Spinal Cord Injury

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Original Author: Mitch Harris, MD; March 2004

New Author: Michael J. Vives, MD; Revised January 2006

Updated Author: Robert Morgan, MD; Revised November 2010

Overview

- Epidemiology
- Pathophysiology
- Classification of SCI’s & descriptive terms
- Natural History & functional prognosis
- Treatment Strategies

Spinal Cord Injury

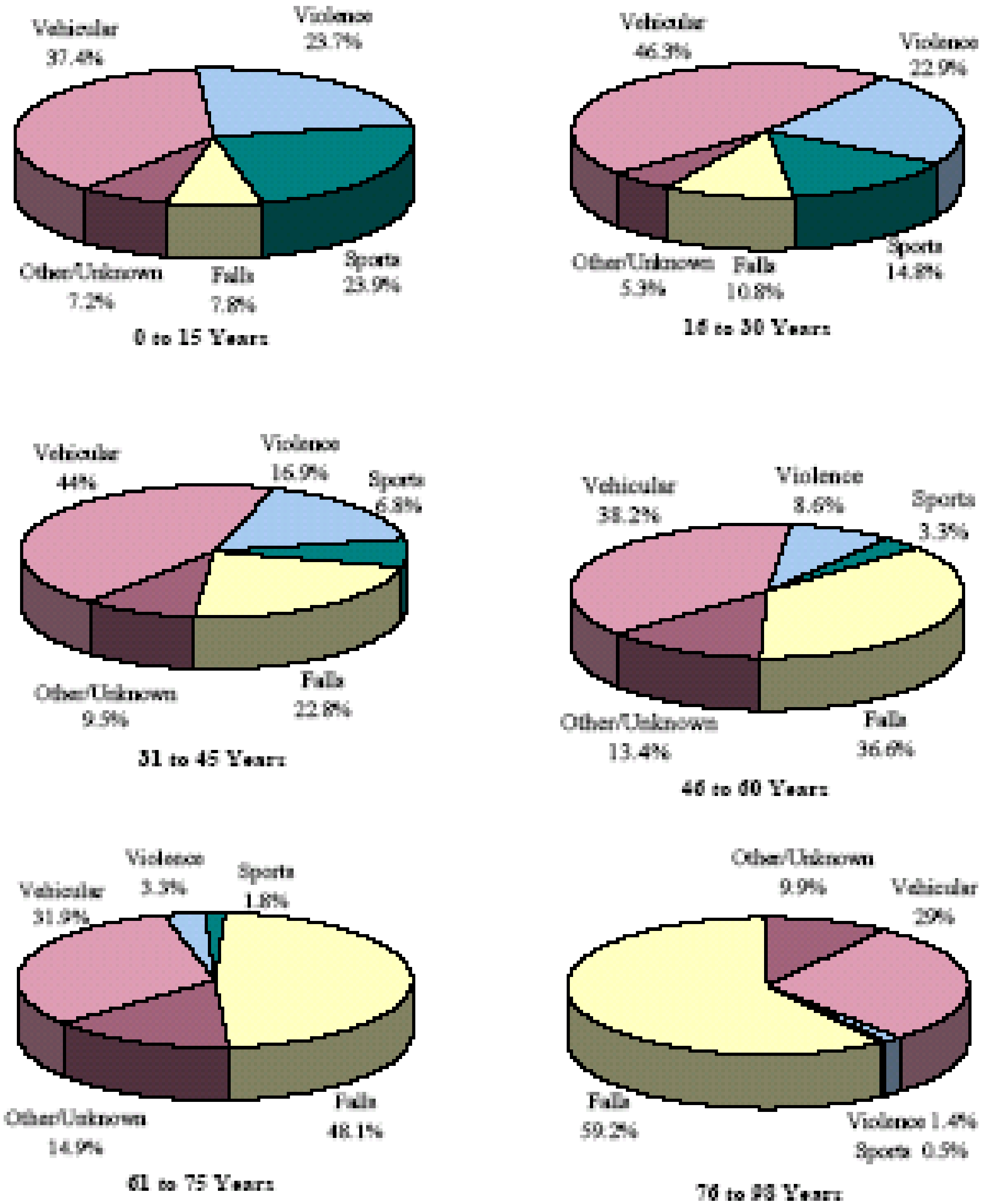
epidemiology

- Incidence: 10-12,000/ yr
- 80-85% males (usually 16-30 y/o), 15-20% female
- 50% of SCI's are *complete*
- 50-60% of SCI's are cervical
- Immediate mortality for complete cervical SCI ~ 50%

