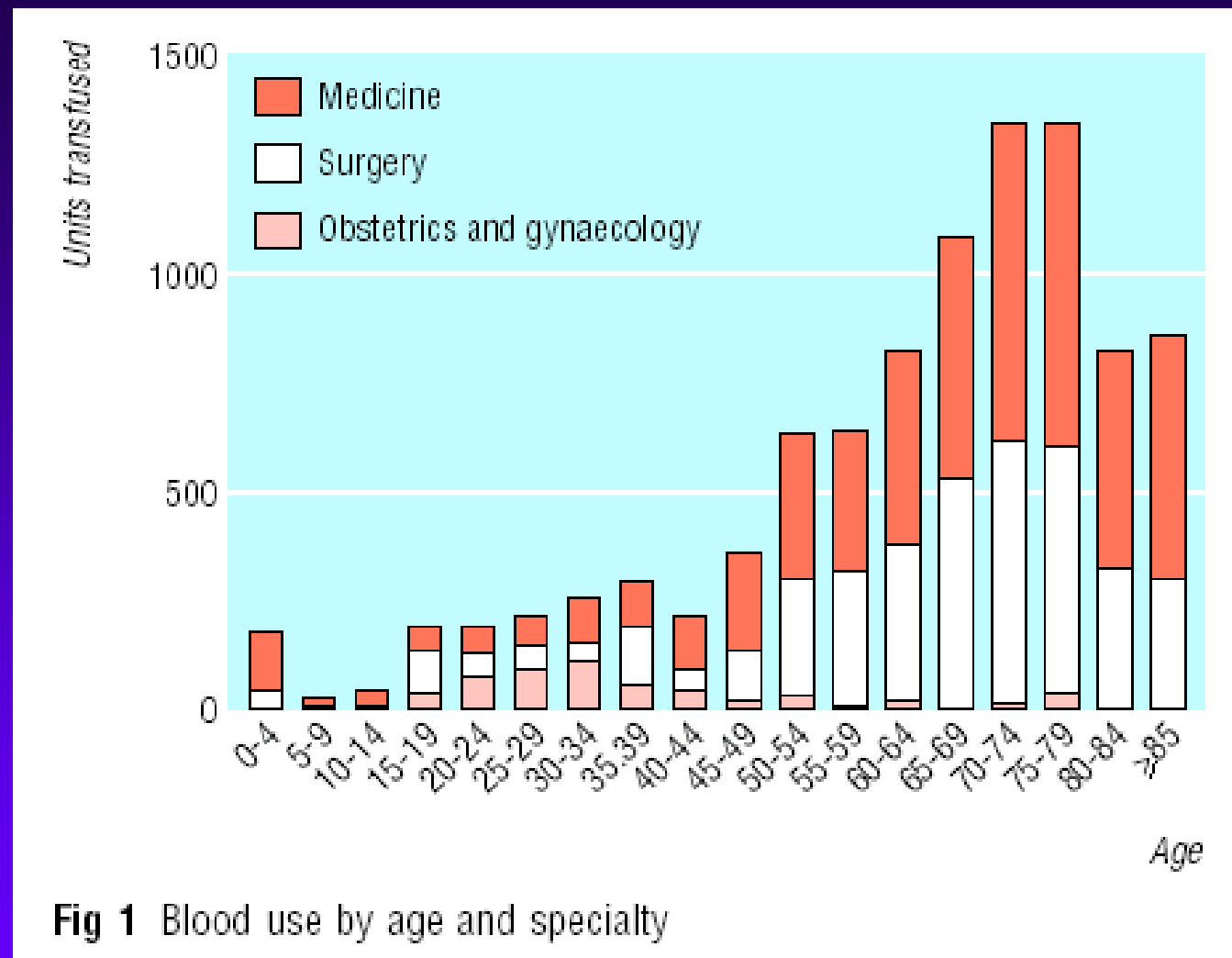


Transfusing the Neonate

Current Guidelines

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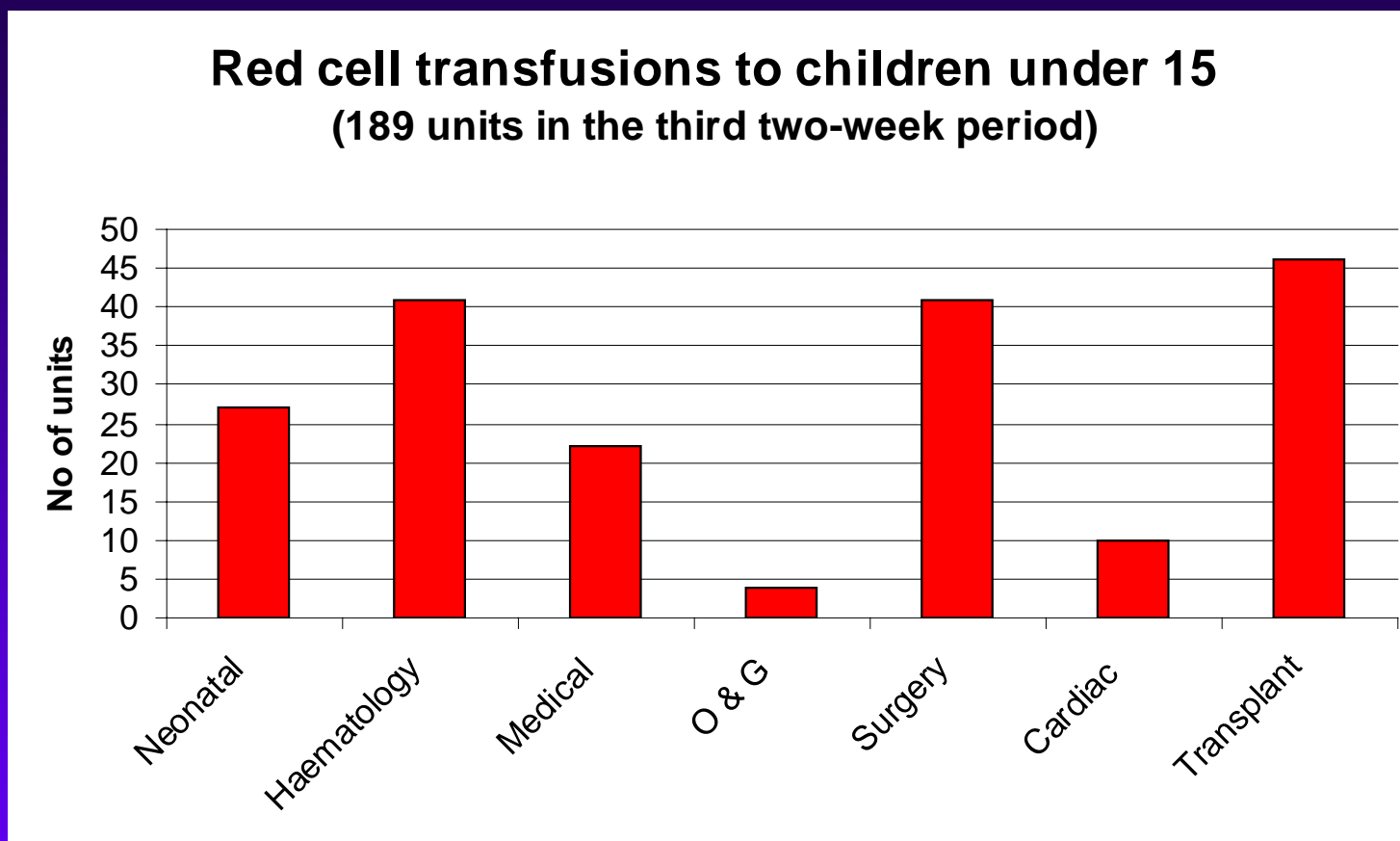
Red cell transfusion in blood banks served by Newcastle



(From Wells et al. eBMJ 2002; 325)

Pop 2.9 mill

Where does blood go? Data from Newcastle Blood Centre



Total units for children over the 6 weeks was 451 units (3%)
3.0% all blood used.
(Data made available by Angus Wells and Jonathan Wallis)

SHOT - Adverse events in paediatrics

- 89/1148 (7.7%) in 5 years
- 78% (69) incorrect component transfused
 - 8 of these occurred because lab staff or clinician lacked understanding of the special needs of neonates
- 3/7 children died with transfusion related acute lung injury (TRALI)
- 2/2 children with TA-GVHD died

Why do neonates need transfusion?

- To ensure adequate tissue oxygenation (but how to measure?)
- To treat clinically significant anaemia

To ensure adequate tissue oxygenation

Depends upon:

- Concentration and type of Hb
- Concentration of 2,3 DPG
- Cardiopulmonary function of neonate

Measure:

- peripheral oxygen extraction by spectroscopy
- lactate?

