



ΕΛΛΗΝΙΚΗ ΕΤΑΙΡΕΙΑ ΑΙΜΑΦΑΙΡΕΣΗΣ

15 ΠΕΡΙΦΕΡΕΙΑΚΗ  
ΔΙΗΜΕΡΙΔΑ  
ΕΛΛΗΝΙΚΗΣ ΕΤΑΙΡΕΙΑΣ  
ΑΙΜΑΦΑΙΡΕΣΗΣ

Λέσχη Αξιωματικών  
Ενόπλων Δυνάμεων  
(ΛΑΕΔ)  
Σαρόγλειο Μέγαρο  
Αθήνα

27 &  
28  
Σεπτεμβρίου  
2024

# Ο ρόλος της θεραπευτικής αφαίρεσης στη ΜΕΘ Χρειάζεται ο Νεφρολόγος

Χρήστος Πλέρος  
Νεφρολόγος  
ΠΑΓΝΗ

# Θεραπευτική αφαίρεση στη ΜΕΘ



- Ενδείξεις θεραπευτικής αφαίρεσης
- Συχνότητα – επίπτωση
- Ιδιαιτερότητες ασθενών και περιβάλλοντος
- Τεχνικά ζητήματα
- Σήψη
- Χρειάζεται ο νεφρολόγος;

**Table 1 Indications for therapeutic plasma exchange (TPE) in the ICU: absolute (likely or less likely to be used), relative, and rescue therapy**

Disease	Rationale	Replacement fluid	Adjunct therapeutic options	Strategy <sup>a</sup> and Endpoints	Parameters to monitor	Additional comments
<b>Absolute indications: disorders for which TPE is a recognized first-line treatment [2]</b>						
Acute inflammatory demyelinating polyradiculoneuropathy (Guillain-Barré syndrome)	Removal of antibodies	Albumin or plasma	IVIg	1–1.5 TPV, 5–6 sessions over 10–14 days <i>until</i> clinical improvement	Clinical response	Consider TPE if failed to respond to IVIg and/or impending respiratory failure
Anti-glomerular basement membrane disease (Goodpasture syndrome)	Removal of pathogenic autoantibodies (including anti-GBM antibodies)	Albumin; plasma if bleeding	Corticosteroids, cyclophosphamide, rituximab	1–1.5 TPV daily or on alternate days over 10–20 days <i>until</i> disease control	Renal function Clinical response	Anti-GBM antibodies may fall to undetectable levels within 2 weeks; TPE course should be ≥ 10–20 days and should continue until resolution of glomerular or pulmonary injury The presence or absence of antibody should not guide decisions to initiate or end TPE
Hyper-viscosity syndrome (in hypergammaglobulinemia, especially Waldenström macroglobulinemia)	Removal of paraproteins, thereby reducing the plasma viscosity	Albumin or Albumin/saline	Systemic chemotherapy or immunotherapy	1–1.5 TPV daily <i>until</i> symptoms subside, most often 1–3 procedures	Clinical response M component (mainly IgM levels)	Symptoms are more reliable than concrete values of viscosity or immunoglobulins to guide therapy
Catastrophic antiphospholipid syndrome	Removal of antibodies (including antiphospholipid antibodies), cytokines, and complement factors; administration of coagulation factors	Plasma (± albumin)	Anticoagulation, corticosteroids, IVIg, rituximab or eculizumab	1–1.5 TPV daily or alternate days; <i>until</i> clinical response	Clinical response	
Myasthenia gravis	Removal of autoantibodies (including antiacetylcholine receptor antibodies) and immunomodulation	Albumin	Cholinesterase inhibitors, corticosteroids, immunosuppression, IVIg, thymectomy, eculizumab	1–1.5 TPV; 3–6 sessions over 10–14 days, <i>until</i> disease control	Clinical response	More effective if initiated during myasthenic crisis, especially with bulbar or severe generalized response; more effective than IVIg in patients with MuSK-Ab
N-Methyl-D-aspartate receptor antibody encephalitis	Removal of antibodies (including anti-neuronal autoantibodies)	Albumin	High dose corticosteroids, IVIg, occasionally rituximab or cyclophosphamide Tumor resection (when tumor is present)	1–1.5 TPV; 5–12 sessions over 1–3 weeks <i>until</i> clinical response	Clinical response	Check for ovarian tumors and other tumors (germ cell tumors, carcinoma, teratoma, lymphoma)



**Table 1 (continued)**

Disease	Rationale	Replacement fluid	Adjunct therapeutic options	Strategy <sup>a</sup> and Endpoints	Parameters to monitor	Additional comments
Thrombotic thrombocytopenic purpura	Administration of ADAMTS13 protease and removal of anti-ADAMTS13 autoantibodies	Plasma	Corticosteroids, rituximab, Caplacizumab (recombinant ADAMTS13?)	Daily <i>until</i> platelet count > 150 × 10. <sup>9</sup> /L, LDH approaching normal and resolution of non-fixed neurologic symptoms then Continue for 2 more sessions then stop	Platelet count, LDH, ADAMTS13 activity	Recovery of ADAMTS13 activity to > 10% within 7 days is associated with clinical response
Acute liver failure <sup>a</sup>	Removal of albumin-bound and water-soluble toxins Replacement of plasma proteins including clotting factors Immunomodulation Reduction of proinflammatory response	Plasma	Multiorgan support	High-volume TPE if possible (target 8–12 L); otherwise, 1–1.5 TPV daily <i>until</i> clinical improvement or transplantation	Clinical response Supportive care as a bridge to liver transplantation	Always consider TTP in the differential in specific scenarios (e.g., pregnancy and acute liver failure) Supportive care may improve nontransplant outcome Support care may stabilize while awaiting liver transplant

**Relative indications: Disorders for which TPE is a recognized second-line treatment (alone or combined)**

Thyroid storm (refractory)	Removal of autoantibodies, catecholamines, and cytokines	Plasma, albumin	Propylthiouracil, corticosteroids, β-blockers, cholestyramine, organ support	Daily to every 3 days, <i>until</i> control of systemic response	Clinical response	Although a category II per 8th ASFA guidelines, TPE could be considered in refractory cases
ANCA-associated vasculitis with diffuse alveolar hemorrhage	Removal of autoantibodies and inflammatory mediators	Plasma	Corticosteroids, rituximab, cyclophosphamide	1–1.5 TPV daily or every other day <i>until</i> disease control	Clinical response (resolution of pulmonary hemorrhage)	PEXIVAS trial suggested no benefit on death or end stage kidney disease Now category II per recent ASFA update [73]
Acute disseminated encephalomyelitis	Removal of presumed pathogenic autoantibodies	Albumin	Corticosteroids, IVIG	1–1.5 TPV every other day <i>until</i> disease control	Clinical response	
Thrombotic microangiopathy-complement-mediated (formerly known as atypical hemolytic syndrome (aHUS))	Recommended while investigations for TTP and other forms of TMA are in progress or if eculizumab is not available	Plasma	Eculizumab	1–1.5 TPV daily <i>until</i> TTP ruled out	Platelet count	
Autoimmune hemolytic anemia	Removal of pathogenic immune complexes, autoantibodies and complement components	Albumin	Corticosteroids, rituximab, IVIG, immunosuppression, monoclonal antibody therapy, splenectomy	TPV 1–1.5 daily <i>until</i> disease control	Clinical response	

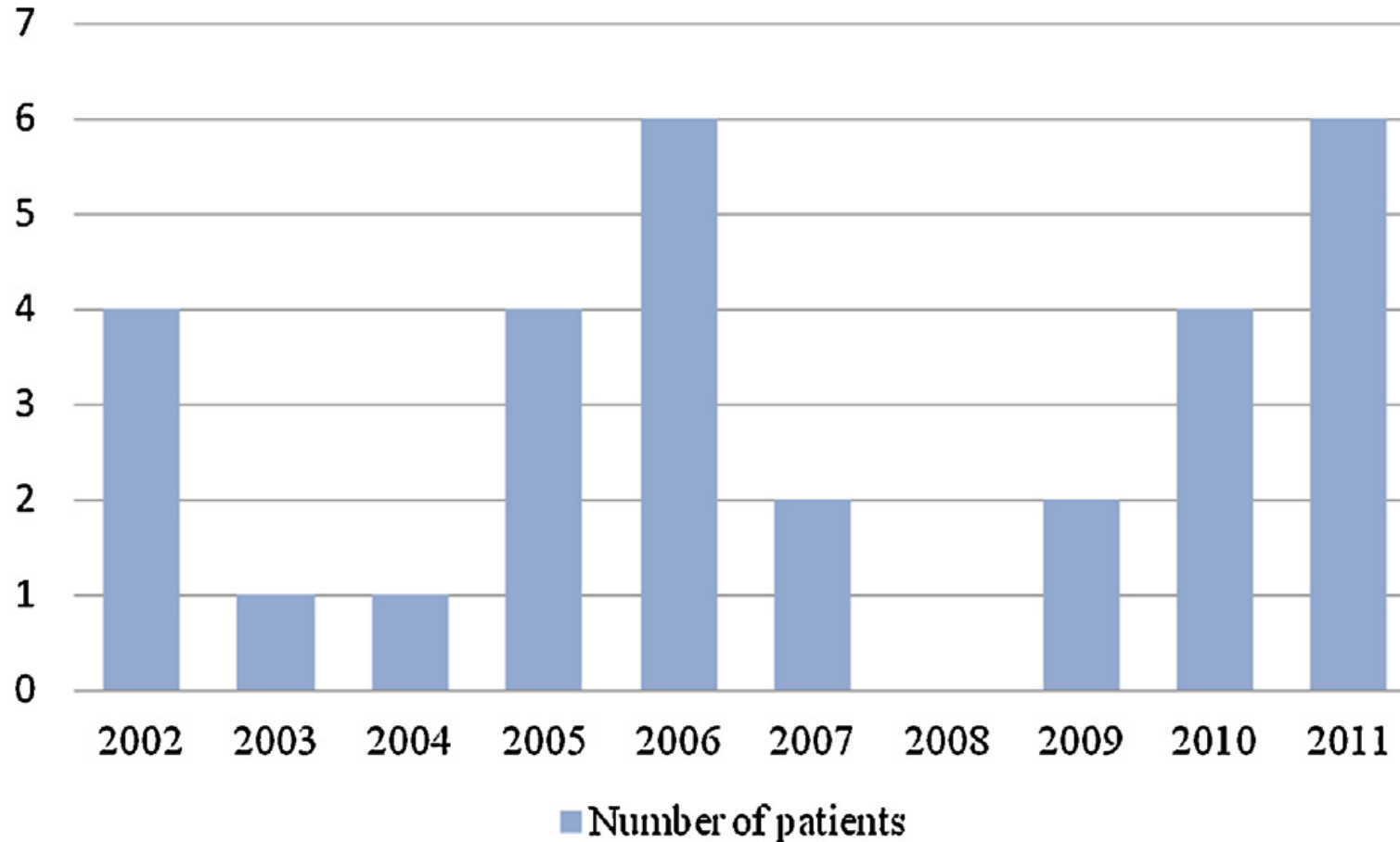




## Plasma exchange in the intensive care unit: A 10 year retrospective audit

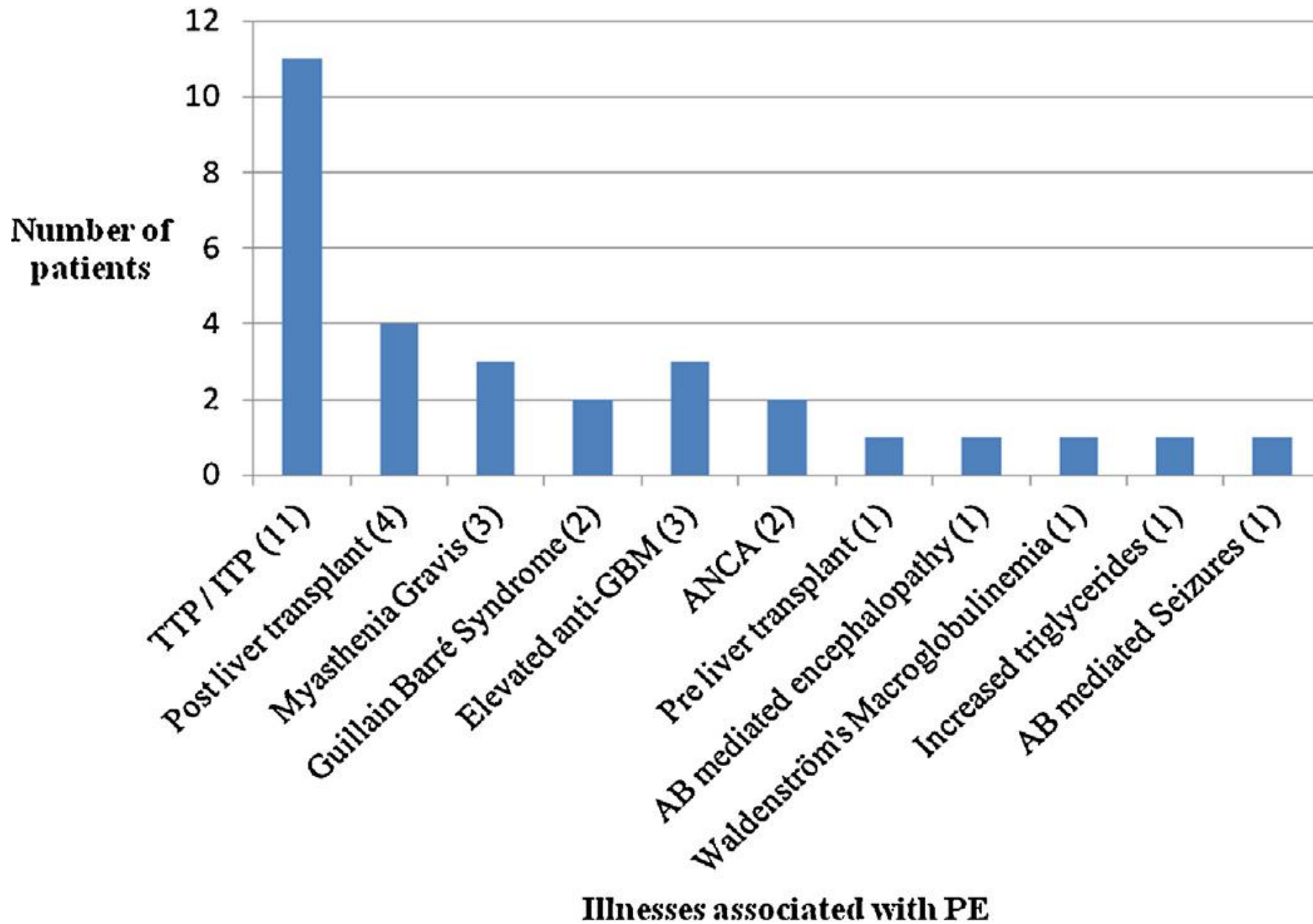
Emily Paton RN, Grad. Dip (Crit Care Nurs), ACCCN\*,  
Ian C. Baldwin RN, PhD, (ICU Cert), ACCCN<sup>1</sup>

