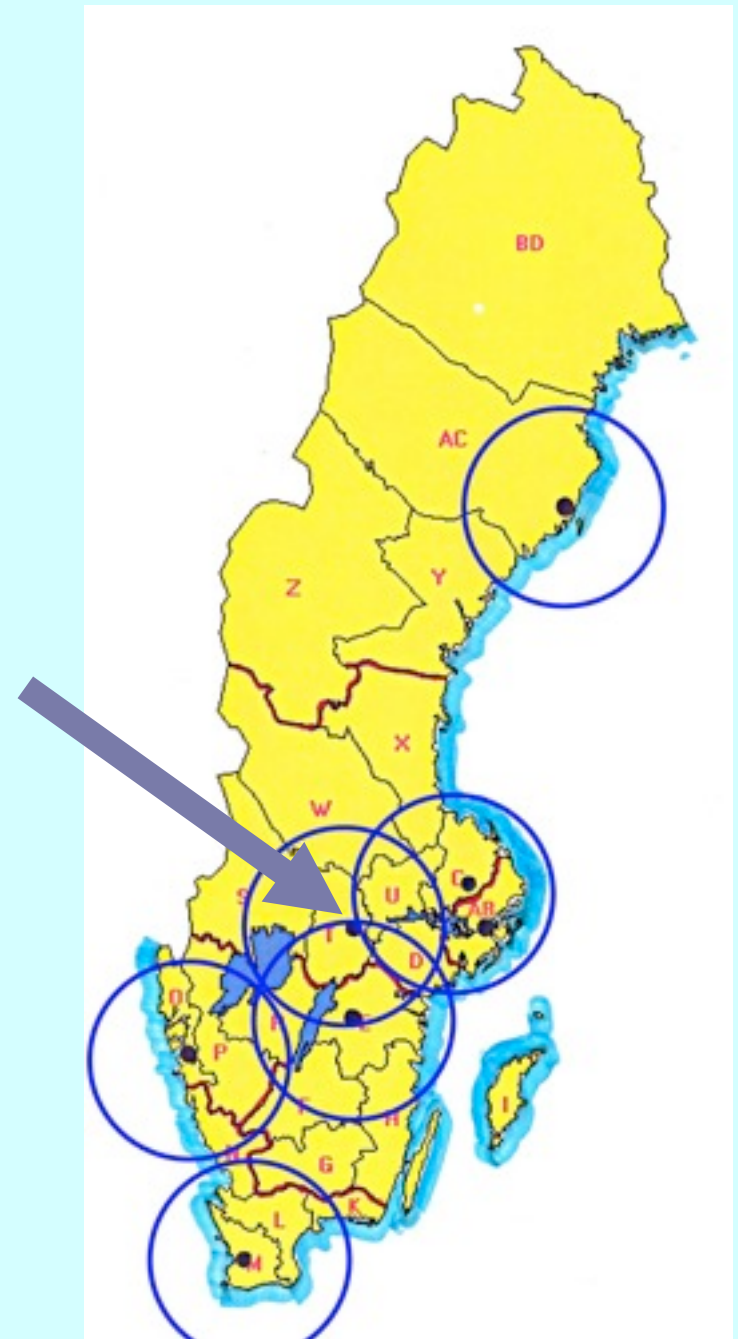


Olle Berséus

MD, PhD, Ass.professor
Medical advisor in transfusion medicine
to the Swedish Armed Forces.

Department for Transfusion Medicine
Örebro University Hospital
Sweden



Adverse patient effects from transfusion of ABO-incompatible plasma (1)

Immediate effects

- Formation of A-/B-immunocomplexes
- Agglutination and hemolysis of the red cells
- Activating mononuclear cytotoxic cells
- Formation and release of acute phase reactants (complement factors, cytokines)
- Activation and aggregation of platelets
- Activation of the coagulation system (DIC?)

