Paediatric Cases n=132

22

Authors: Anne Kelly and Helen New

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.

Key SHOT messages

- It is essential that those who request laboratory tests understand the significance of test results. Unexpected results should be challenged or repeated to avoid acting on erroneous results
- Understanding the significance of abnormal coagulation in children and when to call for specialist interpretation is vital
- Errors in calculation of blood component volumes and specific requirements still occur. Induction training of paediatric staff should include specific requirements and safe blood prescribing
- Following the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) review (2019), recipients born after 1995 can now receive United Kingdom (UK) plasma (non pathogen-inactivated), and either apheresis or pooled platelets. This will therefore affect specific requirements not met (SRNM) reporting for next year

Abbreviations used in this chapter

ADU	Avoidable, delayed and under/overtransfusion
APTT	Activated partial thromboplastin time
BSH	British Society for Haematology
CMV	Cytomegalovirus
DAT	Direct antiglobulin test
FAHR	Febrile, allergic and hypotensive reactions
FFP	Fresh frozen plasma
Hb	Haemoglobin
HSCT	Haemopoietic stem cell transplant
HSE	Handling and storage errors
HTR	Haemolytic transfusion reactions
IBCT	Incorrect blood component transfused
Ig	Immunoglobulin
IT	Information technology
IUT	Intrauterine transfusion
IV	Intravenous
MB	Methylene blue-treated
NM	Near miss
PICU	Paediatric intensive care unit
PT	Prothrombin time
RBRP	Right blood right patient
SaBTO	Advisory Committee on the Safety of Blood, Tissues and Organs
SD	Solvent-detergent treated
SRNM	Specific requirements not met
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
TANEC	Transfusion-associated necrotising enterocolitis
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection
UCT	Uncommon complications of transfusion
UK	United Kingdom
WCT	Wrong component transfused

Recommendations

- Errors in prescription of blood components continue to occur. Training of paediatric and neonatal staff involved in transfusion needs to be ongoing and occur at induction to new posts
- Dissemination of resources such as the 'bookmark' and awareness of the Blood Components mobile application (NHS 2018) and the British Society for Haematology (BSH) guidelines are vital (New at al. 2016)
- The SHOT paediatric video, available on the SHOT website (https://www.shotuk.org/resources/current-resources/videos/), should be viewed for key educational messages from the last 10 years of paediatric SHOT reports

Action: Transfusion practitioners and hospital transfusion teams

Introduction

Common themes for transfusion errors remain consistent over time in both children and neonates.

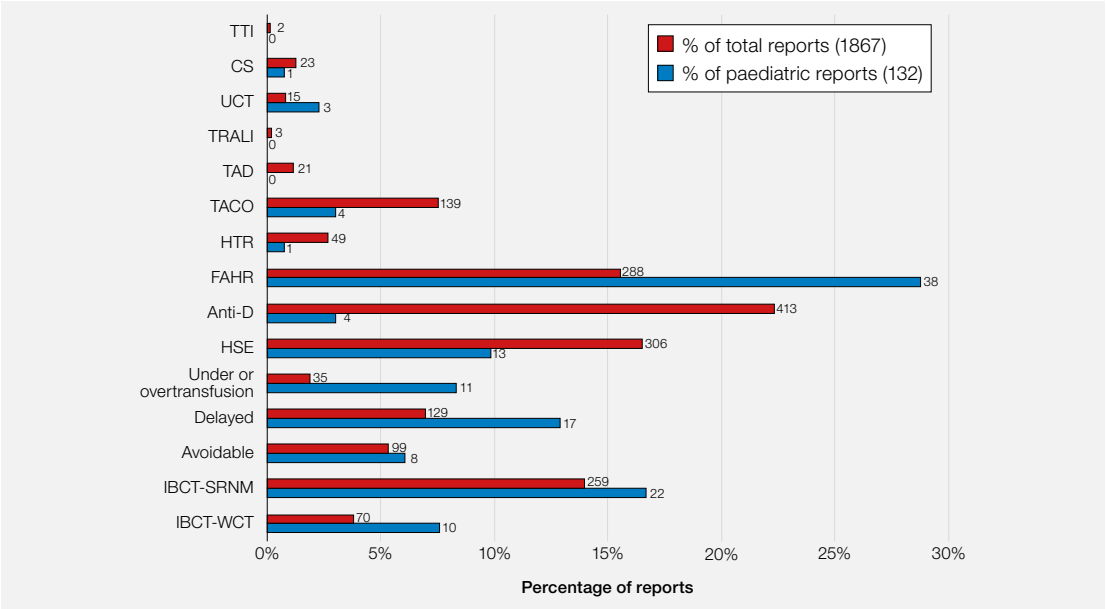
The number of reports is similar to last year (2018) at 132/1867 (7.1%), and if near miss (NM) and right blood right patient (RBRP) are included, 245/3397 (7.2%). The split between categories remains similar (Figure 22.1).

