

**INDICAZIONI  
CLINICHE ALLO  
SCAMBIO  
PLASMATICO**

*La plasmaferisi terapeutica (TPE) consiste nello scambio di grandi quantità di plasma e il suo rimpiazzo con soluzioni colloidali quali albumina o plasma allogenico.*

*Questa tecnica si è resa effettuabile con l'introduzione dei separatori cellulari dalla metà degli anni '70.*

*I criteri principale per l'applicazione della TPE sono:*

- 1) L'esistenza nel plasma di una sostanza patogena.*
- 2) La possibilità di rimuovere questa sostanza dal plasma più rapidamente di quanto sia riimmessa in circolo.*

*Inoltre in rare condizioni come la porpora trombotica trombocitopenica (TTP) sembra esistere in aggiunta alla presenza di sostanze tossiche indesiderate, che devono essere rimosse, la mancanza di un fattore plasmatico che è fornito in quantità sufficiente dal rimpiazzo con plasma fresco congelato (FFP) o plasmacriodepleto.*

*Il volume di plasma scambiato per ogni procedura è solitamente equivalente al volume del plasma del paziente, la pratica comune consiste in un ciclo di 4-5 procedure da effettuare in 7-10 giorni anche se il volume e la frequenza degli scambi plasmatici varia in rapporto al tipo di patologia, alle condizioni cliniche del paziente e al protocollo seguito da ogni centro per quella determinata patologia.*

*Rimuovendo 40 ml di plasma per chilo di peso corporeo per procedura è stato dimostrato che si rimuove approssimativamente il 60% di una sostanza intravascolare (patogena) anche se alcune caratteristiche specifiche di ogni sostanza possono modificare questo valore (diffusione intra-extravascolare della sostanza, emivita, frazione di risintesi della sostanza rimossa).*

*Il fenomeno di rebound è molto importante nella plasmaferesi quando vengono rimossi anticorpi o immunocomplessi.*

*In questi casi, il contemporaneo uso di terapia immunosoppressiva è da considerarsi il trattamento di scelta, riducendo la TPE, la quantità di farmaci immunosoppressori necessari e di conseguenza gli effetti collaterali dei farmaci stessi.*

# LIQUIDI DI SOSTITUZIONE

*In generale il volume di rimpiazzo per ogni TPE è uguale al volume rimosso (TPE isovolemica) sebbene pazienti in sovraccarico idrico possano ricevere un volume inferiore e pazienti con ridotto volume plasmatico un volume maggiore per prevenire fenomeni ipotensivi.*

*Ad eccezione per la TTP, per la quale il plasma è il liquido di sostituzione di scelta, la composizione del liquido di sostituzione è poco importante e ogni centro ha il suo protocollo.*

*Un grande numero di centri usa routinariamente uguali quantità di soluzione fisiologica e albuminata al 4-5%.*

*Si è scritto molto sulle possibili conseguenze della diminuzione dei fattori della coagulazione, ma non sono stati descritti sanguinamenti importanti.*

*Immediatamente dopo la TPE si ha un significativo prolungamento del tempo di protrombina, di tromboplastina parziale e di trombina con riduzione dei valori di fibrinogeno e di AT III. Entro 4 ore la maggior parte dei fattori compreso il numero delle piastrine ritorna ai valori precedenti la procedura e a 24 ore tutti i valori sono tornati nella norma.*

*Nei pazienti a rischio di sanguinamento (epatopatici, DIC) può essere necessario l'uso del FFP (plasma fresco congelato) e nei pazienti gravemente dispropidemici ed emoconcentrati l'uso di soluzioni albuminate al 5% come unico liquido di sostituzione.*

*Gli svantaggi dell'utilizzo del FFP come liquido di sostituzione sono:*

- aumento dell'incidenza della tossicità da citrato e delle reazioni orticarioidi e anafilattiche*
- trasmissione di infezioni virali*
- trasferimento passivo di anticorpi quali Ab anti-HLA responsabili di complicazioni polmonari severe ed eventualmente fatali (TRALI).*

*Perciò il liquido di sostituzione ideale sarebbe il plasma del paziente stesso privato della componente patogenetica. Sfortunatamente i metodi per la rimozione selettiva di costituenti plasmatici non è priva di rischi e, al momento attuale, applicabile solo a un esiguo numero di patologie.*

# SOSTANZE PATOGENE DA RIMUOVERE

## 1) *Anticorpi:*

- *alloanticorpi (anti-A; anti-B; anti-HPA-1a; anti-D; anti-HLA)*
- *Autoanticorpi (anti-AChR; anti-membrana basale; anti-inibitore fattore VIII; anti-mielina)*

