# THERAPEUTIC PLASMA EXCHANGE - COMPLICATIONS

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# INTRODUCTION

- ***<u>Therapeutic plasma exchange (TPE):</u>***

- - is an extracorporal treatment
- - denotes selective removal of plasma from the circulation
- - removal of certain pathologic substances will ↓ organ or tissue damage

# Prevention of volume depletion during TPE

The volume of patient plasma that is removed should be replaced by appropriate amounts of:

- plasma

- 5-20% albumin + substitution fluid

- crystalloid or

- a combination of these fluids

# General rule

**Donor plasma** should be **avoided**, if possible, if apheresis is used to remove a protein or other non-cellular pathological factor.

The main exception: **donor plasma** is used for thrombotic thrombocytopenic purpura **(TTP)** because it provides the ADAMTS13 enzyme.

# TPE complications

Related to:

- vascular access

- replacement fluids

- the procedue itself

- the use of anticoagulants

# Main TPE complications

- Hypocalcemia
- Vascular complications
- Volume overload
- Hypotension
- Removal/clinically relevant decrease in certain proteins or medications

# The frequency and types of TPE complications

Depend on:

- patient factors and overall patient condition

- the number of procedures

- replacement fluid and

- the approach to venous access

# The frequency and types of TPE complications

- In >50,000 procedures (7142 patients): 5.8% complications[1]
- The most common complications:
- - paresthesias (citrate anticoagulant-associated-hypocalcemia)
- - vascular access issues

- In >15,000 TPE treatments[2]: adverse reactions were substantially more common with plasma than albumin replacement (20 vs 1.4 %)


- 1. Transfus Apher Sci. 2016;54(1):2
- 2. Am J Kidney Dis. 1994;23(6):817

# Any replacement fluid

A common issue is **citrate-induced hypocalcemia** (binding of ionized (free) Ca by citrate that is used as an anticoagulant during the procedure).

Symptoms include:

- perioral and distal extremity paresthesias or numbness

- nausea and vomiting

- muscle cramps

- chest pain

- hypotension

- tetany or arrhythmias such as QT prolongation (extreme situations)

# Citrate-induced hypocalcemia

In patients with normal liver function, citrate is generally metabolized within approximately 1.5 hours

Electrocardiographic monitoring and intra-procedural evaluation of ionized calcium levels are appropriate:

- in symptomatic patients who are receiving intravenous calcium infusions

- are at risk of significant citrate sensitivity

- patients with altered mental status or pediatric patients (who may not be able to communicate early symptoms of hypocalcemia)

Apheresis Principles and Practice, 4th ed, Dunbar N, Winters J (Eds), AABB, Bethesda 2020.

# Strategies to reduce citrate-induced hypocalcemia

Slowing the exchange rate

Administer by slow intravenous push one 10 mL ampule of 10% Ca chloride over 15 - 30 minutes;

Pre- and intra-procedural oral Ca supplements can mitigate and/or possibly treat mild hypocalcemia in certain groups such as stable outpatients;

Administration of 5 - 10 mL of 10 % Ca gluconate intravenously over 10 - 15 minutes as in intravenous push can reduce symptoms when oral Ca is not effective;

Apheresis Principles and Practice, 4th ed, Dunbar N, Winters J (Eds), AABB, Bethesda 2020.

# Citrate-induced metabolic alkalosis

Often in patients with concurrent kidney failure due to anti-GBM disease (Goodpasture disease)

Can be managed by hemodialysis

Patients with kidney failure requiring therapeutic apheresis may require hemodialysis following apheresis to restore acid-base, electrolyte, and fluid balance as needed.

Pearl RG, Rosenthal MH. Am J Med. 1985;79(3):391

# Removal of/reduction in medications

Substantial drug removal by TPE:

- medications that are highly protein-bound

- medications that have a small volume of distribution

Administration of these medications should occur **after TPE**:

- rituximab, eculizumab

- total parenteral nutrition

- intravenous immune globulin (IVIG)

- cyclophosphamide

# Vascular catheter complications

Potential complications include:

- infection
- thrombosis
- perforation
- air embolism
- pain
- nerve damage

# Non-plasma replacement fluids for plasma exchange

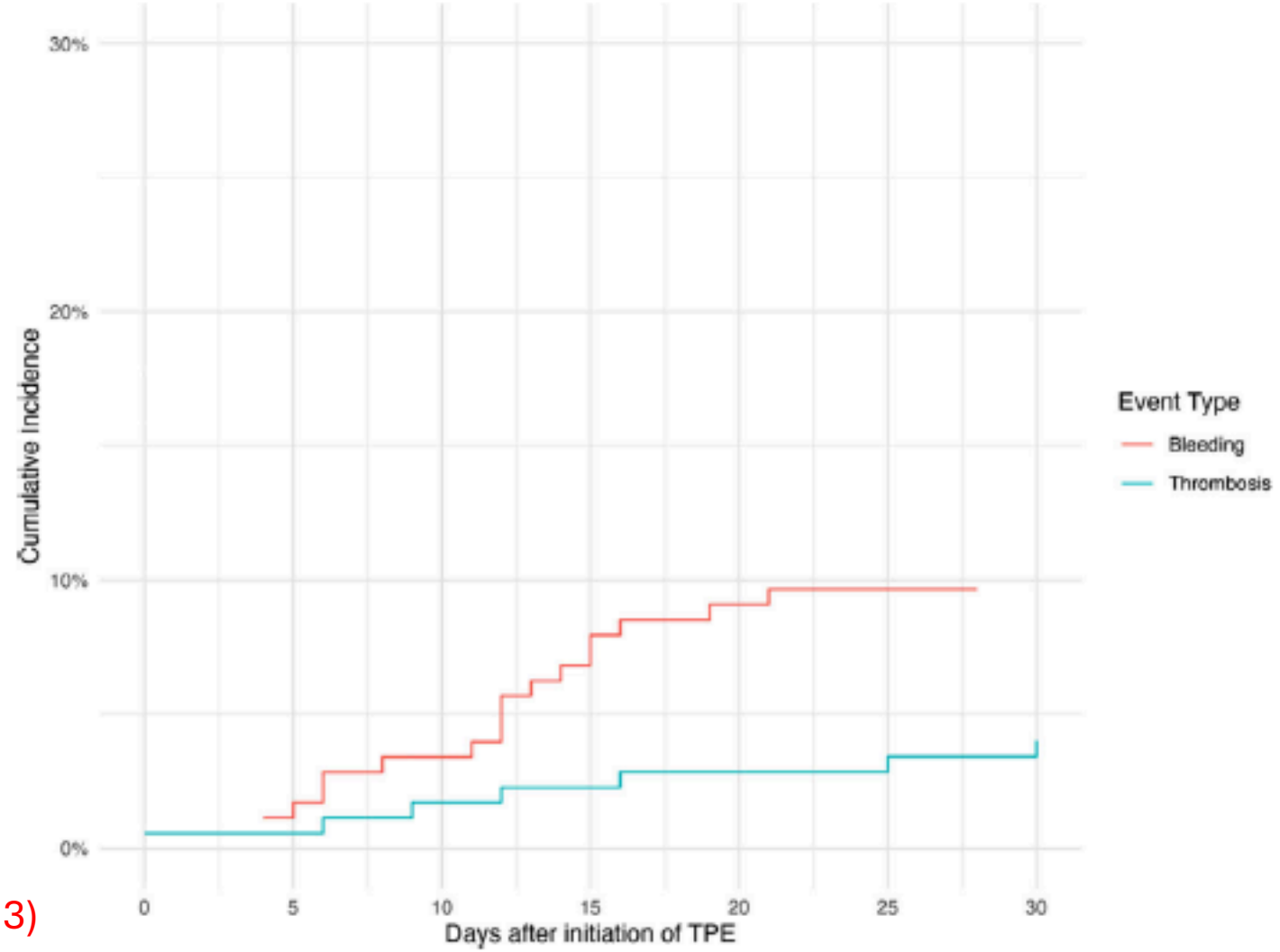
May cause:

- **hypokalemia** ( up to 25 % ↓ in plasma K concentration in the post-apheresis period)

- **reduction in coagulation factors** (the greatest risk factors for bleeding were CKD and hypertension)

- patients with high bleeding risk (immediately after a kidney biopsy): one or more liters of plasma may be substituted as the replacement fluid at the end of TPE

FIGURE 1 Cumulative incidence of clinically relevant bleeding and thrombotic events. [Color figure can be viewed at wileyonlinelibrary.com]




145 patients
890 TPE procedures

Risk for bleeding:
Older age, OR 1.08 (95% CI 1.03-1.13)
CKD, OR 4.68 (95% CI 1.33-14.9)

Transfusion. 2025; 65: 1509-17.

