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P Bolton, Elaine Harrison

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Serious Hazards of Transfusion in Children (SHOT)

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Serious Hazards of transfusion in Children (SHOT)

Elaine Harrison. Transfusion Practitioner. Royal Hospital for Sick Children, Yorkhill, Dalnair St. Glasgow G3 8SJ. Scotland, UK.

Dr Philip Bolton. Consultant Anaesthetist. Royal Hospital for Sick Children, Yorkhill, Dalnair St. Glasgow G3 8SJ. Scotland UK.

Correspondence to philbolton2000@yahoo.co.uk

Introduction

The Serious Hazards of Transfusion (SHOT) is the United Kingdom's national audit of clinical transfusion practice. It has been collecting data since 1996 and in the first ten years it collected 3239 reports of adverse reactions relating to the transfusion of labile blood components (from a total of 23.4 million). SHOT is funded by the four United Kingdom blood transfusion services and is affiliated to the Royal College of Pathologists. Strategic direction is provided by a steering group which has wide representation from UK Royal Colleges and professional bodies including the Royal College of Anaesthetists and the Intensive Care Society.

Whilst reporting to SHOT has historically been voluntary, a number of governing bodies and laboratory accreditation organisations have made reporting compulsory. Reporting of serious adverse events and reactions related to blood transfusion is now a legal requirement, following implementation of the Blood Safety and Quality Regulations in 2005 (1) for which the Medicines and Healthcare products Regulatory Agency is the competent authority. This means that SHOT has near universal up take by all UK blood transfusion laboratories. SHOT produces an annual report where a break down of the previous year's incidents are presented and discussed. New and continuing trends are identified and recommendations on how to improve practice are then suggested.

4.2% of red cells are transfused to patients less than 18 years old and 1.7% to children less than 1 year old (2). Looking at SHOT data for these groups, there is a disproportionate number of adverse reactions in these groups, which can be estimated at 18:100,000 transfusions for children less than 18 years of age and 37:100,000 in

1 those under 1 year. (3) The adult rate is only 13:100,000. So why do children have a
2
3 higher incidence of adverse reactions during transfusion of blood products with nearly
4
5 three times the adult rate in infants? To answer this, the figures need to be broken
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7 down.
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11
12 SHOT classifies incidents reported into 12 different categories. (table 1)
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14
15

- 16
17 1. Incorrect blood component transfused
 - 18 a. Special requirements not met
 - 19 b. Administrative
 - 20 c. Laboratory error
- 21
22 2. Inappropriate / Unnecessary transfusion
- 23
24 3. Handling and storage
- 25
26 4. Acute transfusion reaction
- 27
28 5. Autologous
- 29
30 6. Transfusion transmitted infection
- 31
32 7. Transfusion related acute lung injury
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34 8. Delayed transfusion reaction
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36 9. Transfusion related circulatory overload
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38 10. Post transfusion purpura
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40 11. Graft v's host disease
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42 12. Anti-D related
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44 13. Transfusion associated dyspnoea
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Incorrect blood component transfused

This was the most common category in both adults and children, but it was particularly common in children, making up more than 80% of reports (3).

Special requirements not met

Many children have very specific requirements. CMV negative blood is required for all children less than one year of age. Blood must be irradiated to kill any remaining white cells if the recipient is immunocompromised (for example Di George syndrome).

Omission of CMV negative or irradiated blood were the most common mistakes seen in this group. Failure to use irradiated blood in an immunocompromised child can put them at risk of graft versus host disease. This is an extremely rare, but universally fatal complication of transfusion.

Another example occurred (4) when an exchange transfusion was undertaken in a neonate with blood which was more than 5 days old. This caused in an electrolyte imbalance leading to serious arrhythmia. Methylene blue treated plasma must be used in all children born after 1996 to minimise the theoretical risk of transmission of nvCJD. This problem can be minimised by electronically flagging up all children born after this date to minimise the risk of this occurring.