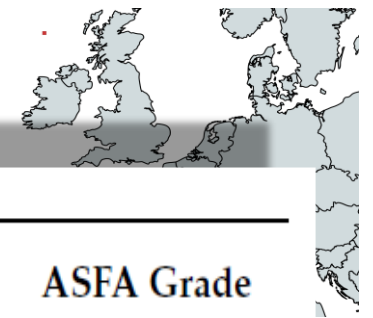
Department of Intensive Care, Austin Health, 145 Studley Rd, Heidelberg, Melbourne 3084, Australia



**$N = 19.728$**

**$n = 30$**





Article

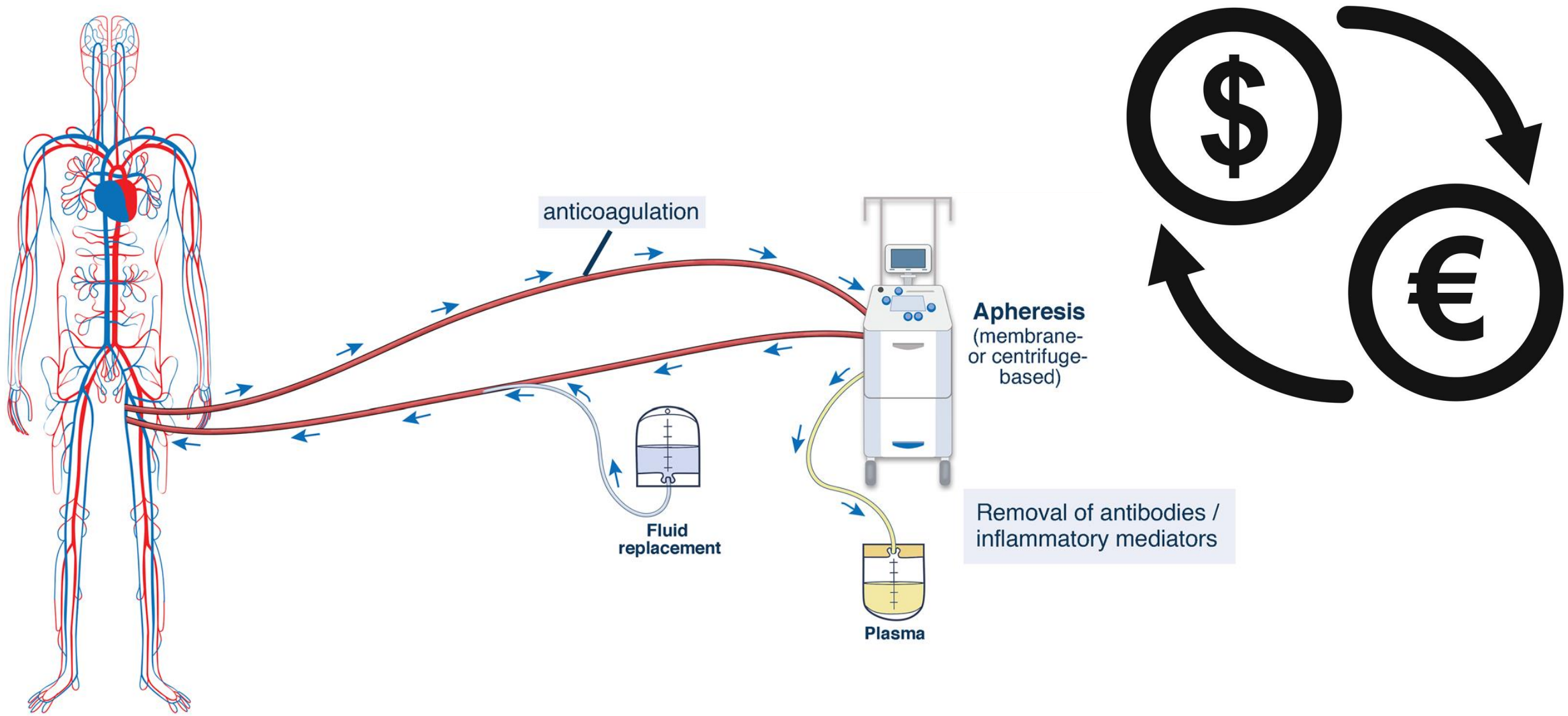
# Indications and Outcomes of Patients Receiving Therapeutic Plasma Exchange under Critical Care Conditions:

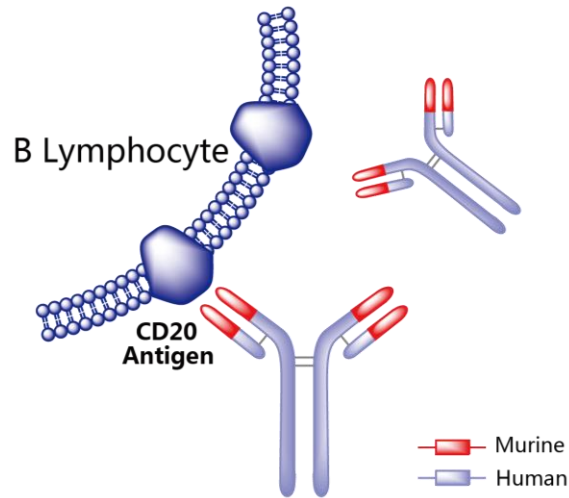
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Indication	Number of Patients n (%)	Median TPE Sessions (IQR)	ASFA Category	ASFA Grade
Anti-IgG5-associated encephalopathy	1 (0.95)	2	unclear	unclear
Systemic sclerosis	1 (0.95)	4	I	1A
Chronic inflammatory demyelinating neuropathy	1 (0.95)	1	I	1B
Postpartum microangiopathy	1 (0.95)	7	I or III	1A or 2C
Miller-Fisher Syndrome	1 (0.95)	1	I	1A
Polyradiculoneuritis	1 (0.95)	1	unclear	unclear
Paraneoplastic neurological syndrome	1 (0.95)	8	III	2C
Catastrophic antiphospholipid syndrome	1 (0.95)	4	I	2C
acute demyelinating neuropathy	1 (0.95)	1	unclear	unclear
Hyperviscosity in hypergammaglobulinemia	1 (0.95)	2	I	1B

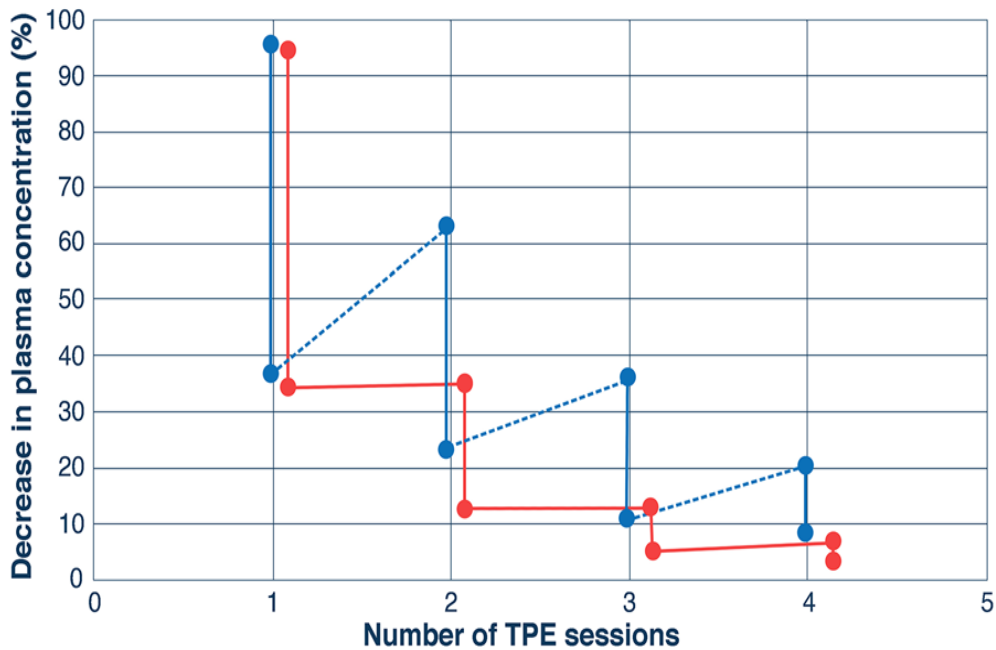
**Total=105**





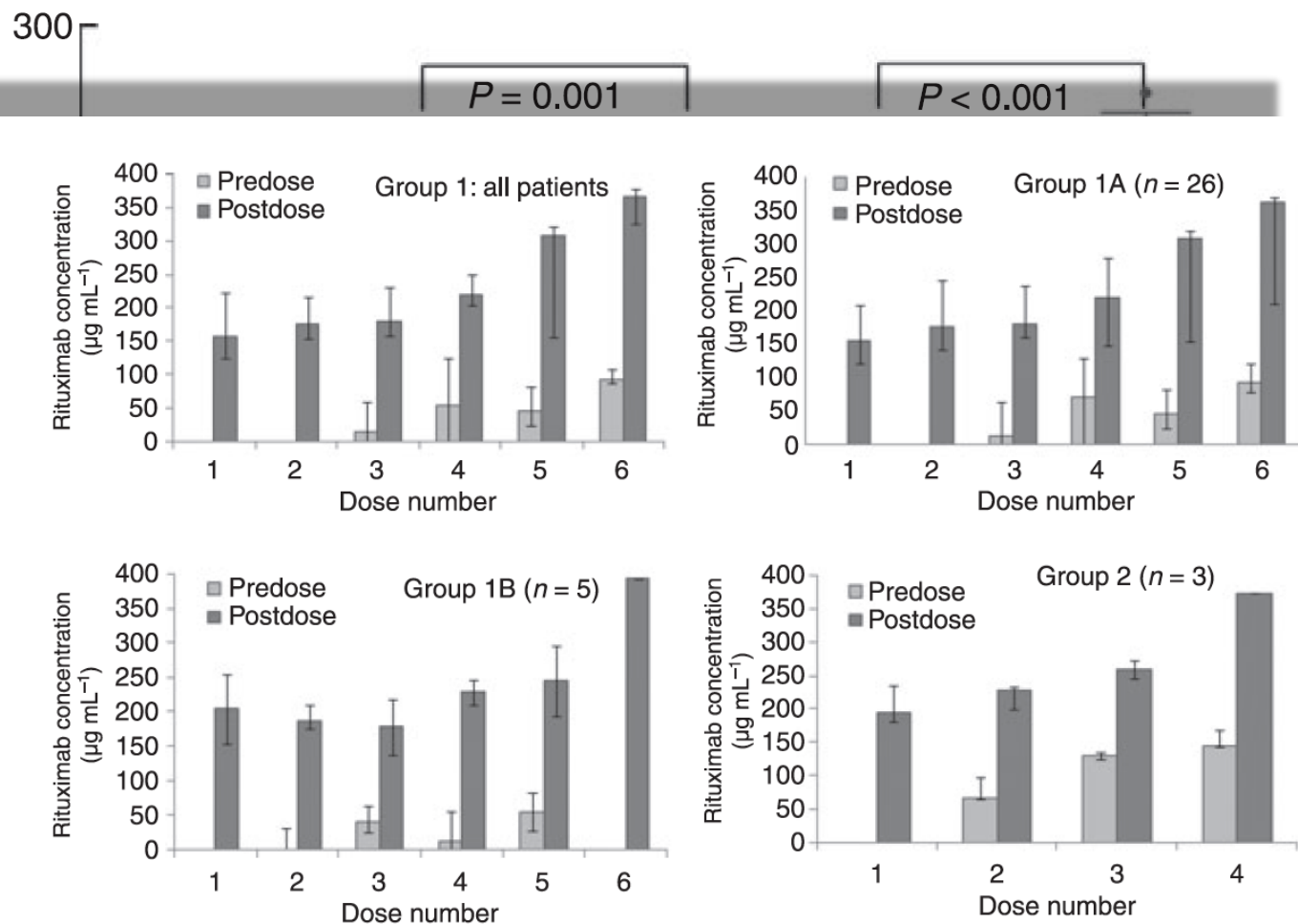
— Represents changes of concentration of substance with small molecular weight and large volume of distribution (25-30% intravascular) (e.g., IgG immunoglobulins)

— Represents changes of concentration of substance with large molecular weight that stays > 90% intravascular (e.g., IgM immunoglobulins)



*Bauer et al. Intensive Care Med 2022*

Serum rituximab concentration ( $\mu\text{g mL}^{-1}$ )

