Apheresis Review Session
Clinical Applications: Therapeutics

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## ASFA Categories

### Indications for Therapeutic Apheresis – ASFA 2016 Categories

<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>

## Recommendation Grades

**Grading recommendations adopted from Guyatt et al**

<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>
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<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>

Hyperleukocytosis

- Hyperleukocytosis
  - White blood cell count $\geq 100,000/\mu L$.
  - Due to the presence of leukemia.
  - Extremely elevated counts can result in:
    - Hyperviscosity
    - Leukostasis
    - Tumor lysis syndrome
Hyperleukocytosis

- Complications of Leukostasis/Hyperviscosity
  - Hemorrhage
  - Pulmonary infarction
  - Alveolar capillary block
  - Cerebral hemorrhage
  - Retinal infarct
Hyperleukocytosis

• Complications of Tumor Lysis Syndrome
  • Hyperkalemia
  • Hyperphosphatemia
  • Hyperuricemia

• Results in disseminated intravascular coagulation and/or renal failure
Hyperleukocytosis

• Response to leukocytapheresis
  • Higher short-term mortality rates with WBC >100,000 compared to counts <50,000.
  • Leukocytapheresis can:
    • Lessen or reverse symptoms
    • Improve 2 to 3 week mortality
    • Does not affect long-term or overall survival
Hyperleukocytosis

- Course of apheresis therapy
  - 8 to 10 liters or 2 blood volumes processed
  - No correlation between reduction and survival
    - Resolution of symptoms the end-point of treatment
- Concurrent chemotherapy MUST be initiated
- More mature phenotype addition of HES may be necessary
Hyperleukocytosis

• Symptomatic
  • ASFA Category - II
  • ASFA Recommendation Grade - 1B

• Prophylaxis
  • ASFA Category - III
  • ASFA Recommendation Grade - 2C

<table>
<thead>
<tr>
<th></th>
<th>RCT</th>
<th>CT</th>
<th>CS</th>
<th>CR</th>
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<tbody>
<tr>
<td>AML</td>
<td>0</td>
<td>6(437)</td>
<td>16(473)</td>
<td>14(16)</td>
</tr>
<tr>
<td>ALL</td>
<td>0</td>
<td>3(366)</td>
<td>6(57)</td>
<td>2(2)</td>
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</tbody>
</table>
Thrombocytosis

- Platelet count $\geq 500,000/\mu L$
- May be primary (e.g. polycythemia vera) or secondary (e.g. splenectomy)
- Results in:
  - Hemorrhage - predominantly mucocutaneous
  - Thrombosis – microvascular and macrovascular
- Complications in:
  - 56% of primary causes
  - 4% of secondary causes
# Thrombocytosis

<table>
<thead>
<tr>
<th>Thrombosis</th>
<th>Increasing age</th>
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<tbody>
<tr>
<td></td>
<td>Previous thrombotic event</td>
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<tr>
<td></td>
<td>Longer duration of thrombocytosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemorrhage</th>
<th>Platelet count &gt;2,000,000/µL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NSAID ingestion</td>
</tr>
</tbody>
</table>
Thrombocytosis

• Response to thrombocytapheresis
  • No controlled trials have been performed.
  • Symptom improvement observed during treatment.
Thrombocytosis

- Course of apheresis therapy
  - 1 to 1.5 blood volumes processed or 3 hours.
  - No correlation between platelet count and complications
  - Resolution of symptoms the end-point of treatment
  - Concurrent chemotherapy MUST be initiated
Thrombocytosis

- **Symptomatic**
  - ASFA Category - II
  - ASFA Recommendation Grade - 2C
- **Secondary or prophylactic**
  - ASFA Category - III
  - ASFA Recommendation Grade - 2C

<table>
<thead>
<tr>
<th></th>
<th>RCT</th>
<th>CT</th>
<th>CS</th>
<th>CR</th>
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<tbody>
<tr>
<td>Symptomatic</td>
<td>0</td>
<td>0</td>
<td>7(180)</td>
<td>25(30)</td>
</tr>
<tr>
<td>Prophylactic</td>
<td>0</td>
<td>0</td>
<td>2(39)</td>
<td>3(4)</td>
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Sickle Cell Anemia

• Incidence: 1 in 200 to 500 births in the US
• >60,000 African-Americans affected
• Autosomal recessive disorder

• Arisen in four separate locations
  • Africa
  • Middle East
  • Mediterranean basin
  • India

