Paediatric Cases n=136

22

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Definition:

Paediatric cases comprise all reports for patients under 18 years of age, including all paediatric cases from the other chapters in this report. Paediatric reports have been subdivided by recipient age group: neonates ≤28 days; infants >28 days and <1 year; children ≥1 year to <16 years and young people aged 16 to <18 years.

Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion	**Ig**	Immunoglobulin
BSH	British Society for Haematology	**IT**	Information technology
CAS	Central alerting system	**ICU**	Intensive care unit
CS	Cell salvage	**MB**	Methylene blue-treated
CMV	Cytomegalovirus	**MHP**	Major haemorrhage protocol
DAT	Direct antiglobulin test	**NEC**	Necrotising enterocolitis
ECG	Electrocardiogram	**NM**	Near miss
ED	Emergency department	**RBRP**	Right blood right patient
FAHR	Febrile, allergic and hypotensive reactions	**SRNM**	Specific requirements not met
FFP	Fresh frozen plasma	**TACO**	Transfusion-associated circulatory overload
FY2	Foundation year 2	**TAD**	Transfusion-associated dyspnoea
Hb	Haemoglobin	**TRALI**	Transfusion-related acute lung injury
HSE	Handling and storage errors	**TTI**	Transfusion-transmitted infection
HT	High-titre	**UCT**	Uncommon complications of transfusion
HTR	Haemolytic transfusion reactions	**WCT**	Wrong component transfused
IBCT	Incorrect blood component transfused		

Key SHOT messages

- Clinical staff must be trained and be aware of the specific transfusion requirements for patients with haemoglobin disorders. These requirements should be communicated to the transfusion laboratory staff in a timely manner
- All staff must be aware of the paediatric major haemorrhage protocol in their hospitals
- Hospitals should ensure the correct use of the paediatric red cell transfusion formula, with the Hb units in g/L (BSH New et al. 2016)
- There remains uncertainty over the precise definitions of paediatric pulmonary complications, particularly for neonates. Clinicians should be alert to the possibility of the diagnosis in these patients
- Hyperkalaemia is a recognised complication of large volume transfusion in neonates and infants, and 'fresh' red cells are recommended for this situation to reduce risk

Recommendations

- Paediatric medical and nursing education must include specific transfusion requirements for patients with haemoglobinopathies and processes must be in place to ensure these are communicated effectively to the hospital transfusion laboratories to ensure safe transfusions
- Protocols must be in place for the management of massive haemorrhage in infants and children. These should include guidance on the appropriate component volumes to be used in resuscitation. Staff involved in paediatric transfusions must be trained and aware of the content of this protocol

Action: Hospital transfusion teams, hospital transfusion laboratories, Royal College of Paediatrics and Child Health, clinical leads, medical and nursing educators

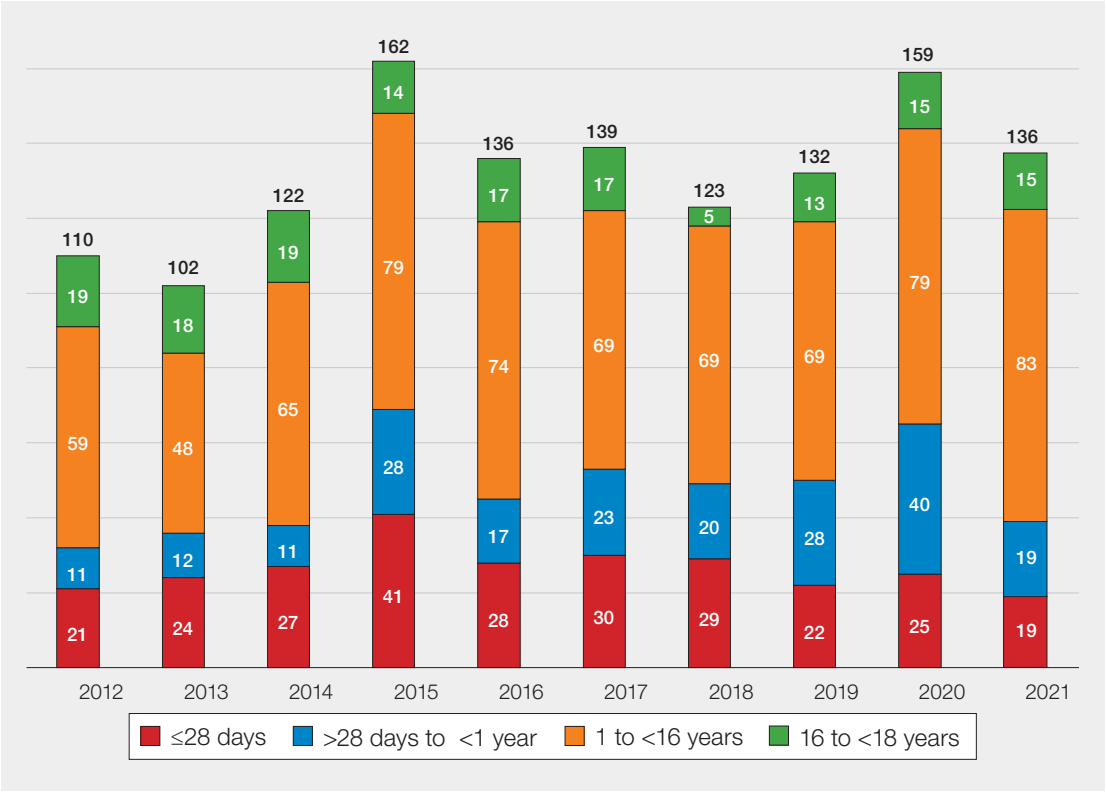
Introduction

There were fewer paediatric cases overall in 2021 compared to 2020 (136 vs 159), with reporting levels this year similar to 2019. Paediatric cases were 7.6% (136/1790) of total cases analysed excluding NM and RBRP and 7.7% (244/3161) if NM and RBRP are included.

