Received: 29 December 2017 | Revised: 31 July 2018 | Accepted: 3 September 2018

DOI: 10.1002/jca.21666

WILEY Journal of Clinical Apheresis ASFA

RESEARCH ARTICLE

Hemostasis testing and therapeutic plasma exchange: Results of a practice survey

Nicole D. Zantek[1] | Monica B. Pagano[2] | Marian A. Rollins-Raval[3] | Roy E. Smith[4] | Amy E. Schmidt[5] | Jason E. Crane[6] | Leonard I. Boral[7] | Yanhua Li[8] | Annika M. Svensson[9] | Chisa Yamada[10] | Yanyun Wu[11] | Edward C. C. Wong[12,13]

[1]Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota

[2]Department of Laboratory Medicine, University of Washington, Seattle, Washington

[3]Department of Pathology and Laboratory Medicine, University of North Carolina, Chapel Hill, North Carolina

[4]Hematology/Oncology Division, University of Pittsburgh Medical Center Presbyterian-Shadyside Hospital, Pittsburgh, Pennsylvania

[5]Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, New York

[6]LifeSource Blood Center, Illinois

[7]Department of Pathology and Laboratory Medicine, University of Kentucky, Lexington, Kentucky

[8]Department of Pathology and Laboratory Medicine, New York University, New York, New York

[9]Consultant, Denver, Colorado

[10]Department of Pathology, University of Michigan, Ann Arbor, Michigan

[11]Bloodworks, Seattle, Washington

[12]Department of Coagulation, Quest Diagnostics Nichols Institute, Virginia

[13]Departments of Pediatrics and Pathology, George Washington School of Medicine and Health Sciences, Washington, DC

Correspondence
Nicole D. Zantek, University of Minnesota, 420 Delaware Street SE, MMC 609, Minneapolis, MN 55455, USA.
Email: zant0005@umn.edu

Abstract

Introduction: Performing therapeutic plasma exchange (TPE) with albumin replacement decreases coagulation factor and platelet levels. No defined guidelines exist regarding laboratory testing to assess hemostasis in patients undergoing TPE.

Materials and methods: A survey to evaluate hemostasis testing with TPE was distributed using online survey software. One response per institution was analyzed based on a hierarchical algorithm, excluding membrane filtration users, resulting in a maximum of 120 respondents per question. Descriptive analysis was performed with results reported as the number and/or frequency (%) of respondents to each question.

Results: The practices represented vary by institution type, number of apheresis procedures per year, and performance of TPE on children. Prior to TPE planned with albumin replacement, many respondents obtain laboratory studies for almost all patients (54.9% outpatients and 68.7% inpatients); however, some do not routinely obtain laboratory studies (9.7% outpatients and 4.4% inpatients). Hemoglobin/hematocrit, platelet count, fibrinogen, partial thromboplastin time (aPTT), and international normalized ratio (INR) are obtained prior to all TPE by 62.5%, 53.4%, 31.0%, 18.1%, and 17.7% of respondents, respectively; however, 1.0%, 8.7%, 29.0%, 38.3%, and 35.4%, respectively, do not routinely obtain these studies. Variation was observed in laboratory threshold values for action; the most common reported were hemoglobin/hematocrit <7 g/dL or 21% (31.0%), platelet count $<50 \times 10^9$/L (24.1%), fibrinogen <100 mg/dL (65.3%), aPTT >reference range and >1.5 times reference range (tied, 28.1%), and INR >1.5 (20.7%).

Conclusions: Practice variation exists in hemostasis laboratory testing and threshold values for action with TPE. Further studies are needed to determine optimal hemostasis testing strategies with TPE.