Paediatric cases continue to be over-represented as percentages of total reports in several categories, particularly in under and overtransfusion, 11/35 (31.4%) cases, Figure 22.1. Neonates are disproportionally represented in the incorrect blood component transfused (IBCT) category in comparison with other categories (Figure 22.2).

Overall numbers of paediatric reports whilst having increased since 2009 have been broadly stable in all age categories for the last 4 years. Interestingly the proportion of neonatal reports has dropped compared to a peak in 2015 (Figure 22.3).

The proportion of paediatric error reports primarily from the laboratory was 34/86 (39.5%) which is similar to last year. These were in the following categories: IBCT-wrong component transfused (WCT) n=5, IBCT-SRNM n=17, avoidable, delayed and under/overtransfusion (ADU) n=10, and handling and storage errors (HSE) n=2.

Figure 22.1: 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; IBCT-SRNM=incorrect blood component transfused-specific requirements not met; IBCT-WCT=IBCT-wrong component transfused

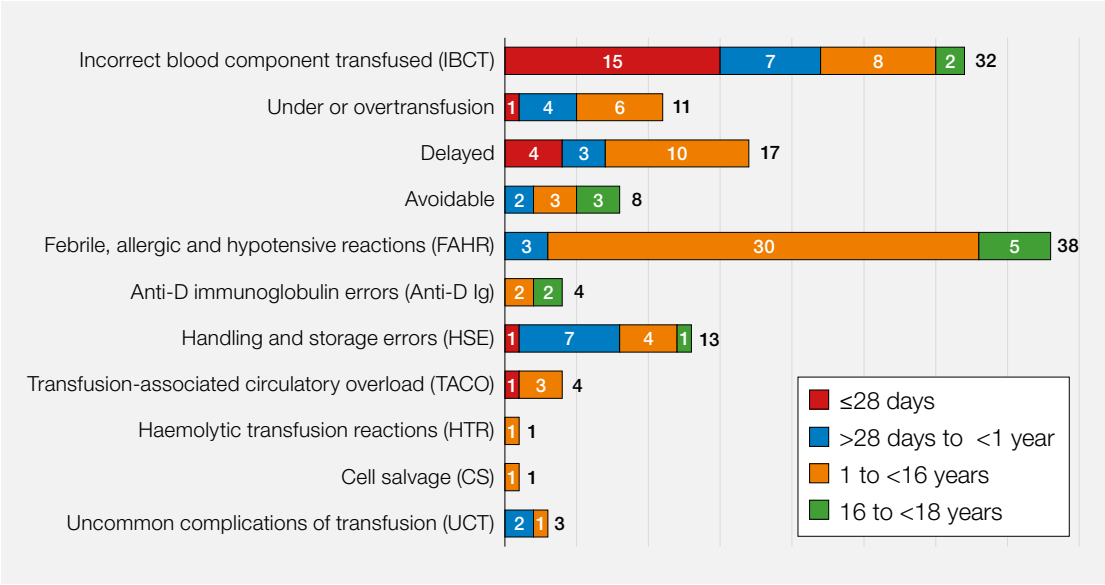


Figure 22.2: Summary of paediatric cases by category and age 2019

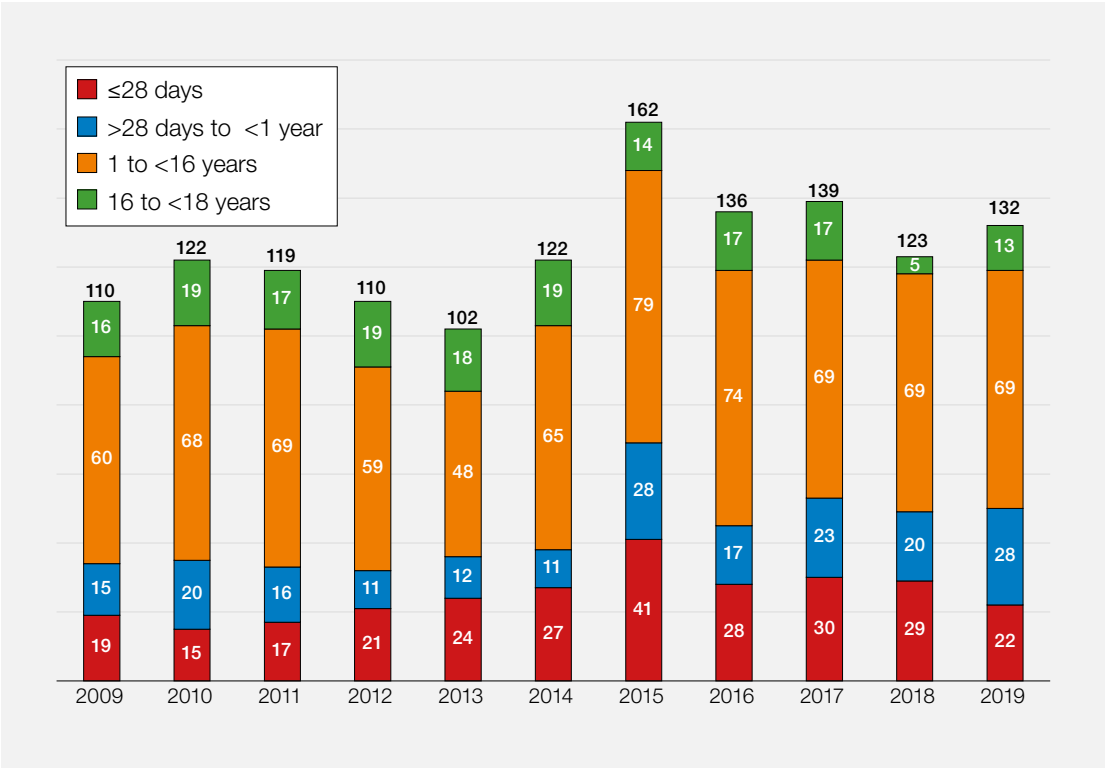


Figure 22.3: Trends in paediatric cases from 2009-2019

Death n=1

There was only 1 death that was determined to be possibly related to transfusion: a case of transfusion-associated necrotising enterocolitis (TANEC) (UCT category; imputability possible =1).

Case 22.1: A case of TANEC

A very preterm baby who was a few months of age, received two red cell transfusions for anaemia within 12 hours. The baby had had a previous bowel perforation. Around 2 hours after starting the second transfusion they developed increasing nasogastric aspirates and worsening abdominal distension. The baby died 24 hours later from multiorgan failure.

A notable ADU case is discussed below as although the recipient died of complications unrelated to the transfusion, the error raises important learning points (see also Case 11a.4 in Chapter 11a, Delayed Transfusions for further discussion).

Case 22.2: Failure to recognise importance of an isolated severely prolonged APTT in a male child leading to delay in appropriate treatment of an infant with haemophilia

