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Impact of a Novel Structured Transfusion Medicine Curriculum on Pediatric Residents' Knowledge and Self-Reported Confidence Levels

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Impact of a Novel Structured Transfusion Medicine Curriculum on Pediatric Residents' Knowledge and Self-Reported Confidence Levels

Cover Page Footnote

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INTRODUCTION:

Optimal training of physicians in transfusion medicine (TM) is essential to prevent unnecessary transfusions and complications of transfusion that can lead to patient harm as well as wastage of valuable resources. In 2013, pediatric transfusions accounted for 5-10% of all blood transfusions administered across the country[1]. A multicenter study of pediatric academic centers showed that 4.8% of hospitalized children required a blood transfusion[2]. Transfusion in the pediatric population follows the principles utilized in adults, but there are physiological differences that lead to different dosage guidelines, volume considerations, and other safety measures for children that pediatricians should be aware of[3]. There is also evidence to suggest that the rate of transfusion reactions is higher in children compared to adults[4]. Therefore, it becomes imperative for pediatric residents to attain a strong foundation of knowledge on this topic including age-related specifics, transfusion reactions and recommended practices in common case scenarios needing transfusion. In most institutions, however, there is limited interaction between the departments of Pediatrics and Transfusion Medicine, leading to lack of effective TM learning opportunities, whether at bedside or through formal didactics.

Medical students receive some education on TM during pre-clinical didactic years and clinical clerkships[5]. However, the curriculum varies among institutions and the pediatric patient population is often overlooked. Studies evaluating TM knowledge in pediatric residents have reported average scores of 37-41% on written tests with most interns describing TM education during medical school as "either one lecture or none at all"[6,7]. A more recent global survey across medical schools, including several United States schools, confirmed this knowledge gap and suggested enhancement of TM education during residency[5]. A multi-center study across Canada and the United Kingdom describes successful implementation of a "Transfusion Camp" with lectures and seminars to residents across different specialties leading to significant improvement in post-test scores and self-rated abilities to manage TM scenarios[8]. There are no published studies evaluating TM teaching techniques dedicated to pediatric residents.

Problem-based learning (PBL) has been studied extensively in the past and shown to improve the utilization of skills in clinical practice[9]. Lecture-based learning (LBL) is historically the most common method of teaching for medical students and residents, but there is mounting evidence that the use of actively engaging strategies improves learning and knowledge retention[10]. It is also important for the teaching material to incorporate input from all the relevant experts. Hence, a curriculum consisting of interactive LBL combined with PBL was created by a multidisciplinary team of pediatric hematologists and TM specialists at our institution. The objective of our study was to assess the impact of this novel curriculum on pediatric residents' knowledge and self-reported confidence levels

regarding management of transfusion. In addition, we evaluated whether sex, year of residency training, or PBL attendance made a difference in the improvement of transfusion knowledge, and ultimately if this curriculum had any effect on institutional practice patterns of pediatric transfusion.

METHODS:

This prospective, interventional study was approved by the University of Texas Health Science Center at Houston Institutional Review Board. Informed consent was obtained from each participating post-graduate trainee, called a "learner" henceforth.
Residents attending the pediatric residency weekly didactic sessions were the target trainee group for a novel transfusion curriculum called Transfusion for Pediatric Residents (TPR). The residents were recruited for study participation by providing information about the curriculum via email prior to the delivery of the curriculum.

Methodology and Intervention:

Specific learning objectives were developed based on review of literature and consensus between a pediatric hematologist and a TM specialist (Table 1). The TPR curriculum was created through a collaboration between the Hematology division in the Department of Pediatrics and the Blood Bank Division in the Department of Pathology at our institution. The content of the curriculum was guided by essential topics identified using a modified Delphi method and validated for physician TM knowledge[11]. All the information was gathered carefully through a review of the most recent literature, either evidence-based or expert consensus-based where evidence was scarce. TPR was delivered in 2 sessions within a timeframe routinely dedicated to didactic sessions for pediatric residents.

Table 1: Learning objectives for pediatric resident transfusion medicine curriculum.

Learning objectives of Transfusion Medicine curriculum (TPR)
1. To understand the indications, goals, rate, volume and complications of red blood cell transfusion in children 2. To understand the indications, goals, rate, volume and complications of platelet transfusions in children 3. To understand the indications, goals, rate, volume and complications of plasma transfusions in children 4. To understand the indications of cryoprecipitate 5. To learn the principles of warfarin reversal.

Learning objectives of Transfusion Medicine curriculum (TPR)
6. To know how and when to contact a transfusion medicine specialist. 7. To understand the importance of correct recipient administration and risks of uncrossmatched blood. 8. To review the identification and management of different types of transfusion reactions.

The first session was a 35-minute lecture steered by two faculty members (one from each of the divisions mentioned above) using "Poll Everywhere" to record responses to case-based questions. Topics covered included types of blood products; indications for their transfusion; methods of their preparation, storage, and administration; correct orders for transfusion; and complications, namely transfusion reactions and transfusion-transmitted infections.

This was followed two weeks later by an 80-minute PBL session consisting of six pediatrics-specific case vignettes (Figure 1). The vignettes were kept brief, with an estimated duration of 10–15 minutes of discussion per vignette. For this session, the residents were divided into seven subgroups, each moderated either by a faculty member/fellow from one of the two divisions, or by one of the pediatric chief residents. Each moderator was provided with suggested questions for discussion (Figure 1) with answers, and a resource sheet per case vignette, containing written information and pertinent references (Supplemental Material). All the material was distributed to the moderators one week prior to the PBL session. The resource sheets were also shared with the learners after they completed the PBL session, to review in their own time.

Figure 1: Pediatric transfusion-specific PBL case vignettes with suggested discussion questions

Acute Severe Anemia

Jake is a 2-year-old boy weighing 14kg. He is admitted from his primary care physician's office after he was found to be significantly pale during a well child check. He is otherwise asymptomatic with no other significant physical exam findings. He drinks 40 ounces of cow's milk per day.

Labs showed a hemoglobin (Hb) of 3.2g/dl, mean corpuscular volume (MCV) 56, white blood cell count (WBC) 4.2K/cu.mm with normal differential and Platelet count of 646K/cu.mm. A ferritin, iron panel, reticulocyte count and bilirubin level are pending at this time, but you strongly suspect iron deficiency anemia and consider a transfusion.

1. Is transfusion indicated?

2. What is your goal?

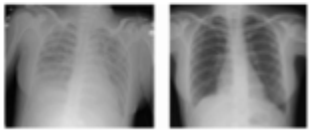
3. What are the complications to watch for?

4. What rate and volume will you use?

5. How would management differ if this was a case of acute autoimmune hemolytic anemia (AIHA) with same Hb?

Transfusion-Associated Lung Injury

A 17 y/o cheerleader with no past medical history gets admitted for multiple splenic lacerations after a sports event. She underwent surgical repair successfully, and received 4 units of FFP along with crystalloid fluids during the procedure. 4 hours after plasma transfusion while in the post-anesthesia care unit, the patient developed severe shortness of breath and fever. Her vital signs: were as follows:
Temp= 101F, Blood pressure = 70/40mmHg, heart rate= 120bpm, oxygen saturation = 70%. Chest X-ray showed bilateral infiltrates. You place the patient on O2, administer iv fluids and order a blood culture followed by antibiotics for possible sepsis. You order additional labs while suspecting a transfusion reaction.



