A General Overview of Plasmapheresis and a Review of TTP

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Objectives

- To briefly review the plasmapheresis in terms of prescription, complications and indications
- To review the literature supporting the use of plasmapheresis in TTP. Additionally, the specifics of prescribing PLEX in TTP will be covered.
- To review specific areas of the TTP literature with a focus on diagnosis, predicting response to therapy and novel therapeutic agents.
Pheresis prescription
Access

- Central line
  - Hemodialysis catheter - Gamcath
  - Apheresis catheter - Mahukar
  - Required for acute pheresis, particularly in the setting where the patient will require multiple daily sessions

- Peripheral veins
  - Acceptable for infrequent runs

- AVF
  - Recurrent disease requiring frequent interventions
Blood Removal/Return

- Intermittent
- Continuous – need double lumen catheter or two needles in patient
- We do continuous blood removal/return
Plasma Separation

- **Centrifuge**
  - Seems old school
  - Advantage - can do cytapheresis

- **Filter**
  - Akin to dialysis, except pores are large enough to allow plasma to flow through
  - Can only do plasmapheresis/exchange
Fig. 3  Principle of membrane plasma separation
Anticoagulation

- Regional
  - Citrate with calcium

- Systemic
  - Heparin
Replacement Fluid

- **Saline**
  - Most frequently used unless there is a risk of/ongoing bleed

- **Albumin**
  - Use for TTP
  - Use to correct coagulopathy or in patients that are bleeding
  - High risk of transfusion reactions

- **FFP**
Complications

- Access
  - Pneumo
  - AVF
  - Infection
  - Thrombosis
  - Bleeding

- Anti-coagulation
  - Bleeding
  - Hypocalcemia
Complications

- Tubing
  - Hemolysis from kinked tubing
  - Activation of cold agglutinins

- Blood products
  - Allergic reaction: urticaria, anaphylaxis, TRALI
  - Infections: Hepatitis, prions

- Drugs
  - Theoretical risk of cardiac collapse with ACE-I
  - Will remove drugs, particularly protein bound and intravascular drugs
  - Give steroids and antibiotics after pheresis
  - Follow levels
Complications

- **Plasma removal**
  - The patient is coagulopathic while they are on pheresis due to the removal of clotting factors
  - Avoid procedures/surgeries that put patients at risk of bleeding within 48h of pheresis
  - If this is to be done, FFP should be used as at least part of the replacement fluid
Indications

- Renal
  - Anti-GBM/Goodpasture’s*
    - Pulmonary hemorrhage
    - Creat < 600
  - Wegener’s
    - Pulmonary hemorrhage
    - Creat > 500*
    - Anti-GBM positive*
  - ? Cryoglobulinemia
    - Pulmonary hemorrhage
    - Digital necrosis
  - RPG N
Indications

- **Hematology**
  - TTP****
  - Macroglobulinemia and hyperviscosity*
  - Antiphospholipid antibody syndrome crisis
  - ? Myeloma/Cast Nephropathy
  - Stem cell harvest

- **Neurology**
  - Devic’s/NMO = Ab mediated MS*
  - GBS/CIDP
  - Myasthenia Gravis*
    - Crisis or pre-thymectomy
  - ADEM
  - Eaton Lambert
Indications

- Transplant
  - Highly sensitized patients*
  - Acute anti-body mediated rejection*
  - Recurrent GN (FSGS)
  - De-novo GN (Anti-G BM)

- Miscellaneous
  - Hypertriglyceridemia
  - Drug removal
  - Sepsis
  - Liver failure
    - Intractable pruritus
    - Bridge to transplant
Review of Selected Topics in TTP
Pathogenesis of TTP
ADAMTS-13

- ADAMTS-13
  - A Disintegrin-like And Metalloprotease with ThromboSpondin type 1 repeats member 13
  - vWF cleaving protease
    - vWF is assembled in large multimers in endothelial cells (ULvWF)
    - These are presented to the plasma and degraded by ADAMTS-13
ADAMTS-13

A Normal Subject
- Cleaved unusually large multimers of von Willebrand factor
- ADAMTS 13
  - Binding site
  - Secretion of multimers from Weibel-Palade body