Delayed effects

Adverse patient effects from transfusion of ABO-incompatible plasma (2)

Delayed effects

within 2h
(up to 4 days)

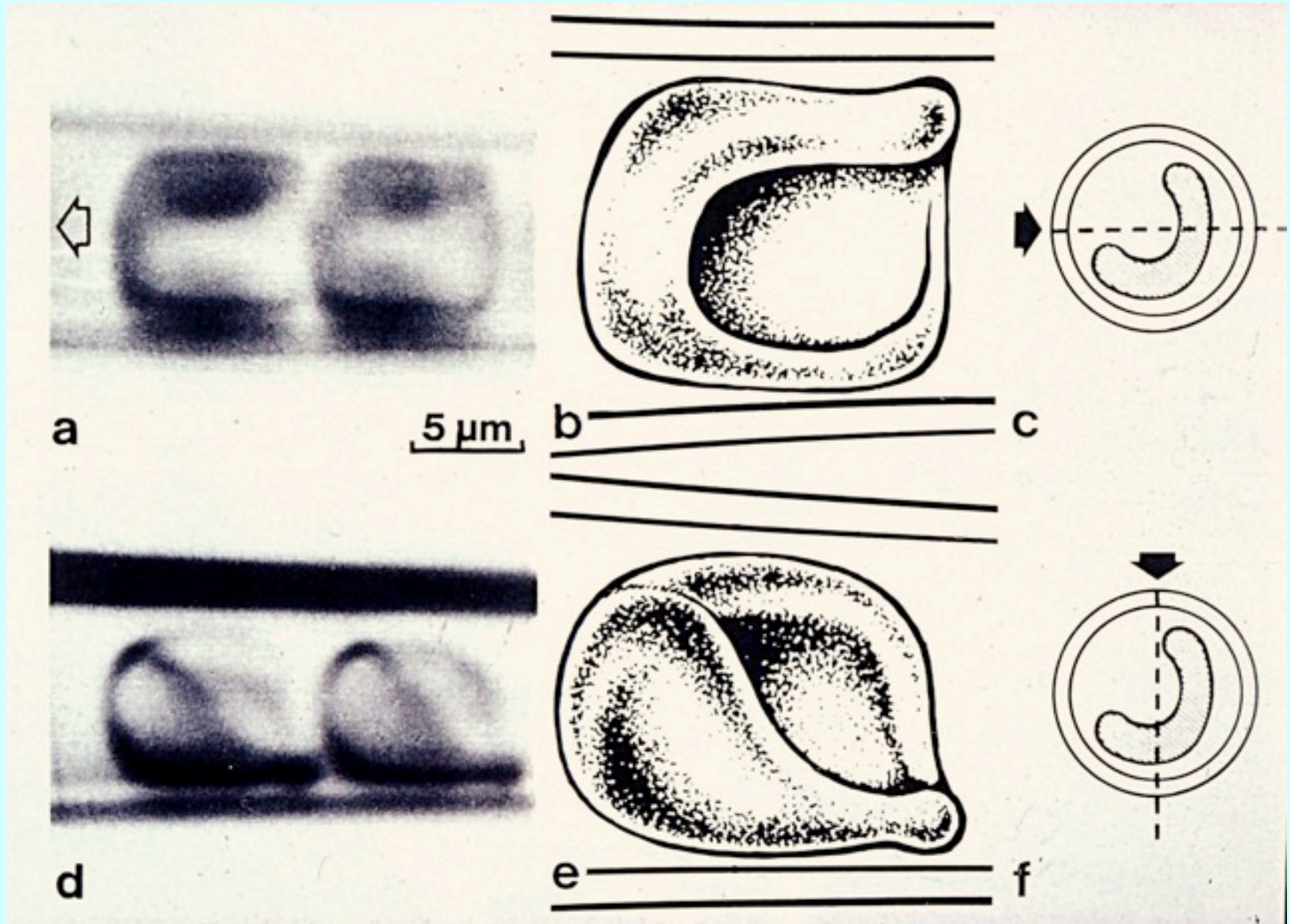
- Febrile reactions
- Increased osmotic fragility of the red cells
- Persistent heme induced activation of the inflammatory response
- Persistent thrombocytopenia
- Coagulopathies and increased fibrinolysis
- Part in the pathogenesis of transfusion related acute lung injury (TRALI)

