LOCAL PRODUCTION OF DRIED BLOOD PLASMA

- A MEASURE FOR LOCAL AND NATIONAL EMERGENCY PREPAREDNESS

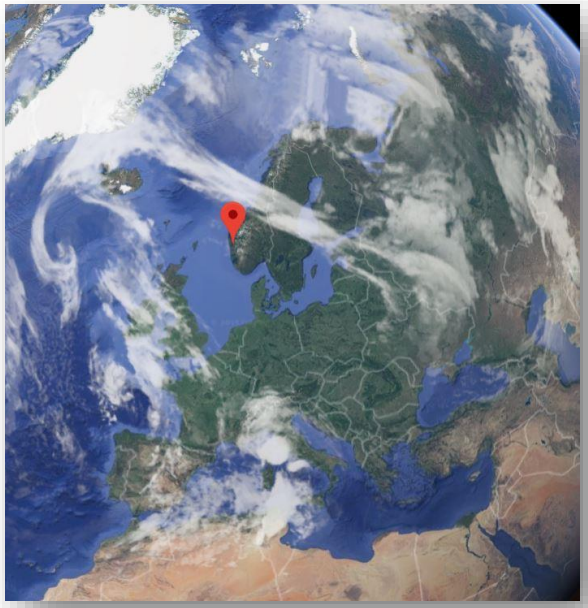
Torunn Apelseth
Overlege
Avdeling for immunologi og transfusjonsmedisin
Haukeland universitetssjukehus, Helse Bergen
Epost: *torunn.oveland.apelseth@helse-bergen.no*

HELSE BERGEN
Haukeland universitetssjukehus

Haukeland universitetssjukehus, Helse Bergen, Norway

Second largest hospital in Norway.

- 900 beds, 945 000 patient consultation per year
- Adult and pediatric patients (including neonatal unit)
- Close collaboration with the University of Bergen
- Extensive research activiy



<u>Services include:</u>

National Burn Center

Regional level 1 trauma center

Regional Cardiac Surgery unit

Regional Stem-cell transplantation unit

Department of Immunology and Transfusion Medicine, Helse Bergen

Hospital Based Blood Bank

- Second largest in Norway
- Collects blood and produces blood components for our hospital and three surronding hospitals
    - Donations per year: 19000
- Transfusion Service
    - RBC transfusions per year: 15000
    - Plasma transfusions per year: 5000

The Nordic Collaborative Dried Plasma Project

Initiated by the Blood Far Forward program in Bergen

- Established January 2019
- Aim: To introduce dried plasma in the Nordic Countries
- Nordic Civilian-Military Collaborative project:
  - Norway: Geir Strandenes, Torunn Apelseth, Einar Kristoffersen, Tor Hervig
  - Sweden: Agneta Wikman, Patrik Hansson
  - Finland: Jouni Lauronen, Jaako Keranen
  - Denmark: Jakob Stensballe

Scientific Advisory Board:
Simon Stanworth (UK)
Patrick Thompson (UK, South Africa)
Andrew Cap (US)
Elon Glasberg (I)
Gabriel Skallsjø (S)

HELSE BERGEN
Haukeland universitetssjukehus

History of Dried Plasma

- 1930: Pooled lyophilized plasma (1,2)
- 1940: WWII: High use
  - UK and US: Pooled lyophilized plasma (3, 4)
  - Sweden: Spray dried plasma(5)

WWII Production
British produced >500,000 U lyophilized plasma during WWII.
US produced >6,000,000 U lyophilized plasma during WWII.
US/British distributed world-wide.
Sweden produced approximately 17,000 U spray dried plasma for Sweden and Finland.