## 2) *Immunocomplessi e macromolecole (crioglobuline)*

## 3) *Proteine monoclonali (IgM; polimeri di IgG o IgA)*

## 4) *Costituenti olasmatici prodotti in eccesso (acido fitanico; LDL)*

**INDICATIONS FOR PLASMAPHERESIS  
ACCORDING TO THE AMERICAN SOCIETY FOR APHERESIS**


CATEGORY	PLASMAPHERESIS	CYTAPHERESIS
I. Standard and acceptable under certain circumstances, including primary therapy	Acute inflammatory demyelinating polyradiculoneuropathy Anti-glomerular basement membrane antibody disease Chronic inflammatory demyelinating polyradiculoneuropathy Demyelinating polyneuropathy with IgG/IgA Myasthenia gravis Phytanic acid storage disease Posttransfusion purpura Thrombotic thrombocytopenia purpura	Cutaneous T-cell lymphoma: photopheresis Erythrocytosis/polycythemia vera Familial hypercholesterolemia: <i>lipid adsorption</i> Leukocytosis syndrome: leukodepletion Sickle cell diseases: red cell exchange Thrombocytosis: platelet depletion

II. Sufficient evidence to suggest efficacy; acceptable therapy on an adjunctive basis

ABO incompatible marrow transplant (recipient)  
Acute CNS inflammatory demyelinating disease  
Coagulation factor inhibitors  
Cryoglobulinemia  
Cryoglobulinemia with polyneuropathy  
Familial hypercholesterolemia  
Lambert-Eaton syndrome  
Myeloma/acute renal failure  
Myeloma/paraproteins/hyperviscosity  
PANDAS (*pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections*)  
Polyneuropathy with IgM ( $\pm$  Waldenström's)  
Rapidly progressive glomerulonephritis  
Sydenham's chorea

Chronic graft vs host disease: photopheresis  
Erythrocytosis/polycythemia vera: RBC depletion  
Hyperparasitemia—Malaria/babesiosis: RBC exchange  
Idiopathic thrombocytopenic purpura: immunoadsorption  
RA: immunoadsorption


<p>III. Inconclusive evidence for efficacy or uncertain benefit-risk ratio</p>	<p>Acute hepatic failure  Aplastic anemia/pure RBC aplasia  Autoimmune hemolytic anemia  Heart transplant rejection  Hemolytic disease of the newborn  Hemolytic uremic syndrome  Inclusion-body myositis  Multiple myeloma with polyneuropathy  Multiple sclerosis (progressive)  Multiple sclerosis (relapsing)  Overdose poisoning  Platelet alloimmunization and refractoriness  Paraneoplastic neurologic syndromes  POEMS (plasma cell dyscrasia with <i>poly</i>neuropathy, <i>organomegaly</i>, <i>endocrinopathy</i>, <i>monoclonal protein</i>, and <i>skin changes</i>) syndrome  Polymyositis or dermatomyositis  Rasmussen's encephalitis  Raynaud's phenomenon  Recurrent focal glomerulosclerosis  Renal transplantation (presensitization)  Scleroderma/progressive systemic sclerosis  SLE  Stiff-man syndrome  Vasculitis</p>	<p>Cutaneous T-cell lymphoma: leukodepletion  Demyelinating polyneuropathy with IgG/IgA: immunoadsorption  Heart transplant rejection: photopheresis  Multiple sclerosis, progressive: lymphocytapheresis  Paraneoplastic neurologic syndromes: immunoadsorption  Platelet alloimmunization and refractoriness: immunoadsorption  Polyneuropathy with IgM (<math>\pm</math> Waldenström's): immunoadsorption</p>
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IV. Lack of efficacy in controlled trials	Renal transplantation rejection RA Systemic (AL) amyloidosis	Inclusion-body myositis: leukapheresis Polymyositis or dermatomyositis
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Data from McLeod BC. Introduction to the third special issue: Clinical applications of therapeutic apheresis. *Journal of Clinical Apheresis* 15:1–5, 2000.



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***Guidelines on the Use of Therapeutic Apheresis  
in Clinical Practice—Evidence-Based Approach  
from the Apheresis Applications Committee  
of the American Society for Apheresis***

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*Extracorporeal photopheresis (ECP)*

