Acute Transfusion Reactions

How will *you* react?

Definition of acute reaction

An unintended response in a patient that is associated with the transfusion of blood or components

The BCSH guideline can be accessed at http://www.bcshguidelines.com/4_HAEMATOLOGY_GUIDELINES.html?dtype=Transfusion&dpage=0&sspage=0&ipage=0#gl

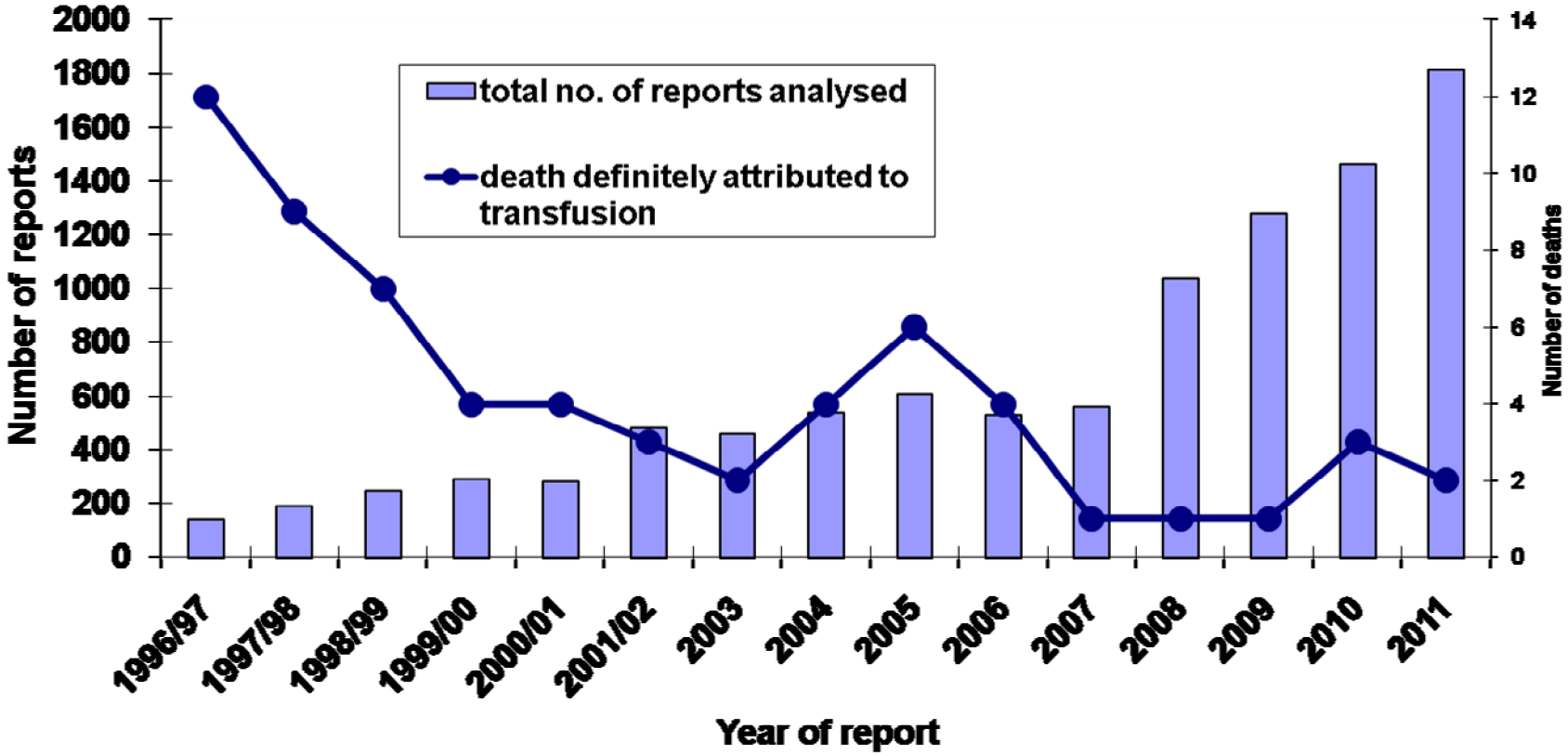
What is the commonest cause of transfusion-related death?

- A TACO (Transfusion Associated Circulatory Overload)
- B Viral infection (e.g. hepatitis B, C, HIV)
- C “Wrong blood”
- D TRALI (Transfusion-Related Acute Lung Injury)

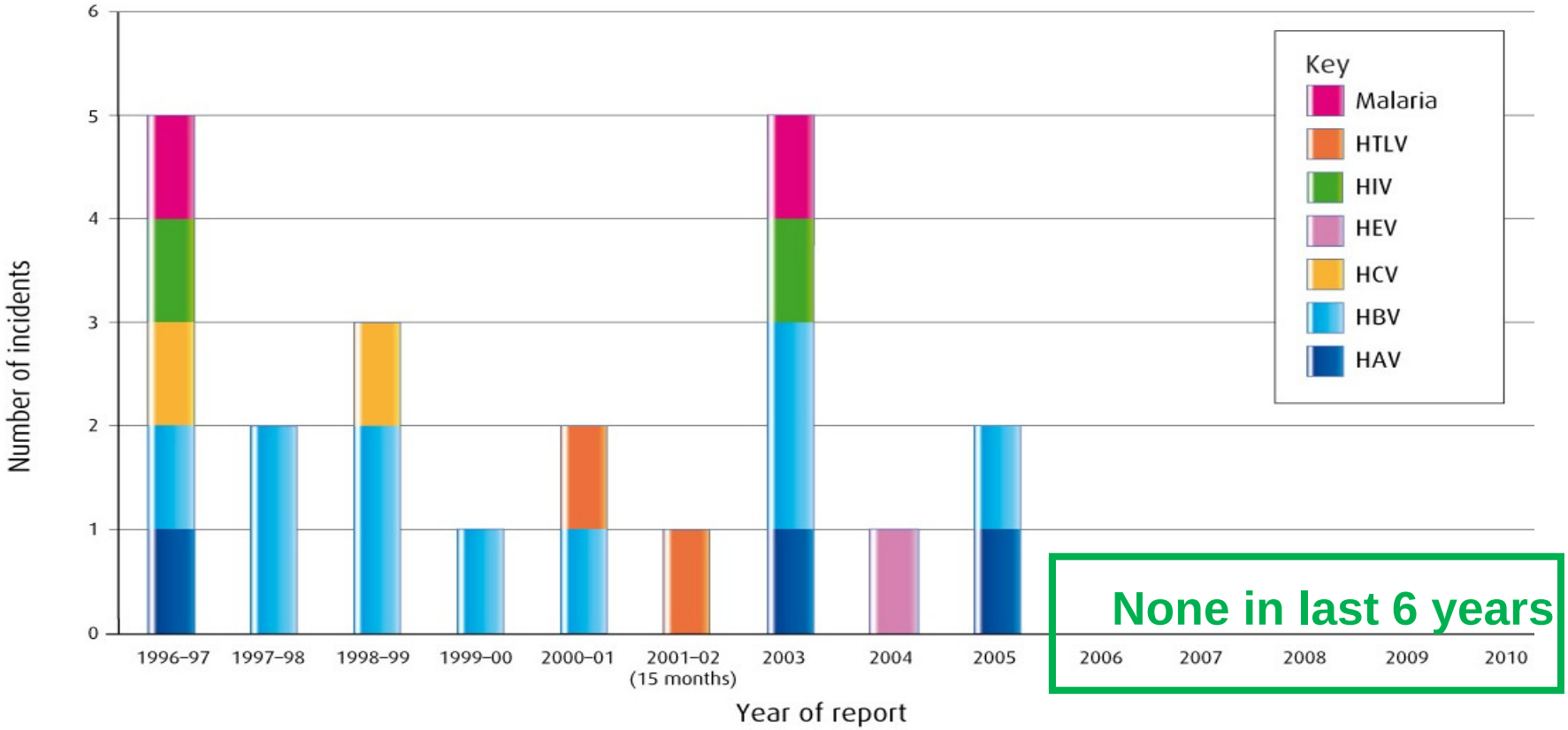
Major Morbidity and Mortality per 1,000,000 components issued in 2011