At the event Normal

1. What is your differential for the type of transfusion reaction this patient may have?

2. What is the next step at this point?

3. What is your most likely diagnosis; especially after initial labs rule out acute hemolytic transfusion reaction?

4. What are the specific steps to take after Transfusion associated lung injury is diagnosed?

Neonatal Alloimmune Thrombocytopenia

Born to a 25 yo primigravida otherwise healthy mom with no antenatal or perinatal complications, and with birth weight 3.2kg, baby boy John was found to have petechiae and bruises over arms and legs a few hours after birth with no physical anomalies, hepatosplenomegaly, pallor, or active bleeding. Complete blood count (CBC) showed normal hemoglobin (Hb) and WBC, but a platelet count of 20,000/cu.mm. Maternal platelet count was normal. Neonatal alloimmune thrombocytopenia is suspected as the underlying cause and you consider a platelet transfusion, while ordering an ultrasound head to look for intracranial hemorrhage and testing of parents for platelet antibodies and platelet antigen typing.

1. Is platelet transfusion indicated?

2. How should platelets be ordered?

3. How can platelet refractoriness be addressed?

4. What is another important complication of platelet transfusion in general?

Neonatal Purpura Fulminans

An otherwise healthy term newborn, born to a multigravid mom with birth weight 2.8kg, has a widespread vascular appearing skin lesion on his trunk and limbs. Mom's pregnancy work-up for hypercoagulable disease was negative. Baby's initial CBC and disseminated intravascular coagulation (DIC) panel are normal, but the lesion begins to show areas of necrosis and bleeding by 24hr of life. Repeat labs show PT prolonged to 21secs and fibrinogen down to 110ng/ml. You consider an FFP or cryoprecipitate transfusion.

Your differential includes sepsis, vascular malformation with early DIC, and neonatal purpura fulminans (seen in severe protein C or S deficiency) associated with DIC. Computer tomography Head was done to rule out vascular lesions and/or hemorrhage. Instead it showed a venous infarct and suspected sinus vein thrombosis. On further evaluation, protein C level was found to be 20% after FFP transfusion.

Is transfusion indicated?

What is the dose and further management?

When should you use cryoprecipitate instead of FFP?

Warfarin Induced Coagulopathy

A 9-year-old boy was placed on warfarin for antithrombin III deficiency that was diagnosed when he developed extensive right lower extremity deep vein thrombosis after an acute episode of gastroenteritis. His dose was closely monitored at first but family no-showed for monthly INR checks after a few months and he presented to the emergency department after a random check by his primary care provider showed an INR of 10.5. His parents report no bleeding.

1. Is fresh frozen plasma (FFP) transfusion indicated in this patient?

2. What would be a definite indication to give FFP?

3. If FFP is needed, what are some of the important considerations?

Sickle Cell Disease

Precious is a 6-year-old girl with HbSS disease on hydroxyurea (25mg/kg/day), with baseline hemoglobin (Hb) 8-9g/dl and reticulocyte count 11%. She developed pain in both legs after playing outside for several hours on a hot afternoon day.

Her parents gave her oral hydration along with ibuprofen (10mg/kg/dose) and Norco (0.1mg/kg hydrocodone per dose) alternating every 3-4hours with no improvement after 24hours and then brought her to the emergency room (ER). Her Hb was 7.5g/dl and reticulocyte count 20%, with normal electrolytes. She received iv hydration and iv Morphine 0.1mg/kg per dose every 30 minutes x3 doses with little improvement and then got admitted to the floor. The ER team considers a transfusion.

The next day you are in charge of her care. Overnight, she developed fever, chest pain and left lower lobe crackles on lung exam along with hypoxia to 88% on room air. Repeat labs in the morning show a Hb of 7g/dl. You suspect acute chest syndrome, and consider a transfusion.

1. Is (or was) transfusion indicated on the day of ER presentation and admission?

2. Is transfusion indicated the next day after diagnosis of acute chest syndrome?

3. How would you proceed with transfusion? (type of transfusion: simple or exchange, volume)

4. What are some special considerations for transfusion in ?

5. What if this patient did not have hypoxia or any other signs of respiratory distress?

All the residents participating in LBL during the routine didactic session submitted responses to a preliminary test (pre-test) called BEST-TEST3, a 21-question exam validated for assessment of TM knowledge among pediatric residents[12]. They took the pre-test just prior to the LBL session over 20–25 minutes. A study consent form was attached to the test. Those who consented to the study were contacted to take the test again after completing the curriculum (post-test), at which time answers with explanations were also provided. Of note, the test questions and answers were not discussed directly with the learners at any point during the curriculum.

A survey addressing self-reported ability (SRA) or confidence levels regarding different aspects of transfusion management was included at the time of the pre-test and re-distributed among consented learners at the end of the academic year. A satisfaction survey was also included at the end of the curriculum. All tests and surveys were distributed through a web-based software called Qualtrics (Qualtrics XM®, Seattle, WA) using a link and/or a QR code. Each consenting learner received a gift card for their participation.

Outcome measures:

Attendance records were obtained from the department for each session, and learners were included in the study if they met one of the following criteria:

1. Attended PBL and LBL sessions
2. Attended the LBL session and confirmed reviewing resource sheets from the PBL session
3. Attended the PBL session and confirmed reviewing slides from the LBL session

The primary outcome measure was knowledge gain, defined as the change in the BEST-TEST3 score from before to after attending the TM curriculum.

Secondary outcome measures included comparison of changes to mean BEST-TEST3 scores based on sex, postgraduate year of training (PGY), and number/type of sessions attended; satisfaction scores immediately following curriculum delivery; and change in scores on the SRA survey assessing self-reported impact on transfusion management. To assess changes in the pattern of transfusions at our institution following the curriculum, we retrospectively reviewed hospital records of pediatric transfusions given during the last 3 months of the academic year (April to June) before versus after curriculum implementation (2021 versus 2022). Patients receiving transfusions in the neonatal intensive care unit (NICU) and cardiovascular intensive care unit (CVICU) were excluded because these transfusions are guided by specific protocols that were not discussed in the curriculum. Patients receiving transfusions in the units where pediatric residents do not rotate were also excluded.

Statistical methods:

We reported continuous variables as mean and standard deviation (SD), or median and interquartile range (IQR) where appropriate. Categorical variables were reported as frequency and percentages. For univariable comparison of pre- and post-test scores, we used paired sample t-test or the Wilcoxon signed-rank test as its non-parametric equivalent. To explore whether the difference between pre- and post-scores is dependent on other covariates including sex, PGY and attendance of PBL session, we used the generalized estimating equations (GEE) models that account for within-subject correlations. Specifically, we included an interaction term between timing of the test (before or after the TPR curriculum) and each of the covariates in separate GEE models. A significant *P*-value for the interaction term would indicate that the covariate has a modifying effect on the changes in the test scores. All statistical tests were performed at 0.05 level of significance and conducted using SAS statistical software version 9.4[13].

RESULTS

Learner characteristics (Table 2)

Thirty-one out of 55 (56%) residents who participated in the TPR course consented to participate in the study, including 23 in the Pediatrics program, six in the combined Internal Medicine/Pediatrics program, one in the Child Neurology program and one in the combined Medical Genetics/Pediatrics program. Twenty one out of 31 (67%) learners were female, and learners were from all training levels, with the smallest cohort being PGY-4 learners at 11%. Two learners were not able to attend the LBL session but submitted the pre-test under the supervision of a faculty member at a separate time followed by review of the lecture slides and attendance of the PBL session. Of the 29 learners who attended the lecture, 22 (76%) attended the PBL session.