Red cell storage

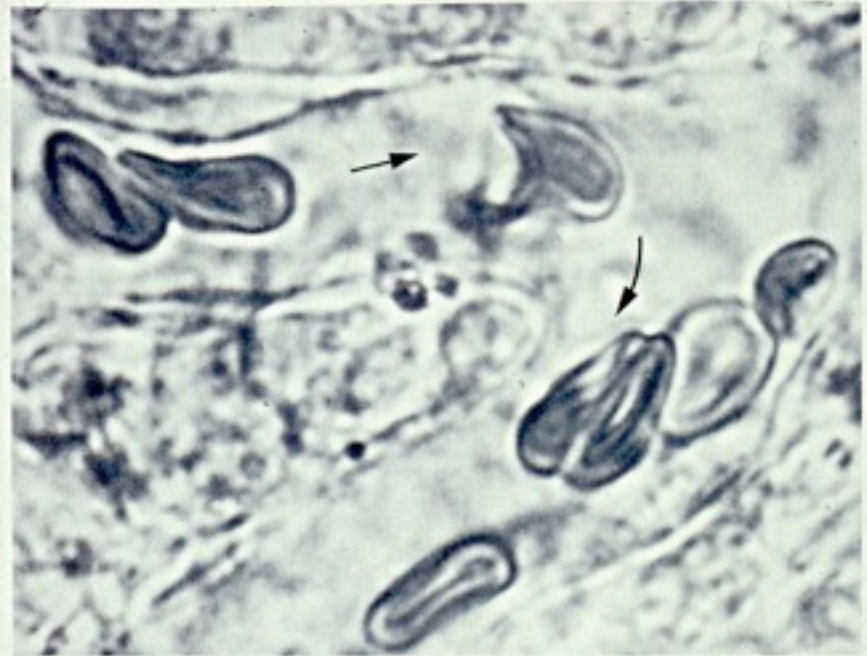
Whole blood
red cells after
storage for
3 weeks in
ACD-solution



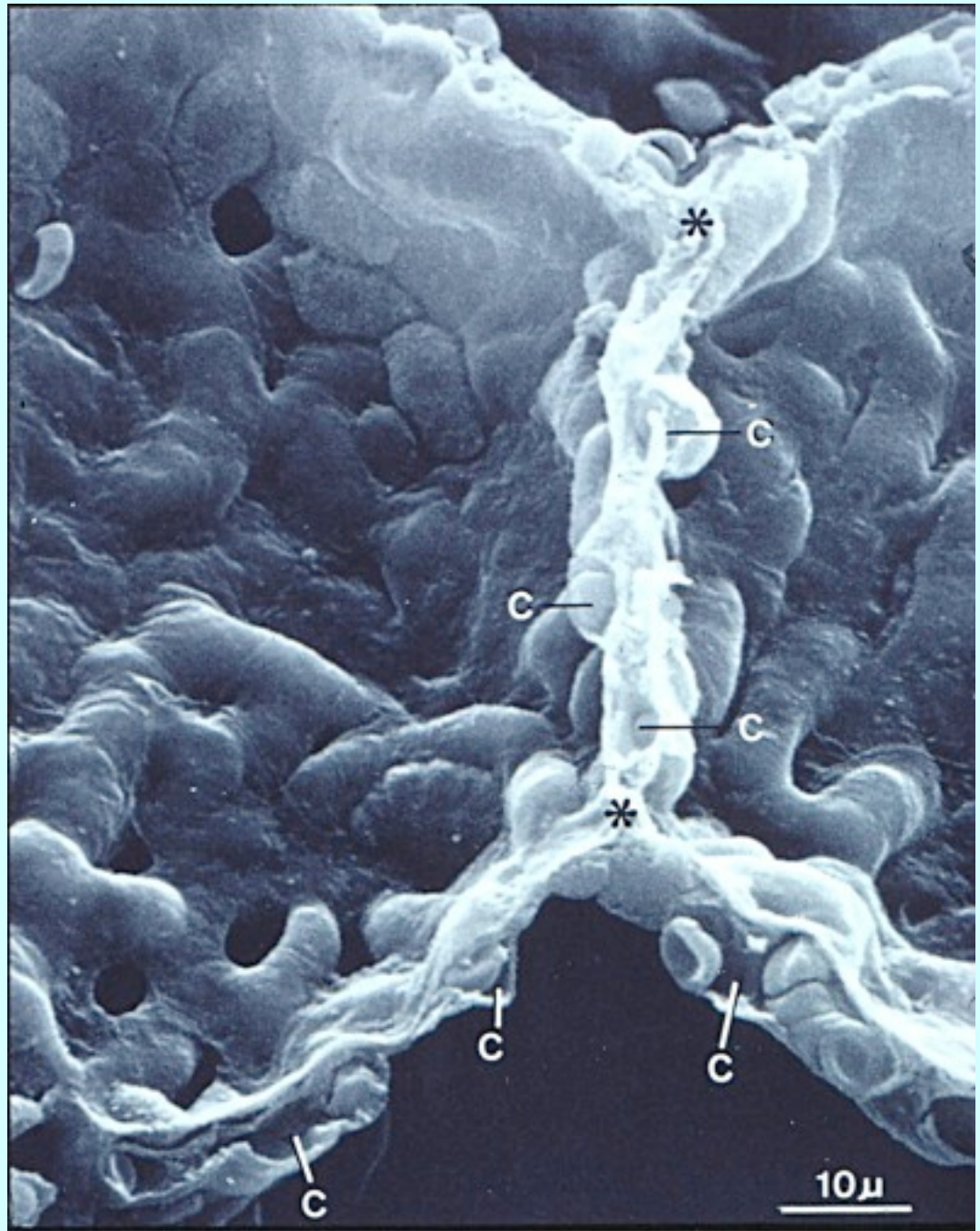
Erythrocyte-plasticity (1)