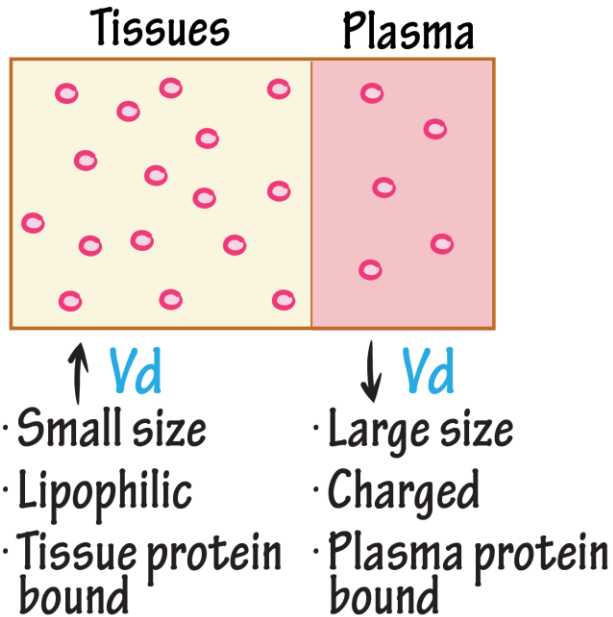


*McDonald et al. J Thromb Haemost 2009*

# Volume of Distribution

$$\frac{F \times \text{Dose}}{TC} = Vd$$

- Vd - Volume of Distribution
- TC - Target Plasma Concentration
- F - Bioavailability



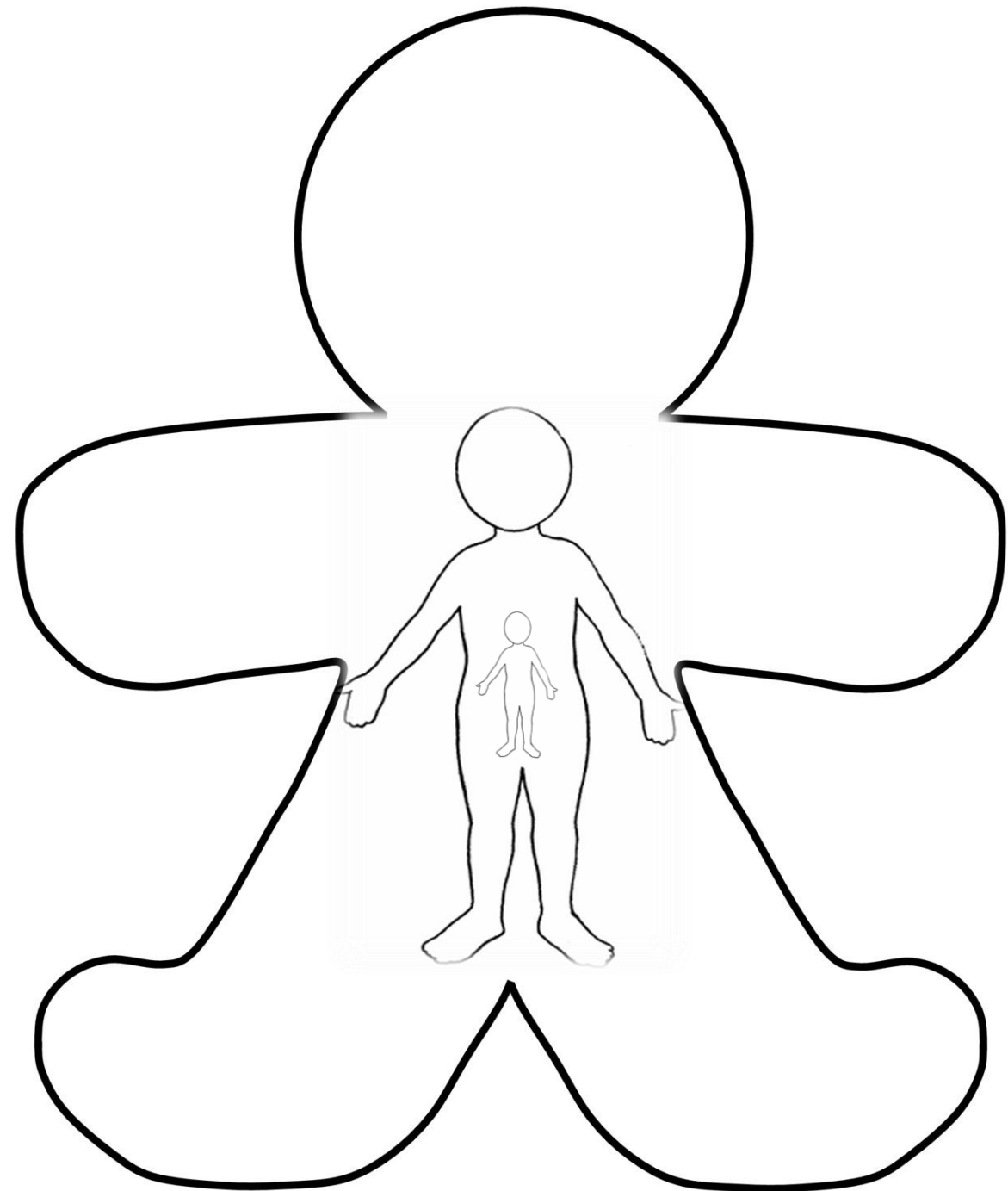
## EXAMPLE

$$\frac{0.50 \times 500\cancel{\text{mg}}}{5\cancel{\text{mg/L}}} = 50\text{L}$$

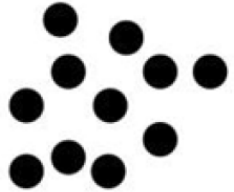
## LOADING DOSE



$$\text{Dose} = \frac{Vd \times TC}{F}$$

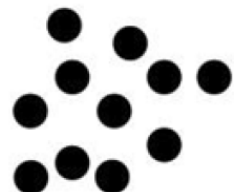


Healthy Volunteers



Standard Dose

Critically Ill Patients



Standard Dose

**Table 1 Antibiotic Physicochemical Characteristics**

Hydrophilic	Lipophilic
Beta-Lactams	Fluoroquinolones
Aminoglycosides	Macrolides
Glycopeptides	Lincosamides
Linezolid	Tetracyclines and Tigecycline
Daptomycin	Daptomycin
Polymyxins	Rifampicin
	Metronidazole
	Azoles
	Echinocandins

Table 1. Effect of Plasma Exchange on Various Classes of Drugs (continued)

Drug Class, Drug	Type of Publication	Indication	Plasma Exchange	
			Drug Removal	Time After Last Dose (hrs) <sup>a</sup>
Ceftriaxone (continued)	Phase II parallel-group trial (n=11) <sup>37</sup>	Early vs late administration	No; 12.6% (early) or 5.7% (late) of 2-g dose	3 or 15
Ceftazidime	Phase II trial (n=11) <sup>38</sup>	Various; $Cl_{cr} > 50$ (6 patients) or $< 50$ (5 patients) ml/min	No; 5% of administered dose	0.25–2
Chloramphenicol	Case report (n=1) <sup>39</sup>	Intoxication	Yes	29
Tobramycin	Case report (n=1) <sup>40</sup>	TTP	Yes; 11% of total body stores	NR
	Case report (n=2) <sup>41</sup>	Hyperviscosity syndrome and myasthenia gravis	Yes; 4.3–6.1% of total body stores	0.66–5.5
	Case report (n=1) <sup>42</sup>	Myositis	Yes; 6.8–10.8% of total stores	18, 1 <sup>d</sup>
Gentamicin	Phase II trial (n=15) <sup>35</sup>	Neonatal sepsis and hyperbilirubinemia	Yes; 33.1% mean drop in concentration	2–10
	Phase II trial (n=7, 8 controls) <sup>43</sup>	Neonatal hyperbilirubinemia	Yes; ~5% of single dose	~9.5
	Phase II trial (n=7) <sup>44</sup>	Neonatal sepsis and hyperbilirubinemia	Yes; 62% reduction in concentration	3–12
	Phase II trial (n=12) <sup>45</sup>	Neonatal coagulation abnormalities and hyperbilirubinemia	Yes; ~26% drop in concentration	NR
Vancomycin	Case report (n=1) <sup>46</sup>	TTP	No	~24
	Phase II trial (n=12) <sup>47</sup>	Various	No; 6.3% of total body stores	2.75–134.25
	Case report (n=1) <sup>48</sup>	Sickle cell disease	Yes	NR
	Case report (n=1) <sup>49</sup>	TTP, acute renal failure	Yes; 27% reduction in concentration	NR
Teicoplanin	Case report (n=1) <sup>50</sup>	Hemolytic anemia	Yes; 48.5% mean drop in concentration	NR
	Phase II trials (n=12) <sup>51</sup>	Various	Yes; ~20% of dose	0
Antiepileptics Phenytoin	Case report (n=1) <sup>52</sup>	TTP	Yes; 10% of total body stores	NR
	Case report (n=2) <sup>53</sup>	Myasthenia gravis	No; 5% of total body stores	1–1.5
	Case report (n=1) <sup>54</sup>	Overdose	No; 5% of total body stores	4 days
	Case series (n=5) <sup>55</sup>	Healthy (1 patient) or various (4 patients)	No; ~4% of total body stores	12 (4 patients), 2 (1 patient)
	Case report (n=1) <sup>56</sup>	Renal failure due to lupus nephritis	No; ~3% of total body stores	NR
	Case report (n=1) <sup>57</sup>	TTP	No; ~4% of total body stores	NR
	Case report (n=1) <sup>58</sup>	TTP	No; ~9% of total body stores	NR
	Case report (n=1) <sup>59</sup>	TTP	No; 4.6% of total body stores	NA <sup>e</sup>
	Oxcarbazepine	Case report (n=1) <sup>60</sup>	Seizures	No; ~6% of total body stores; 4% of dose
Carbamazepine	Case report (n=1) <sup>61</sup>	Overdose	No; ~6% of total body stores	32
	Case report (n=1) <sup>62</sup>	Overdose	Yes	> 2 days
	Case report (n=1) <sup>63</sup>	Accidental ingestion	Yes	26

