Therapeutic Plasma Exchange in Glomerular Diseases

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• No conflicts of interest to declare.
Overview

- Therapeutic plasma exchange (TPE)
  - Instrumentation
  - Mechanism of removal
  - Replacement fluids
- American Society for Apheresis (ASFA)
  - Special Issue/Guidelines
- Glomerular diseases treated with TPE
  - Top 4 diseases with best evidence for use of TPE
TPE

- Apheresis
  - Derived from the Greek word “aphairesis”
  - “To remove” or “to separate”

- Plasmapheresis = removal of plasma

- TPE is different
  - Plasma is removed and then replaced by an alternative fluid
TPE Instrumentation at UNC

Cobe Spectra Apheresis System

Spectra Optia Apheresis System
TPE Mechanism of Separation

- Centrifugation

1 = whole blood*
2 = plasma
3 = buffy coat
4 = red cells
5 = waste plasma

*Anticoagulated with citrate
TPE Kinetics

• Very effective at removing
  – Plasma proteins, particularly of higher molecular weights (>30,000 Daltons)
  – Compounds bound to plasma proteins (>80%)
  – Substances with a low volume of distribution ($V_d$) (<0.2 L/kg body mass)

• Not a targeted removal methodology
  – Pathologic and non-pathologic substances removed by TPE

*Ther Apher 5:351-357 (2001)*
$Y/Y_0 = e^{-X}$
## TPE Kinetics

<table>
<thead>
<tr>
<th>Plasma Volume Removed</th>
<th>Fraction Removed (%)</th>
<th>Fraction Remaining (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>40</td>
<td>60</td>
</tr>
<tr>
<td>1.0</td>
<td>63</td>
<td>37</td>
</tr>
<tr>
<td>1.5</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>2.0</td>
<td>86</td>
<td>14</td>
</tr>
<tr>
<td>2.5</td>
<td>91</td>
<td>9</td>
</tr>
<tr>
<td>3.0</td>
<td>94</td>
<td>6</td>
</tr>
</tbody>
</table>
TPE Kinetics

Total Body Water Volume

Extracellular Fluid Volume

Intracellular Fluid Volume, 25 L

Interstitial Fluid Volume, 12 L

Plasma Volume, 3 L
## Candidate Plasma Protein Characteristics

<table>
<thead>
<tr>
<th>Protein</th>
<th>mg/mL</th>
<th>Molecular Weight (Daltons)</th>
<th>Percent Intravascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>IgG</td>
<td>12.1</td>
<td>150,000</td>
<td>45</td>
</tr>
<tr>
<td>IgM</td>
<td>0.9</td>
<td>950,000</td>
<td>76</td>
</tr>
<tr>
<td>Albumin</td>
<td>42</td>
<td>66,000</td>
<td>40</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>3</td>
<td>340,000</td>
<td>80</td>
</tr>
<tr>
<td>α2-macroglobulin</td>
<td>2.6</td>
<td>820,000</td>
<td>100</td>
</tr>
</tbody>
</table>

Alterations in Blood Constituents by 1.0 Plasma Volume TPE*

<table>
<thead>
<tr>
<th>Constituent</th>
<th>Decrease from Baseline Immediately after TPE</th>
<th>Recovery 48 hours after TPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coagulation factors</td>
<td>As much as -50%</td>
<td>As much as +100%</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>-63%</td>
<td>+65%</td>
</tr>
<tr>
<td>Immunoglobulins</td>
<td>-63%</td>
<td>+45%</td>
</tr>
<tr>
<td>Liver enzymes/Bilirubin</td>
<td>As much as -60%</td>
<td>+100%</td>
</tr>
<tr>
<td>Platelets</td>
<td>As much as -30%</td>
<td>As much as +100%</td>
</tr>
</tbody>
</table>

*Replacement fluid contains no plasma

Replacement Fluids

- 5% albumin in physiologic saline
  - Most commonly used replacement fluid
  - Slightly hyperoncotic compared with plasma
  - No coagulation factors
  - Considered sterile
    - Can still have allergic reactions
  - Use associated with volume-refractory hypotension
    - Significant generation of kinin via contact pathway
    - No ACE in replacement fluid
    - If patient taking ACE inhibitor, no metabolism of kinin
    - Discontinue ACE inhibitors for 24-48 hours