# Non-plasma replacement fluids for plasma exchange

- **reduction in immunoglobulins levels:** may lead to an immunodeficient state, leaving the patient susceptible to infection

- **patient undergoing aggressive TPE** (2-3 plasma volume replacements per procedure and/or consecutive daily procedures without plasma replacement):

baseline IgG level should be obtained

IgG level falls below 500 mg/dL and who have a systemic infection → single infusion of intravenous **immune globulin** (IVIG; 100 to 400 mg/kg)

# Non-plasma replacement fluids for plasma exchange

- **hypotension** if the patient is taking an ACE inhibitor

- rarely, symptoms resembling **anaphylaxis** such as flushing, hypotension, abdominal cramping, and other gastrointestinal symptoms, have been reported during TPE in patients receiving ACEi (increased kinin generation?)

recommendation that ACEi be withheld for 24 to 48 hours prior to TPE or

transitioning to an angiotensin II receptor blocker should be considered

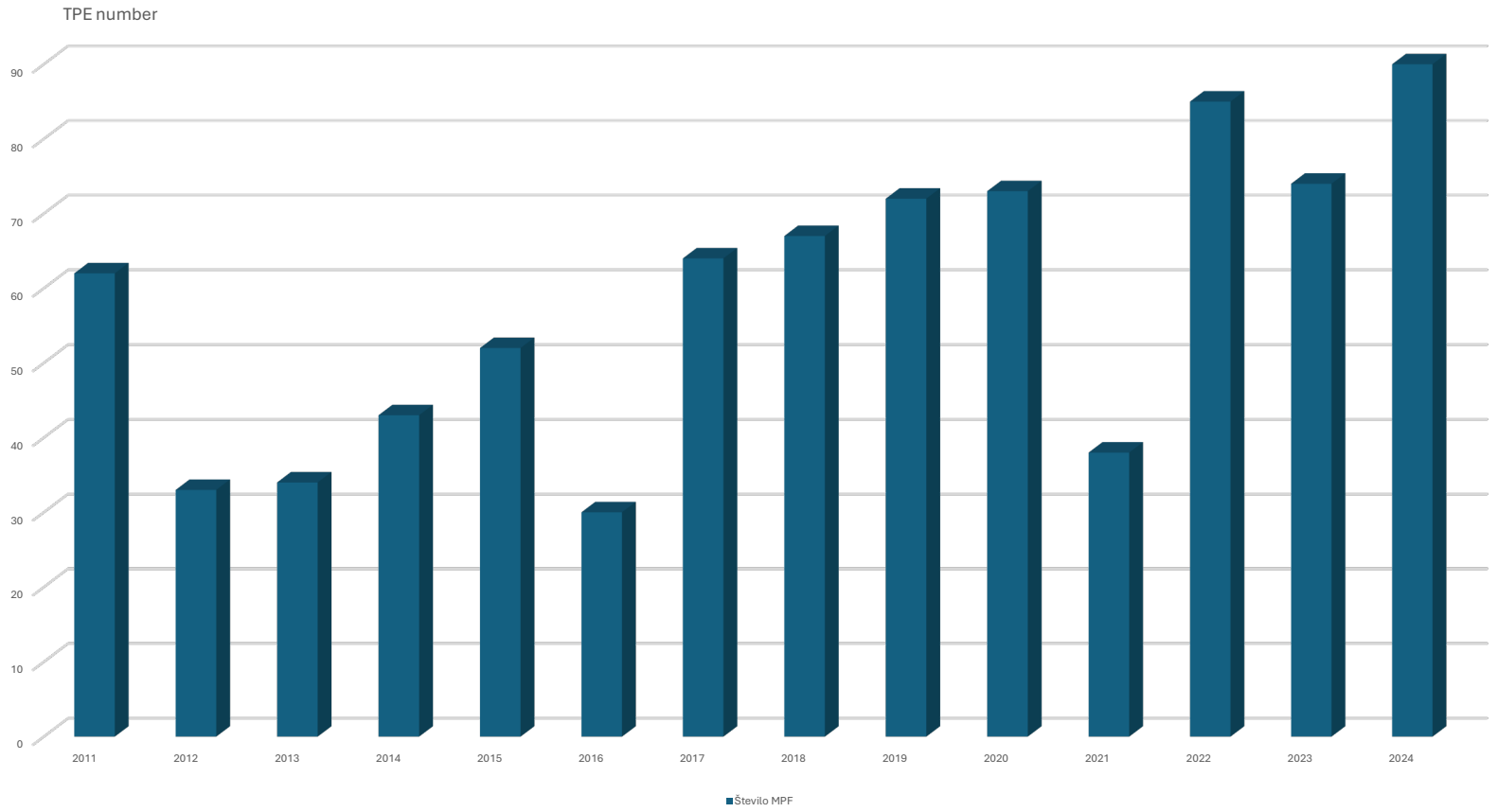
# Donor plasma or RBC exposure

- May cause serious complications such as:
- - **hemolytic transfusion** reactions especially if incompatible products are given;
- - severe **anaphylactic reactions** (in up to 21% of patients);
- - transfusion-related acute **lung injury** (TRALI) (antibodies in donor plasma reacts with "matching" antigens on patient neutrophils, leading to leukoagglutination in the pulmonary circulation and noncardiogenic pulmonary edema);
- - a potential increase in the risk of exposure to transfusion-**transmitted pathogens**;

