Evidence and Decision Making in Apheresis Medicine

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Dr. Weinstein has no conflicts, financial or otherwise, to disclose.
Rationale for Apheresis Therapy

blood substance → clinical disorder
remove substance → improve disorder
The “Harvard Death”

No patient should die without...

circa 1960: ...being restored to normal fluid and electrolyte status

circa 1970: ...a trial of corticosteroids

circa 1980: ...a course of plasma exchange
The Safety, Efficacy, and Cost Effectiveness of Therapeutic Apheresis (Office of Technology Assessment)

- A last resort in a wide range of diseases.
- Very few high quality studies document efficacy in actually improving health.
- Effective acute therapy in a few obscure diseases.
- Convincing proof of clinical efficacy lacking in most diseases in which apheresis is used.
- Optimal role and treatment parameters unknown.

adapted from CTA-HCS-23, July 1983
Plasma Exchanges Charged to US Medicare 2003-2017

Year
Plasma
Exchange
Procedures
12000
14000
16000
18000
20000
22000
24000
26000
28000
30000
32000

$R^2 = 0.958$
Leading Indications for Plasma Exchange in the United States

2017
- Complications of transplanted organs and tissues: 15.99%
- Inflammatory Polyneuropathy: 13.53%
- Multiple Sclerosis: 6.53%
- Other necrotizing vasculopathies: 8.69%

2010
- Myoneural Disorders: 22.9%
- Plasma protein metabolic disorder: 5.6%
- Polyarteritis Nodosa: 8.10%
- Complication of specific procedure: 7.5%
US Specialties Performing Therapeutic Plasma Exchange 2017

- **Nephrology**: 38.07%
- **Pathology**: 36.70%
- **Heme or Onc**: 5.35%
- **Internal Medicine**: 4.30%
- **Phys Med & Rehab**: 3.70%
- **Pain Management**: 3.18%
- **Physician's Assistant**: 2.40%
- **Neurology**: 2.07%
- **Anesthesiology**: 1.55%
- **Other**: 2.68%
2010 Revised ASFA Indication Categories *(with examples)*

| Category I       | First-line therapy: primary stand-alone treatment or in conjunction with other modes of treatment.  
|                  | *Acute Guillain-Barré Syndrome; Myasthenia Gravis* |
| Category II      | Second-line therapy: stand-alone treatment or in conjunction with other modes of treatment.  
|                  | *Photopheresis for chronic GVHD after corticosteroid failure* |
| Category III     | Optimum role of apheresis therapy not established. Decision making should be individualized.  
|                  | *DCM; Sepsis with Multiorgan Failure* |
| Category IV      | Published evidence indicates apheresis to be ineffective or harmful. IRB approval is desirable.  
|                  | *Plasma Exchange for Active Rheumatoid Arthritis* |

Definition of the Quality of Evidence: ACCP Modification of GRADE

<table>
<thead>
<tr>
<th>Evidence Quality Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>A</td>
</tr>
<tr>
<td>Moderate</td>
<td>B</td>
</tr>
<tr>
<td>Low</td>
<td>C</td>
</tr>
</tbody>
</table>

Based on:
- Guyatt GH et al. BMJ 2008;336:924-6
- Guyatt GH et al. Chest 2008;133:123S-131S
Modified GRADE System for Recommendations for Clinical Practice

<table>
<thead>
<tr>
<th>Grade of Recommendation</th>
<th>Implications for Decision-making</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>For Patient</td>
</tr>
<tr>
<td><strong>Strong (Grade 1)</strong></td>
<td>Most patients <em>would want</em></td>
</tr>
<tr>
<td>“We recommend”</td>
<td>recommended intervention under</td>
</tr>
<tr>
<td></td>
<td>similar circumstances</td>
</tr>
<tr>
<td><strong>Weak (Grade 2)</strong></td>
<td>Most patients would</td>
</tr>
<tr>
<td>“We suggest”</td>
<td>want the recommended intervention</td>
</tr>
<tr>
<td></td>
<td>under similar circumstances,</td>
</tr>
<tr>
<td></td>
<td><em>but many might not</em></td>
</tr>
</tbody>
</table>

adapted from Guyatt GH et al. Chest 2008;133:123S-131S
Fact Sheets: the Seventh ASFA Guidelines

