10. Document the procedure.
A procedure note in the patient's chart written by the trainee and cosigned or attested by the attending serves as physician documentation**.** Document the service/attending requesting the procedure and construct a brief clinical note, including the indication for the procedure (provide the ICD10 codes specific for the diagnostic indication and procedure), the procedure parameters, complications, and plan going forward. When finished, sign the note to send it to the attending for cosignature/attestation. This must be done prior to leaving the hospital for the day, unless note completion will cause you to stay past midnight (ONLY in that event can the note be written the following morning). Update the Apheresis Inpatient log on the Pathology Intranet with the patient information, procedure parameters, complications, and plan.

Summary Checklist—Before Starting Apheresis Procedure:

- ☐ Obtain relevant medical history
- ☐ Attending approval
- ☐ The primary physician's request for apheresis (EPIC order)
- ☐ Notify charge/on-call nurse
- ☐ Documentation of correct line placement
- ☐ Informed consent for therapeutic apheresis
- ☐ Informed consent for blood products (if applicable)
- ☐ EPIC procedure orders

Common Apheresis Procedures

Therapeutic apheresis
Therapeutic apheresis is a general term for a procedure in which a patient's blood is passed through an extracorporeal medical device which separates components of blood to treat a disease.

Therapeutic plasma exchange (TPE): Blood is passed through an apheresis device that separates out plasma from the other blood components. The plasma is then replaced with plasma or albumin. Many indications for TPE involve removal of antibodies in the patient's blood.

Red blood cell exchange: Red blood cells are separated from the other blood components and replaced with donor red blood cells. Red cell exchange is most commonly performed for acute and chronic complications of sickle cell disease.

Erythrocytapheresis (red blood cell depletion): Red blood cells are separated and removed; the other blood components are returned to the patients. Red cell depletion is typically requested for patients with polycythemia and inability to tolerate therapeutic phlebotomy.

Leukocytapheresis (leukapheresis, leukoreduction): White blood cells are separated and removed, and the other blood components are returned. Leukocytapheresis may be requested when a patient has acute leukemia with hyperleukocytosis and is exhibiting symptoms or signs of leukostasis.

Extracorporeal Photopheresis (ECP): White blood cells (buffy coat) are separated, treated with a psoralen compound with subsequent activation by UV light exposure to induce DNA damage in lymphocytes (specifically targeting T cells), and then returned back to the patient. ECP is typically a long-term treatment and is performed for cutaneous T cell lymphoma, graft-versus-host disease and cellular mediated solid organ transplant rejection.

Thrombocytapheresis (plateletpheresis): Platelets are separated and removed; the other blood components are returned to the patient. Thrombocytapheresis is typically requested for patients with essential thrombocythemia (ET) and thrombotic complications.

Therapeutic Phlebotomy: Collection of whole blood from a peripheral vein (resembling whole blood donation) for therapeutic purposes, typically for patients with polycythemia vera (PV), porphyria cutanea tarda, and iron overload due to hemochromatosis.

Donor apheresis

Peripheral Blood Mononuclear Cell collections: White blood cells are collected from the peripheral blood by apheresis for a variety of therapeutic purposes, including for hematopoietic stem cell transplantation (autologous and allogeneic), donor lymphocyte infusions, and collection for manufacturing (for example, chimeric antigen receptor, or CAR, T cells).

Common Adverse Reactions

Although generally considered safe, apheresis procedures are not without risk. Below highlight some commonly encountered adverse events and strategies to mitigate them.

Hypocalcemia: Hypocalcemia can occur during apheresis due to use of anticoagulant citrate dextrose (ACD)-A. Symptoms initially include parasthesias (peripheral, perioral), followed by muscle spasm, nausea/vomiting, and/or hypotension; if untreated, cardiac arrhythmias or seizures can develop. Severe hypocalcemia can develop with large processing volumes or blood product replacement (also contain ACD-A). Calcium replacement can be oral (calcium carbonate) or IV (calcium gluconate).