# Shortness of breath-differential diagnosis

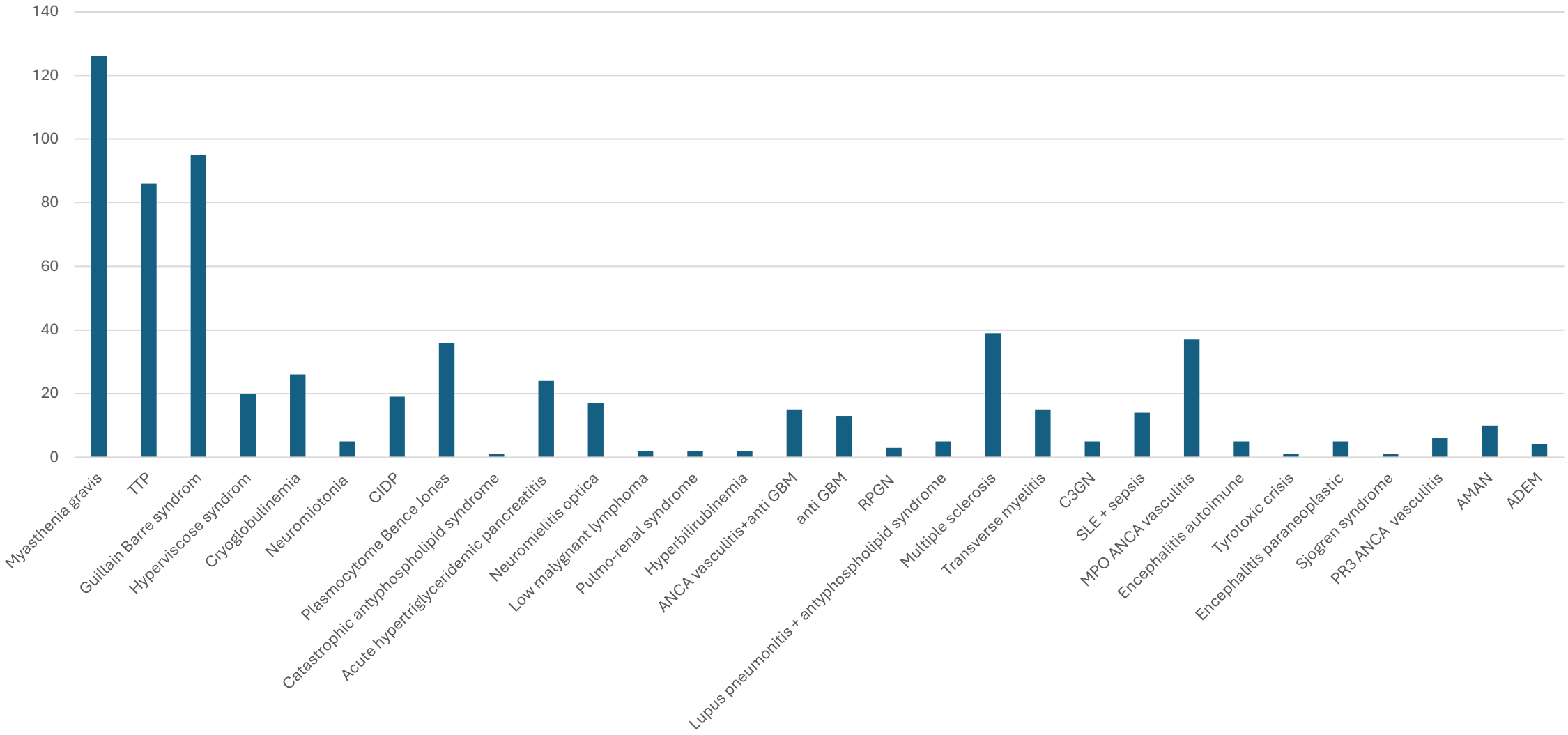
- **Transfusion-related acute lung injury** should be considered if plasma is infused.
- **Pulmonary edema** due to fluid overload.
- **Bronchospasm**, hives, or mucous membrane swelling may be a sign of an impending **anaphylactic reaction** that can be due to plasma in RBCs.
- **Air emboli** caused by air or bubbles in the line, or **pulmonary emboli** due to inadequately anticoagulated blood that contains clots.
- **Complement-mediated membrane bioincompatibility** or sensitivity to ethylene oxide used as a membrane sterilant (very rarely).

# Therapeutic plasma exchange - Department of Dialysis UKC Maribor




Together 817 TPE

# Department of Dialysis UKC Maribor



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- **Analysys of 110 TPE – complications:**
- - 1x hypotension after TPE
- - 1x dysphagia
- - 2x lumbalgia
- - 1x nausea + anxiety before TPE +headache after TPE
- - 1x pruritus + urticaria
- - 1x coagulation of extracorporal circuit system


THANK YOU FOR YOUR ATTENTION.