Spinal Cord Injury
epidemiology

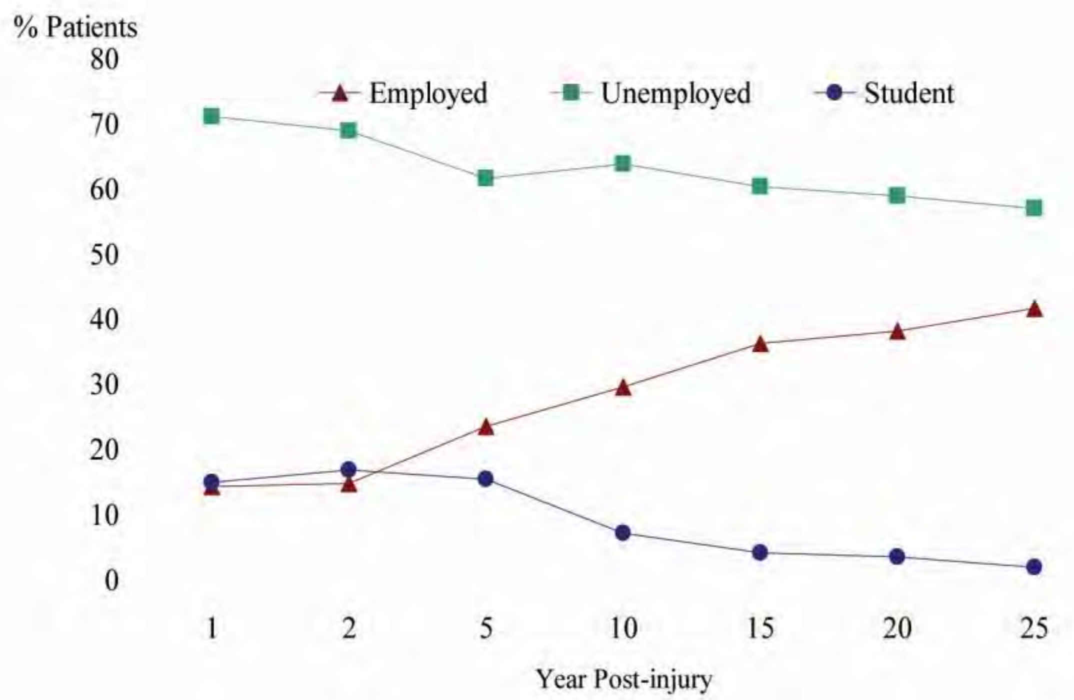
- Cause
  - MVC 42%
  - Fall 20%
  - GSW 16%
- Gender
  - Male 81%
  - Female 19%
- Level of Education
  - To 8th Grade: 10%
  - 9th to 11th: 26%
  - High School: 48%
  - College: 16%