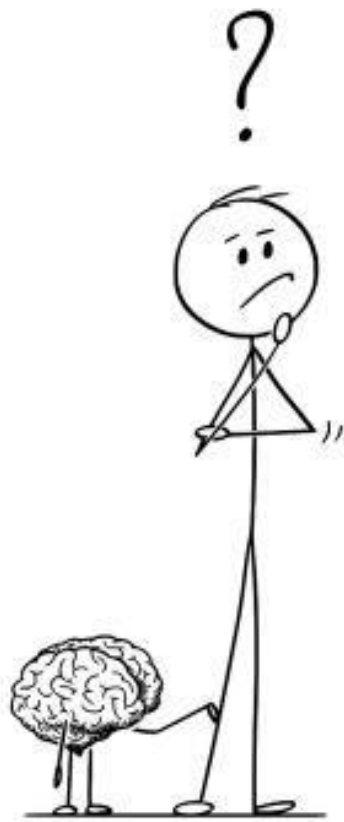


Figure 1A. Dose-Response Curves for Wide Therapeutic Index Medications

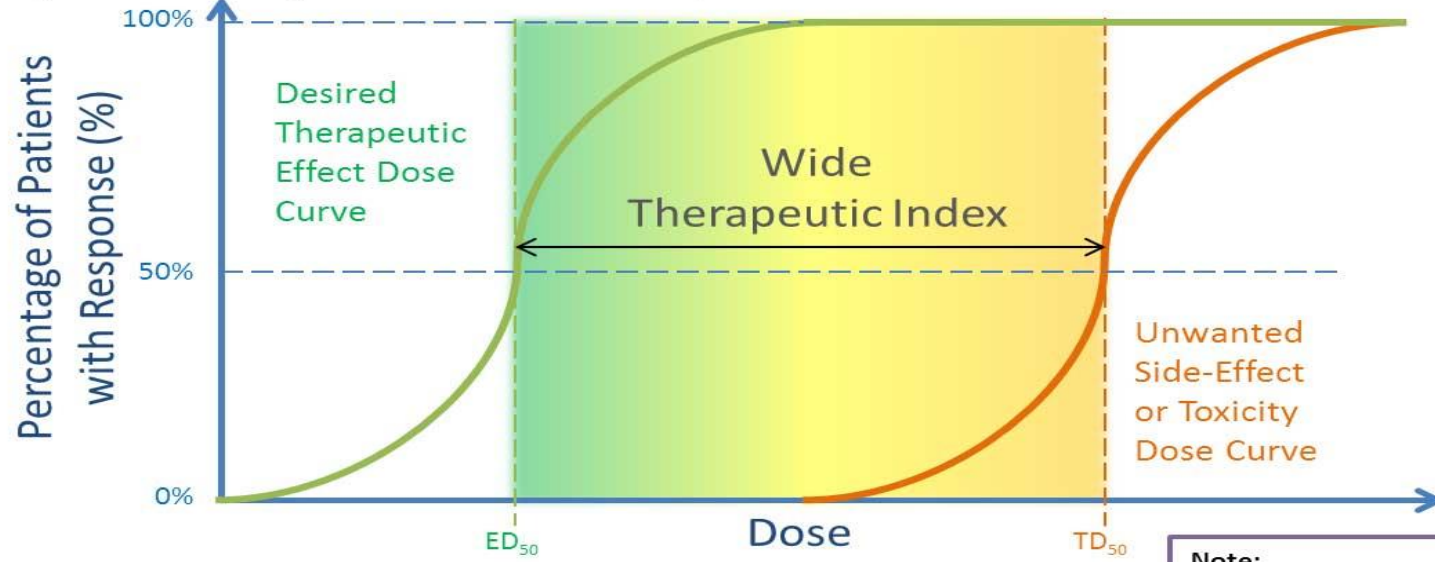
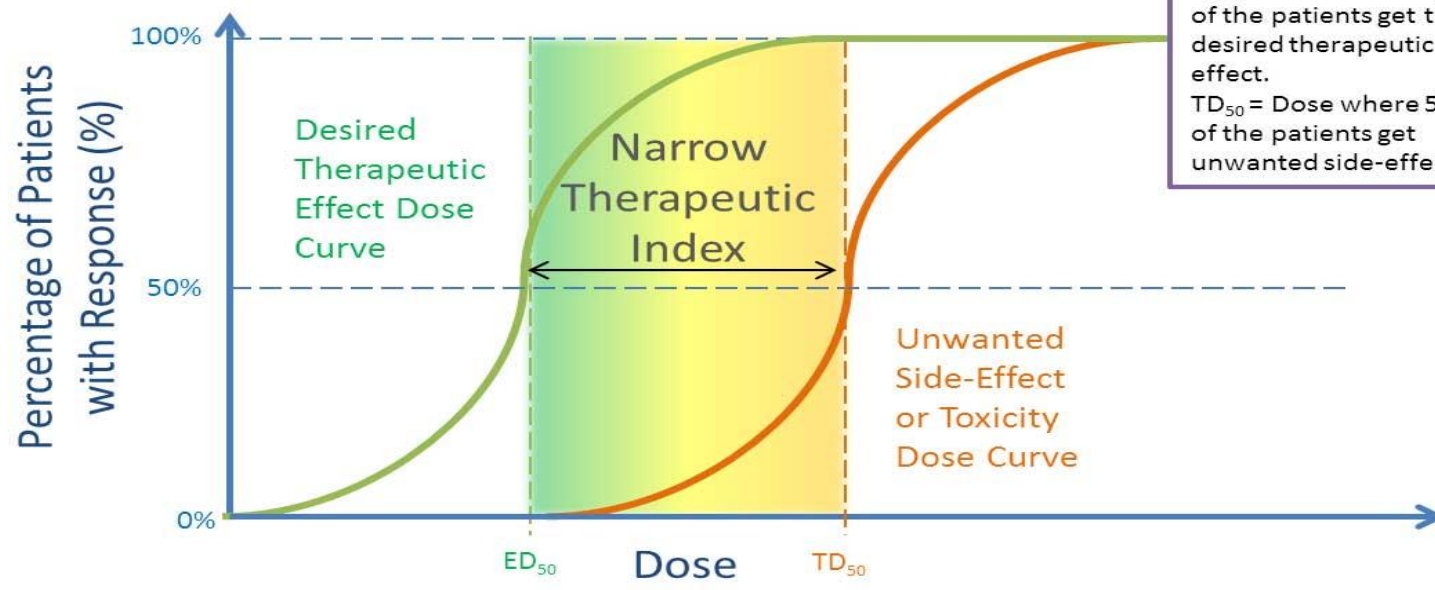
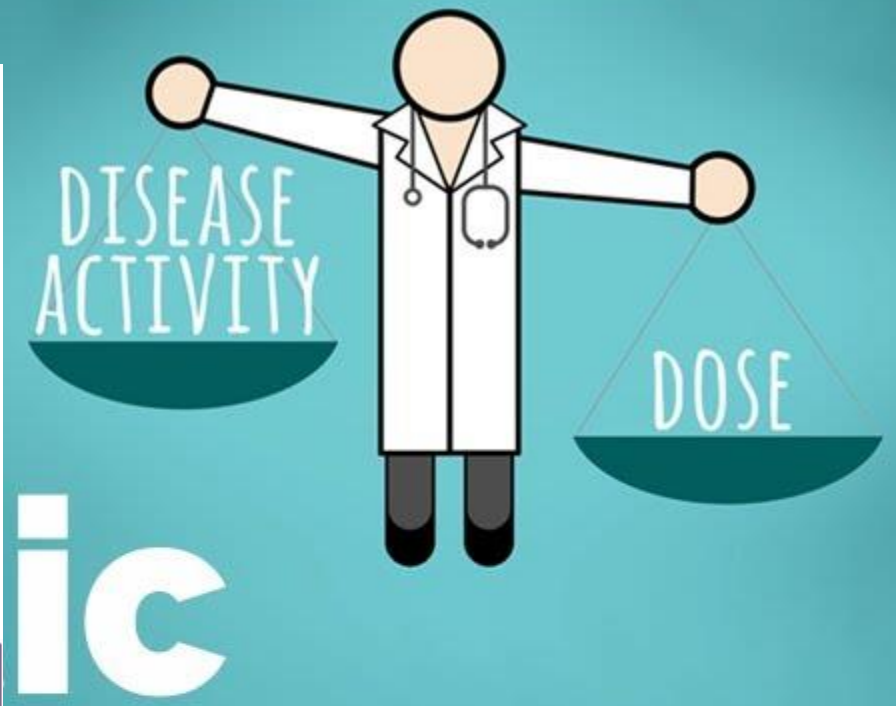


Figure 1B. Dose-Response Curves for Narrow Therapeutic Index Medications



**Note:**  
 $ED_{50}$  = Dose where 50% of the patients get the desired therapeutic effect.  
 $TD_{50}$  = Dose where 50% of the patients get unwanted side-effect.



**Table 5**

Most common findings of mild specified AE/10,000 procedures.

Symptom, reason	AE/10,000
Access problems	130
Hypotension	36
Tingling	19
Device problems	17
Urticaria	12
Nausea/vomiting	12
Hematoma at puncture site	10
Hypertension	5
Flush	2
Phlebitis	2
Shivering, fever	2
Arrhythmia	1
Back pain	1
Vertigo	1

**Table 6**

Most common findings of moderate specified AEs/10,000 procedures.

Symptom, reason	AEs
Tingling	174
Urticaria	45
Hypotension	30
Nausea	9
Technical problems	6
Hypertension	6
Chills and fever	6
Flush	5

**Table 7**

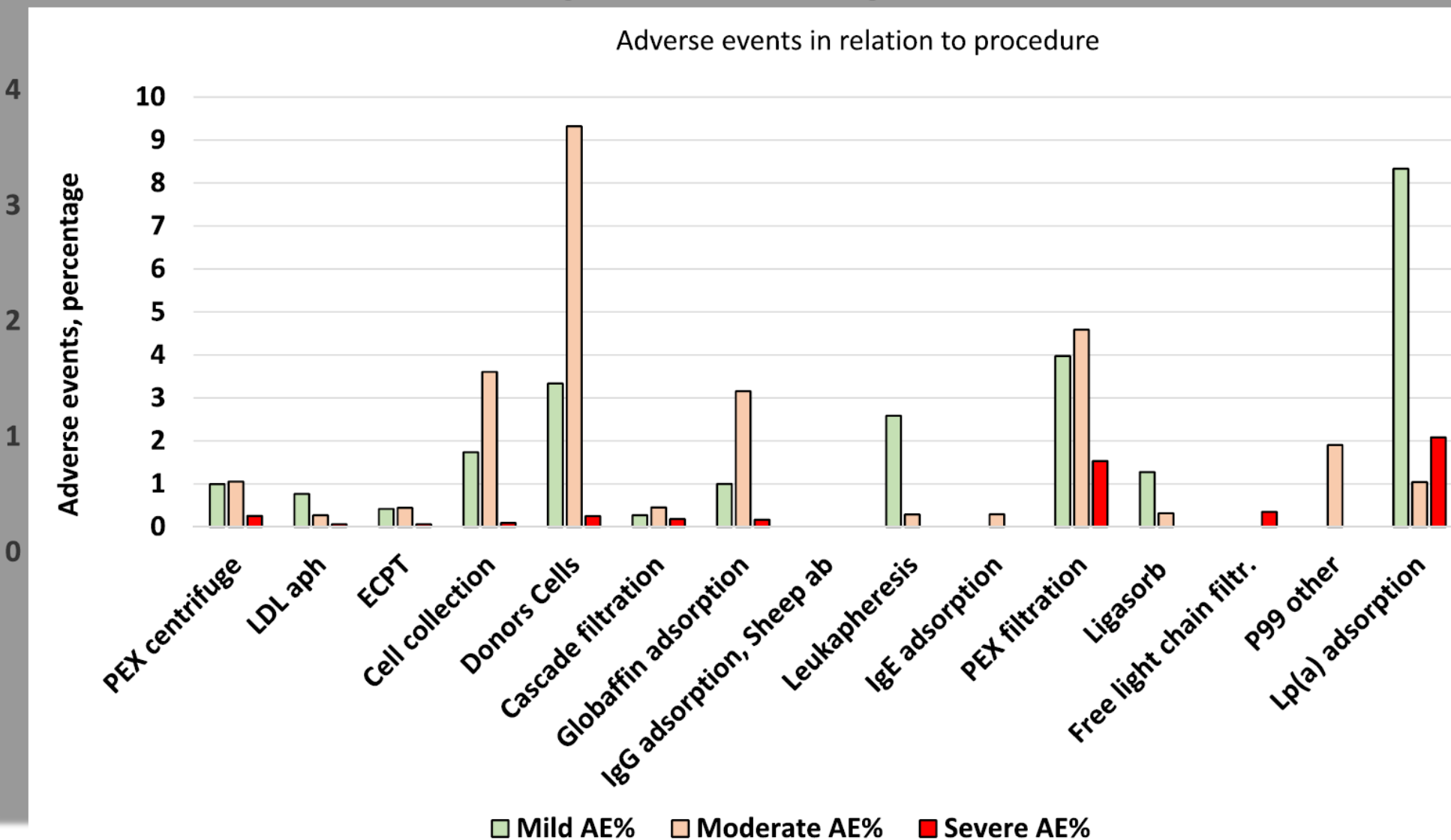
Severe adverse events (primary reason in 168 procedures) resulting in interruption of apheresis given as specified AEs/10,000 procedures.

Symptom, reason	AEs
Hypotension, syncope	11
Urticaria	6
Fever, chills	3
Nausea, vomit	2
Access problem	2
Flush	2
Tingling, stitching	2
Arrhythmia	2
Bronchospasm	1
Quincke edema	1
Technical problem	0.8
Abdominal pain	0.8
Back pain	0.8
Epilepsy	0.6
Hypertension	0.4
Spasm	0.4
Asystolia	0.2
TRALI chest pain	0.2
Anaphylaxis	0.2
Gastro intestinal bleeding	0.2
Wrong plasma	0.2
Adverse event to drug	0.2
Chest pain	0.2
Anxiety + hyperventilation	0.2

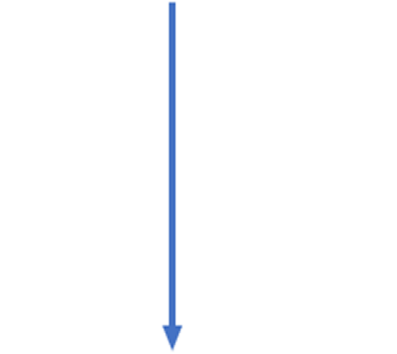
## Adverse events in % of procedures /year

Adverse events, %

Percentage of Adverse events



**Number of admissions to ICUs**  
2015-2019 : 15,000 patients



**Eligible patients by screening**  
« plasma exchange » using the  
PMSI : 131

**Patients excluded :**  
7 did not undergo TPE

**Included patients : 124**  
Plasmafiltration : 68 (55%)  
Double cascade filtration : 50 (40%)  
Centrifugation : 15 (12%)  
  
(711 TPE sessions)

**N (%) or Median [Q1–Q3]** **Patients (n = 124)**

Indication for TPE	
Thrombotic microangiopathy	32 (26)
Myasthenia	25 (20)
Acute polyradiculoneuritis	12 (10)
Catastrophic antiphospholipid syndrome	9 (7)
ANCA vasculitis	8 (6)
Other	38 (31)

TPE modality and characteristics (711 sessions)	
Plasma filtration	68 (55)
Double cascade filtration	50 (40)
Centrifugation	15 (12)

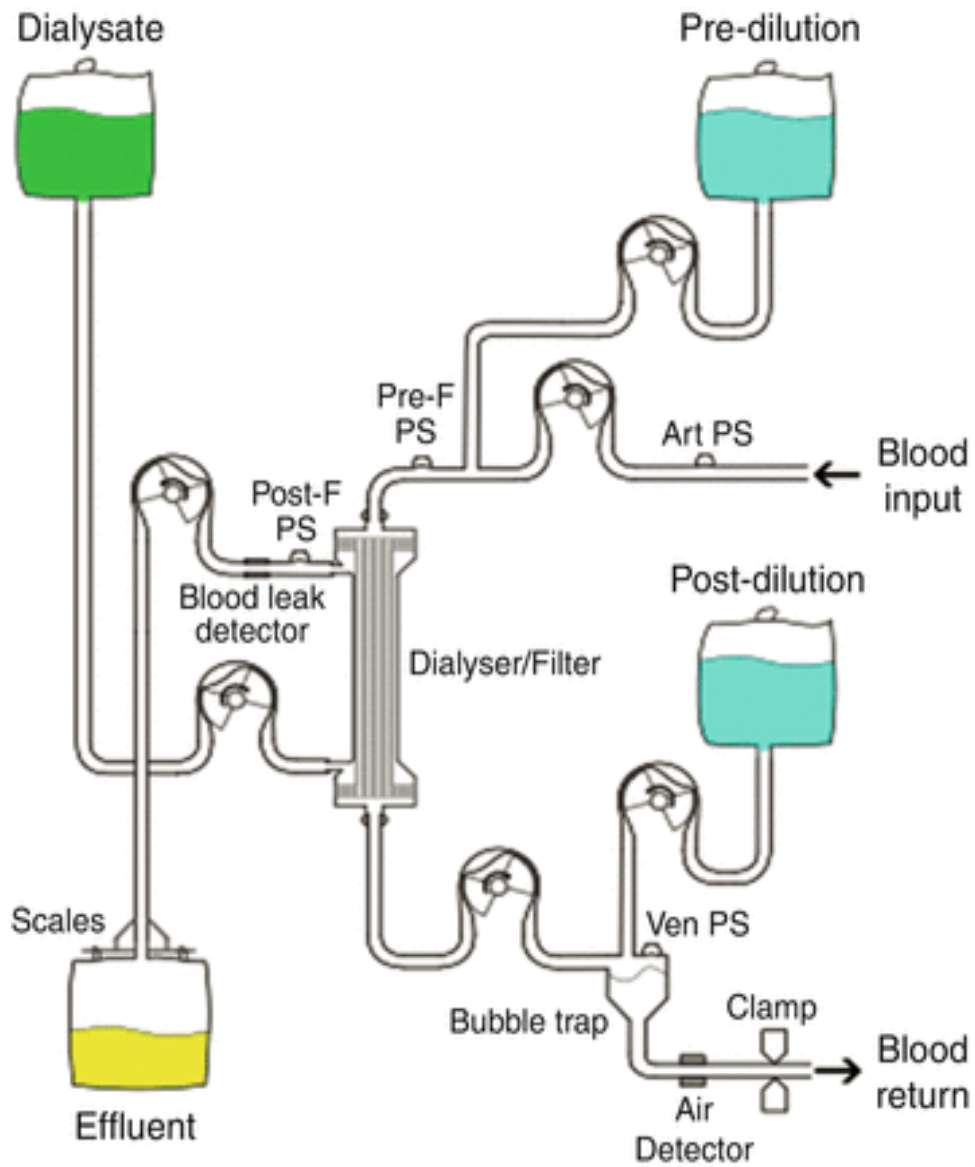
No. of sessions per patient	5 [2–7]
Duration of treatment, d	7 [3–12]
Volume of plasma treated, mL/kg	52 [45–60]
Substitute products	
Plasma alone	53 (43)
Albumin alone	46 (37)
Plasma + albumin	35 (28)