	Mortality	Major morbidity
Total	**2.7**	**39.6**
All errors	***0.7***	***5.4***
Acute transfusion reacns.	0.7	17.9
Haemolytic trans. reacns.	0.0	3.7
TRALI	0.3	2.7
TACO	0.7	8.1
Trans-assoc. dyspnoea	0.0	1.0
Post-trans. purpura	0.0	0.3
Paediatric cases	0.3	5.1

Deaths definitely attributed to transfusion 1996/97 - 2011



Number of viral and parasitic TTI incidents, by year of report and infection type (Scotland included from 10/1998)

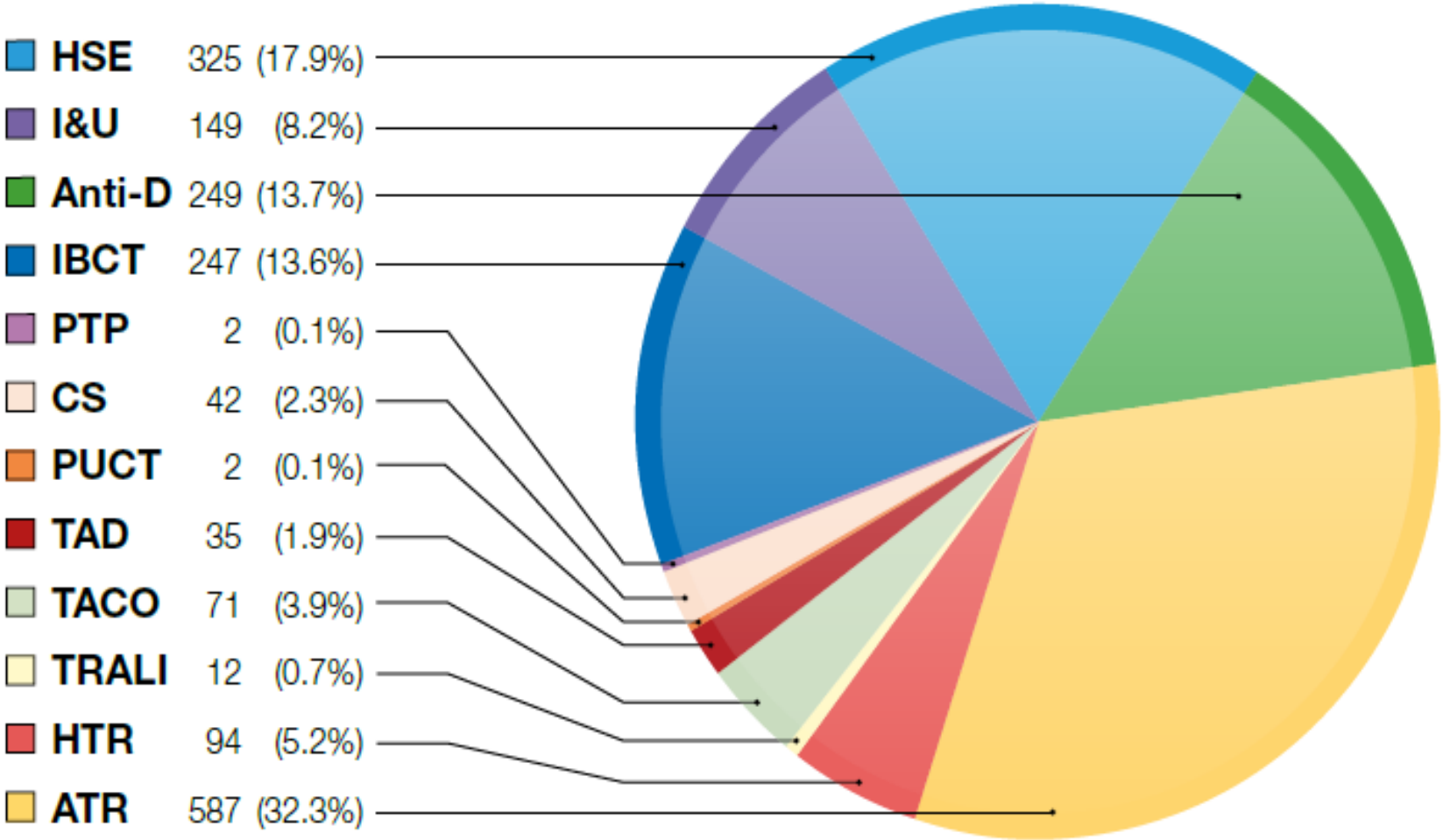


None in last 6 years

Current estimated risks in the UK per million donations

HBV	1.5	Death	2.7
HCV	0.01	Major morbidity	39.9
HIV	0.20		
HTLV1	0.06		

Cases reviewed in 2011 (excluding near miss and instances where the patient received a correct component despite errors having occurred – RBRP)
n=1815



Adverse clinical events – WHEN?