KEYWORDS

coagulation, fibrinogen, international normalized ratio, partial thromboplastin time, plasmapheresis

1 | INTRODUCTION

Therapeutic plasma exchange (TPE) is a procedure in which plasma is removed from a patient and replaced with an alternate fluid, typically albumin or plasma. The primary intent of the exchange is to remove pathogenic substances (eg, toxins, autoantibodies, paraproteins) that have a role in the pathophysiology of the disease in order to ameliorate disease progression and provide clinical benefit to the patient. The removal of the pathogenic substance is nonselective and

physiologic (eg, immunoglobulins, complement, coagulation factors) or therapeutic (eg, medications) substances, and cells (eg, platelets) may also be removed. The unintended removal of coagulation factors is especially critical when replacement fluids other than donor plasma is used, and has a potentially important hemostatic effect on patients undergoing invasive procedures immediately before or after TPE.

The removal of proteins involved in the coagulation cascade has been extensively evaluated and is well characterized.[1–13] In addition, the platelet count may decrease with TPE.[2,4,5,9] Less is known about how to monitor TPE associated coagulopathy and the risk of bleeding, especially when there is ongoing anticoagulation and antiplatelet therapy.[1–3,14,15] A number of tests have been shown to be reflective of this coagulopathy, including fibrinogen levels, prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), and more recently, rotational thromboelastometry (ROTEM).[16,17] Furthermore, there are currently no defined guidelines regarding the frequency of testing, type of tests to perform, and actionable thresholds for patients undergoing TPE treatment.

The aim of this study is to describe and characterize current laboratory testing practices which are used to evaluate the hemostatic capacity of patients undergoing TPE.

2 | MATERIALS AND METHODS

A survey to evaluate laboratory testing patterns associated with performing TPE was developed by members of the Coagulation Subcommittee of the American Society for Apheresis (ASFA) Applications Committee. The survey consisted of 37 questions, including demographic information, questions regarding laboratory testing, case examples to determine routine practice for TPE, and questions regarding hemostasis management, particularly replacement fluid choice (Supporting Information, 1). This article contains data on the laboratory practices portion of the survey and the hemostasis management practices are described in the associated article by Zantek et al.[18] The survey was beta tested by members of the committee and additional members of ASFA. More than 5000 email addresses in the ASFA distribution lists received an email invitation to take the survey which was administered through an online survey tool (Survey Monkey). The initial survey invitation was sent on February 12, 2016.

A total of 167 responses were received. Sixteen duplicate responses were removed, retaining the response with the most complete answers. When the institution was provided by the respondent, only one response per institution was analyzed utilizing the following hierarchy: (1) Director and one of the following—physician, residency/fellowship program director, or member of physician teaching staff; (2) Residency/fellowship program director; (3) Member of physician teaching staff; (4) Physician; (5) Other when listed as physician assistant or nurse practitioner; (6) Director of apheresis; (7) Nurse; (8) Technician; and (9) Resident/Fellow, resulting in 24 additional responses removed from analysis. One respondent entered multiple answers for the question regarding position (physician, nurse, and member of nonphysician teaching staff) and regarding physician specialty responded "I am not a physician." This respondent was included in the nurse category and not included in the physician category in Table 1. Data from an additional 5 respondents were excluded from analysis as they indicated the method typically used for cell separation was membrane filtration or centrifugation and membrane filtration and these numbers are too small to analyze. This resulted in a maximum of 122 potential respondents per question; however, in the data presented here, the maximum number of responses per question was 120. The number of respondents to each question generally decreased through the survey.

Descriptive statistical analysis was performed using Excel 2010 (Microsoft Corporation, Redmond, WA). Results are presented as the number and frequency (%) of respondents for that particular question. Due to rounding, the total percent may not equal 100%. Data analysis was conducted by one author and reviewed by additional authors. All authors had access to the data and contributed to aspects of survey development, data analysis, writing the article, and/or critical review and edit of the article.

3 | RESULTS

Demographic information of the survey respondents is presented in Table 1. In the analyzed data set, respondents were primarily physicians (including physicians-in-training) and nurses, in part due to the algorithm used to remove duplicate responses from the same institution. While only 4 physicians indicated their specialty was pediatrics, 68.1% ($n = 81$ of 119 respondents) performed TPE on children. In a follow-up question, a pediatric procedure was predominately defined by age rather than weight, with the most common threshold for age being 18 years. A wide variety of thresholds were used for weight, ranging from 5 to 50 kg.