B Patient with Thrombotic Thrombocytopenic Purpura
- Adhesion and aggregation of platelets
- Uncleaved unusually large multimers of von Willebrand factor
  - ADAMTS 13
  - Binding site
  - Secretion of multimers from Weibel-Palade body
TTP and ADAMTS-13 Deficiency
- First characterized in a family with congenital TTP
- Deficiency can be either absolute or functional
- Results in:
  - Accumulation of ULvWF in the plasma
  - Platelet Clumping
  - Platelet aggregation → MAHA → End organ damage
ADAMTS-13

- Vesely 2003
  - Series of 48 patients with idiopathic TTP
  - Characterized ADAMTS-13 deficiency into 4 categories (function and inhibitor measured)
    - < 5% (severe); 5-9%; 10-25%; > 25%
    - 16/48 had severe deficiency
    - Patients from all groups responded well to PLEX
    - Clinical characteristics and outcomes were the same amongst groups

Blood 2003 Jul 1;102(1):60-8
# ADAMTS-13

## Table 5. Relation of presenting features and clinical outcomes of 48 patients with clinically diagnosed idiopathic TTP-HUS to the presence or absence of severe ADAMTS13 deficiency

<table>
<thead>
<tr>
<th>Presenting features</th>
<th>Severe ADAMTS13 deficiency (n = 16)</th>
<th>Not severe ADAMTS13 deficiency (n = 32)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y (minimum, maximum)</td>
<td>39 (19, 71)</td>
<td>50 (9, 85)</td>
<td>.007</td>
</tr>
<tr>
<td>Sex (% female)</td>
<td>12 (75)</td>
<td>23 (72)</td>
<td>1.000</td>
</tr>
<tr>
<td>Race (% African American)</td>
<td>8 (50)</td>
<td>8 (25)</td>
<td>.083</td>
</tr>
<tr>
<td>Obesity (% BMI ≥ 30 kg/m²)</td>
<td>8 (50)</td>
<td>10 (31)</td>
<td>.206</td>
</tr>
<tr>
<td>Neurologic abnormalities (%)</td>
<td>8 (50)</td>
<td>17 (53)</td>
<td>.838</td>
</tr>
<tr>
<td>Acute renal failure (%)</td>
<td>1 (6)</td>
<td>11 (34)</td>
<td>.040</td>
</tr>
<tr>
<td>Median platelet count, 10⁹/L (minimum, maximum)</td>
<td>11 (4, 27)</td>
<td>15 (2, 95)</td>
<td>.085</td>
</tr>
<tr>
<td>Median hematocrit, % (minimum, maximum)</td>
<td>21 (15, 30)</td>
<td>22 (14, 32)</td>
<td>.509</td>
</tr>
<tr>
<td>Median LDH, U/L (minimum, maximum)†</td>
<td>1524 (436, 3909)</td>
<td>1107 (302, 12 587)</td>
<td>.094</td>
</tr>
</tbody>
</table>

## Clinical outcomes

| Response (%) | 14 (88) | 24 (75) | .460 |
| Exacerbation (%)| 8/14 (57) | 3/24 (38) | .240 |
| Median no. of plasma exchange (minimum, maximum)‡ | 20 (5, 74) | 16 (3, 68) | .429 |
| TTP-HUS–associated death (%) | 3 (19) | 7 (22) | .730 |
| All Death (%) | 3 (19) | 12 (38) | .123 |
| Relapse (%)§ | 6/14 (43) | 2/25 (8) | .016 |

Patients with idiopathic TTP-HUS who had severe ADAMTS13 deficiency (activity < 5%) were compared with the patients with idiopathic TTP-HUS who did not have severe deficiency (ADAMTS13 activity > 5%). The 2 patients with severe ADAMTS13 deficiency who had TTP-HUS associated with pregnancy are not represented in this table. Presenting features and clinical outcomes are defined in "Patients and methods." Laboratory data are the most abnormal values on the day of diagnosis ± 7 days.

*LDH values were adjusted to an upper limit of normal value of 200 U/L.
†The denominator is the number of patients who achieved a response.
‡The number of plasma exchange treatments is given for all patients who achieved a remission.
§The denominator is the number of patients who achieved a remission.
Conclusion

- TTP is not characterized by severe ADAMTS-13 deficiency alone
- PLEX should be initiated based on clinical suspicion
- Idiopathic TTP are more likely to have severe deficient
Many retrospective studies suggest that severe deficiency is associated with a higher rate of relapse.