Paediatric cases continue to be over-represented in FAHR, ADU (particularly overtransfusion) and IBCT. This year there is also a relative increase in paediatric HTR reports. However, the large increase seen last year in the FAHR reports following platelet transfusion has not been sustained.

This year 53/83 (63.9%) of paediatric error reports were considered clinical errors and only 30/83 (36.1%) laboratory errors. This constitutes both an increase in the number of clinical errors and decrease in the number of laboratory errors. There has been a drop in total laboratory reports overall, discussed in Chapter 14, Laboratory Errors; it is not clear whether this is due to improvement in practice or a reduction in reporting. The paediatric categories with high percentages of clinical errors in 2021 were ADU (28/33, 84.8%), HSE (14/15, 93.3%) and all the reports in cell salvage (n=1) and anti-D Ig categories (n=3).

Figure 22.1: Trends in paediatric reports 2012-2021



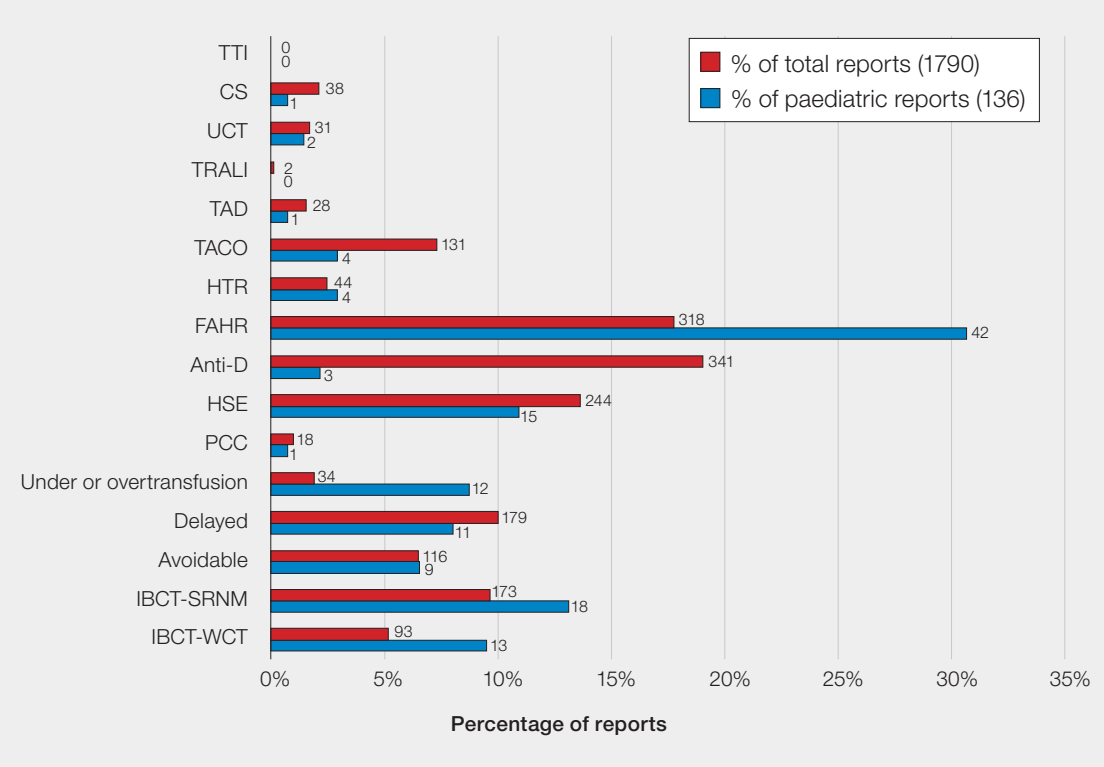


Figure 22.2: Percentages of paediatric and total reports in each category

TTI=transfusion-transmitted infection; CS=cell salvage; UCT=uncommon complications of transfusion; TRALI=transfusion-related acute lung injury; TAD=transfusion-associated dyspnoea; TACO=transfusion-associated circulatory overload; HTR=haemolytic transfusion reactions; FAHR=febrile, allergic and hypotensive reactions; HSE=handling and storage errors; PCC=prothrombin complex concentrate; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; IBCT-WCT=IBCT-wrong component transfused

