Managing Transfusion Risk
A clinical and laboratory perspective

Jonathan Wallis
15 years of reports

Marked reduction in:

- ABO incompatibility
- TRALI
- PTP
- TaGVHD
- Bacterial infections

Increase in:

- ATR, allergic and other
- DHTR
- TACO/overtransfusion
## Overall risk of blood transfusion

<table>
<thead>
<tr>
<th>UK Blood services 2010</th>
<th>1996-2010</th>
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<tbody>
<tr>
<td>Red cells</td>
<td>2.18 million</td>
</tr>
<tr>
<td>Platelets</td>
<td>246,000</td>
</tr>
<tr>
<td>FFP</td>
<td>292,000</td>
</tr>
<tr>
<td>Cryo</td>
<td>120,000</td>
</tr>
<tr>
<td><strong>Total units</strong></td>
<td>2.9 million</td>
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Lottery jackpot 1 in 14 million
5 numbers 1 in 55,500 (£1500)
SHOT report forward 1997

‘It is not sufficient that the blood system be safe
- it must be considered safe’
Kreever Commission of enquiry Canadian Blood services 1997

‘…transfusion now exists in a climate, familiar to industries such as nuclear power, where regulatory bodies and public opinion require us to pursue the unattainable goal of absolute safety or zero risk at almost any cost.’
“A product is defective when it does not provide the safety which a person is entitled to expect....

The legitimate expectation of people generally was not that blood would be 100% clean but that all legitimately expectable (reasonably available) precautions had been taken.
Medical interventions are intended to benefit but all have a capacity for harm.

In medical practice we balance benefit vs harm.

We are constrained to consider the cost of all medical interventions.
Assessing safety measures for transfusion

1. **Efficacy**- does the measure reduce risk of harm?
   Eg. Will red cell filters reduce the risk of vCJD?

2. **Does the measure harm the product?**
   Eg. Is MB FFP as good as standard FFP

3. **Does the measure harm the patient?**
   Eg. Do psoralens for pathogen inactivation do harm to the patient?

4. **Cost**
   Could we spend the money elsewhere to better effect?
Units of risk
Ronald Howard, Stanford Un. & David Spiegelhalter Cambridge

• A **Micromort** is a 1-in-a-million chance of dying

• Each day 50 people die of non-natural causes in England and Wales (about 50 million)

• So just living means that we experience a micromort every day (on average)
How far can you travel per micromort?

- Walk: 15 miles
- Cycle: 20 miles
- Motor Bike: 6 miles
- Car: 250 miles
1 in 290,000 chance of death due to transfusion of one unit of any component

= 3.5 micromorts

Hang Gliding = 8 mM
One night in hospital = 75 mM
One week on the slopes = 3.5 mM
Occasional versus Regular harm

You are knocked down by a car

You inhale exhaust fumes
A 18 yr old male has 150 mM per year of using roads
Road traffic accidents UK

Population of 50 million

2500 deaths per year,

23% pedestrians

= 575 deaths per year

Assume accidents on average happen at 35 yrs

Each year 575 x 35 yrs are lost = 20,125 years
Traffic fumes

Lung cancer/respiratory disease

Average life shorter by $\frac{1}{10^{th}}$ year

$\frac{1}{10^{th}}$ year over 50 years = $\frac{1}{500^{th}}$ year pa

Average loss per year = 100,000 years
Life-years lost per year crossing the road....

Accidents 20,125 years

Lung disease 100,000 years
A unit of chronic risk?
David Spiegelhalter

The *microlife*
*1 millionth of a life*

30 minutes off your life-expectancy
Lose 1 microlife from ---

(5 Kg per day)

3 microlives  ?? microlives  180 microlives
Original Article

Duration of Red-Cell Storage and Complications after Cardiac Surgery

Colleen Gorman Koch, M.D., Liang Li, Ph.D., Daniel I. Sessler, M.D., Priscilla Figueroa, M.D., Gerald A. Hoeltge, M.D., Tomislav Mihaljevic, M.D., and Eugene H. Blackstone, M.D.

N Engl J Med
Volume 358(12):1229-1239
March 20, 2008
Kaplan-Meier Estimates of Survival and Death

Figure 4. Kaplan–Meier survival curve showing the cumulative proportion of patients who died over time according to whether patients had had an RBC transfusion.

Risk or Hazard

Number at risk:
Not transfused: 3689 3529 2925 2383 1842 1261 772 391
Transfused: 4909 4449 3913 3340 2773 2213 1713 1073

Trials on outcome

FOCUS trial Carson et al NEJM 2012
No difference in outcome between restrictive and liberal transfusion post #hip repair

TRACS trial JAMA 2010 Hajjar et al
No difference in outcome between restrictive and liberal transfusion post CABG

Titre study UK (Gavin Murphy) results awaited

ABLE study on age of blood in critically ill patients
What are the microlifes associated with transfusion?