Adverse events during TPE	
Arterial hypotension	22 (21)
Fever	12 (12)
Electrolyte disturbance	9 (9)
Arrhythmia	7 (7)
Pruritus-urticaria	3 (3)
Nausea-vomiting	2 (2)
Cardiac arrest	1 (1)

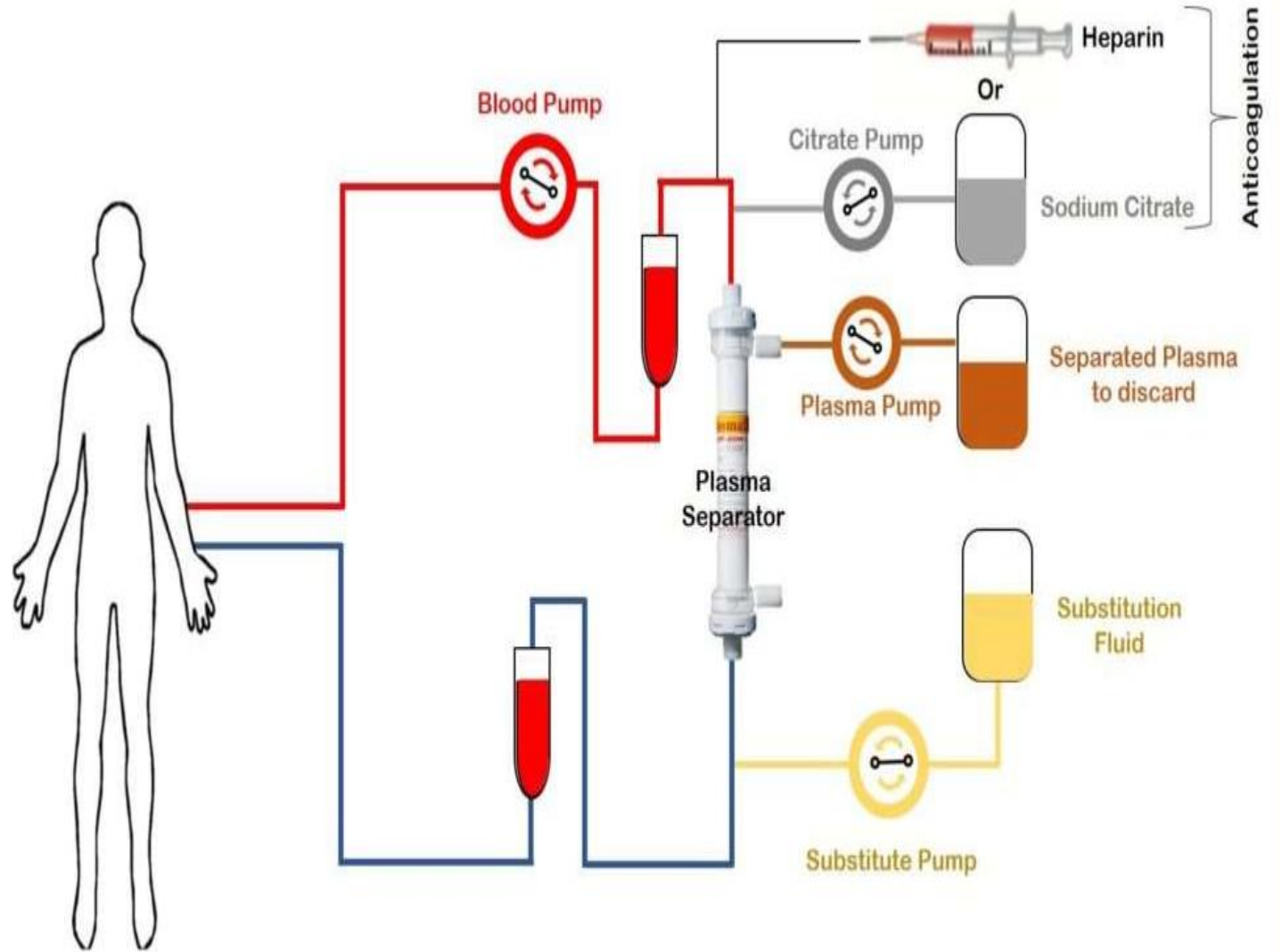
Infectious complications	
At least one infectious event	60 (48)
Pneumonia	
Nosocomial pneumonia	13 (10)
Ventilator-associated pneumonia	42 (34)
Viral reactivation	
Bacteremia	18 (14)
Catheter-related infection	
Elapsed time to first infectious complication, d	
From ICU admission	9 [4–14]
From TPE initiation	5 [2–8]

**TABLE 3.****Comparison of the Studied Population to the Control Group**

<b>N (%) or Median [Q1–Q3]</b>	<b>Control Group (n = 124)</b>	<b>Therapeutic Plasma Exchange Group (n = 124)</b>	<b>p</b>
Age, yr	56 [41–68]	54 [39–72]	0.76
Gender (male)	73	55	0.22
Sequential Organ Failure Assessment	6 [3–9]	5 [2–8]	0.50
Simplified Acute Physiology Score II	43 [31–60]	36 [25–51]	0.01
Invasive mechanical ventilation	80 (64)	78 (63%)	0.79
Duration, d	13 [6–20]	14 [7–22]	0.75
Renal replacement therapy	25 (20)	36 (29)	0.11
Duration, d	4 [1–7]	10 [3–17]	0.06
Vasopressor support	78 (63)	56 (45)	0.01
Duration, d	4 [3–10]	6 [2–11]	0.79
ICU Length of stay, d	14 [6–24]	14 [6–26]	0.74
Mortality			
ICU	19 (15)	18 (14)	0.86
In-hospital	22 (18)	27 (22)	0.35
Withdrawal of life-sustaining treatments	26 (21)	20 (16)	0.33
Infectious events			
At least one infectious event	36 (29)	60 (48)	0.01
Ventilator-associated pneumonia	27 (22)	42 (34)	0.03
Pneumonia	4 (3)	13 (10)	0.24
Catheter-related infection	9 (7)	6 (4)	0.28
Blood stream infection	7 (5)	12 (9)	0.91
Septic shock	8 (6)	19 (15)	0.03
Viral reactivation	8 (6)	14 (11)	0.06

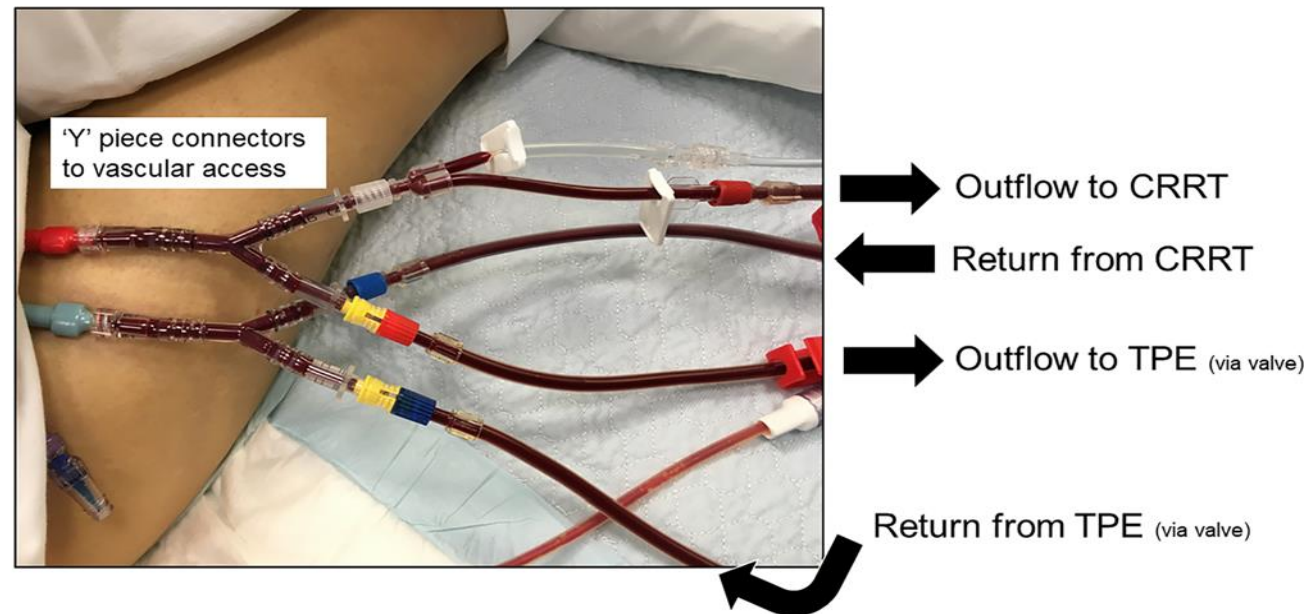
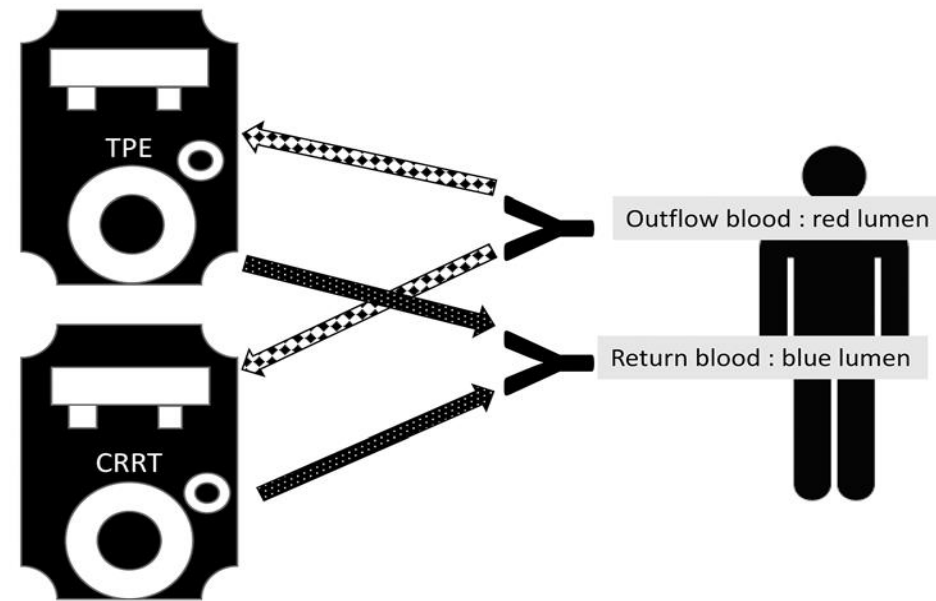
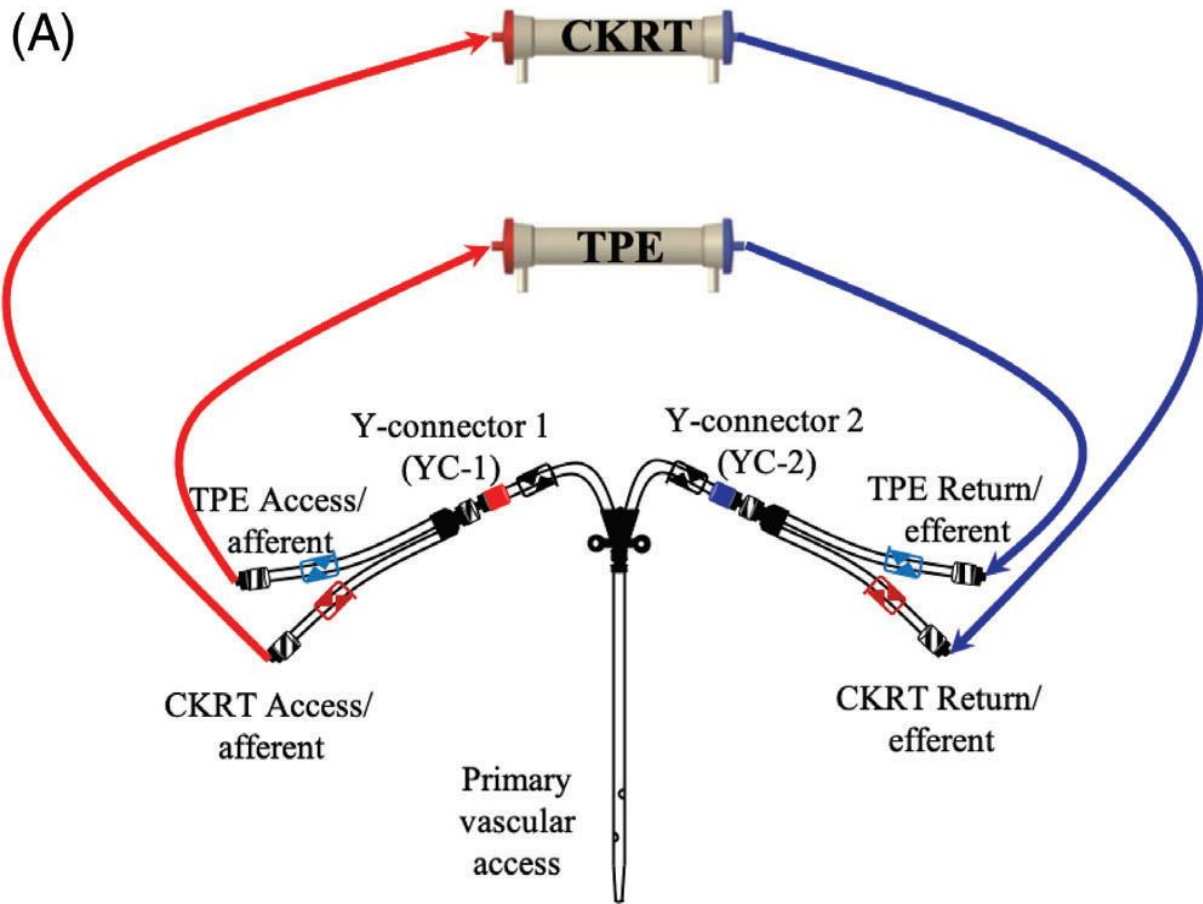