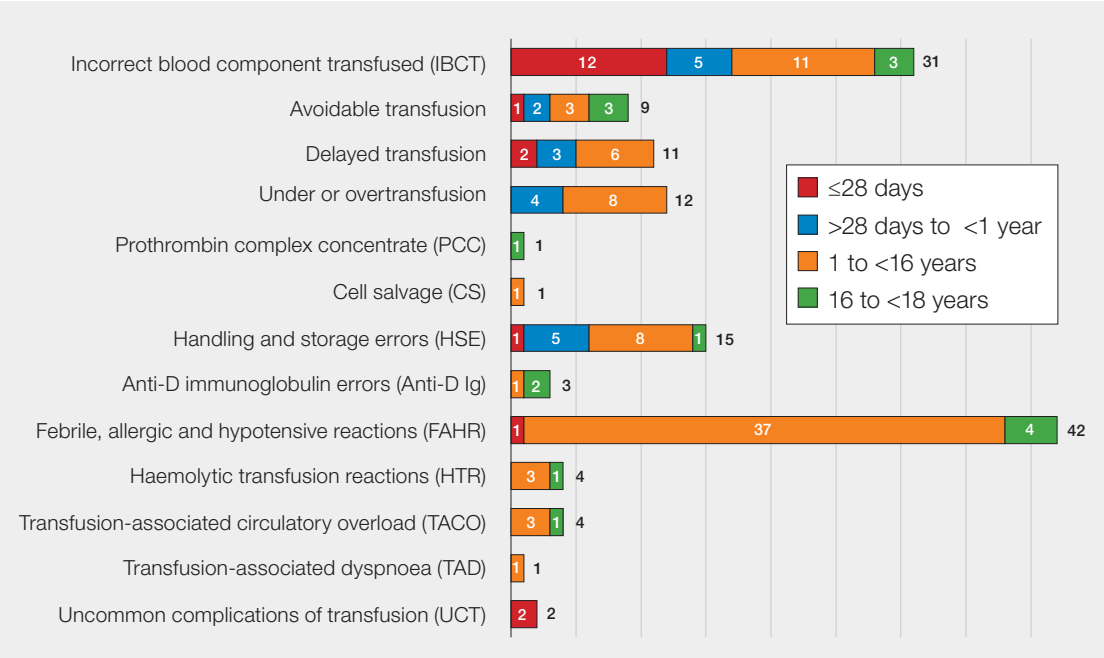


Figure 22.3: Summary of paediatric cases by category and age 2021

Deaths related to transfusion n=2

There were 2 paediatric deaths felt to be possibly related to transfusion. One of these deaths was in the ADU category and was a delay in transfusion. The other was in the UCT category and was a case of transfusion-associated necrotising enterocolitis.

The delay in transfusion is discussed below and was in the emergency provision of red cells. This highlights the importance of robust communication pathways in an emergency.

Case 22.1: Communication failure resulting in delay in provision of red cells

A preterm baby was born in a poor condition and required resuscitation. The Hb on a blood gas was 50g/L. Due to a communication error, the call for emergency blood was not received by the transfusion laboratory and no red cell units were provided before attempts at resuscitation were abandoned.

Case 22.2: Case of necrotising enterocolitis following transfusion

An extremely preterm baby with respiratory distress, sepsis (site unspecified) and hypoglycaemia developed falling oxygen saturation and became pale with distended, tense abdomen 7 hours following a red cell transfusion for severe anaemia. The baby continued to deteriorate despite resuscitation and abdominal X-ray showed a perforation. Death was felt to be possibly related to transfusion. This was a suspected case of transfusion-associated necrotising enterocolitis.

Major morbidity n=20

There were similar numbers of cases this year which were judged to have resulted in major morbidity, with the largest category being FAHR.

There were 14 in the FAHR category, 1 of which is illustrated below. It is a reminder that significant hypotension can occur in association with transfusion reactions including in very tiny babies (Bolton-Maggs et al. 2016). FAHR should be considered if there is unexpected hypotension following transfusion, although this can be difficult to distinguish from complex underlying diagnoses.

Case 22.3: Hypotension during MB-FFP infusion in child with pre-existing cardiac condition

A preterm baby developed significant hypotension and drop in oxygen saturation 5 minutes into an infusion of MB-FFP. The baby responded to resuscitation. Of note the baby had pre-existing fetal arrhythmia and reduced ventricular function so it is difficult to know the contribution of the pre-existing condition to the episode of hypotension.

There were 3 cases in TACO, 1 of which was an episode of TACO in a young child following FFP infusion, which resulted in ICU admission.

Two cases were in the HTR category with 1 being a complex case involving both an allo anti-Jk^{b} and autoantibodies (auto anti-c and anti-E) with positive DAT in a child following a multi-visceral transplant. The other was a teenager with sickle cell disease and hyperhaemolysis with anti-S and anti-Fy^{a}.

The final case was in the ADU category and was a delayed transfusion due to lack of awareness of a paediatric MHP (discussed in the ADU section of this chapter).

Error related reports n=83

Apart from a set of IBCT reports in 2020 from a single centre due to a look back exercise, the number of paediatric error reports is broadly similar over the last 3 years.

