The 2019 guidelines from the American Society for Apheresis: what's new?

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Purpose of review
For over 30 years, the American Society for Apheresis (ASFA) has published practice guidelines on the use of therapeutic apheresis in the *Journal of Clinical Apheresis* (JCA) Special Issue. These guidelines are periodically reviewed with the addition of new indications, retirement of some former indications and the provision of updated recommendations for current indications based on new published literature. During the last 12 years, updated guidelines have been published every 3 years to provide a reflection of current evidence-based apheresis practice. Recently, the eighth special issue was published. Significant updates and changes to the last edition are discussed in this review.

Recent findings
This review provides a description of the development of the eighth special issue with the evolution of the ASFA guidelines since introduced in 1986. There are no new indications for therapeutic apheresis listed in the 2019 edition, however, several recommended category changes to existing indications have been made. There are also several organizational changes with the renaming of some fact sheets.

Summary
ASFA has recently published its latest guidelines for therapeutic apheresis in the *Journal of Clinical Apheresis* 'Eighth Special Edition'. This review describes the evolution of the ASFA guidelines and highlights significant changes to the prior edition.

Keywords
American Society for Apheresis, eighth special issue, evidence-based guidelines, therapeutic apheresis

INTRODUCTION

The American Society for Apheresis (ASFA) *Journal of Clinical Apheresis* Special Issue Writing Committee publishes evidence-based indications for the use of therapeutic apheresis in human disease every 3 years. The eighth special issue, published in 2019, is the latest contribution to the field [1▪▪]. This update is based on a stringent review of new literature in the field and a standardized analysis of the quality of evidence supporting the use of therapeutic apheresis for each disease and/or indication, including the strength of the recommendation based on the quality of evidence. This review describes the evolution of the *Journal of Clinical Apheresis* Special Issue from the first edition in 1986 to the current eighth edition. Significant changes in the latest edition, as compared with the seventh special issue published in 2016, are highlighted.

EVOLUTION OF APHERESIS GUIDELINES

The first issue of apheresis practice guidelines was published in the *Journal of Clinical Apheresis* in 1986 [2]. This was updated in 1993 with publication of the second issue, which introduced the use of category definitions based on available evidence to guide clinical use of apheresis therapy [3]. These definitions were further refined in the third issue published in 2000 [4]. The fact sheet format that is in use today first appeared in the fourth issue published in 2007 [5]. The fourth issue also introduced a new methodology to assign strength of evidence based on a structured review of published literature along with a new category 'P' to describe therapeutic

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KEY POINTS

- Every 3 years, the *Journal of Clinical Apheresis* Special Edition provides updated evidence-based recommendations for the use of therapeutic apheresis.
- Improved methodologies in presenting the recommendations have evolved since the first edition was published in 1986.
- The writing committee consider new potential indications for therapeutic apheresis, and review and retire category IV indications for which there has been no new literature since the last publication.
- The eighth special edition has recently been published with several indications having a change in their category recommendations.

apheresis modalities undergoing clinical trials or not yet approved in the United States. With the publication of the fifth issue in 2010, the frequency for updating these guidelines increased from every 7 years to every 3 years [6]. The fifth issue further refined the category definitions, eliminated the 'P' category, and implemented the use of the GRADE system to assess the quality of published evidence [7,8]. The sixth special issue, published in 2013, eliminated the use of level of evidence in favor of continued use of the GRADE system [9]. In the sixth issue, many diseases with multiple clinical presentations and/or situations were individually graded and categorized, continuing to expand the number of indications relative to the number of fact sheets (Fig. 1). This practice continued with the publication of the seventh special issue in 2016 [10]. In the seventh issue, several fact sheets for several category IV diseases, where published evidence suggests apheresis to be ineffective or harmful, were retired because of a lack of any new evidence supporting therapeutic apheresis for these indications. The seventh issue also divided the multiple indications for therapeutic apheresis in the setting of thrombotic microangiopathy into separate fact sheets based on disease pathophysiology.