Information regarding how the respondents routinely perform TPE was obtained with a series of questions regarding general management of a patient case which were asked at the end of the data presented here. There was a gradual decline in responses throughout the survey, such that only 112 participants responded to the question regarding plasma separation method: 107 centrifugation, 5 membrane filtration alone or with centrifugation, and 10 did not answer this question. The 5 who indicated they use membrane filtration were excluded from all analysis, as the numbers are too small to analyze. The most common volume of TPE performed ($n = 106$) would be 1.0 plasma volume (63.2%), followed by 1.5 plasma volume (13.2%), 1.3 plasma volume

TABLE 1 Demographic information of survey respondents and apheresis programs

Question (number of responders)[a]	Number (%)[b]
Position at institution[b] ($n = 120$)[d]	
Physician (including physician in training-resident/fellow)	74 (61.7)
Director of apheresis service	27 (36.5)[c]
Member of physician teaching staff	22 (29.7)
Residency/fellowship program director	6 (8.1)
Other	6 (8.2)
Nurse	32 (26.7)
Director of apheresis service	2 (6.2)
Member of nonphysician teaching staff	2 (6.2)
Other	6 (19.4)
Director of apheresis (did not indicate physician or nurse)	10 (8.3)
Member of nonphysician teaching staff	1 (10.0)
Other	4 (3.3)
Type of institution ($n = 120$)	
Academic medical center	81 (67.5)
Blood collection facility	16 (13.3)
Non-academic medical center	7 (5.8)
Contract provider of apheresis services	6 (5.0)
Outpatient facility that performs apheresis	1 (0.8)
Other	9 (7.5)
Number of beds for medical centers ($n = 97$)	
>500	60 (61.9)
100–500	34 (35.0)
<100	3 (3.1)
Apheresis procedures per year ($n = 117$)	
>700	47 (40.2)
500–700	18 (15.4)
100–500	41 (35.0)
<100	11 (9.4)
Departments which perform or oversee TPE[b] ($n = 117$)[e]	
Pathology	41 (35.0)
Hematology	33 (28.2)
Nephrology	32 (27.4)
Blood collection facility	20 (17.1)
Neurology	15 (12.8)
Rheumatology	7 (6.0)
Medicine	6 (5.1)
Performed by outside source but overseen by pathology	7 (6.0)
Performed by outside source but overseen by neurology	3 (2.6)
Performed by outside source but overseen by hematology	2 (1.7)
Performed by outside source but overseen by nephrology	2 (1.7)
Performed by outside source but overseen by rheumatology	1 (0.8)
Performed by outside source but overseen by medicine	1 (0.8)
Other	22 (18.8)
Physician medical specialty ($n = 104$)	
Pathology	45 (43.3)
Hematology	16 (15.4)
Nephrology	5 (4.8)
Pediatrics	4 (3.8)
Medicine	2 (1.9)
Other	10 (9.6)
I am not a physician	22 (21.1)

(*Continues*)

TABLE 1 (Continued)

Question (number of responders)[a]	Number (%)[b]
Perform TPE procedures on children (n = 119)	
Yes, adults and children	75 (63.0)
No	38 (31.9)
Yes, children only	6 (5.0)

[a] For some questions respondents were requested to check all that apply and the total number of responses is greater than the number of respondents.
[b] For questions that permitted more than 1 response, the percent is based on the number of respondents to the question.
[c] Subcategory percent is based on the number of main category responses.
[d] Total number of responses = 185.
[e] Total number of responses = 192.

(11.3%), 2.0 plasma volume (0.9%), with the remaining respondents selecting other (11.3%). ACD-A would be used for the anticoagulant during the procedure by more than 97% of respondents.