Incorrect blood component transfused (IBCT) n=31

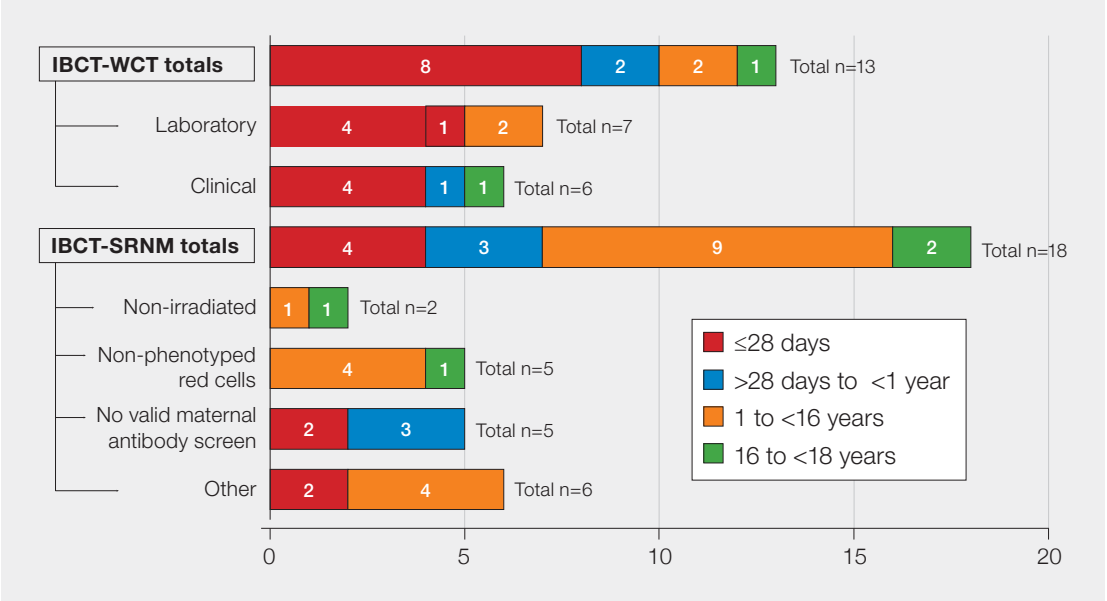


Figure 22.4: Breakdown of incorrect blood component transfused reports

Other includes incomplete testing (n=3), invalid time-expired sample (n=1), failure to provide CMV-negative (n=1) and inappropriate D-positive component (n=1)

IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met; CMV=cytomegalovirus

IBCT wrong component transfused (WCT) n=13

IBCT-WCT clinical errors n=6

Adult O D-negative red cells to a neonate n=5

There remain a significant number of reports of adult specification O D-negative red cells being administered to children under 1 year of age. Of these, 3 were neonatal resuscitation, and suitable neonatal specification units were available. The other 2 incidents were emergency situations involving infants where adult specification units were used but neonatal units could have been provided.

Incorrect blood component to haemopoietic stem cell transplant recipient n=1

A child post haemopoietic stem cell transplant (patient's blood group was A D-positive and stem cell donor was O D-positive) received incorrect but compatible blood components due to a lack of communication from the clinical team to the transfusion laboratory about the transplant status.

IBCT-WCT laboratory errors n=7

Issues with grouping n=3

All cases involved neonates. One case involved issue against another patient's sample, 1 involved lack of two historical groups and the other resulted in incorrect provision of FFP based on an inconclusive blood group.

Adult specification component to a neonate or infant n=2

One of these was FFP and 1 red cells.

Wrong ABO/D blood components provided to a haemopoietic stem cell transplant recipient n=2

Two cases involved issues around communication resulting in provision of components of the wrong ABO (although compatible) or D-type to a haemopoietic stem cell transplant recipient.

IBCT-specific requirements not met (SRNM) n=18

IBCT-SRNM clinical errors n=1

A child with sickle cell disease was admitted to ICU following transfer from another hospital and received non-phenotyped red cells which were also not sickle negative due to poor communication. This highlights the importance of communication of specific requirements between clinicians and laboratory.

IBCT-SRNM laboratory errors n=17

Most paediatric SRNM reports were primarily due to errors in the laboratory.

In 5 cases (all infants aged 1 month old and younger), there was a failure to perform an antibody screen on a maternal sample. In 3 cases testing was incomplete. Of these, 1 child only had a single group and save sample, 1 child the DAT was not complete prior to issue, and in the 3rd, 1 infant had platelets issued when their blood group was not known. There were 4 children (3 with sickle cell and 1 with thalassaemia) that received non-phenotyped non-HbS negative blood.

Case 22.4: Alloimmunisation in a patient with thalassaemia resulting from failure to provide phenotype matched red cells

A teenager with thalassaemia had previously had red cell phenotyping performed. There was no alert on the laboratory system indicating that this patient required phenotyped red cells and they were transfused with E-positive red cells. The patient developed an anti-E.

Two patients (1 child and 1 teenager) with Hodgkin's disease were given non-irradiated blood components. There was 1 case reported where the maternal sample was invalid and had expired.

Another patient received D-positive blood components inappropriately due to a selection error (patient was group A D-variant and should have been transfused D-negative red cells), and in the final case a CMV-negative teenager received two units of CMV untested granulocytes against local policy.

Learning points

- Provision of appropriate blood components with the correct specification for chronically transfused patients is vital
- Transfusion errors where specific requirements for paediatric haemoglobinopathy patients have not been met continue to be reported to SHOT. BSH guidelines (BSH New et al. 2016) recommend that children with haemoglobinopathies should have extended red cell phenotyping or genotyping. It is considered good practice for these same recommendations to apply to children on chronic transfusion programmes, such as bone marrow failure syndromes
- The All-Party Parliamentary Group 'No One's Listening' report (Sickle Cell Society 2021) into poor care for patients with sickle cell anaemia has made several recommendations to improve standards of care provided for these patients and enhance patient safety

SHOT
Serious Hazards of Transfusion

Avoidable, delayed, under or overtransfusion (ADU) n=33

Avoidable transfusions n=9

In 4 cases erroneous results were acted upon. These included looking the result of wrong baby (n=1), acting on previous results (n=2) and acting on a dilute sample when a repeat showing a much higher Hb was available (n=1).

For 3 children, O D-negative components were used when in all cases crossmatched blood was appropriate and available.

One case involved lack of knowledge of recommended transfusion thresholds and was exacerbated by poor handover between clinical staff. In the final case an additional platelet unit was given in error to a child with aplastic anaemia as the IT system did not allow a unit to be ordered but merely be on 'stand-by' in case needed.