Transfusion 34:891-894 (1994)
Replacement Fluids

• Plasma
  – Used in cases with active bleeding or high-risk of bleeding
  – Physiologic amounts of all plasma substances
  – Contains all pro- and anticoagulant factors
  – Risk of transfusion-transmitted disease
  – Transfusion reactions can occur
  – Can start TPE even if patient is taking ACE inhibitor
    • ACE in plasma replacement fluid
ASFA Special Issue/Guidelines

• Every 3-7 years, panel of apheresis experts convenes to review relevant literature

• Based on the published evidence
  – Disease-specific indications and guidances for use of therapeutic apheresis technologies are assigned
  – Accompanying fact sheets for disease pathophysiologies, current treatment options, and rationales for therapeutic apheresis
## TABLE I. Indications for Therapeutic Apheresis—ASFA 2013

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Disorders for which apheresis is accepted as first-line therapy, either as a primary standalone treatment or in conjunction with other modes of treatment.</td>
</tr>
<tr>
<td>II</td>
<td>Disorders for which apheresis is accepted as second-line therapy, either as a standalone treatment or in conjunction with other modes of treatment.</td>
</tr>
<tr>
<td>III</td>
<td>Optimum role of apheresis therapy is not established. Decision making should be individualized.</td>
</tr>
<tr>
<td>IV</td>
<td>Disorders in which published evidence demonstrates or suggests apheresis to be ineffective or harmful. IRB approval is desirable if apheresis treatment is undertaken in these circumstances.</td>
</tr>
</tbody>
</table>
### TABLE III. Modified McLeod’s Criteria for Evaluation of Therapeutic Apheresis Efficacy

<table>
<thead>
<tr>
<th>Evidence</th>
<th>McLeod’s criteria</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mechanism</td>
<td>“Plausible Pathogenesis”</td>
<td>The current understanding of the disease process supports a clear rationale for the use of therapeutic apheresis modality.</td>
</tr>
<tr>
<td>Correction</td>
<td>“Better Blood”</td>
<td>The abnormality, which makes therapeutic apheresis plausible, can be meaningfully corrected by its use.</td>
</tr>
<tr>
<td>Clinical Effect</td>
<td>“Perkier Patients”</td>
<td>There is a strong evidence that therapeutic apheresis confers benefit that is clinically worthwhile, and not just statistically significant.</td>
</tr>
</tbody>
</table>
### TABLE II. Grading Recommendations adopted from Guyatt and coworkers

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Description</th>
<th>Methodological quality of supporting evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1A</td>
<td>Strong recommendation, high-quality evidence</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>Grade 1B</td>
<td>Strong recommendation, moderate quality evidence</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
<td>Strong recommendation, can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>Grade 1C</td>
<td>Strong recommendation, low-quality or very low-quality evidence</td>
<td>Observational studies or case series</td>
<td>Strong recommendation but may change when higher quality evidence becomes available</td>
</tr>
<tr>
<td>Grade 2A</td>
<td>Weak recommendation, high quality evidence</td>
<td>RCTs without important limitations or overwhelming evidence from observational studies</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
</tr>
<tr>
<td>Grade 2B</td>
<td>Weak recommendation, moderate-quality evidence</td>
<td>RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies</td>
<td>Weak recommendation, best action may differ depending on circumstances or patients’ or societal values</td>
</tr>
<tr>
<td>Grade 2C</td>
<td>Weak recommendation, low-quality or very low-quality evidence</td>
<td>Observational studies or case series</td>
<td>Very weak recommendations; other alternatives may be equally reasonable</td>
</tr>
</tbody>
</table>