Prior to and starting TPE procedures using replacement fluid that does not contain plasma or cryoprecipitate laboratory studies are obtained at least rarely by 102 of 113 respondents for outpatients (90.3%) and 110 of 115 respondents for inpatients (95.7%) (Supporting Information, 2). To determine if respondents obtain hemostasis testing prior to TPE with planned albumin replacement more often for inpatients versus outpatients, the individual responses from each respondent for these two questions were compared (Supporting Information, 3). Of the 113 respondents who answered both inpatient and outpatient, 82 (72.6%) have the same practice for outpatients and inpatients and 30 (26.5%) obtain testing more for inpatients.

Respondents were next asked regarding which clinical situations laboratory studies are obtained to assess a patient's hemostatic function prior to TPE (n = 114) (Figure 1). Of the 5 (4.4%) respondents who reported not routinely obtaining laboratory studies, 3 indicated they do not obtain testing for any of the conditions listed in Figure 1. In contrast, laboratory studies are routinely obtained for all of the conditions listed in Figure 1 by 11 (9.6%) respondents.

If the replacement fluid does not include plasma or cryoprecipitate, respondents varied on what and when they would obtain specific laboratory tests prior to and starting TPE (Table 2). Only 1 respondent indicated they do not routinely obtain any of these 6 laboratory parameters and 6 respondents indicated they obtain all 6 laboratory parameters prior to all procedures.

The laboratory threshold values at which the respondents would change the procedure parameters or act upon also varied (Table 3). While a fibrinogen level of <100 mg/dL was the most common threshold reported (65.3%), 27.8% used a higher threshold of <150 or < 200 mg/dL. The INR threshold value was reported by the least number of respondents (n = 58), but 53.4% (n = 31) reported they would use a threshold of 1.5 or higher.

4 | DISCUSSION

TPE causes significant hemostatic changes in patients undergoing treatment. Use of replacement fluids without coagulation factors (eg, 5% albumin) results in a decrease in coagulation factors which may increase bleeding risk in susceptible patients.[1–13] In addition, platelet count may decrease with TPE.[2,4,5,9] Treatment frequency and the degree of exchange are other factors that can impact depletion of coagulation factors involved in both primary and secondary hemostasis. For example, in the absence of extravascular redistribution of coagulation factors and significant synthesis, ~60%-70% of plasma constituents is immediately depleted with a 1.0 plasma volume exchange using 5% albumin and may be accompanied by a depletion of circulating platelets.[2,7,19] In particular, significant declines in procoagulant coagulation factors such as factor V (FV), FVII, FVIII, FIX, FX, and VWF activity occur.[6,12,13] However, coagulation factors are replenished at different rates. For example, activities of FVIII, FIX, and VWF may return to normal within 4 h after TPE, whereas other coagulation factors may require 24 h or more to achieve pre-TPE activity

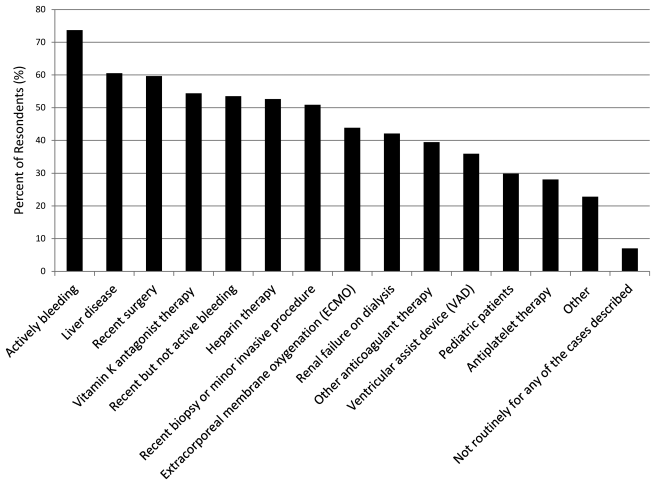

FIGURE 1 Conditions for which laboratory studies are performed to assess hemostasis prior to therapeutic plasma exchange (TPE). Respondents were requested to select all conditions that apply. A total of 114 respondents answered this question. Data represent the percentage of respondents that would obtain testing for each condition