Delayed transfusions n=11

Five errors directly involved communication issues, including the case of the neonate who died (Case 22.1). In 1 case there was a delay in clinical decision making and in another a calculation error was noted and had to be corrected before the child received the blood component. Three errors involved laboratory processes: not thawing FFP in a timely manner, incorrect rejection of a sample that was not a duplicate, and not reserving red cells for a blood prime for an apheresis procedure. In the final case, management of a major haemorrhage was delayed due to lack of awareness of the paediatric MHP.

Prothrombin complex concentrate (PCC) n=1

There was a delay in the management of the coagulopathy in a teenage patient with acute promyelocytic leukaemia due to confusion around the optimal recommended components and/or blood products (PCC had been prescribed).

Case 22.5: Lack of awareness of paediatric MHP

The paediatric MHP was activated in the ED. The laboratory scientist was not aware that there was a separate protocol for children and advised the ED to contact the on-call consultant paediatric haematologist instead of preparing packs, resulting in a 20-minute delay in provision of the blood components.

SHOT
Serious Hazards of Transfusion

Learning points

- The importance of MHP was highlighted in the 2022 CAS Alert (SHOT 2022) and was also discussed in the 2020 Annual SHOT Report paediatric chapter (Narayan et al. 2021). The recently published 2018 paediatric National Comparative Audit found that only 21% of reporting sites had an MHP for children (as distinct from adults) and that the MHP was only activated in 55% of cases of paediatric major haemorrhage (NCA 2021)
- All staff, clinical and laboratory, involved in paediatric and neonatal transfusions must be familiar with the paediatric MHP protocol

Overtransfusions n=12

Most (9/12) paediatric overtransfusion events were related to incorrect prescribing. All were transfusions of red cells except 1 infant who received an excess of platelets. Prescribing errors included whole adult units given to children, correct volume prescribed but whole unit given in error, and a mis-transcription of a child's weight (see Case 22.11 in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2021/).

In 2 cases illustrated below, erroneous use of the formula to calculate the red cell transfusion volume required (using Hb in g/dL rather than g/L) resulted in a 10-fold volume error. Hb has been measured in g/L rather than g/dL for several years and guidance on using the calculation formula is given in the paediatric transfusion guidelines, including a reminder to use Hb in g/L, to double-check that the final volume calculated is not excessive, and that the final volume should not exceed the maximum normally transfused to an adult in a similar situation (BSH New et al. 2016).

In 7/12 cases, overtransfusions were prescribed by paediatric staff, 2 by paediatric haematologists and 1 by a gynaecologist (2 were not specified). Where specified these clinicians were speciality registrars in 6, consultants in 2 and a FY2 in 1 case.

Case 22.6: Calculation error that illustrates the pitfalls but also safety mechanisms that worked

An infant received an overtransfusion due to a calculation error. The Hb was 68g/L and there was an error in calculating the required dose (mL) of red cells. The registrar used g/L (68) to calculate the volume rather than g/dL still in use in this department (6.8). The intended amount therefore was a tenfold error (432mL rather than 43.2mL). A safety net on the formula states a maximum transfusion volume of 20mL/kg (170mL) therefore this is how much was prescribed. The nurses checking prescription both stated they did not check the formula themselves. After handover a different nurse realised patient had received 110mL (12mL/kg) and paused the pump as it is unusual to give more than 10mL/kg to a patient with liver disease. Repeat testing showed Hb was 96g/L.

The outcome of this episode was to revise the formula for blood transfusion to reflect g/L and no longer use g/dL.

Two further cases in this category are described in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2021/).

Learning points

- Prescribing errors for blood components in children are common. Hospitals should review their paediatric transfusion guidelines and ensure they contain updated units and calculations. The Hb values used for that the calculations should be in g/L and not g/dL
- When a calculation (BSH New et al. 2016) is performed to determine the volume of red cells required, it is vital to 'sense check' that the volume prescribed is <20mL/kg, other than for specific large volume transfusions, and if not recheck the calculation
- The patient's weight (child or neonate) should be recorded accurately as this is the basis for all calculations including transfusion support
- Electronic prescribing systems can assist in prevention of paediatric prescribing errors by limiting the total volume of blood component that can be authorised. However, the design of such systems can be complex as they must allow for large volumes transfusions either in emergency or for exchange transfusion

Cell salvage (CS) n=1

Relatively few CS reports are seen in the paediatric age group probably reflecting the proportion of paediatric patients receiving this form of transfusion. It is even more critical that all members of staff involved understand the process when a procedure is performed less frequently for a patient group.

Case 22.7: Communication issues resulted in confusion about whether to utilise salvaged blood

Autologous re-transfusion was not performed for a teenager following scoliosis surgery despite the Hb being below the local postoperative transfusion threshold. On review there had been uncertainty as to whether to give the transfusion of the salvaged blood to this patient and the blood expired before it could be transfused.

Handling and storage errors (HSE) n=15

Most of the HSE were primarily clinical rather than laboratory (14 out of 15).

There were 7 technical administration errors. Of these, 4 were errors in transfusion rate, 2 involved incorrect prescription and 2 incorrect pump programming. One error involved running red cells alongside an incompatible fluid and the other 2 were problems with the giving set.

In 3 cases, duration of transfusions were greater than 5 hours for 2 red cell transfusions and nearly 2 hours for a platelet transfusion, although in the latter case the patient had a sudden deterioration in the middle of the transfusion (felt to be unrelated to the transfusion) and this was the reason given for the long duration.