If symptoms of hypocalcemia develop, pause the procedure (to temporarily stop ACD-A flow into patient), order a STAT ionized calcium level (iCa), and administer IV calcium gluconate following general guidelines outlined below:

- Administer Calcium gluconate IV based on iCa level:
    - iCa <4.5 mg/dL: 1 gram calcium gluconate IV, rate: 1 gram over 15 minutes
    - iCa level <3.5 mg/dL: 2 grams calcium gluconate IV, rate: 1 gram over 15 minutes
- Re-check the ionized calcium
    - If iCa >4 mg/dL, increase calcium gluconate infusion rate of 1 or 2 grams over the remainder of the procedure
- If symptoms persist, further adjustments may be necessary
- If >10 grams are administered, evaluation of hypomagnesemia might be warranted

Hypotension: Some patients (e.g. those with autonomic instability or negative fluid balance) may become hypotensive during the procedure. Prebolus for prevention or bolus for treatment, of 250mL 5% albumin helps manage hypotension. Prebolus or priming the machine with albumin is needed if the extracorporeal volume is ≥15% of the patient's total blood volume.

ACE inhibitors: Patients generally should not receive ACE inhibitors while undergoing therapeutic apheresis, particularly TPE with albumin replacement, due to risk for adverse reactions from increased bradykinin levels. Symptoms can include hypotension, flushing and GI upset. Waiting 24 hours after the last ACE inhibitor dose prior to initiation of apheresis is preferred, unless emergent. This effect does not apply to angiotensin receptor blockers (ARBs).

Transfusion reactions: In some TPEs and all RBC exchanges, patients receive several blood products in rapid succession, all of which pose a risk for transfusion reaction. Patients may receive premedication with acetaminophen and/or diphenhydramine. If a transfusion reaction occurs, the procedure must be stopped, the patient evaluated and given supportive therapy (IV fluids, acetaminophen, diphenhydramine, call rapid response team if acute hemodynamic instability), and machine lines flushed. Unless a mild allergic reaction, a transfusion reaction investigation should be sent to the blood bank. Regardless of the nature of the reaction, the implicated unit must not be used. If the procedure is restarted, a new unit must be used.

Transient coagulopathy: Coagulation factor levels are transiently lowered during TPE when albumin is the sole replacement fluid (see table). Generally, most patients with adequate liver function maintain sufficient levels, but PT/INR and/or fibrinogen may be monitored on the day of procedures prior to starting. If coagulopathy is suspected, bleeding risk factors are present, TPE is performed perioperatively, the patient has undergone recent operative procedures and/or ECMO (which uses heparin) or ventricular assist devices (VADs - can lower anti-thrombin levels which may precipitate thrombotic complications), use of plasma to varying degrees as replacement fluid is warranted. For partial plasma replacement, the procedure is started with albumin replacement with transition to a defined amount of plasma (by volume, percentage or number of units) replacement. Another mitigation strategy to consider in patients with isolated labs suggestive of transient coagulopathy is delaying the procedure by an additional day if warranted and clinically appropriate.

Estimated alterations in blood constituents after 1 plasma volume TPE with albumin*

Constituent	Percent decrease from baseline	Percent recovery in 48 hours
Clotting Factors	25-50	80-100
Fibrinogen**	25-50	65
Immunoglobulins	63	45
Paraproteins	30-60	Variable
Liver Enzymes	55-60	100
Bilirubin	45	100
C3	63	60-100
Platelets	25-30	75-100

* Replacement fluid consists of 4-5% albumin in 0.9% sodium chloride

**Recovery rate for fibrinogen is quite variable between patients varying from 0.5 -10 mg/hour

At the end of a 1.5 PV TPE:

- All FFP: no anticipated major changes in amount of coagulation factors
- All Albumin: residual patient plasma ~22%, plasma removed ~78%
- Half and half (first half albumin and last half plasma): factor activity about ~75% of pre-TPE
- Last liter plasma: factor activity is about ~50% of pre-exchange

Volume Overload: Patients receiving apheresis can be susceptible to volume overload due to fluids given (albumin prebolus, ACD-A); patients with heart failure or significant renal dysfunction may be particularly susceptible. Knowledge of patient history and fluid status and communication with the clinical team are important considerations. It is our responsibility to manage patients with fluid overload during collections. Strategies may include use of diuretics with or without potassium and/or magnesium supplementation, if necessary, or heparin for anticoagulation to decrease amount of fluid used. Patients undergoing cellular therapy collections may be referred to the BMT clinic for IV magnesium infusion following apheresis. Contact the transplant coordinator and BMT fellow/ attending when considering interventions.

Indications for Apheresis

Common Indications for apheresis encountered at BJH (by procedure type) are described below.

