Supplement:

Table 1S. Responses to TPE

Diagnosis	Indicators of clinical response to TPE
Immuno-hematology	
Thrombotic thrombocytopenic purpura (TTP)	Recovery of ADAMTS13 activity to more than 10% within 7 days is significantly associated with a rapid clinical response
ANCA-associated vasculitis	Median number of TPE sessions is 7 over a median of 14 days; up to 12 sessions reported to result in further improvement in patients with severe renal failure or diffuse alveolar hemorrhage
Neurology	
Acute inflammatory demyelinating polyneuropathy (Guillain-Barré syndrome)	1) TPE is effective within 7 days of disease onset. 2) Frequency: 5–6 sessions over 10–14 days; accelerates motor recovery and reduces time on mechanical ventilation
Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	1) TPE is initiated early to stop the inflammatory demyelination and prevent secondary axonal degeneration. 2) Therapeutic response is measured by improvement or stabilization of individual neurological response. 3) Frequency: 2–3/week until improvement, then tapered, e.g., to weekly or monthly
Myasthenia gravis	1) TPE is more effective if initiated during a myasthenic crisis, particularly in patients with bulbar or severe generalized response. 2) Time to clinical benefits may be < 24 hours or up to a week. 3) Frequency: Acute attack/relapse or unstable disease activity: 3–4 sessions over 10–14 days; weekly to bi-weekly for chronic treatment tailored to each patient

	4) Apheresis may be more effective than IVIG in patients with MuSK- MG.
Nephrology	
Rapid progressive glomerulonephritis; Goodpasture syndrome (with diffuse alveolar hemorrhage)	1) Anti-GBM antibodies fall to undetectable levels within 2 weeks, requiring a TPE course of ≥10–20 days. 2) The presence or absence of antibody should not be used to initiate or terminate therapy, because antibody is not demonstrable in a few patients with the disease and may be present in patients without active disease. In patients with active disease, TPE should continue until resolution of evidence of ongoing glomerular or pulmonary injury. 3) Plasma angiopoietin-2 levels reported to decline to near-normal with ≤4 TPE sessions.

Abbreviations: RBC, red blood cells; IVIG, intravenous immunoglobulins; MuSK-MG, myasthenia gravis with muscle-specific tyrosine kinase autoantibodies; GBM, glomerular basement membrane; TPE, therapeutic plasma exchange

Table 2S. Anticoagulation for TPE

	Heparin	**Citrate**	**Epoprostenol**
Advantages	Considerable experience	Regional anticoagulation (rapidly reversible with calcium) decreases the bleeding risk	No systemic anticoagulation
	Monitoring available (aPTT or antiXa activity)		low bleeding risk
	Antagonist available (protamine)		Short half life
	Inexpensive		
Drawbacks	Systemic anticoagulation with bleeding risk	Risk of hypocalcemia and metabolic acidosis from citrate accumulation	Risk of hypotension
	Monitoring is difficult due to unpredictable kinetics and heparin removal in TPE circuit	Risk of metabolic alkalosis from citrate metabolism, hypernatremia, hypomagnesemia	Weaker anticoagulant
	Action is antithrombin-dependent, and antithrombin loss through TPE should be considered	Higher blood flows require closer monitoring	
	Risk of heparin-induced thrombocytopenia	Dose adjustment may be necessary to compensate for the plasma citrate content	

Abbreviation: aPTT: activated partial thromboplastin time

Table 3S. Replacement fluids used for TPE

	5% albumin	Fresh frozen plasma	Saline[a]
Advantages	Iso-oncotic with plasma	Iso-oncotic with plasma	Inexpensive
		Replacement of clotting factors or immunoglobulins	
	Reduced risk of viral contamination	Replacement of missing elements in plasma	Readily available
	Can be stored at ambient temperature	May not be easily available and less expensive than albumin	Can be stored at ambient temperature
	Compatible with all blood types		Compatible with all blood types
	Adverse events are rare		Adverse events rare
Drawbacks	Depletion of coagulation factors	Higher risk of viral transmission and allergic reactions	Hypo-oncotic with risk of hypotension
	Depletion of immunoglobulins		Higher volume required
	No replenishment of missing plasma components	Contains citrate with risk of hypocalcemia and metabolic alkalosis	
	May carry risk of acidosis	Risk of transfusion-related adverse events	Hyperchloremic acidosis
	Expensive	ABO compatibility required	

Abbreviation: TPE, therapeutic plasma exchange; FFP, fresh frozen plasma. [a]Only considered as partial fluid replacement (<30%) combined with albumin or plasma

Table 4S. Summary of the main studies on TPE over the past 20 years with reported rate of complications

Publication	TPE sessions (n)[a]	Study design	Population	Vascular access	Replacement fluid	Complication rate
Lemaire 2017	260	Prospective	ICU adults TMA>hyperviscosity>ANCA vasculitis	CVC 90%	FFP 87%	26.9%
Yilmaz 2011	1188	Retrospective	ICU adults Mixed indications	CVC 98%	90% FFP	2.1%
Szczeklik 2013	370	Retrospective	ICU adults MG>GBS	CVC	FFP + albumin	11.1%
Cortina 2018	244	Retrospective	Children in ICU Mixed indications	CVC	FFP	21.2%
Sik 2020	635	Retrospective	Children, sepsis with MOF++	CVC	90% FFP	16.3%
Basic-Jukic 2005	4857	Retrospective	MG >> TMA/SLE/GBS	Peripheral 72%	80% albumin / 20% FFP	4.8%
Shemin 2007	1727	Prospective	TTP>FSGS>MG	NA	60% albumin / 40% FFP	36%
Bramlage 2009	883	Retrospective	TMA>MS>MG	CVC	70% albumin / 30% FFP	25.6%
Lu 2019	1201	Retrospective	Children Poisoning/Rheumatological /Kidney/Neurological	CVC	FFP	12.7%
McGuckin 2014	2067	Retrospective	TMA	CVC 90%	FFP	6–10%
Som 2012	302 patients	Registry	TTP	CVC++	FFP	24%
Korach 2001	134 938	Registry	Mixed indications	Peripheral 66%	60% albumin	4.6%–11.9%
Yeh 2004	2502	Retrospective	92% neurological disorders	CVC 63%	Saline / albumin	26.3%

[a]Except for the study by Som et al.

Abbreviation: ICU, intensive care unit; TMA, thrombotic microangiopathy; ANCA, antineutrophil cytoplasmic antibodies; MG, myasthenia gravis; GBS, Guillain-Barré syndrome; MOF, multiorgan failure; SLE, systemic lupus erythematosus; TTP, thrombotic thrombocytopenic purpura; FSGS, focal segmental glomerulosclerosis; MS, multiple sclerosis; CVC, central venous catheter; NA, not applicable; FFP, fresh frozen plasma