The remaining cases included 4 reports where time-expired or wasted units were transfused, and in 1 case there was an error in the cold chain.

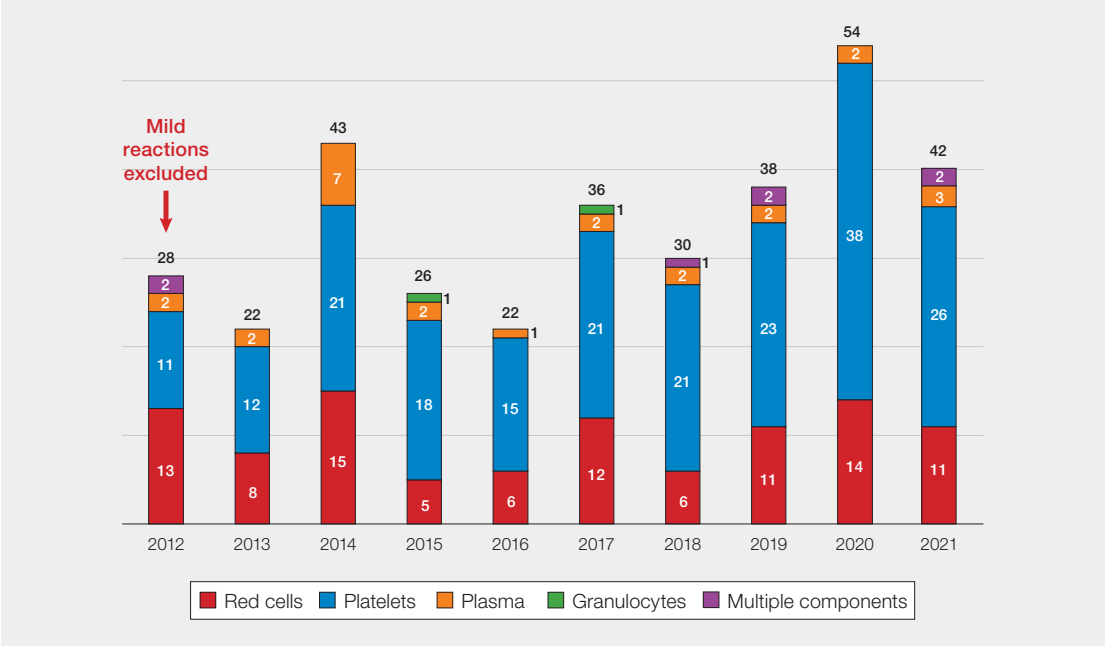
Anti-D immunoglobulin (Ig) n=3

One case involved failure to give anti-D Ig to a D-negative teenager who received D-positive platelets. The other 2 cases were failure to give anti-D Ig prophylaxis to D-negative teenage mothers.