Administration errors

There are a number of unique problems seen in children with regard to identification. Neonates may not have been named and young children can not confirm their identity. Twins have the same date of birth and surname and can often be cared for in the same neonatal unit. SHOT 1999 illustrated this problem where the wrong identical twin neonate was transfused in error(6). There were 2 cases where blood samples were

1 taken simultaneously from a mother and baby and mislabelled. In one case it resulted
2
3 in a group O baby transfused with group A blood (7) Another problem peculiar to
4
5 children is the potential to treat members of the same family together. An example of
6
7 the potential for confusion occurred when 2 brothers who were both to be transfused
8
9 for thalassaemia major swapped beds for a prank between the checking of the blood
10
11 and it's administration and received each others blood.(8)
12
13
14
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16
17

18 Lab errors

19
20 These remain most common in the neonatal group reflecting the complicated nature of
21
22 transfusion in this age group. For example incompatible transfusions were reported
23
24 (4,9) with a number of neonates because of maternal antibodies which had not been
25
26 detected in the baby's sample. The mother's sample had mistakenly not been taken
27
28 into account during the crossmatch process.
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37 **Inappropriate / Unnecessary transfusion**

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41 While blood can be transfused on the strength of a mistaken haemoglobin to an adult
42
43 or a child there are a number of situations where children are at particular risk of over
44
45 transfusion. The importance of clear prescription and communication can be illustrated
46
47 by 2 examples. In the first a prescription for 50ml of blood to be given over 4 hours
48
49 was misunderstood as 50ml/hour of blood for 4 hours, resulting in morbidity (6). In the
50
51 second case a 2-year old child was under shared care for treatment of a malignancy.
52
53 The central hospital requested that the shared care hospital transfuse 2 paedipacks of
54
55 red cells without mentioning the number of mls required. Two adult units were
56
57 transfused resulting in a very high haemoglobin which required venesection.
58
59
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1
2
3 Both of these cases highlight the importance of having a standardised method to
4
5 prescribe blood which is unlikely to be misunderstood and to always use mls as the
6
7 volume rather than units.
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10 11 12 **Handling and Storage Errors**

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17 The strict requirements for neonatal transfusion are also seen in this category with half
18
19 of the errors reported in this category involving neonates. For example the blood for
20
21 exchange transfusion in a neonate was more than 5 days old at the time it was given.
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25 (10)
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28 29 **Acute Transfusion Reactions**

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34 This is the most common non-error related category, making up around a quarter of all
35
36 cases reported. The overall incidents in children is similar to adults. Neonates are
37
38 rarely seen in this group. There are a number of possible explanations for this.

39
40 Neonates are relatively immunosuppressed and therefore may not mount such an
41
42 obvious reaction to blood products. Also neonates requiring blood are commonly
43
44 unwell and a transfusion reaction may be thought to be due to other factors. Platelets
45
46 have made up about half of all acute transfusion reactions. This increased in 2008 to
47
48 72% of the total (10). Since platelet transfusions make up a very small amount of the
49
50 total units transfused, it is apparent that acute transfusion reactions are at least 5 – 6
51
52 times more likely in this group (11) The high incidence of reaction to platelets is not
53
54 seen in adult practice where red cell transfusion most commonly cause acute
55
56 reactions. The reactions reported in children also tended to be more severe than in
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1 adults with 52% in 2008 being classed as severe allergic / anaphylactic type
2
3 compared to 20% of adult reactions. (10)
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10 **Autologous transfusion problems**

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15 This category relates mostly to intra-operative cell salvage and re-transfusion. Only 2
16 of the 28 reports in 2008 relate to children (10), but it is mentioned here because of
17 the potential increase in use in paediatric surgery in the future. The 2 children reported
18 were teenagers having orthopaedic surgery. There were technical difficulties with the
19 cell salvage equipment resulting in abandoning of the technique without any harm to
20 either child. Looking at the adult data from this year, the most common report (5
21 cases) was of hypotension during re-infusion of the blood. Common factors in all of
22 these reports were:-
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- 33 • Use of acid citrate dextrose as anticoagulant
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- 35 • Use of a leucodepletion filter during reinfusion of red cells
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43 These patients may have been relatively hypovolaemic and thus more susceptible to
44 vasoactive cytokines present in the blood. All of these episodes were transient, being
45 corrected by stopping the infusion +/- vasopressors. There were no long term
46 sequelae.
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Transfusion Transmitted Infections

This is the category that most members of the general public (and some clinical staff) worry about, after the problems of hepatitis B & C, HIV and more recently concern of the possibility of nvCJD. The fact is, however this is a rare event, making up 2% of all paediatric reports. In the last 2 years (2007-8) there has been only one report of a bacterial infection which was the result of a platelet transfusion. There were no viral infections reported in the last 4 years in children. The last recorded episode was in 2004 when a 2-year old girl was infected with hepatitis B from a regular platelet donor during the very early acute phase of infection. (SHOT 2004)

When considering the possibility of long incubation infections occurring in children, it is important to remember that the transfusion recipients may be living with the consequences for many decades into the future. While nvCJD remains vanishingly rare, with no reports of infection in children, new, unexpected and novel infections may occur in the future, so vigilance is vital.