**CRRT**



**Plasmapheresis**

(A)



# Regional Citrate Anticoagulation

Potassium will need to be added unless the patient is hyperkalemic



SID in vitro

SID in vivo



35

35



0

54

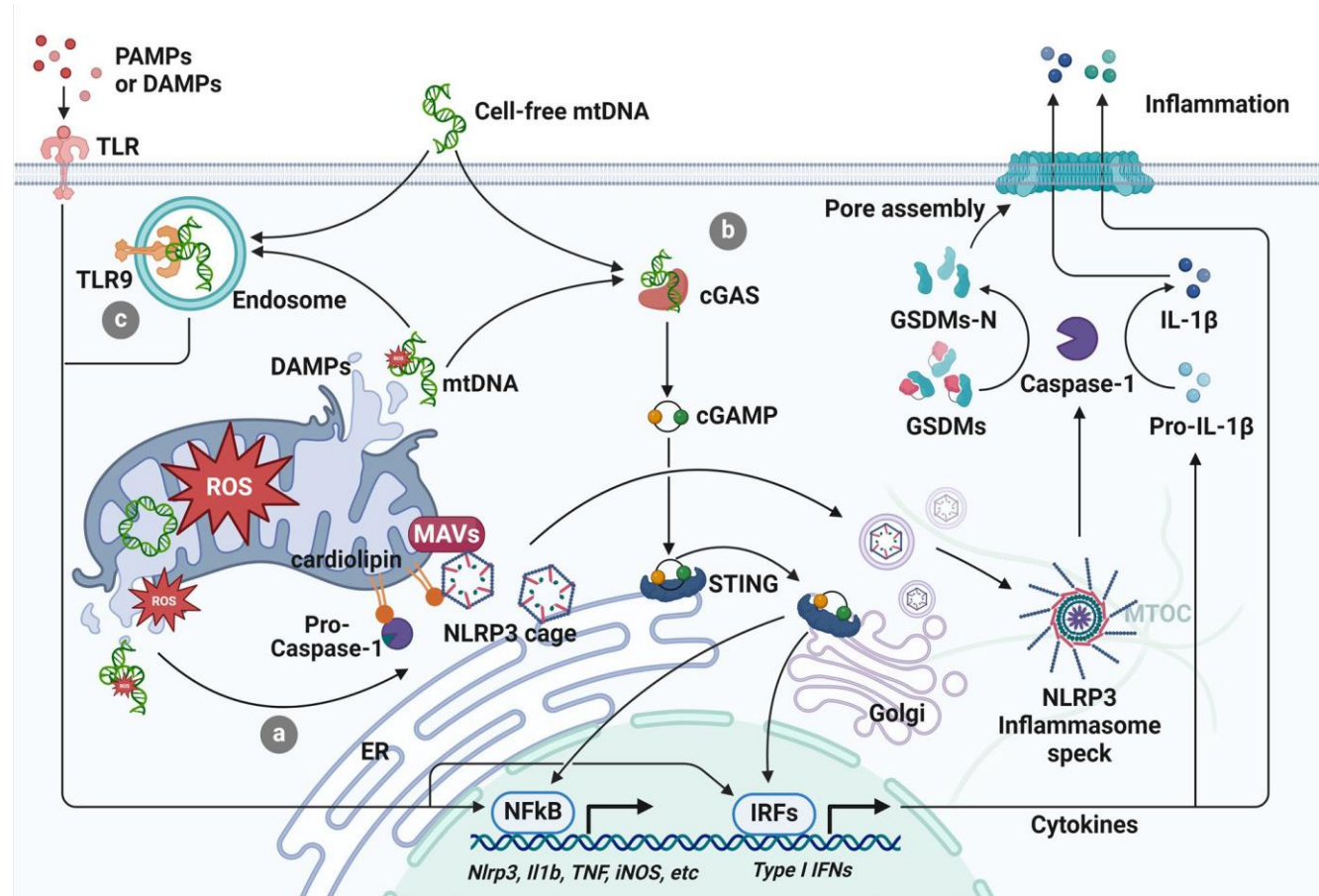
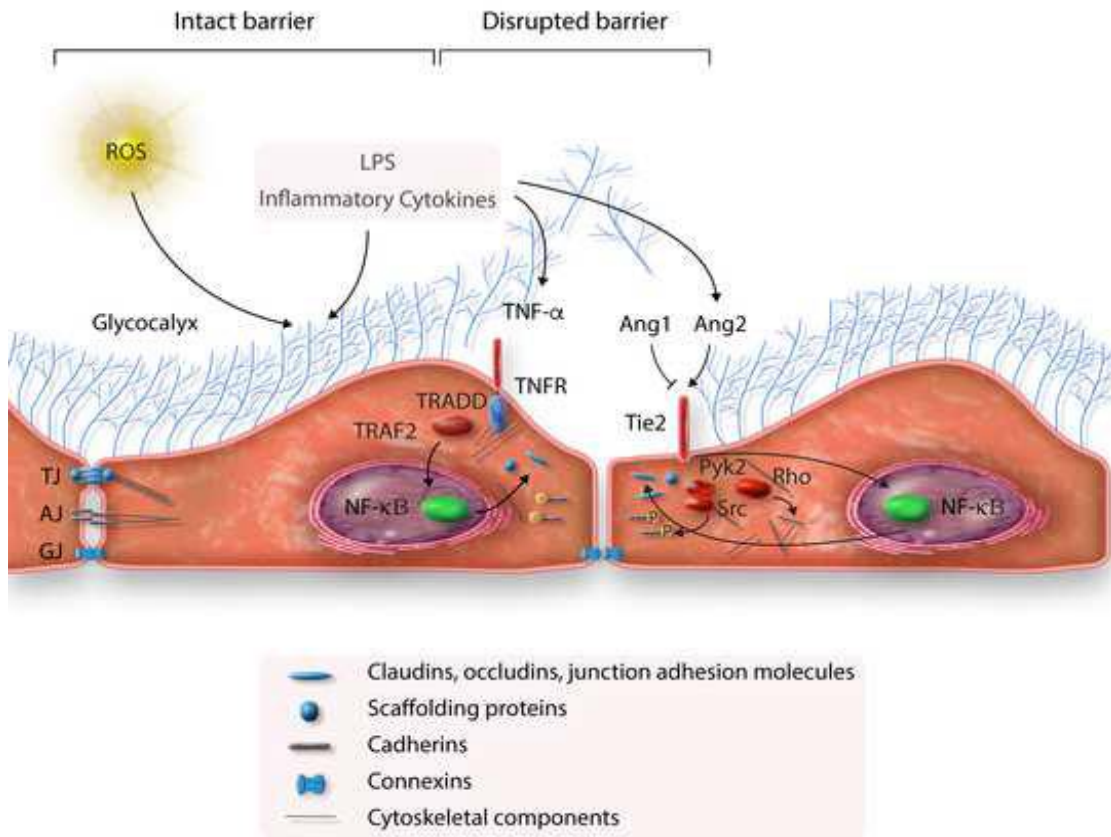