Interestingly, mortality has not been shown to be different amongst these groups.
The role of PLEX in TTP
Natural History of TTP

- Progressive renal failure and neurologic deterioration with death was the most common outcome.

- Mortality
  - Pre-PLEX – 90%
  - Now - ~12-14%

Why does PLEX work?

- TTP is caused by decreased ADAMTS-13 activity
  - Absolute deficiency: Congenital/Genetic
  - Functional deficiency: Antibodies/Congenital
Why does PLEX work?

- PLEX has multifactorial mechanisms by which it may be beneficial in the treatment of TTP
- It removes the circulating antibodies to ADAMTS-13
- It removes the accumulation of ultralong vWF multimers
- It repletes ADAMTS-13 with the use of plasma as the exchange fluid

**PLEX Literature**

- **Canadian Apheresis Study Group – 1991**
  - **Subjects:** 102 patients with presumed primary TTP
  - **Methods:**
    - Randomized to PLEX vs. Plasma infusion
    - Above carried out on 7 of first 9 days
    - PLEX group received 3x more Plasma
    - All patients were given ASA and Dipyridamole
  - **Outcomes:** Day 9 and at 6 months
    - Response (increase in platelets)
    - Mortality

*N Engl J Med 1991 Aug 8;325(6):393-7*
PLEX Literature

- CASG – 1991
  - Outcomes
    - Day 9 – Favours PLEX
      - Response: 24/51 vs. 13/51 (p = 0.025)
      - Mortality: 2/51 vs. 8/51 (p = 0.035)
    - 6 months – Favours PLEX
      - Response: 40/51 vs. 25/51 (p = 0.002)
      - Mortality: 11/51 vs. 19/51 (p = 0.036)

- Conclusion
  - PLEX is better than Plasma exchange, BUT is this related to plasma volume?
Henon 1991

- Subjects: 40 patient with primary TTP
- Methods:
  - Randomized to PLEX vs. Plasma Infusion at equivalent doses of plasma
  - All on anti-platelet agents
- Results – Favours PLEX
  - Response: 16/20 vs. 11/20 (p < 0.02)
  - Mortality: 3/20 vs. 8/20 (p < 0.02)
PLEX Literature

- Henon 1991
  - Conclusion
    - PLEX still favoured, but a higher mortality rate with the lower plasma volume.
### TABLE 6. Study protocol and outcome of two randomized clinical trials in thrombotic thrombocytopenic purpura/hemolytic uremic syndrome

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Rock et al. (Ref. 57)</th>
<th>Henon (Ref. 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FFP exchanges on 7 of the first 9 days</td>
<td>FFP exchanges</td>
</tr>
<tr>
<td></td>
<td>21.5 ± 7.8 L</td>
<td>15 ml/kg in HA 45 ml/kg</td>
</tr>
<tr>
<td>Responses, n</td>
<td>49</td>
<td>16</td>
</tr>
<tr>
<td>Fatalities, n</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total FFP volume</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma exchange</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FFP transfusion</td>
<td>FFP transfusion on 7 of the first 9 days</td>
<td>FFP transfusion</td>
</tr>
<tr>
<td></td>
<td>6.7 ± 6.7 L</td>
<td>15 ml/kg</td>
</tr>
<tr>
<td>Responses</td>
<td>43</td>
<td>11</td>
</tr>
<tr>
<td>Fatalities</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Total FFP volume</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ther Apher 6(4) 2002
### TABLE 7. Outcome in primary and secondary thrombotic thrombocytopenic purpura/hemolytic uremic syndrome