Twenty-five learners who completed both the pre-test and the post-test were included in the final analysis, with the post-tests completed within 15 days of the PBL session by all participants. All consented learners completed the satisfaction survey and 19 (76%) of them completed the SRA survey before and after the curriculum.

Table 2: Pediatric resident participant characteristics of the whole cohort (N=31)

Variable		N=31 [a]	N =25[*]
Sex Male Female		 10 (33.3 %) 21 (66.7 %)	 9 (36.0 %) 16 (64.0 %)
PG year 1 2 3 4		 10 (32.3 %) 11 (35.5 %) 7 (22.5 %) 3 (9.7 %)	 9 (36.0 %) 9 (36.0 %) 5 (20.0 %) 2 (8.0 %)
Comparison of pre-test and post-test n (N=25)		29 (93.5 %)	23 (92.0 %)
Sex	Male (n=9)		
	Female (n=16)		
PG year	1 (n=9)		
	2 (n=9)		
	3 or 4 (n=7)		
PBL attended	Yes (n=19)		
	No (n=6)		
Lecture attended (yes)			
PBL attended (yes)		22 (71.0 %)	19 (76.0 %)

[a] Six participants did not take the post-test
[*] Characteristics of the participants who have taken both the pre- and post-test

Pre-and post-curriculum assessments

The mean pre-test score was 7.9 (SD 1.8, n=25) out of 21 total questions (37.6% correct), improving to a post-test score of 9.7 (SD 2.3, n=25, 46.2% correct) with P <0.001. The post-test score improved regardless of learners' PGY level, sex, or attendance of PBL session (interaction P > 0.14 for all). Although test scores for all PGY levels showed improvement, the improvement was statistically significant for PGY-2 learners (P =0.047) and marginally significant for PGY-1 and PGY-3&4 learners (P = 0.08 and 0.055, respectively) (Table 3).

Table 3: Score improvement by sex, PGY, and PBL session attendance

Comparison of pre-test and post-test means by sex, PGY and whether the participant attended PBL (N=25)					
		Mean Score (SD)		*P*	Interaction *P*
		Pre-test	Post-test		
Sex	Male (n=9)	9.1 ± 1.5	10.7 ± 2.0	0.02	0.59
	Female (n=16)	7.2 ± 1.6	9.2 ± 2.3	< 0.01	
PG year	1 (n=9)	7.7 ± 1.7	9.3 ± 2.6	0.08	0.95
	2 (n=9)	8.1 ± 1.8	10.0 ± 2.0	0.047	
	3 or 4 (n=7)	7.9 ± 2.0	9.9 ± 2.5	0.055	
PBL attended	Yes (n=19)	7.9 ± 1.9	9.4 ± 2.5	0.01	0.14
	No (n=6)	7.8 ± 1.6	10.7 ± 1.2	<0.01	

The SRA survey utilized a 5-point Likert scale and showed significantly increased confidence levels across all categories of transfusion management assessed (Table 4).

Table 4: Self-rated ability survey results

Comparison of self-rated ability survey pre- and post- curriculum scores					
Survey question	n [a]	Likert Scale Scores Median (IQR)			*P* [b]
		Before curriculum	At the end of curriculum	Difference	
Self-related ability on indications for transfusion (SRAI)	16	2.0 (1.0)	4.0 (1.0)	-1.0 (1.0)	<0.01
Self-related ability to manage transfusion reactions (SRAR)	19	1.0 (1.0)	3.0 (0)	-2.0 (1.0)	<0.01
Self-related ability regarding different types of blood products (SRAP)	19	1.0 (1.0)	3.0 (1.0)	-1.0 (1.0)	<0.01
Self-related ability to manage specific cases needing transfusions (SRAS)	19	2.0 (1.0)	3.0 (0.0)	-1.0 (1.0)	<0.01
Self-related ability to obtain consent for transfusion (SRAC)	19	3.0 (1.0)	4.0 (1.0)	-1.0 (1.0)	<0.01
Self-related overall ability to manage TM related issues (SRA)	19	2.0 (1.0)	3.0 (1.0)	-1.0 (1.0)	<0.01
IQR: Interquartile range. [a] Number of participants who answered the survey both before and after the curriculum; [b] *P*-value based on Wilcoxon signed-rank test.					

The feedback survey results showed that the curriculum was well received (Table 5). Eighty percent of learners stated they were likely or very likely to recommend the curriculum to others and 80% of learners felt that PBL was useful. Sixteen percent of learners were not comfortable expressing opinions or asking questions. Learners described positive aspects of the curriculum as “useful in real-world practice” and “relevant to their everyday clinical duties.” Suggestions for

improvement included more time for discussion during the PBL sessions, multiple PBL sessions, and combining the LBL and PBL into one session.

Table 5: Pediatric resident transfusion medicine satisfaction survey results (N=25)

Question 1	Very Likely N (%)	Likely N (%)	Neither likely nor unlikely N (%)	Unlikely N (%)	Very unlikely N (%)
Overall, how likely are you to recommend this course to another learner?	12 (48)	8 (32)	5 (20)	0 (0)	0 (0)
Question 2	Very Comfortable N (%)	Somewhat Comfortable N (%)	Neither comfortable nor uncomfortable N (%)	Somewhat Uncomfortable N (%)	Very uncomfortable N (%)
How comfortable did you feel expressing your opinions or asking questions in this course?	7 (28)	11 (44)	3 (12)	4 (16)	0 (0)
Question 3	Very Useful N (%)	Useful N (%)	Neither useful nor useless N (%)	Useless N (%)	Very useless N (%)
How useful were the discussions after the problem based learning sessions in your understanding of the course material?	12 (48)	8 (32)	5 (20)	0 (0)	0 (0)

Test questions' details

The knowledge test questions were categorized under three broad topics, namely indications and types/preparation of transfusion (seven questions), complications of transfusion (10 questions), and specific case scenarios (four questions). The first

category had the highest pre-test average score of 63%, and significantly improved to 72% following TPR (P = 0.036). For the second category, the test score significantly improved from 29% to 40% (P = 0.001). The questions on special transfusion topics had the lowest average score of 16% before and 17% after TPR (P = 0.960).

Six out of the 10 questions with a pre-test score of less than 25% were related to transfusion reactions, one was related to transfusion transmitted infection, and the remaining three were about specific case scenarios.

Retrospective records review of transfusions (Table 6)

One hundred and seventy-four transfusions in children were recorded over the last three months of the 2021 academic year before the educational session, of which seven (4%) were not indicated based on available guidelines and expert consensus[14-17]. Review of records across the same timeframe in the next academic year (2022) showed four out of 120 (3.3%) transfusions that were not indicated. Specifically, we observed a reduction in the percentage of unnecessary platelet (3.3% versus 0%) and red cell (2.9% versus 1.3%) transfusions, but the differences were not statistically significant (P = 0.73 and P = 0.64 respectively).