OVERVIEW OF THE EIGHTH ISSUE

The eighth issue, published in 2019, continues to provide comprehensive, yet succinct information in

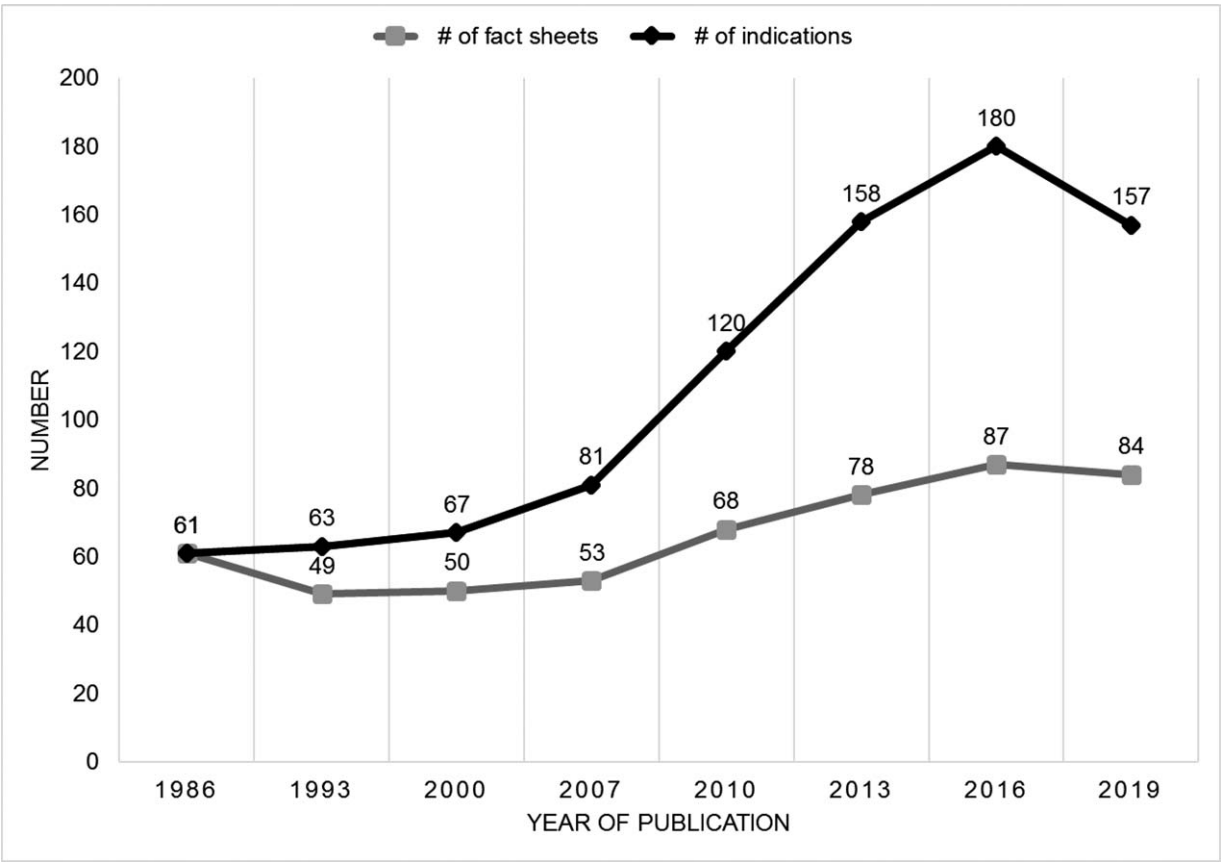

FIGURE 1. Evolution in number of fact sheets and indications in the apheresis guidelines.

a one-page fact sheet format that can be easily shared with healthcare providers requesting information on the potential utility of apheresis in a given clinical setting [1▪▪]. Fact sheets contain updated information on the disease description, current management, rationale for therapeutic apheresis, technical notes (e.g. volumes treated, frequency, replacement fluid), duration and discontinuation of treatment as well as select references highlighting significant studies and/or current reviews. Each disease, therapeutic apheresis modality, and indication is assigned a category and grade recommendation as in the previous edition.