<table>
<thead>
<tr>
<th>Reference</th>
<th>Total patients</th>
<th>Response (%)</th>
<th>Mortality (%)</th>
<th>Relapse (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bell 1991 (51)</td>
<td>78</td>
<td>70</td>
<td>10.3</td>
<td>64</td>
</tr>
<tr>
<td>Roberts 1991 (52)</td>
<td>14</td>
<td>12</td>
<td>14.3</td>
<td>29</td>
</tr>
<tr>
<td>Hayward 1994 (50)</td>
<td>52</td>
<td>48</td>
<td>8.0</td>
<td>21</td>
</tr>
<tr>
<td>Elkins 1996 (33)</td>
<td>11</td>
<td>9</td>
<td>18.2</td>
<td>25</td>
</tr>
<tr>
<td>Sarode 1997 (46)</td>
<td>70</td>
<td>60</td>
<td>14.3</td>
<td>18</td>
</tr>
<tr>
<td>George 1998 (44)</td>
<td>169</td>
<td>138</td>
<td>18.4</td>
<td>—</td>
</tr>
<tr>
<td>Bandarenko 1998 (43)*</td>
<td>115</td>
<td>102</td>
<td>10.4</td>
<td>37</td>
</tr>
<tr>
<td>Ramanan 1999 (54)</td>
<td>15</td>
<td>13</td>
<td>13.3</td>
<td>40</td>
</tr>
<tr>
<td>Lara 1997 (55)</td>
<td>122</td>
<td>110</td>
<td>9.8</td>
<td>13</td>
</tr>
<tr>
<td>Dervenoulas 2000 (45)</td>
<td>48</td>
<td>43</td>
<td>10.4</td>
<td>22.5</td>
</tr>
<tr>
<td>Total</td>
<td>694</td>
<td>605</td>
<td>12.7% (mean)</td>
<td>30% (mean)</td>
</tr>
</tbody>
</table>

* Multicenter survey in U.S.A.
PLEX Literature

- Von Baeyer 2002
  - Results from uncontrolled trials
    - 694 patients
    - Sustained hematologic response in 605 (88%)
    - Mortality 12%
    - Relapse rate 13-64%
## Outcomes in subsets of secondary TTP

<table>
<thead>
<tr>
<th>Constellation</th>
<th>Series (n)</th>
<th>Total (n)</th>
<th>Response (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug-induced</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ticlopidine (60,61)</td>
<td>2</td>
<td>39</td>
<td>71.9</td>
</tr>
<tr>
<td>Clopidogrel (62)</td>
<td>1</td>
<td>11</td>
<td>90.9</td>
</tr>
<tr>
<td>Cancer chemotherapy (40,64)‡</td>
<td>2</td>
<td>65</td>
<td>69.2</td>
</tr>
<tr>
<td>High-dose chemotherapy (23)</td>
<td>1</td>
<td>11</td>
<td>27</td>
</tr>
<tr>
<td>Gemcitabine (65)</td>
<td>1</td>
<td>5</td>
<td>100</td>
</tr>
<tr>
<td>Tacrolimus (66–69)</td>
<td>4</td>
<td>8</td>
<td>100</td>
</tr>
<tr>
<td><strong>Miscellaneous causes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative (28,29)</td>
<td>2</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>HIV infection (70,71)</td>
<td>2</td>
<td>20</td>
<td>90</td>
</tr>
<tr>
<td>Quinine in beverages (72)</td>
<td>1</td>
<td>9</td>
<td>100</td>
</tr>
<tr>
<td><strong>Pregnancy-related</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TTP/HUS in pregnancy (50,63,73)</td>
<td>3</td>
<td>22</td>
<td>72.7</td>
</tr>
<tr>
<td>Persistent HELLP (32,69,74,75)</td>
<td>4</td>
<td>10</td>
<td>100</td>
</tr>
</tbody>
</table>

* All patients received PAL.
Cochrane Review 2006

- No real changes to management or conclusions
- Added RR calculation based on two RCTs
  - remission at two weeks (RR 1.48, 95% 1.12 to 1.96) and all-cause mortality (RR 1.91, 95% 1.09 to 3.33)
Typical PLEX Rx for TTP
PLEX Rx

- Daily PLEX with 150% Exchange with plasma
- Once platelets are increasing consistently and approaching normal (>100), decrease volume of exchange to 100%
- PLEX daily for a minimum of 7 days or until the platelets are normal and stable for 3 consecutive days
  - Whichever is longer
- Begin slow wean
  - Every other day x 3
  - Every third day x 3 etc until off
ADJUNCTIVE Therapies
Why do we need adjunctive rx?