Erythrocyte- plasticity (2)



Red cells in a lung capillary



Levels of blood group immunization (1)

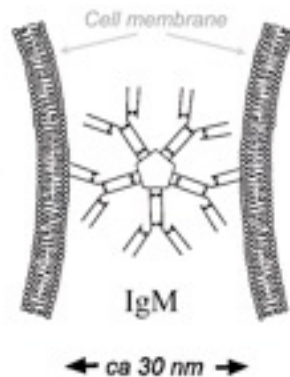
Age

0 – 3 months

No blood group antibodies present

3 months –

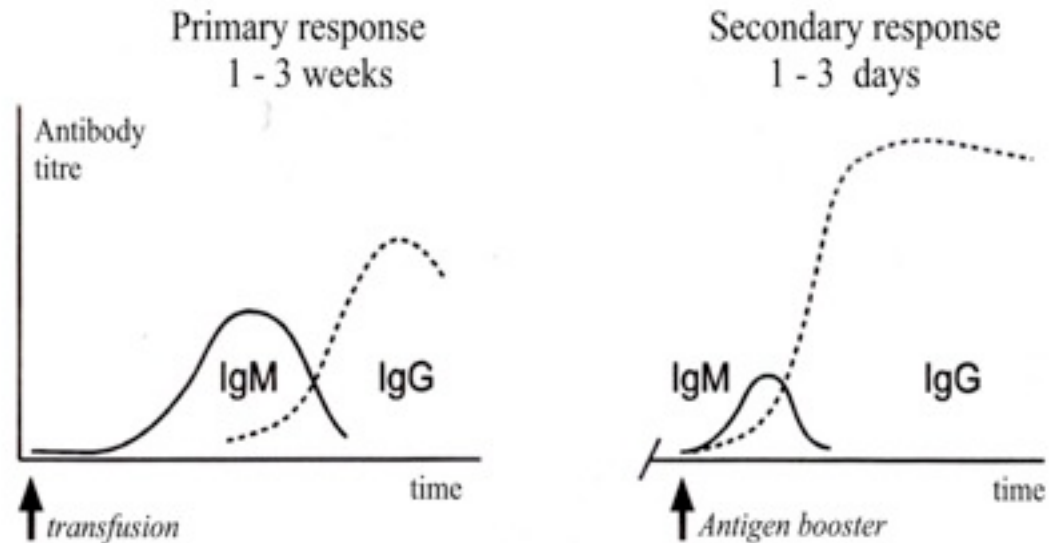
Bacterial A and B blood group substances from the normal intestinal bacterial flora induce the formation of A- and or B-antibodies of IgM-class (the "natural antibodies")



Levels of blood group immunization (2)

After pregnancy or transfusion of a blood product

Active immunization with the production of specific blood group antibodies of both IgM and IgG class