- Immediate and life-threatening
  ABO incompatibility; anaphylaxis
- Hours: pulmonary complications, bacterial infections, transfusion reactions
- Days: Haemolytic reactions
- Late (months or years): viral infections; iron overload

HOW do they present?

- Transfusion reactions may have many overlapping symptoms and signs with varying severity
- Fever, chills, rigor, myalgia, nausea, urticaria, itching, swelling, respiratory symptoms.....etc.
- Advise patients to report any adverse events in 24 hrs after transfusion

Case 1

- A 56 year old man with acute myeloid leukaemia is having a platelet transfusion
- 5 minutes into the transfusion he feels unwell
  - Temp 1.5 C rise
  - Transient rigors

What is your first action?

(Choose 1)

- A Telephone the laboratory
- B Call a doctor
- C Check details on the bag
- D Stop the transfusion

What is the most likely cause? (Choose 1)

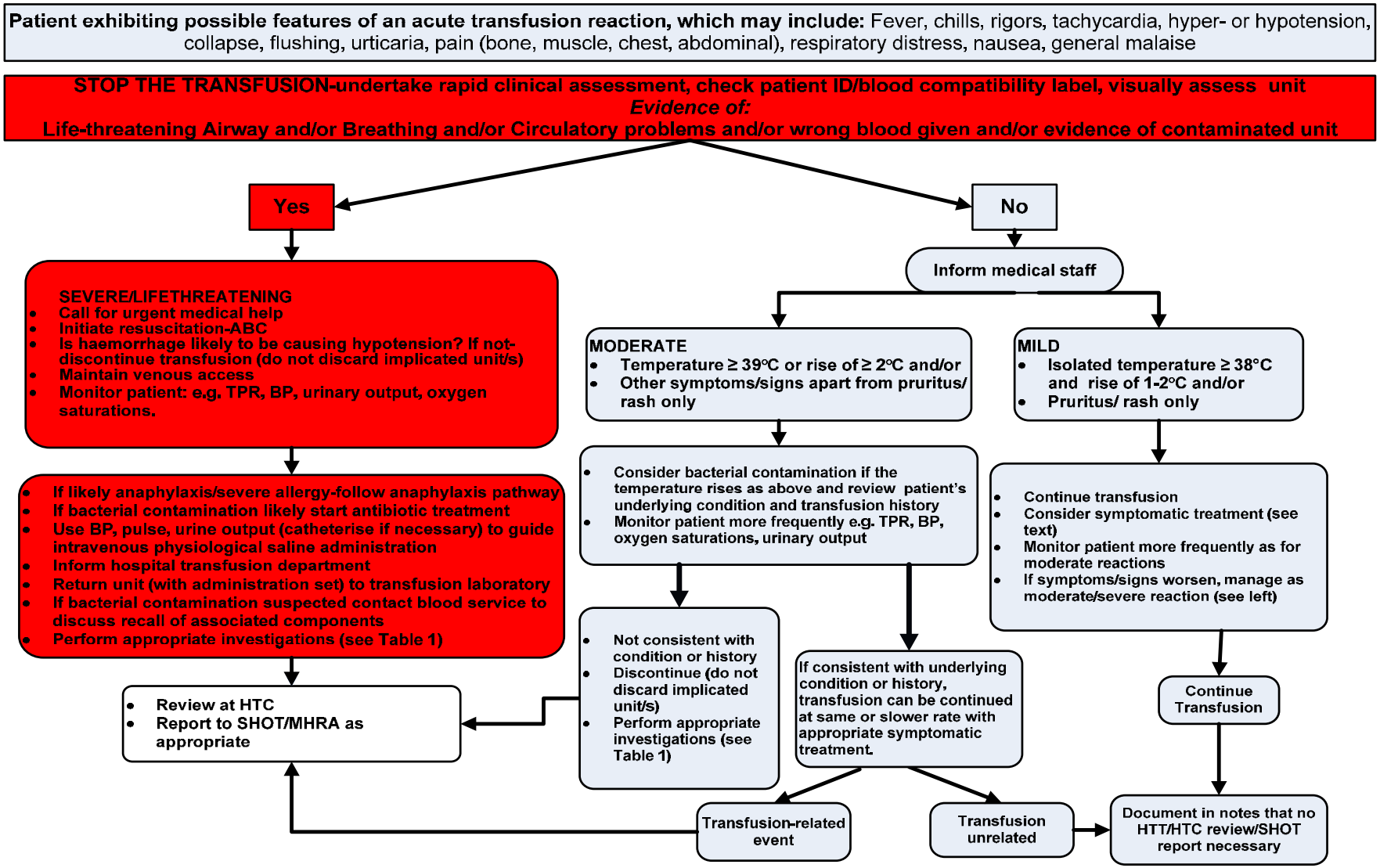
- A Allergic reaction
- B Haemolytic reaction
- C Infection in central venous line
- D Infection in platelet bag

What do we worry about when we see hypotension with fever?

- ABO incompatibility
  - Contact laboratory immediately
- Bacterial infection
  - Central and peripheral blood cultures
  - Start broad spectrum antibiotics
  - Inform laboratory and haematologist to arrange culture of the unit
  - Inform the Blood Service

What to do for an immediate transfusion reaction?