**ANCA-ASSOCIATED RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (GRANULOMATOSIS WITH POLYANGIITIS AND MICROSCOPIC POLYANGIITIS)**

<table>
<thead>
<tr>
<th>Incidence: 8.5/1000,000/yr</th>
<th>Indication</th>
<th>Procedure</th>
<th>Recommendation</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dialysis dependence(^a)</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>

| No. of reported patients: >300 | RCT 8 (296) | CT 1 (26) | CS 22 (347) | CR NA |

\(^a\)At presentation, defined as Cr > 6 mg/dL. DAH=diffuse alveolar hemorrhage

---

**ANTI-GLOMERULAR BASEMENT MEMBRANE DISEASE (GOODPASTURE’S SYNDROME)**

<table>
<thead>
<tr>
<th>Incidence: 1/1000,000/yr</th>
<th>Indication</th>
<th>Procedure</th>
<th>Recommendation</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Dialysis dependence(^a), no DAH</td>
<td>TPE</td>
<td>Grade 2B</td>
<td>III</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 1B</td>
<td>I</td>
</tr>
</tbody>
</table>

| No. of reported patients: >300 | RCT 1(17) | CT 0 | CS 19 (468) | CR 21 |

\(^a\)At presentation, defined as Cr > 6 mg/dL. DAH=diffuse alveolar hemorrhage

Grade of Recommendation vs. Indication Category

ASFA 2016 Guidelines

<table>
<thead>
<tr>
<th>Number of Indications</th>
<th>Grade of Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>10</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>20</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>30</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>40</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>50</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>60</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>70</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
<tr>
<td>80</td>
<td>1A, 1B, 1C, 2A, 2B, 2C</td>
</tr>
</tbody>
</table>

- Category I (n=32)
- Category II (n=40)
- Category III (n=96)
- Category IV (n=13)

McLeod’s Criteria for Likelihood of Benefit of Apheresis Therapy

“Plausible Pathogenesis”  A secure understanding of the disease process suggests a clear rationale for apheresis therapy.

“Better Blood”  The abnormality that makes apheresis plausible is meaningfully corrected by apheresis therapy.

“Perkier Patients”  There is strong evidence that apheresis therapy confers clinical benefit that is meaningful (not only statistically significant).

Acute Guillain-Barré Syndrome

- Idiopathic inflammatory demyelinating polyneuropathy
  - Ascending, progressive muscle weakness, areflexia
  - Association with antecedent Campylobacter jejuni infection (60%)
  - Annual incidence: 1 to 4 per 100,000 worldwide

- Clinical course
  - Assisted ventilation: 10-25%
  - Death: 4-15%
  - Persistent mild neurological deficits: 67%
  - Persistent disabling neurological deficits: 5-15%

- Autoimmune disorder
  - Complement fixing IgM anti-peripheral nerve myelin antibodies
  - Anti-GM\(_1\) antibodies (severe axonal involvement)
  - Anti-GQ\(_{1b}\) antibodies (Fisher’s syndrome: ataxia, ophtalmoplegia, areflexia)
Rapid Response of Acute Guillain-Barré Syndrome to Plasma Exchange

from the French Cooperative Group Trial:
Ann Neurol 1987;22:753-761

109 TPE vs 111 controls
92% ≥ grade 3

<table>
<thead>
<tr>
<th></th>
<th>TPE</th>
<th>Control</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to grade 2 (days*)</td>
<td>70</td>
<td>111</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital stay (days*)</td>
<td>28</td>
<td>45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Full strength by 1 year</td>
<td>71%</td>
<td>52%</td>
<td>0.007</td>
</tr>
</tbody>
</table>