A male infant <6 months of age was admitted to his local hospital 6 days after a fall down the stairs. Two coagulation screens showed an un-clottable activated partial thromboplastin time (APTT) with a normal prothrombin time (PT) and the patient was given vitamin K prior to transfer. This result was not communicated at the time to a haematologist. Further investigations, in particular coagulation factor assays, were not performed. The infant was transferred to a tertiary centre and the APTT was noted to be 101 seconds with a normal PT. The biomedical scientist noted in the report that these were abnormal and requested a repeat, but the abnormal results were not discussed with a haematologist. The infant was given fresh frozen plasma (FFP) with a partial improvement in APTT but not full correction. The results were not discussed with the haematology department until over 24 hours after admission, and the infant received three transfusions of solvent detergent (SD)-FFP. The infant was subsequently diagnosed with severe haemophilia A. He died of an intracranial bleed caused by an arteriovenous malformation.

This case illustrates the vital importance of understanding the significance of abnormal laboratory results and of early discussion with a haematologist. An isolated prolonged APTT in a bleeding infant should have triggered urgent further investigation (ideally factor assays). FFP does not contain sufficient factors VIII or IX to provide sufficient correction of levels in patients with haemophilia. Recombinant factor VIII would have been the appropriate treatment of the infant's Factor VIII deficiency in association with a bleed.

Learning points

- Severe abnormalities of coagulation in a bleeding patient require urgent discussion with a haematologist
- Severe bleeding disorders can present in neonates and early childhood in the absence of family history
- In the neonatal period and up to 6 months of life the interpretation of coagulation results can be complex and normal ranges appropriate for age and gestation should be used, thus underlining the need for early specialist input

Major morbidity n=14

There were 14 cases associated with major morbidity. There were 12 cases in the FAHR category which met the criteria for major morbidity. The other 2 cases were in TACO and UCT categories and are discussed in the relevant sections.

Error-related reports n=86

Incorrect blood component transfused (IBCT) n=32

IBCT wrong component transfused (WCT) n=10

There were fewer reports in this category (n=10) compared to the 2018 Annual SHOT Report (Narayan et al. 2019) where there were 17 cases.