• Heterozygotes protected from *Plasmodium falciparum* malaria

Images from Ohio State University Parasite and Parasitology Resources
(http://www.biosci.ohio-state.edu/~parasite/home.html)
Sickle Cell Anemia

• Single nucleotide substitution
• Glutamic acid to valine substitution
• Polymerization of Hb at low pO₂:
  • Vascular occlusion
  • Red cell membrane damage
    • Water loss and cell dehydration
    • K⁺ and Na⁺ leakage
    • Hemolysis
    • Increased expression of adhesion molecule receptors
• Cells are “sticky” increasing viscosity

Image from www.pathologystudent.com
Sickle Cell Anemia

- **Acute Chest Syndrome**
  - Fever, tachycardia, chest pain, leukocytosis, and pulmonary infiltrates
  - Cause found in 38% of patients
    - Pneumonia – 29%
    - Fat embolism – 9%
- 20 to 50% of patients with SCD
- 14 to 33% of all hospitalizations in SCD
- Progressive respiratory failure leading to death
Sickle Cell Anemia

- Priapism
  - 30 to 80% of male SCD patients
  - Associated with dehydration and hypoventilation
  - Sickling within the corpus cavernosa
  - May result in:
    - Stuttering - multiple episodes all less than 3 hours
    - Fulminant cases - lasting >6 hours
    - 25% will have erectile dysfunction
Sickle Cell Anemia

• Increased risk of acute chest syndrome, renal failure, stroke, and pain crisis with surgery.
  • Due to:
    • Hypoxia
    • Dehydration
    • Hypothermia
    • Acidosis

• Current anesthesiology practice minimizes these.
Sickle Cell Anemia

• Red Cell Exchange
  • Avoids hyperviscosity by replacing sticky HbS cells with normal cells.
  • Performed by manual or automated methods.
  • Automated method superior:
    • Shorter time involved
    • Greater efficiency of HbS reduction
Sickle Cell Anemia

- Indications for red cell exchange:
  - Cerebrovascular disease
  - Arterial hypoxemia syndrome
  - Acute chest syndrome
  - Priapism
  - Initiation of chronic transfusion
  - Preoperative preparation
  - Retinal arterial vaso-occlusion
  - Cerebral angiogram (using hyperosmotic contrast agents)
  - Hepatic failure
  - Septic shock
Sickle Cell Anemia

• Course of apheresis therapy
  • Goal is to remove HbS containing red blood cells and replace them.
  • Targets:
    • Hematocrit of 30%
    • <30% of the cells containing HbS
Sickle Cell Anemia

- **Acute stroke**
  - ASFA Category - I
  - ASFA Recommendation Grade - 1C

- **Acute chest syndrome**
  - ASFA Category - II
  - ASFA Recommendation Grade - 1C

- **Prophylaxis for stroke**
  - ASFA Category - I
  - ASFA Recommendation Grade – 1A

- **Multi-organ failure**
  - ASFA Category - III
  - ASFA Recommendation Grade - 2C
Sickle Cell Anemia

• Priapism
  • ASFA Category - III
  • ASFA Recommendation Grade - 2C

• Splenic sequestration
  • ASFA Category - III
  • ASFA Recommendation Grade - 2C

• Recurrent vaso-occlusive pain crisis
  • ASFA Category - III
  • ASFA Recommendation Grade - 2C

• Pre-operative preparation
  • ASFA Category - III
  • ASFA Recommendation Grade - 2A
# Sickle Cell Anemia

<table>
<thead>
<tr>
<th>Condition</th>
<th>RCT</th>
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<tbody>
<tr>
<td>Acute Stroke</td>
<td>0</td>
<td>1(52)</td>
<td>7(160)</td>
<td>8(10)</td>
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<tr>
<td>Acute Chest Syndrome</td>
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<td>2(121)</td>
<td>13(145)</td>
<td>8</td>
</tr>
<tr>
<td>Priapism</td>
<td>0</td>
<td>0</td>
<td>1(5)</td>
<td>1</td>
</tr>
<tr>
<td>Multiorgan failure</td>
<td>0</td>
<td>0</td>
<td>3(10)</td>
<td>3</td>
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<tr>
<td>Hepatic sequestration</td>
<td>0</td>
<td>0</td>
<td>1(52)</td>
<td>3(4)</td>
</tr>
<tr>
<td>Splenic sequestration</td>
<td>0</td>
<td>0</td>
<td>3(204)</td>
<td>0</td>
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<td>Stroke prophylaxis</td>
<td>2(326)</td>
<td>1(36)</td>
<td>20(335)</td>
<td>3</td>
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<tr>
<td>Vaso-occlusive pain crisis</td>
<td>1(130)</td>
<td>1(21)</td>
<td>3(18)</td>
<td>1</td>
</tr>
<tr>
<td>Pre-operative management</td>
<td>3(1035)</td>
<td>4(184)</td>
<td>3(957)</td>
<td>0</td>
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Thrombotic Thrombocytopenic Purpura (TTP)