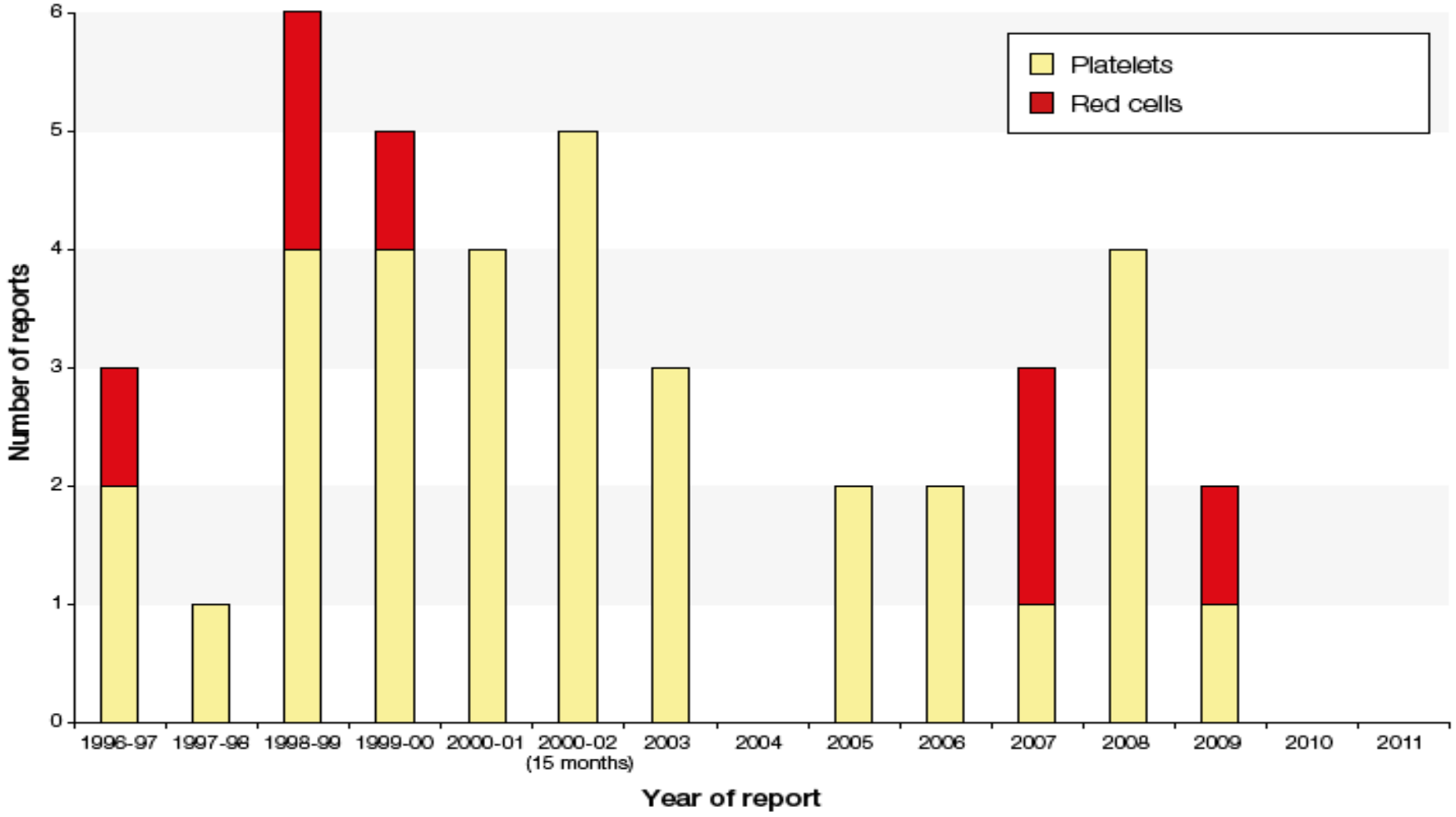
- Stop the transfusion, maintain IV access with saline and check the bag and patient ID
- Rapid medical assessment
- Inform the transfusion laboratory
- Blood culture and return blood bag to lab
- Renal function
  - Monitor fluid balance (input and output)
  - Collect first and subsequent urine samples


Patient exhibiting possible features of an acute transfusion reaction, which may include: Fever, chills, rigors, tachycardia, hyper- or hypotension, collapse, flushing, urticaria, pain (bone, muscle, chest, abdominal), respiratory distress, nausea, general malaise
STOP THE TRANSFUSION-undertake rapid clinical assessment, check patient ID/blood compatibility label, visually assess unit
Evidence of:
Life-threatening Airway and/or Breathing and/or Circulatory problems and/or wrong blood given and/or evidence of contaminated unit
Yes
No
SEVERE/LIFETHREATENING
Call for urgent medical help
Initiate resuscitation-ABC
Is haemorrhage likely to be causing hypotension? If not-discontinue transfusion (do not discard implicated unit/s)
Maintain venous access
Monitor patient: e.g. TPR, BP, urinary output, oxygen saturations.
If likely anaphylaxis/severe allergy-follow anaphylaxis pathway
If bacterial contamination likely start antibiotic treatment
Use BP, pulse, urine output (catheterise if necessary) to guide intravenous physiological saline administration
Inform hospital transfusion department
Return unit (with administration set) to transfusion laboratory
If bacterial contamination suspected contact blood service to discuss recall of associated components
Perform appropriate investigations (see Table 1)
Review at HTC
Report to SHOT/MHRA as appropriate
Inform medical staff
MODERATE
Temperature ≥ 39°C or rise of ≥ 2°C and/or
Other symptoms/signs apart from pruritus/ rash only
MILD
Isolated temperature ≥ 38°C and rise of 1-2°C and/or
Pruritus/ rash only
Consider bacterial contamination if the temperature rises as above and review patient's underlying condition and transfusion history
Monitor patient more frequently e.g. TPR, BP, oxygen saturations, urinary output
Continue transfusion
Consider symptomatic treatment (see text)
Monitor patient more frequently as for moderate reactions
If symptoms/signs worsen, manage as moderate/severe reaction (see left)
Not consistent with condition or history
Discontinue (do not discard implicated unit/s)
Perform appropriate investigations (see Table 1)
If consistent with underlying condition or history, transfusion can be continued at same or slower rate with appropriate symptomatic treatment.
Continue Transfusion
Transfusion-related event
Transfusion unrelated
Document in notes that no HTT/HTC review/SHOT report necessary

Bacterial transmission

- In 6 years from 1996 to 2002, 24 bacterial transmissions (6 fatal) were reported to SHOT
  - 6 cases in 1998-1999, 5 in 1999-2000