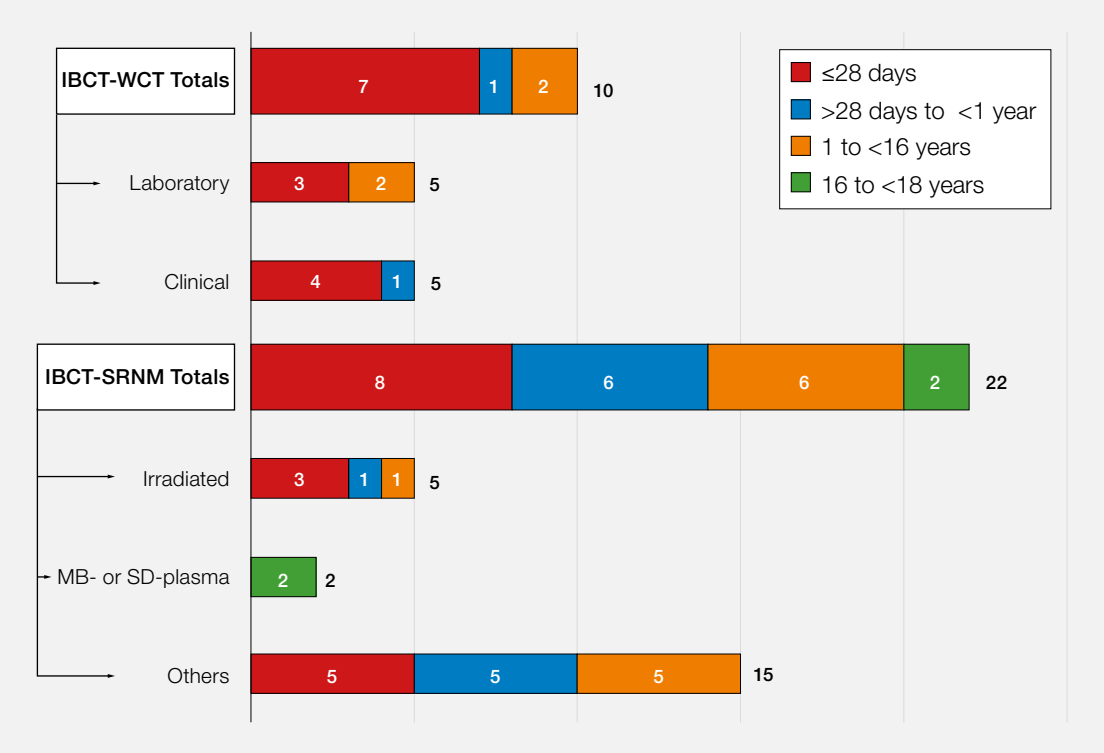


Figure 22.4: Breakdown of incorrect blood component transfused reports

IBCT-WCT=incorrect blood component transfused-wrong component transfused; IBCT-SRNM=IBCT-specific requirements not met; MB=methylene blue-treated; SD=solvent-detergent treated

IBCT-WCT clinical errors n=5

Adult emergency blood given to neonates n=2

There were 2 reports of adult specification red cell components given to neonates. The first was a newborn who received blood from an adult O D-negative red cell unit which was subsequently found to be cytomegalovirus (CMV)-positive. This child died from complications unrelated to the transfusion. The other case was a newborn baby who received 15mL of an O D-positive unit which was intended for the mother and was therefore not of neonatal specification. Fortunately, it was ABO and D-compatible as both mother and baby were B D-positive. Of note a 2-person bedside check did not detect the error and it was noticed by the transfusion laboratory.

Failure to communicate relevant medical history n=2

Communication errors were noted in 2 patients where the wrong specification component was given. One was a post liver transplant patient who should have only received group O components, but this was not communicated to the transfusion laboratory by the treating team. Therefore, they received a group B red cell unit. There were no significant clinical consequences.

Case 22.3: Failure to communicate history of haemopoietic stem cell transplant (HSCT)

A young child who was post HSCT for juvenile myelomonocytic leukaemia received group O platelets instead of group B. The transplant protocol and therefore the change in the child's transfusion requirements had not been shared with the hospital transfusion laboratory. There were no clinical sequelae.

Other n=1

A retrospective review uncovered that a pair of preterm twins had inappropriately had a single unit of FFP shared between them, which is contrary to guidelines.

Learning points

- Children who undergo either solid organ or stem cell transplantation may have a change in their transfusion requirements post transplant
- Communication between the transplanting team and the hospital transfusion laboratory is vital to ensure the correct components are issued
- Where care is delivered post transplant closer to children's homes (e.g. by paediatric oncology shared care units), there should be mechanisms in place to ensure that this information is shared between units

IBCT-WCT laboratory errors n=5

There were 5 errors in the laboratory category. Three of these involved issue of a D-positive component in error; 1 to a baby whose D-type was unknown, 1 to a female D-negative child and 1 to a D-negative patient whose group switched post HSCT.