*median
### “McLeod’s Criteria” Applied to Conditions Treated by Apheresis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Plausible Pathogenesis</th>
<th>Better Blood</th>
<th>Perkier Patients</th>
<th>Recommended Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute GBS Cat I Grade 1A</td>
<td>Anti-myelin Antibody</td>
<td>Antibody↓ with TPE</td>
<td>Randomized trials</td>
<td>Based on clinical trials</td>
</tr>
</tbody>
</table>

*adapted from McLeod BC J Clin Apheresis 2002;17:124-132*
Myasthenia Gravis
An Autoimmune Disorder of the Neuromuscular Junction

- Autoantibody mediated
  - Acetylcholine receptor (AChR) antibodies
  - Anti-muscle-specific receptor tyrosine kinase
- Thymoma in 10-15%, esp. ♂ >40 yrs
- Variable weakness of voluntary muscles
  - Accentuated by repetitive motion
  - Alleviated by rest
  - Bulbar, extremity, trunk muscles
- Treatment
  - Acetylcholinesterase inhibitors
  - Immunosuppression
- Major role of TPE
  - Pre-op preparation for thymectomy
  - Acute exacerbations

Compilation of Level II Evidence Regarding TPE for Myasthenia Gravis

Seven open studies of at least 15 patients

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>patients</th>
<th>Pred</th>
<th>Immunosuppressor</th>
<th>TPE/pt</th>
<th>L exchanged</th>
<th>Effect (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behan</td>
<td>1979</td>
<td>21</td>
<td>Y</td>
<td>Y</td>
<td>?</td>
<td>16-32</td>
<td>100</td>
</tr>
<tr>
<td>Dau</td>
<td>1981</td>
<td>60</td>
<td>48</td>
<td>48</td>
<td>9-33</td>
<td>73</td>
<td></td>
</tr>
<tr>
<td>Olarte</td>
<td>1981</td>
<td>21</td>
<td>13</td>
<td>12</td>
<td>2-10</td>
<td>81</td>
<td></td>
</tr>
<tr>
<td>Perlo</td>
<td>1981</td>
<td>17</td>
<td>?</td>
<td>?</td>
<td>3-5</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Fornasari</td>
<td>1985</td>
<td>33</td>
<td>11</td>
<td>11</td>
<td>4-8</td>
<td>61</td>
<td></td>
</tr>
<tr>
<td>Antozzi</td>
<td>1991</td>
<td>70</td>
<td>?</td>
<td>?</td>
<td>2</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>Chiu</td>
<td>2000</td>
<td>94</td>
<td>?</td>
<td>?</td>
<td>4-5</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>316</td>
<td></td>
<td></td>
<td></td>
<td>76.4</td>
<td></td>
</tr>
</tbody>
</table>

“No adequate randomised controlled trials have been performed to determine whether plasma exchange improves the short- or longterm outcome for myasthenia gravis. However, many case series studies report short-term benefit from plasma exchange in myasthenia gravis, especially in myasthenic crisis. Further research is need to compare plasma exchange with alternative short-term treatments for myasthenic crisis and to determine the value of long-term plasma exchange for treating myasthenia gravis.”

