European bank of frozen blood

Concept, current status and future

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Johan Lagerberg

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History

- 1950 Audrey Smith showed that glycerol protects RBC from injury from freezing
- 1956 Chelsea Naval Hospital in Boston starts with large scale freezing of RBC
- 1962 Dr Krijnen Central Laboratory of the Blood Transfusion Service of the Dutch Red Cross started a bank of frozen blood
    - Uncommon and rare phenotypes
- 1968 Foundation of the Blood Bank for the Council of Europe in Amsterdam
    - Rare phenotypes
- 1960-1970--> Military storage in USA and UK
- 2001 FDA licence Haemonetics ACP 215 sterile freezing and thawing (2 weeks)

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Why are red cells kept in frozen storage? (1)

- Diagnostics
  - (Identification)panels
  - donor RBC with rare typing
  - Reference RBC
  - Quality controls
- Research
  - population genetics
  - typed red cells

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Why are red cells kept in frozen storage? (2)

- Transfusion
  - º Typed blood (back up storage, uncommon combinations)
  - º Rare typings
  - º Autologous blood
    - Combination of antibodies
    - HTR without detectable antibodies
    - Antibodies against a high frequency antigen

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How are rare donors discovered?

- Patients with antibodies against HFA who are send in for a serological work up (e.g. in need of a transfusion, pregnant)
- Relatives of patients with a rare typing
- Random screening of donors for HFA
  - Restriction: test reagents
  - Future: DNA typing

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How are red blood cells frozen?

- -196°C liquid nitrogen, low glycerol (Council of Europe)
  - *High yield (90%-95%)*
  - *Long tenability > 40 year (indefinite?)*
  - *Reliable storage*
- -80°C, high glycerol
  - *Yield 80%-90%*
  - *Tenability 10 years (European guidelines, FDA)*
  - *Can be fully automated and closed sterile circuit possible: shelf-life*
  - *More sensitive for disturbances in technology*

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How are red blood cells frozen?

Both methods are expensive

- Initial and ongoing costs of specialized equipment and automated devices to process cells
- Storage facilities
- Trained staff
- Disposables

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Freeze and thaw method (1)

Freeze

- Leukocyte depleted erythrocyte concentrate
- Removal of SAGM
- Addition of freezing solution: *glycerol, (sorbitol, NaCl)*
- Aluminium container

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Freeze and thaw method (2)

Thawing and reconstitution

- Thaw in water bath 40^{o}C
- Remove glycerol
- Wash with sorbitol (hypertone) and NaCl
- Reconstitution