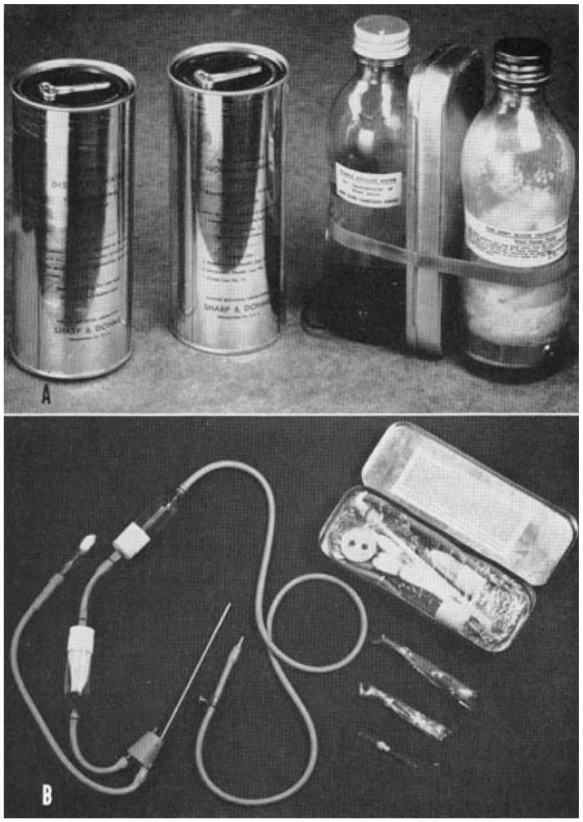


Fig. 1. (A) British (right) and US Army dried plasma units. (B) British dispensing set for plasma. Available from: https://upload.wikimedia.org/wikipedia/en/thumb/9/95/Britain_and_ us_plasma_packages_wwii.jpg/162px-Britain_and_us_plasma_ packages_wwii.jpg, accessed 30 Sept 2015.

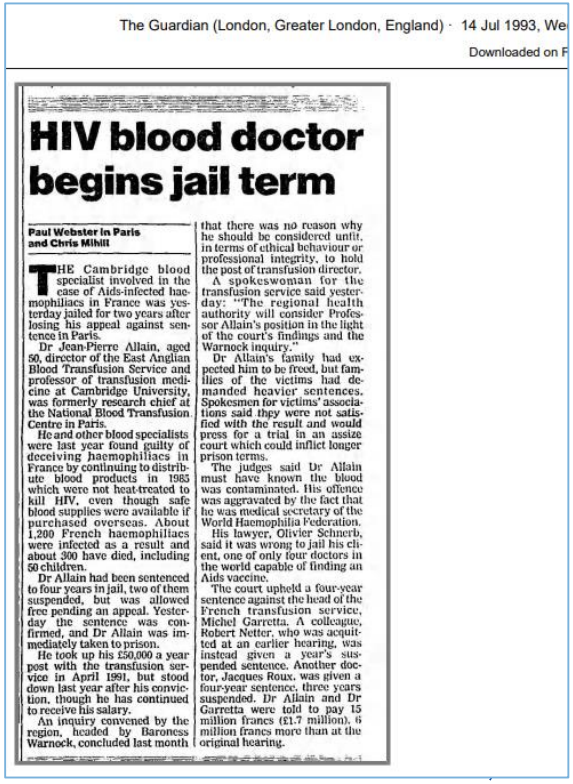
Referanser.

1) *Pusateri AE, Given MB et al. Dried plasma: state of the science and recent devlopements. Transfusion. 2016; 56:S128-S139*
2) *Flosdorf EW, Mudd S. Procedure and apparatus for preservation in "Lyophile" form of serum and other biological substances. J Immunol 1935;29:389-425.*
3) *Schmidt PJ. The plasma wars: a history. Transfusion 2012;52: 2S-4S.*
4) *Harding AJ. A brief history of blood transfusion. Biomed Sci 2005;49:1147-57.*
5) *Octapharma Annual Report. 2002. [Accessed 2015 Sept 5] Available from: http://www.haemophiliaonline.com/corporate/02_the_company/04_financial/docs/annual report_2002.pdf*

HELSE BERGEN
Haukeland universitetssjukehus

History cont.

- 1945: Transfusion associated hepatitis first discovered (6-10)
- 1968: National Research Council Committee on Plasma and Plasma Substitutes US: *"the use of whole, pooled human plasma be discouraged and even discontinued unless a clear cut case can be made for its unique requirements."* (11)
- 1985: French production stopped (12)



The Guardian (London, Greater London, England) · 14 Jul 1993, We

Downloaded on F

HIV blood doctor begins jail term

Paul Webster in Paris and Chris Mihill

THE Cambridge blood specialist involved in the case of Aids-infected haemophiliacs in France was yesterday jailed for two years after losing his appeal against sentence in Paris.

