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Hemostasis Testing and Therapeutic Plasma Exchange: Results of a Practice Survey

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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, 68.7% inpatients); however, some do not routinely obtain laboratory studies (9.7% outpatients, 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 <7g/dL or

21% (31.0%), platelet count $<50 \times 10^9/L$ (24.1%), fibrinogen $<100 \text{mg/dL}$ (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.

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 (e.g. 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 (e.g. immunoglobulins, complement, coagulation factors) or therapeutic (e.g. medications) substances, as well as cells (e.g. 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.

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 (Supplement 1). This manuscript 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 5,000 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 non-physician 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 manuscript and/or critical review and edit of the manuscript.

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 50kg.

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 (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%) (Supplement 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 (Supplement 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 <100mg/dL was the most common threshold reported (65.3%), 27.8% used a higher threshold of <150mg/dL or <200mg/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.

DISCUSSION

TPE causes significant hemostatic changes in patients undergoing treatment. Use of replacement fluids without coagulation factors (e.g. 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, approximately 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 hours after TPE, whereas other coagulation factors may require 24 hours or more to achieve pre-TPE activity levels.^{1,6,10,13} One exception is fibrinogen, which achieves 66% of pre-apheresis levels by 72 hours.^{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 (e.g. 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 practice²⁰ and a small survey on anticoagulation and apheresis²¹ 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 <100mg/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 (e.g. 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 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 post-analytical factors (e.g. heparin contamination from central lines causing a falsely elevated aPTT), test misinterpretation by providers to indicate a higher or lower risk for bleeding risk, and higher costs.^{30,31-33}

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 (e.g. 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, 5 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.

CONCLUSION

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

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Table 1 Demographic information of survey respondents and apheresis programs.

Question (Number of Responders)*	Number (%)**
Position at institution** (n=120) [†]	
Physician (including physician in training-resident/fellow)	74 (61.7)
Director of apheresis service	27 (36.5)***
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 non-physician teaching staff	2 (6.2)
Other	6 (19.4)
Director of Apheresis (did not indicate physician or nurse)	10 (8.3)
Member of non-physician 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** (n=117) ^{††}	
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)
Perform TPE procedures on children (n=119)	
Yes, adults and children	75 (63.0)
No	38 (31.9)
Yes, children only	6 (5.0)

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

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* (n=94) (%)	INR* (n=96) (%)	aPTT* (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

* PT=prothrombin time, INR=international normalized ratio, aPTT=activated partial thromboplastin time.

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*	>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*	>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	26.2

	volume of the extracorporeal circuit	
	Other	3.6
Platelet count	<reference range	7.2
(n=83)	<10 x10 ⁹ /L	9.6
	<20 x10 ⁹ /L	20.5
	<50 x10 ⁹ /L	24.1
	<100 x10 ⁹ /L	9.6
	<150 x10 ⁹ /L	3.6
	Other	25.3

*INR = international normalized ratio, aPTT=activated partial thromboplastin time.

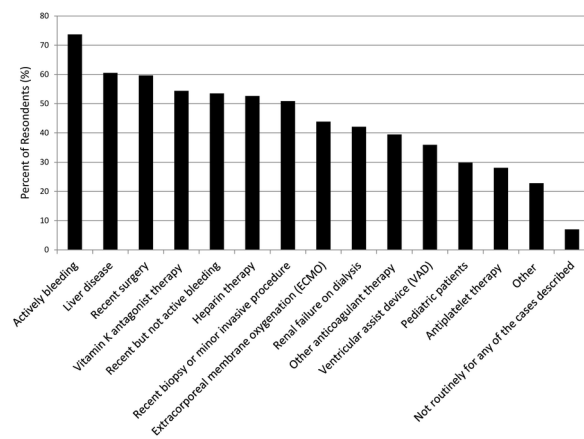
Supplement 3. Comparison of individual respondent testing practices in inpatients versus outpatients.

Inpatient Response	Comparison to Outpatient Response			
	Same	More Inpatient	More Outpatient	Answered Only Inpatient
No	5	0	0	0
Yes, rarely	7	2	1	1
Yes, some patients	8	12	0	0
Yes, almost all	62	16	0	1

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 percent of respondents that would obtain testing for each condition.

Supplement 1. American Society for Apheresis Coagulation Subcommittee Practice Survey

Supplement 2. Inpatient versus outpatient obtainment of laboratory studies to assess hemostasis/coagulation prior to therapeutic plasma exchange (TPE) planned with albumin replacement. A total of 115 responses were received regarding inpatient testing and 113 responses were received regarding outpatient testing.