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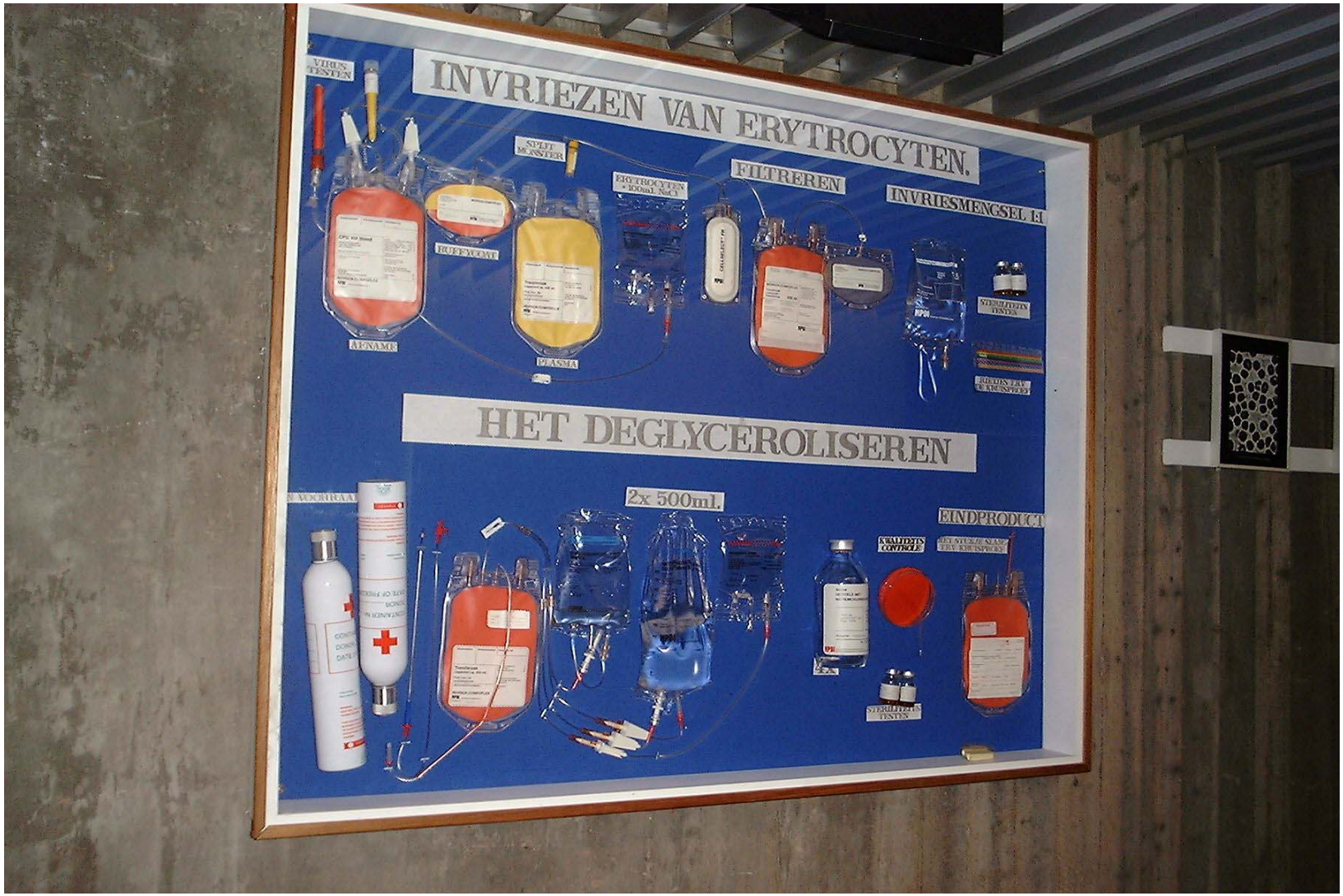
INVRIEZEN VAN ERYTROCYTEN.
FILTREREN
INVRIESMENGSEL 1:1
HET DEGLYCEROLISEREN
2x 500ml.
EINDPRODUCT

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Case 1
Exploding containers

Request:	Berlin – Germany
18/4/05	4 ECs Ko, female patient, 76 yrs, anti-Ku (O D+) Cardiac surgery scheduled for 20 April
20/4/05	4 units are thawed 2 units explode: 1 back up unit is thawed: 3 units are transported by plane
	1 extra unit is thawed and transported with a second flight

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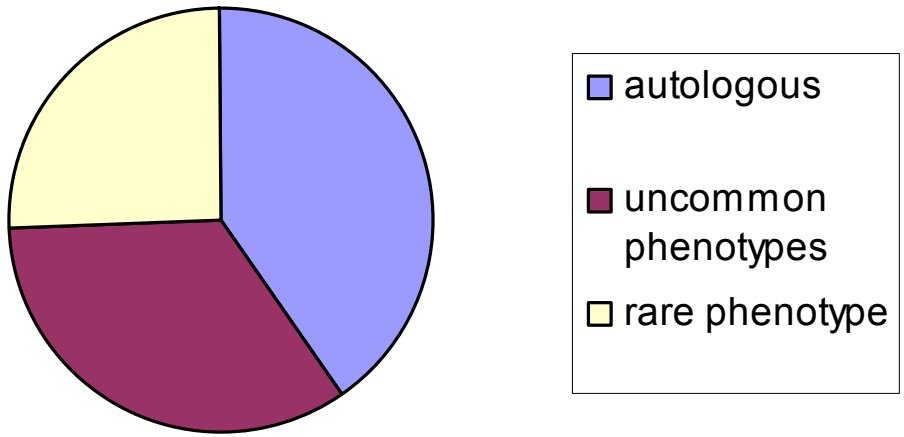
Current status