Table 6: Summary of non-indicated transfusions from retrospective chart review with referenced guidelines

Age in years (y) or months (m)	Underlying diagnosis	Product transfused	Transfusion details
Before TPR			
13y	Trauma	Platelets	The patient was clinically unstable after major bleeding requiring multiple transfusions, but platelet count was 269K with no functional deficits based on thromboelastogram (TEG) testing (14)
12y	Trauma	FFP	The patient was critically ill, but there was no active bleeding and there were no laboratory abnormalities in coagulation studies (15)
8y	Biliary atresia status post repair and liver transplant	FFP	The patient had severe anemia due to melena, but there was no laboratory evaluation of coagulation status to guide therapy (15)

Age in years (y) or months (m)	Underlying diagnosis	Product transfused	Transfusion details
3y	Malnutrition	FFP	The patient's coagulation studies showed a slightly prolonged PT (20.7 sec) and PTT (39.2 sec), but was hemodynamically stable with no scheduled procedures or active bleeding (15)
18y	Postoperative bleeding	pRBC	The patient was bleeding from the mouth and hemoglobin dropped from 12.8g/dl to 11.1g/dL, but the patient was hemodynamically stable with no scheduled procedures (16)
9y	Intestinal perforation	pRBC	The patient was transfused in anticipation of a wound vac replacement procedure, but was hemodynamically stable with a hemoglobin of 9.6 g/dL (16)
2m	Trauma	pRBC	The patient presented in an unresponsive state due to subdural hemorrhage, but had already received two pRBC transfusions and was hemodynamically stable with a hemoglobin of 9.8 g/dL prior to this third transfusion (16)
After TPR			
4y	Trauma	FFP	The patient's coagulation studies showed a slightly prolonged PT (17.1 sec) and normal PTT, but was hemodynamically stable with no scheduled procedures or active bleeding (15)
15m	Acute respiratory illness	FFP	The patient's coagulation studies showed a slightly prolonged PT (19.4 sec) and normal PTT, but was hemodynamically stable with no scheduled procedures or active bleeding (17)
7y	Trauma	FFP	The patient was critically ill with active bleeding, but there were no laboratory abnormalities in coagulation studies (15)
7y	Trauma	pRBC	The patient was critically ill, but was hemodynamically stable with no clinical symptoms of anemia and a hemoglobin of 8.7 g/dL with no scheduled procedures or active bleeding (16)

Key: Fresh Frozen Plasma (FFP), packed red Blood Cells (pRBC), Prothrombin Time (PT), Partial Thromboplastin Time (PTT)

DISCUSSION

Transfusion management in the pediatric population requires knowledge of numerous details beyond the principles of adult care. The development of the TPR curriculum stimulated an unprecedented collaboration between the departments of Pediatrics and Pathology at our institution, leading to discussions and exchange of ideas that benefited both departments, academically as well as clinically. Prior to this study, pediatric residents at our institution engaged in informal discussions about TM with intensivists and hospitalists, watched a video about transfusion reactions and consent-taking at the beginning of their oncology rotation, and attended a lecture presented by a pediatric hematologist or a TM specialist once every 2-3 years. Our study established the feasibility of implementing a more structured curriculum on this important topic.

A 5-day course was conducted across multiple centers in a previous study, but only half the learners were able to attend it for 4 days or more[8]. Our study assessed the effect of a more practically feasible curriculum delivered within the time constraints of resident education at most academic institutions, with 20 of the 31 (64%) consented learners able to attend the whole curriculum.

The mean pre-test score in our study (37.6%), is similar to the results of an international study that assessed pediatric resident knowledge using the same test (37.1%)[6]. The score improved by 1.8 points after two sessions, compared to 2.7 points after five sessions of lectures and team-based learning (TBL) in a previous study using a much larger population[8]. These results imply an average score improvement of 1.8 questions per learner. Improvement of 1-2 questions per learner may not appear to be a significant gain in knowledge in the grand scheme of resident education. However, given the fact that the curriculum was not created around the test questions, but to address all relevant TM topics, and still led to improved scores, we feel confident that with repetition of the curriculum over several years, and incorporation of different PBL cases, the scores will improve further as foundational transfusion knowledge accumulates. TBL is like PBL in engaging small groups of learners in an active learning process[18]. However, it includes a preparatory assignment that learners must complete prior to class, and this can be difficult for residents on busy clinical rotations. Critics of PBL emphasize the need of "a working memory" for this teaching technique, and the pediatric residents already have baseline knowledge of TM from medical school, making PBL a suitable supplemental resource to prepare them for similar real-world scenarios without needing to do any preparatory work[9]. A study evaluating learner response to replacement of PBL with TBL in the medical curriculum described the presence of content experts as one of its biggest strengths[19]. However, the simultaneous availability of multiple clinical experts is challenging for most residency programs. PBL does not depend on the content expertise of each

moderator and each moderator receives common resource sheets and instructions in advance. Hence, despite different levels of content expertise amongst the moderators, we were able to uniformly moderate each PBL group. Overall, PBL enabled the use of practically relevant transfusion cases, specific to pediatrics, to promote clinical reasoning and self-directed learning skills. LBL and information handouts after the PBL helped to cover the remaining learning objectives and provide clinically relevant information related to TM.

The improvement in test scores was highest for the PGY-2 residents and this may be because they had a better "working memory" described earlier than PGY-1 learners, but less overall knowledge of TM compared to PGY-3 learners. Interestingly, the PGY-3 and PGY-4 residents' pre-test scores were lower than PGY-2 learners, but this may be because this category included residents from outside the pediatric residency program (with likely less baseline pediatric TM knowledge).

The improvement in self-rated ability of the learners to manage TM cases exceeded that of the test scores. Although this is a subjective finding, it is reflective of an increased confidence level among trainees that paves the way for discussions (and hence more learning) with the TM and hematology specialists at their institution. The feedback from the learners was largely positive and their praise for the interactive lecture led to an invitation from our hospitalist faculty members for a similar presentation at their monthly clinical conference.

Although most learners found the PBL sessions to be helpful, the feedback survey also revealed that some learners were not comfortable expressing themselves in a group forum. This may be related to less exposure to group-based learning during residency. PBL has been introduced into the curriculum by many medical schools over the last 3 decades, but it is not widely used by residency programs. One study evaluating students' perception of PBL over time found that positive reflections remained unchanged while negative comments reduced in frequency over a period of 12 weeks of weekly PBL sessions[20]. Hence, supplementing lectures with PBL in different areas of residency program didactics may increase the comfort level of residents over time.

Most of the pre-test questions answered correctly by less than 25% of the learners were related to transfusion reactions, similar to a previous study evaluating pediatric residents[6]. This confirms the lack of baseline knowledge of pediatric residents on this clinically relevant topic which the American Board of Pediatrics prioritizes under topics tested in its certification exam for General Pediatrics. The questions related to specific case scenarios had the lowest average pretest scores reiterating the need for case-based learning techniques. Only 1 out of the 4 cases (massive transfusion, hemolytic disease of newborn, warfarin overdose, and autoimmune hemolytic anemia) was included in the TPR PBL session, but with

introduction of more PBL cases over the 3-year duration of residency, the residents are likely to enhance their knowledge on all these topics.

The percentage of non-indicated pediatric transfusions ordered by resident-based hospital teams did not significantly change after the TPR course, but the continued implementation of TPR during the following academic years is anticipated to lead to improvement. Of note, this chart review was not a direct measure of pediatric resident knowledge, as information regarding the physician ordering each transfusion was not available and he/she may not have been one of the TPR learners. It did however show a pattern of non-indicated transfusions mostly related to plasma. This finding is in consonance with the fact that there is paucity of literature regarding the use of plasma as a blood product and hence minimal evidence to support guidelines on its transfusion[15]. This review of transfusion practices at a major pediatric tertiary hospital highlights the need for more research related to plasma transfusion in pediatric patients.