TABLE 2 Laboratory testing routinely performed prior to therapeutic plasma exchange (TPE), if the replacement fluid does not include plasma or cryoprecipitate

	Fibrinogen ($n = 100$) (%)	PT[a] ($n = 94$) (%)	INR[a] ($n = 96$) (%)	aPTT[a] ($n = 94$) (%)	Hemoglobin or hematocrit ($n = 104$) (%)	Platelet count ($n = 103$) (%)
Not routinely obtained	29.0	37.2	35.4	38.3	1.0	8.7
Obtained only prior to the first procedure	2.0	13.8	12.5	10.6	8.6	9.7
Obtained prior to some but not all procedures	38.0	31.9	34.4	33.0	27.9	28.2
Obtained prior to all procedures	31.0	17.0	17.7	18.1	62.5	53.4

[a] Abbreviations: aPTT = activated partial thromboplastin time; INR = international normalized ratio; PT = prothrombin time.

levels.[1,6,10,13] One exception is fibrinogen, which achieves 66% of pre-apheresis levels by 72 h.[5,12] Decreased coagulation factors and other hemostatic elements such as platelets do not necessarily equate with bleeding risk as adequate hemostasis may occur with deficiency of these factors. In addition, TPE also removes natural anticoagulants (eg, antithrombin and protein C), so the risk of bleeding may not be as high as predicted based on removal of procoagulant factors only.[6,10,11,13] As a result, guidelines do not exist regarding appropriate laboratory testing and thresholds for action for patients undergoing TPE. Consistent with this lack of guidelines is the wide variation in practice on when laboratory testing is obtained, what tests are obtained, and what are important actionable thresholds. A survey on pediatric practice[20] and a small survey on anticoagulation and apheresis[21] also reported practice variation among centers. However, the survey on pediatric practice did not survey coagulation screening or monitoring practice.[20]

The impact of this wide variation in practice on clinical outcomes is largely unknown. For illustrative purposes consider testing for fibrinogen. A fibrinogen threshold of <100 mg/dL was the most common threshold reported (as indicated by 65.3% of respondents), but it is unknown if a different threshold would better balance the risk of bleeding and potential use of replacement fluids containing coagulation factors (eg, plasma and cryoprecipitate). The optimal frequency for laboratory testing is unknown and is likely based on institutional or physician practice, which may not be evidenced based. Testing prior to every procedure (performed by 31.0% of respondents) may result in many patients getting unnecessary testing, but not routinely obtaining testing (as is done by 29.0% of respondents) may result in a patient undergoing TPE with a replacement fluid without coagulation factors in the setting of already marked hypofibrinogenemia.

Furthermore, in patients undergoing TPE, bleeding/hematoma rates are low, ranging from 0.26% to 2.46%.[22,23] Laboratory studies such as the INR, aPTT, and platelet count have been found to be poor predictors of bleeding risk.[24,25] Thus, testing with these common coagulation tests may not readily identify who is at greatest risk for bleeding.

Inappropriate over test utilization may have a negative impact on the patient.[26–29] Potential negatives include a

TABLE 3 Laboratory threshold values used to change the procedure or act upon

Parameter	Threshold value	%
Fibrinogen	<Reference range	1.4
($n = 72$)	<50 mg/dL	2.8
	<100 mg/dL	65.3
	<150 mg/dL	20.8
	<200	6.9
	Other	2.8
INR[a]	>Reference range	20.7
($n = 58$)	>1.25	10.3
	>1.5	20.7
	>1.75	6.9
	>2.0	17.2
	>2.5	1.7
	>3.0	5.2
	>4.0	1.7
	Other	15.5
aPTT[a]	>Reference range	28.1
($n = 57$)	>1.25 times the reference range	8.8
	>1.5 times the reference range	28.1
	>1.75 times the reference range	5.3
	>2.0 times the reference range	12.3
	Other	17.5
Hemoglobin or hematocrit	<Reference range	3.6
($n = 84$)	<6 g/dL or 18%	7.1
	<7 g/dL or 21%	31.0
	<8 g/dL or 24%	20.2
	<9 g/dL or 27%	8.3
	Threshold determined based on the patients hemoglobin and blood volume relative to the volume of the extracorporeal circuit	26.2
	Other	3.6
Platelet count	<Reference range	7.2
($n = 83$)	$<10 \times 10^9$/L	9.6
	$<20 \times 10^9$/L	20.5
	$<50 \times 10^9$/L	24.1
	$<100 \times 10^9$/L	9.6
	$<150 \times 10^9$/L	3.6
	Other	25.3