The remaining cases were 1 occasion of administration of a group O component to a group A patient (FFP, with no haemolytic sequelae reported), and 1 occasion of administration of a group O component (cryoprecipitate) when the patient group was unresolved.

IBCT-specific requirements not met (SRNM) n=22 (17 laboratory; 5 clinical)

Failure to provide irradiated components n=5

Five children had received non-irradiated components due to a failure to communicate the need for irradiated components by the clinical team. Two of these were neonates who had received intrauterine transfusion (IUT) and of note there was no transfusion-associated graft-versus-host disease. SHOT has received 20 reports since 2007 where irradiation was missed for transfusion following IUT, with no adverse outcome. These errors usually occur due to failure in communication and often lead to significant anxiety for families and clinical staff. Of the other cases, 1 child had a previous HSCT, 1 had received Campath and 1 a purine analogue.

Learning point

- All staff involved in paediatric transfusions must be aware of the specific requirements for transfusions, especially in cases with previous intrauterine transfusions (IUT). Paediatric transfusion prescribing including choosing the right component should be the focus of ongoing education in hospitals and staff should be familiar with available guidelines. Effective communication is vital in preventing such incidents

Failure to provide appropriate blood for patients with sickle cell disease n=4

Sickle patients have specialised red cell requirements including the need for a baseline extended red cell phenotype and provision of Rh phenotyped, HbS-negative components. Four children did not have these requirements met.

Failure of pre-transfusion compatibility testing or component selection n=8

Of these cases, 6 were due to failure to perform an antibody screen on a maternal sample and upon subsequent investigation it was found that 5 mothers had previous known positive antibody screens (4 anti-M and 1 with both anti-Le^a and anti-Le^b). One of the babies with maternal anti-M was retrospectively noticed to have a significant drop in haemoglobin in the weeks following transfusion, possibly due to haemolysis. The other 2 cases were failure to provide antigen-negative red cells to children under 4 months of age with history of maternal antibodies.

Failure to provide imported plasma for a recipient born after 1995 n=2

Two teenagers received UK plasma (non-pathogen inactivated). Of note the requirement for non-UK plasma for patients born after 1995 has now been removed.

Other n=3

In 1 report, CMV-unscreened red cells were provided in error. Another child received pooled rather than apheresis platelets. In the 3rd case electronic issue was used in error for a post stem cell transplant patient.

Learning point

- Following the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO) review (2019), recipients born after 1995 can now have United Kingdom (UK) plasma (non pathogen-inactivated) and either apheresis or pooled platelets. This will therefore affect specific requirements not met (SRNM) reporting for next year (SaBTO 2019)

Avoidable, delayed, under or overtransfusion (ADU) n=36

Avoidable n=8

There were 8 avoidable transfusions, with 5 due to misinterpretation of results. Of these 5 reports, 4 were due to lack of questioning of unexpected results and 1 was due to a transcription error (see Case 22.4). There were 2 cases where emergency O D-negative red cells were used when fully crossmatched units should have been given. In the final case a teenage patient received two units of FFP to correct coagulation results which were not sufficiently deranged to warrant correction.

Case 22.4: Transcription error resulting in transfusion based on erroneous results

A young infant who was unwell had a full blood count sent to the laboratory. The platelet count was telephoned through to the ward by a member of the laboratory team and was written down as 23.8x10^9/L. The child was unwell and it was presumed that the count was valid and so a platelet transfusion was given. Subsequently when the result was available on the computer it was seen that the true result was 238x10^9/L.

Learning points

- Platelet counts are not reported with decimal points
- When results are telephoned through from the laboratory to ward areas it is critical that the members of staff check that they have heard correctly. Results should be uploaded onto electronic format as soon as possible so that the ward staff can check them

Overtransfusion n=11

In total 11 patients received excessive volumes of component. Of these, 6 were related to failure to prescribe the correct volume, once again highlighting the importance of correctly calculating and prescribing in mL for babies and children. Electronic prescribing systems which incorporate prompts or reminders are ideally placed to avoid transfusion of excessive volumes in children.

Case 22.5: Prescription error of 10 times the required red cell volume

Red cell transfusion was prescribed for a 3kg infant (pre-transfusion Hb 79g/L): the volume was discussed in a ward round and 300mL was prescribed. An electronic system was used to prescribe the blood but there was no in-built error message to prevent prescription of such a large volume. 138mL (46mL/kg) was administered before the error was realised. Post-transfusion Hb was 141g/L.

Of the remaining reports, 2 were errors in setting the infusion pump and 1 was failure to communicate the pump settings at a change of staff. There was 1 error when an incorrect weight was used for the calculation of transfusion volume, and in 1 report national transfusion guidance was not followed where a non-bleeding adult sized teenager received three red cell units without any check of Hb between units.