*Erythrocytapheresis (RBC exchange)*

*Filtration selective removal*

*Immunoabsorption (IA)*

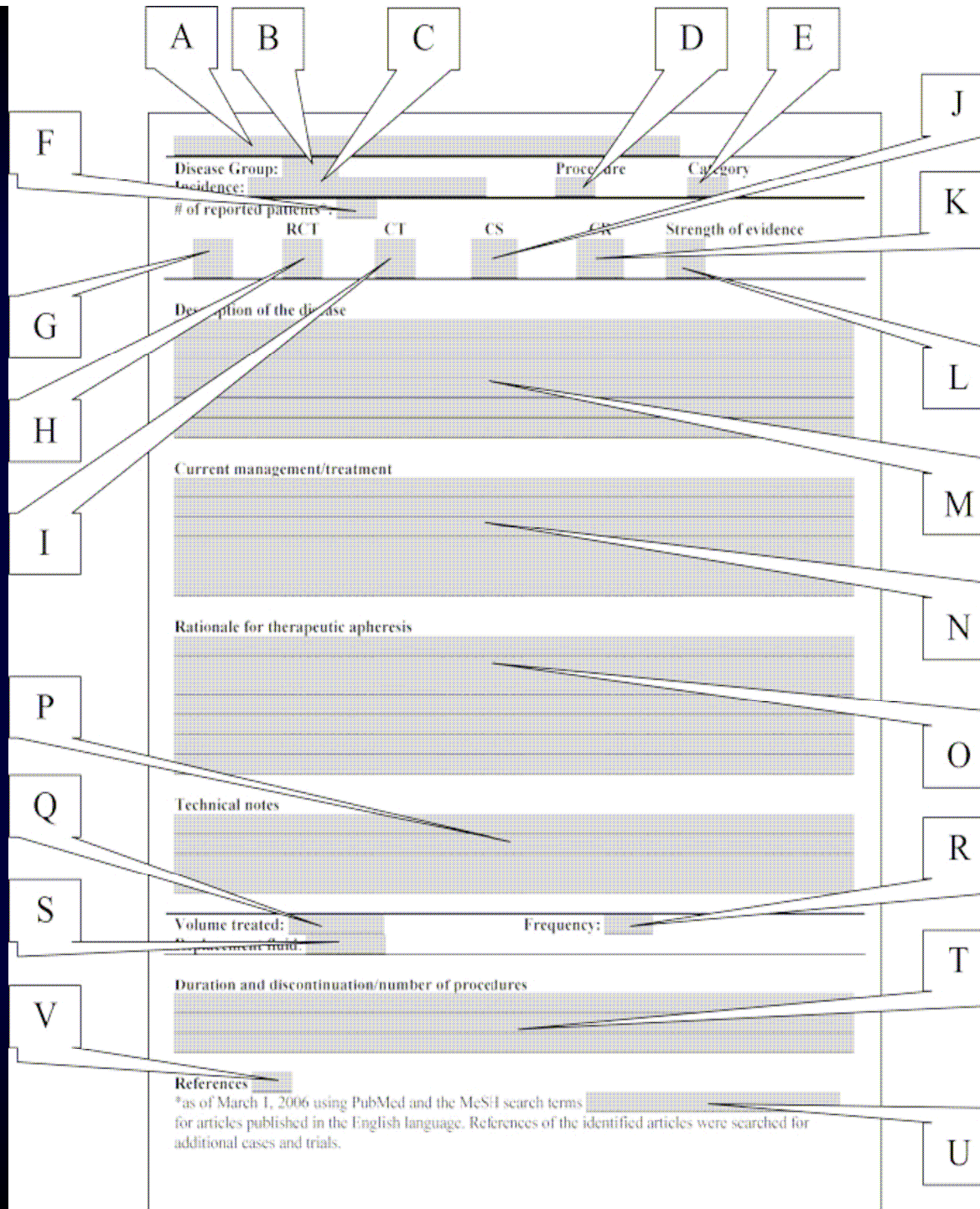
*LDL Apheresis*

*Leukocytapheresis (LCP)*

*Plasma exchange (TPE)*

*Therapeutic apheresis (TA)*

*Trombocytapheresis*



References  
 \*as of March 1, 2006 using PubMed and the MeSH search terms [redacted]  
 for articles published in the English language. References of the identified articles were searched for additional cases and trials.

*A The name of the disease as well as its eponym when appropriate.*

*B Each disease entity was assigned a disease group. The disease groups are primarily based on the ASFA Special Issue 2000 with minor modifications. The following are the disease groups used in the ASFA Special Issue 2007: autoimmune, hematologic, metabolic, miscellaneous, neurological, renal, rheumatic, and transplantation. The subcommittee recognizes that some of the diseases can be assigned to multiple groups, in such situations a primary and secondary group was used. However, only the primary assigned group was used in the Tables.*

*C This section lists the incidence and/or prevalence of the disease in the US and other selected geographic region, when appropriate. In some instances when the incidence varies between genders, ethnicity or race, this information was noted as well. For certain diseases with insufficient data on either incidence or prevalence, other terms such as rare or unknown were used. The reader is cautioned to use this information only as an indicator of disease prevalence. It is possible prevalence may vary by geographical area.*

