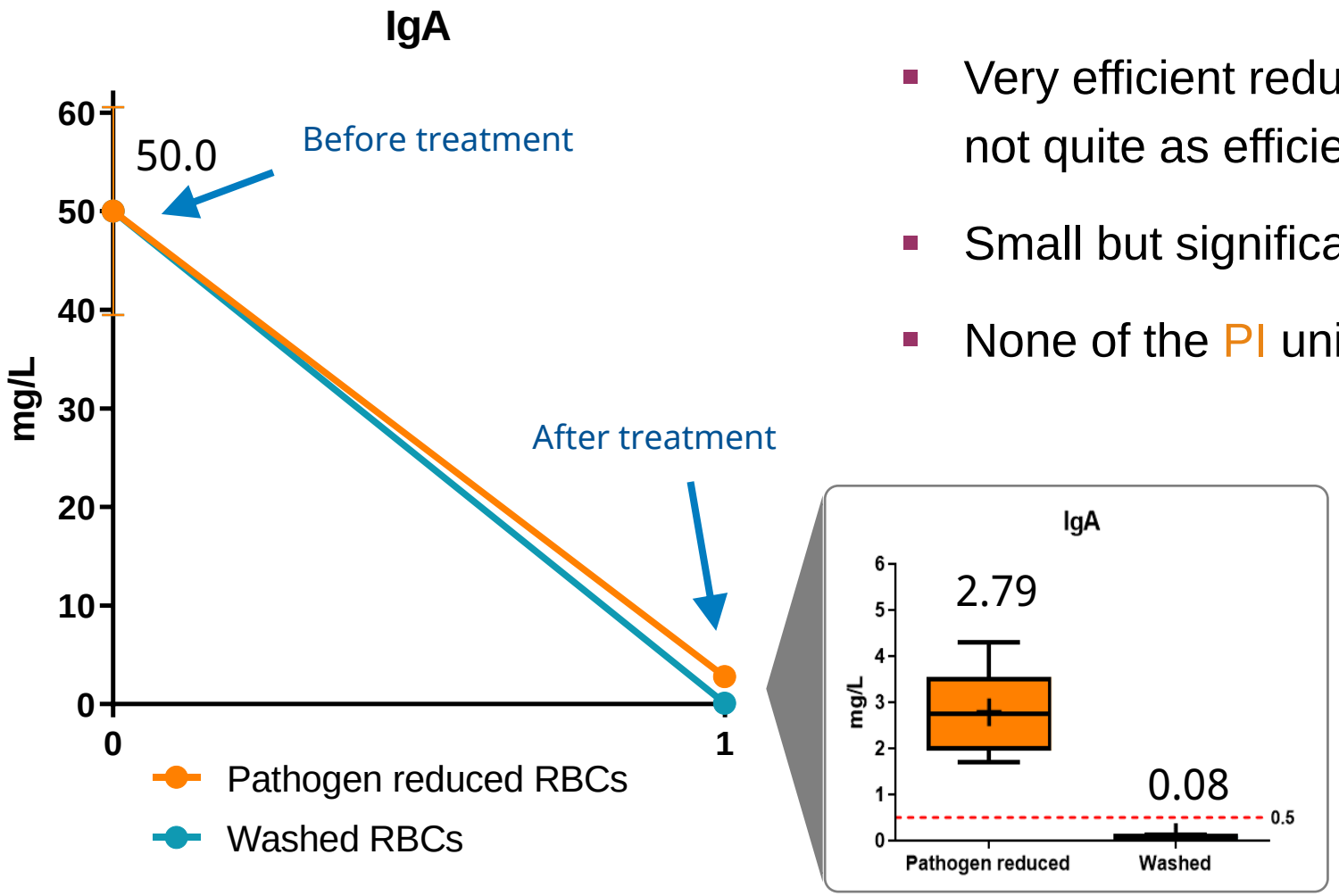
- ATP increased directly after PI. The difference remained >1 µmol/g Hb throughout storage.
- 2,3-DPG was depleted faster after PI treatment. On d14, all PI units were depleted.
- Probably related to lower pH in PI units

→ Suggests a better preserved metabolism after PI than after washing or irradiation

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Pathogen reduced red cells



- Very efficient reduction of IgA by PI (94.4%), but not quite as efficient as by washing (99.8%)
- Small but significant difference (p<0.001)
- None of the PI units met AABB limit (<0.5 mg/L)

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Potential benefits of pathogen inactivation for the blood supply

- **Pathogen reduced red cells*** possess **superior membrane preserving qualities** compared to both irradiated and washed red cells

*with the INTERCEPT pathogen inactivation technology

- **Similar** in vitro quality as **untreated red cells** → proposing up to 42 days shelf life

- **Full shelf life**, also for customised blood components like irradiated or washed red cells, may **reduce outdating** and **facilitate inventory management** of secondary-processed red cells
  - May be extra beneficial in locations where red cells otherwise are irradiated or washed on demand

Awareness



- Not all the pathogen inactivation systems are the same: **pathogen inactivation capacity** and **component quality** varies depending on manufacturer
  - Publications on competing systems where the red cells are harmed and quality is not very great → the potential of longer shelf life is lost
  - Differences in **which pathogens** that are inactivated, and **how well** they are inactivated
- Initial pathogen inactivation systems have been developed using DEHP plasticiser
  - Need to re-assess in DEHP-free systems – results may differ
- Consideration should be given to further development of the centrifugation protocol to optimise the IgA reduction / plasma removal
  - The INTERCEPT pathogen inactivation system was not developed for this purpose

Conclusion

Pathogen inactivation technology does **not only** increase blood safety by targeting potential pathogens. It holds the potential to **replace both washed and irradiated red cell components** with a single component, maintaining **as long shelf life** as a **conventional** red cell concentrate.

This could help **reducing outdating rate** and **ensure the supply** of secondary-processed red cells available for **immediate transfusion**. Such a replacement would be advantageous for both the **blood supply** and the **patient safety**.

Thank you for your kind attention!



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Read the full publication:

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