There were several limitations to our study. Firstly, only 56% of eligible trainees consented to the study. The low rate of consents may partly be related to the fact that we needed the name of each participant to accurately collect data before and after. Although it was clearly stated that the results of the test and/or survey would not affect their overall residency performance, the study may have had more participation if the data was collected anonymously. To achieve optimal data collection, the consented learners were sent reminders after completion of the curriculum to fill out the surveys. An additional session was also arranged for all the trainees to submit their post-test, during which bonus questions and answers were discussed. Ultimately, a complete dataset before and after TPR for comparison of knowledge was available in 45% of total eligible trainees, and data on self-reported ability was available in 35% of them. The overall participation rate is most likely affected by busy trainee schedules, and there is also the possibility of a selection bias for trainees more comfortable with and/or more interested in TM. Secondly, the test assessing knowledge did not cover all the relevant pediatric topics that were included in our curriculum, so that the test scores may have underestimated the improvement in the learners' knowledge. Thirdly, the curriculum had to be conducted virtually due to the Omicron variant surge of the COVID-19 pandemic, and PBL has traditionally been conducted and studied in an in-person setting. Regardless, we were able to modify all the material to ensure its optimal delivery through Webex, email communication and online links. We also acknowledge that the reported *P* values in this study were not adjusted for multiple statistical comparisons and replication of our findings in larger populations is warranted.

To conclude, a structured, collaborative, and interactive curriculum on transfusion medicine for pediatric residents, including components of small group learning like PBL, was well-received by the learners and improved their knowledge

as well as self-rated ability regarding transfusion in children. It also enhanced the working relationship between the departments of Pediatrics and Pathology and in the long run, may lead to improvement of institutional transfusion practices. Although our study findings are limited to a single institution, they provide a framework for the development of a standardized TM curriculum through inter-institutional collaboration and assessment of its impact through a multicenter study in the future. Our work has the potential to improve pediatric transfusion education and ultimately patient care, across the world.

List of Abbreviations
CVICU: Cardiovascular Intensive Care Unit
GEE: Generalized Estimating Equations
IQR: Interquartile Range
LBL: Lecture-based Learning
NICU: Neonatal Intensive Care Unit
PBL: Problem-based Learning
PGY: Postgraduate Year
SD: Standard Deviation
SRA: Self-reported Ability
TBL: Team-based Learning
TPR: Transfusion for Pediatric Residents

REFERENCES

1. Whitaker B, Rajbhandary S, Kleinman S, Harris A, Kamani N. Trends in United States blood collection and transfusion: results from the 2013 AABB Blood Collection, Utilization, and Patient Blood Management Survey. *Transfusion.* Sep 2016;56(9):2173-2183.
2. Slonim AD, Joseph JG, Turenne WM, Sharangpani A, Luban NL. Blood transfusions in children: a multi-institutional analysis of practices and complications. *Transfusion.* Jan 2008;48(1):73-80.
3. New HV. Transfusion in neonates and older children: Principles and updates. *Transfusion clinique et biologique : journal de la Societe francaise de transfusion sanguine.* Sep 2019;26(3):195-196.
4. Oakley FD, Woods M, Arnold S, Young PP. Transfusion reactions in pediatric compared with adult patients: a look at rate, reaction type, and associated products. *Transfusion.* Mar 2015;55(3):563-570.
5. Al-Riyami AZ, Louw VJ, Indrikovs AJ, et al. Global survey of transfusion medicine curricula in medical schools: Challenges and opportunities. *Transfusion.* Feb 2021;61(2):617-626.

6. Wheeler AP, Delaney M, Fung M, et al. Pediatric resident knowledge of transfusion medicine: Results from the BEST-TEST3 international education needs assessment. *Transfusion.* Aug 2021;61(8):2487-2495.
7. O'Brien KL, Champeaux AL, Sundell ZE, Short MW, Roth BJ. Transfusion medicine knowledge in Postgraduate Year 1 residents. *Transfusion.* Aug 2010;50(8):1649-1653.
8. Lin Y, Tilokee E, Charge S, et al. Transfusion Camp: a prospective evaluation of a transfusion education program for multispecialty postgraduate trainees. *Transfusion.* Jun 2019;59(6):2141-2149.
9. Neville AJ. Problem-based learning and medical education forty years on. A review of its effects on knowledge and clinical performance. *Medical principles and practice : international journal of the Kuwait University, Health Science Centre.* 2009;18(1):1-9.
10. Handelsman J, Ebert-May D, Beichner R, et al. Education. Scientific teaching. *Science.* Apr 23 2004;304(5670):521-522.
11. Haspel RL, Lin Y, Mallick R, et al. Internal medicine resident knowledge of transfusion medicine: results from the BEST-TEST international education needs assessment. *Transfusion.* Jun 2015;55(6):1355-1361.
12. Haspel RL, Lin Y, Fisher P, Ali A, Parks E, Biomedical Excellence for Safer Transfusion C. Development of a validated exam to assess physician transfusion medicine knowledge. *Transfusion.* May 2014;54(5):1225-1230.
13. Institute S. SAS 9.4. *SAS Institute Inc.* 2013.
14. Kaufman RM, Djulbegovic B, Gernsheimer T, et al. Platelet transfusion: a clinical practice guideline from the AABB. *Annals of internal medicine.* Feb 3 2015;162(3):205-213.
15. Lu W. A Concise Synopsis of Current Literature and Guidelines on the Practice of Plasma Transfusion. *Clinics in laboratory medicine.* Dec 2021;41(4):635-645.
16. Carson JL, Guyatt G, Heddle NM, et al. Clinical Practice Guidelines From the AABB: Red Blood Cell Transfusion Thresholds and Storage. *Jama.* Nov 15 2016;316(19):2025-2035.
17. Demaret P, Emeriaud G, Hassan NE, et al. Recommendations on RBC Transfusions in Critically Ill Children With Acute Respiratory Failure From the Pediatric Critical Care Transfusion and Anemia Expertise Initiative. *Pediatric critical care medicine : a journal of the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies.* Sep 2018;19(9S Suppl 1):S114-S120.
18. Mourad A, Jurjus A, Hussein IH. The What or the How: a Review of Teaching Tools and Methods in Medical Education. *Medical Science Educator.* 2016;26(4):723-728.

19. Burgess A, Bleasel J, Hickson J, Guler C, Kalman E, Haq I. Team-based learning replaces problem-based learning at a large medical school. *BMC medical education.* Dec 7 2020;20(1):492.
20. Kong AP. Students' perceptions of using Problem-Based Learning (PBL) in teaching cognitive communicative disorders. *Clinical linguistics & phonetics.* Jan-Feb 2014;28(1-2):60-71.

Supplemental Material: PBL Case Moderator Notes

Case 1 Moderator Notes: Anemia

Suggested Q&A for discussion (color coded to match the information at the bottom)
Is transfusion indicated?
Yes, because Hb<5-7g/dl. (A thorough history and physical exam is important regardless to manage appropriately)
What is your goal?
Goal is to improve pallor and prevent complications of anemia, as well as to avoid complications of fluid overload during transfusion..
15ml/kg (210ml) is estimated to bring Hb up to around 6g/dl. Ask blood bank to hold on to the rest of the unit (1 unit is 250-350ml) and transfuse that too, so that overall donor exposure remains the same with maximum benefit from the transfusion.
What are the complications to watch for?
Congestive heart failure (CHF) due to fluid overload
Stroke due to severe anemia
Transfusion reactions
What rate and volume will you use?
We can give 30ml/hr (1-3ml/kg/hr) or a rule of thumb often used is for severe anemia with Hb< or =5g/dl is: For a Hb of 5g/dl; give 5ml/kg at a time, for 4g/dl, give 4ml/kg; for 3g/dl, give 3ml/kg and so on.
Practically, the pRBCs ordered from the Blood Bank have to be used within 4hours. So:
-Order 45mls (around 3ml/kg) over 2-3 hours, then another 45ml over next 2-3hours.
-Check a CBC to assess response
-Serial exams to assess congestive heart failure
-Continue to transfuse without waiting for the Hb result as long as there are no signs of congestive heart failure
-Give another 100ml over 3hours
-Give remainder of the unit (60-160ml) over another 2-3hours

How would management differ if this was a case of acute autoimmune hemolytic anemia (AIHA) with same Hb?
-Acute anemia is usually symptomatic and goal would be to relieve symptoms and signs in addition to preventing complications of anemia
-Rate can be faster since the anemia did not develop over many months, but still it is important to monitor for CHF.
-It will be hard to find compatible blood due to pan agglutinins but still transfuse the least incompatible unit.
-Assessing response (clinical exam and CBC) is important because it may not be optimal due to peripheral destruction of pRBCs

Information and references that will be provided to residents after the case discussion
-When deciding to transfuse a critically ill child, one must consider not only the Hb concentration, but also the overall clinical context (e.g. symptoms, signs, physiological markers, laboratory results) and the risks, benefits, and alternatives to transfusion.