Berséus 2011

Vaccination mediated A and B immunization

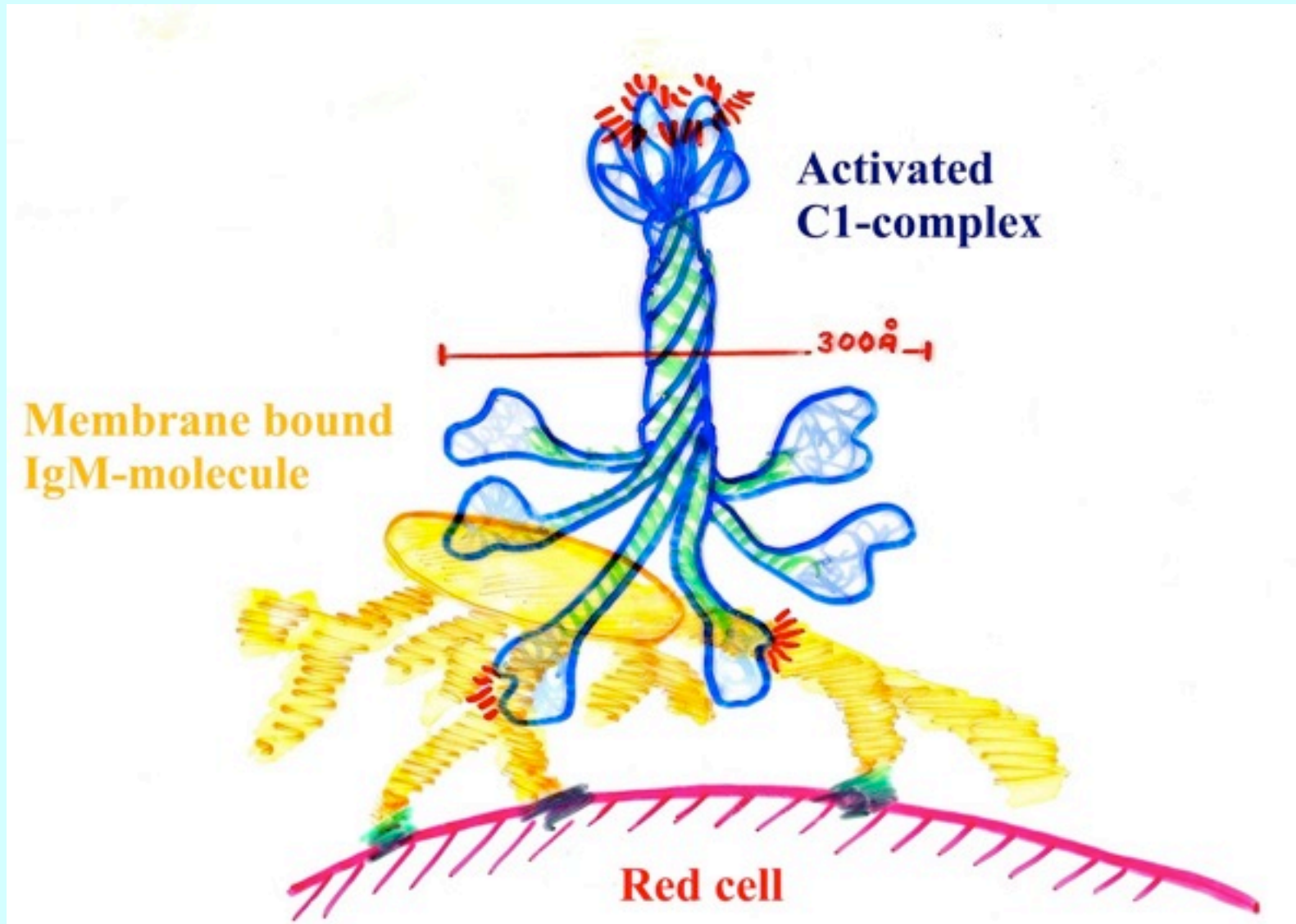
Elevated levels of both IgM and IgG class anti-A and/or anti-B have been reported after vaccinations with vaccines against:

tetanus, typhoid, diphtheria, plague, meningococcus, hemophilus influenza, influenza virus A/B

