Transfusion Guidelines

Blood, Platelet and Factor

Children's Hospital of Philadelphia®
Division of Neonatology

Title CHOP Transfusion Guidelines: Blood, Platelet and Factor

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Abstract

Evidence supports a more conservative approach to blood, platelet, plasma and cryoprecipitate transfusions for neonates. Blood transfusion guidelines are based on the TOP Transfusion thresholds with reference to clinical illness and age of neonate. Platelet transfusions have shown to increase the risk of IVH and mortality in neonates, a more conservative approach is recommended with threshold for well appearing neonates of 25 $x10^3$/L for transfusion of platelets. Plasma should be used only with active bleeding or oozing and abnormality of coagulation studies (normal values provided, abnormal consider more than twice normal age-based values). No new evidence exists to change current ECMO transfusion practices, although in the future more conservative platelet transfusion practices may be considered. Although there is a low incidence of Transfusion associated NEC, at this time there is not strong evidence to recommend holding feeds during a blood transfusion, recommendation is to continue current volume of feeds during a blood transfusion.

Consensus Goals

Evidence based guidelines for blood transfusions.
Evidence based guidelines for platelet transfusions.
Evidence based updated guidelines on transfusions guidelines for patients on ECMO.
Evidence based and expert opinion for factor transfusion guidelines for newborns.
Evidence based and expert opinion about Transfusion Associated NEC.

Background

Blood, platelet and factor transfusions are all common practice in the neonatology. Newer evidence has emerged in the past 5 years to show that liberal blood transfusions do not lead to improved neurodevelopmental outcomes or survival in the NICU. Platelet transfusions have been shown to have a detrimental impact on neonatal survival, without improvement in decreasing IVH rates. In fact, using a more conservative platelet count for transfusions decreased risk of mortality in neonates. Transfusion practices with regards to use of factors has not been well studied in neonates and is at times derived from pediatric and adult practices. Obtaining routine coagulation studies in neonates has decreased over the past epochs of neonatology and is not routinely recommended. Use of fresh frozen plasma has also been shown to be inappropriate in terms of intravascular fluid replacement, there are few studies to

discuss appropriate factor transfusions parameters in neonates. ECMO transfusion practices are often expert and practice opinion based, ELSO guidelines, derived also from mainly adult practices guide parameters for transfusion for neonates on ECMO. Evidence in regards to transfusion associated NEC (TANEC) or transfusion associated gut injury (TRAGI) is varying and large meta-analysis have shown that the association is weak. Practice varies widely in regards to holding of neonatal feeds or decreasing the volume of feeds during a blood transfusion.

Previous Consensus Statement or Data from Division of Neonatology (if applicable)
None

Literature Search

Title	Author	Level of Evidence	Primary Outcome & Results	Key Findings/Conclusions
Premature Infants in Need of Transfusion (PINT) Study	Kirpalani et al Journal of Pediatrics 2006	Randomized Control Trial of Low vs High Transfusion Threshold. 10 NICUS in US/Canada/Australia	Eligibility criteria: <1kg at birth, <31 weeks, <48hrs of age at enrollment Primary Outcome: death before DC or survival with severe ROP, BPD, brain injury (e.g. PVL) All transfusions 15 ml/kg with rate by local policy. Nothing in protocol setting when/how often to check H/H	Groups similar re: maternal and infant variables Low threshold n=223 mean 4.9 units transfused. High threshold n=228 mean 5.7 units transfused (p=0.070) Fewer infants transfused (89% v 95%, p=0.037) in low group Rate of primary outcome 74% (low) vs 69.7% (high) p=0.25 Individual components of primary outcome except brain injury favored high threshold group but not statistically significant Key Conclusions: little evidence of benefit in maintaining a higher hemoglobin
Randomized trial of liberal versus restrictive guidelines for red blood cell transfusion in preterm infants	Edward F Bell, et al. Pediatrics 2005	Randomized controlled study at single center NICU	Statistical difference 1) number of transfusions 2) Frequency of apnea 2X higher in restrictive vs liberal absolute number if <1 per day.	More restrictive criteria may lead to more apnea – but absolute number may have no/little impact