Hemostasis Testing and TPE REV 1 Figure 1.tif.tif

Thank you for taking time to complete this survey from the American Society for Apheresis (ASFA). This survey has been developed by the Coagulation Subcommittee of the ASFA Applications Committee. Your response will provide insight into how providers of apheresis manage patients with disorders of hemostasis. If at any time you have questions, comments, or concerns about the survey please contact the ASFA Head Office at asfa@apheresis.org or Dr. Nicole Zantek, Chair, Coagulation Subcommittee at zant0005@umn.edu. It is estimated that it will take you approximately 20 minutes to complete the survey.

1. Does your institution provide therapeutic plasma exchanges?
 - a. Yes
 - b. No

2. What is the name of your institution? This is only used to determine if duplicate survey responses are received.

3. Can we contact you if we have questions regarding your responses?
 - a. Yes
 - b. No

4. If yes, please provide your contact information below.
 - a. Name: _____
 - b. E-mail: _____
 - c. Phone: _____

5. Please specify if you are replying as
 - a. Representative of your institution
 - b. Individual respondent

6. Are you an ASFA member?
 - a. Yes
 - b. No

7. Please indicate your position at your institution (Check all that apply)
 - a. Physician
 - b. Physician in training – resident/fellow
 - c. Nurse
 - d. Technician
 - e. Residency/Fellowship program director
 - f. Director of apheresis service
 - g. Member of physician teaching staff
 - h. Member of non-physician teaching staff
 - i. Other (please specify): _____

8. What type of institution are you located at:
 - a. Academic Medical Center
 - b. Blood collection facility

- c. Contract provider of apheresis services
 - d. Non-Academic Medical Center
 - e. Outpatient facility that performs apheresis
 - f. Other (please specify): _____
9. If you are a Medical Center, how many beds (including NICU) does your institution have?
 - a. <100
 - b. 100-500
 - c. >500
10. How many apheresis procedures does your institution perform per year?
 - a. <100
 - b. 100-500
 - c. 500-700
 - d. >700
11. Which department(s) in your institution perform(s) therapeutic plasma exchanges (TPE)? (Check all that apply)
 - a. Blood Collection Facility
 - b. Hematology
 - c. Medicine
 - d. Nephrology
 - e. Neurology
 - f. Pathology
 - g. Rheumatology
 - h. Performed by outside source, but is overseen by hematology
 - i. Performed by outside source, but is overseen by medicine
 - j. Performed by outside source, but is overseen by nephrology
 - k. Performed by outside source, but is overseen by neurology
 - l. Performed by outside source, but is overseen by pathology
 - m. Performed by outside source, but is overseen by rheumatology
 - n. Performed by outside source, but is overseen by ordering provider
 - o. Other (please specify): _____
12. If you are a physician, what is your medical specialty?
 - a. I am not a physician
 - b. Hematology
 - c. Medicine
 - d. Nephrology
 - e. Neurology
 - f. Pathology
 - g. Pediatrics
 - h. Rheumatology
 - i. Other (please specify): _____

13. Do you perform TPE procedures on children?
 - a. No
 - b. Yes, adults and children
 - c. Yes, children only

14. How do you define a pediatric procedure?
 - a. Do not perform TPE on pediatric patients.
 - b. Based on age
 - c. Based on weight

15. If based on age, what age?

16. If based on weight, what weight?

17. For the majority of your TPE procedure, who makes the decision about what replacement fluid is used during the TPE procedures?
 - a. The Apheresis Medicine physician makes the decision
 - b. The requesting provider makes the decision
 - c. The decision is made jointly by the Apheresis Medicine physician and requesting provider.
 - d. Other (please specify): _____

18. Do you obtain laboratory studies to assess hemostasis/coagulation prior to TPE planned with albumin replacement?
Inpatients?
 - a. Yes, all most all patients
 - b. Yes, some patients
 - c. Yes, rarely
 - d. No

19. Do you obtain laboratory studies to assess hemostasis/coagulation prior to TPE planned with albumin replacement?
Outpatients?
 - a. Yes, all most all patients
 - b. Yes, some patients
 - c. Yes, rarely
 - d. No

20. Which of the following situations do you routinely obtain laboratory results to assess hemostasis (e.g. PT, INR, PTT, fibrinogen) prior to TPE? (Check all that apply)
 - a. Do not routinely obtain laboratory results for any of the cases below
 - b. Actively bleeding
 - c. Recent but not active bleeding
 - d. Recent surgery
 - e. Recent biopsy or minor invasive procedure

- f. Liver disease
- g. Vitamin K antagonist therapy (e.g. warfarin, Coumadin)
- h. Heparin therapy
- i. Other anticoagulant therapy (e.g. fondaparinux, rivaroxaban, apixaban, dabigatran, argatroban)
- j. Antiplatelet therapy (e.g. aspirin, clopidogrel)
- k. ECMO (extracorporeal membrane oxygenation)
- l. Ventricular assist device (VAD)
- m. Renal failure on dialysis
- n. Pediatric patients
- o. Other (please specify): _____

What tests do you routinely perform prior to and starting TPE, if TPE replacement fluid does not include plasma or cryoprecipitate?