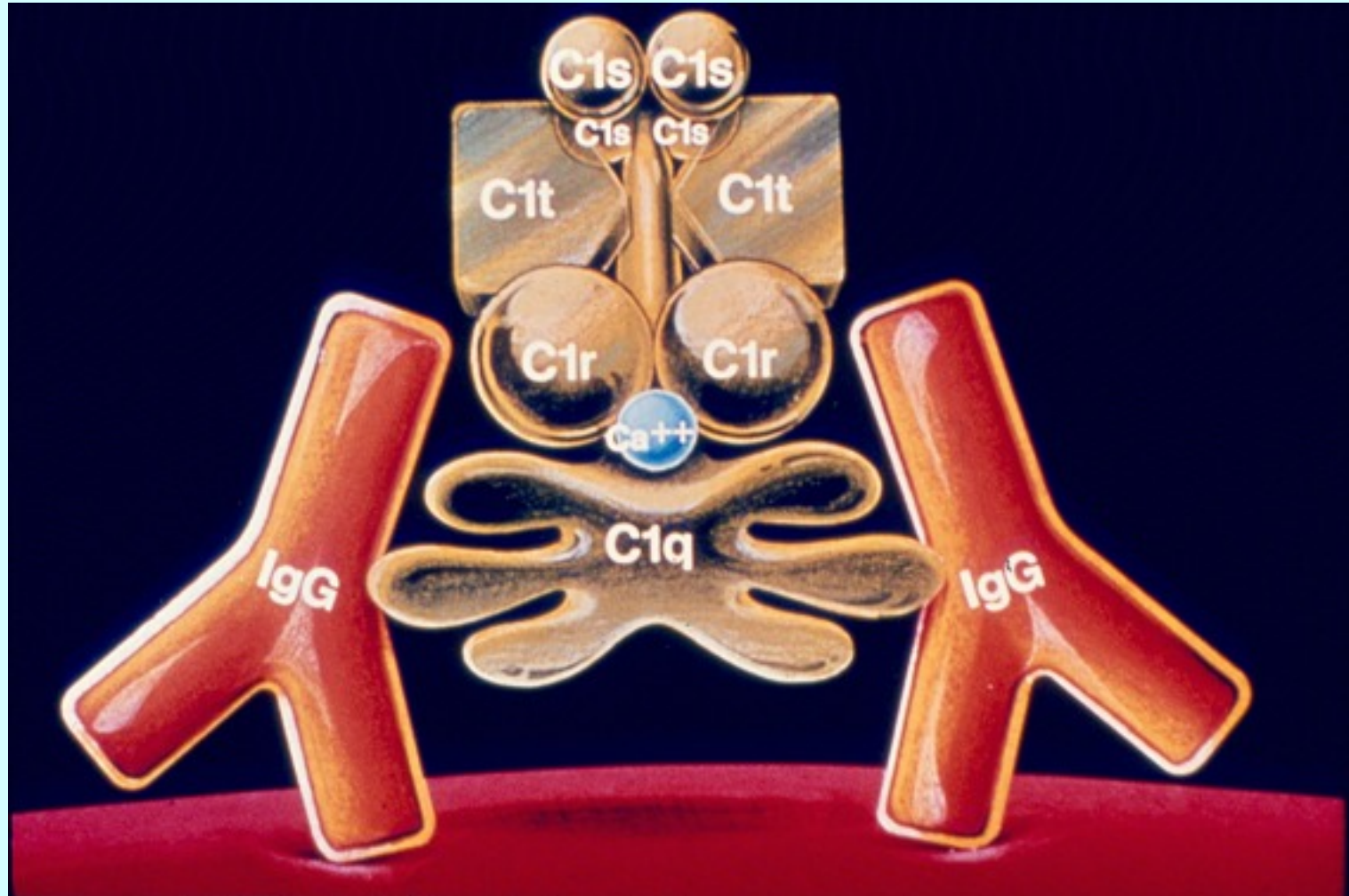
The stimulative activity varies with the different brands of the same vaccin

Very high levels of IgM and IgG class anti-B has been described in a group A donor after per oral intake of a commercial probiotic containing lactobacillus