The “classic pentad”:

- Thrombocytopenia
- Microangiopathic hemolytic anemia
  - Schistocytes and an elevated LDH
- Neurologic dysfunction
- Fever
- Renal dysfunction
Thrombotic Thrombocytopenic Purpura (TTP)

Mechanism behind TTP

• Deficient ADAMTS13 activity.

• ADAMTS13 cleaves vWF into smaller multimers.

• Ultra-large vWF multimers bind to platelets via GPIb producing microthrombi.

Sadler J E Blood 2008;112:11-18
Thrombotic Thrombocytopenic Purpura (TTP)

- Plasma infusion:
  - Replaces the ADAMTS13

- Plasma exchange:
  - Removes the autoantibody
  - Removes the ultra-large vWF multimers
  - Replaces the ADAMTS13
Thrombotic Thrombocytopenic Purpura (TTP)

- Course of TPE therapy
  - 1 to 1.5 plasma volume exchanges with plasma
  - Cryopoor plasma indicated for refractory patients
  - Daily treatment until:
    - Platelet count $>150,000/\mu L$ for two days
    - LDH near normal
    - Resolution of neurologic symptoms
  - Withdrawal versus tapering
Thrombotic Thrombocytopenic Purpura (TTP)

- ASFA Category - I
- ASFA Recommendation Grade – 1A

<table>
<thead>
<tr>
<th>RCT</th>
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<th>CS</th>
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<tbody>
<tr>
<td>7(301)</td>
<td>2(133)</td>
<td>38(1541)</td>
<td>NA</td>
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</tbody>
</table>
Hyperviscosity in monoclonal gammopathies

- Viscosity determined: hematocrit, red blood cell aggregation, plasma protein levels, vasculature condition
- Hyperviscosity characterized by:
  - Mucous membrane bleeding
  - Retinopathy
  - Neurologic impairment

- Neurologic impairment:
  - Headache
  - Dizziness
  - Vertigo
  - Nystagmus
  - Hearing loss
  - Visual impairment
  - Somnolence
  - Coma
  - Seizures

- Other symptoms:
  - Congestive heart failure
  - Respiratory compromise
  - Fatigue
  - Peripheral polyneuropathy
  - Anorexia
Hyperviscosity in monoclonal gammopathies

• Most common in Waldenström’s macroglobulinemia

• Paraprotein levels:
  • IgM >3g/dL
  • IgA >6 to 7 g/dL
  • IgG3 >4 g/dL

• Serum viscosity does NOT correlate with symptoms.
  • Normal: 1.4 to 1.8 Ostwald units
  • Some symptomatic as low as 3 or 4
  • Most symptomatic between 6 and 7
  • Some asymptomatic between 8 to 10
Hyperviscosity in monoclonal gammopathies

- Response to plasma exchange
  - Rapid improvement in neurologic symptoms
  - Length of response depends upon the rate of monoclonal protein production.
Hyperviscosity in monoclonal gammopathies

- Course of TPE therapy
  - 1 to 1.5 plasma volume exchanges with albumin
  - Daily treatment until acute symptoms resolve, usually 1 to 3 treatments
  - Relationship between serum viscosity and paraprotein levels is exponential
    - Small changes in concentration result in large changes in viscosity
  - Concurrent chemotherapy MUST be initiated
Hyperviscosity in monoclonal gammopathies

• Symptomatic
  • ASFA Category - I
  • ASFA Recommendation Grade - 1B
• Prophylaxis prior to rituximab administration
  • ASFA Category - I
  • ASFA Recommendation Grade - 1C

<table>
<thead>
<tr>
<th></th>
<th>RCT</th>
<th>CT</th>
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</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td>0</td>
<td>3(46)</td>
<td>18(263)</td>
<td>NA</td>
</tr>
<tr>
<td>Prophylaxis for rituximab</td>
<td>0</td>
<td>0</td>
<td>3(45)</td>
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</table>
Acute Inflammatory Demyelinating Polyneuropathy (Guillain-Barré Syndrome)