-In hemodynamically stable children, RBC transfusion is not recommended if the Hb concentration is ≥ 7 g/dL. It is recommended at Hb concentration<5g/dl (even if asymptomatic) and reasonable to consider at Hb 5-7g/dl based on clinical judgement. This also applies to critically ill patients, although with some exceptions like severe acute hypoxemia, a chronic cyanotic condition, acute brain injury (trauma or stroke), and congenital or acquired heart disease where higher thresholds of 9-10g/dl (or even higher for some cardiac cases) are used.

-10-15ml/kg of pRBCs will increase hemoglobin (Hb) by 2-3g/dl.
-Post transfusion goal Hb is to address the indication for transfusion, and may not necessarily achieve normal Hb for age.

-It is important to do a baseline exam and then periodically monitor for signs of congestive heart failure during the transfusion (atleast once at the end of each planned aliquot), including but not limited to tachycardia, tachypnea, hepatomegaly, jugular venous distension, pulmonary rales and S3 gallop.
--Slower rates of transfusion are desired in chronic anemia to decrease the risk of cardiac failure (for example 1-3ml/kg/hr has been studied and found to be well tolerated).
-For oncology and bone marrow transplant patients, a threshold of 7-8g/dl is mostly used for transfusion.

--Always address and manage the underlying cause of anemia (For example, iron therapy for iron deficiency anemia and steroids for AIHA)

References

McCormick M, Delaney M. Transfusion Support: Considerations in Pediatric Population. Seminars in Hematology 2020

Olgun H, Buyukavci M et al. Comparison of safety and effectiveness of two different transfusion rates in children with severe anemia. J Pediatr Hematol Oncol. 2009

Valentine SL, Membea M et al. Consensus Recommendations for Red Blood Cell Transfusion Practice in Critically Ill Children from the Pediatric Critical Care Transfusion and Anemia Expertise Initiative. Pediatr Crit Care Med. 2018

Case 2 Moderator Notes: Neonatal Alloimmune Thrombocytopenia

Suggested Q&A for discussion (color coded to match the information at the bottom)

Is platelet transfusion indicated?

Yes.

How should platelets be ordered?

With severe thrombocytopenia and high risk of ICH in this case scenario, give a higher dose of 10ml/kg or more quickly; so 40mls of platelets over 30 minutes.

How can platelet refractoriness be addressed?

Since NAIT occurs due to antibodies against platelet antigens, most commonly HPA-1a and HPA-5b, there is a high risk of platelet refractoriness.

-HPA-1a and 5b negative platelets are preferred but not immediately available in most cases.

-Another option if feasible is maternal platelets to be obtained for transfusing the baby.

-Since both the options above can be time-consuming and studies show at-least partial response to random platelets, it is best to give random platelets as soon as possible while waiting for other options to materialize.

-Give IVIG concurrently

-Check platelet count 30min to 1hr post transfusion to assess refractoriness

What is another important complication of platelet transfusion in general?

-Sepsis due to bacterial contamination of platelets. Clinicians need to monitor for signs of sepsis after platelet transfusion even after application of bacterial mitigation strategies (strategies vary according to institution) and report any adverse reactions, so that the platelet suppliers may be notified.

Information and references that will be provided to residents after the case discussion

-There are no randomized controlled trials evaluating platelet count threshold transfusions for pediatric patients, except for a neonatal study in preterms (PlaNeT-2 trial) and some studies with pediatric and adult oncology patients combined together. Guidelines are mostly based on expert consensus.
-Platelet transfusion should be considered in any child with platelet count<100,000/cu.mm in the presence of intracranial or other life-threatening bleeding, traumatic brain injury, and multiple traumatic injuries.
-Platelets are transfused for platelet count<50,000-75,000/cu.mm for major surgeries; higher thresholds of up to 100,000/cu.mm are recommended prior to ocular surgery or neurosurgery.
-For cancer and stem cell transplant pediatric patients, transfuse at platelet count <10,000/cu.mm or if actively bleeding. Higher thresholds are used for specific situations like mucositis (20K), bone marrow aspirate/biopsy, central line insertion (20K), and lumbar puncture (40-50K).
-For neonates, a threshold of 20,000-30,000/cu.mm is commonly used for transfusion. Higher thresholds of up to 50,000/cu.mm babies are used for specific situations like personal h/o intracranial hemorrhage (ICH), NAIT with family h/o ICH, coagulopathy and invasive procedures.
-There is no prescribed transfusion threshold for thrombocytopenia due to hypo-proliferative conditions like aplastic anemia, platelet dysfunction or immune thrombocytopenia. In the absence of bleeding, observation is often recommended.
-Platelets are dosed at 5-10ml/kg per AABB guidelines, up to the maximum adult dose. Routine adult dose is 1 unit (300mls), with higher doses considered in severe thrombocytopenia cases associated with bleeding at a critical site.
-Bacterial contamination resulting in post-transfusion infection is one of the biggest challenges in platelet transfusion. This is overcome by specific blood bank techniques.
-Another important complication to recognize is platelet refractoriness which can be non-immune mediated (more common) due to clinical situations like DIC/bleeding/splenomegaly, or immune mediated due to alloimmunization.

References

McCormick M, Delaney M. Transfusion Support: Considerations in Pediatric Population. Seminars in Hematology 2020
Prodger CF et al. Platelet transfusion: alloimmunization and refractoriness. Seminars in Hematology 2020
National Institute for Health and Care Excellence (NICE). Transfusion; Platelets: dose. NICE Guideline NG24 2015
Chapter 24: Neonatal and Pediatric Transfusion Practice. P680. Technical Manual, 2020. AABB 20th ed.
Curley A et al. Randomized Trial of Platelet Transfusion Thresholds in Neonates. New England Journal of Medicine 2019

Case 3 Moderator Notes: Warfarin induced coagulopathy

Suggested Q&A for discussion (color coded to match the information at the bottom)
Is FFP indicated for this patient?
No. This patient can be treated by stopping warfarin and giving vitamin K.
What would be a definite indication to give FFP?
Presence of intracranial hemorrhage or other serious bleeding
If FFP is needed, what are some important considerations?
Time lag for cross-matching, risk of fluid overload.
Information and references that will be provided to residents after the case discussion
-Warfarin acts as an anti-coagulant by reducing the synthesis of vitamin K-dependent clotting factors synthesized in the liver namely factors 2, 7, 9 and 10. It also reduces the synthesis of anti-coagulant factors protein C and S.
-Warfarin's half-life is 20-60hours, meaning it affects coagulation long after the last dose is taken.
-Reversal treatments for warfarin induced coagulopathy (WIC) included vitamin K, FFP, recombinant factor 7a (NovoSeven) , and prothrombin complex concentrates (PCC).
-Vitamin K (1-10mg in children) takes 24hours before a significant effect is seen.
-FFP is indicated for the reversal of WIC when serious or life-threatening bleeding occurs, regardless of INR.
-When FFP is decided to be given, it is important to send a sample for type and screen ASAP to initiate the process of obtaining it.
-While transfusing FFP, close monitoring of fluid status and avoidance of fluid overload is imperative.
-Cryoprecipitate does not contain enough amounts of vitamin K dependent factors; hence it is not a good choice for WIC.
References
Widermann CJ, Stockner I. Warfarin-induced bleeding complications- clinical presentation and therapeutic options. Thrombosis Research 2008.
Hall AB, Carson BC. Reversal of warfarin-induced coagulopathy: review of treatment options. J Emerg Nurs 2012.