shock

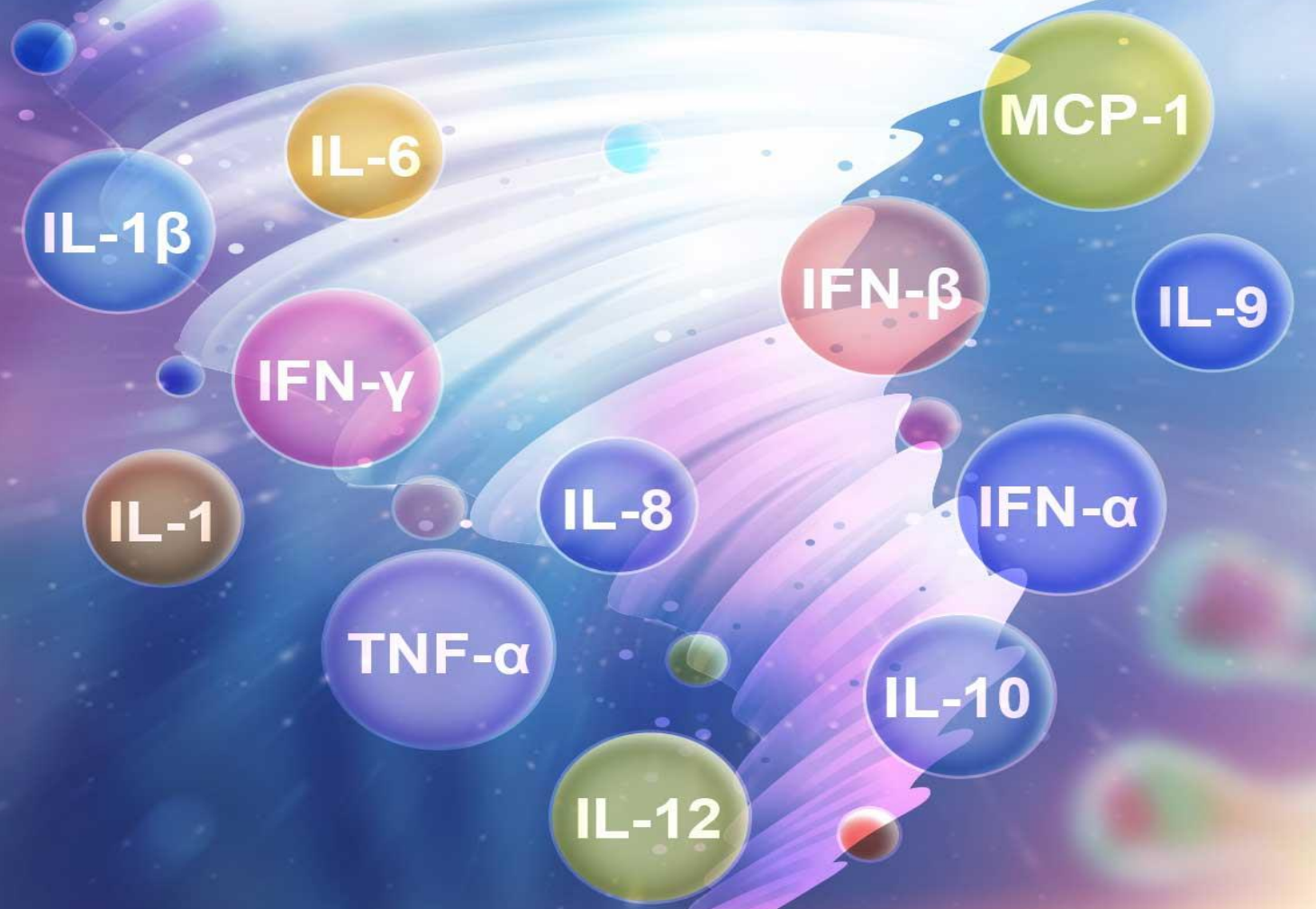


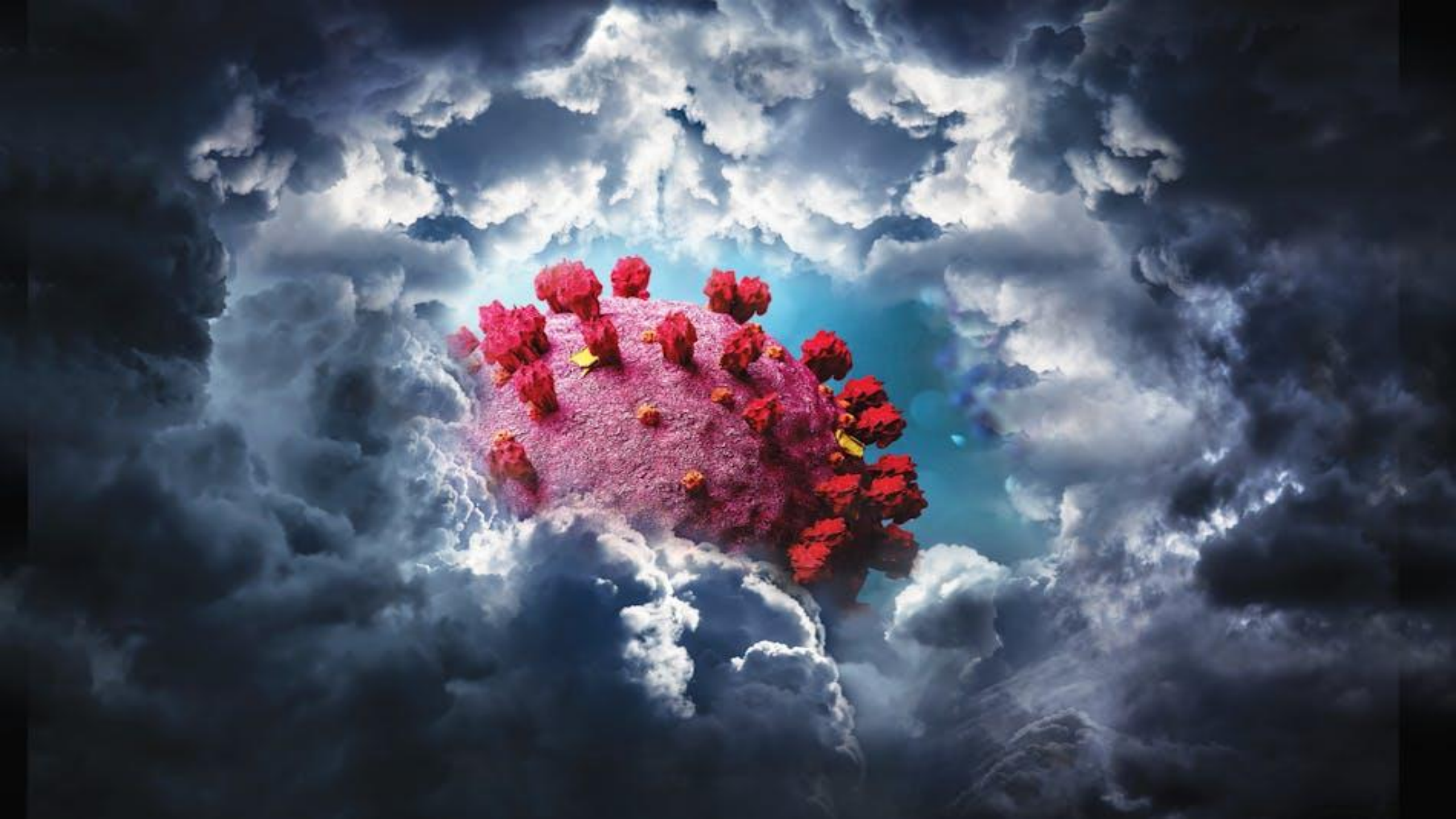
# SEPTIC OF FLESH

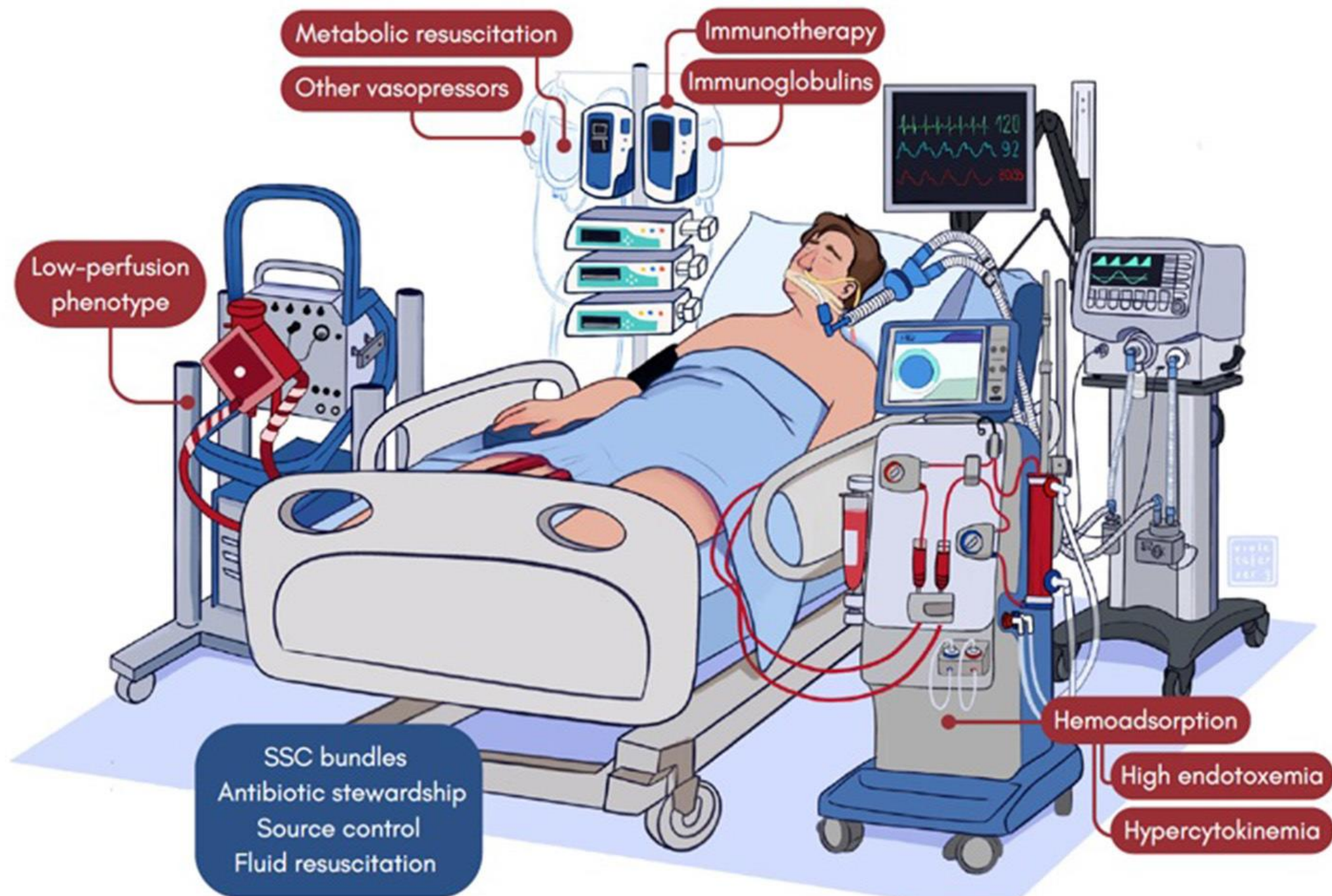
THE GREAT MASS



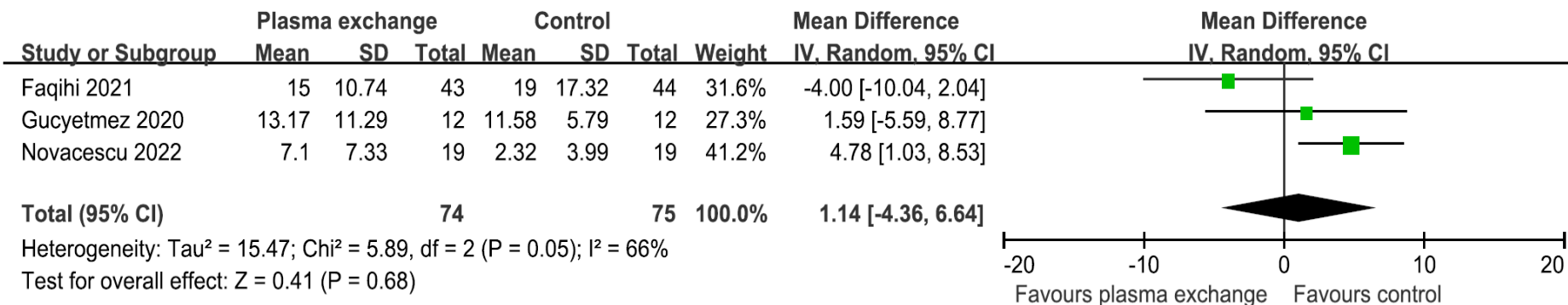
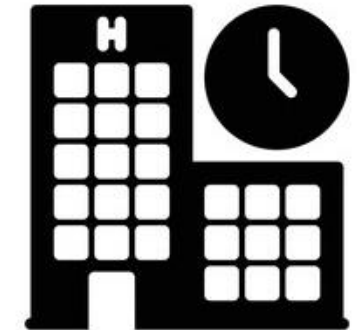
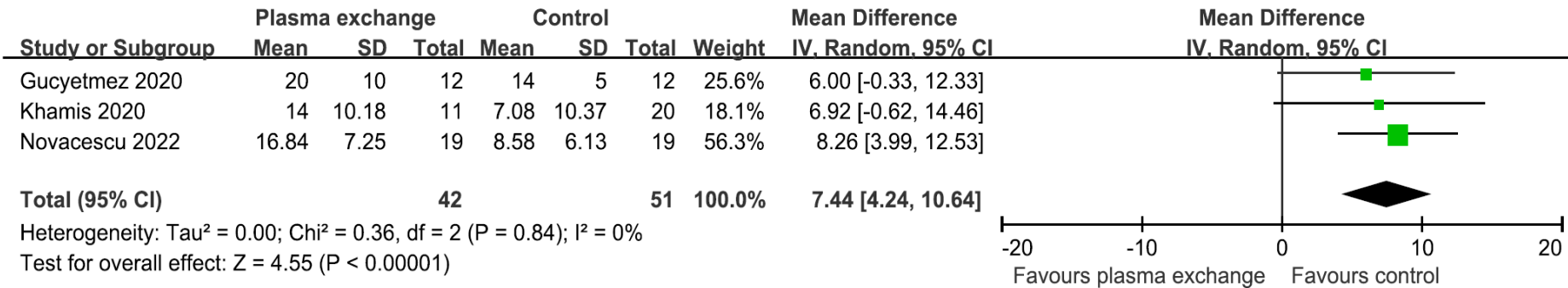
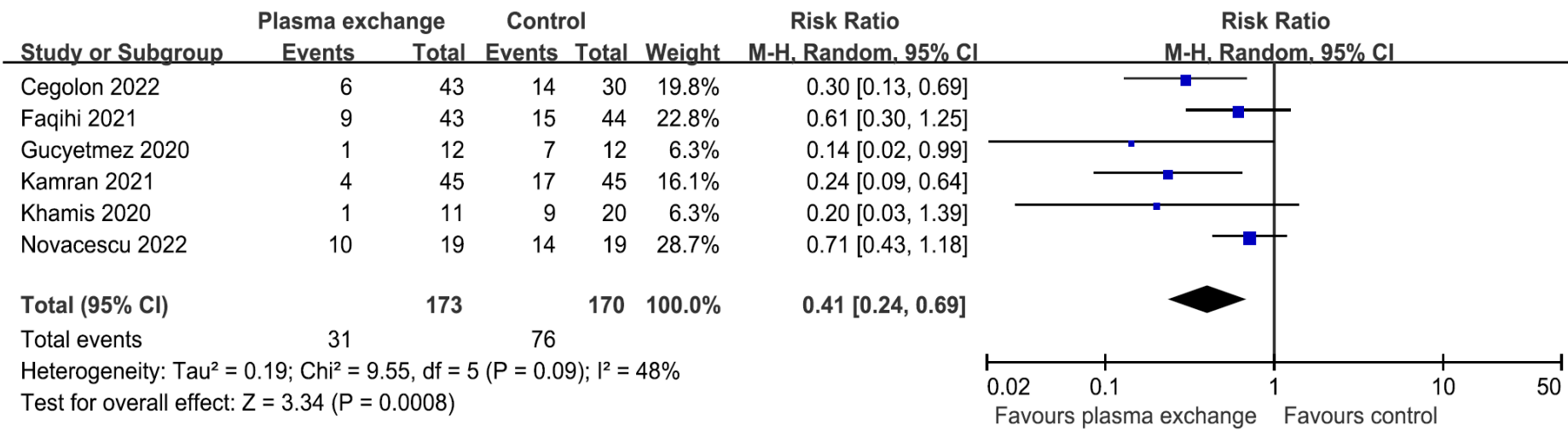
# Cytokine Storm

