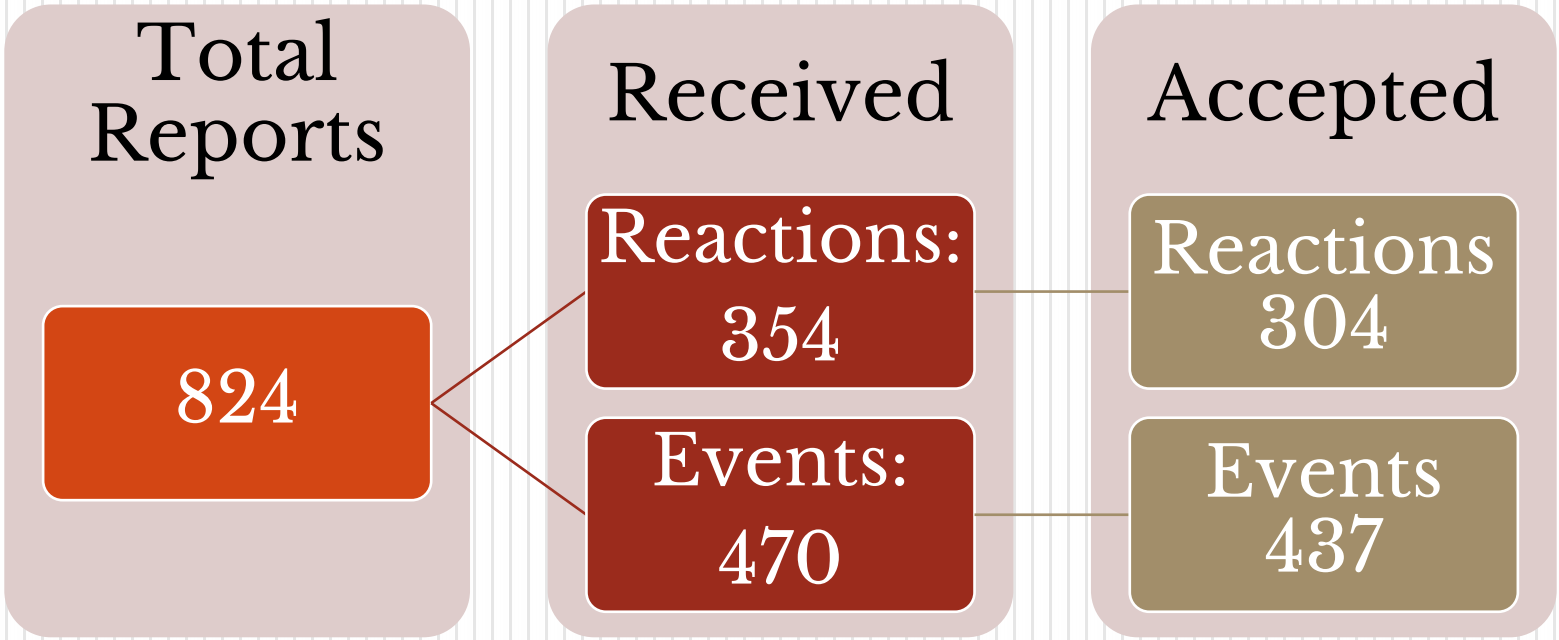
Serious Adverse Reactions 2016-2017

Joanne Scanlon
National Haemovigilance Office

NHO Findings 2016-2017



Findings 2016-2017

In total 824 SAR and SAE reports submitted to the NHO with 741 reports accepted

304 accepted reports fall into the category of SAR

118 SAR Reports Mandatory (16%)

50 SAR Reports Did Not Progress

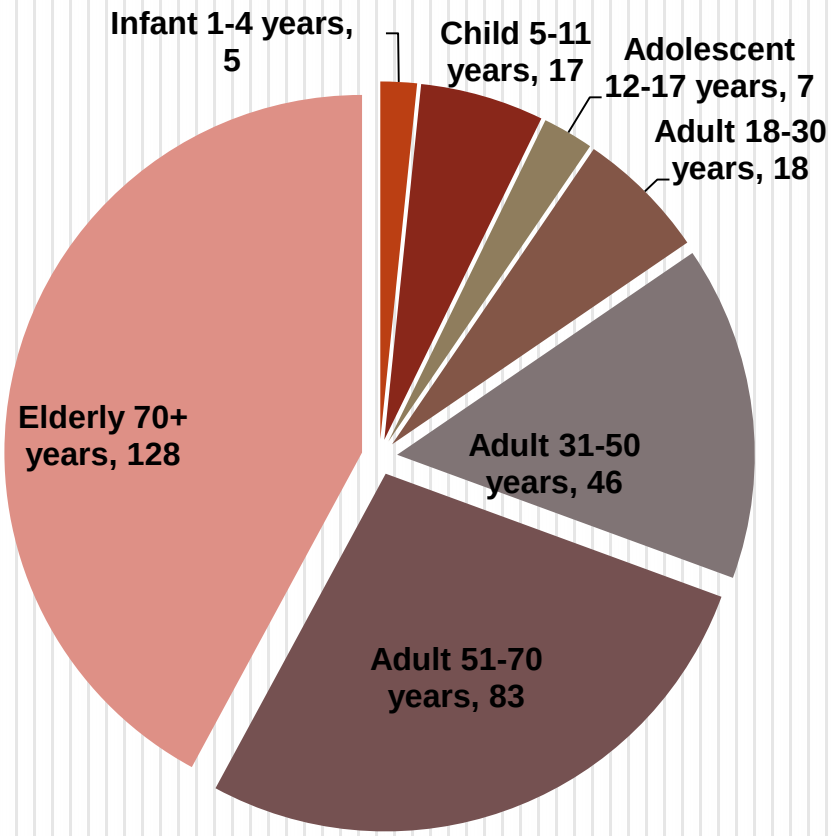
30 SAR reports involving paediatric patients received and 29 accepted

No reports accepted in relation to:

- ***Suspected transfusion transmitted infection (bacterial)***
- ***Transfusion Associated Graft versus Host Disease (TA-GvHD)***
- ***Post Transfusion Purpura***

Serious Adverse Reactions accepted by the NHO		2015	2016	2017
Acute Transfusion Reactions	Immunological haemolysis due to ABO Incompatibility	1	1	0
	Immunological haemolysis due to other allo-antibody (Acute < 24 hrs.)	0	0	1
	Anaphylaxis/hypersensitivity (AA)	41	51	42
	Febrile Non Haemolytic Transfusion Reaction	65	52	54
	Unclassified SAR	5	6	3
Delayed Haemolytic Transfusion Reactions	Immunological haemolysis due to other allo-antibody (Delayed > 24 hrs.)	8	10	7
Delayed Serological Transfusion Reaction	Delayed Serological Transfusion Reaction	168	N/A	N/A
Transfusion Transmitted viral infection (HBV)	Transfusion Transmitted viral infection (HBV)	0	0	1
Respiratory Complications of transfusion	Transfusion Associated Circulatory Overload (TACO)	38	32	41
	Transfusion Associated Dyspnoea	2	1	1
	Transfusion related acute lung injury (TRALI)	0	1	0
Totals		328	154	150

Breakdown of age groups



Acute Hemolytic Transfusion Reactions (AHTR)

AHTR is defined as a reaction occurring within 24 hours of a transfusion where clinical and/or laboratory features of haemolysis are present (ISBT Working Party, 2011). Acute haemolysis may be caused by ABO incompatibility, other antigen incompatibility or to non-immunological factors.

Immunological Haemolysis due to ABO incompatibility (n=1)

Background

90yr old admitted with bradycardia/GI bleed

Hb: 6.9 g/dl, transfused 2 A+ RCC

What went wrong

In ED sample taken from incorrect pt

2 days post transfusion patient was routinely recrossmatched, error discovered

Report initially categorized as an event.