Transfusion reactions n=54

Febrile, allergic and hypotensive reactions (FAHR) n=42

Figure 22.5 Summary of FAHR reports by component type from 2012 to 2021

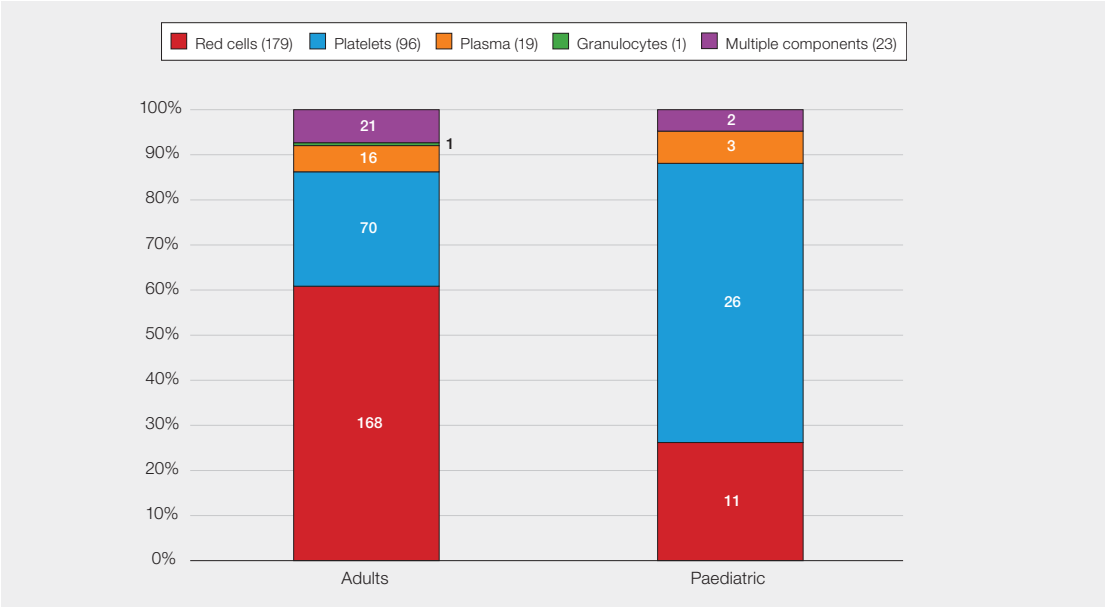


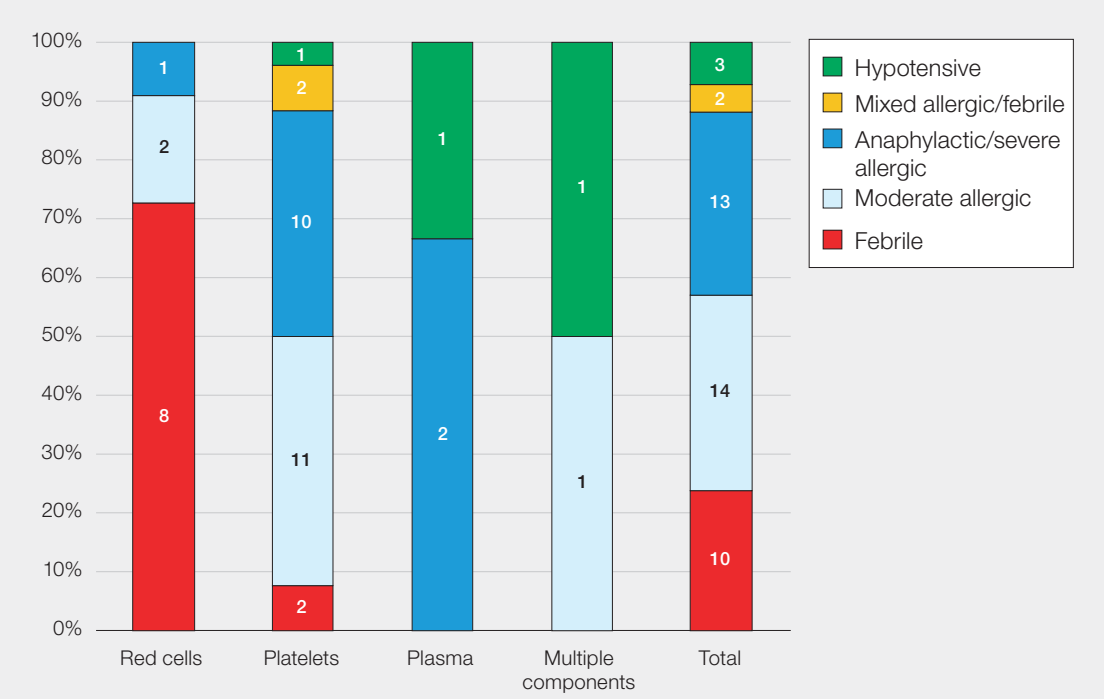
The total number of reports have reduced from a peak of 54 in 2020 (Figure 22.5). Platelet reactions continue to account for a higher proportion of paediatric FAHR as compared to adults, 26/42 (61.9%) (Figure 22.5), although these were fewer than the previous year. It is unknown whether paediatric platelet transfusion demand has changed in this period.

The relative frequency, and often severity, of paediatric FAHR to platelets is a reminder that prophylactic platelet transfusions should only be given according to guidelines. For neonates, this message is accentuated by the findings of the PlaNeT-2 trial showing evidence of harm of prophylactic platelet transfusions given above a threshold of $25x10^9$/L (Curley et al. 2019).

There was 1 possible reaction in a preterm neonate with pre-existing cardiac condition, discussed in the major morbidity section (Case 22.3). This case is a reminder that reactions can occur in this age group, sometimes hypotensive, and may be difficult to identify or distinguish from other complex co-morbidities.

Figure 22.6: Paediatric FAHR reports a. Comparison of proportions of adult and paediatric FAHR related to different components





b. Percentages of reaction types of each component for paediatric reports

Haemolytic transfusion reaction (HTR) n=4

There were 4 cases reported. Two of these cases resulted in major morbidity and are described in the relevant section above (a case of auto/alloantibodies in a multi-visceral transplant patient and the other a case of hyperhaemolysis in a patient with sickle cell disease).

A young child developed a bilirubin rise following a group A platelet transfusion of non-HT negative group A platelets to a group AB child. This case is a reminder that for ABO minor-mismatched platelet transfusions to children, platelets should be tested and negative for high-titre antibodies (anti-A and anti-B; New et al. 2016). The other case was of a delayed HTR following a red cell exchange, and an eluate showed an auto anti-C and anti-E. See Chapter 18, Haemolytic Transfusion Reactions (HTR) for further details of both cases.

Pulmonary complications of transfusion in neonates and children

Identification of pulmonary complications of transfusion in children remains challenging without age-specific definitions, and reports in this age category are few and intermittent. There has been no pattern in reporting of pulmonary complications evident over the last 10 years.