• Incidence
  • 1-2/100,000

• Demographics
  • Male predominance
  • Increasing incidence with age (1/100,000 <30 versus 4/100,000 >75)

• Signs and Symptoms
  • Symmetrical muscle weakness and paresthesia that spread proximally
  • Progresses over 12 hours to 28 days
  • May involve respiratory and oropharyngeal muscles
    • 10 to 23% require ventilator assistance
  • Autonomic dysfunction may be present
Acute Inflammatory Demyelinating Polyneuropathy (Guillain-Barré Syndrome)

- **Associations**
  - Infectious illness in weeks prior to onset in 75%
  - *Campylobacter jejuni, CMV, EBV, varicella-zoster, Borrelia burgdorferi, Mycoplasma pneumoniae, HIV*
  - Influenza vaccine

- **Pathophysiology**
  - Demyelination of peripheral neurons due to autoantibodies toward GM1, GD1a, GT1a, and GQ1b
  - Evidence of axonal damage in some patients involving motor and sensory neurons (AMSAN) or only motor neurons (AMAN)
Acute Inflammatory Demyelinating Polyneuropathy (Guillain-Barré Syndrome)
Acute Inflammatory Demyelinating Polyneuropathy (Guillain-Barré Syndrome)

- Treatment
  - Spontaneous recovery
    - 66-75% residual deficits
  - Supportive care
  - IVIG
  - Plasma exchange
Acute Inflammatory Demyelinating Polyneuropathy (Guillain-Barré Syndrome)

- Response to plasma exchange
  - Cochrane database found 6 eligible trials enrolling 649 patients
    - Shorter time to recovery of walking, smaller percentage requiring artificial ventilation, shorter duration of ventilation, better muscle strength at 1 year, fewer severe deficits at 1 year
    - “First and only treatment proven superior to supportive care”
  - Second Cochrane database study found equivalence between TPE and IVIG though IVIG course more likely to be completed
  - Recent economic analysis found the costs of IVIG therapy to be twice that of TPE
Acute Inflammatory Demyelinating Polyneuropathy  
(Guillain-Barré Syndrome)

• Response to plasma exchange
  • Axonal involvement has been reported to be more responsive to TPE than IVIG
  • Retrospective studies suggest that TPE in the setting of failure to respond to IVIG has limited benefit

• Course of TPE therapy
  • 1 to 1.5 plasma volume exchanges with albumin as replacement
  • Mild AIDP – 2 TPE
  • Moderate to severe AIDP – 4 TPE
  • Greatest benefit if started within 7 days of symptom onset
Acute Inflammatory Demyelinating Polyneuropathy (Guillain-Barré Syndrome)

- **AIDP**
  - ASFA Category - I
  - ASFA Recommendation Grade – 1A

- **AIDP after failure of IVIG**
  - ASFA Category - III
  - ASFA Recommendation Grade – 2C

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<tr>
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<th>RCT</th>
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<tbody>
<tr>
<td>AIDP</td>
<td>19(1770)</td>
<td>0</td>
<td>9(369)</td>
<td>NA</td>
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<tr>
<td>After IVIG</td>
<td>0</td>
<td>0</td>
<td>1(46)</td>
<td>NA</td>
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</table>
Chronic Inflammatory Demyelinating Polyneuropathy

• Incidence
  • 1-2/100,000

• Demographics
  • Male predominance

• Signs and Symptoms
  • Symmetrical proximal and distal muscle weakness with or without numbness that progresses and relapses over two or more months
  • Pain in 42% of patients
  • NCV demonstrates slow conduction, conduction block, and prolonged latencies in more than 1 nerve
  • CSF demonstrates protein >55 mg/dL with cell count <10/µL
Chronic Inflammatory Demyelinating Polyneuropathy

• Associations
  • Hepatitis, inflammatory bowel disease, Hodgkin disease, connective tissue diseases, HIV, diabetes mellitus

• Pathophysiology
  • Inflammatory demyelination of peripheral nerves with secondary axonal degeneration
  • Both humoral and cell-mediated immune responses have been documented
  • Antibodies to myelin components GM1, P0, and MAG have been identified in some patients
Chronic Inflammatory Demyelinating Polyneuropathy