# Glomerular Diseases and TPE

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>TPE</th>
<th>Dialysis dependence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCA- associated rapidly progressive glomerulonephritis</td>
<td>TPE</td>
<td>Dialysis dependence</td>
</tr>
<tr>
<td>(Granulomatosis with polyangiitis; Wegener’s Granulomatosis)</td>
<td>TPE</td>
<td>Dialysis independent</td>
</tr>
<tr>
<td>Anti-glomerular basement membrane disease (Goodpasture’s syndrome)</td>
<td>TPE</td>
<td>Dialysis dependent and no DAH</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>TPE</td>
<td>Symptomatic/severe</td>
</tr>
<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>TPE</td>
<td>Recurrent in transplanted kidney</td>
</tr>
<tr>
<td>Hemolytic uremic syndrome, atypical</td>
<td>TPE</td>
<td>Complement gene mutations</td>
</tr>
<tr>
<td></td>
<td>TPE</td>
<td>Factor H antibodies</td>
</tr>
<tr>
<td></td>
<td>TPE</td>
<td>MCP mutations</td>
</tr>
<tr>
<td>Hemolytic uremic syndrome, infection-associated</td>
<td>TPE</td>
<td>Shiga toxin associated</td>
</tr>
<tr>
<td></td>
<td>TPE</td>
<td>S. pneumoniae associated</td>
</tr>
<tr>
<td>Henoch-Schonlein purpura</td>
<td>TPE</td>
<td>Crescentic</td>
</tr>
<tr>
<td></td>
<td>TPE</td>
<td>Severe extrarenal disease</td>
</tr>
<tr>
<td>Immune complex rapidly progressive glomerulonephritis</td>
<td>TPE</td>
<td></td>
</tr>
<tr>
<td>Immunoglobulin A nephropathy</td>
<td>TPE</td>
<td>Crescentic</td>
</tr>
<tr>
<td></td>
<td>TPE</td>
<td>Chronic progressive</td>
</tr>
<tr>
<td>Scleroderma (Progressive systemic sclerosis)</td>
<td>TPE</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>TPE</td>
<td>Severe</td>
</tr>
<tr>
<td></td>
<td>TPE</td>
<td>Nephritis</td>
</tr>
<tr>
<td>Thrombotic microangiopathy, HSCT associated</td>
<td>TPE</td>
<td>Variable</td>
</tr>
</tbody>
</table>

Immunosuppression & TPE
UNC Therapeutic Apheresis Likes Kidney Biopsies

www.netterimages.com; www.med.unc.edu
ANCA-Associated RPGN

- Progressively rapid loss of kidney function
- Attributed to P-ANCA or C-ANCA in the plasma

- Can be limited to kidney or involve other organ systems
  - Involvement of the lung with subsequent diffuse alveolar hemorrhage (DAH) is associated with increased risk of mortality

Images from J.C. Jennette, www.unckidneycenter.org
ANCA-associated RPGN

Images from J.C. Jennette, www.unckidneycenter.org
Inflammation of the vessel wall (vasculitis) caused by white blood cells that have been stimulated by ANCA.
Evidence for TPE in ANCA-associated RPGN

• ANCA characteristics favorable for removal
  – High molecular weights
  – Low turnover rates and long half-life

• ANCA is an inciting factor for tissue damage

• Most “pauci-immune” glomerulonephritis is proving to be ANCA-associated, there is justification in using older studies

• Older trials found no generalizable benefit for TPE in non-anti-GBM-associated RPGN

<table>
<thead>
<tr>
<th>Trial</th>
<th>Index of Severity</th>
<th>TPE</th>
<th>No TPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mauri 1985</td>
<td>Creatinine &gt; 9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial creatinine</td>
<td>13.5 (6 pts)</td>
<td>13.1 (5 pts)</td>
<td></td>
</tr>
<tr>
<td>Creatinine after 3 yrs</td>
<td>8.7*</td>
<td>13.4</td>
<td></td>
</tr>
<tr>
<td>Glockner 1988</td>
<td>Dialysis dependent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial creatinine</td>
<td>7.4 (8 pts)</td>
<td>9.2 (4 pts)</td>
<td></td>
</tr>
<tr>
<td>Creatinine after 6 mos</td>
<td>1.7*</td>
<td>5.5</td>
<td></td>
</tr>
<tr>
<td>Pusey 1991</td>
<td>Dialysis dependent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial # pts on dialysis</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Pts off dialysis at 12 mos</td>
<td>10*</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Cole 1992</td>
<td>Dialysis dependent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial # pts on dialysis</td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Pts off dialysis at 12 mos</td>
<td>3*</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Jayne 2007</td>
<td>Creatinine &gt;5.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial # of pts</td>
<td>70</td>
<td>67</td>
<td></td>
</tr>
<tr>
<td>Pts off dialysis at 12 mos</td>
<td>57*</td>
<td>40</td>
<td></td>
</tr>
</tbody>
</table>