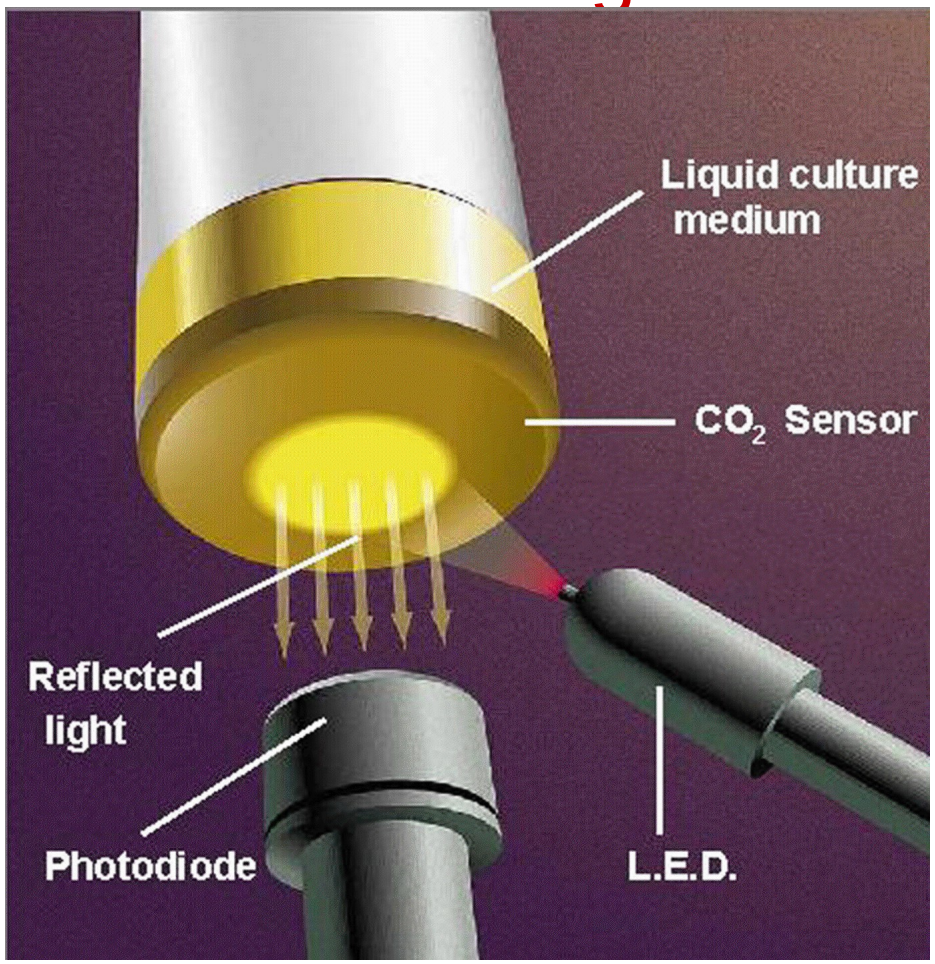
Bacterial TTIs 1996 - 2011



Strategy to reduce bacterial TTI

- Donor screening
- Post donation information
- Arm cleaning
- Diversion pouches
- Bacterial screening
- Withdrawing associated components when adverse reactions reported

Colourimetric sensor detects CO2 given off as a result of bacterial growth



Case 2

- An elderly male patient received the first unit of FFP to reverse warfarin.

- Half-way through the unit, he developed a widespread urticarial rash, shortness of breath with wheeze and marked hypotension (from 100/60 to 50/20)

What would you do?
(Choose 2)

- A Call a doctor
- B Give hydrocortisone and piriton
- C Give adrenaline
- D Try a different unit

Acute transfusion reactions

- Allergic or anaphylactic reactions are unpredictable and usually occur early
- This is why all patients having blood products must be monitored
- Adrenaline is the treatment of choice for severe allergy or anaphylaxis and should be available in all areas where transfusions take place
  - In most clinical areas it should be given IM
  - In ITU, theatres it may be appropriate to give IV

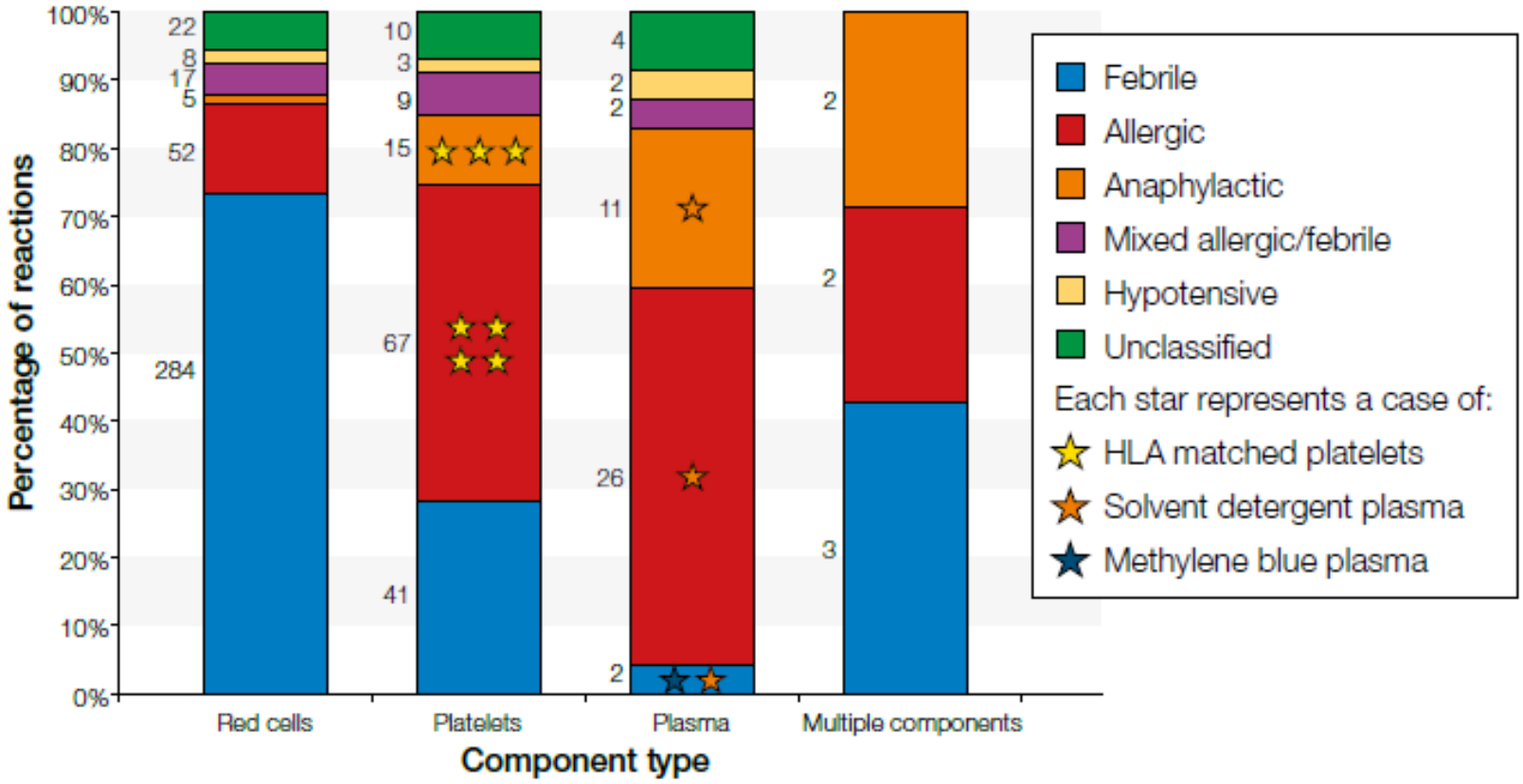
Anaphylaxis

- Life threatening
- Requires immediate intervention
- Follow UKRC guidelines
- Adrenaline
- Support the airway (oxygen)
- Longer term: discuss with immunologist how to manage future transfusions