*D The type of therapeutic apheresis procedure is listed here. Only diseases which were categorized are listed. More information on category IV indications can be found in a separate publication in this Special Issue. For certain diseases there are several apheresis based modalities available. In such instances (e.g., hypercholesterolemia) all types of therapeutic apheresis procedures are listed.*

*E The ASFA category is listed for each therapeutic apheresis modality discussed. See the article in this Special Issue discussing the process of category assignment. Some categories have additional information to further specify a subgroup of patients for whom the category was assigned. It is important to recognize that an ASFA category was assigned only in this particular subset of patients.*

*More information is always available in the text of the fact sheet.*

*F This section lists the number of patients reported in the literature who were treated with therapeutic apheresis. The committee used three categories: fewer than 100, between 100 and 300, and more than 300. This entry will help readers in judging how often this entity was reported to be treated with TA. However, the number of patients treated is less important than the quality of the scientific reports and sometimes can be misleading as negative results tend to be published less frequently.*

*G This section is used when there are several different TA procedures used and it was necessary to subdivide available scientific reports. Not all entries will have this section.*

*H Randomized controlled trials (RCT). The number of randomized controlled trials and the total number of patients studied. For example, 4 (250) indicates that there were 4 randomized controlled trials with 250 enrolled patients. The 250 patients include all patients irrespectively of randomization to either treatment group with TA or control arm. Some trials have more than two arms and therefore simplification was necessary. The minimum requirement for these studies was randomization to a control arm and a test arm the quality of the study is not reflected here. Example: Two randomized studies with 50 patients in each arm and one randomized study with 75 patients in each arm will be denoted as 3 (350).*

*I Controlled trials (CT): the notation is similar to randomized controlled trials. Studies listed here were not randomized. The control group could be historical or concurrent to the treatment group.*

*J Case series (CS). Number of case series (with total number of patients reported). We required that the case series described at least 3 patients. Case series with two patients were included in case reports. Example: 4 (56) implies that there were 4 case series with the total number of reported patients of 56.*

*K Case reports (CR). Number of case reports (with total number of patients reported) – this information was derived also from abstract case reports from ASFA, ASH, AABB Annual meetings and meetings of other organizations relevant to the discussed entity starting January 1, 2001. The committee decided that if the report has not been published in peer reviewed literature within 5 years it will not be included in the total number of case reports. If there are more than 50 case reports or there is a significant number of larger studies either >50 or NA (not applicable) was used, respectively.*

*L The strength of evidence was assigned based on the grading system used by the University HealthSystem Consortium as discussed in the introductory article in this Special Issue. If there were multiple TA modalities used the attempt was made to assign strength of evidence to each modality.*

*M A brief description of the discussed entity is provided here. Typically this entry contains information on clinical signs and symptoms, pathophysiology, typical presentation and the severity of the disease.*

*N This section provides a brief description of therapeutic modalities available to treat the disease. The committee attempted to cover all reasonable modalities (e.g., medications, surgical procedures, etc) however, this section is not intended to provide extensive discussion of any treatment modality. In addition, for some entities the management of standard therapy failure is discussed (e.g., steroid), especially when the failure of established therapies may trigger the use of therapeutic apheresis.*

*O This section discusses a rationale for therapeutic apheresis as well as supporting evidence of its use. Most important reports are briefly discussed here. If a TA treatment was determined as category III indication, a rationale for this decision is provided as either limited data and/or conflicting data. The effort was made to discuss a rationale for TA in the context of the current understanding of pathophysiology.*

*P This section briefly describes technical suggestions relevant to the treated disease, which the committee believed were important to improve quality of care or increase chances of positive clinical outcome. Not all diseases have specific technical notes, in such instances a general statement referring to the introductory article is provided.*

*Q This section specifies commonly used volumes of plasma or blood treated. Typically this value for plasma exchange is between 1 and 1.5 total plasma volumes (TPV).*

*R The proposed frequency of treatment is listed here. The frequency is based on the data from the published reports however, due to variability of such reports; the committee suggested what is believed to be the clinically most appropriate frequency. When used, “every other day” generally indicates 3 procedures per week. Application of this information is left to discussion between the treating physician and the apheresis physician.*

*S The type of replacement fluid most frequently used is listed here based on published literature. Terms such as plasma or albumin were used to denote the type of replacement fluid. No attempt was made to include all possible variations (e.g., 4% vs. 5% albumin; plasma vs. thawed plasma). In addition, blood component modifications are listed here, if relevant (e.g., RBC modifications for erythrocytapheresis). “Not applicable” is used when there is not replacement fluid necessary (i.e. photopheresis).*