Etiology of SCI by Age

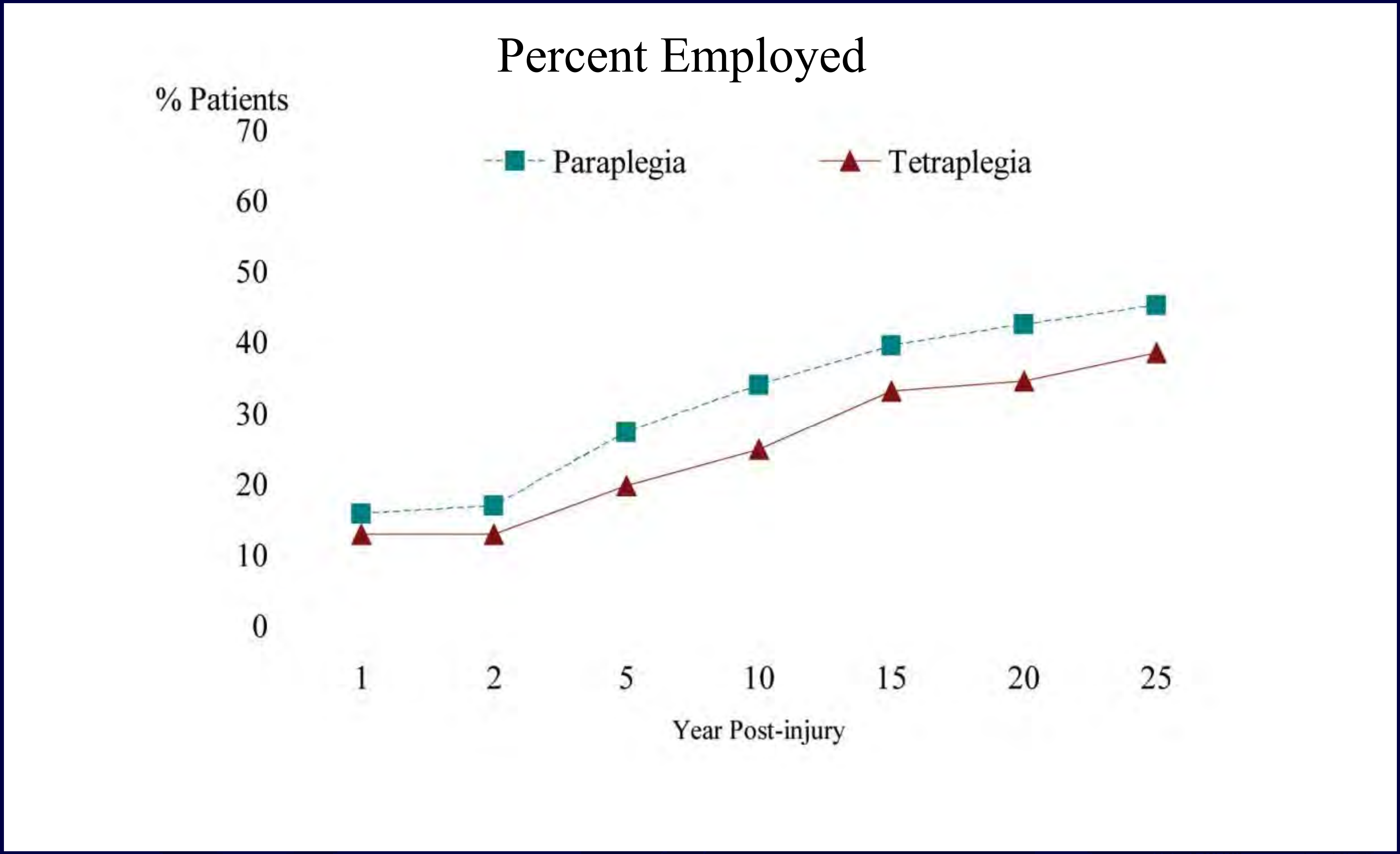


Source: National Spinal Cord Injury Statistical Center, University of Alabama at Birmingham, 2004
Annual Statistical Report, June, 2004

Employment Status



Source: National Spinal Cord Injury Statistical Center, University of Alabama at Birmingham, 2004 Annual Statistical Report, June, 2004



Source: National Spinal Cord Injury Statistical Center, University of Alabama at Birmingham, 2004 Annual Statistical Report, June, 2004

Spinal Cord Injury
pathophysiology

Primary injury

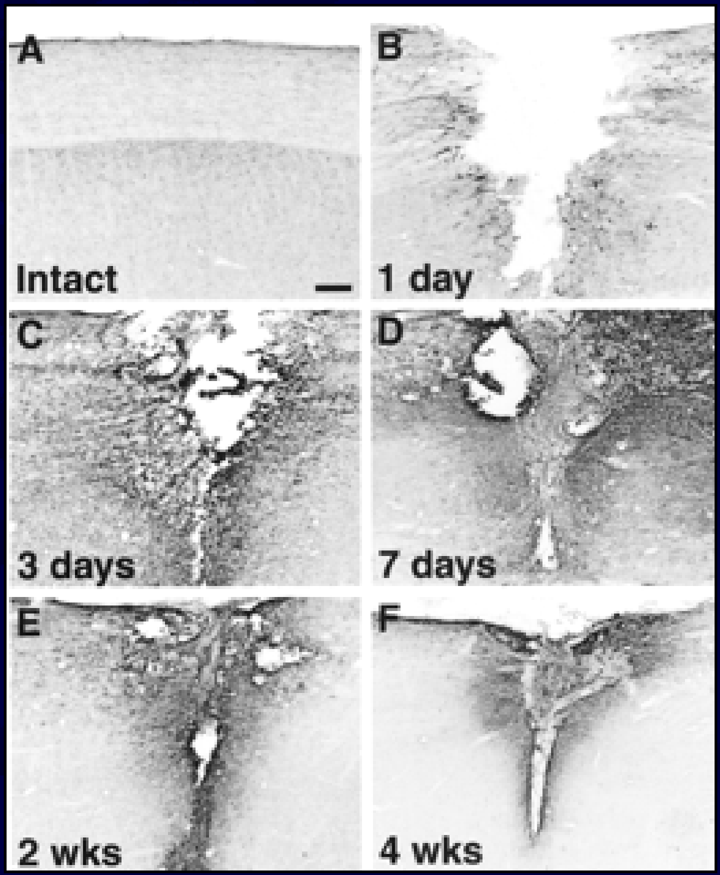
- **Initial insult to cord**
- **Local deformation**
- **Energy transformation**