However signs of a mild haemolysis reaction evident (↑Bilirubin, ↓Hb, DCT +)

Report captured as a reaction secondary to an event with an imputability of possible

Pt received an incompatible unit. Pt group O Rh Neg and patient received A Rh Pos unit

Recommendation

- ***There is no substitute for Correct Patient Identification at all stages in the transfusion process (Key SHOT message 2015)***
- ***It is imperative that patients are robustly and correctly identified at all stages of the transfusion process and that all spelling and number sequences on the patient ID band and all transfusion-associated documentation are correct and legible (BSH 2017)***

Immunological haemolysis due to other allo-antibody (Acute < 24 hrs) n=1

- 72 yr old with history of ovarian ca admitted with bowel obstruction
- Referral sample sent for crossmatch
- Finding: Autoantibody and an allo-anti-c detected
- Patient received 2 units RCC
- Prior to 1st unit Hb: 8.4 g/dl, bili: 14
- Prior to 2nd unit Hb: 9.5 g/dl, bili: 4
- Patient developed haematuria and severe back pain (5 hours post transfusion of 2nd unit)

Case Study 2 …contd

Post Transfusion Investigations

- Dropping Hb
- Anti c and Anti Jk^a identified
- Haemosiderin negative (requested)
- Pre-transfusion sample reviewed and Anti Jk^a identified
- 2^{nd} unit transfused positive for the Jk^a antigen

Outcome

- Complete recovery
- Reaction noted due to error

What went wrong?

- Error in deduction – Human Error
- Anti Jk^a excluded in error at crossmatch
- Jk^a neg units should have been issued
- MS on duty was working alone, out of hours in the evening
- No second person available to check
- MS involved was fully trained and experienced

CAPA

Hospital informed of error

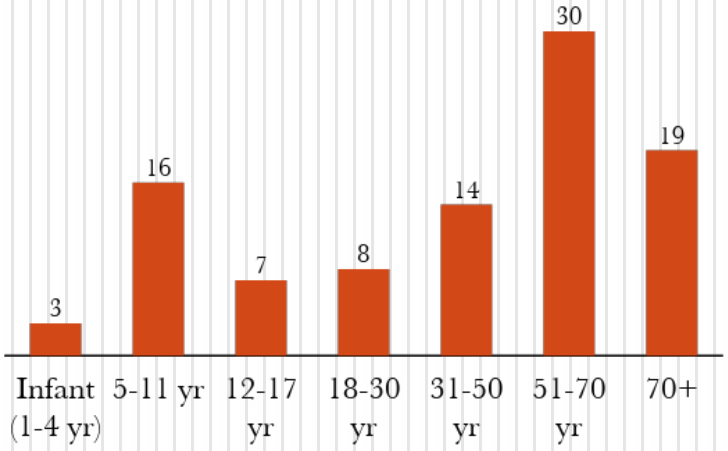
Antibody identification is a manual process requiring interpretation. An error was made and MS has ‘reflected on action’

Anaphylaxis/Hypersensitivity (n=93)

Findings

- 99 Reports Received
- 93 Reports Accepted
- 57 Mandatory

Demographics



Components

- RCC: 27
- Plt Aph: 51
- Pooled Plt: 14
- Multiple Components:3

Investigations

- IgA levels: 30 (all NAD)
- Bact screening unit: 30
- Bact screening pt: 31

Clinical Outcome

- Complete Recovery: 89
- Minor Sequelae: 4 (All admitted overnight for observation)

Case Study 3

Background

- Female in 70's received RCC transfusion for management of anaemia (Hb 6.4g/dl o/a)
- 3 units prescribed
- No iron studies carried out pre transfusion
- Baseline obs: T:36.5^{o}c, HR: 73bpm, BP: 104/60mmhg

Symptoms

- 5-10 mins into transfusion patient felt head & neck swelling/choking sensation
- BP ↑204/81mmhg
- Heart rate ↑121 bpm
- Patient nauseated and vomited
- 1 hour post transfusion temperature spiked 38.3^{o}c