Delay in transfusion n=17

One of these errors was the missed diagnosis of haemophilia resulting in a delay in the child receiving the appropriate recombinant coagulation factor. The other errors included 6 communication errors, 1 information technology (IT) error, 3 internal hospital logistics errors, 1 delay in cannulation, 4 equipment failures and 1 case where one of the samples from a pair of brothers was discarded in error as it was thought to be a duplicate.

Cell salvage (CS) n=1

In 1 case during cell salvage black particles were seen in the bag from the first processed bowl of red cells. This was linked to a series of other cases in the same centre and is discussed in more detail in Chapter 21, Cell Salvage (CS).

Handling and storage errors (HSE) n=13

Four errors were made setting infusion pumps, with 3 involving infants less than 6 months of age. There were 5 temperature-related errors, 4 resulting in failure of cold chain for red cells and 1 a failure of temperature control on a platelet incubator. There were 2 traceability failures where a retrospective review at a hospital could not determine whether 2 paediatric patients had received the component prescribed. Two related to timing: in 1 a red cell unit had expired by the time the transfusion was completed due to miscommunication between laboratory and clinical staff; in the other a child received a transfusion over 6 hours.

Anti-D Ig n=4

There were 4 cases in teenage girls who had delay in receiving anti-D Ig; 1 due to late booking of a pregnancy, 2 for delay in administration following a sensitising event, and 1 incorrect administration for a D-negative fetus. For more details of anti-D administration errors, see Chapter 8, Adverse Events Related to Anti-D Immunoglobulin (Ig).

Transfusion reactions n=46

Febrile, allergic and hypotensive reactions (FAHR) n=38

The number of reports has been fairly stable over the last 3 years. The majority (35/38) were in children >1 year of age. Once again there were no reports in the <28 day (neonatal) category a possible reflection of immunological immaturity or of difficulty in recognising reactions in this transfused patient group many of whom are sick preterm babies. The predominance of reactions to platelets can again be seen when compared to the adult data although does not necessarily indicate a difference in reaction rate in proportion to number of platelets transfused to the two groups (Figure 22.5a).

Of the reactions to platelet components (n=23) most (14/23) were allergic-type reactions and the rest were febrile (4/23) or a mixture of allergic and febrile (5/23). Three of the components were pooled platelet components the rest were apheresis.

There were 11 reports related to red cells. In 8/11 these involved fever, 2 were allergic, and 1 was a mixture of allergic and febrile features.

Two reactions were reported due to SD-FFP (Octaplas®).

The data for reaction by component type is summarised in Figure 22.5b below.