- Response to plasma exchange
  - Dyck – 29 patients randomized to shame versus TPE twice weekly for three weeks. Significantly better NCV testing and clinical improvement.
  - Hahn – 18 patients randomized to shame versus 10 TPE over 5 weeks followed by washout period and opposite therapy. 80% with substantial improvement. 66% relapsed within 1 to 2 weeks but responded to additional TPE.
  - Dyck – 20 patients randomized to IVIG versus TPE. Both with significant improvement but no difference between the two.
Chronic Inflammatory Demyelinating Polyneuropathy

- Course of TPE therapy
  - 1 to 1.5 plasma volume exchanges with albumin as replacement
  - 3 TPE per week for 2 weeks followed by 2 per week for 4 weeks.
  - Relapse occurs within 2 weeks of cessation but responds to additional TPE.
  - With relapse, maintenance therapy necessary with frequency adjusted to control symptoms.
Chronic Inflammatory Demyelinating Polyneuropathy

- ASFA Category - I
- ASFA Recommendation Grade – 1B

<table>
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<th>RCT</th>
<th>CT</th>
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<tbody>
<tr>
<td>3(67)</td>
<td>0</td>
<td>32(1021)</td>
<td>31(32)</td>
</tr>
</tbody>
</table>
Myasthenia Gravis

• Incidence
  • 1/100,000

• Demographics
  • Most prevalent in 20 to 40 year-old women

• Signs and Symptoms
  • Weakness and fatigability with repetitive physical activity that improves with rest
  • Ptosis, diplopia, facial weakness, bulbar weakness, and limb weakness
  • Bulbar weakness associated with dysphagia, aspiration, and respiratory failure
Myasthenia Gravis

• Associations
  • Thymic pathology in 75%
    • 85% thymic hyperplasia
    • 15% tumor, predominantly thymoma

• Pathophysiology
  • Autoantibodies directed against acetylcholine receptors (AChR) or muscle-specific receptor tyrosine kinase (MuSK) on the postsynaptic motor end plate results in decreased number of AChR and decreased action potentials on stimulation
  • 80 to 90% of patients have IgG1 or IgG3 antibodies to AChR
  • 40 to 70% of “seronegative” cases have IgG4 antibodies to MuSK
    • MuSK recruits AChR binding proteins leading to AChR clustering and neuromuscular junction formation
Myasthenia Gravis

• Response to plasma exchange
  • 3 randomized controlled trials comparing TPE to IVIG have found equivalency
  • One comparison study of IVIG and TPE found IVIG to be more cost effective with a shorter length of hospital stay but patients in the study treated with TPE more likely to be on ventilator and have respiratory failure
  • Trials of routine TPE prior to thymectomy versus supportive care have shown equivalency
Myasthenia Gravis

• Course of TPE therapy
  • 1 to 1.5 plasma volume exchanges with albumin as replacement
  • 5 to 6 TPE daily or every-other-day
  • Mild exacerbations in stable patients can be treated with 2 to 3 TPE
  • Maintenance TPE at weekly intervals followed by weaning may be performed
Myasthenia Gravis

• MG moderate to severe
  • ASFA Category - I
  • ASFA Recommendation Grade – 1B

• MG pre-thymectomy
  • ASFA Category - I
  • ASFA Recommendation Grade – 1C

<table>
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<th>RCT</th>
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<tbody>
<tr>
<td>Moderate - severe</td>
<td>8(279)</td>
<td>8(2837)</td>
<td>30(556)</td>
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<tr>
<td>Pre-thymectomy</td>
<td>0</td>
<td>5(342)</td>
<td>2(51)</td>
<td>NA</td>
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</table>
Multiple Sclerosis

- **Incidence**
  - 5-30/100,000

- **Demographics**
  - Female predominance
  - Most common in Caucasians of Northern European ancestry
  - More common in temperate climates
  - Genetic predisposition

- **Signs and Symptoms**
  - Variety of neurologic symptoms resulting from multifocal demyelination of the central nervous system
  - Include fatigue, visual problems, bladder/bowel dysfunction, sensory changes, emotional changes, weakness, balance difficulty, cognitive changes, etc.
Multiple Sclerosis

• Disease course
  • 80 to 85% relapsing and remitting
    • Acute focal or multifocal inflammatory demyelination
    • Development of symptoms over days to weeks
  • Symptoms plateau in 1 to 2 weeks
  • Gradual recovery within 3 months
    • May take up to 6 to 12 months
  • 15% primary progressive
    • Chronic demyelination, axonal loss, and gliosis
    • Progression of disability from onset with no or only minor remissions or plateaus
Multiple Sclerosis