Case Study 3 contd…

Treatment/Investigations

- Transfusion discontinued
- Reviewed by Doctor
- Treated with IV Hydrocortisone and IV Piriton
- Blood Cultures taken – no growth
- All serological investigations – negative

Clinical Outcome

Complete Recovery

Points to note AA Reactions

- 78/99 cases reported received antihistamines post reaction
- 65/99 cases received steroids
- 60/99 cases received both

Recommendation (BSH 2012)

For patients with **recurrent moderate or severe allergic reactions**, other than those in which the patient is IgA deficient, options for further transfusion include:

➢ Use of directly monitored transfusion of standard components in a **clinical area with resuscitation facilities**

➢ Anaphylaxis should be treated with **intramuscular adrenaline**

➢ Transfusion of **washed red cells or platelets**

➢ **Consider antihistamine prophylaxis** (although the evidence for efficacy is low, the risks are also low)

Febrile Reactions (n=106)

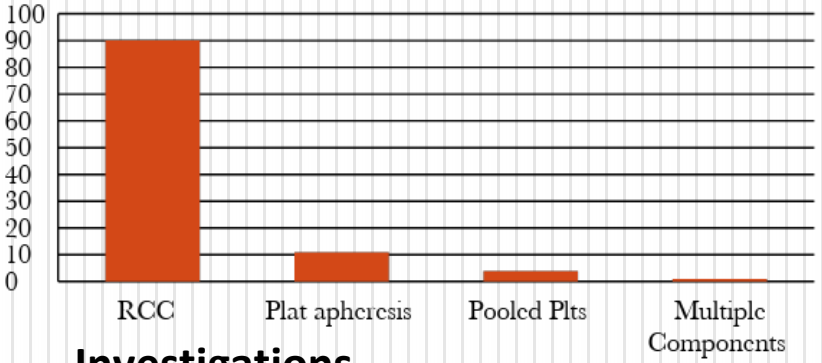
Findings

- 112 Reports received
- 106 Reports accepted
- 15 Reports Mandatory

Demographics

- 1-4 yr: 1
- 5-11 yr: 1
- 18-30 yr: 8
- 31-50 yr: 23
- 51-70 yr: 29
- 70+: 44

Components



Investigations

- Bact screening of unit: 69
- Bact screening of pt: 88
- Bact screening of both pt and unit: 50

Clinical Outcome

- Complete Recovery: 98
- Minor Sequelae: 8(all 8 bar one required overnight admission)

Case Study 4

Background

25 yr old oncology female transfused with a pool of platelets for a plt count of 2

Signs & Symptoms

	BP	Pulse	Temp	RR
Pre Transfusion	104/62	105	37.0	16
15 mins	110/58	98	36.5	17
End time	108/68	104	36.4	16
2 hours post commencement	144/90	149	38.4	26

Case Study 4

Patient also experienced chills/rigors, weakness and breathlessness

Investigations

- DAT negative
- Chest Xray unchanged from previous Xray
- Bacterial investigation of patient – all negative

Treatment/Outcome

- 4L O2 for 2+ hours
- Patient already on antibiotics
- Symptoms all resolved within 2 hours and patient made complete recovery

Future Transfusions

- Patient to receive Hydrocortisone and Piriton pre future Platelet Transfusion

Febrile and allergic reactions: targeted treatment

Key SHOT messages

- For febrile reactions alone, give paracetamol
- For allergic reactions give an antihistamine as first line; give adrenaline if anaphylaxis is suspected. The effect of steroids is delayed by several hours, will have no immediate effect, and should only be used to prevent a late recurrence. The use of steroids may further immunosuppress already immunocompromised patients and increase the risk of side effects such as infection

Reaction	Treatment	Prevention of recurrent reactions
Febrile	Paracetamol	Paracetamol 60 minutes before anticipated time of reaction
Allergic	Antihistamine (steroid should not be used routinely) If anaphylaxis, adrenaline is essential	If previous reaction with apheresis platelets try pooled platelets in PAS If reactions continue, give pre-transfusion antihistamine If reactions continue, consider washed platelets/red cells; for fresh frozen plasma (FFP) try a pooled component e.g. solvent-detergent treated plasma