## Controlled Trials of TPE in Myasthenia Gravis

<table>
<thead>
<tr>
<th>Authors</th>
<th>Study Design</th>
<th>Population</th>
<th>Intervention</th>
<th>Outcome Measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goti P et al. Thorax 1995;50:1080-6</td>
<td>Non-randomized, baseline to treatment</td>
<td>9 patients with grade IIb myasthenia</td>
<td>Baseline of treatment with pyridostigmine compared to treatment with TPE</td>
<td>• Pulmonary volumes &lt;br&gt; • Inspiratory and expiratory muscle force &lt;br&gt; • Respiratory muscle strength, Ventilatory pattern  &lt;br&gt;   o Inspiratory time  &lt;br&gt;   o Expiratory time  &lt;br&gt;   o Total time of respiratory cycle  &lt;br&gt;   o Tidal volume</td>
<td>Decrease in FRC and RV &lt;br&gt; Increase in FEV1, MIP &lt;br&gt; Increase in MEP &lt;br&gt; TPE vs pyridostigmine (p&lt;0.05).</td>
</tr>
<tr>
<td>Nagayasu T et al. Jpn J Thorac Cardiovasc Surg 2005;53:2-7</td>
<td>Retrospective, cohort study</td>
<td>51 patients with MG treated with trans-sternal thymectomy</td>
<td>19 patients: 1 TPE prior to thymectomy. 32 patients: thymectomy alone.</td>
<td>• Incidence of MG crisis &lt;br&gt; • Pharmacologic remission and improvement rate, evaluated by graded scale</td>
<td>TPE vs CONTROL &lt;br&gt; • Crisis within 1 year post-op: 5.3% vs 28.1% (p=0.049);  &lt;br&gt; • Crisis within 30 days post-op: 0 vs 15.6% (p=0.0724). &lt;br&gt; • Improvement rate: 100% vs 81.3% (p=0.0466).  &lt;br&gt; • Complete remission (5-7 yrs): 79% vs 50% (p=0.0427).</td>
</tr>
</tbody>
</table>

*adapted from Cortese I et al. Neurology 2011;76:294-300*
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<tr>
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<td>Anti-myelin Antibody</td>
<td>Antibody↓ with TPE</td>
<td>Randomized trials</td>
<td>Based on clinical trials</td>
</tr>
<tr>
<td>Myasthenia Gravis Cat I Grade 1B</td>
<td>ACh-receptor Antibody</td>
<td>↓ ACh receptor Antibody</td>
<td>Strong but anecdotal</td>
<td>? optimal regimen</td>
</tr>
</tbody>
</table>
Focal Segmental Glomerulosclerosis

- 15-20% of idiopathic nephrotic syndrome
- 30% recurrence post-transplant
  - 50% graft loss within 2 years
  - Higher risk with presentation before age 20
  - Up to 80% recurrence in subsequent graft
- Circulating permeability factor? \((\text{suPAR?})\)
  - Disease transferable to animals with patient plasma
  - 30-50 kDa protein
  - Sensitive to heat, proteolysis, \([\text{NH}_4\text{]}_2\text{SO}_4\)
- Treatment: controversial?
  - Corticosteroids, cytotoxic drugs
  - ACE inhibitors
  - Apheresis approach to circulating permeability factor?
Permeability Factor and Proteinuria in Focal Segmental Glomerulosclerosis

Plasma Exchange in Recurrent FSGS After Kidney Transplant

<table>
<thead>
<tr>
<th>Patient number</th>
<th>FSGS diagnosis post transplant</th>
<th>Recurrence days post transplant</th>
<th>Number of PE Procedures</th>
<th>Urinary protein (U.P.) (g/24 h)</th>
<th>Percentage decrease in U.P.</th>
<th>Post PE follow-up U.P.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Clinical</td>
<td>3</td>
<td>6</td>
<td>4.0</td>
<td>92</td>
<td>0.3 g/24 h 2 weeks</td>
</tr>
<tr>
<td>2</td>
<td>Clinical</td>
<td>3</td>
<td>10</td>
<td>40.0</td>
<td>99</td>
<td>0.2 g/24 h 2 months</td>
</tr>
<tr>
<td>3</td>
<td>Biopsy</td>
<td>5</td>
<td>8</td>
<td>11.0</td>
<td>45</td>
<td>Not available</td>
</tr>
<tr>
<td>4</td>
<td>Clinical</td>
<td>7</td>
<td>5</td>
<td>5.9</td>
<td>93</td>
<td>0.2 g/24 h 1 year</td>
</tr>
<tr>
<td>5</td>
<td>Clinical</td>
<td>7</td>
<td>11</td>
<td>4.0</td>
<td>92</td>
<td>0.3/4 h 3 months</td>
</tr>
<tr>
<td>6</td>
<td>Clinical</td>
<td>7</td>
<td>5</td>
<td>4.2</td>
<td>85</td>
<td>Negative 1.5 years</td>
</tr>
<tr>
<td>7</td>
<td>Biopsy</td>
<td>11</td>
<td>5</td>
<td>8.0</td>
<td>70</td>
<td>0.3 g/24 h 11 months</td>
</tr>
<tr>
<td>8</td>
<td>Biopsy</td>
<td>26</td>
<td>5</td>
<td>4.0</td>
<td>8</td>
<td>0.2 g/dl 2.5 year</td>
</tr>
<tr>
<td>9</td>
<td>Biopsy</td>
<td>66</td>
<td>5</td>
<td>6.1</td>
<td>97</td>
<td>Negative 9 months</td>
</tr>
<tr>
<td>10</td>
<td>Biopsy</td>
<td>52</td>
<td>11</td>
<td>11.0</td>
<td>45</td>
<td>0.8 g/24 h 11 months</td>
</tr>
<tr>
<td>11</td>
<td>Biopsy</td>
<td>&gt; 700</td>
<td>6</td>
<td>3.0</td>
<td>50</td>
<td>0.4 g/24 h 5.5 year</td>
</tr>
</tbody>
</table>

