

Acute Therapies: Steroids, IVIG, Plasmaexchange and Cyclophosphamide

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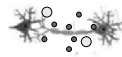
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[Disclosures: none]

Stages of Disease



Chronic Degeneration

Stages of Disease



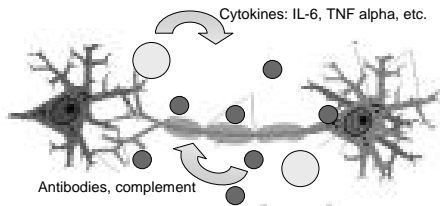
Acute Inflammation

Stages of Disease



Endogenous Repair

Acute Inflammation



Immune Mediated Neurologic Disease

INTERVENTIONS

TRIGGER

Avoidance
Vaccines

ACUTE INFLAMMATION

Anti-inflammatories
Neuroprotection

CHRONIC DEGENERATION

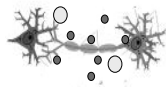
Neuroprotection
Prevent Recurrence

ENDOGNEOUS REPAIR

Promote Repair
Repair it Iatrogenically

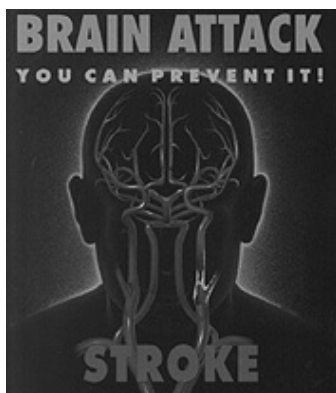
Acute Therapy

- Goals of acute therapy
- Mechanisms
- Lessons from transverse myelitis



Drugs/Strategies Used as Acute Therapy and Their Mechanism of Action

- Steroids
 - dampens the inflammatory cytokine cascade
 - inhibits the activation of T cells
 - decrease the extravasation of immune cells into the CNS
 - facilitate the apoptosis of activated immune cells



Drugs/Strategies Used as Acute Therapy and Their Mechanism of Action

- IVIG
 - neutralization of pathogenic autoantibodies
 - suppression of pathogenic autoantibody production
 - acceleration of native IgG degradation
 - inhibition of complement binding
 - blockage of Fc binding mediated phagocytosis
 - interruption of antigen recognition
 - suppression and neutralization of T-helper cell cytokines, metalloproteinase and chemokine production

Goals of Acute Therapy

- Limit Inflammation
 - Preventing more cells from infiltrating blood brain barrier
 - Eliminate members of the immune system that are in inappropriate places
- Limit substances that lead to nervous system damage
 - Directly inhibit substances that are neurotoxic (i.e. IL-6)
- Protect components of the nervous system
 - “neuroprotective” strategies aim to shield neurons from damage even in the presence of inflammation.

Drugs/Strategies Used as Acute Therapy and Their Mechanism of Action

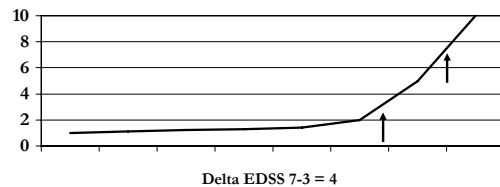
- Plasmaexchange (plasmapheresis/PLEX)
 - reduces the amount of circulating antibodies in a patient through filtration
- Cyclophosphamide
 - Alkylating agent, destroys proliferating lymphocytes

Difficulties Encountered When Designing Acute Strategies

- Limited clinical trials
- Difficulty for designing prospective, blinded trials
 - Small numbers
 - Difficulty blinding patients and physicians
- Heterogeneity of disorders obscures data
 - Lumpers versus splitters
- Outcome measures are limited
 - Subjective and objective data

Measures of Outcome

- Delta EDSS



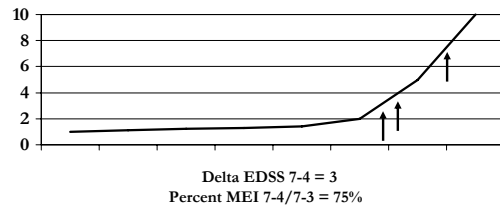
American Spinal Injury Association

ASIA IMPAIRMENT SCALE

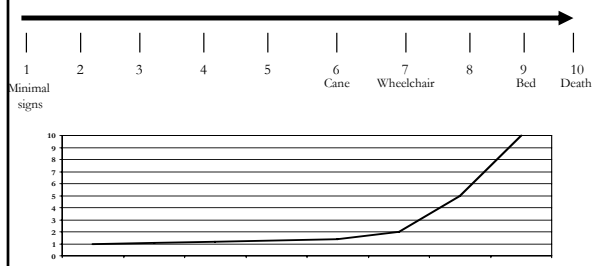
- A = **Complete:** No motor or sensory function is preserved in the sacral segments S4-S5.
- B = **Incomplete:** Sensory but not motor function is preserved below the neurological level and includes the sacral segments S4-S5.
- C = **Incomplete:** Motor function is preserved below the neurological level, and more than half of key muscles below the neurological level have a muscle grade less than 3.
- D = **Incomplete:** Motor function is preserved below the neurological level, and at least half of key muscles below the neurological level have a muscle grade of 3 or more.
- E = **Normal:** motor and sensory function are normal

Measures of Outcome

- Percent Maximum Expected Improvement



Kurtzke Expanded Disability Status Scale

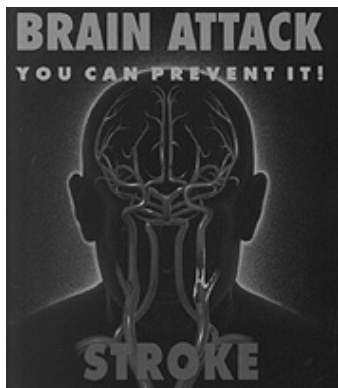


Acute Management of Transverse Myelitis: A Retrospective Study of Intravenous Steroids, Plasma Exchange, and Cyclophosphamide

Benjamin M. Greenberg, MD, MHS, Katherine P. Thomas BS, Chitra Krishnan MHS,
Peter A. Calabresi MD, Adam Kaplin, MD, PhD, Douglas A. Kerr MD/PhD

Neurology, *in press*

1. What therapies work?
2. How well do they work?
3. Are there subsets of patients who should have certain therapies?



Thank You

- Project RESTORE
- Transverse Myelitis Association
- The Cody Unser First Step Foundation

Spine Attack



Thank You



Conclusions from Transverse Myelitis

- Patients with transverse myelitis secondary to systemic autoimmune disease respond best to regimens that include cyclophosphamide
- Patients who are ASIA A at nadir respond significantly better to regimens with cyclophosphamide, regardless of other factors.
- Patients who are non-ASIA A and who do not have signs of autoimmune disease do not necessarily have improved outcomes from the addition of cyclophosphamide to their regimen.
- Time is cord!!

Thank You

- Our patients, who face each day with courage and accept our faults and uncertainty with grace.
- Our patients' families who advocate for, support and care for their loved ones.

- And most importantly, thank you to