Unclassified SAR

Findings

- 30 Reports Unclassified Reactions received
- 20 of these reports did not progress, categorized as DSTR's which NHO ceased collecting Jan 2016
- 1 further report not accepted
- 9 reports accepted

	Component Transfused	Imputability	Description
1	Red Cells	Possible	**Patient became hypotensive and drowsy**
2	Red Cells	Possible	**Patient developed symptoms of nausea and vomiting**
3	Red Cells	Possible	**Patient became tachycardic**
4	Red Cells	Possible	**Patient developed hypotension and vomiting**
5	Red Cells	Possible	**Arm pain and pleuritic chest pain**
6	Red Cells	Likely/Probable	**Patient became hypotensive, developed a fever, nauseous, very anxious and had blurred vision/dizziness**
7	Plat Aph	Possible	**Patient became hypertensive**
8	Red Cells	Possible	**Patient became tachycardic**
9	Red Cells	Possible	**Patient became tachycardic and developed palpitations**

Delayed Transfusion Reactions:

Immunological Haemolysis due to other allo-antibody (delayed n=17)

- 18 Reports received
- 17 Reports accepted

Age Range

No Paediatrics

All reactions ranged from 31 years to 70+ year age group with a mean age of 69yrs

Death Related to transfusion (n=0)

4 reports of death following transfusion but all unrelated

Minor Sequelae (n=1)

Patient readmitted with jaundice 15 days post transfusion, resolved 22 days following transfusion

Most Common antibodies identified

Antibody Identified	Total
Anti Jk^a	3
Anti Jk^b	3
Anti E	3
Anti Fy^a	2
Anti Fy^b	1
Anti K	1
Anti s	1
Anti Lu^a	1
Anti D	1
Anti Jk^b & Anti E	1

Recommendations

- Lifesaving transfusion should not be withheld due to a history of alloantibodies.
- Robust methods of recording patients antibody history should be developed and supported with patient education

Transfusion Transmitted Infections

Findings

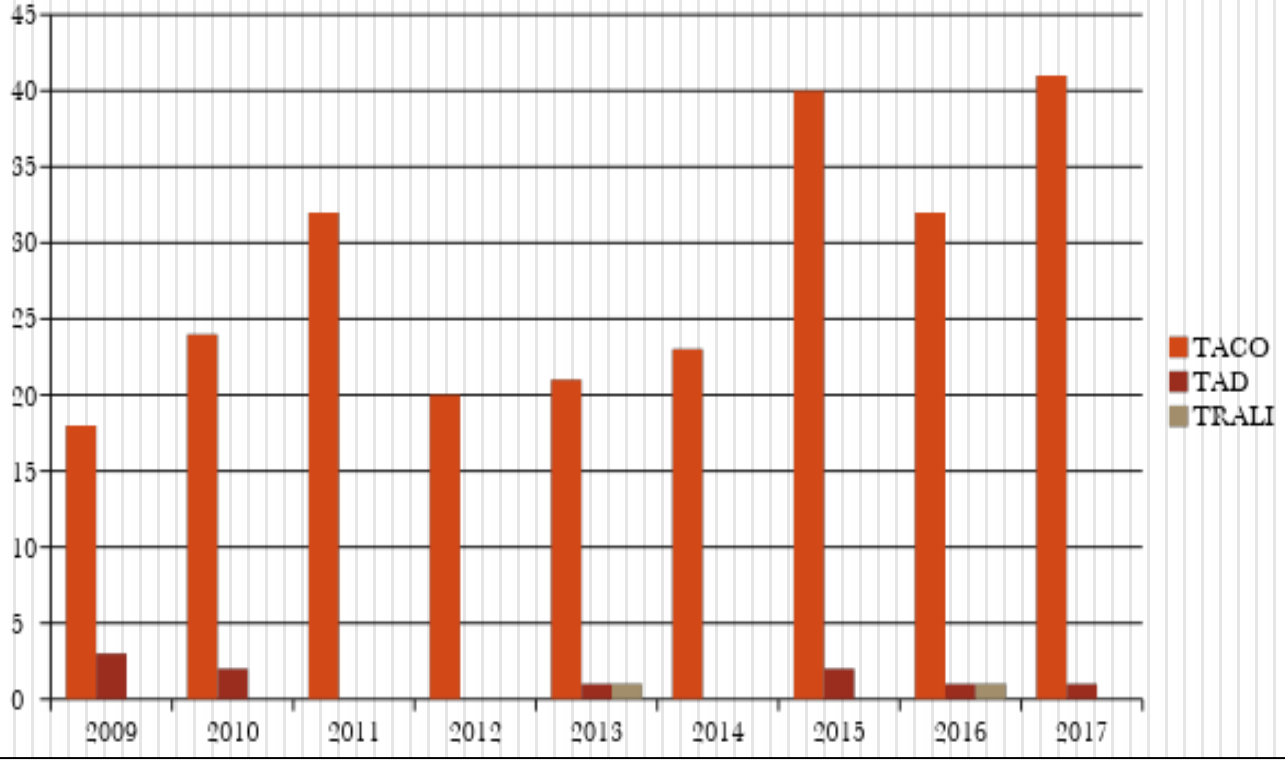
Between 2016 and 2017 the NHO have received 7 Reports of Suspected Transfusion Transmitted Infections and in all but one case transfusion transmitted infection has been excluded or considered unlikely as a result of extensive investigations carried out by the IBTS.