Complement activating IgM molecule



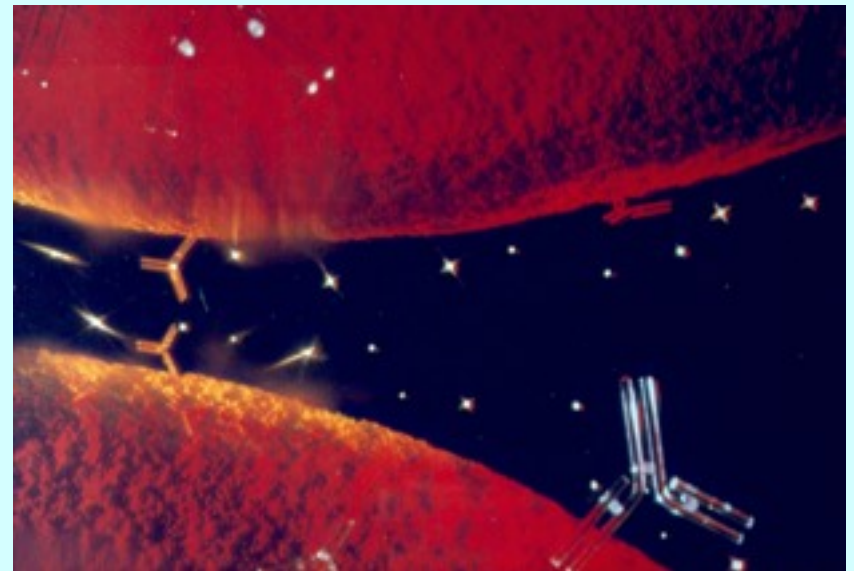
Complement activating IgG molecule



Agglutination of red cells by IgM antibodies

IgM antibodies with
molecular weight 900
kD easily agglutinates
antigen positive red
cells.

IgG antibodies with
molecular weight 150
kD cannot agglutinate
antigen positive red cells



Quantification of anti-A and anti-B

Titration: in a saline medium (*only IgM*)
with antiglobulin method (*IgG and/or IgM*)

Technique: agglutination in test tubes
agglutination, separation in gel tubes

Flow cytometry: specific quantification of antibody
technically complicated, expensive
"Gold standard"

Quantification of anti-A and anti-B

Titration: in a saline medium (*only IgM antibodies*)
with antiglobulin method (*IgG and/or IgM antibodies*)

Technique: agglutination in test tubes
agglutination and separation in gel tubes

Flow cytometry: specific quantification of the antibody
technically complicated and expensive
"Gold standard"

No functioning standardization or reference value

No generally recognized method for routine laboratory work

Reports of hemolytic reactions by transfusion of group O blood to non-group O recipients

1911 Ottenberg proposes group O blood donors as "universal donors"

1945-1986 15 non military publications with case reports of severe hemolytic reactions after a transfusion of group O blood or plasma to non-group O recipients has been found and reviewed.

Antibody titres varied from 16 to >8000 (IgM / IgG)

Volume of infused plasma varied from 25 mL to 800 mL

All patients recovered except for 2 fatalities

Military experiences of the transfusion of group O blood to non-group O recipients

World War II

Group O blood used universally in US armed forces

In 1944 reports of haemolytic reactions in blood units with high titres anti-A/B. Only "low titre"* group O blood units are being sent to military hospitals.

No further reports of haemolytic reactions

* Anti- A and or anti-B saline titre < 250

Military experiences of the transfusion of group O blood to non-group O recipients

World War II

Group O blood used universally

1944 hemolytic reactions with high titres anti-A/B and only "low titre" group O blood is sent to military hospitals
No further reports of hemolytic reactions

Korean War

Only "low titre" group O blood used

1952 >60000 transfusions no hemolytic reactions

Severe IHTR after return to recipient's blood group.
After massive transfusion continue group O blood.

Military experiences of the transfusion of group O blood to non-group O recipients

Vietnam war

"Low titre" group O blood used universally.