Planning future transfusions

- Discussion with immunologist/allergist
- In this man's case (warfarin reversal), FFP was inappropriate
  - Learning opportunity

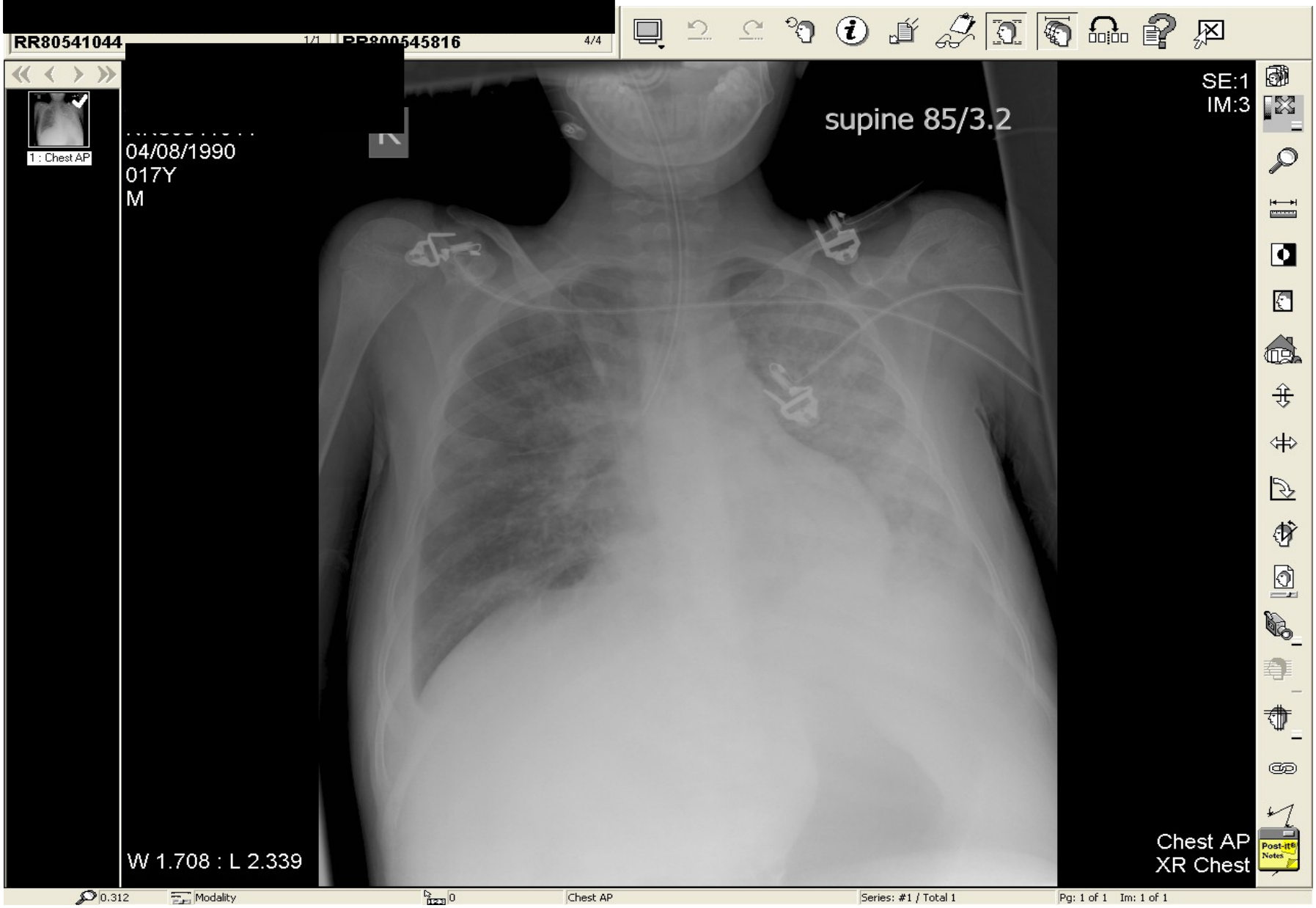
Reaction by component type



Case 3: Unexpected dyspnoea

- Teenage boy with history of liver disease transfused with female apheresis platelets for an elective surgical procedure
- Developed hypoxia, hypotension and pyrexia within 30 minutes of transfusion. Hb increased from 8g/dl before procedure to 18 after
- Required cardio-respiratory support on ITU
- When ET tube inserted, developed fountain like pulmonary oedema

30 mins post transfusion



What is the most likely diagnosis (Choose 1)

- A TACO (Transfusion Associated Circulatory Overload)
- B Chest infection
- C Acute myocardial infarction
- D TRALI (Transfusion-Related Acute Lung Injury)