Therapeutic Plasma Exchange (TPE)

Thrombotic Thrombocytopenic Purpura (TTP):
TTP is a potentially fatal disease with a rapidly progressive course. TPE is initiated as soon as possible, even pending definitive diagnosis. Ensure a sample is collected for testing ADAMTS-13 activity and inhibitor before starting the first procedure. Patients typically undergo TPE daily, with 1.5 plasma volume exchanged with all plasma replacement fluid (to replace deficient ADAMTS13), until the platelet count is ≥150K/cumm for 2-3 days, after which TPE is either stopped or tapered as agreed upon with the hematology service. Daily labs to monitor include CBC daily (platelets), with LDH, haptoglobin and creatinine if needed. Ensure there is a current type and screen for plasma.

Myasthenia Gravis (MG):
Urgent/emergent indications for TPE in MG include (1) signs or symptoms of respiratory failure and/or (2) dysphagia with risk of aspiration, in which cases TPE is initiated urgently to prevent intubation or hasten ventilator independence. Less urgent indications include (1) dysphagia (without aspiration risk) (2) muscle weakness (3) diplopia (4) pending thymectomy. Patients typically undergo 5 TPE procedures, with the first 2 on successive days, and then the last 3 every other day , with 1 plasma volume exchanged with albumin. Clinical improvement typically occurs relatively quickly over the duration of TPE; respiratory parameters to follow daily are negative inspiratory force (NIF) and forced vital capacity (FVC). Patients with MG can exhibit autonomic instability and hypotension, so 250mL albumin prebolus is typically given unless the patient is hypertensive or has volume overload.

Guillain-Barre Syndrome (GBS):
GBS is an acute autoimmune inflammatory neuropathy. If respiratory failure is imminent, patients are treated emergently. The standard course is 1.0 plasma volume exchanged with 5% albumin for a total of 5 procedures, performed daily or every other day for the first two procedures, then every other day for the remaining three procedures. Patients with GBS may exhibit autonomic instability and hypotension, and may benefit from an albumin prebolus to minimize procedure-related hypotension.

Solid organ antibody-mediated transplant rejection:
Donor-specific HLA antibodies (DSA) in solid organ (specifically heart, lung and kidney) transplant recipients are strongly associated with antibody-mediated rejection. TPE is performed to decrease DSA levels. Pre-transplant TPE may be considered when the transplant occurs across an immunological barrier (pre-existing DSA or positive crossmatch). Patients typically undergo 1 pre-transplant TPE and post-transplant procedures daily or every other day for 5-7 total procedures. Post-transplant TPE may be based on positive HLA crossmatch, continued DSA detection, or HLA antibody titer increase. Presence of DSA together with organ dysfunction is sufficient for diagnosis. Discuss replacement fluid (albumin vs. FFP) with the primary service as some transplants have lower risks of severe bleeding (i.e. kidney transplant), and moderate coagulation defects may be tolerable. Around post-transplant day 3, if coagulation test results are favorable and no post-operative bleeding, transition to partial FFP replacement may be considered, and patients further out can be considered for albumin replacement.

Hematopoietic stem cell transplant (HSCT) with pre-transplant donor specific antibodies (DSAs):
In patients undergoing HSCT across immunologic barriers (known HLA DSAs), TPE to decrease DSA levels (i.e. desensitization) can be considered. DSA testing should be performed on recent serum specimens. Patients typically undergo 5 TPEs pre-HSCT, every other day, with 1 plasma volume exchanged (and IVIG given by primary team between TPEs), usually starting as outpatient and transitioning to inpatient (LMR responsible) the day before transplant. An HLA antibody screen must be ordered on the recipient before initiation of the final procedure to determine need for post-HSCT TPE. If the HLA DSA mean fluorescent intensity (MFI) is >2,000 before TPE #5, 2 more TPEs are performed days 1 and 2 post-HSCT. If the HLA DSA MFI <2,000, no additional post-HSCT procedures are required.

Red Cell Exchange

Acute complications of sickle cell disease:
RBC exchange has been best established for evolving stroke and acute chest syndrome, both of which are considered emergent indications. Target hematocrit and %HbS goals are decided with the Hematology service (see below). Review history of recent transfusions, transfusion reactions, and RBC alloantibodies (could increase search time for blood products). If the patient is unknown to the BJH blood bank but has a known or reported history of transfusion, it is important to attempt to obtain a transfusion history from other blood banks so the most appropriate blood can be ordered. Contact the BJH blood bank before the procedure to determine how best to approach obtaining this history. Sickle-dex negative donor RBCs matched or antigen negative for C, E, and K RBC antigens are used. Ensure a pre- and post-procedure Hb analysis and a post-procedure CBC are collected. Premedication with diphenhydramine and acetaminophen may reduce incidence and/or severity of allergic or febrile transfusion reactions, respectively.