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Effects of Liberal vs Restrictive Transfusion Thresholds on Survival & Neurocognitive Outcomes in Extremely Low-Birth-Weight Infants: The ETTNO Randomized Clinical Trial	Franz AR et al, ETTNO Investigators, August 2020, JAMA	Multicenter randomized control trial 36 level III/IV NICUs in Europe, 1013 infants weighing 400-999g at birth, randomized within 72 hrs of birth	Death or NDI by 24 mo was present in 44% of infants in liberal group vs. 42.9% of infants in restrictive group, for risk difference of 1.6% (95% CI, −4.8% to +7.9%) and an odds ratio of 1.05 (95% CI, 0.80-1.39; P = .72)	Among ELBWs, at follow up at 24 mo corrected, a liberal RBC strategy compared to restrictive did NOT reduce likelihood of composite outcome of death or NDI or secondary outcomes
Transfusion of Prematures (TOP Trial)	Kirpalani et al New England Journal of Medicine	Randomized Control Triap Level II	Multicenter RCT 1000g or less & 22 0/7-28 6/7 were randomly assigned within 48 hrs to higher vs lower HGB threshold for transfusion Until 36 weeks PMA or discharge Primary outcome death or neurodevelopmental impairment at 22-26 months	Higher hemoglobin thresholds did not improved survival without neuro-developmental impairment
Platelet Transfusion Practices Among Very-Low-Birth-Weight Infants	Sparger, Katherine et al. published in JAMA Peds May 2016	Multicenter retrospective cohort study (6 US NICUs including Boston, Iowa, several in Utah)	231 (24%) of the population received at least 1 plt transfusion, with a mean of 4.3 transfusions per infant (range 1-63) 65% of transfusions given for thresholds of at least 50K 28% given in the first week of life, of which 66% of patient days given for counts < 50K Infants transfused more likely to be male, more premature, and smaller (statistically significant for all three items) 28% of transfusions given in first 7 days of life	Large proportion of transfusions given to those with counts > 50K Severity of illness influenced decision to transfuse There was no correlation between severity of thrombocytopenia and IVH Transfusions didn't have an effect on the incidence of IVH Limitations of study: retrospective, not randomized so unable

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			402 days total with a platelet count < 100, 000 Transfusion given on 212 (52.7%) of those days 93.4% had at least 1 marker of severe illness or bleeding on these days	to assess for causation, not very generalizable to infants with counts < 50 K as there was a low number of patient days with these counts Highlighted need for randomized trials
Randomized Trial of Platelet-Transfusion Thresholds in Neonates.	Curley et al. Jan 2019 in NEJM	Multicenter Randomized trial	**High threshold** Group (<50,000) 90% of infants (296 of 328 infants) received at least 1 transfusion 26% of infants (85 of 324) had new major bleeding episode or death occurred through trial day 28 15% Died **Low threshold** Group (<25,000) 53% of infants (177 of 331 infants) received at least 1 transfusion 19% of infants (61 of 329) had new major bleeding episode or death occurred through trial day 28 10% died	Conclusion: Use of platelet count of 50,000 resulted in higher rate of death or major bleeding
Preterm neonates benefit from low prophylactic platelet transfusion threshold despite varying risk of bleeding or death	Susanna F Fustolo-Gunnink Blood December 2019	Clinical Trials & Observations Regular Article	Multivariate logistic regression model in PlaNet-2 data to predict baseline risk of major bleeding +/- mortality for all 653 neonates. Based on baseline risk, they were categorized into 4 risk quartiles and then absolute-risk difference between $50x10^9$/L & $25x10^9$/L threshold groups was assessed.	Conclusion: The $25x10^9$/L threshold was associated with absolute-risk reduction in all risk groups. Recommendation: $25x10^9$/L threshold can be adopted in all preterm neonates, irrespective of predicted baseline outcome risk
Benefits of lower neonatal platelet transfusion thresholds.	Hasan R, Saifee NH Transfusion. 2021; 61: 1672-1675	Rapid Review article	1-Neonatal platelet physiology is a distinct hemostatic balance:Transfusing adult plts into neonate is a developmental mismatch	There are implications for platelet transfusions in adults and neonates. Increasing evidence for role of platelets in