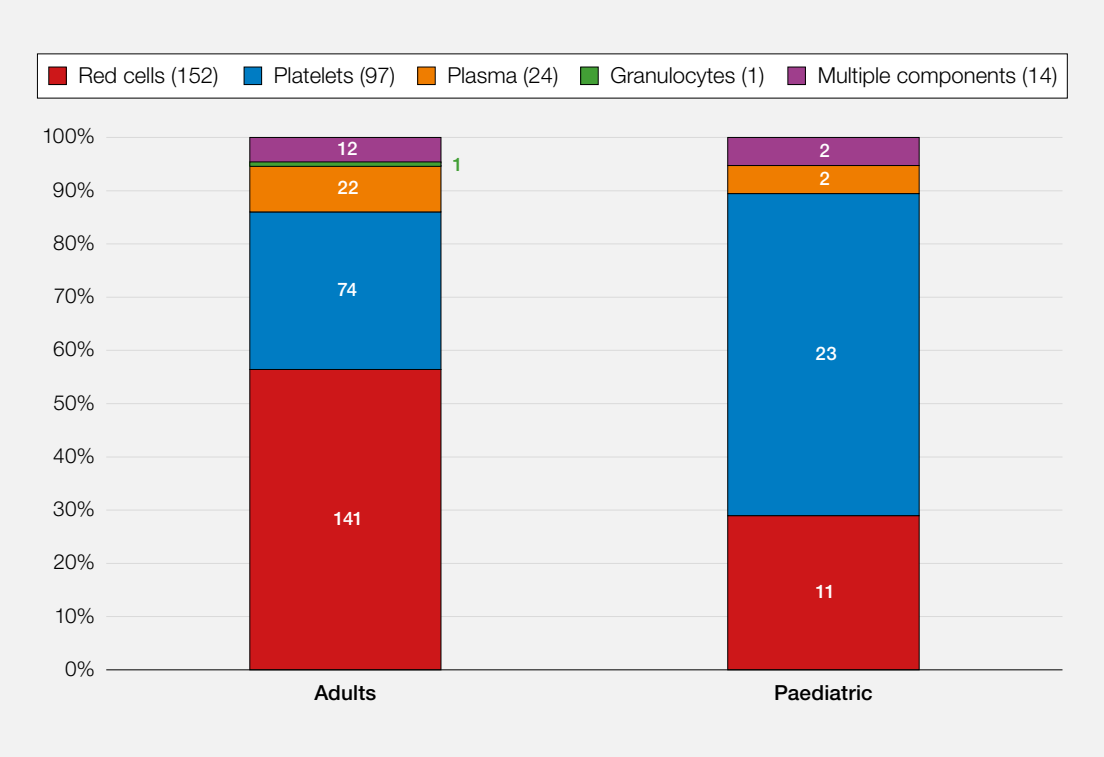
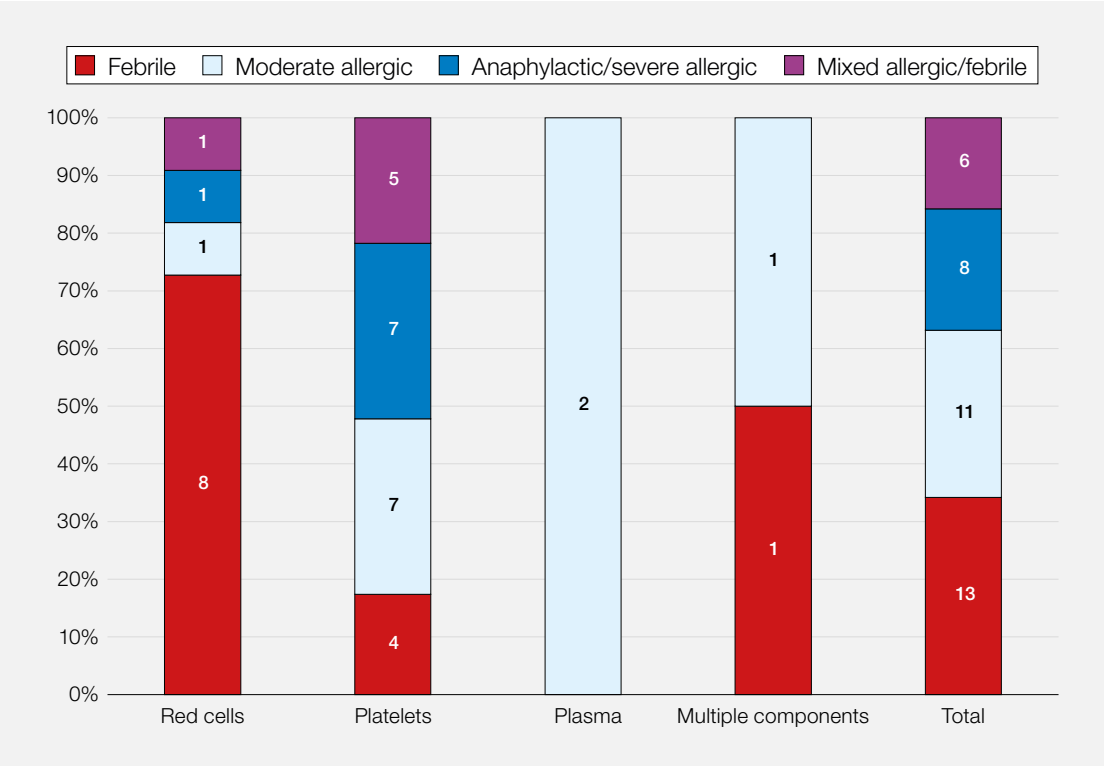


Figure 22.5: Paediatric febrile, allergic and hypotensive reaction (FAHR) reports

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=1

There was 1 case of a haemolytic transfusion reaction in a child with acute lymphoblastic leukaemia, a rare occurrence in this population (see Chapter 18, Haemolytic Transfusion Reactions (HTR)).

Case 22.6: Acute haemolysis secondary to an anti-E in a child with acute leukaemia

A child with acute lymphoblastic leukaemia who had a negative pre-transfusion antibody screen was transfused with two units of red cells. Near the end of the second unit they developed rigors and dark urine. A positive direct antiglobulin test (DAT) and a strongly positive antibody screen was found in the post-transfusion sample. Anti-E was eluted from the patient's red cells. The pre-transfusion sample was then retested and a weak (1+) antibody was detected but only on the homozygous E-positive cells. The Rh type of the transfused units was subsequently confirmed and one unit was negative but the other unit was heterozygous (Ee). The child made a complete recovery with supportive care.