New Transfusion Guidelines for Neonates and Older Children

- Transfusion Task Force, BCSH
- Lack of suitable evidence – mostly level 3 and 4 (i.e. based on case reports, comparative studies and ‘expert’ opinion)
- Update from previous guidelines of 1994

(bcshguidelines.com and *BJHaem* 2004;124; 433-453)

How to administer?

- All products must go through a 170-200 micron mesh filter
- There are several giving sets on the market; both free flow and ones which can run through a pump
- Some paediatric centres like to have an integral burette
- Microaggregate (40 micron) are never necessary

Transfusion-associated GvHD

- Immune suppression
 - Congenital (SCID, di George syndrome)
 - Stem cell transplants
 - Purine antagonists (fludarabine)
 - Hodgkin's disease
 - ? B cell malignancies
- Prevent transfusion of viable lymphocytes by irradiation to 25Gy

Plasma and Platelet compatibility

- Platelets should be ABO and RhD identical with recipient. Haemolysis may occur with group O.
- Rh compatible FFP because contains red cell stroma

Exchange Transfusion

- Severe anaemia at birth
- Severe hyperbilirubinaemia
- Haemolytic disease of the newborn
- Done infrequently now that Rh D sensitisation is largely prevented
 - 250-300 per annum in Newcastle in 1950s
- Needs expertise

Exchange Transfusion

- Disagreement about optimal product
 - Whole blood (Hct 0.35-0.45)? Strongly advocated South of Birmingham
 - Plasma-reduced blood (0.5-0.6)? Used as routine by many centres
- Questionnaire

'The absence of data bears no relationship to the strength of opinions held' James George, 1997

Dilemmas

- Whole blood (Hct 0.35-0.45) in exchange transfusion for anaemia may lead to an insufficient rise in Hb
- Packed cells (Hct 0.75) may lead to too high Hct and need diluting with its attendant risks
- Cannot guarantee that 'plasma-reduced' blood will not have Hct >0.55

Exchange Transfusion guidelines

- Plasma-reduced red cells with Hct 0.50-0.60 should be suitable for exchange for both groups
- Group O or ABO compatible with maternal and neonatal plasma; negative for any red cell antigens determined by maternal antibody status
- CMV negative; less than 5 days old
- Irradiated (essential if previous IUT) and transfused within 24 h

Irradiation

- Always required for granulocytes, all cellular transfusions between family members or HLA matched products
- Never required – no cellular contents- FFP, cryoprecipitate
- Required under specific circumstances

Irradiation of red cells and platelets for babies – When?

- Intrauterine transfusions
- Top-up transfusions to neonates who have received IUT
- Exchange transfusion in neonates
 - Essential for those who have had IUT
 - Preferable for others unless unreasonable delay

Irradiation of red cells and platelets for babies – What?

- For exchange and large volumes (e.g. cardiac surgery) use blood <5 days old and within 24h
- For top-ups use blood irradiated within 14 days of donation and up to 14 days from irradiation.

Other blood products

- FFP is only indicated for documented coagulation disturbances
 - It is virally inactivated with methylene blue for children born since 1.1.96 (increased cost)
 - It will be sourced from US plasma
- Cryoprecipitate is only indicated for correction of a low fibrinogen (less than 0.8-1.0g/l)

Treatment of coagulation disorders

- Make the right diagnosis
 - Specific factor concentrates may be indicated
 - Inherited disorders are rare, and paediatricians will not think of them
 - Vitamin K deficiency can be treated with Vitamin K, not FFP

Transfusion – a hazard in SCBU

Changes in practice

- Use of multiple satellites up to expiry date (up to 35 days)
- Reduction in the transfusion trigger
- Acceptance that Hb may not be the best indicator

10-20 mls

No routine frusemide

Infants >1000g never transfused

<u>Year</u>	<u>%</u>
1982	17
1989	33
1993	64

Widness et al. J.Pediatr 1996: 129; 680-7

Transfusion of neonates and children up to 1 year of age, and for intrauterine transfusions

- Donors must have given at least 1 donation in the previous 2 yrs which is negative for mandatory viral markers

Who needs CMV negative products?