Transfusion Related Acute Lung Injury (TRALI)

This is a rare condition in children with only 2 reports in 2008 (10). Both were teenagers. It may be an important category however in anaesthesia and intensive care medicine, since it is probably under reported. It is hard to diagnose, since an isolated deterioration in lung function can commonly being attributed to other causes in sick and unstable patients. This may also be the reason why there are so few reports of TRALI in neonates, although this may be due to an impaired immune response in this group.

1 More than 95% of the cases in the last ten years have been caused by plasma or
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3 platelets.
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9 Recommendations

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12 SHOT makes recommendations at the end of every annual report which reflects any
13 changes in practice or trends which are developing. The reports also comment on
14
15 previous recommendations and discusses how they have progressed. SHOT 2007 re-
16
17 emphasised the importance of Laboratory staff being appropriately trained and aware
18
19 of the special requirements for children under the age of 16. Also the importance of
20
21 ward staff who prescribe blood products being suitably trained and experienced to
22
23 calculate the appropriate volume of blood required for a transfusion in a child. This
24
25 prescription must always be in mls, never in units.
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34 The British Committee for Safety in Haematology has produced formal guidelines for
35
36 transfusion of neonates and older children, which are based on the evidence from
37
38 SHOT(12).
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46 Discussion

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48
49 The majority of adverse reactions in children were error related. Often the error was
50
51 from the issuing laboratory, but errors from clinical staff were an important factor in
52
53 many incidents. Anaesthetists treat a wide range of children requiring transfusion
54
55 support who are often unstable with a complex clinical picture. In this environment,
56
57 changes in the clinical condition of a child may be due to many factors. Suspicion that
58
59 a drop in blood pressure may be the result of an acute transfusion reaction or
60

1 worsening ventilation may be the result of a transfusion related acute lung injury is
2
3 helped when the anaesthetist is aware of what group of children are most at risk and
4
5 which products most commonly are associated with these conditions.
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10 Neonates are a particular challenge for anaesthetists. Knowledge of their specific
11
12 transfusion requirements will help to prevent inappropriate and potentially dangerous
13
14 practice from occurring. This is particularly true when a specific diagnosis or treatment
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16 is being managed, such as Di-George syndrome or ECMO. Good communication with
17
18 the issuing blood bank is vital to ensure that the correct blood is issued in these very
19
20 complicated cases.
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27 Conclusion

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30 The advances in surgical and medical care for children, such as cardiac surgery and
31
32 oncology have been paralleled by the advances in transfusion practice, without which
33
34 the clinical work would have been impossible. Continued reporting of adverse events
35
36 and reactions to SHOT will contribute to a growing body of evidence on transfusion
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38 hazards that can influence future transfusion safety strategies and improve education.
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40 Improved quality of practice is already suggested by the increasing number of reports
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42 over the last 10 years while the number of serious events has declined. All of this
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44 should result in improved patient outcome.
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Elaine Harrison. Transfusion Practitioner. Royal Hospital for Sick Children, Yorkhill, Dalnair St. Glasgow G3 8SJ. Scotland, UK.

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4
5 children improve their care during surgery? To answer this, the figures need to be
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This was the most common category in both adults and children, but it was particularly common in children, making up more than 80% of reports (3).

Special requirements not met

Many children have very specific requirements for blood products. There are a number of reasons for this. In the first year of life, children have an immature immune system and are at particular risk of certain blood born infections. A number of congenital syndromes are associated with the requirement for neonatal surgery. If the diagnosis has not been confirmed, a precautionary policy is required with blood transfusion.

CMV negative blood is required for all children less than one year of age. Blood must be irradiated to kill any remaining white cells if the recipient is immunocompromised (for example Di George syndrome). Omission of CMV negative or irradiated blood were the most common mistakes seen in this group. Failure to use irradiated blood in an immunocompromised child can put them at risk of graft versus host disease. This is an extremely rare, but universally fatal complication of transfusion.