Dr Jean-Pierre Allain, aged 50, director of the East Anglian Blood Transfusion Service and professor of transfusion medicine at Cambridge University, was formerly research chief at the National Blood Transfusion Centre in Paris.

He and other blood specialists were last year found guilty of deceiving haemophiliacs in France by continuing to distribute blood products in 1985 which were not heat-treated to kill HIV, even though safe blood supplies were available if purchased overseas. About 1,200 French haemophiliacs were infected as a result and about 300 have died, including 50 children.

Dr Allain had been sentenced to four years in jail, two of them suspended, but was allowed free pending an appeal. Yesterday the sentence was confirmed, and Dr Allain was immediately taken to prison.

He took up his £50,000 a year post with the transfusion service in April 1991, but stood down last year after his conviction, though he has continued to receive his salary.

An inquiry convened by the region, headed by Baroness Warnock, concluded last month that there was no reason why he should be considered unfit, in terms of ethical behaviour or professional integrity, to hold the post of transfusion director.

A spokeswoman for the transfusion service said yesterday: "The regional health authority will consider Professor Allain's position in the light of the court's findings and the Warnock inquiry."

Dr Allain's family had expected him to be freed, but families of the victims had demanded heavier sentences. Spokesmen for victims' associations said they were not satisfied with the result and would press for a trial in an assize court which could inflict longer prison terms.

The judges said Dr Allain must have known the blood was contaminated. His offence was aggravated by the fact that he was medical secretary of the World Haemophilia Federation.

His lawyer, Olivier Schnerb, said it was wrong to jail his client, one of only four doctors in the world capable of finding an Aids vaccine.

The court upheld a four-year sentence against the head of the French transfusion service, Michel Garretta. A colleague, Robert Netter, who was acquitted at an earlier hearing, was instead given a year's suspended sentence. Another doctor, Jacques Roux, was given a four-year sentence, three years suspended. Dr Allain and Dr Garretta were told to pay 15 million francs (£1.7 million), 6 million francs more than at the original hearing.

Referanser

6) Rappaport EM. Hepatitis following blood or plasma transfusions. JAMA 1945;128:932-9.

7) Murphy WG, Workman WP. Serum hepatitis from pooled irradiated dried plasma. JAMA 1953;152:1421-3.

8) Kendrick DB. Blood program in World War II. Washington (DC): Office of the Surgeon General, Department of the Army; 1964.

9) Rappaport EM. Hepatitis following blood or plasma transfusions. JAMA 1945;128:932-9.

10) Murphy WG, Workman WP. Serum hepatitis from pooled irradiated dried plasma. JAMA 1953;152:1421-3.

11) Statement on normal (whole pooled) human plasma by Committee on Plasma and Plasma Substitutes of the Division of Medical Sciences, National Research Council. Transfusion 1968;8:57-9.

12. Sailliol A, Martinaud C, Cap AP, et al. The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service. Transfusion 2013;53(Suppl):65S-71S.

Why do we want to transfuse plasma to our bleeding patients?

Improved survival

Research

JAMA | Original Investigation

Association of Prehospital Blood Product Transfusion During Medical Evacuation of Combat Casualties in Afghanistan With Acute and 30-Day Survival

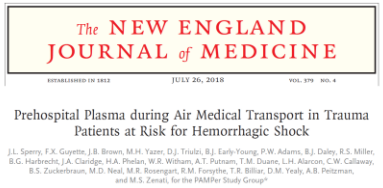
Stacy A. Shackelford, MD; Deborah J. del Junco, PhD; Nicole Powell-Dunford, MD; Edward L. Mazuchowski, MD, PhD; Jeffrey T. Howard, PhD; Russ S. Kotwal, MD, MPH; Jennifer Gurney, MD; Frank K. Butler Jr, MD; Kirby Gross, MD; Zsolt T. Stockinger, MD