HEREDITARY HEMOCHROMATOSIS

Incidence: 1-2/100,000/yr		**Procedure**	**Recommendation**	**Category**
		Erythrocytapheresis	Grade 1B	I
# reported patients: >300	**RCT**	**CT**	**CS**	**CR**
	3(146)	2(98)	13(122)	NA

Description of the disease

Hereditary hemochromatosis (HH) includes several inherited disorders that result in iron deposition in the liver, heart, pancreas and other organs. The genetic mutation, accounting for >90% of cases (and almost all cases in Caucasians of Northern European ancestry) is homozygosity for a single missense mutation in *HFE* on chromosome 6p21 that results in substitution of cysteine with tyrosine at amino acid 282 (C282Y), known as type I HH. The prevalence of type I HH is approximately 1:200 among Caucasians. Abnormalities of *HFE* result in abnormal iron sensing in the deep crypt cells of gut epithelium and thus inappropriate iron uptake despite abundant iron stores in the body. Other genetic mutations coding for hemojuvelin (*HFE2*, type IIA), hepcidin (*HAMP*, type IIB), transferrin receptors (*TFR2*, type III) or ferroportin (*SLC40A1*, type IV), have been described in rare families with non-HFE HH. In HH, iron accumulation can ultimately result in liver failure (cirrhosis, hepatocellular carcinoma), diabetes, hypogonadism, hypopituitarism, arthropathy, cardiomyopathy and skin pigmentation. Diagnosis is suggested by a persistent serum transferrin saturation of ≥ 45% and/or unexplained serum ferritin of ≥300 ng/mL in men or ≥200 ng/mL in premenopausal woman. The clinical penetrance of disease is variable, with only 70% of homozygotes developing clinical manifestations of disease, only 10% any end-organ complications, and <1% full-blown complications.

Current management/treatment

Because HH is a disease of iron overload, iron removal by therapeutic phlebotomy has been the mainstay of treatment both to remove iron and to increase erythropoiesis to mobilize stored iron. Phlebotomy is recommended when serum ferritin is elevated even in the absence of symptoms or signs of end-organ damage. Typically, 1 whole blood unit is removed weekly or biweekly until the serum ferritin is <50 ng/mL without resultant anemia. Patients with tissue complications of hemochromatosis usually have a ferritin >1000 ng/mL and present with upward of 20 gm of excess iron. Thus, with 250 mg of iron removed per phlebotomy, two years may be needed to achieve therapeutic iron depletion. Thereafter 2-4 phlebotomies per year are usually adequate to maintain the ferritin ≤50 ng/ml. Malaise, weakness, fatigability and liver transaminase elevations often improve during the first several weeks of treatment, but joint symptoms may initially worsen before eventually improving (if at all). Cardiomyopathy and cardiac arrhythmias may resolve with phlebotomy, but insulin-dependent diabetes generally will not. The risk of hepatocellular carcinoma correlates strongly with cirrhosis and persists despite iron depletion. In situations where therapeutic phlebotomy is contradicted, iron chelation can be used as an alternative treatment, although it is costly and has side effects.