Spinal Cord Injury
pathophysiology

<u>*Secondary injury*</u>

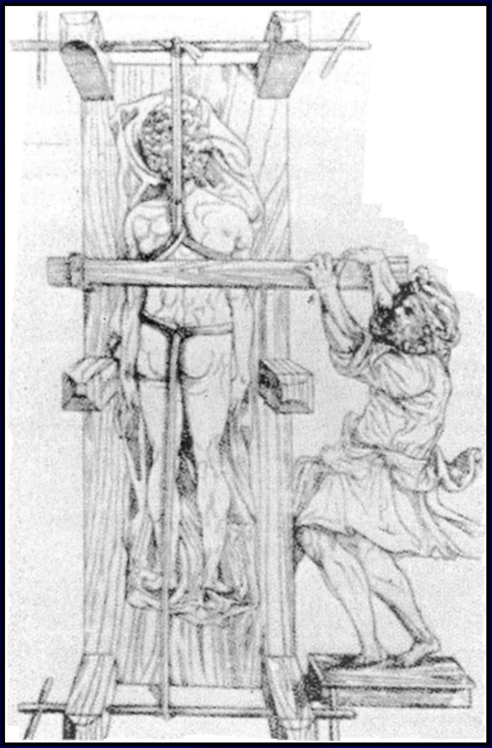
- **Biochemical cascade**
- **Cellular processes**