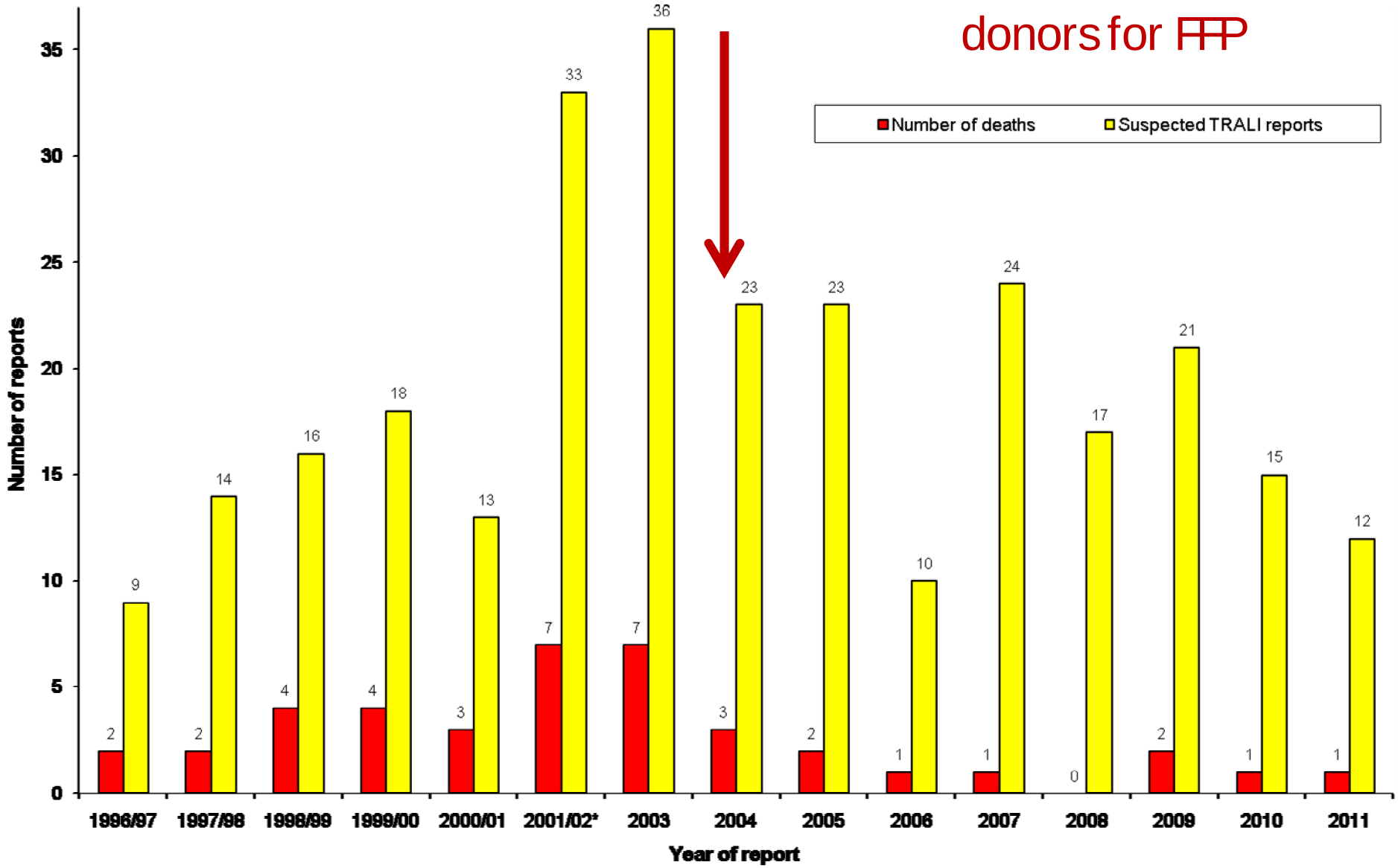
TRALI

- Serious complication of transfusion, almost always with plasma rich components
- Donor has antibody to recipient leucocytes
  - HLA or HNA
- Reduced
  - Universal leucodepletion
  - Male donors
- Dyspnoea, hypoxia (pyrexia) usually within 6 hours
- Commoner in certain groups of patients-”two-hit” hypothesis

TRALI – relative risk from different components 1996-2003

	Red cells	Cryo	FFP	Platelets
TRALI cases	33	2	31	27
Components issued	18,370,000	634,000	2,515,000	1,842,000
Risk/ component issued	1:556,000	1:317,000	1:81,000	1:68 000
Relative risk compared to red cells	**1**	**2**	**7**	**8**

Decision to use male donors for FFP



Learning points

- TACO is much more common than TRALI and it can be difficulty to confirm the cause of acute respiratory symptoms
- Elderly patients are particularly at risk of TACO
- Even small transfusions may be enough
- All patients need careful monitoring and appropriate investigation

Case 4: Serious reaction

- An 83-year-old male with refractory anaemia related to CKD received 2 units of RBCs, each over approximately 1.5–2.5 hours.
- He had continuing bradycardia during the second unit. He remained stable, but the bradycardia persisted at 40–45 bpm.
- Within 15 minutes of the start of the 3rd unit of RBC, he became unresponsive with no cardiac output.

What is the most likely diagnosis (Choose 1)

- A TACO (Transfusion Associated Circulatory Overload)
- B Chest infection
- C Acute myocardial infarction
- D TRALI (Transfusion-Related Acute Lung Injury)

TACO

- Any 4 of the following occurring within 6h of transfusion
  - Acute respiratory distress
  - Tachycardia
  - Increased blood pressure
  - Acute or worsening pulmonary oedema
  - Evidence of positive fluid balance