- Still recommended up to 1yr of age
 - Greatest risk in infants >1500g
- Leucocyte depletion to $<5 \times 10^6$ /unit is safe from CMV
- Leucocyte depletion is adequate certainly in an emergency

Intra-uterine transfusion - 1

- Fetal anaemia due to
 - Red cell alloimmunisation (D, c, K)
 - Parvovirus infection
- To prevent hydrops and to allow pregnancy to progress until delivery is safe
 - Start as late as possible and transfuse large volumes to minimise invasive procedures
- Fetal thrombocytopenia

Intrauterine transfusion - 2

- Gp O, low haemolysin and D neg (K neg)
- IAT cross match compatible with maternal serum and neg for relevant antigen
- <5 d old, CPD
- CMV neg and irradiated
- Hct not more than 0.75
- Not transfused direct from 4°C
- Rate 5-10 ml/min (but slower for platelets)

Pretransfusion testing for Neonates and infants within the first 4 months

- Maternal sample
 - ABO and Rh group
 - Screen for irregular antibodies
- Infant sample
 - ABO and RhD by cell only with repeat on same sample (serum will contain maternal antibodies)
 - Direct antiglobulin test
 - If no maternal sample, screen for irregular antibodies by indirect antiglobulin technique

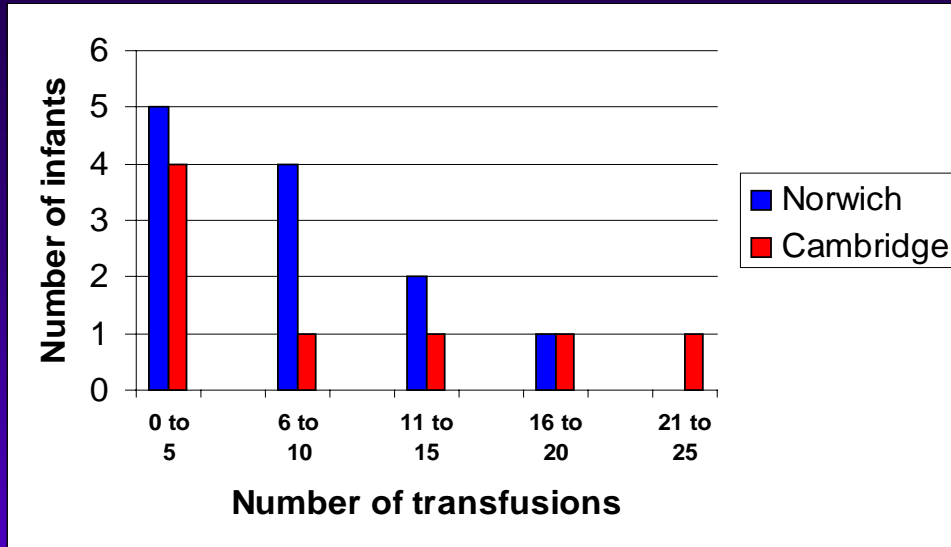
Selection of blood

- Neonate's own ABO and Rh group
- Compatible with any ABO or atypical red cell antibody in maternal or neonatal plasma
- Caution if using electronic selection
 - ABO identical adult blood transfused to a neonate with maternal anti-A or –B may haemolyse even if the DAT is negative due to stronger ABO expression on adult cells