[a] PTT = activated partial thromboplastin time; INR = international normalized ratio.

small risk of injury and infection with phlebotomy or accessing central venous catheters or fistulas, iatrogenic blood loss due to phlebotomy, false-positive or -negative results or spurious results due to a number of pre- and postanalytical factors (eg, heparin contamination from central lines causing a falsely elevated aPTT), test misinterpretation by providers to a indicate a higher or lower risk for bleeding risk, and higher costs.[30–33]

Due to lack of published studies on laboratory testing and TPE and the subjective nature of our study design, future studies need to be conducted to determine the best laboratory testing practice for improved clinical outcomes and cost effectiveness. Clinical history and patient factors should be considered when determining if, what, and when to perform laboratory testing. It would be reasonable to obtain a basic laboratory evaluation of hemostasis (such as hemoglobin/hematocrit, platelet count, PT/INR, PTT, and fibrinogen) for most patients prior to the initial TPE in a series. More extensive evaluations or ongoing testing should be based on the patient's medical history and potential hemorrhage or thrombosis risk, if the results would change management. This action is also supported by the ASFA Choosing Wisely recommendations, part the Choosing Wisely initiative of the ABIM Foundation, which states "Do not routinely monitor coagulation tests during a course of therapeutic plasma exchange, unless the procedure is performed daily."[34]

Additional studies are needed to establish the clinically appropriate laboratory action thresholds. These thresholds should not be based exclusively on the laboratory reference range. For example, many respondents use action levels well outside of the laboratory reference interval (eg, 68.1% of respondents used a fibrinogen of <100 mg/dL or lower which is well below typical fibrinogen reference range limits of 150-200 mg/dL).

This study has several limitations. The survey respondents were largely from U.S. centers so it is unclear if the survey results can be generalized to non-U.S. apheresis practice. Participant response progressively decreased during the survey likely due to survey fatigue and the large number of questions being asked. In addition, five centers reported using membrane filtration and were excluded from analysis and 15 respondents dropped out of the survey prior to this question so their method of plasma separation is unknown. Furthermore, we did not inquire about other tests of hemostasis such as thromboelastography (TEG) and rotational elastometry (ROTEM).[17,35] However, based on the authors' experiences, the use of TEG and ROTEM was considered not to be a test routinely utilized during TPE treatment and therefore was not queried.

5 | CONCLUSION

This survey demonstrates wide variation in hemostasis testing practice in the setting of TPE. These descriptive data do not establish what should be the best practice, but identify areas of equipoise. Future studies need to be conducted to determine the best laboratory testing practice for improved clinical outcomes and cost effectiveness.

ACKNOWLEDGMENTS

The authors would like to acknowledge the respondents who participated in our survey, members of the ASFA Clinical Applications Committee who provided feedback during development and beta testing of the survey, and the ASFA head office staff for their assistance with the distributing the survey and administrative support throughout the project.

DISCLOSURE OF INTERESTS

NDZ: Research funding: Octapharma, Terumo BCT, Bayer HealthCare, Verax Biomedical; Financial interest: Endo International PLC, Boston Scientific. MBP: Research funding: Terumo BCT. MAR: Advisory Boards: Bayer and NovoNordisk. ECCW: Consultant: Comprehensive Care Services. YW: Consultant: Verax Biomedical. The other authors have no conflict of interest to disclose.