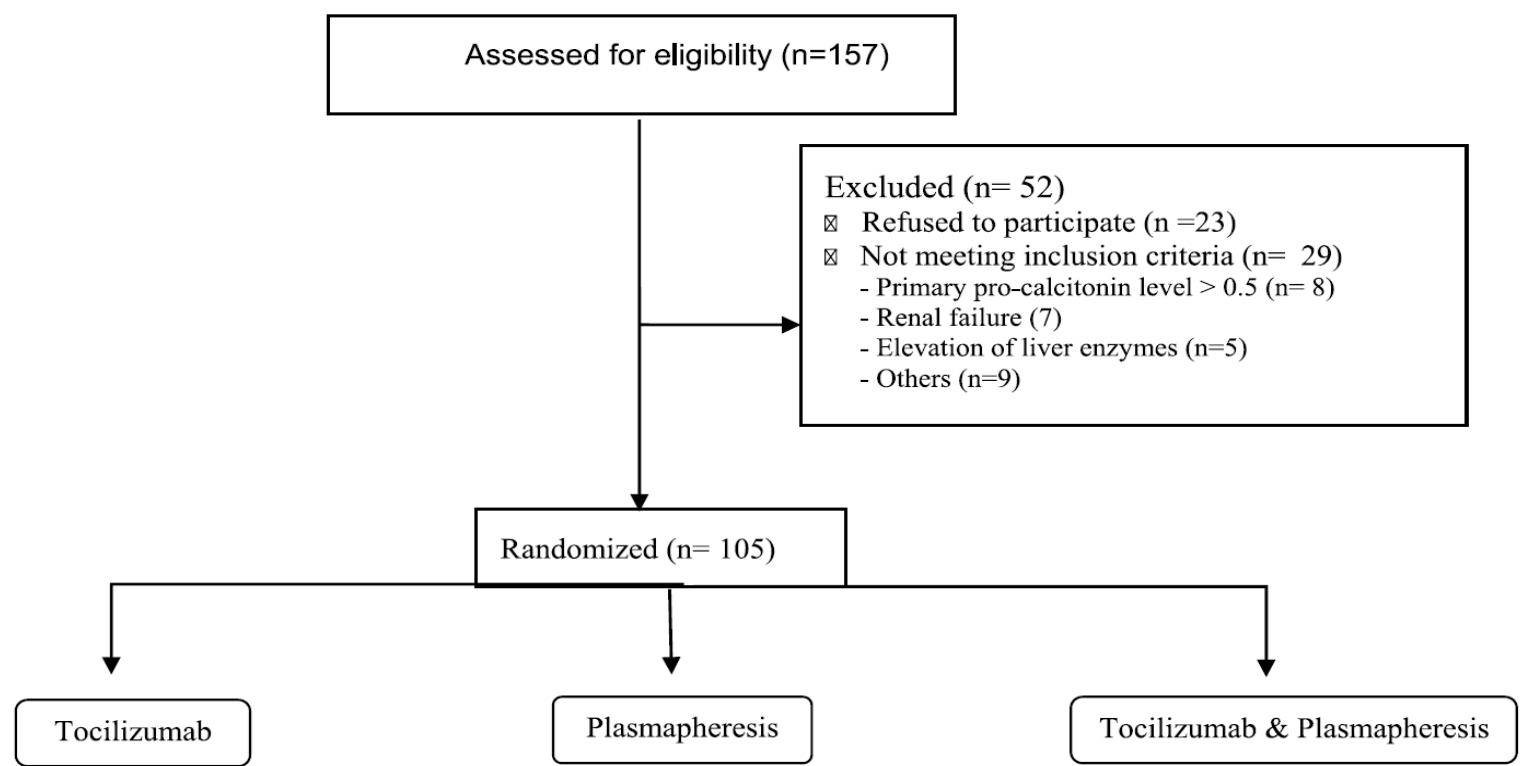
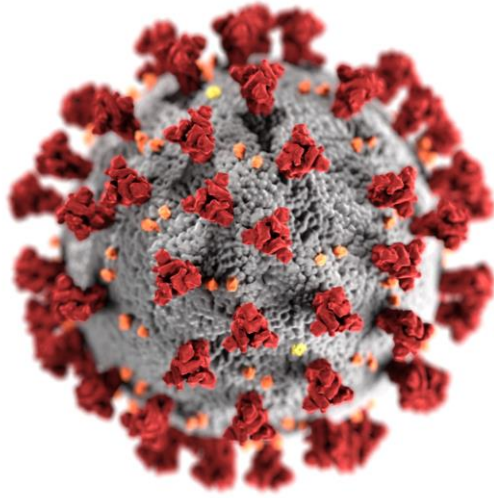








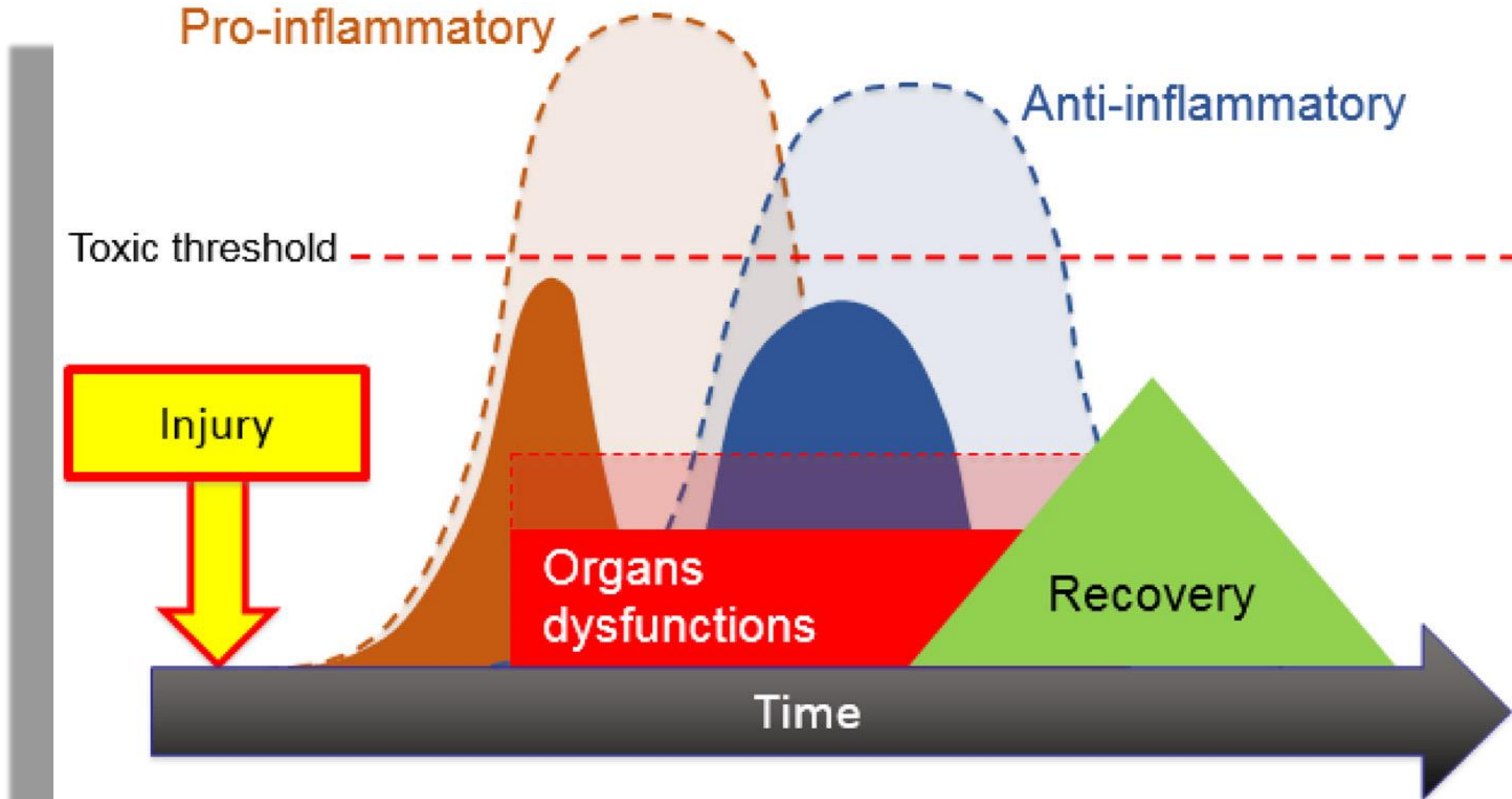




**Table 3**

Comparison of Outcomes & Complications before and after the intervention in the study groups.

Variable	Tocilizumab	Plasmapheresis	Plasmapheresis & Tocilizumab	p-value
Hospital length of stay, Mean (SD)	12.29(4.71)	13.30(4.57)	13.12(4.90)	0.68
ICU length of stay, Mean (SD)	9.82(4.06)	11.15(4.07)	10.48(4.52)	0.48
O2 saturation ranges at discharge with supplementary o2, Mean (SD)	91.68(1.64)	92.20(2.12)	92.88(2.12)	0.12
Intubation, F (%)	6(21.4)	9(27.3)	8(24.2)	0.87
NIPPV, F (%)	15(53.6)	15(45.5)	13(39.4)	0.54
Death, F (%)	7(25)	9(27.3)	8(24.2)	0.96
Discharge, F (%)	22(78.6)	25(75.8)	26(77.7)	0.95
<b>Complication</b>				
Infection, F (%)	5(17.9)	10(30.3)	6(18.2)	0.40
GI. Bleeding, F (%)	3(10.7)	5(15.2)	2(6.1)	0.49
Thrombosis, F (%)	1(3.1)	3(9.1)	0	0.18



VOLUME in intensive care; NA, not applicable; PAMP, pathogen-associated molecular patterns; RCT, randomized controlled trial; SOFA, sequential organ failure assessment; TNF, tumor necrosis factor.

A large teal circle is centered on the page, containing the text. The background is a grayscale anatomical illustration of a human torso, showing the ribcage, spine, and internal organs like the kidneys and bladder.

## Reasons To See a Nephrologist

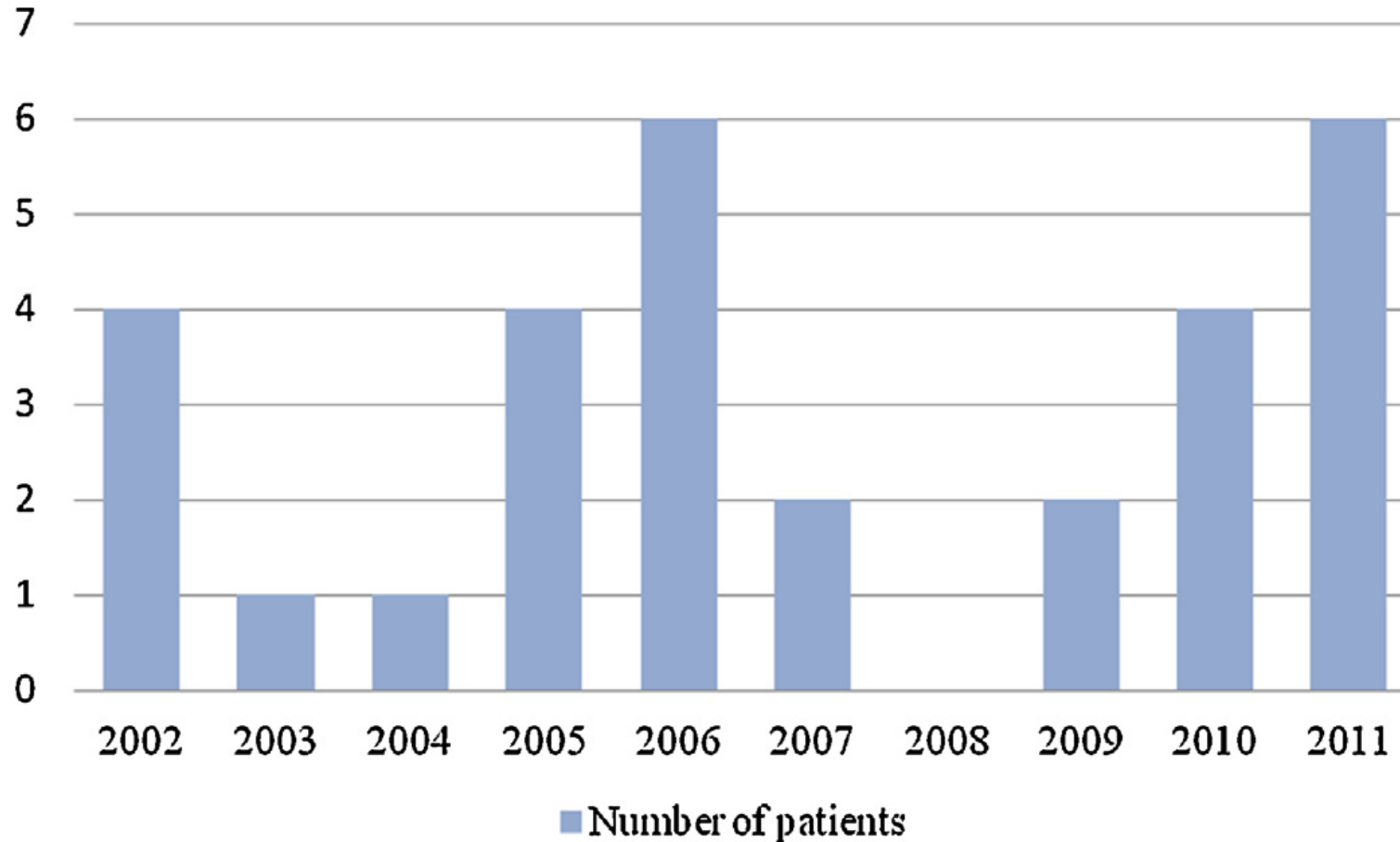




## Plasma exchange in the intensive care unit: A 10 year retrospective audit

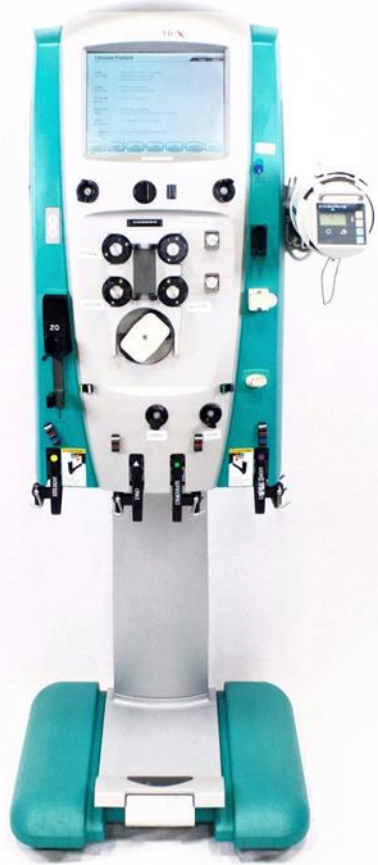
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**$N = 19.728$**

**$n = 30$**



# Moving Points

## Debates in Nephrology

Kidney360

*Intensive Care Med*  
DOI 10.1007/s00134-017-4788-y

*Intensive Care Med*  
DOI 10.1007

### EDITORIAL

# A nephrologist should be consulted in all cases of acute kidney injury in the ICU: We are not sure



CrossMark

360

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