ORGANIZATIONAL CHANGES

In this edition, several previously published fact sheets were renamed in an effort to group fact sheets together by similar disease pathology and/or treatment. All fact sheets involving transplantation have been renamed according to the naming convention 'Transplantation, <<transplant-type>>'. Vasculitis-associated fact sheets were renamed 'Vasculitis, ANCA-associated', 'Vasculitis, IgA (Henoch-Schönlein purpura)' and 'Vasculitis, other.' In keeping with the 2016 edition, which expanded the number of fact sheets for thrombotic microangiopathies, the 'Thrombotic thrombocytopenic purpura'' fact sheet has been renamed 'Thrombotic microangiopathy, thrombotic thrombocytopenic purpura'.

ADDITIONS AND DELETIONS

The eighth edition is the first since 1993 to have fewer fact sheets than the previous edition (Fig. 1). Changes in the number of fact sheets in the eighth edition reflect the merging of several fact sheets, the discontinuation of one fact sheet, and no new fact sheets in this edition. On the basis of all of the above changes, the total number of diseases addressed in the eighth issue is 84 compared with 87 in the seventh edition.

Select fact sheets in the 2016 issue were merged in the 2019 issue based on similar disease pathophysiology. For example, the 'Prevention of RhD alloimmunization after red blood cell exposure' and 'Red cell alloimmunization in pregnancy' fact sheets were combined into a new fact sheet named 'Red cell alloimmunization, prevention and treatment'. Similarly, the 'Aplastic anemia; pure red cell aplasia' and 'Hematopoietic stem cell transplant ABO incompatible' fact sheets were combined into a new fact sheet named 'Transplantation, hematopoietic stem cell, ABO incompatible'.

The 'Dermatomysitis/polymyositis' fact sheet, first introduced in 2013 and with a category IV designation for both therapeutic plasma exchange (TPE) and extracorporeal photopheresis (ECP) in the 2016 edition, was retired as per other category IV indications retired in 2016 without significant new evidence since the last publication [10].

Several diseases or conditions underwent review in consideration for the development of new fact sheets: Alzheimer's disease, Antisynthetase syndrome, Autoimmune myofasciitis, Composite tissue transplantation, Fulminant meningococcemia, Mechanical red cell hemolysis, Methemoglobulinemia, Necrotizing myopathy, Pancreatic transplantation, Platelet transfusion allorefractoriness, Preeclampsia and Recurrent pregnancy loss. 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 research group. On the basis of these criteria, there were no new disease categories added to the eighth issue. Strong consideration was given for the addition of a new fact sheet on Alzheimer's disease based on preliminary data from the recently concluded phase IIb/III Alzheimer Management by Albumin Replacement (AMBAR) study [11▪]. However, published peer-reviewed evidence supporting the use of TPE in Alzheimer's is currently lacking. As more evidence becomes available, this and other indications may warrant inclusion in future editions.

The eighth edition is also the first since 1986 to have fewer indications than the previous edition (Fig. 1). Changes in the number of indications in the eighth edition reflect the practice of combining indications with similar category and grade recommendations to conserve space and maintain the one-page fact sheet format. Specifically, if more than one type of apheresis modality is used for the same clinical indication within the same disease, and if the assigned recommendation grade and category are identical for each modality, it was assigned as a single indication in the eighth edition. This resulted in a decrease in the number of indications from 180 in seventh issue to 157 in the eighth issue.