Rationale for therapeutic apheresis

An RCT compared biweekly erythrocytapheresis of 350-800 ml of RBCs to a minimum post-procedure Hct of ≥30% with weekly phlebotomy of 500 mL among 38 patients with newly diagnosed HFE HH. The mean number of procedures and treatment duration to achieve ferritin of ≤50 ng/mL were 9 and 20 weeks for the erythrocytapheresis group versus 27 and 34 weeks ($p < 0.001$ and $p < 0.002$), respectively, for the phlebotomy group. No difference in adverse events and no significant difference in total treatment costs were observed (the higher cost of erythrocytapheresis was offset by a significant reduction in lost work productivity due to phlebotomy visits) (Rombout-Sestrienkova, 2012). A second RCT enrolled 30 patients for biweekly apheresis (400 mL) and 32 patients for weekly whole blood phlebotomy (450 ml). Time to normalization (50ng/mL) of ferritin was equivalent; cost for apheresis was 3x higher in this study (Sundic, 2014). A CT using another apheresis platform removed 300-550 ml of RBCs in patients with Hct >37%, weight >50 kg and age 18-65 years with mean reduction of 405 mg of iron per procedure (Grabmer, 2015). A crossover clinical trial randomized 46 HH patients to either erythrocytapheresis or phlebotomy to keep ferritin at 50 μg/L or below for one year and then switched groups (Rombout-Sestrienkova, 2016). In this study, mean number of procedures per treatment year was significantly higher using phlebotomy versus erythrocytapheresis (3.3 vs. 1.9; mean difference, 1.4; 95% confidence interval, 1.1-1.7). The median intertreatment time was 2.3 times longer for erythrocytapheresis. Eighty percent of the patients expressed preference for the erythrocytapheresis over phlebotomy. The cost and ability to rapidly lower ferritin and iron stores differ by the ability of RBC reduction per apheresis procedure, which varies by apheresis technology, and patient's weight and height. The reduction in the number of required procedures per year to maintain a goal ferritin level may give a cost benefit of erythrocytapheresis over phlebotomy.

Technical notes

The volume removed and pre-procedure HCT vary by height, bodyweight and gender. The actual volume of erythrocytes to be removed (VR) with each procedure can be calculated as:

VR = [(starting HCT - target HCT) ÷ 79] × [blood volume (mL/kg) × body weight (kg)].

Volume treated: Erythrocytapheresis of up to 800 ml of RBCs	**Frequency:** Every 2-3 weeks, keeping the pre-procedure HCT ≥30-36% and post-procedure HCT ≥30%
Replacement fluid: Replace at least ⅓-½ of removed RBC volume with saline	

Duration and discontinuation/number of procedures

Erythrocytapheresis every 2-3 weeks, or as tolerated, until serum ferritin <50 ng/mL. Maintenance treatment can follow with less frequent therapeutic phlebotomy or erythrocytapheresis.

Keywords: hemochromatosis, erythrocytapheresis, phlebotomy

TABLE 2 Category Definitions for Therapeutic Apheresis

Category	Description
I	Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.
II	Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.
III	Optimum role of apheresis therapy is not established. Decision making should be individualized.
IV	Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.

IRB = Institutional Review Board

has been incorporated into the "Transplantation, hematopoietic stem cell, ABO incompatible" fact sheet. The "Hashimoto's encephalopathy" fact sheet has been renamed "Steroid-responsive encephalopathy associated with autoimmune thyroiditis (Hashimoto's encephalopathy)." The "Immunoglobulin A nephropathy" has been renamed "IgA nephropathy (Berger's Disease)." The "Thrombotic thrombocytopenic purpura" fact sheet has been renamed "Thrombotic microangiopathy, thrombotic thrombocytopenic purpura." The "Red cell alloimmunization in pregnancy" fact sheet was combined with "Prevention of RhD alloimmunization after RBC exposure" and renamed "Red cell alloimmunization, prevention and treatment." The Dermatomyositis/polymyositis fact sheet was retired. The total number of diseases and indications addressed in the Eighth Edition are 84 and 157, respectively. Distribution by category and grade is shown in Figure 3.

2 | METHODOLOGY

2.1 | Evidence-Based Approach

The JCA Special Issue 2007 (Fourth Edition) incorporated evidence-based medicine into well-defined and widely accepted ASFA Categories and quality of the evidence (Szczepiorkowski, 2007). In the JCA Special Issue 2010 (Fifth Edition), this system was modified to revise category definitions, maintain quality of the evidence, and add strength of the recommendation (Szczepiorkowski, 2010). In the JCA Special Issue 2013 (Sixth Edition), this was further refined

TABLE 3 Grading Recommendations, Strength and Quality of Evidence

Recommendation	Description	Methodological Quality of Supporting Evidence	Implications
Grade 1A	Strong recommendation, high-quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1B	Strong recommendation, moderate quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Strong recommendation, can apply to most patients in most circumstances without reservation
Grade 1C	Strong recommendation, low-quality or very low- quality evidence	Observational studies or case series	Strong recommendation but may change when higher quality evidence becomes available
Grade 2A	Weak recommendation, high quality evidence	RCTs without important limitations or overwhelming evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2B	Weak recommendation, moderate-quality evidence	RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Weak recommendation, best action may differ depending on circumstances or patients' or societal values
Grade 2C	Weak recommendation, low-quality or very low-quality evidence	Observational studies or case series	Very weak recommendations; other alternatives may be equally reasonable

RCT = Randomized controlled trial
Adopted from Guyatt, 2006; 2008.