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			with higher risk for hyperreactivity. 2-Global Variability in Platelet thresholds for Neonates. 3- Severity of thrombocytopenia does not predict major bleeding: PlaNeT-1 a prospective observational trial in median age 27wks infants with risk factors for bleeding including prior IVH showed 91% did not have major hemorrage even with plt of <20. 4-Lower transfusion thresholds may have better outcomes in neonates: PlaNeT-2 RCT showed increase in 7% more death in a higher plt transfusion threshold of 50 vs 25. Secondary outcome showed higher rate of BPD at 36 wks in higher threshold.	disrupting hemostasis, thrombogenesis, and inflammation. No conclusive evidence of benefit for platelet transfusion on major bleeding. Need for future studies include platelet dosing, long term outcomes, risk of bleeding and platelet therapy.
Implementation of a neonatal platelet transfusion guideline to reduce non-indicated transfusions using a quality improvement framework	Davenport et al, J Perinatology 2021	A quality control framework based on historical controls for the unit	The number of non-indicated platelet transfusions per month decreased from a mean of 7.3 before to 1.6 after guideline implementation, with significant special cause variation on c-chart SPC analysis (Fig. 2 run chart). Analysis of balancing measures showed that rates of major bleeding, including ICH, remained stable over time (Table 4). No differences in the rates of sepsis, necrotizing enterocolitis, thrombosis, or overall mortality were found.	The biggest reduction in non-indicated platelet transfusions came from withholding transfusions in non-bleeding, critically ill neonates with platelet counts between 25 and 50 × 10^9/L, who were historically transfused at the higher threshold of 50 × 10^9/L due to their severity of illness. In agreement with previous trial data, despite the decrease in platelet transfusion thresholds and decrease in non-indicated platelet transfusions, they did not see a change in the incidence of major

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				bleeding, including ICH.
Fresh frozen plasma transfusion in the neonatal population	**Sokou *et al, Blood Rev* 2022)**	Metanalysis Level I	Meta-analysis of 40 NICU studies to assess FFP transfusion practices in neonates.	Practices vary widely Most FFP given prophylactically. Improves coags but does not improve clinical outcomes Transfusion reactions are likely under-diagnosed, under-estimated, under-reported FFP includes all coags/factors/inhibs at mean concentration 1 IU/mL 10-15ml/kg FFP infusion should be an effective dose (raises factor levels by 10-15%). Prevalence of FFP transfusion varies – 0.17% up to 24% in extremely preterm infants Most babies get FFP due to abnormal coags w/o bleeding NICU makes more inappropriate FFP transfusions than other units 21% FFP transfusions were used as volume expander (inappropriate)
Pediatric non-red cell blood product transfusion practices: what's the evidence to guide transfusion of the 'yellow'	Steinbicker *et al, Curr Opin Anesthesiol* 2020		Daily practice for bleeding and nonbleeding children very often includes FFP, cryoprecipitate, platelets, or fibrinogen concentrate without a well-defined clinical indication. Evidence is weak, high quality studies limited	FFP may be of benefit prior to invasive procedures with a risk of significant coagulopathic bleeding, and in patients who have an abnormal coagulation profile