The remaining case (HBV) was accepted.

Respiratory Complications

Categories:

- Transfusion Associated Circulatory Overload (TACO)
- Transfusion related Acute Lung Injury(TRALI)
- Transfusion Associated Dyspnoea (TAD)



Transfusion Associated circulatory Overload (TACO)

Findings

- 78 Reports received
- 73 Accepted
- 14 Mandatory

Demographics

- 18-30 yr: 2
- 31-50 yr: 4
- 51-70 yr: 15
- 70+: 52

Components

- RCC: 72
- RCC & SD Plasma: 3

Clinical Outcome

- Complete Recovery: 52
- Minor Sequelae: 8
- Serious Sequelae: 4
- Death: 9 – 5 unrelated to transfusion and 4 related to transfusion

Reporting TACO to the NHO

- No change on current Definition
- International Group with representation from SHOT, ISBT, IHN and AABB continue to review reporting criteria of TACO
- ROI have been involved in validation studies (2016-2017)
- Workshop Autumn 2018
- TRALI definitions also being reconsidered (different taskforce in contact with the ISBT group)

Case History 5

Background

- 66yr old male (hx of Multiple Myeloma)
- Admitted to ED – Generally unwell, chest tightness, cough
- Hb 8.6 patient prescribed 2 units of RCC

Baseline obs

- Temp: 36.4, HR: 70, BP: 122/65

Timeline

- 12.17 Transfusion commenced (prescribed over 4 hours)
- 13.30 Patient complains of feeling breathless, O2 2L commenced
- 14.00 Transfusion completed. SHO review, O2 ↑15L, HR: 105, Right side crepitations on exam
- 15.45: No urine output
- 16.00: BP 200/100, HR: 100-120 bpm

Case History 5

- Patient unable to speak
- Patient catheterised
- IV 40mg frusemide administered
- Arterial line inserted
- HLA samples taken, BNP (elevated) and Urine
- Rapid alert for ? TRALI sent to IBTS
- Patient transferred to ICU
- 21.30: Good Diuresis. HR: 93. BP: 110/47mm/hg
- Chest Xray changes, bilateral creps (new)

DAY 2

- Reviewed following day. Noted unit transfused over 1hr40mins (prescribed over 4 hours)
- Decision to capture reaction as TACO
- 3 Days later Chest Xray had no evidence of pulmonary oedema
- Category of TRALI outruled

Case History 5

- **Outcome**

Following discussion with Haematology Consultant the patient had acute detioriation due to TACO

Unit transfused too quickly to an already at risk patient (RCC prescribed over 4 hrs, given over 1hr40 mins!!)