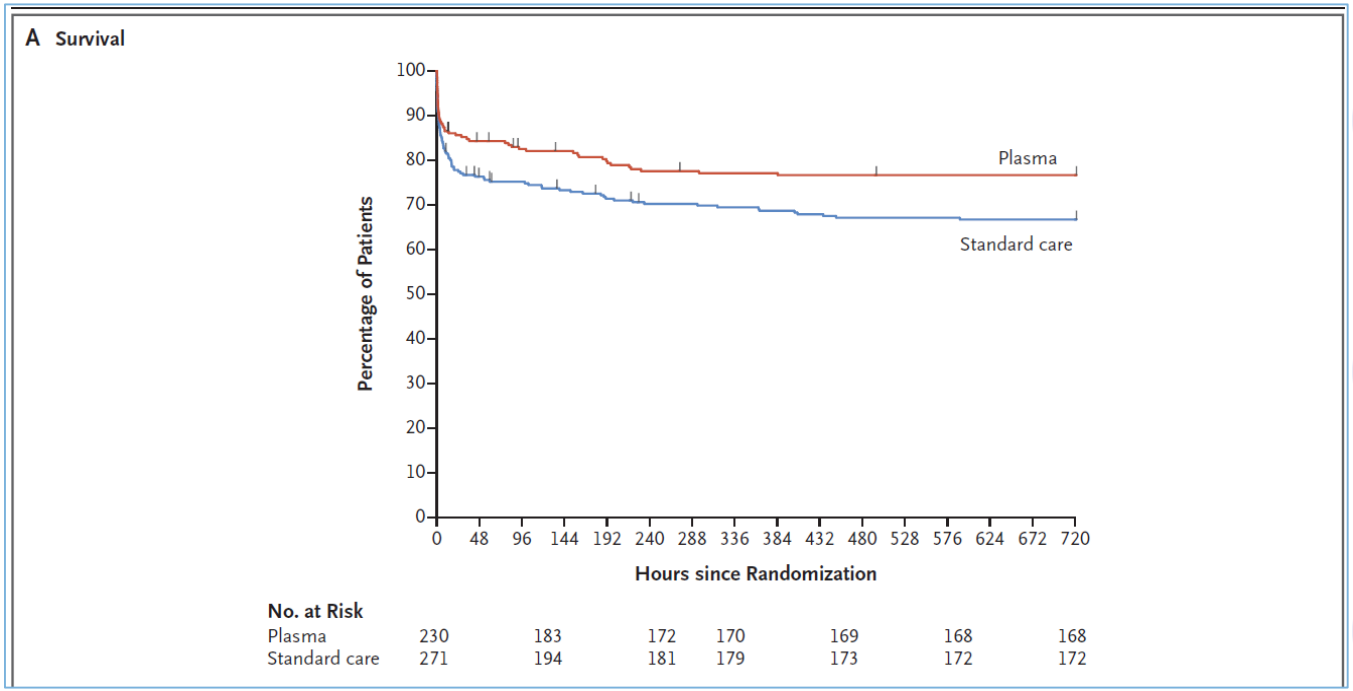
Aim: To investigate the effect of transfusion (red cells, plasma or both) during evacuation of bleeding soldiers on survival outcomes

Results:

- Early prehospital blood transfusion was associated with increased 24 hour and 30 day survival in US military combat casualities
- Timing is critical, benefit depends on starting transfusion early
- 70 % of deaths occurred within the first hour after MEDEVAC rescue. More early deaths among non-recipients.

Prehospital plasma transfusion in civilian air ambulance service improve 30 day survival and is safe (PAMPer Study)





RESULTS: Mortality at 30 days was significantly lower in the plasma group than in the standard-care group (23.2% vs. 33.0%; difference, −9.8 percentage points; P=0.03). No significant differences between the two groups were noted with respect to multiorgan failure, acute lung injury–acute respiratory distress syndrome, nosocomial infections, or allergic or transfusion-related reactions.