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blood products?			Can be clinically efficacious to treat coagulopathic bleeding But ~50% FFP transfusions are prophylactic Dose-dependent increase in serious transfusion reactions (often underappreciated/underreported). Allergic reactions, fever, transfusion-related acute lung injury, and transfusion-related acute cardiac overload, hemolysis and venous thrombosis	PT or aPTT significantly above the normal gestational and post-natal age-related reference range FFP should not be given prior to surgery or invasive procedure with minor prolongation of PT/aPTT FFP should not be given as volume replacement Cryoprecipitate withdrawn from some European countries because of risk of immunologic reactions and potential transmission of infectious agents. Insufficient evidence to recommend therapeutic or prophylactic Cryo in neonates and infants The recommended dosage is 5ml/kg body weight Massive Transfusion Protocols No consensus for ratio of RBC:FFP
Anticoagulation and Transfusion management during neonatal and pediatric ECMO: A survey of medical directors in the US	Caroline P. Ozment, MD Briana L. Scott, MD Melania M. Bembea, MD Philip C. Spinella, MD PCCM Journal, June 2021 • Volume 22 • Number 6	Survey Level IV	79 surveys filled out by medical directors August - December 2019 For Neonates, Data showed: Most units had anticoagulation and transfusion guidelines Default Heparin starting dose mostly 21-30Most institutions give FFP for AT3 <80 ACT goals mostly 180-220 Anti-Xa goal mostly 0.3-0.7 PTT goal mostly 60-80	Transfusion thresholds, especially for platelets, varied CHOP Anticoagulation Guidelines not significantly different from the practices at other institutions

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			Most institutions monitored Heparin with Anti-Xa and ACTs	
Withholding Feeds and Transfusion-Associated Necrotizing Enterocolitis in Preterm Infants: A Systematic Review	B. Jassani Australia *Advances in Nutrition*, Volume 8, Issue 5, September 2017, Pages 764–769, https://doi.org/10.3945	Study population VLBW and LBW (6) one <34 weeks Moderate (although observational study, upgraded 2 levels because of large sample size, narrow CI and very low *p value*	Review of 7 articles where feeds withheld Incidence of NEC pre and post implementation calculated Total of 7492 infants estimated risk with feed 107/4534 and with withholding 22/2958 Relative effect 0.47 (0.28 vs 0.8, *p 0.0005)*	Withholding feeds in the peri-transfusion period reduces the incidence of TANEC in preterm infants. Given the limitations of the studies included in our meta-analysis, adequately powered RCTs are needed to confirm these findings.
Characteristics and incidence of transfusion-associated necrotizing enterocolitis in the UK	Christopher M Faraday *Journal of Maternal-Fetal & Neonatal Medicine on 1st October 2018*	Retrospective study 8007 consecutive ICN admissions reviewed oct 2011-Nov 2014 NEC: modified VON criteria, excluded perforation TANEC: NEC within 48hrs of Tx	68 developed NEC (All were VLBW infants out of 1608 VLBW) Incidence 4.2% in VLBW 19 (28%) no Tx 34 had transfusion but did not match TANEC criteria 15 of 68 (22%) had TANEC, Incidence 0.93% in all VLBW 60% were transfused for asymptomatic	TANEC does exist although incidence was very small and there was unit to unit variation in NEC as well as TANEC incidences Difficult to design a prospective study with specific intervention Further work is needed to clarify causation, pathophysiology, and possible mechanisms of prevention of TANEC.
Effect of withholding feeds on transfusion-related acute gut injury in preterm infants: a pilot randomized controlled trial	Susan Shin et al Journal of Maternal-Fetal and Neonatal Medicine March 2019	RCT withhold feeds for 12hrs or continue feeds Population: <32 weeks or <1500gm at birth Primary outcome NEC stage >2 or = within 72hrs	154 transfusions 74 NPO, 80 fed No difference in incidence (0 vs 3.4% p 0.49) Slightly higher feeding intolerance but not statistically significant	This pilot study does not support withholding feedings during transfusion but is not adequately powered to test the hypothesis that NPO decreases NEC rates. Adequately powered well-designed multicenter trials are still required.
Transfusion related gut injury and NEC	Allison Rose Clinical Perinatology June 2020	Discussion of various studies	Animal model to understand TRAGI shows possible mechanism of gut injury related to anemia and transfusion	Anemia (priming step) and RBC transfusion (activating step) may play a role in gut injury. Results from ongoing RCTs of transfusion