• Pathophysiology
  • T-cells and B-cells penetrate blood-brain barrier with injury to myelin and axons
  • Both cell mediated immunity and humoral immunity involved

Lucchineti CF Neurol Clin 2005;23:77-105
Multiple Sclerosis

• Response to plasma exchange
  • Acute CNS demyelination unresponsive to steroids – Blinded trials have demonstrated moderate to marked improvement in 42% of patients. Case series have reported improvement in 37 to 100% of treated patients
  • Primary progressive MS – Meta-analysis of 6 prospective trials found decreased odds of worsening at 12 and 24 months and increased odds of improvement at 6 and 12 months
Multiple Sclerosis

• Course of TPE therapy
  • Acute CNS demyelination unresponsive to steroids
    • 1 to 1.5 plasma volume exchanges with albumin as replacement
    • 5 to 7 TPE over 14 days
  • Primary progressive MS
    • 1 to 1.5 plasma volume exchanges with albumin as replacement
    • Weekly long-term therapy with tapering as tolerated
Multiple Sclerosis

- Acute CNS demyelination unresponsive to steroids
  - ASFA Category – II
  - ASFA Recommendation Grade – 1B
- Primary progressive
  - ASFA Category – III
  - ASFA Recommendation Grade – 2C
- Chronic progressive
  - ASFA Category – III
  - ASFA Recommendation Grade – 2B

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<tbody>
<tr>
<td>Acute CNS demyelination</td>
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Anti-Basement Membrane Disease

- Anti-basement membrane disease (Goodpasture’s syndrome)
- Autoantibody to the c terminus of $\alpha_3$ chain of type IV collagen
  - Restricted to glomerular and alveolar basement membrane
- Results in complement mediated damage to these membranes producing:
  - Glomerulonephritis
  - Alveolar hemorrhage
Anti-Basement Membrane Disease

- Response to plasma exchange
  - More rapid decline in anti-basement membrane antibody titers
  - Lower serum creatinine levels
  - Fewer patients progressing to renal failure
  - Decreased mortality (40% versus 85%)
Anti-Basement Membrane Disease

Plasma exchange should be instituted early!!!

- Recovery correlates with a serum creatinine of <5 mg/dl and <50% crescents on biopsy
- Recovery infrequent with plasma exchange if:
  - Oliguric
  - Serum creatinine > 6.8 mg/dl
  - Dialysis required at presentation
- Reserve plasma exchange for pulmonary hemorrhage in patients unlikely to respond
Anti-Basement Membrane Disease

• Course of TPE therapy
  • 1 to 1.5 plasma volumes exchange with albumin
  • Daily for 7 to 14 days following:
    • Urine output
    • Serum creatinine
    • Anti-GBM titers
  • Concurrent chemotherapy MUST be initiated
Anti-Basement Membrane Disease

- Dialysis independent
  - ASFA Category - I
  - ASFA Recommendation Grade - 1B
- Diffuse alveolar hemorrhage
  - ASFA Category - I
  - ASFA Recommendation Grade - 1C
- Dialysis dependent
  - ASFA Category - III
  - ASFA Recommendation Grade - 2B

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ANCA Associated Rapidly Progressive Glomerulonephritis

- 40% of patients with RPGN - Wegner’s granulomatosis, polyarteritis nodosa, or “renal-limited” pauci-immune glomerulonephritis
- 80% progress to end-stage renal disease
ANCA Associated Rapidly Progressive Glomerulonephritis

- Response to plasma exchange
  - No statistically significant difference in renal outcome in mild RPGN!
    - No difference in mean serum creatinine, changes in creatinine values, dialysis dependency
  - Effective adjuvant therapy for severe disease as defined by dialysis dependency or creatinine > 9 mg/dl!
    - Discontinuation of dialysis or decrease in serum creatinine by at least 50% has been seen in these patients
ANCA Associated Rapidly Progressive Glomerulonephritis

- Course of TPE therapy
  - 1 to 1.5 plasma volume exchange with albumin
  - 7 exchanges per week following:
    - Urine output
    - Serum creatinine
    - ANCA titers (?)
  - Concurrent chemotherapy MUST be initiated
ANCA Associated Rapidly Progressive Glomerulonephritis

- Dialysis independent
  - ASFA Category - III
  - ASFA Recommendation Grade - 2C
- Diffuse alveolar hemorrhage
  - ASFA Category - I
  - ASFA Recommendation Grade - 1C
- Dialysis dependent
  - ASFA Category - I
  - ASFA Recommendation grade - 1A

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Questions?