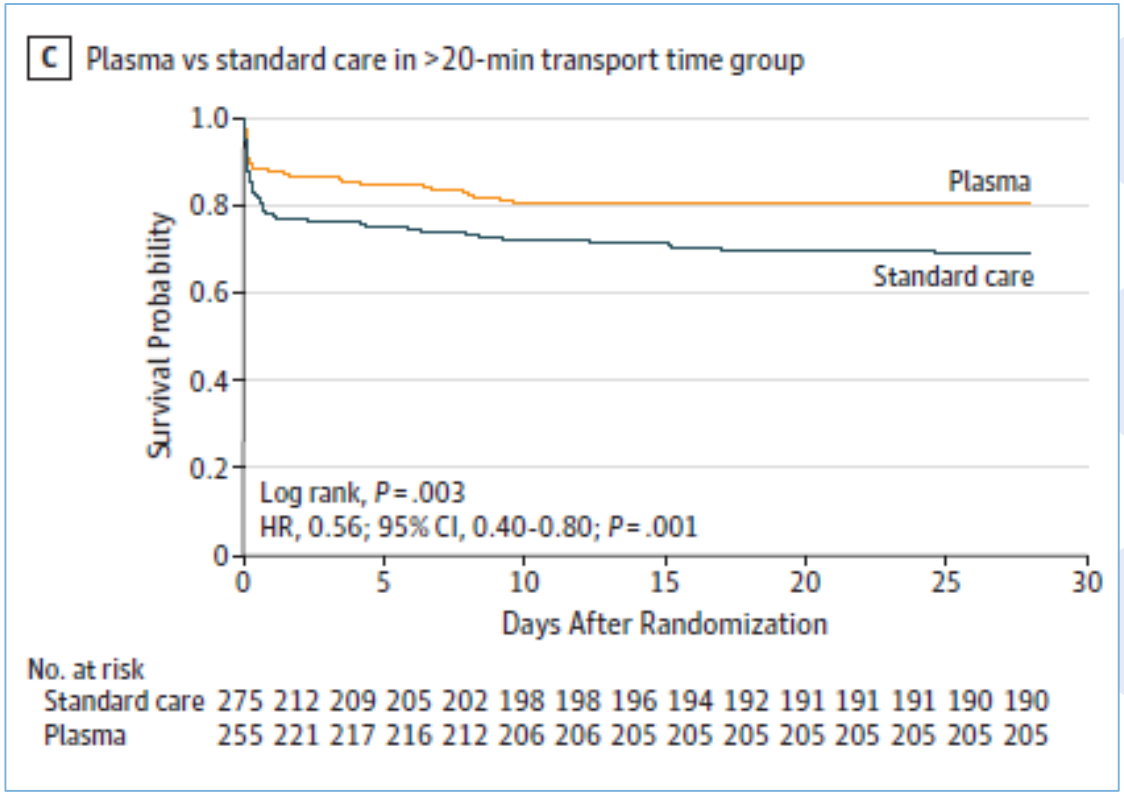
Improved survival with prehospital plasma transfusion if transport time more than 20 minutes (PAMPer and COMBAT study combined)

JAMA Surgery | Original Investigation

Association of Prehospital Plasma Transfusion With Survival in Trauma Patients With Hemorrhagic Shock When Transport Times Are Longer Than 20 Minutes

A Post Hoc Analysis of the PAMPer and COMBAT Clinical Trials

Anthony E. Pusateri, PhD; Ernest E. Moore, MD; Hunter B. Moore, MD, PhD; Tuan D. Le, MD, DrPH; Francis X. Guyette, MD, MPH; Michael P. Chapman, MD; Angela Sauaia, MD, PhD; Arsen Ghasabyan, MPH; James Chandler; Kevin McVaney, MD; Joshua B. Brown, MD; Brian J. Daley, MD; Richard S. Miller, MD; Brian G. Harbrecht, MD; Jeffrey A. Claridge, MD; Herb A. Phelan, MD, MSCS; William R. Witham, MD; A. Tyler Putnam, MD; Jason L. Sperry, MD, MPH



Results:

In 625 patients with hemorrhagic shock, increased mortality with standard care (crystalloids) if preshospital transport time more than 20 minutes

HELSE BERGEN
Haukeland universitetssjukehus

Dried plasma as a bridge to definitive care

Karmsund bro, Rogaland, Norge

HELSE BERGEN
Haukeland universitetssjukehus

Commersially available dried plasma in the world today:

A. French Lyophilized Plasma, FLYP (French Military Blood Institute, Centre de Transfusion Sanguine des Armees, CTSA)

B. Lyoplas N-w, (German Red Cross)

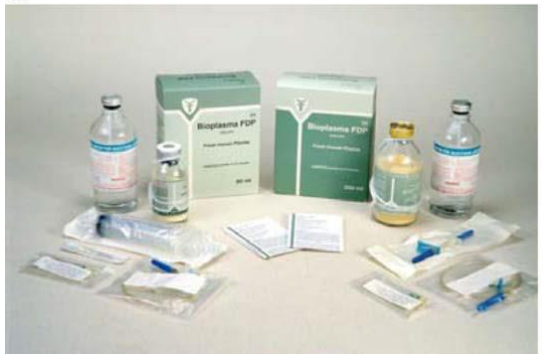
C. Bioplasma FDP (National Bioproducts Institute, Pinetown, South Africa)

→ **Large centralized production units**

A.

B.

C.

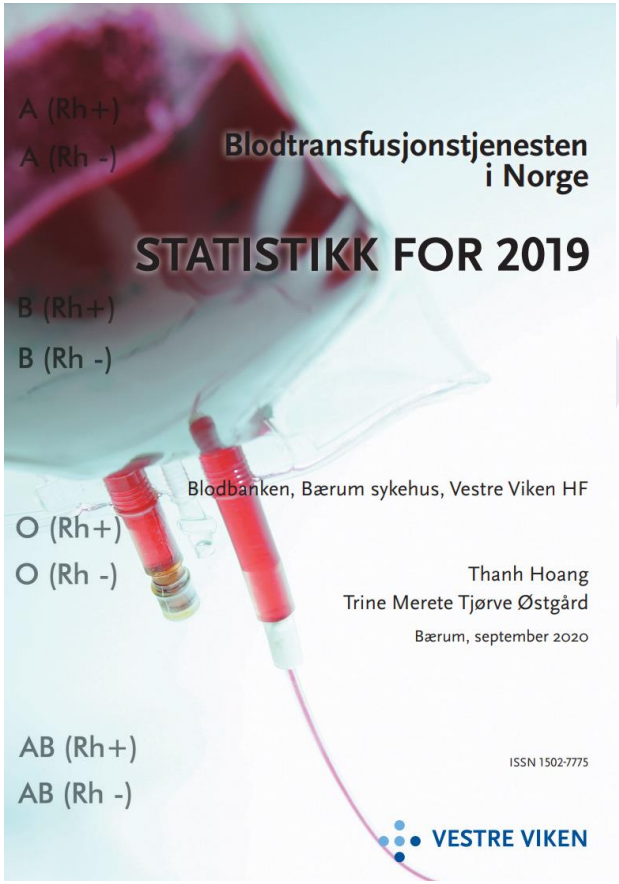


Plasma transfusions in Norway

Total number of plasma transfusions in hospitals in Norway 2019: **40195**

<u>Type of plasma products in use:</u>

- Solvent-Detergent Pooled plasma
- LyoPlas N-w (German Red Cross)

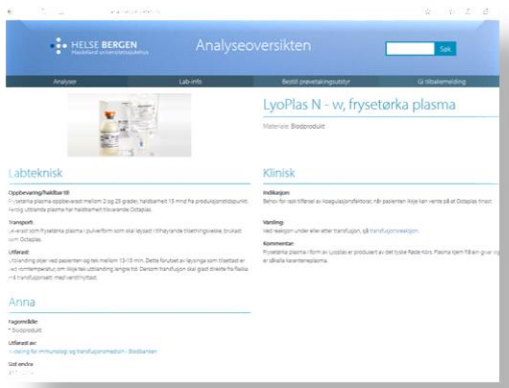


Ref. https://www.helsedirektoratet.no/rapporter/transfusjonsstatistikk

Where is dried plasma used in Norway today?