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				thresholds as well as feeding practices during RBC transfusion should inform important clinical decisions surrounding approaches to RBC transfusions and enteral feedings during transfusion.
Feeding practices and effects on transfusion-associated necrotizing enterocolitis in premature neonates.	Killion E., Gephart S.M. and Quinn M Advances in Neonatal Care 2021		Discussed various NPO protocols No consensus for about adequate period for premature infants to be maintained NPO in an attempt to reduce the risk of TANEC	- Need large, multicenter RCTs to evaluate interventions such as establishing transfusion threshold protocols and implementing peritransfusion feeding protocols. - Individual institutions should standardize their enteral feeding policies to reflect best practice.
Slow enteral feeding decreases risk of transfusion associated necrotizing enterocolitis.	Dako J., Buzzard J., Jain M., Pandey R., Groh-Wargo S. and Shekhawat P. Journal of Perinatology 2018	Retrospective A single center and a small sample size	- With introduction of SSEF protocol in 2009 the incidence of NEC decreased to 0.3% to 0.75% and only one case of TANEC recorded during observation period. - delay in onset of NEC from a median of 21 days to 52 days (p = 0.003)	The practice of withholding feeds around the time of transfusion was not protective against TANEC where cohort of patients more infants were kept NPO in the TANEC group (p = 0.01). NPO status during any blood transfusion did not prevent TANEC. Our results show a significant decrease in NEC and almost complete prevention of TANEC after the introduction of a SSEF protocol in our institution, suggesting that NEC and TANEC are both related to feeding practices.

Title	Author	Level of Evidence	Primary Outcome & Results	Key Findings/Conclusions
				SSEF can significantly reduce the incidence of TANEC without impairing growth; SSEF can prevent NEC/TANEC.
FEEding DURing red cell transfusion (FEEDUR RCT): a multi-arm randomized controlled trial	Tim Schindler, Kee Thai Yeo , Srinivas Bolisetty, Joanna Michalowski, Alvin Hock Kuan Tan and Kei Lui BMC pediatrics 2020 20.346	Open, multi arm, parallel group RCT in a single center 20 transfusions in 3 arms so very limited data	Sensors are placed on forehead and abdomen to measure oxygenation 3 arms: withhold feeds for 12 hrs, continue feeds, restrict feeds to 120 mL/kg: Splanchnic-cerebral O2 ratio and splanchnic O2 extraction at 0, 1hr, 3hr, 12hr and 24hrs: No difference in each group, no NEC, or other complications	Larger trial feasible It is feasible to measure splanchnic oxygenation non-invasively with near infrared spectroscopy (one of the factor thought to play the role in TA-NEC) No difference seen in splanchnic oxygenation during feeds with transfusions
Feeding during transfusion and the risk of necrotizing enterocolitis in preterm infants.	Bajaj et al. (2019) Journal of Perinatology (Vol 39, Issue 4)	Retrospective Chart Review: Pre and post feeding protocol change which included holding feeds for 12-24 hours during PRBC transfusion <1250 grams Feeding protocol emphasize BM, trophics, slow advance Transfused based on EBM protocol	125 infants included, 57 pre and 68 post protocol Mean GA 27.1 weeks 19 had NEC overall TRAGI in 6 15.8% TRAGI pre versus 14.7% post Post-natal hydrocortisone was associated with TRAGI after multivariable regression analysis 381 transfusions with 189 pre an 192 post, no difference in TRAGI, higher rate of blood steam infections post period	There was no benefit to holding feeds for 12-24 hours during and after transfusion on rates of TRAGI TRAGI rates were consistent with reported literature. More studies required to determine etiology of disease and guide future management recommendations
Epidemiology of NEC: New Considerations Regarding the Influence of Red Blood Cell Transfusion and Anemia	Saroha et al. (2019) Clinical Perinatology (Vol46, Issue 1)	Review Discussion of Epidemiology with small meta-analysis	Transfusion Hb threshold NEC within 48h of transfusion Does level of anemia affect NEC	Clear advantage not present in regards to Hb threshold Studies not adequate to state NEC associated with transfusion