From 1965 all blood groups used at major military hospitals, group O blood in the periphery

1967-69 >230000 transfusions

Only 1 IHTR from transfusion with group O blood
(A high titre unit by mistake released from hospital
the patient had uneventful recovery)

Case reports of hemolytic transfusion reactions in plt transfusions containing ABO-incompatible plasma

Publication	Year	Patient blood group	Patient age (y) /sex	Infused volume, mL	Renal complication	Severe coagulopathy	Titre anti-A and anti-B		Diagnosis / (recovered = R, died = D)
							saline	AHG	
Lundberg (43)	1975	A ₂ B	40 / M	80	none	none	NR	NR	Leukemia (R)
Zoes (44)	1976	AB	44 / F	500	none	none	A: 256 B: 64	256 NR	Leukemia (R)
McLeod (45)	1982	A	45 / M	200	none	none	A: 1280	10240	Erythroleukemia (R)
Siber (10)	1982	A	20 / M	199	none	none	A: NR	8192	Leukemia (R)
Conway (46)	1984	A	15 / F	200	dialysis	DIC	A: 8192	4096	Leukemia, BMT (R)
Pierce (47)	1985	A B	2 1/2 / F 58 / F	200 50	uremic none	DIC none	A: 51 B:512	32000 16384	Leukemia, ABMT (D) Cardiac surgery (R)
Ferguson (48)	1988	A	66 / M	50	none	none	A: 256	>4000	Leukemia (R)
Reis (49)	1989	B	56 / M		none	none	B: NR	4096	Aplastic anemia (R)
Murphy (50)	1990	A	30 / F		uremic	none	A: 512	2048	Leukemia, ABMT (R)
Chow (51)	1991	AB	18 / F	NR	none	none	A: 1024	NR	Leukemia (R)
Mair (14)	1998	A	28 / M	225	none	none	A: 128	NR	Neuroblastom (R)
McManigal (52)	1999	AB	78 / F	300	none	none	A: NT	NR	Cardiac surgery (R)
Larsson (53)	1999	A	44 / F	371	none	none	A: 16384	NR	Leukemia (R)
Valbonesi (54)	2000	A A	55 / F 16 / F	35 35	none dialysis	none none	A: 128 A: 128	8000 8000	Breast cancer (R) Aplastic anemia (R)
Sauer-Heilbom (55)	2002	B	35 / M	526	uremic	none	B: 4096	2048	BMT (R)
Gresens (56)	2003	A	29 / M	250	none	none	A: 1024	NR	Gunshot, abdomen (R)
Ozturk (57)	2003	A	21 / M	600	dialysis	none	NR	NR	Myelodysplasia (R)
Josephson (15)	2004	A A	Adult /NR Adult /NR	50 50	none none	none none	A: 256 A: NR	8192 1024	Leukemia (R) Leukemia (R)
Fauzie (58)	2004	A A	NR / NR NR / NR	598 390	none none	none none	A: 256 A: 32	512 32	Leukemia Leukemia
Angiolillo (59)	2004	A	8months/M	15 / kg	anuria	mult.-organ failure	A: 128	NR	Langerhans cell histiocytosis (D)
Reinhardt (in 60)	2005	A	NR / NR	NR	none	none	A: 512	NR	NR
Sapatnekar (61)	2005	A	2 / F	145	none	DIC	A: 2048	16384	Medulloblastoma (R)
Sadani (62)	2006	A	65 / F	200	none	none	A: 128	1220	Leukemia (R)
Harris (63)	2007	A	8 / F	300	none	none	A:256	4096	Leukemia (R)
Daniel-Johnson (12)	2009	B B	40 / M 5 / M	100 37	none none	none none	B: 16384 B: 16384	16384 16384	Leukemia (R) Aplastic anemia (R)

Case reports of hemolytic transfusion reactions in plt transfusions containing ABO-incompatible plasma

Summary of 26 case reports 1975 – 2009:

21 patients with systemic malignancies 2 fatalities
4 surgical patients 0 fatalities

In all patients but one the transfused plasma had anti-A / anti-B titres above 100 (saline) and 400 (antiglobulin).

All patients with less than 200 mL transfused plasma had anti-A / anti-B titres above 1000 (antiglobulin).

Conclusion:

In emergency life saving support the risks for an IHTR from the transfusion of group O blood or blood products to a non-group O recipient constitutes a minor risk which with good margins is outweighed by the benefit.

Whenever possible all “universal” donors should be screened for low titres of anti-A and anti-B preferably for antibodies of both IgM (saline technique) and IgG (antiglobulin technique).

For non emergency situation the above mentioned screening for anti-A and anti-B of both IgM and IgG classes should be mandatory.