**TABLE I. Evolution of Treatments and Outcomes for Patients with TTP**

<table>
<thead>
<tr>
<th>Period</th>
<th>Treatment</th>
<th>Survival (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1925–1964</td>
<td>Corticosteroids, antiplatelet agents, splenectomy</td>
<td>10</td>
</tr>
<tr>
<td>1964–1982</td>
<td>Plasma infusion, beginning use of PEX</td>
<td>46</td>
</tr>
<tr>
<td>1982–2008</td>
<td>PEX, inconsistent use of adjuvant treatments</td>
<td>80</td>
</tr>
<tr>
<td>2008–2012</td>
<td>PEX, corticosteroids, beginning use of rituximab</td>
<td>~90</td>
</tr>
</tbody>
</table>

**TABLE III. Adjunctive Treatment for TTP: Goals**

- Decrease duration of PEX treatment required to achieve remission
- Decrease complications from PEX treatment
- Decrease frequency of relapse

Prednisone

- A lack of strong evidence
  - No placebo controlled RCTs

- Steroids were known to be beneficial in TTP even before PLEX was used.
  - Do steroids add anything to PLEX?

- Based on unpublished registry data (Oklahoma)
  - Steroids should be used as adjunctive therapy in severe ADAMTS-13 deficiency
  - They reduce the amount of PLEX required to achieve a sustained remission
  - They may reduce relapse

Prednisone

- RCT comparing high dose versus low dose steroid therapy in patients with TTP
  - 30 patients randomized to standard dose (1mg/kg/day)
  - 30 patients randomized to high dose (10mg/kg/day x 3 days, then 2.5mg/kg/day)
  - All Rx was done with IV methylprednisolone
  - Patients with a good response at Day 9 were continued on the same dose of steroid for one week and then a half dose for another week
  - All patients were on ASA once plt's > 30
  - Primary end point was a “good” response at Day 9 and secondary end point was “Incomplete response” or death at day 23.
Prednisone

- **Results:**
  - No difference in primary endpoint
  - 16 of 30 failed to achieve a complete remission at Day 23 in the standard dose arm versus the high dose arm (7 of 30)

- **Conclusions**
  - High dose steroid is more effective than standard dose
  - Compared with CASG study from 2003 (steroids were prohibited), the rate of remission at Day 9 was 76.6% in the high dose steroid group versus 62% in the Canadian study …
  - Also, standard dose remission rate was 56.6%, suggesting that this dose of steroids did not help PLEX
Rituximab

- Largely observational data suggesting
  - Decreased exacerbations when PLEX stopped
  - Fewer relapses
<table>
<thead>
<tr>
<th>Patients</th>
<th>No.</th>
<th>Follow-up duration (mo)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAMTS13 &lt;10%, treated during initial episode</td>
<td>10</td>
<td>54 (19–96)</td>
<td>One patient has relapsed, 30 months after rituximab</td>
</tr>
<tr>
<td>ADAMTS13 &lt;10%, treated for relapsed episode</td>
<td>11</td>
<td>42 (1–83)</td>
<td>Two patients have relapsed again, 32 and 34 months after rituximab</td>
</tr>
<tr>
<td>ADAMTS13 ≥10%</td>
<td>14</td>
<td>28 (6–96)</td>
<td>No patients have relapsed</td>
</tr>
<tr>
<td>Suspected ADAMTS13 &lt;10%</td>
<td>6</td>
<td></td>
<td>One patient (ADAMTS13 activity 95%) was subsequently recognized to have quinine-induced TTP-HUS. In the other five patients (ADAMTS13 activity 11, 36, 75, 80, and 100%) no alternative etiologies were recognized.</td>
</tr>
</tbody>
</table>

**Autoimmune disorders**

- **Systemic lupus erythematosus**
  - 4
  - Patients initially diagnosed as TTP, then a previous diagnosis of SLE was determined to be the indication for treatment.

- **Bronchiolitis obliterans organizing pneumonia**
  - 1
  - Patient initially diagnosed as TTP, then a new diagnosis of BOOP was the indication for treatment.

- **Primary immune thrombocytopenia (ITP)**
  - 1
  - Patient initially diagnosed as TTP, then a subsequent diagnosis of ITP was the indication for treatment.

- **Acquired Factor VIII inhibitor**
  - 1
  - Patient had two previous episodes of TTP with ADAMTS13 <10%.