Title	Author	Level of Evidence	Primary Outcome & Results	Key Findings/Conclusions
			Discuss several mechanisms related to associations Feeding during transfusion	Anemia does not independently contribute to NEC Discuss hypoxemia, dysregulated blood flow, inflammation Equivocal, some studies say negative association, some say no association WHEAT- withholding enteral feeds around transfusion study- on-going

Literature Summary

Evidence based guidelines for blood transfusions.
The PINT study, followed by the Iowa Trial set the precedence that potentially more conservative blood transfusion guidelines would be appropriate for premature neonates. The ETTNO study (2019) and TOP Trial (2020) both showed that a liberal blood transfusion policy did not lead to increase survival without neurodevelopmental impairment at 24 months corrected gestational age.

Evidence based guidelines for platelet transfusions.
Sparger et al in 2016 showed that liberal platelet transfusions did not impact intraventricular hemorrhage or risk of bleeding. Curley et al showed that use of platelet count of 50,000 versus 25,000 resulted in higher rate of death or major bleeding in neonates. Further studies by the Fustolo Gunninck in 2019 showed $25x10^9$/L threshold can be adopted safely in all preterm neonates, irrespective of predicted baseline outcome risk with the data from the PLANET-2 Trial.

Evidence based and expert opinion for factor transfusion guidelines for newborns.
Sokou in a review (Blood 2022) discussed that practices vary widely in regards to plasma transfusions for neonates. Most plasma given prophylactically. Improvement in coagulation results do not improve clinical outcomes and that transfusion reactions are likely under-diagnosed, under-estimated, under-reported. Neonatal intensive care units are most likely to give inappropriate transfusions of plasma, and that plasma is not appropriate as intravascular volume expander. Steinbricker (2020) discussed that plasma may be of benefit prior to invasive procedures with a risk of significant coagulopathic bleeding, and in patients who have an abnormal coagulation profile (PT or aPTT significantly above the normal gestational and post-

natal age-related reference range). Plasma should not be given prior to surgery or invasive procedure with minor prolongation of PT/aPTT.

Evidence based and expert opinion about Transfusion Associated NEC.
Jassani et al showed in a meta-analysis of multiple smaller studies that withholding feeds during a blood transfusion may reduce the risk of TANEC—but commented on the need for a large RCT as this was based on many smaller trials. Although Faraday et al did find that TANEC did exist they incidence was extremely low. Schindler et al during the FEEDUR RCT showed that splanchnic oxygenation did not change during feeds and a blood transfusion. A majority of the literature shows there is little correlation between feeding, NEC and blood transfusion.

Delphi Survey Round Results (if applicable)
Survey questionnaire sent out in January and results collected by February (2023), 102 responses received from throughout the CHOP Division of Neonatology, CHOP Newborn Care Network as well as surrounding outside hospital systems.
Results showed the following:
73% of neonatologist (73/102) do not hold feeds during a blood transfusion.
60% of neonatologist continue feeds at their current volume during a blood transfusion. (7 people do half volume and 6 people did trophic feeds)
82% of neonatologist do not consider the level of anemia, while 18% do consider the level of anemia.
Of those who are currently holding feeds during a blood transfusion, 94% said they would.
Of those who are currently holding feeds, 78% said would be willing to continue feeds at a lower volume.
90% of people do not feel that there is evidence to support NPO status during blood transfusion.