Helse Bergen import dried plasma and distribute for local, regional and national use:

- Air ambulance
- Oil industry health care
- Hospitals
- Military Health Services

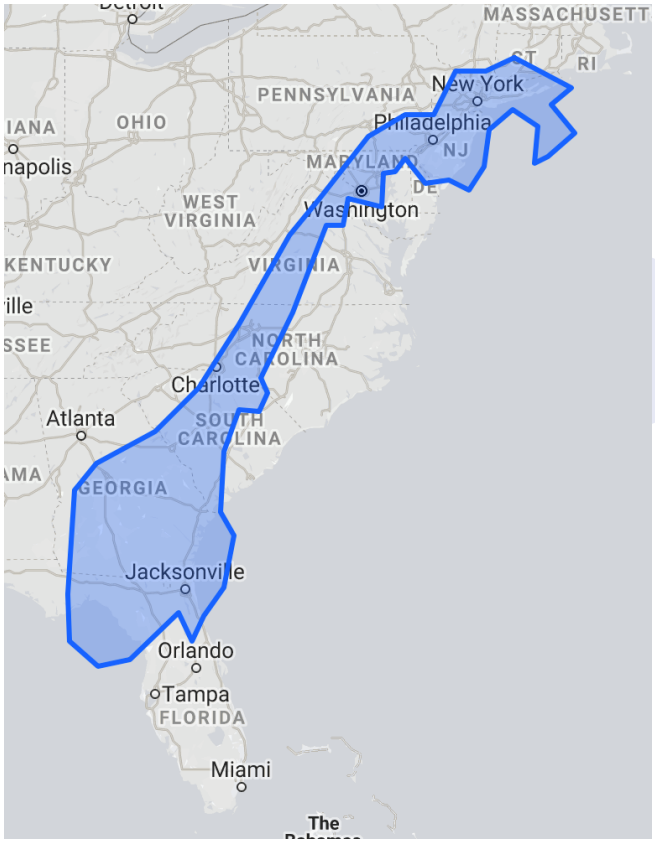


Challenge

1. Norway is not self-sufficient with dried plasma.
    - ➢ This makes us vulnerable in emergency situations and creates a unnecessary uncertainty with regards to availability of treatment.

2. We do not have enough dried plasma to supply our need.
    - ➢ To ensure early access to plasma for all bleeding patients in Norway, plasma should be available at all treatment levels

Patient transport in Norway:
How far du you get in 20 minutes…



HELSE BERGEN
Haukeland universitetssjukehus

Where are plasma needed?

Level 1 Trauma Centers

Local Community Hospital

Ambulance Services

General practice

HELSE BERGEN
Haukeland universitetssjukehus

The solution is to produce our own dried blood plasma

Local production of dried blood plasma:

1. Better use of blood donor resources
2. Enables us to adjust production according to need
   - ✓ Increased need (major incidents, terrorist attacks, natural disasters or war)
   - ✓ Reduced access (pandemic)

→ **Improved preparedness**

HELSE BERGEN
Haukeland universitetssjukehus

Project objective:

- **To develop and implement a solution for local production of dried plasma in Helse Bergen**

To expand this technology to Blood Banks in Norway and in the Nordic Countries, which will ensure an efficient and predictable access to dried blood plasma and better blood preparedness.