Learning points

- Acute transfusion reactions in children can take place in a variety of clinical settings
- Paediatricians and neonatologists need to be aware of the symptoms and signs of transfusion reaction and instigate appropriate management
- The hospital transfusion practitioner, haematology team and transfusion laboratory are key sources of advice in terms of management

Pulmonary complications of transfusion in neonates and children

Pulmonary complications of transfusion in babies and children are almost certainly under-reported. This may be an issue of education but there is also poor standardisation of definitions as discussed by Gauvin et al. (2020). Diagnosis is compounded by the complexities of the patients involved such as extremely preterm babies.

There were no cases of TAD or TRALI in patients <18 years reported in 2019.

Transfusion associated circulatory overload (TACO) n=4

There were 4 cases of TACO and 1 of these cases was associated with major morbidity. This was a child with complex cardiac disease (tetralogy of Fallot) who developed respiratory distress following a red cell transfusion. Symptoms did not resolve with intravenous (IV) frusemide and they were transferred to the paediatric intensive care unit (PICU) for respiratory support. In 3 patients the implicated component was red cells and 1 to platelets.

Case 22.7: Tachypnoea following a platelet transfusion

A young child with neuroblastoma received a 15mL/kg apheresis platelet transfusion prior to a procedure. They developed tachypnoea 6 hours following transfusion with drop in oxygen saturations to 92% on air. Chest X-ray showed pulmonary oedema. The child responded to frusemide. They had also received IV chemotherapy and hydration fluids the same day and therefore there was uncertainty as to the relative contribution of the platelet transfusion as the cause of the fluid overload.

Learning points

- Complexities of paediatric patients and even more so extreme preterm babies can make the diagnosis of transfusion-associated circulatory overload (TACO) very difficult
- A universal set of diagnostic criteria in children is lacking and risk factors are extrapolated from the adult population
- The SHOT ABCDE assessment of transfusion (see Figure 4.2 in Chapter 4, Key Messages and Recommendations) and risk factors such as fluid overload, low albumin, existing respiratory or cardiac dysfunction should be considered

Transfusion-transmitted infection (TTI) n=0

There were no cases of TTI in patients <18 years reported in 2019.

Uncommon complications of transfusion (UCT) n=3

There were 2 cases of TANEC in preterm babies, 1 resulted in death and is discussed at the beginning of this chapter (see Chapter 19, Uncommon Complications of Transfusion (UCT) for further commentary). The other resulted in major morbidity. The baby started bleeding per rectum 90 minutes post transfusion and required transfer to another hospital for a subtotal colectomy.

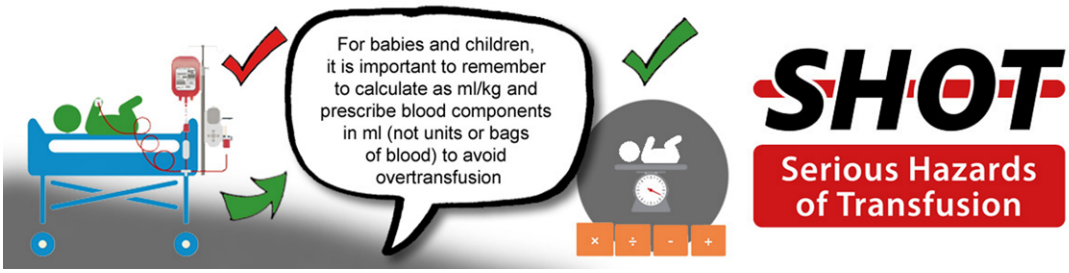
One young child developed severe back pain following red cell transfusion. There was no evidence of haemolysis.

Near miss (NM) n=53, NM–wrong blood in tube (WBIT) n=43, right blood right patient (RBRP) n=17

See relevant chapters (Chapter 12, Near Miss (NM) Reporting and Chapter 13, Right Blood Right Patient (RBRP)) for further details.

Recommended resources

The transfusion handbook has a useful summary of management of transfusion reactions
https://www.transfusionguidelines.org/transfusion-handbook/5-adverse-effects-of-transfusion/5-2-non-infectious-hazards-of-transfusion



References

BSH New HV, Berryman J, Bolton-Maggs P, et al. (2016) Guidelines on transfusion for fetuses, neonates and older children. Br J Haematol 2016;**175(5)**:784-828.

Gauvin F and Robitaille N. (2020) Diagnosis and management of transfusion-associated circulatory overload in adults and children. *International Society of Blood Transfusion, ISBT Science Series* 2020;**15(1)**:23-30.

Narayan S (Ed), Poles D, et al. (2019) on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2018 Annual SHOT Report. https://www.shotuk.org/shot-reports/ [accessed 08 June 2020].

NHS (2018) Blood Components. (version 1.3.0) [mobile app] [accessed 20 April 2020].

SaBTO (2019) Importation of plasma and use of apheresis platelets as risk reduction measures for variant Creutzfeldt-Jakob Disease. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/829906/SaBTO_PC_report.pdf [accessed 09 June 2020].