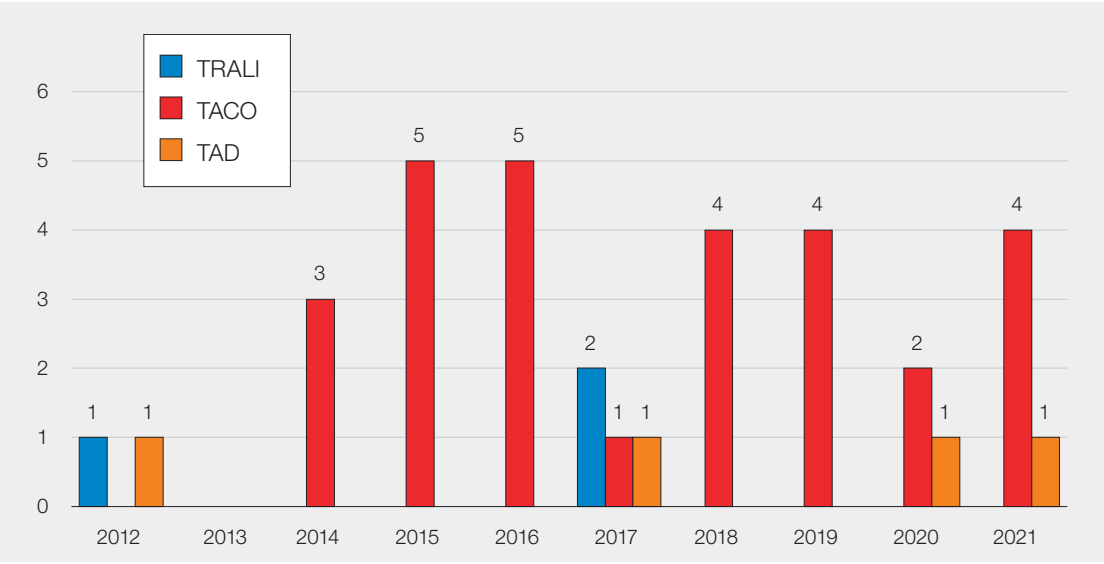
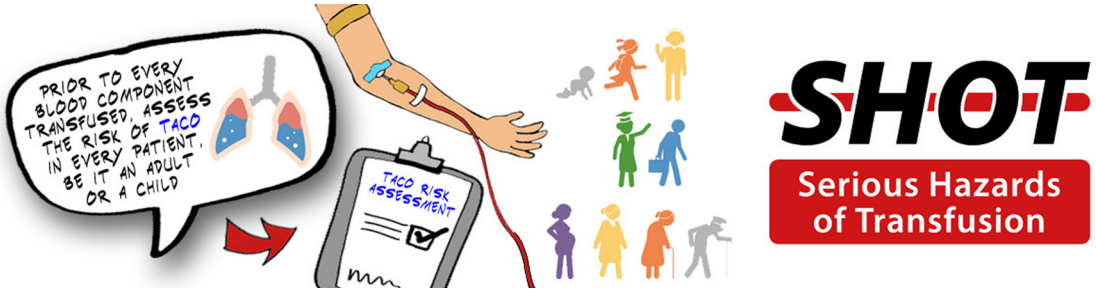


Figure 22.7: Pulmonary complications in children and neonates 2012-2021

Transfusion-associated circulatory overload (TACO) n=4

There were 4 cases of TACO in 2021. One of these followed red cell transfusion alone, 1 apheresis platelets. Two followed transfusions of multiple components. The range of age of presentation was 2 to 16 years. Of note there is an established SHOT checklist for TACO in adult patients and although not validated in children several of the main points in the checklist are relevant.



Non-TACO pulmonary case n=1

One case was classified as TAD but also involved an overtransfusion.

Case 22.8: Overtransfusion of a young child resulted in TAD

A child with leukaemia had been correctly prescribed 10mL/kg of red cells over 1 hour. However due to an error in the pump programming 40mL/kg was administered over 4 hours. This resulted in tachycardia and increased respiratory rate. This settled without any specific treatment and no chest X-ray was performed and thus did not meet the criteria for TACO. Both the nurses checking the transfusion were inexperienced in checking transfusions and one had not performed this role at the hospital before.

There were no cases of TRALI in 2021.

Learning points

- Pulmonary complications of transfusion can be difficult to identify in young children, particularly in neonates who may have multiple causes that could result in respiratory deterioration
- It is vital that those caring for children and infants are aware of TACO/TAD/TRALI as a potential cause of respiratory deterioration following transfusion

Transfusion-transmitted infection (TTI) n=0

There were no cases of paediatric TTI in 2021.

Uncommon complications of transfusion (UCT) n=2

There were 2 uncommon complications of transfusion in children in 2021. One was a case of NEC (Case 22.2) which resulted in the neonatal death. Causality of red cell transfusion in relation to NEC is still unclear. The other was a case of hyperkalaemia following rapid transfusion of red cells irradiated several days previously.

Case 22.9: Iatrogenic hyperkalaemia secondary to transfusion of large volume of irradiated red cells

An infant with Di-George syndrome with lymphopenia was taken to theatre for washout of infected cardiothoracic surgical wound. The infant had a surgical complication and required urgent large volume, rapid red cell transfusion due to significant bleeding. The red cell unit had been irradiated approximately 7 days previously. The child developed abnormal ECG secondary to hyperkalaemia from the transfused blood with an arterial blood gas showing a potassium of 8.5. This was managed appropriately and the infant recovered and survived.

Learning points

- Hyperkalaemia following transfusion is recognised. Significant clinical sequelae including cardiac arrest are rare, but risk factors include hypovolaemia, and large volume transfusions in particular to neonates and infants (Vraets et al. 2011, Burke et al. 2021)
- In order to reduce the risk of hyperkalaemia following transfusion, the use of red cells within 5 days of donation, and if irradiated, within 24 hours of irradiation, is recommended for large volume neonatal and infant transfusions, including for cardiac surgery (BSH New et al. 2016)
- Use of irradiated red cells in an emergency to treat major haemorrhage can increase the risk of hyperkalaemia following transfusion so it is probably safer to avoid unless irradiated blood is otherwise indicated (BSH Foukaneli et al. 2020)

Recommended resources

SHOT Video: Paediatric SHOT
SHOT Video: Delayed Transfusions in Major Haemorrhage
https://www.shotuk.org/resources/current-resources/videos/

SHOT Bite No. 4: Paediatrics
SHOT Bite No. 8: Massive Haemorrhage Delays
https://www.shotuk.org/resources/current-resources/shot-bites/

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