Evidence for TPE in ANCA-associated RPGN

<table>
<thead>
<tr>
<th>Incidence: 8.5/1,000,000/yr</th>
<th>Condition</th>
<th>Procedure</th>
<th>Recommendation</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dialysis dependence</td>
<td>TPE</td>
<td>Grade 1A</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>DAH</td>
<td>TPE</td>
<td>Grade 1C</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td>Dialysis independence</td>
<td>TPE</td>
<td>Grade 2C</td>
<td>III</td>
</tr>
</tbody>
</table>

# of reported patients*: >300

<table>
<thead>
<tr>
<th>RCT</th>
<th>CT</th>
<th>CS</th>
<th>CR</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 (296)</td>
<td>1 (26)</td>
<td>22 (347)</td>
<td>NA</td>
</tr>
</tbody>
</table>

*At presentation, defined as Cr>6 mg/dL. DAH = diffuse alveolar hemorrhage.

- **Volume treated**
  - 1-1.5 TPV

- **Frequency**
  - Daily procedures in fulminant cases (particularly with DAH)
  - Every 2-3 days
  - Total of 6-9 procedures

Anti-Glomerular Basement Membrane (GBM) Disease

• Attributed to
  – IgG autoantibodies to α3 chain of type IV collagen

• Typically impacts both the kidneys and lungs
  – The autoantibody target is enriched in both alveolar and glomerular basement membranes
  – Up to 40% cases are renal-limited

• 30% of patients will also have detectable ANCA

Anti-GBM Disease

• Autoantibodies bind to the basement membrane
  – Attract and activate leukocytes
  – Leukocyte-induced injury of capillary walls
  – Alveolar capillaritis and glomerulonephritis

• Glomerular deformation
  – Red cell and protein losses from damaged capillaries
  – Cellular proliferation
Anti-GBM Disease

Cells lining the inner surface (endothelial cells)
Blood plasma (liquid with proteins)
Neutrophil type of white blood cell
Other type of white blood cell
Red blood cell
Basement membrane surrounding the vessel

Blood vessel (capillary wall)
Neutrophil type of white blood cell
Basement membrane

Inflammation of the vessel wall caused by white blood cells that have been stimulated by anti-GBM bound to capillary basement membranes (GBM)

Images from J.C. Jennette, www.unckidneycenter.org
Anti-GBM Disease

Renal Biopsy Finding in Anti-GBM Glomerulonephritis

Normal glomerulus

Anti-GBM crescentic glomerulonephritis

Red blood cells in the urine caused by rupture of glomerular capillaries

Abnormal crescent-shaped accumulation of cells in the urine surrounding a glomerulus (a crescent)

The bright green color shows the location of anti-GBM antibodies bound to the GBM of capillaries in a glomerulus from a patient with anti-GBM disease (by immunofluorescence microscopy)

Images from J.C. Jennette, www.unckidneycenter.org
Evidence for TPE in Anti-GBM Disease

• TPE is effective at removing the autoantibody from plasma
• Only one randomized controlled study of TPE
  – Adjunct to immunosuppression
  – Modest use of TPE (once every 3 days)
  – Non-TPE group had greater kidney injury
• Multiple other nonrandomized and case-controlled studies support TPE use
  – → Lower post-treatment Cr and ESRD rates