Case 4 Moderator Notes: Transfusion Reaction

Suggested Q&A for discussion (color coded to match the information at the bottom)
What is your differential for the type of transfusion reaction this patient may have?
Acute hemolytic transfusion reaction (AHTR): occurs during or within 24hrs of cessation of transfusion with pain/fever/hematuria/hypotension/oliguria

Febrile, non-hemolytic transfusion reaction (FNHTR): occurs during or within 4hrs with fever
Transfusion associated circulatory overload (TACO): occurs within 12hrs with respiratory distress/pulmonary edema/elevated BNP
Transfusion related acute lung injury (TRALI): occurs during or within 6hours with hypoxia/pulmonary infiltrates/no signs of circulatory overload
Transfusion-associated dyspnea (TAD): occurs within 24hrs with respiratory distress not attributed to any of the above

What is the next step at this point?
-Stop the transfusion, check patient ID and unit ID, talk to the Blood Bank and obtain first tier labs for suspected transfusion reaction: CBC, DAT, Repeat Blood typing, plasma hemoglobin.
-Also obtain BNP
-Ongoing supportive care: O2/ventilation/fluids/pressors.

What is your most likely diagnosis; especially after initial labs rule out AHTR?
TRALI
There is increased risk of TRALI in the ICU setting and perioperative setting.

What are the specific steps to take after TRALI is diagnosed?
-An event report must be made
-Avoid transfusion from that donor in the future
Information and references that will be provided to residents after the case discussion
-Rash and/or itching with or without a fever is seen in allergic and/or anaphylactic reactions as well as hemolytic transfusion reactions (HTR).
-Fever without a rash is also seen in febrile non-hemolytic transfusion reaction and sepsis
-Respiratory symptoms should prompt an evaluation for TRALI or TACO
-Hypotension can be an associated feature of acute HTR, anaphylactic reaction, sepsis or TRALI
-Transfusion Reaction Laboratory Investigation Process is shown in the table below from Lancet 2016:

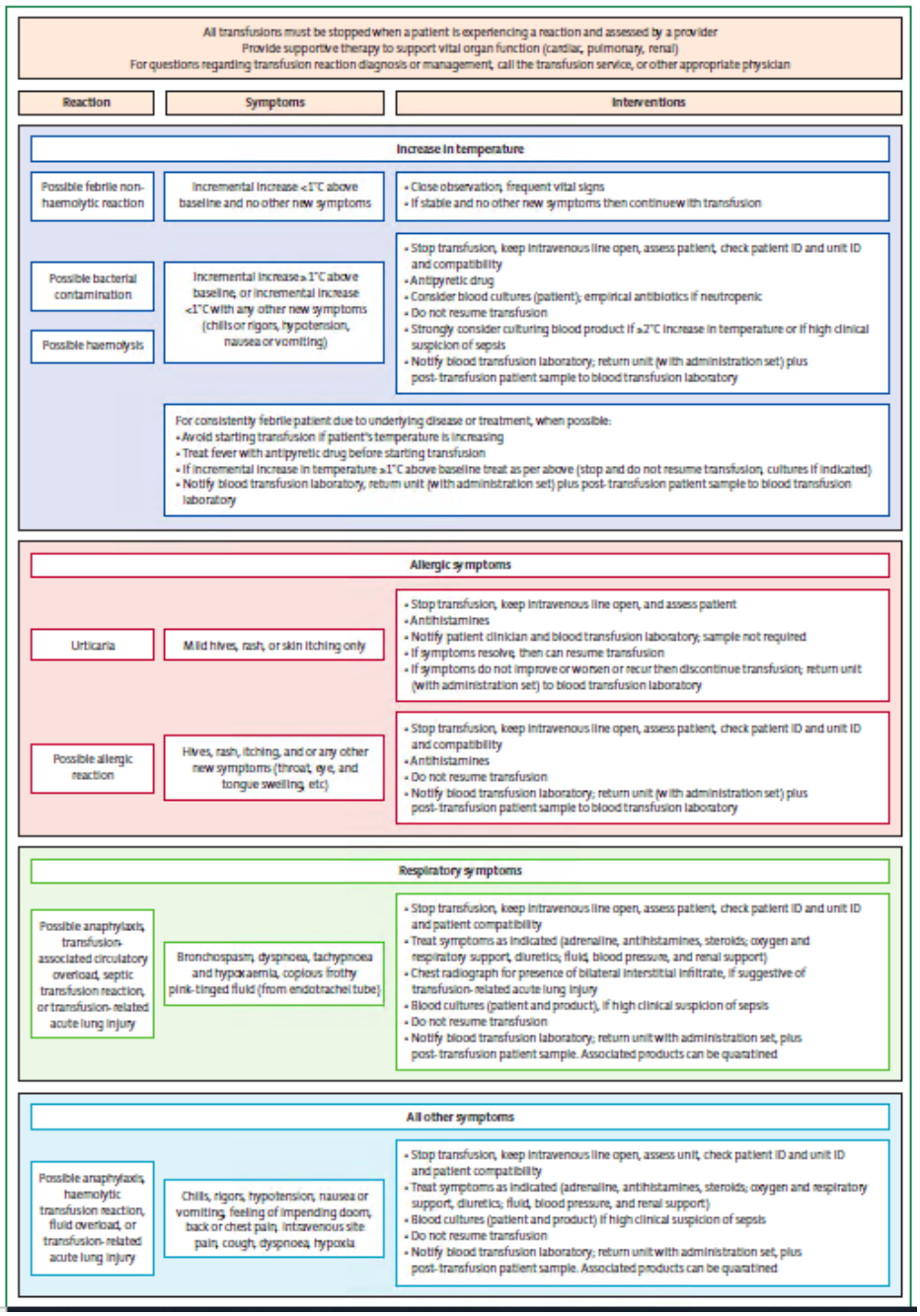


Figure 2: Transfusion reaction decision-tree
Algorithm to guide assessment and actions to takewhen a transfusion reaction is initially identified. Actions should go from left to right.

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-Pathophysiology of TRALI is not well understood, but a 2-hit model is suggested for TRALI with a pre-existing medical condition being the first hit (risk factors include shock, systemic inflammation, positive fluid balance, current smoking,

chronic alcohol abuse) and the second hit conveyed by the transfused blood product (anti-HLA,, anti-HNA, other factors in the transfusion product).
-The 2-hit model also applies to TACO (specific risk factors are different)
-Survivors of TRALI can receive additional blood products in the future, and transfusion of needed blood products should not be withheld. Importantly, however, individuals should not receive blood products from the implicated donor.

-Event report of all TRALI reactions is necessary in order to consider donor deferral depending on their antibody testing results.