Low level risk may be worse than rare but fatal risk

A 30-minute loss per unit transfused is equivalent to one death aged 50 from ABO incompatibility

We should spend proportionate amounts of effort on investigating and reducing low level risk due to blood transfusion and improving the quality of components
Leucodepletion and the law of unintended consequences

• Introduced as a measure to reduce vCJD transmission
• Frank Dobson ‘I Hope it is a waste of money ...’
• Reduced
  – TaGvHD
  – PTP
  – Allergic reactions
  – Platelet refractoriness
  – ??vCJD
• ?increased risk of bacterial infection
Figure 18
Number of bacterial TTI incidents, by year of report and type of unit transfused (Scotland included from 10/1998)
Platelets: options to prevent bacterial infection

1. Pathogen inactivation

2. In storage bacterial screening

3. Pre-transfusion testing
In storage bacterial screening

Platelets collected at time 0
Say 1400 hrs on Monday

Culture performed at 24 hours
1400hrs on Tuesday

Released on day 3
1400 hrs on Wednesday

Transfused on day 4
1400hrs on Thursday

Time before Transfusion = 72 hours
2/3rds of platelets are used for prophylaxis

Platelet days per pack  $3 \times 10^{11}$
= $0.3 \times 10^d$
+ $0.3 \times 9d$
+ $0.3 \times 8d$  etc

Total = $16.5 \times 10^{11}$ platelet days
Platelet days per pack  $3 \times 10^{11}$

$= .3 \times 10d$

$+ .3 \times 9d$

$+ .3 \times 8d$ etc

Total = $16.5 \times 10^{11}$ platelet days

Platelet days per pack  $3 \times 10^{11}$

$= .3 \times 7d$

$+ .3 \times 6d$

$+ .3 \times 5d$ etc

Total = $8.4 \times 10^{11}$ platelet days
At 6 days
Survival x recovery vs fresh
0.75 x 0.65 = 0.5
Assessing safety measures for transfusion

1. Efficacy- does the measure reduce risk of harm?
2. Does the measure harm the product?
3. Does the measure harm the patient?
4. Cost

- Plado study (Slichter et al 2010) showed that transfusion frequency was higher with lower doses
The precautionary principle or precautionary approach states that if an action or policy has a suspected risk of causing harm to the public or to the environment, in the absence of scientific consensus that the action or policy is harmful, the burden of proof that it is not harmful falls on those taking the action.
Alternatives?

Limit storage to 3 days

Guarantee viral testing and release within 12 hrs

Issue fresh directly to hospitals
Shower or Bath?

2009 UK: 33 deaths due to accidental drowning in bath

Jean Paul Marat, one time denizen of Newcastle upon Tyne
Cost/Benefit of Electronic bedside checks

ABO incompatible transfusion
Average recipient 65 yr old
Life expectancy = 15 years
Risk of dying as a result = 1 in 15
On average 1 yr of life lost
Freq of event 1 in 250,000 units
Units transfused per year = 25,000
Cost of prevention = £1,000,000
£1,000,000 per yr of life

NICE £30,000 per quality adjusted year
A patient with a haematemesis was in need of an urgent blood transfusion. The patient’s wristband was contaminated with blood and could not be read. As a consequence the electronic bedside checking system was not used.

There was 1 case of major morbidity reported as a result of an ABO incompatible transfusion.
An elderly patient with an underlying heart condition was transfused, during hip arthroplasty….

An elderly patient was admitted as an emergency during the night with chest pain, ECG changes, chest infection and iron deficiency anaemia, and was deteriorating….

ITU patient receives ABO-incompatible transfusion despite electronic bedside device…

Cancer day unit: Incorrect unit collected and transfused despite training, competency-assessment and fridge locking system…

Man receives emergency transfusion which is both ABO and D incompatible with no ill effects…
Patient grouped as AB

AB units selected
2 unit crossmatch
1 unit incompatible
Further units Xmatched and 2 compatible units transfused
NHSBT received sample and found it to be group A
Group AB red cells

Possibly fatal to 95% of all known patients
Are there alternatives?

Sampling errors...mainly out of hours

Administration errors…mainly non-elective Tx

Use fresh Group O blood for all non elective transfusions
Collect more group O red cells with apheresis

Apheresis red cells from all male donors

Use AB donors for FFP only

50,000 AB male donors

2 donations of 2u by apheresis per year = 200,000 u
Summary

1. Cost of safety measures must be considered
   - NICE should include blood transfusion

2. Low level risk may be as important as headline risk
   - Component quality and efficacy

3. Rethink how we use donors to make transfusion safer
   - Reduce risk and demystify transfusion

Thank you for listening