- **Atypical HUS**
  - 1
  - Congenital complement factor H (CFH) deficiency with CFH antibody was the indication for treatment.
Rituximab

- Phase II trial
  - 40 patients with acute TTP (clinical diagnosis)
  - Treated with steroids as per local protocol (1gm pulse of Solu-medrol x3 days)
  - Given 375mg/m² of Ritux x 4 weeks
  - Patients could receive an additional 4 infusions if ADAMTS-13 levels remained low
  - Progressive cardiac and neurologic symptoms were treated with BID PLEX
  - Compared to 40 historical controls
Rituximab
Rituximab

- Conclusion
  - Reduce relapse rate compared with controls
  - Reduced inpatient admission days in non-ICU patients
  - Reduced the number of PLEX runs in Caucasian patients
  - Should be used in all patients with “severe” TTP
    - End organ dysfunction
    - Particularly Neuro and Cardiac
Cyclophosphamide

- Literature is sparse
  - No RCTs

- Expert opinion suggests to use this in patients that are not responsive to PLEX, steroids, or Rituximab
Cyclophosphamide

- Patients were identified over a 10 year period who did not respond to PLEX, steroids, vincristine, or rituximab.
- All patients were severe ADAMTS-13 deficient
- Patients underwent splenectomy and/or treatment with cyclophosphamide
Cyclophosphamide

- 18 patients
  - 13 patients had a splenectomy (average 19 days from presentation)
    - 1 patient died post-op
    - The remaining patients improved until Day 6, at which 6 transiently worsened and re-improved
  - Durable PLT recovery observed in all at Day 13
  - 3 relapses (5 months, 2.5 years, 4.5 years)
- 5 patients received pulse cyclophosphamide (average 12 days after presentation).
  - All patients recovered PLT count by 10 days post drug
  - One relapse at 3.5 years

Overall survival was 94% after 2.5 years of follow-up
New Drugs

- Eculizumab
  - Terminal complement C5 monoclonal Ab

- ADAMTS-13 Nanobodies
  - A molecule that prevents the interaction of PLTs with vWF
  - Clinical Trial ongoing

- rADAMTS-13
  - Recombinant ADAMTS-13
  - Initial indication is for congenital TTP
Eculizumab

- ASN Abstracts – Study not yet published
  - 20 patients who had PLEX dependent TTP were enrolled
  - Intervention was Eculizumab
  - Primary outcome was “TMA Event Free Status”
    - Stable PLT counts
    - Absence of PLEX
    - No new dialysis
  - At 12 weeks, 15 patients had achieved the primary endpoint
  - Pharmaceutical sponsored trial
New Directions for Apheresis
Dr. Fritzler and I are (once again) collaborating to bring this test to Calgary
Dr. Klassen, Dr. Muruve, Dr. Scott-Douglas, Dr. Quinn and Dr. Girard

Goal is to create an electronic research platform on Citrix that can communicate with any other Citrix based database (AKDN, APPROACH etc).

We will hire a research nurse +/- unit clerk to enroll all patients who consent into the registry

Enrolment data will be of high quality and focused (Dr. Quinn)

Patients who are enrolled will have RCT level data (i.e. research coordinator will do BVAS scores on ANCA patients)

Outcomes will also be clearly defined and try to be as objective as possible. This will vary by disease.
Biobank (Dr. Muruve)

Currently a grant is being submitted for the AKDN to have a biobank

We have proposed to do the same with this registry
  - We will store blood, tissue, and pheresis effluent etc in the biobank
  - Graduate students and labs will then be able to use the biobank to do genomics, proteomics etc

This will be quite powerful as these basic science projects can then be linked to outcomes in our registry or any other registry that it can communicate with.
Apheresis Interest Group

- Clearly, the indications and increasing applications for pheresis require a group with diverse expertise

- Group members:
  - Representatives from – Hematology, Neurology, Transplant and Nephrology
  - Ideally representatives will include both Pediatrics and Adult

- Quarterly meetings
Conclusions

- The indications for PLEX are increasing
  - We need to start filling in the knowledge gap
  - RCTs may not always be feasible, but at minimum a solid prospective registry is required
  - Biobank is also very exciting

- ADAMTS-13
  - Not the be all and the end all
  - Not clinically useful in acute settings
  - Bringing the test here and increasing the speed of obtaining the result would help this
Conclusions

- TTP is a potentially fatal disease with a relapse rate of ~50%
- Any other antibody mediated disease with these characteristics is treated with induction immune Rx
- Should we be doing more at the start? Steroids? Ritux? Cyclophosphamide?
- A group consensus approach to this questions would be very useful; particularly in the setting of a registry

- We need to draw on the expertise of all of our colleagues to ensure the best possible patient care
Questions?