Current frozen stock, appx 1700 units



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National stock

Rare combinations

- O R1R1 (CCDee)
- O R2R2 (ccDEE)
- O rr (ccdee)

With Fya neg or Fyb neg; Jka neg or Jkb neg; S neg or s neg, k neg

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International stock

Null types

- *Bombay*
- *Rhesus Null*
- *Kell Null*
- *Lua-b-*
- *Fya-b-*
- *Jka-b-*
- *U neg; S-s-*
- *pp;Tja neg; P1-.Pk-,P-;*

Negative for HFA

- *Kpb*
- *Lub*
- *Vel*
- *Ge*
- *Coa*
- *Lan*
- *Yta*

Antigen combinations

- *CCdee*
- *ccdEE*
- *k neg en Fya neg*

or k neg en Jka neg,S neg etc.

Incoming Units

	1997	1998	1999	2000	2001	2002	2003	2004	Total
Netherlands	27	32	45	33	20	16	11	10	**194**
Finland	7	5	1	2					**15**
Swiss		1	1	11	14	14	10		**51**
Sweden	11	14	19	13	16	10	15	13	**111**
Denmark		1	4	2					**7**
Italy									
Austria									
Hungary									
Germany									
Norway		6							**6**
Belgium									
Spain									
UK	7		3						**10**
Total	**52**	**59**	**73**	**61**	**50**	**40**	**36**	**23**	**394**

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Outgoing Units

	1997	1998	1999	2000	2001	2002	2003	2004	Total
Netherlands	22	29	9	25	21	18	9	37	**170**
Finland		3							**3**
Swiss	2			2					**4**
Sweden		4	2				2		**8**
Denmark			2			4			**6**
Italy			17			2			**19**
Austria			4						**4**
Hungary			4						**4**
Germany	9	13	19	5	5	2	5		**58**
Norway	3		3			2			**8**
Belgium	2	4	6	17	6				**35**
Spain					8				**8**
UK									**0**
Rejected	6	9	17	2	5		5	5	**49**
Total	**44**	**62**	**83**	**51**	**45**	**28**	**21**	**42**	**376**

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Balance-sheet

	1997	1998	1999	2000	2001	2002	2003	2004	Total
Netherlands	5	3	36	8	-1	-2	2	-27	24
Finland	7	2	1	2					12
Swiss	-2	1	1	9	14	14	10		47
Sweden	11	10	17	13	16	10	13	13	103
Denmark		1	2	2		-4			1
Italy			-17			-2			-19
Austria			-4						-4
Hungary			-4						-4
Germany	-9	-13	-19	-5	-5	-2	-5		-58
Norway	-3	6	-3			-2			-2
Belgium	-2	-4	-6	-17	-6				-35
Spain					-8				-8
UK	7		3						10
Total	14	6	7	12	10	12	20	-14	67

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Logistics incoming units

- Processing of viral test results from country of origin
- Retesting according to the Dutch Guidelines (+ additional testing)
- Storage of sample for additional testing
- Freezing within 7 days after blood draw
- Check ABO, Rhesusphenotype (each time), complete typing (2x) and rare typing (each time)

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Blood transmissable infectious diseases

HBsAg

Lues

HIV 1&2 as

HCV as

HTLV 1&2 as

HB core as (USA)

ALT (USA)

HCV NAT

HIV NAT

No British donors

No tf in donor history

…..

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Logistics delivery

- **Order by telepone and confirmation on paper (fax or email) including current requirements in receiving country**
- Acceptance of potentially deliverable units (fax)
- Thawing and inclusion results viral testing
- Transport via World Courier
- Administration within 24 hours after thawing

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Request for erythrocytes from the Bloodbank of the Council of Europe

Name					
Date of birth			Male/ Female		
Bloodgroup/ Rhesus					
Antibodies					
If necessary confirmed by					
Erythrocyte-typing required					
Physician		Date of requirement			
Institute					
Address					
Telephone		Fax			
Number of units required		Leucocyte-depleted		Other requests	
Clinical information					
Current operative bloodinfectious tests required in your country THIS MUST BE STATED					

Please complete this form and return by fax.