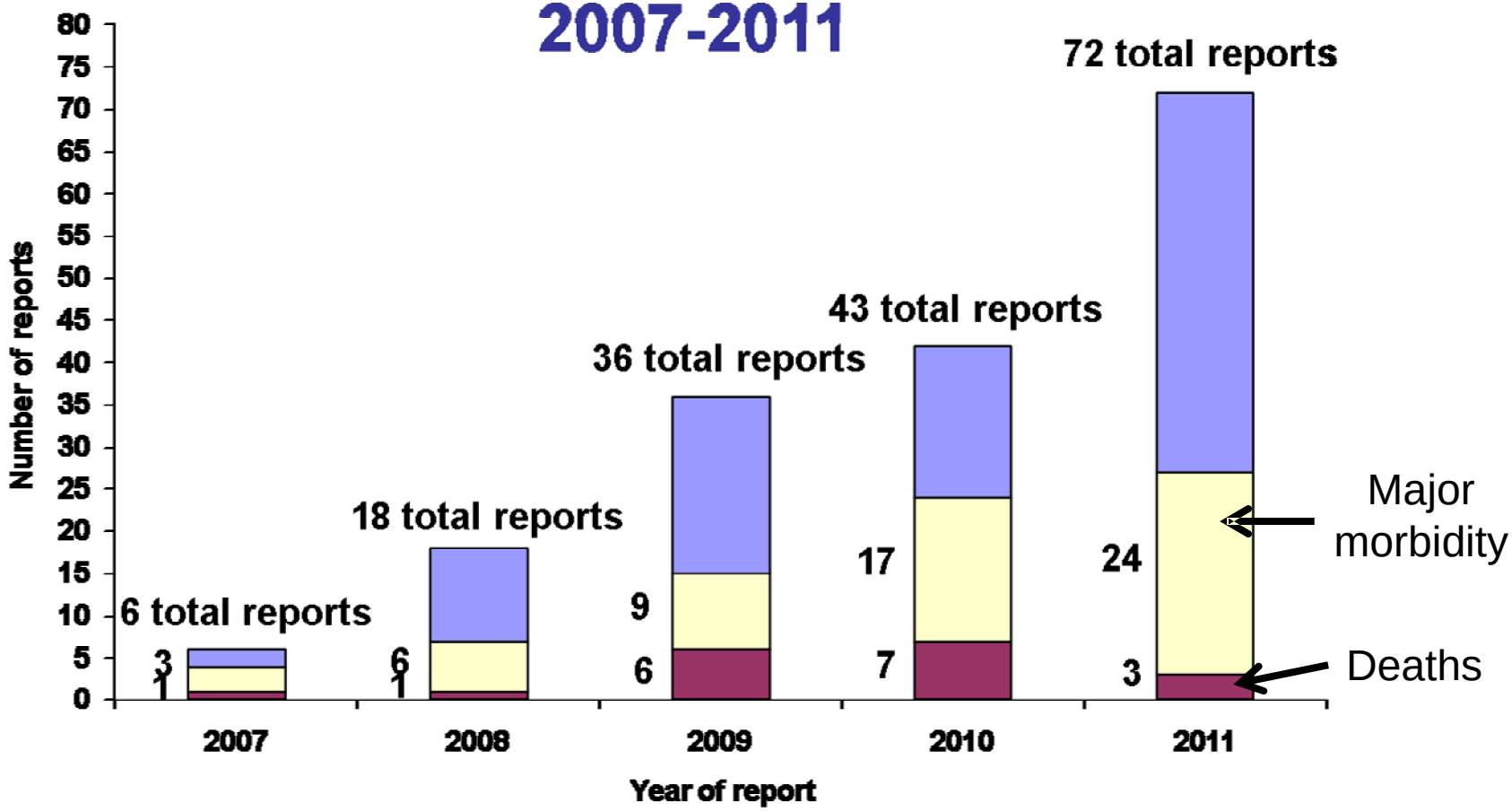
TACO risk factors

- Small stature
- Age> 70 is likely factor
- Co-morbidities including poor renal function, cardiac disease, low albumin

Features of TACO and TRALI

	TRALI	TACO
Type of component	Usually plasma or platelets	Any
BP	Often reduced	Often raised
Temperature	Often raised	Normal
Echo	Normal	Abnormal
Diuretics	Worsen	Improve
Fluid loading	Improves	Worsens

18 TACO-related deaths and 59 Cases of major morbidity 2007-2011



*Includes 4 deaths and 5 cases of major morbidity from I&U

Further information

- Resuscitation was ultimately unsuccessful.
- A post-mortem examination showed acute LVF, hypertensive heart disease with mitral valve prolapse and hypertensive nephropathy.

Learning points

- “Individualise” transfusions
- Note patient’s height and weight
- Careful monitoring and attention to fluid balance

Acute haemolytic transfusion reaction

- Patient A, blood group O RhD negative, was transfused 2 units of A RhD positive blood during cardiac surgery
- On arrival in ICU he received two more group A units without apparent adverse events.
- Following transfusion, the patient showed evidence of haemolysis, with a fall in Hb requiring further transfusions, and rise in bilirubin to 241mmol/L within 6 days
- He had an extended stay in ITU.

What was the cause?

- Patient A and patient B were sampled at the same time in a preoperative clinic. The nurse was distracted while bleeding patient A, did not complete the process at the bedside, and so patient details were transposed when labelling the samples.
- **Near Miss**: Patient B's mislabelled sample was detected in the laboratory, because a historical group was available.
- **Adverse event**: Patient A had no historical group and the error was not detected.

How can you reduce the risk?

- A All staff have regular training and competency assessment
- B Positive patient ID: who are you?
- C Label at the bedside: Stand by me!
- D Electronic tracking

Case 4

- A woman with sickle cell disease was transfused 2 units of red cells after an emergency caesarian section
- 10 days later she presents with Hb 6.7g/dl, fever hypoxia and pain

What is the most likely diagnosis (Choose 1)

- A Sickle cell crisis
- B Bacterial infection
- C Delayed haemolytic reaction
- D Pulmonary embolus

What happened next?

- She underwent exchange transfusion for sickle crisis but still had symptoms
- The Hb dropped below pre-transfusion levels with evidence of haemolysis noted on the blood film

Findings

- DAT positive with anti-Jka detectable in eluate on pre- and post-exchange samples
- Four out of six units for exchange transfusion were Jk(a+)
- The anti-Jka became detectable in the plasma after a couple of days

Learning points

- Delayed transfusion reactions in sickle patients may be confused with sickle crises
- Antibodies may only be detectable by specialised techniques not available in hospital labs (e.g. eluate to detect antibody coating cells)
- Sickle cell disease patients are at particular risk of alloimmunisation and may miss special requirements because clinicians forget to tell the lab

Investigation of moderate or severe transfusion reactions

Symptoms	Investigations
Fever ≥2°C rise or ≥39°C	Standard plus repeat compatibility testing, DAT, LDH and haptoglobin Blood cultures from patient Coagulation screen Do not discard unit Sustained fever: return unit to lab, repeat antibody screen and DAT

NB. Standard investigations for all transfusion reactions
FBC, renal and liver function, assessment of urine for haemoglobin

Symptoms	Investigations
Mucosal swelling	Standard, plus IgA If <0.07g/l and no general hypogammaglobulinaemia confirm and look for IgA antibodies
Dyspnoea, wheeze or features of anaphylaxis	Standard, plus oxygen saturation/blood gases, CXR; consider mast cell tryptase (MCT)
Hypotension (isolated fall systolic of ≥ 30mm resulting in level ≥ 80mm	Investigate as for fever If allergy suspected, IgA Consider MCT

A particular problem in ITU?

- A woman in her 60s has just been admitted to ITU after CABG, complicated by moderate perioperative haemorrhage. She is just finishing the 3rd unit of a red cell transfusion: her BP at the start was 94/52, at the end it was 72/42
- A 4th unit of red cells is started and her BP becomes unrecordable

Is this:

- A A hypotensive transfusion reaction?
- B Continued bleeding?

Hypotensive reactions

- Rare, but can be severe
- Appear to be commoner after bypass surgery or prostate surgery
- Difficult decision: transfuse more as blood loss or stop transfusion

Post-transfusion purpura

- Definition: sudden onset of thrombocytopenia occurring 5-12 d following red cell transfusion associated with antibodies in the patient directed against human platelet antigen systems. Commoner in women, rare (1-2 pa).
- Management: IVIg
- Women are at risk of neonatal alloimmune thrombocytopenia in future pregnancies

Late complications of transfusion

- Viral infections
  - Identify and report
  - Establish link with previous transfusion
  - Counselling and management
- Iron overload
  - Think of this in any chronically transfused patient and do regular assessment of iron loading
  - May be missed in young patients undergoing cancer chemotherapy?

So, to summarise..

- Stop transfusion, check patient and blood compatibility
- Manage symptoms and signs first, classification comes later
- Plan immediate management
- Consider how to manage subsequent transfusions
- Reporting and classification

Acknowledgements

- The BCSH writing group for helping me write the guidelines
- Hospitals for reporting cases to SHOT
- SHOT experts and incident specialists
- Paula Bolton-Maggs, medical director of SHOT for letting me use her slides
- And you for your enthusiastic participation