Consensus Statement and Clinical Recommendations

CHOP Transfusion Guidance

Platelet Transfusion Guidelines

Platelet Count Threshold (x 10^3/L)	Non Bleeding Neonate	Bleeding Neonate **
<25	**Transfuse** (10ml/kg over 2 hours)	**Transfuse** (10ml/kg over 2 hours)
25-50	Stable- No transfusion ***Consider Transfusion*** • Critically ill <1000 gram and <1 week*** • Hemodynamically unstable • Previous major bleeding <1 week of age* • Current minor bleeding ** • Concurrent coagulopathy • Pre/Post operative (72hr) • Pre IR procedure or Lumbar puncture	**Transfuse**
50-100	Do Not transfuse	**Transfuse**
>100	Do Not transfuse	Do Not Transfuse

* Grade III or IV IVH, intracranial bleeding or pulmonary hemorrhage (new onset)
** Petechia, puncture site oozing, blood streaked ET secretions
***Please use clinical judgement in specific circumstances

Please contact Hematology if platelet qualitative defect suspected

Red Blood Cell Transfusion Guidelines, <35 weeks GA

	Hgb(g/dL)/Hct (%) Threshold	
Week of life	Critical Illness	Non Critical Illness
1	11/32	10/29.5
2	10/29.5	8.5/25
≥3	8.5/25	7/21

Feedings should continue at their current volume during a blood transfusion

* Critical Illness: High Flow Nasal Cannula ≥ 4L and/or FiO2 ≥ 30% ; Hemodynamic instability
** Recommended transfusion volume of 15-20ml/kg over 3 hours
*** Discretion of the provider to be used in terms of transfusions in unique clinical situations
Conservative evidence based transfusion thresholds not based on superiority

Plasma and Cryoprecipitate Transfusion Recommendations

Recommend against routine evaluation of coagulation studies in neonates
- Use clinical judgement, obtain lab work as appropriate

Recommend against using Plasma (FFP) or Cryoprecipitate for intravascular volume
- Consider crystalloid (normal saline) or 5% albumin for intravascular volume

Consider Plasma or cryoprecipitate **(5-10ml/kg over 1 hour)** for at-risk neonates **with signs/symptoms of bleeding**
- *At risk neonates include*:
  Neonates with active bleeding or uncontrolled oozing
  HIE undergoing cooling with bleeding or oozing
  Pre-surgical neonates with active bleeding

Normal ranges for ages < 6 months

Test	Reference Range
PT	10.5-13.0 seconds
PTT	25-37 seconds
Fibrinogen	131-405 mg/dL

Values change rapidly in the neonatal period and are dependent on gestational age at delivery

From CHOP Dept. of Pathology & Laboratory Medicine Reference Ranges Document
https://media.chop.edu/data/files/pdfs/chop-labs-reference-ranges.pdf

Reference values for coagulation tests in healthy premature infants (30-36 weeks' gestation) during first 6 months of life

Test	Day 1	Day 5	Day 30	Day 90
PT (sec)	13 (10.6-16.2)	12.5 (10-15.3)	11.8 (10-13.6)	12.3 (10-14.6)
PTT (sec)	53.6 (27.5-79.4)	50.5 (26.9-74.1)	44.7 (26.9-62.5)	39.5 (28.3-50.7)
INR	1 (0.61-1.70)	0.91 (0.53-1.48)	0.79 (0.53-1.11)	0.88 (0.53-1.32)
Fibrinogen (mg/dL)	243 (150-373)	280 (160-418)	254 (150-414)	246 (150-352)

Many studies transfuse if values reach 2x normal value

Mean (95% Confidence Interval)
From Nathan & Oski's Hematology of Infancy and Childhood, 8th Ed, Table A1-4 Original Data: Andrew et al, Blood 1988 (PMID 3179444)

Further Goals

Nationwide survey to practicing Neonatologist through the AAP—pending IRB approval
Follow Up survey to assess standardization of practice within the network in 6 months (Sept 2023)

QI Metrics

Pending as needed following post implementation 6 month survey

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