- **CAPA**

Use of pumps for transfusion in ED

Further and on-going vigilance required

SHOT Recommendation (2017)

A formal pre-transfusion Risk assessment for Transfusion-associated circulatory overload (TACO) should be performed wherever possible as TACO is the most commonly reported cause of death and major morbidity

Transfusion related deaths 2010 to 2017

- Total deaths :55
- 9 Possibly/Probably related to transfusion
- **All 9 related to TACO**

➢All 9 received RCC

➢All 9 similar symptoms including hypertension, tachycardia, dyspnoea

➢3 reports were mandatory

➢3 reports were as a result of an error (dilute sample processed, unit prescribed too quickly, 2 units administered with one prescribed)

LEARNING POINTS TACO

- TACO is the leading cause of death following transfusion reported by the UK Serious Hazards of Transfusion (SHOT) report in 2016
- Consider risk factors for TACO prior to transfusion
- Elderly particularly at risk
- Be cautious about using estimated weights
- If Hb low and symptomatic, consider blood early before fluid challenge
- Consider the need for transfusion based on symptoms
- Don’t give unit two without review!

Transfusion Associated Dyspnoea

- Between 2016 and 2017 two reports of TAD received and accepted
- Both in the elderly 70 + age group
- RCC implicated in both reactions
- Clinical outcome was complete recovery in both reactions

Transfusion Related Acute Lung Injury (n=1)

Two cases of TRALI reported to the NHO with one report captured as a Possible TRALI

Background:

3 yr. old male with an oncology/haematology disorder with overwhelming sepsis in ICU.

Pt has had multiple transfusions in past.

Case History 6

Timeline:

- 15.00: Unit of plt commenced. Pt on CPAP and pressure support at this time
- 15.00: C-xray shows pleural effusions and pulmonary oedema
- 16.00: Following plt transfusion patient in a negative fluid balance
- 19.00: Pt. received GCSF
- 21.00: Pts condition deteriorated, desaturated to 80%, tachynopneic
- 22.30: HB 8.9, 1 unit RCC commenced

Case History 6

- 23.00: Tachycardic(118), Desaturated to 60%, B/P elevated to 147/96 following 96mls RCC, rash noted to face, frothy secretions
- Ventilation required however patient became difficult to ventilate. Commenced on high frequency osscilating ventilation
- 23.40: Diuretics administered with no effect
- 24.00: C-xray now showing worsening Pulmonary Oedema and pulmonary effusions
- IBTS and NHO informed of possible TRALI, rapid alert initiated

Case History 6

Clinical Outcome

Patient made a complete recovery. Required osscilator ventilation for 12 hours. Moved onto CPAP for 2 days and was then discharged self-ventilating from ICU.

Differential Diagnosis of Possible TACO

Findings of dyspnoea, hypertension, tachycardia and chest X-ray changes were consistent with the ISBT definition of TACO.

However there was no evidence of diuresis following administration of diuretic. BNP levels were not carried out.

Case History 6

Results of follow up donor investigations

2 Donors were implicated in this reaction. The platelet donor was not tested as it was a male donor with no history of transfusion.

The RCC donor tested negative

- ***TRALI is therefore a clinical syndrome and neither presence of anti-HLA or anti-HNA antibodies in donor(s) nor confirmation of cognate antigens in recipient as required for diagnosis (ISBT 2013)***

Take Home Notes

- Blood transfusion is extremely safe
- But deaths & major morbidity do occur
- Look at the patient
- Monitor patient
- Consider the need for transfusion based on symptoms
- Don’t give unit two without review
- Avoid inappropriate & unnecessary transfusions.

Thank You