CHANGES IN CATEGORY RECOMMENDATIONS

The definitions of the four ASFA categories in the eighth edition remain unchanged from those used in the sixth and seventh editions (Table 1) [9,10]. The following fact sheets contain category assignments updated following a careful review of new developments in the current management and treatment of the disease or condition and/or any changes in the evidence surrounding the use of therapeutic apheresis as a treatment modality.

Table 1. Category definitions for therapeutic apheresis

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

Age-related macular degeneration, dry

Rheopheresis for high-risk dry age-related macular degeneration was changed from category I to category II based on clinical use as second-line therapy where this apheresis modality is currently available.

Catastrophic antiphospholipid syndrome

In the eighth edition, TPE for catastrophic antiphospholipid syndrome (CAPS) was changed from category II in the 2016 edition to category I (i.e. first-line therapy) based on reassessment of existing evidence and new clinical evidence supporting therapeutic apheresis as first-line therapy. This change was based largely on data from the International CAPS registry [12]. A triple therapy approach of anticoagulation with glucocorticosteroids and TPE and/or IVIG is the recommended approach to treatment [13▪] and is independently associated with higher survival among CAPS patients [14▪].

Focal segmental glomerulosclerosis

Lipoprotein apheresis for focal segmental glomerulosclerosis (FSGS) was changed from category III in the 2016 edition to category II based on improved outcomes for patients with nephrotoxicity associated with persistent hyperlipidemia [15]. The category II recommendation (i.e. second-line therapy) is consistent with US Food and Drug Administration approval for Lipoprotein apheresis for adult and pediatric FSGS patients with nephrotic syndrome who fail or do not tolerate standard treatment options, including corticosteroid and/or calcineurin inhibitors.

Multiple sclerosis

Immunoadsorption for acute attack/relapse in multiple sclerosis (MS) was also changed from category III in the 2016 edition to category II based on a recent study demonstrating significant numbers of patients that showed marked improvement of symptoms after immunoadsorption during pregnancy or breastfeeding, a situation when the first-line therapy of high-dose steroids may be contraindicated [16].

Progressive multifocal leukoencephalopathy associated with natalizumab

TPE for progressive multifocal leukoencephalopathy (PML) associated with natalizumab was changed from category I to category III based on new evidence suggesting that TPE may not be associated with decreased morbidity or mortality [17▪].

Sickle cell disease

Red blood cell (RBC) exchange for sickle cell disease (SCD) with recurrent vaso-occlusive pain crisis or during pregnancy was also changed from category III in the 2016 edition to category II based on data from new studies. One study demonstrated improved maternal and fetal outcomes in pregnant women with SCD who received early RBC exchange [18]. Another study showed a reduction in utilization of hospital services by patients with recurrent vaso-occlusive pain crisis receiving regular RBC exchange [19].

Thyroid storm

TPE for thyroid storm was also changed from category III in the 2016 edition to category II based on a large case series demonstrating rapid reduction in levels of free T4 and T3 with TPE used as a second-line therapy in patients with thyrotoxicosis [20].

CONCLUSION

The ASFA 'JCA Special Edition' continues to provide apheresis prescribers and users, up-to-date recommendations for the use of therapeutic apheresis

based on the latest published literature available. Since the introduction of the first edition, not only has there been an increase in contributing indications for apheresis, but the special edition has also seen improved developments to the methodology used to convey the evidence-based recommendations to the readers. The special edition has seen the development of fact sheets and the replacement of the 'level of evidence' with the GRADE system to assess the quality of evidence that has been published. The special edition writing committee reviews all potential new indications for therapeutic apheresis based on the amount and quality of the evidence in the published literature. It reviews current published indications where apheresis is no longer or seldom used and updates current indications with changes to grade of evidence and category if required. The organizational changes of the special edition as well as any additions or deletions and, considerations of potential indications are discussed in the introduction of the special edition. These changes as well as changes in category recommendations made in the new eighth special edition have been summarized in this review.

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Conflicts of interest

There are no conflicts of interest.

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- ■ of special interest
- ■■ of outstanding interest

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