TABLE 4 Therapeutic Apheresis Modality Definitions

Procedure/term	Definition
Adsorptive cytapheresis	A therapeutic procedure in which blood of the patient is passed through a medical device, which contains a column or filter that selectively adsorbs activated monocytes and granulocytes, allowing the remaining leukocytes and other blood components to be returned to the patient.
$ß_2$-microglobulin column	A therapeutic apheresis procedure that uses a column containing porous cellulose beads specifically designed to bind to ß2-microglobulin as the patient's blood passes over the beads.
Double filtration plasmapheresis (DFPP)	A filter based therapeutic procedure that removes pathogenic substances from separated plasma based on their size, which is mainly determined by molecular weight and three-dimensional configuration (e.g., autoantibodies, immune complexes, lipoproteins, etc.), by using plasma filters with different pore sizes.
Erythrocytapheresis	A procedure in which blood of the patient or donor is passed through a medical device which separates red blood cells from other components of blood. The red blood cells are removed and replaced with crystalloid or colloid solution, when necessary.
Extracorporeal photopheresis (ECP)	A therapeutic procedure in which the buffy coat is separated from the patient's blood, treated extracorporeally with a photoactive compound (e.g., psoralens) and exposed to ultraviolet A light then subsequently reinfused to the patient during the same procedure.
Immunoadsorption (IA)	A therapeutic procedure in which plasma of the patient, after membrane based or centrifugal separation from the blood, is passed through a medical device (adsorber column) which has a capacity to remove immunoglobulins by binding them to select ligands on the backing matrix surface (membranes or beads) of the adsorber column.
Leukocytapheresis	A procedure in which blood of the patient is passed through a medical device which separates out white blood cells (e.g., leukemic blasts or granulocytes), collects the selected cells and returns the remainder of the patient's blood with or without addition of replacement fluid such as colloid and/or crystalloid solution.
Lipoprotein apheresis (LA)	The selective removal of lipoprotein particles from the blood with the return of the remaining components. A variety of methodologies are available and include double filtration plasmapheresis (DFPP), HELP-apheresis, polyclonal-sheep-anti-apoB-immunoadsorption, dextran-sulfate plasma adsorption, dextran-sulfate whole blood adsorption, and polyacrylate whole blood adsorption.
RBC exchange	A therapeutic procedure in which blood of the patient is passed through a medical device which separates red blood cells from other components of blood. The patient's red blood cells are removed and replaced with donor red blood cells and colloid solution.
Rheopheresis	A therapeutic procedure in which blood of the patient is passed through a medical device which separates out high-molecular weight plasma components such as fibrinogen, α2-macroglobulin, low-density lipoprotein cholesterol, and IgM in order to reduce plasma viscosity and red cell aggregation. This is done to improve blood flow and tissue oxygenation. LA devices and selective filtration devices utilizing two filters, one to separate plasma from cells and a second to separate the high-molecular weight components, are used for these procedures.
Therapeutic plasma exchange (TPE)	A therapeutic procedure in which blood of the patient is passed through a medical device which separates out plasma from other components of blood. The plasma is removed and replaced with a replacement solution such as colloid solution (e.g., albumin and/or plasma) or a combination of crystalloid/colloid solution.
Thrombocytapheresis	A therapeutic procedure in which blood of the patient is passed through a medical device which separates out platelets, removes the platelets and returns the remainder of the patient's blood with or without addition of replacement fluid such as colloid and/or crystalloid solution.

to provide information on categorization, and strength of recommendation based on the GRADE system (Guyatt 2006; 2008), which takes methodological quality of supporting evidence into account, while eliminating the need for "Level of Evidence" information used in previous fact sheets (Schwartz, 2013). The current edition follows the format used in the Sixth and Seventh Editions (Schwartz, 2016) and provides information on ASFA category (Table 2), and quality of supporting evidence that forms the basis of the grading recommendation (Table 3).

2.2 | ASFA Categories

The definition of the four ASFA categories in the Eighth Edition remains unchanged from the definition used in the Sixth and Seventh Editions (Table 2). This allowed us to

summarizes the evidence for the use of TA in a specific disease entity or medical condition. The Eighth Edition comprises 84 fact sheets for relevant diseases and medical conditions, with 157 graded and categorized indications and/or TA modalities. The Eighth Edition of the JCA Special Issue seeks to continue to serve as a key resource that guides the utilization of TA in the treatment of human disease.