For each test you will be asked whether you routinely obtain the test and, if so, what threshold value you change the procedure or act upon. For example, if you check fibrinogen to make decisions about replacement fluid, list the value for which you would decide to change the replacement fluid.

21. Fibrinogen

- a. The laboratory test is
 - i. Not routinely obtained
 - ii. Obtained only prior to the first procedure
 - iii. Obtained prior to some but not all procedures on the patient
 - iv. Obtained prior to all procedures on the patient
- b. Threshold value
 - i. < reference range
 - ii. <50 mg/dL
 - iii. <100 mg/dL
 - iv. <150 mg/dL
 - v. <200 mg/dL
 - vi. Other

22. Prothrombin time (PT)

- a. The laboratory test is
 - i. Not routinely obtained
 - ii. Obtained only prior to the first procedure
 - iii. Obtained prior to some but not all procedures on the patient
 - iv. Obtained prior to all procedures on the patient
- b. Threshold value
 - i. > reference range for laboratory
 - ii. >1.25 times the reference range
 - iii. >1.5 times the reference range
 - iv. >1.75 times the reference range
 - v. >2.0 times the reference range
 - vi. Other

23. International Normalized Ratio (INR)

- a. The laboratory test is
 - i. Not routinely obtained
 - ii. Obtained only prior to the first procedure
 - iii. Obtained prior to some but not all procedures on the patient
 - iv. Obtained prior to all procedures on the patient
- b. Threshold value
 - i. > reference range for laboratory

- ii. >1.25
- iii. >1.5
- iv. >1.75
- v. >2.0
- vi. >2.5
- vii. >3.0
- viii. >3.5
- ix. >4.0
- x. Other

24. Partial Thromboplastin time (PTT)

- a. The laboratory test is
 - i. Not routinely obtained
 - ii. Obtained only prior to the first procedure
 - iii. Obtained prior to some but not all procedures on the patient
 - iv. Obtained prior to all procedures on the patient
- b. Threshold value
 - i. > reference range for laboratory
 - ii. >1.25 times the reference range
 - iii. >1.5 times the reference range
 - iv. >1.75 times the reference range
 - v. >2.0 times the reference range
 - vi. Other

25. Hemoglobin or Hematocrit

- a. The laboratory test is
 - i. Not routinely obtained
 - ii. Obtained only prior to the first procedure
 - iii. Obtained prior to some but not all procedures on the patient
 - iv. Obtained prior to all procedures on the patient
- b. Threshold value
 - i. < reference range for laboratory
 - ii. <6 g/dL or 18%
 - iii. <7 g/dL or 21%
 - iv. <8 g/dL or 24%
 - v. <9 g/dL or 27%
 - vi. <10 g/dL or 30%
 - vii. <11 g/dL or 33%
 - viii. <12 g/dL or 36%
 - ix. <13 g/dL or 39%
 - x. Threshold determined based on the patients hemoglobin and blood volume relative to the volume of the extracorporeal circuit
 - xi. Other

26. Platelet count

- a. The laboratory test is

- i. Not routinely obtained
 - ii. Obtained only prior to the first procedure
 - iii. Obtained prior to some but not all procedures on the patient
 - iv. Obtained prior to all procedures on the patient
- b. Threshold value
 - i. < reference range for laboratory
 - ii. $<10 \times 10^9/L$
 - iii. $<20 \times 10^9/L$
 - iv. $<50 \times 10^9/L$
 - v. $<100 \times 10^9/L$
 - vi. $<150 \times 10^9/L$
 - vii. Other

A patient presents for TPE. A series of 5 TPE approximately every other day are scheduled. Regarding this patient, what is your most common (typical) practice?