References

National Healthcare Safety Network (NHSN) Biovigilance Component: Hemovigilance Module Surveillance Protocol v2.6. March 2021; Section 3: 8-21.
Delaney M et al. Transfusion reactions: prevention, diagnosis and treatment. Lancet 2016
Semple JW et al. Transfusion-Associated Circulatory Overload and Transfusion-Related Acute Lung Injury. Blood 2019.

Case 5 Moderator Notes: Neonatal purpura fulminans

Suggested Q&A for discussion (color coded to match the information at the bottom)

Is transfusion indicated?

Yes, given the presence of active symptoms and coagulopathy at first
Later on, protein C deficiency is diagnosed. The symptoms are hard to recognize at first as a bleeding versus clotting complication, but regardless, FFP is appropriate while the diagnosis is being confirmed because it replenishes both pro-coagulant and anticoagulant factors.

What is the dose and further management?

10-15ml/kg is around 40ml FFP. Check PT/PTT/fibrinogen 1 hour after completion of FFP and reassess clinical situation. Either a repeat dose or alternative treatment (like protein C concentrate) to replace protein C should be considered if there is worsening of the lesions. In the absence of bleeding, repeat FFP dose is unlikely to be needed just for the prolonged PT and/or low fibrinogen.

When should you use cryoprecipitate instead of FFP?

If and when there is worsening DIC with a need to avoid fluid overload, and/or fibrinogen deficiency. It is not beneficial to use in cases of fluid overload when PT/PTT are prolonged without fibrinogen deficiency.
It is unlikely to be needed in this case scenario.

Information and references that will be provided to residents after the case discussion

-There is minimal evidence in the pediatric population regarding plasma transfusions. Adult guidelines are commonly used in children as well. FFP dosing, even in adults, is guided by non-randomized studies.
-FFP is indicated for coagulopathies when there is active bleeding or prior to invasive procedures. Causes of coagulopathy include acquired deficiency of multiple clotting factors due to DIC, treatment with vitamin K antagonists like warfarin (when prothrombin complex concentrates are not available, FFP is used), and inherited clotting factor deficiencies with no specific concentrates available for replacement therapy (Factors 2, 5, 10, 11).
-FFP is also indicated for replacement of other plasma proteins like for purpura fulminans/severe thromboses (in protein C deficiency, protein S deficiency, antithrombin III deficiency, and warfarin induced skin necrosis), thrombotic microangiopathies (TTP, HUS), and hereditary angioedema when specific C1-esterase inhibitors are not available.
-FFP (and cryo) may cause adverse outcomes in critically ill patients, like TRALI, TACO, multi-organ failure and increased risk of infection. The risks are more than benefits for prophylactic use just for prolonged PT/PTT use without any bleeding or upcoming invasive procedure. Hence it is not recommended.
-Patients with an INR< or =2 may not benefit from FFP and can undergo invasive procedures at the bedside in the ICU without any serious bleeding. In fact, several guidelines recommend against FFP prior to certain invasive procedures (see Reference 3 for details).
-FFP is dosed at 10-15ml/kg followed by reassessment of clinical condition and coagulation tests post-transfusion followed by further doses if needed.
-Cryoprecipitate use should be restricted to DIC and congenital fibrinogen deficiency in the presence of active bleeding and fibrinogen <150mg/dl. It can also be used in certain inherited factor deficiencies when specific concentrates are not immediately available for replacement therapy (Factors 8, 13 and vWF).
-Cryoprecipitate at 1U/10kg or 5-10ml/kg (1 unit contains 15-20mls), to a maximum adult dose of 10units, should result in an increase in fibrinogen of 60-100mg/dl.
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References

McCormick M, Delaney M. Transfusion Support: Considerations in Pediatric Population. Seminars in Hematology 2020
National Institute for Health and Care Excellence (NICE). Transfusion; FFP. NICE Guideline NG24 2015
Lu W. A Concise Synopsis of Current Literature and Guidelines on the Practice of Plasma Transfusion. Clinics in Laboratory Medicine 2021

Case 6 Moderator Notes: Sickle Cell Disease

Suggested Q&A for discussion (color coded to match the information at the bottom)
Is (or was) transfusion indicated on the day of ER presentation and admission?
No.
Is transfusion indicated the next day after diagnosis of acute chest syndrome?
Yes.
How would you proceed with transfusion? (type of transfusion: simple or exchange, volume)
Simple transfusion can be done since the Hb level is 7g/dl. 10-15ml/kg pRBCs is expected to raise the Hb to 9-10g/dl which is not too high to cause hyper-viscosity complications like stroke.
What are some special considerations for transfusion in SCD?
The risk of alloimmunization and long-term risk of iron overload.
The aim of transfusion in SCD is not just to improve O2 carrying capacity but also to reduce HbS level.
What if this patient did not have hypoxia or any other signs of respiratory distress?
It is best to discuss each specific case with the hematologist. Milder cases of acute chest syndrome with fever and CXR infiltrate but no respiratory distress or severe anemia can be monitored carefully for improvement without a transfusion, keeping in mind that they may need one if clinical course worsens.
Information and references that will be provided to residents after the case discussion
-Aims of transfusion in SCD are both to increase O2 carrying capacity and reduced HbS level relative to HbA level, in order to prevent or reverse the complications of vaso-occlusion.
-Consensus guidelines recommend against the use of transfusion for an uncomplicated pain crisis.
-Indications for acute transfusion include symptomatic anemia, acute severe splenic sequestration, aplastic crisis, acute chest syndrome (ACS) with hypoxia or other signs of respiratory distress, sickle cell hepatopathy, priapism not responding to initial measures, severe sepsis, and pre-operatively (for surgeries needing general anesthesia and lasting >1 hour to prevent post-op sickling complications like pain and ACS).
-Indications for chronic transfusions include primary stroke prevention in the presence of abnormal Transcranial doppler studies (TCD), secondary stroke prevention after occurrence of stroke, and recurrent complications of SCD like ACS or priapism not controlled by other measures.
-In acute situations, the volume of pRBCs should be calculated to achieve a Hb of 9-11g/dl to avoid hyper-viscosity related to higher Hb values. Sometimes this is not

achievable with a simple transfusion and hence exchange transfusion is needed: for example, severe acute chest syndrome with pre-transfusion Hb>10-11g/dl.

-In acute situations needing rapid lowering of HbS level, exchange transfusion is preferred: for example, stroke.

-In patients on long-term transfusions, if HbS level is maintained at <30-40%, Hb can be safely maintained at a higher level with less risk of hyper-viscosity.

-Patients should undergo extended RBC antigen typing (meaning beyond ABO/RhD) at baseline, including antigens C/c, E/e, Kell (K), along with a full crossmatch and screen for new antibodies prior to each transfusion.

-Patients should be administered blood products matched for C, E and Kell to avoid alloimmunization, especially since alloimmunization is more common in SCD than other patient populations.

-The main concerns with alloimmunization, namely, Delayed Hemolytic Transfusion reactions (DHTR) and hyper-hemolysis syndrome, are also more common in SCD. These need to be recognized and managed appropriately with immunosuppressive therapy if needed.

-Another important complication of transfusion in SCD is iron overload, either due to repeated acute transfusions over time or chronic transfusions.

References

McCormick M, Delaney M. Transfusion Support: Considerations in Pediatric Population. Seminars in Hematology 2020

Chou ST et al. American Society of Hematology 2020 Guidelines for Sickle Cell Disease: Transfusion support. Blood Advances 2020

Howard J. Sickle cell disease: When and How to Transfuse. Hematology ASH Education Program 2016