(2 years)

All were on immunosuppressive drugs.

Shariatmadar S and Noto TA. J Clin Apheresis 2002;17:78-83
10 High-Risk Patients with FSGS who Received TPE Peri-Transplantation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Follow-up (days)</th>
<th>Induction therapy*</th>
<th>Current immuno-suppression**</th>
<th>Recurrence</th>
<th>Proteinuria (g/day)</th>
<th>Rejection</th>
<th>Serum creatinine (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1258</td>
<td>T</td>
<td>T/M/P</td>
<td>N</td>
<td>0.30</td>
<td>N</td>
<td>1.0</td>
</tr>
<tr>
<td>2</td>
<td>980</td>
<td>B</td>
<td>T/M/P</td>
<td>N</td>
<td>0.19</td>
<td>N</td>
<td>1.1</td>
</tr>
<tr>
<td>3</td>
<td>959</td>
<td>B</td>
<td>T/M/P</td>
<td>N</td>
<td>0.39</td>
<td>Y</td>
<td>1.8</td>
</tr>
<tr>
<td>4</td>
<td>749</td>
<td>T</td>
<td>T/I</td>
<td>Y</td>
<td>4.75</td>
<td>N</td>
<td>2.6</td>
</tr>
<tr>
<td>5</td>
<td>735</td>
<td>B</td>
<td>T/M/P</td>
<td>N</td>
<td>0.81</td>
<td>Y</td>
<td>1.3</td>
</tr>
<tr>
<td>6</td>
<td>699</td>
<td>T</td>
<td>R/I/P</td>
<td>N</td>
<td>0.39</td>
<td>N</td>
<td>2.0</td>
</tr>
<tr>
<td>7</td>
<td>644</td>
<td>B</td>
<td>T/M/P</td>
<td>N</td>
<td>0.33</td>
<td>N</td>
<td>1.5</td>
</tr>
<tr>
<td>8</td>
<td>962</td>
<td>B</td>
<td>T/I/P</td>
<td>Y</td>
<td>37.1</td>
<td>N</td>
<td>HD</td>
</tr>
<tr>
<td>9</td>
<td>238</td>
<td>T</td>
<td>T/M/P</td>
<td>Y</td>
<td>7.5</td>
<td>N</td>
<td>HD</td>
</tr>
<tr>
<td>10</td>
<td>287</td>
<td>T</td>
<td>T/M/P</td>
<td>N</td>
<td>0.59</td>
<td>N</td>
<td>0.9</td>
</tr>
</tbody>
</table>

*T = thymoglobulin;  B = basiliximab.