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Sanquin Diagnostics (CLB)
Department: Immunohaematology/diagnostics
Direct dial: +31 20 512 3373
Direct fax: +31 20 512 3685

ACCEPTANCE FORM for unit number: _____

Concerning unit for: _____

Date of birth: _____

Test	Date of unit tested and conform normal standards	Date of unit tested and deviating from normal standards	Unit not tested
antibodies against Human Immunodeficiency Virus HIV)			
Human Immunodeficiency Virus (HIV-NAT, PCR)			
antibodies against Human T-cell lymphotropic virus, type 1 en 2 (anti-HTLV)			
hepatitis B surface antigen			
antibodies against hepatitis B-core antigen			
antibodies against hepatitis C-virus (anti-HCV)			
hepatitis C-virus (HCV-NAT, PCR)			
anti-treponema antibodies			
SGPT/ALAT			

This unit is leucocyte depleted	YES	NO

This unit originates from a non-British donor. However, it is unknown whether the donor has been in the United Kingdom for a longer period than six months between 01-01-1980 - 31-12-1996

☐ It is unknown if the donor of this unit has received a bloodtransfusion after 01-01-1980.
☐ This donor has received bloodtransfusion(s) after 01-01-1980.

Approximate costs per unit:
Approximate costs freight for all units:

Arrival date:
Arrival time:

When accepted, please sign the form and return by fax as soon as possible.

Place:
Name:

Date:
Signature:

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Date			
Your reference			
Our reference	mo/ml/res 2.1	Direct dial	+31 20 512 3373
Division	Sanquin Diagnostics (CLB)	Direct fax	+31 20 512 3685
Department	Immunohaematology-D		

These are the results of the tests performed on donor number.. …….unit number……

TEST	RESULT	DATE TEST PERFORMED
• antibodies against Human Immunodeficiency Virus (HIV)	:	:
• Human Immunodeficiency Virus (HIV-NAT, PCR)	:	:
• antibodies against Human T-cell lymphotropic virus type 1 en 2 (anti-HTLV)	:	:
• hepatitis B surface antigen	:	:
• antibodies against hepatitis B core antigen	:	:
• antibodies against hepatitis C virus (anti-HCV)	:	:
• hepatitis C virus (HCV-NAT, PCR)	:	:
• anti-treponema antibodies	:	:
• SGPT/ALAT	:	:
• Leucocyte depleted	:	

This unit originates from a non-British donor. However, it is unknown whether the donor has been in the United Kingdom for a longer period than six months between 01-01-1980 - 31-12-1996.
It is unknown if the donor of this unit has received a bloodtransfusion after 01-01-1980.

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Drs M.A.M.Overbeeke M.Sc.,
Head of Department of Immunohaematology -D– Sanquin Diagnostics at CLB:

Case 2
Extra fast transportation

Request: Bergen – Norway

3/4/96
Needed: 4 EC Kp(b-), male patient, 37 yrs (O D+)
Oesopagus aneurysm

18/11/96
Needed: 4 EC Kp(b-)
Surgery

27/1/97
Needed: 4 EC Kp(b-)
No direct flight available. In Oslo military plane to Bergen

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Rare blood

- Frozen stocks
  - Germany: Different places
  - Belgium: Antwerp and Liege
  - France: Paris
  - UK: Birmingham
  - Sweden: Umeå and Stockholm

- Rare donor list

WHO
  - rare donor program Bristol
  - ARC list
  - AABB list

IBGRL

aaBB

- Swiss

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Future

- Introduce –80ºC freezing procedure
  - Longer shelf life (sterility)
  - Safer handling

  Cave: Current stock not completely replacable

- Typed donors

  -Large scale serological typing (almost) impossible

  -Large scale genotyping of blood group antigens?

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