Some procedures, which only occur in the pre-natal or neonatal period require very specific blood products, for example intra-uterine transfusion or neonatal exchange transfusion. Failure to adhere to these strict criteria has caused significant electrolyte imbalance in infants leading to serious arrhythmia (4). Children born after 1996 in the UK have in theory avoided exposure to new variant Creutzfeldt-Jakob Disease (nvCJD) in the food chain. In an attempt to avoid the potential for transmission of this infection, methylene blue treated plasma must be used in all children born after this date. Many of these problems can be minimised by using an electronic flagging system based on the patient's date of birth. This recommendation was made in the

1 2007 SHOT report (5). This group of errors however still accounts for the biggest
2
3 difference between children and adults.
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5 6 7 8 *Administration errors* 9

10 There are a number of unique problems seen in children with regard to identification.
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12 Neonates may not have been named and young children can not confirm their identity.
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14 Twins have the same date of birth and surname and can often be cared for in the
15
16 same neonatal unit. SHOT 1999 illustrated this problem where the wrong identical twin
17
18 neonate was transfused in error (7). There were 2 cases where blood samples were
19
20 taken simultaneously from a mother and baby and mislabelled. In one case it resulted
21
22 in a group O baby transfused with group A blood (8). Another problem peculiar to
23
24 children is the potential to treat members of the same family together. An example of
25
26 the potential for confusion occurred when 2 brothers who were both to be transfused
27
28 for thalassaemia major swapped beds for a prank between the checking of the blood
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30 and it's administration and received each others blood (9).
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39 *Laboratory errors* 40

41 These remain most common in the neonatal group reflecting the complicated nature of
42
43 transfusion in this age group. For example incompatible transfusions were reported
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45 (4,10) with a number of neonates because of maternal antibodies which had not been
46
47 detected in the baby's sample. The mother's sample had mistakenly not been taken
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49 into account during the crossmatch process.
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58 **Inappropriate / Unnecessary Transfusion** 59 60

1 While blood can be transfused on the strength of an inaccurate haemoglobin to an
2
3 adult or a child, there are a number of situations where children are at particular risk of
4
5 over transfusion. The importance of clear prescription and communication can be
6
7 illustrated by 2 examples. In the first case, a prescription for 50ml of blood to be given
8
9 over 4 hours was misunderstood as 50ml/hour of blood for 4 hours, resulting in
10
11 morbidity (7). In the second case a 2-year old child was under shared care for
12
13 treatment of a malignancy. The central hospital requested that the shared care
14
15 hospital transfuse 2 paedipacks of red cells without mentioning the number of mls
16
17 required. Two adult units were transfused resulting in a very high haemoglobin, which
18
19 required venesection. Both of these cases highlight the importance of having a
20
21 standardised method to prescribe blood which is unlikely to be misunderstood and to
22
23 always use mls as the volume rather than units.
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32 **Handling and Storage Errors**

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36 The strict requirements for neonatal transfusion are also seen in this category with half
37
38 of the errors reported involving neonates. For example the blood for exchange
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40 transfusion in a neonate was more than 5 days old at the time it was given (11).
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46 **Acute Transfusion Reactions**

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50 This is the most common non-error related category, making up around a quarter of all
51
52 cases reported. The overall incidents in children is similar to adults. Neonates
53
54 however are rarely seen in this group. There are a number of possible explanations for
55
56 this. Neonates are relatively immunosuppressed and therefore may not mount such an
57
58 obvious reaction to blood products. Also neonates requiring blood are commonly
59
60 unwell and a transfusion reaction may be thought to be due to other factors.

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2
3 Platelets have made up about half of all acute transfusion reactions. This increased in
4
5 2008 to 72% of the total (11). Since platelet transfusions make up a very small amount
6
7 of the total units transfused, it is apparent that acute transfusion reactions are at least
8
9 5 – 6 times more likely in this group (12). The high incidence of reaction to platelets is
10
11 not seen in adult practice where red cell transfusion most commonly cause acute
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13 reactions. The reactions reported in children also tended to be more severe than in
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15 adults with 52% in 2008 being classed as severe allergic / anaphylactic type
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17 compared to 20% of adult reactions (11).
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27 **Autologous Transfusion Problems**