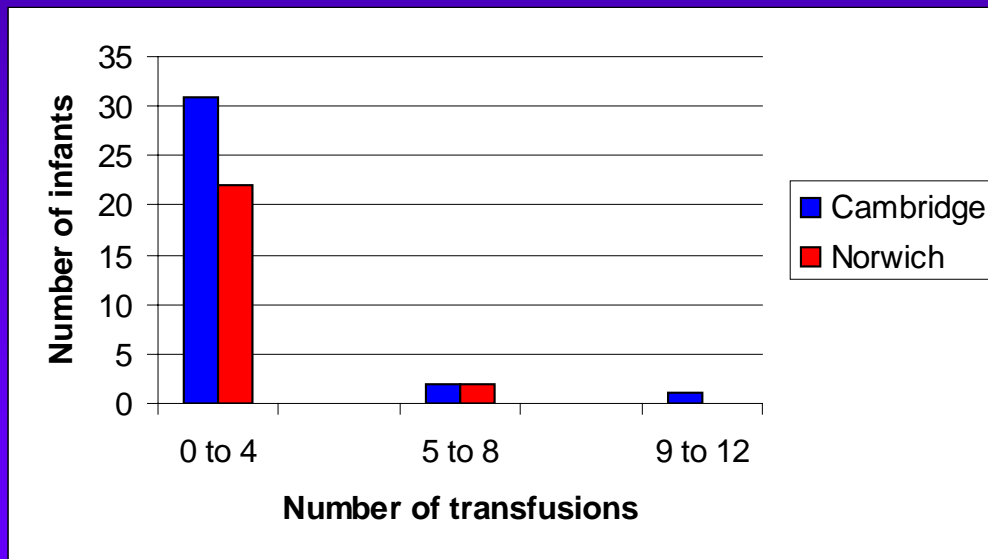
Transfusion of infants

- Small volume transfusions can be given repeatedly over first 4 months
- Infants rarely produce atypical antibodies unless given large volumes of relatively fresh blood

Number of transfusions is related to birth weight



Infants
less than 900g



Infants
more than 900g

Lack of consensus

Data from Dr. Amit Gupta

- Telephone survey of 8 SCBUs in the London Region.
- 3 units issued 8-satellite packs to an individual baby
- 3 units issued 4-satellite packs to an individual baby
- 2 units do not allocate satellite packs from any one donor to a specified baby

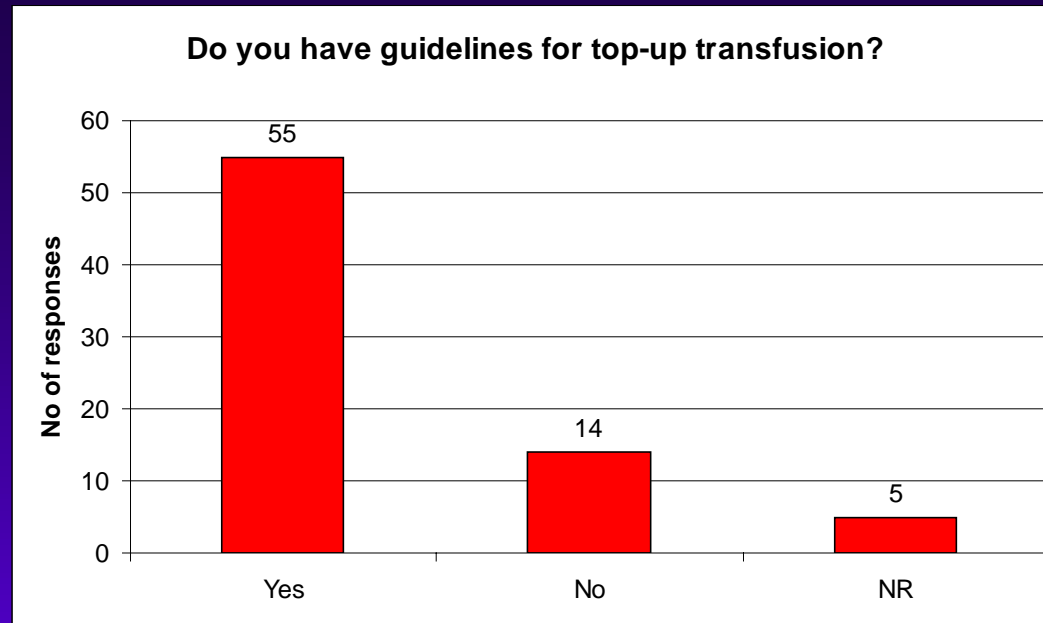
Suggested transfusion thresholds

<i>Infants under 4 months of age</i>	<i>Transfuse at</i>
Anaemia in 1 st 24 h	Hb 12 g/dl
Neonate requiring intensive care	Hb 12 g/dl
Chronic oxygen dependency	Hb 11 g/dl
Late anaemia, stable	Hb 7 g/dl
Cumulative blood loss in 1 week, infant requiring intensive care	10% blood volume
Acute blood loss	10% blood volume

(National Guidelines)

Guidelines from College of American Pathologists 1998

<i>Neonates - criteria</i>	<i>Transfuse at</i>
Absolute anaemia, low retics	Hb 7 g/dl
Neonate with apnoea, bradycardias, sustained tachycardia, mild RDS or cessation of adequate weight gain over 4 days	Hb 8 g/dl
Oxygen dependency – Moderate RDS	Hb 10 g/dl
Severe RDS and ventilation, or severe congenital cyanotic heart disease	Hb 12 g/dl
Cumulative blood loss	Not for low Hb alone unless other criteria
Acute blood loss	10% blood volume



Clinicians who transfuse against agreed local guidelines give fewer transfusions.