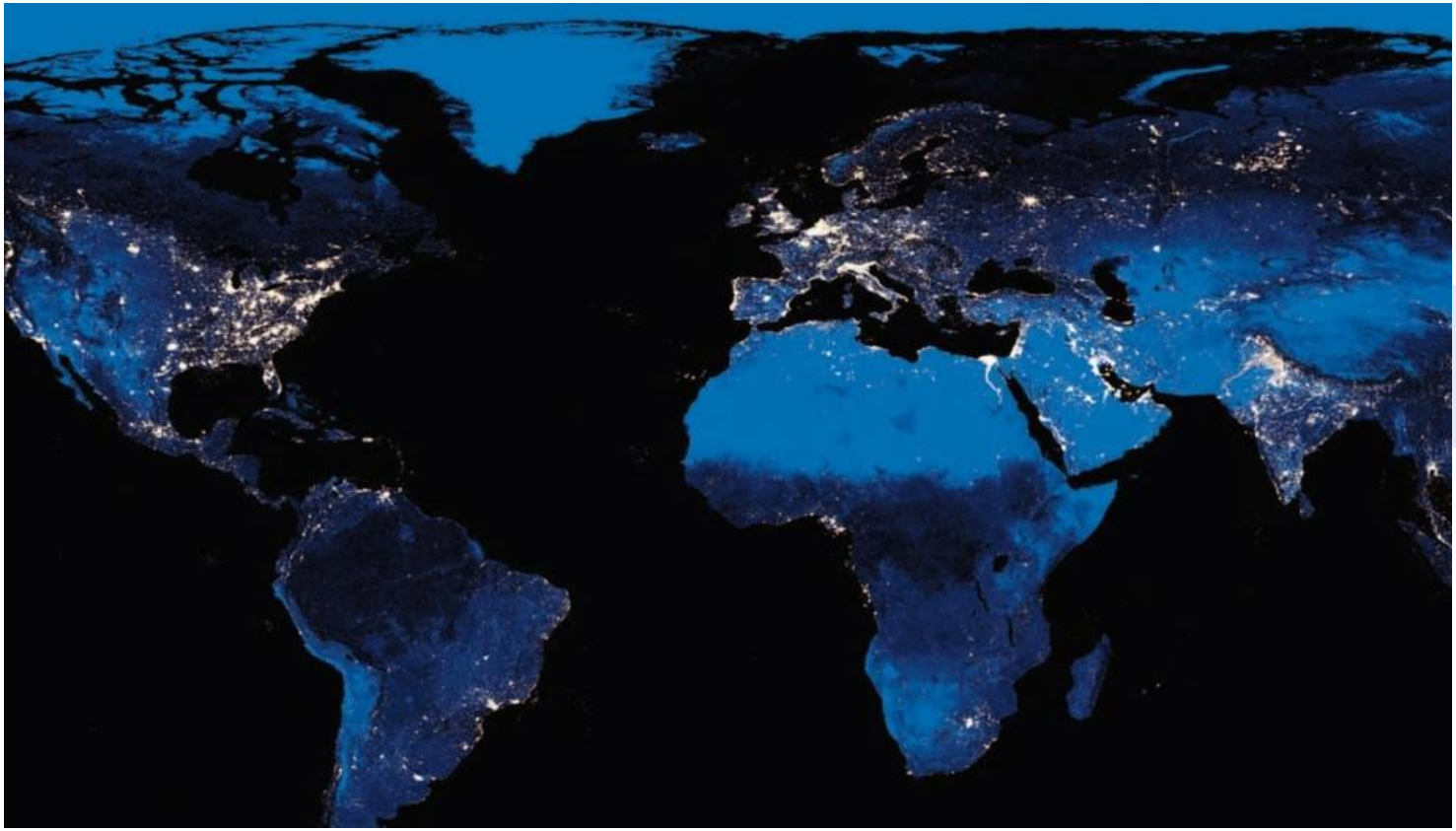
What do we need?

We need technology to produce dried plasma

1. Production
   - ✓ Preferably, to be produced in the Blood Bank
   - ✓ Need to satisfy requirements for blood component production for human use

2. Product
   - ✓ Long storage time
   - ✓ Stored in room temperature or in refridgerator
   - ✓ Easy to carry
   - ✓ To be resolved in water at time of use

Market potential



HELSE BERGEN
Haukeland universitetssjukehus

Do you have the solution to our problem?

THANKS!

To the Blood Far Forward program in Bergen

- Geir Strandenes
- Einar K. Kristoffersen
- Hanne Braathen
- Kristin Gjerde Hagen
- Tor Hervig
- Christopher Bjerkvig
- Turid Helen Felli Lunde
- Joar Sivertsen

To the Nordic Collaborative Dried Plasma project:

- Norway: Geir Strandenes, Torunn Apelseth, Einar Kristoffersen, Tor Hervig
- Sweden: Agneta Wikman, Patrik Hansson
- Finland: Jouni Lauronen, Jaako Keranen
- Denmark: Jakob Stensballe

HELSE BERGEN
Haukeland universitetssjukehus