Evidence for TPE in Anti-GBM Disease

- Majority of patients with serum Cr < 6.6 mg/dL recover kidney function → initiate TPE
- Those with Cr ≥ 6.6 mg/dL almost always do not recover kidney function due to irreversible injury → TPE far less likely to be of benefit
- TPE in DAH is highly effective
  - 90% of patients respond to TPE
  - Due to increased mortality risk there is a low threshold for initiation

Evidence for TPE in Anti-GBM Disease

- **Volume treated**
  - 1-1.5 TPV
- **Frequency**
  - Daily procedures in fulminant cases
  - Every 2-3 days
  - ≥14 day treatment course

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Cryoglobulinemia

• Cryoglobulins
  – Immunoglobulins that reversibly precipitate below normal body temperatures
  – Classified into 3 types
    • Type I: monoclonal immunoglobulins (IgM or IgG)
      – Waldenstrom’s macroglobulinemia or multiple myeloma
    • Type II – monoclonal IgM + polyclonal IgG
      – Hepatitis
    • Type III – polyclonal IgM and IgG
      – Inflammatory disorders
Cryoglobulinemia

• Commonly affects skin, but can impact renal and nervous systems
• Associated with many disorders
  – Viral infections (notably hepatitis B and C)
  – Lymphoproliferative disorders
  – Autoimmune diseases
• Complement activated and leukocytes recruited
Cryoglobulinemia

Images from J.C. Jennette, www.unckidneycenter.org
Evidence for TPE in Cryoglobulininemia

• TPE effectively removes cryoglobulins
• One RCT along with numerous case reports and case series demonstrate 80% clinical improvement with TPE
• General consensus is that TPE is a useful treatment for certain cryoglobulininemia patients

Evidence for TPE in Cryoglobulinemia

- Most often utilized in moderate-to-severe cases with active disease
  - Advanced neuropathy
  - Coalescing purpura
  - Progressive renal failure
- Favorable responses with TPE in chronic management of disease
- Optimal parameters for assessing TPE efficacy are unknown

Evidence for TPE in Cryoglobulinemia

- **Volume treated**
  - 1-1.5 TPV

- **Frequency**
  - Acute disease: 3-8 procedures
  - Chronic disease: Weekly to monthly procedures

- **Important points**
  - Cryocrit is not a marker of disease activity
  - Warm replacement fluid
  - Treat underlying disease

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Focal Segmental Glomerulosclerosis (FSGS)

- Histologically descriptive name
  - Not a specific diagnosis with a specific etiology
- Multiple FSGS variants, but podocyte injury and depletion are present in FSGS pathologies
- 80% cases are idiopathic (primary FSGS)
- 20% cases are secondary
  - Drug induced
  - Hemodynamic adaptive response
  - Mutations in podocyte genes
FSGS

Images from J.C. Jennette, www.unckidneycenter.org
FSGS

- Attributed to a plasma compound of unknown origin
  - Damages filtration barrier and/or increases glomerular permeability
  - Demonstrated induction of significant albumin leakage when FSGS patient plasma is incubated with rodent glomeruli
  - Is detectable in many but not all FSGS patients

FSGS

- ESRD occurs in the majority of patients within 3-7 years
- Patients can receive kidney transplant
  - Recurrences occur in up to 40% of cases
  - Contributes to up to 50% of graft failures
  - Those who lose allografts to recurrent FSGS have >80% likelihood of losing subsequent allografts
  - Recurrences most likely to occur in idiopathic (primary) FSGS patients

Evidence for TPE in Recurrent FSGS

• Treatments goals
  – Abrogate proteinuria
  – Preserve kidney allograft function

• TPE is ideal to remove the poorly characterized pathologic plasma factor posited to have mass of 30,000-50,000 Daltons

• Reductions of this ill-defined factor by TPE has correlated with reductions in proteinuria