**T = tacrolimus;  M = mycophenolate mofetil;  P = prednisone.

from Gohh et al. Am J Transplant 2005;5:2907-12
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</tr>
<tr>
<td>Focal Segmental Glomerular Sclerosis (recurrent post transplant) Cat I Grade 1B (2016)</td>
<td>Permeability factor (PF)</td>
<td>↓ PF ↓ Proteinuria</td>
<td>Largely anecdotal. Small numbers</td>
<td>Variable Not determined</td>
</tr>
</tbody>
</table>
McLeod’s Criteria for Likelihood of Benefit of Apheresis Therapy

**Corollary Considerations**

- Is the problem potentially reversible with apheresis therapy?
- Is there a first-line or standard therapy?
  - Has it been tried?
  - Outcome?
- If apheresis to be tried, is the goal of a therapeutic trial defined?

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**McLeod BC J Clin Apheresis 2002;17:124-132**

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Plausible Pathogenesis”</td>
<td>A secure understanding of the disease process suggests a clear rationale for apheresis therapy.</td>
</tr>
<tr>
<td>“Better Blood”</td>
<td>The abnormality that makes apheresis plausible is meaningfully corrected by apheresis therapy.</td>
</tr>
<tr>
<td>“Perkier Patients”</td>
<td>There is strong evidence that apheresis therapy confers clinical benefit that is meaningful (not only statistically significant).</td>
</tr>
</tbody>
</table>
Individualize Apheresis Decision Making for Patients with Rasmussen’s Encephalitis

- 22 y/o ♀ with RE since age 8 yrs
  - Major partial seizures Q 15 min
  - Cognitive decline (7-8 y/o level)
  - Right hemiparesis (wheelchair)
  - Anti-GluR3 negative

- Therapies applied
  - Anticonvulsants – partial control
  - Surgery – transient↓ seizures
  - IVIG – no response

- Plasma exchange (since 5/2/2008)
  - Initially 3 TPE per week
  - Weekly since Sept 2008
  - Ambulatory
  - ↓↓ seizures
  - ↑ cognitive function

Maintained for many years with intermittent TPE
68 year old ♀ with CMML

**Peripheral Blood:**
- WBC: 45,000/µL
- HCT: 31.8%
- MCV: 73.7 FL
- PLT: 3,000/µL
- Mono: 3,400/µL

**Bone Marrow:**
- Cellularity: 95%
- Morphology: dysplastic
- Megakaryocytes: ↓↓↓
- Iron: absent
Severe Symptomatic Thrombocytopenia

• Clinical manifestations
  – Petechial rash & spontaneous ecchymoses
  – Severe, constant hematochezia
  – Retrotympanic bleeding → hearing loss

• Attempts to manage thrombocytopenia & hemorrhage
  – IVIG
  – Steroids
  – RBC transfusion
  – Platelet transfusion

• HLA phenotype: A23, A66, B7, B41
• > 40% PRA on HLA antibody screen

• HLA antibody specificities
  – Broad spectrum
  – Class I and II

• Initial platelet crossmatching
  – 7 crossmatch panels
  – 2 of 117 (1.7%) apheresis platelet units compatible
Platelet Support of Patient PK

HLA antibody↓56% (35-82%)
41 of 274 (15%) products crossmatch compatible

Platelet Pre-Count
Platelet Post-Count

CCI = \frac{(Post \ Tx \ PLT) - (Pre \ Tx \ PLT)}{* \ # \ of \ Platelets \ Transfused} \times BSA \ (M^2)

*multiples of 10^{11}
Evidence Based Medicine: Caveats

“...integrate individual clinical expertise with the best available external clinical evidence ...”

“Without clinical expertise, practice risks becoming tyrannized by evidence...[which may be] inapplicable to an individual patient.”

“Without current best evidence, practice risks becoming rapidly out of date.”

Using Available Tools for Clinical Decision Making in Apheresis Medicine

- **Indication Categories** – ASFA Fact Sheets
  - Where does apheresis fit into treatment scheme
  - Assessment of strength of published evidence

- **McLeod’s Criteria**
  - Framework for taking stock of available data
  - Plausibility of achieving benefit with apheresis

- **Corollary Considerations**
  - Framework for incorporating clinical judgment
  - Formulation of specific therapeutic trial
Apheresis at the Bedside

Evidence \times \text{Knowledge} \quad \text{Individualized Judgment} = \quad \text{Rational Apheresis Decision Making}