Every unit should have guidelines against which to audit. There is a clear need for ongoing national audit and more research.

Surrogate markers of anaemia in neonates

- Respiratory irregularity
- Tachycardia
- Poor weight gain
- Poor suck
- Increased blood lactate

*Or do these just indicate a need
for volume expansion?*

Other considerations

- Oxygen dependency
 - Infants may benefit from a higher Hb
- FFP – PT or APTT ratio >1.5
 - Use 15 ml/kg and repeat coagulation tests

Is there any role for Epo?

- Several studies – but variable entry criteria and doses/routes of administration
- Does not seem to be of benefit in the most transfused group (<800g), nor in the 1st 2 weeks of life
- Studies showed a reduction in transfusion in the placebo group of 50%

Other effects of Epo

- Receptors on bowel - ? Protective against necrotizing enterocolitis
- Stimulates angiogenesis - ? Adverse effect on retinopathy of prematurity
- Beneficial in bronchopulmonary dysplasia
- Beneficial in late anaemia after IUT

Suggested transfusion thresholds for platelet administration

<i>Infants under 4 months</i>	<i>Administer platelets at</i>
Preterm or term neonate with bleeding	50 x 10 ⁹ /l
Sick preterm or term infant not bleeding	30 x 10 ⁹ /l
Stable preterm or term infant not bleeding	20 x 10 ⁹ /l

(National Guidelines)

Granulocyte transfusions?

- Neonates with severe sepsis
 - Deteriorating
 - Severe neutropenia >24 h
- Dose – $1-2 \times 10^9$ granulocytes/kg
 - ABO compatible
 - Irradiated
 - 2 or more daily infusions

Granulocytes in other settings

- No evidence to support prophylactic use
- Empirical evidence of benefit in severe bacterial or fungal infections
- Risk of platelet refractoriness
- Role in congenital neutropenia with severe infection

Does T-activation matter?

- Neuraminidase-producing organisms strip sialic acid residues exposing the T-crypto-antigen
- Adult plasma almost invariably contains an antibody (IgM) to this, and can cause haemolysis in affected recipients – sick infants with necrotizing enterocolitis

Does T-activation matter?

We don't know the answer

- Recommended that babies with NEC receive SAG-M blood
- Any infant with NEC and haemolysis should be investigated
- Other potentially more hazardous blood products should be given as indicated
- Need for more information

Emergency management

- Bleeding neonates with a possible coagulation disorder
 - Take blood before any blood products are given for coagulation factor assays
 - Sample relevant family members
 - Give FFP 10-20ml/kg
 - Avoid intramuscular injections

Blood group compatibility

- Neonates may have IgM 'naturally occurring' anti-A and anti-B
- Plasma products must be group compatible
 - FFP
 - Cryoprecipitate
 - Platelet concentrates
- Group O plasma is not safe for babies other than those of group O

Normal ranges in neonates

1

- Factor VIII and V are normal adult values
- Von Willebrand factor is elevated
- Vitamin K dependent factors reach adult values at up to 6 months of age

Normal ranges in neonates 2

- Natural anticoagulants are low at birth
 - antithrombin III
 - Protein C
 - Protein S
- Thrombin generation is reduced in the neonate compared to adults

Consequences of neonatal normal ranges

- Accurate diagnosis of heterozygous states for Proteins C and S, and ATIII is difficult
- Vitamin K deficiency is difficult to diagnose - relative
- Acquired disorders such as DIC will be suggested by clinical state as well as pattern of abnormality

Diagnostic pitfalls

- Sample size
- Sample site - heparin in lines
- Method of venepuncture
- Severe haemophilia A can be missed if the sample is traumatic and thus 'activated'.

Acquired coagulopathies

- Vitamin K deficiency
- Anticoagulant reversal
- Liver disease
- Disseminated intravascular coagulation

Component specification

- Infants in the first year of life should receive blood <5 days old, not collected into SAG-M in the first 6 months of life.
- Children older than 12 months may receive blood 5-10 days old

Monitoring (HSC)

- Trusts should ensure a **minimum data set** for each transfusion
- Documented **in the clinical notes**
 - Indication for transfusion
 - Amount of blood transfused
 - Effectiveness of transfusion
 - Adverse effects and their management
- The **clinical indication for transfusion** must be provided on the request form

Transfusion of neonates

- Many questions
- Audit and further research needed to determine best practice

The delicatessen,
not the supermarket