ORCID

Nicole D. Zantek https://orcid.org/0000-0001-5776-6400
Chisa Yamada https://orcid.org/0000-0002-1968-2385
Yanyun Wu https://orcid.org/0000-0001-8410-4349

REFERENCES

1. Volkin RL, Starz TW, Winkelstein A, et al. Changes in coagulation factors, complement, immunoglobulins, and immune complex concentrations with plasma exchange. *Transfusion*. 1982;22(1):54-58.
2. Wood L, Jacobs P. The effect of serial therapeutic plasmapheresis on platelet count, coagulation factors, plasma immunoglobulin, and complement levels. *J Clin Apher*. 1986;3(2):124-128.
3. Tek I, Arslan O, Arat M, Ozcan M, Akdag B, Ilhan O. Effects of replacement fluids on coagulation system used for therapeutic plasma exchange. *Transfus Apher Sci*. 2003;28(1):3-7.
4. Sultan Y, Bussel A, Maisonneuve P, Poupeney M, Sitty X, Gajdos P. Potential danger of thrombosis after plasma exchange in the treatment of patients with immune disease. *Transfusion*. 1979;19(5):588-593.
5. Keller AJ, Chirnside A, Urbaniak SJ. Coagulation abnormalities produced by plasma exchange on the cell separator with special reference to fibrinogen and platelet levels. *Br J Haematol*. 1979;42(4):593-603.
6. Chirnside A, Urbaniak SJ, Prowse CV, Keller AJ. Coagulation abnormalities following intensive plasma exchange on the cell separator. II. Effects on factors I, II, V, VII, VIII, IX, X and antithrombin III. *Br J Haematol*. 1981;48(4):627-634.
7. Chopek M, McCulough J. Protein and biochemical changes during plasma exchange. In: Berkman EM, Umlas J, eds. *Therapeutic Hemapheresis: A Technical Workshop*. Washington, D.C.: American Association of Blood Banks; 1980:13-52.
8. Simon TL. Coagulation disorders with plasma exchange. *Plasma Ther Transfus Technol*. 1982;3:147-152.
9. Domen RE, Kennedy MS, Jones LL, Senhauser DA. Hemostatic imbalances produced by plasma exchange. *Transfusion*. 1984;24(4):336-339.
10. Mannucci PM, D'Angelo A, Vigano S, et al. Decrease and rapid recovery of protein C after plasma exchange. *Transfusion*. 1986;26(2):156-158.
11. Pearlman ES, Litty CA, Edger N, Ballas SK. Effect of therapeutic plasmapheresis on coagulation parameters. *J Clin Apher*. 1994;9(3):202-203.