## Evidence for TPE in Recurrent FSGS

<table>
<thead>
<tr>
<th>Study</th>
<th># Pts</th>
<th># TPE</th>
<th>Meds</th>
<th>Improvement</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valdivia 2005</td>
<td>7</td>
<td>17</td>
<td>No</td>
<td>100% pts with functioning allografts at 10 mos follow up</td>
<td>Include TPE early in treatment plan</td>
</tr>
<tr>
<td>Pardon 2006</td>
<td>9</td>
<td>12-25</td>
<td>No</td>
<td>89% partial or complete remission; 6 pts (67%) still lost their allograft by 5 yr follow up</td>
<td>Benefit transient, particularly if other meds not used</td>
</tr>
<tr>
<td>Garcia 2006</td>
<td>9</td>
<td>10</td>
<td>Yes</td>
<td>55% complete response; 12% partial response</td>
<td>Start TPE as soon as possible after recurrence</td>
</tr>
<tr>
<td>Sener 2009</td>
<td>4</td>
<td>9-15</td>
<td>Yes</td>
<td>100% pts with preserved allograft function at 34 mos follow up</td>
<td>Include TPE early in treatment plan</td>
</tr>
<tr>
<td>Tsagalis 2011</td>
<td>4</td>
<td>20-69</td>
<td>Yes</td>
<td>50% complete remission; 50% partial remission</td>
<td>Include TPE in treatment plan</td>
</tr>
<tr>
<td>Canaud 2009</td>
<td>10</td>
<td>25-39</td>
<td>Yes</td>
<td>90% complete remission at 1 yr follow up</td>
<td>Include TPE in intensive, long-term treatment plan</td>
</tr>
</tbody>
</table>

Evidence for TPE in Recurrent FSGS

- Volume treated
  - 1-1.5 TPV
- Frequency
  - Highly variable
  - Multiple intensities and tapering regimens
  - Tapering is guided by degree of proteinuria
- No clinical or laboratory parameters that predict likelihood of success with TPE treatment

Conclusions

• Likelihood of successful treatment of glomerular diseases with TPE is limited to a handful of pathologies

• Agreed upon and organized institutional protocols between Nephrology and Apheresis services critical to consistent patient care

• Despite published data, there is much to learn about TPE use in glomerular disease
  – This is an opportunity for the GDCN
### Glomerular Diseases and TPE

<table>
<thead>
<tr>
<th>Glomerular Disease</th>
<th>TPE Treatment</th>
<th>Associated Complications</th>
<th>Disease Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANCA- associated rapidly progressive glomerulonephritis (Granulomatosis with polyangiitis; Wegener’s Granulomatosis)</td>
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<tr>
<td>Cryoglobulinemia</td>
<td>TPE</td>
<td>Symptomatic/severe</td>
<td>I</td>
</tr>
<tr>
<td>Focal segmental glomerulosclerosis</td>
<td>TPE</td>
<td>Recurrent in transplanted kidney</td>
<td>I</td>
</tr>
<tr>
<td>Hemolytic uremic syndrome, atypical</td>
<td>TPE</td>
<td>Complement gene mutations</td>
<td>II</td>
</tr>
<tr>
<td>Hemolytic uremic syndrome, infection-associated</td>
<td>TPE</td>
<td>Factor H antibodies</td>
<td>I</td>
</tr>
<tr>
<td>Hemolytic uremic syndrome, infection-associated</td>
<td>TPE</td>
<td>MCP mutations</td>
<td>IV</td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td>TPE</td>
<td>Crescentic</td>
<td>III</td>
</tr>
<tr>
<td>Immune complex rapidly progressive glomerulonephritis</td>
<td>TPE</td>
<td>Severe extrarenal disease</td>
<td>III</td>
</tr>
<tr>
<td>Immunoglobulin A nephropathy</td>
<td>TPE</td>
<td>Crescentic</td>
<td>III</td>
</tr>
<tr>
<td>Scleroderma (Progressive systemic sclerosis)</td>
<td>TPE</td>
<td>Chronic progressive</td>
<td>III</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>TPE</td>
<td>Severe</td>
<td>II</td>
</tr>
<tr>
<td>Thrombotic microangiopathy, HSCT associated</td>
<td>TPE</td>
<td>Nephritis</td>
<td>IV</td>
</tr>
</tbody>
</table>