27. What method of cell separation do you typically use for TPE?
- Centrifugation
 - Membrane filtration
 - Other (please specify): _____
28. What instrument do you typically use for TPE? Please list manufacturer and model
- Terumo BCT Optia
 - Terumo BCT Spectra
 - Other (please specify): _____
29. What volume of TPE will you perform?
- 1.0 plasma volume
 - 1.3 plasma volume
 - 1.5 plasma volume
 - 2.0 plasma volume
 - 2.5 plasma volume
 - 3.0 plasma volume
 - Other (includes fixed volume or other volumes), please specify: _____
30. What anticoagulant will you use for the procedure?
- ACD-A (Anticoagulant citrate dextrose solution A)
 - ACD-A and heparin
 - Heparin
 - Other (please specify): _____
31. What anticoagulant to whole blood ratio do you typically use during a TPE procedure?
- 1:10
 - 1:11
 - 1:12
 - 1:13
 - Other (please specify): _____
32. What replacement fluid will use for the first procedure?
- Albumin
 - Albumin and normal saline (0.9% sodium chloride)
 - Albumin and cryoprecipitate

- d. Albumin and plasma
- e. Plasma
- f. Other (please specify): _____

33. A patient for TPE and has the following associated situations present (these are not the direct reason for the TPE). A series of 5 TPE approximately every other day are scheduled.

Indicate what replacement fluid would use for the procedure. If you would like to share information on why you would use that replacement fluid, please make comments in the box below

	Delay procedure	Albumin	Albumin and normal saline (0.9% sodium chloride)	Albumin and cryoprecipitate	Albumin and plasma	Plasma
No history of a bleeding or clotting disorder						
Active bleeding						
Bleeding disorder due to coagulation factor deficiency (e.g. Hemophilia A, B or C and von Willebrand disease)						
Platelet disorder (inherited or acquired)						
Hypofibrinogenemia (<100 mg/dL) due to recent TPE.						
THERAPEUTIC on continuous IV unfractionated heparin						
SUPRATHERAPEUTIC on continuous IV unfractionated heparin						
THERAPEUTIC on low molecular weight heparin (e.g. enoxaparin)						
SUPRATHERAPEUTIC on low molecular weight heparin (e.g. enoxaparin)						
THERAPEUTIC (INR 2.5) on warfarin.						
SUPRATHERAPEUTIC (INR 4.0) on warfarin.						
Liver disease with a mildly elevated INR (1.5-2.0)						

Other (please specify)/Comments: _____

34. The patient presents for TPE and has recently had or is scheduled to have an invasive procedure, excluding kidney biopsy which will be discussed later.

Indicate what replacement fluid would use for the procedure. If you would like to share information on why you would use that replacement fluid, please make comments in the box.

Examples of minor invasive procedures: liver biopsy, lumbar puncture, colonoscopy with biopsy

Examples of major surgeries: organ transplant, laparotomy, nephrectomy, colectomy

	Delay procedure	Albumin	Albumin and normal saline (0.9% sodium chloride)	Albumin and cryoprecipitate	Albumin and plasma	Plasma
A minor invasive procedure was performed in the morning						
A minor invasive procedure was performed yesterday						
A minor invasive procedure was performed 2 days ago						
A minor invasive procedure was performed 2 days ago and the patient has evidence of bleeding						
Will undergo major surgery in 2 days, no additional TPE before surgery						
Will undergo major surgery tomorrow, no additional TPE before surgery						
Underwent major surgery yesterday						
Underwent major surgery 3 days ago						
Underwent major surgery a week ago						

Other (please specify)/Comments: _____

35. What is your routine practice for use of plasma for replacement fluid after the KIDNEY BIOPSY?
- Do not use plasma routinely after biopsy
 - Use plasma during TPE only if signs of bleeding
 - Use plasma during TPE up to the following post-biopsy day (please note in the comment box)
 - Use plasma during TPE up to hours (please note in the comment box)
 - Use plasma during TPE up to procedure number (please note in the comment box)
- Other/Comment: _____
36. If a patient is on antiplatelet therapy, do you have the patient stop taking the drug during a series of TPE?
- Aspirin
 - Yes
 - No
 - Clopidogrel
 - Yes
 - No
 - Aspirin and Clopidogrel
 - Yes, stop both
 - Yes, stop aspirin only
 - Yes, stop clopidogrel only
 - No
37. Have you performed TPE on patient who was receiving one of the following anticoagulants? If you have performed TPE while on these anticoagulants, please provide information on the procedure.
- Direct factor Xa inhibitor (e.g. rivaroxaban, apixaban, edoxaban)?
 - Yes, Comments
 - No
 - Oral direct thrombin inhibitor (e.g. dabigatran)?
 - Yes, Comments
 - No
 - Intravenous direct thrombin inhibitor (e.g. argatroban, bivalirudin, lepirudin)?
 - Yes, Comments
 - No
- Comments: _____