12. Orlin JB, Berkman EM. Partial plasma exchange using albumin replacement: removal and recovery of normal plasma constituents. *Blood*. 1980;56(6): 1055-1059.
13. Flaum MA, Cuneo RA, Appelbaum FR, Deisseroth AB, Engel WK, Gralnick HR. The hemostatic imbalance of plasma-exchange transfusion. *Blood*. 1979;54(3):694-702.
14. Zantek ND, Morgan S, Zantek PF, Mair DC, Bowman RJ, Aysola A. Effect of therapeutic plasma exchange on coagulation parameters in patients on warfarin. *J Clin Apher*. 2014;29(2):75-82.
15. Kaplan A, Raut P, Totoe G, Morgan S, Zantek ND. Management of systemic unfractionated heparin anticoagulation during therapeutic plasma exchange. *J Clin Apher*. 2016;31(6):507-515.
16. Witt V, Pichler H, Beiglboeck E, Kursten F, Weidner L. Changes in hemostasis caused by different replacement fluids and outcome in therapeutic plasma exchange in pediatric patients in a retrospective single center study. *Transfus Apher Sci*. 2017;56(1):59-65.
17. Tholking G, Mesters R, Dittrich R, Pavenstadt H, Kumpers P, Reuter S. Assessment of hemostasis after plasma exchange using rotational thrombelastometry (ROTEM). *PLoS One*. 2015;10(6):e0130402.
18. Zantek ND, Boral LI, Li Y, et al. Hemostasis management and therapeutic plasma exchange: results of a practice survey. *J Clin Apher*. 2018. Doi: 10.1002/jca.21653 [Epub ahead of print].
19. Winters JL. Plasma exchange: concepts, mechanisms, and an overview of the American Society for Apheresis guidelines. *Hematology Am Soc Hematol Educ Program*. 2012;2012:7-12.
20. Delaney M, Capocelli KE, Eder AF, et al. An international survey of pediatric apheresis practice. *J Clin Apher*. 2014;29(2):120-126.
21. Shunkwiler SM, Pham HP, Wool G, et al. The management of anticoagulation in patients undergoing therapeutic plasma exchange: a concise review. *J Clin Apher*. 2018;33(3):371–379. Doi: 10.1002/jca.21592.
22. Couriel D, Weinstein R. Complications of therapeutic plasma exchange: a recent assessment. *J Clin Apher*. 1994;9(1):1-5.
23. Shemin D, Briggs D, Greenan M. Complications of therapeutic plasma exchange: a prospective study of 1,727 procedures. *J Clin Apher*. 2007; 22(5):270-276.
24. Segal JB, Dzik WH. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. *Transfusion*. 2005;45(9):1413-1425.
25. Callum JL, Dzik WH. The use of blood components prior to invasive bedside procedures. In: MIntz PD, ed. *Transfusion Therapy: Clinical Principles and Practice*. Bethesda, MD: AABB; 2011:1-35.
26. Huck A, Lewandrowski K. Utilization management in the clinical laboratory: an introduction and overview of the literature. *Clin Chim Acta*. 2014; 427:111-117.
27. Rudolf JW, Dighe AS, Coley CM, et al. Analysis of daily laboratory orders at a large urban academic center: a multifaceted approach to changing test ordering patterns. *Am J Clin Pathol*. 2017;148(2): 128-135.
28. Zhi M, Ding EL, Theisen-Toupal J, Whelan J, Arnaout R. The landscape of inappropriate laboratory testing: a 15-year meta-analysis. *PLoS One*. 2013; 8(11):e78962.
29. van Walraven C, Naylor CD. Do we know what inappropriate laboratory utilization is? A systematic review of laboratory clinical audits. *JAMA*. 1998; 280(6):550-558.
30. Favaloro EJ, Lippi G, Adcock DM. Preanalytical and postanalytical variables: the leading causes of diagnostic error in hemostasis? *Semin Thromb Hemost*. 2008;34(7):612-634.
31. Newman RS, Fagin AR. Heparin contamination in coagulation testing and a protocol to avoid it and the risk of inappropriate FFP transfusion. *Am J Clin Pathol*. 1995;104(4):447-449.
32. Mayo DJ, Dimond EP, Kramer W, Horne MK. 3rdDiscard volumes necessary for clinically useful coagulation studies from heparinized Hickman catheters. *Oncol Nurs Forum*. 1996;23(4):671-675.
33. Hinds PS, Quargnenti A, Gattuso J, et al. Comparing the results of coagulation tests on blood drawn by venipuncture and through heparinized tunneled venous access devices in pediatric patients with cancer. *Oncol Nurs Forum*. 2002;29(3):E26-E34.
34. ABIM Foundation. Choosing Wisely [Accessed May 8, 2018]. http://www.choosingwisely.org/clinician-lists.
35. Blasi A, Cid J, Beltran J, Taura P, Balust J, Lozano M. Coagulation profile after plasma exchange using albumin as a replacement solution measured by thromboelastometry. *Vox Sang*. 2016;110(2):159-165.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Zantek ND, Pagano MB, Rollins-Raval MA, et al. Hemostasis testing and therapeutic plasma exchange: Results of a practice survey. *J Clin Apher*. 2019;34:26–32. https://doi.org/10.1002/jca.21666