1 | INTRODUCTION

The Writing Committee of the Journal of Clinical Apheresis (JCA) Special Issue 2019 is pleased to present the Eighth Edition of the JCA Special Issue. After more than 2 years of engaging collaborative work, and the rigorous critical review of fact sheets contained herein, we believe that this document will appeal to both practitioners with a focus in the area of apheresis medicine and other physicians who may need to utilize therapeutic apheresis (TA) occasionally for the care of their patients. This latest iteration of evidence-based ASFA categories is based upon a stringent review of up-to-date literature, analysis of the quality of evidence, and the strength of recommendation derived from this evidence.

This Special Issue is a compilation of fact sheets for 84 diseases (Table 1). To clarify terminology used in this table and throughout this document, **"Disease"** refers to a specific disease or medical condition (e.g., myasthenia gravis [disease]; transplantation, liver [medical condition]) and represents the pathology discussed in the fact sheet. **"Indication"** refers to the use of apheresis in specific situations encountered in the disease (e.g. acute, short-term treatment [indication]). Each disease, TA modality and indication is assigned a category (Table 2) and grade (Table 3) as in previous editions. In this edition, we have continued to use the table format at the start of each fact sheet to summarize disease name, TA modality (Table 4), indication(s), category, and grade. Several diseases or conditions that are category IV, which have been described in detail in previous editions and do not have significant new evidence since the last publication, are summarized in a separate table (Table 5).

The 2019 JCA Special Issue Writing Committee comprised 13 members from diverse fields including Transfusion Medicine/Apheresis, Hematology/Oncology, Pediatrics, Nephrology, and Critical Care Medicine from locations across the United States and Europe. Each disease or condition was assigned to one committee member as primary author. That primary author reviewed any new developments in the understanding, current management, and treatment of the disease or condition as well as any changes in the evidence surrounding the use of TA as a treatment modality. Only peer-reviewed PubMed-indexed publications available in English were considered when reviewing literature published since the last fact sheet update. The primary author updated each fact sheet table, disease description, current management, rationale for TA, technical notes (e.g., volumes treated, frequency, replacement fluid), duration and discontinuation of treatment, and provided a maximum of 20 key references highlighting important or new studies and/or reviews (Figure 1). Two other committee members, along with an external expert for select fact sheets, provided secondary peer-review of each fact sheet. The entire writing committee performed a third and final review of all fact sheets with category and grade assigned by consensus in the same manner as described in previous editions with consistent application of evaluation criteria. This evidence-based approach is designed to achieve several objectives. First, it provides uniformity to ASFA category assignment and disease discussion while minimizing personal bias. Second, it provides the strength of recommendation [strong (1) vs. weak (2)] using a defined grading schema. Finally, it provides comprehensive, yet succinct information easily shared with healthcare providers requesting information on the potential utility of apheresis in a given clinical setting. The entire process of fact sheet development is shown in Figure 2.

Several diseases or conditions underwent review in consideration for the development of a new fact sheet (Table 6). To meet criteria for a new fact sheet, the committee required a minimum of 10 cases published in the last decade in peer-reviewed journals, ideally by more than one group. Based on these criteria, there were no new disease categories added to the JCA 2019 Special Issue. Strong consideration was given for the addition of a new fact sheet on Alzheimer's disease. The published evidence for the use of TPE in Alzheimer's disease is currently limited. Preliminary data from the recently concluded phase IIb/III Alzheimer Management by Albumin Replacement (AMBAR) study is available in abstract form but is not yet published in a peer-reviewed journal. Thus, Alzheimer's disease was not selected for inclusion in the JCA 2019 Special Issue.

Some previously published fact sheets were renamed to group fact sheets together by similar disease pathology and/or treatment. For example, "ANCA-associated rapidly progressive glomerulonephritis" and "Henoch-Schönlein purpura" were renamed "Vasculitis, ANCA-associated" and "Vasculitis, IgA (Henoch-Schönlein purpura)" respectively with a separate fact sheet for "Vasculitis, other." All fact sheets involving transplantation have been renamed "Transplantation, transplant-type…" The "Aplastic anemia, pure red cell aplasia" fact sheet