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32 This category relates mostly to intra-operative cell salvage and re-transfusion. Only 2
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34 of the 28 reports in 2008 relate to children (11), but it is mentioned here because of
35
36 the potential increase in use in paediatric surgery in the future. The 2 children reported
37
38 were teenagers having orthopaedic surgery. There were technical difficulties with the
39
40 cell salvage equipment resulting in abandoning of the technique without any harm to
41
42 either child. Looking at the adult data from this year, the most common report (5
43
44 cases) was of hypotension during re-infusion of the blood. Common factors in all of
45
46 these reports were:-
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- 51 • Use of acid citrate dextrose as anticoagulant
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- 53 • Use of a leucodepletion filter during reinfusion of red cells
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These patients may have been relatively hypovolaemic and thus more susceptible to vasoactive cytokines present in the blood. All of these episodes were transient, being

1 corrected by stopping the infusion +/- vasopressors. There were no long term
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3 sequelae.
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10 **Transfusion Transmitted Infections**

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15 This is the category that most members of the general public (and some clinical staff)
16 worry about, after the problems of hepatitis B & C, HIV and more recently concern of
17 the possibility of nvCJD. The fact is, however this is a rare event, making up 2% of all
18 paediatric reports. In the last 2 years (2007-8) there has been only one report of a
19 bacterial infection which was the result of a platelet transfusion. There were no viral
20 infections reported in the last 4 years in children. The last recorded episode was in
21 2004 when a 2-year old girl was infected with hepatitis B from a regular platelet donor
22 during the very early acute phase of infection (4).
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36 When considering the possibility of long incubation infections occurring in children, it is
37 important to remember that the transfusion recipients may be living with the
38 consequences for many decades into the future. While nvCJD remains vanishingly
39 rare, with no reports of infection in children, new, unexpected and novel infections may
40 occur in the future, so vigilance is vital.
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50 **Transfusion Related Acute Lung Injury (TRALI)**

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55 This is a rare condition in children with only 2 reports in 2008 (11). Both were
56 teenagers. It may be an important category however in anaesthesia and intensive care
57 medicine, since it is probably under reported. It is hard to diagnose, since an isolated
58 deterioration in lung function can commonly being attributed to other causes in sick
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1 and unstable patients. This may also be the reason why there are so few reports of
2
3 TRALI in neonates, although this may be due to an impaired immune response in this
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5 group.
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8 More than 95% of the cases in the last ten years have been caused by plasma or
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10 platelets.
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For Peer Review

Recommendations

SHOT makes recommendations at the end of every annual report which reflects any changes in practice or trends which are developing. The reports also comment on previous recommendations and discuss how they have progressed. SHOT 2007 re-emphasised the importance of Laboratory staff being appropriately trained and aware of the special requirements for children under the age of 16. Also the importance of ward staff who prescribe blood products being suitably trained and experienced to calculate the appropriate volume of blood required for a transfusion in a child. This prescription must always be in mls, never in units.

The British Committee for Standards in Haematology has produced formal guidelines for transfusion of neonates and older children, which are based on the evidence from SHOT (13).

Discussion

The majority of adverse reactions in children were error related. Often the error was from the issuing laboratory, but errors from clinical staff were an important factor in many incidents. There were a number of categories where children were more commonly seen than adults. These include failure to meet special requirements, failure to correctly identify the patient and difficulties with crossmatching. While acute transfusion reactions are equally common in children and adults, platelet reactions are more common in children.

1 Anaesthetists treat a wide range of children requiring transfusion support who are
2 often unstable with a complex clinical picture. In this environment, changes in the
3 clinical condition of a child may be due to many factors. Suspicion that a drop in blood
4 pressure may be the result of an acute transfusion reaction, or worsening ventilation
5 may be the result of a transfusion related acute lung injury is helped when the
6 anaesthetist is aware of what group of children are most at risk and which products
7 most commonly are associated with these conditions.
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20 Neonates are a particular challenge for anaesthetists. Knowledge of their specific
21 transfusion requirements will help to prevent inappropriate and potentially dangerous
22 practice from occurring. This is particularly true when a specific diagnosis or treatment
23 is being managed, such as Di-George syndrome or ECMO. Good communication with
24 the issuing blood bank is vital to ensure that the correct blood is issued in these very
25 complicated cases.
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36 The advances in surgical and medical care for children, such as cardiac surgery and
37 oncology have been paralleled by the advances in transfusion practice, without which
38 the clinical work would have been impossible. Continued reporting of adverse events
39 and reactions to SHOT will contribute to a growing body of evidence on transfusion
40 hazards that can influence future transfusion safety strategies and improve education.
41 Improved quality of practice is already suggested by the increasing number of reports
42 over the last 10 years while the number of serious events has declined. All of this
43 should result in improved patient outcome.
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