Most acute therapies aim to limit secondary injury cascade



Secondary Injury

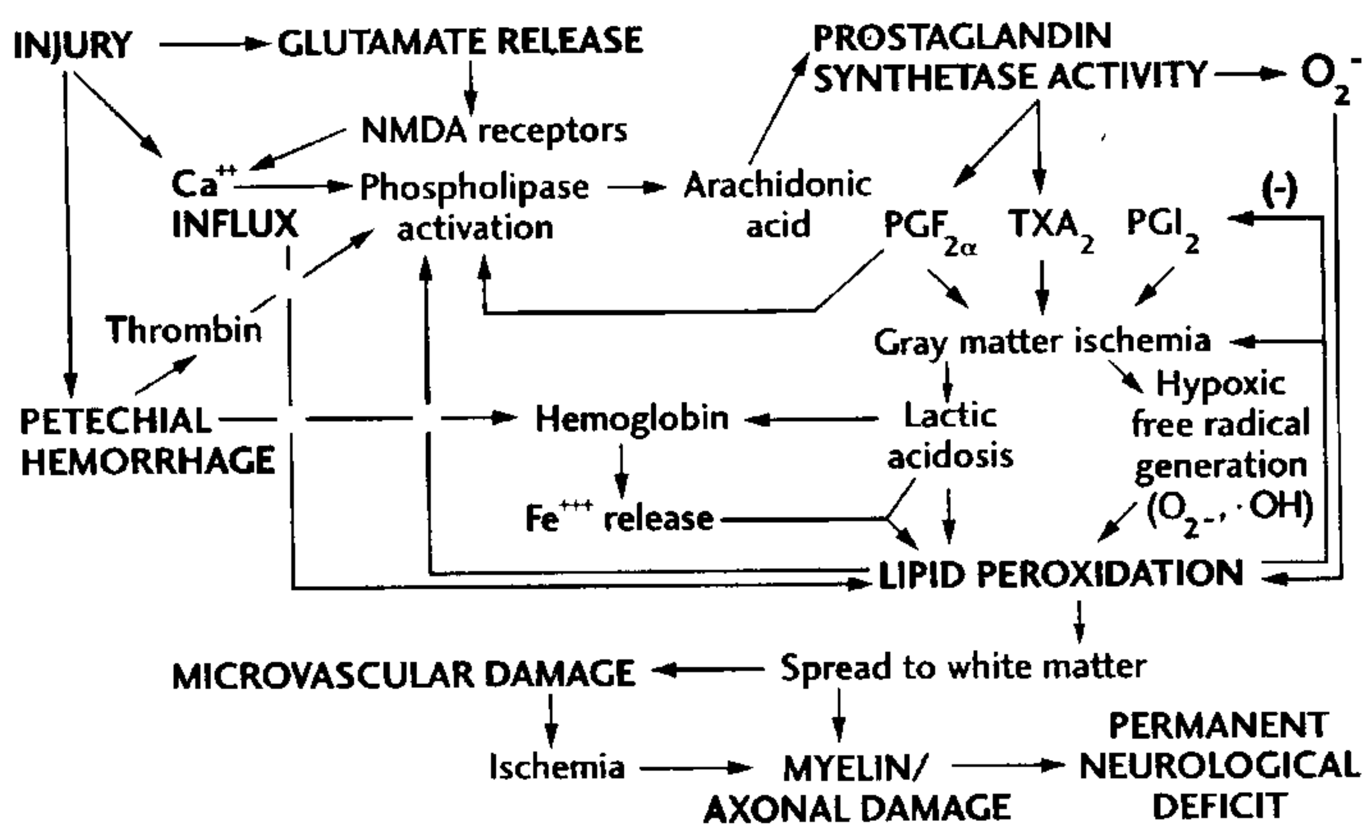
theories



- **1970's: free radicals**
- **1980's: Ca, opiate receptors**
  lipid peroxidation
- **1990/2000's: apoptosis**
  intracellular protein synthesis
  glutaminergic mechanisms

Secondary Injury Cascade

current understanding



Definitions

Spinal shock:

- **transient flaccid paralysis**
- **areflexia (including bulbocavernosus reflex)**
- **while present (usually <48 h), unable to predict potential for neurological recovery.**

Neurogenic Shock:

- **Loss of sympathetic tone, vasomotor and cardiac regulation.**
- **Hypotension with relative bradycardia.**

Classification

Complete

- absence of sensory & motor function in lowest sacral segment after resolution of spinal shock

Incomplete

- presence of sensory & motor function in lowest sacral segment (indicates preserved function below the defined neurological level)

ASIA Examination

Motor level (MLI) = lowest normal level with 3/5 strength (& level above = 5/5)

Each muscle has 2 root innervations, 3/5 strength = full innervation by the more rostral root level.

(4/5 acceptable with pain, de-conditioning)

- Motor Index Score (MIS) = total 100 pts
- **Superiority of Motor level versus Sensory Level

Neurologic Examination

- American Spinal Injury Association (ASIA)
  - A = Complete – No Sacral Motor / Sensory
  - B = Incomplete – Sacral sensory sparing
  - C = Incomplete – Motor Sparing (<3)
  - D = Incomplete – Motor Sparing (>3)
  - E = Normal Motor & Sensory

ASIA Sensory Exam

- 28 sensory "points" (within dermatomes)
- Test light touch & pin-prick pain

Importance of <u>sacral</u> <u>pin testing</u>

- 3 point scale (0,1,2)
- "optional": proprioception & deep pressure to index and great toe ("present vs absent")
- deep anal sensation recorded "present vs absent"

Motor Examination

- 10 “key” muscles (5 upper & 5 lower extremity)

C5-elbow flexion	L2-hip flexion
C6-wrist extension	L3-knee extension
C7-elbow extension	L4-ankle dorsiflexion
C8-finger flexion	L5-toe extension
T1-finger abduction	S1-ankle PF

  – Sacral exam: voluntary anal contraction (present/absent)

Motor Grading Scale

- 6 point scale (0-5) …..(avoid +/-'s)
  - 0 = no active movement
  - 1 = muscle contraction
  - 2 = active movement without gravity
  - 3 = movement thru ROM against gravity
  - 4 = movement against some resistance
  - 5 = movement against full resistance

STANDARD NEUROLOGICAL CLASSIFICATION OF SPINAL CORD INJURY

MOTOR

KEY MUSCLES

	R	L	
C2			
C3			
C4			
C5			Elbow flexors
C6			Wrist extensors
C7			Elbow extensors
C8			Finger flexors (distal phalanx of middle finger)
T1			Finger abductors (little finger)
T2			
T3			
T4			
T5			
T6			
T7			
T8			
T9			
T10			
T11			
T12			
L1			
L2			Hip flexors
L3			Knee extensors
L4			Ankle dorsiflexors
L5			Long toe extensors
S1			Ankle plantar flexors
S2			
S3			
S4-5			Voluntary anal contraction (Yes/No)

0 = total paralysis
1 = palpable or visible contraction
2 = active movement, gravity eliminated
3 = active movement, against gravity
4 = active movement, against some resistance
5 = active movement, against full resistance
NT = not testable

TOTALS ☐ + ☐ = ☐ **MOTOR SCORE**

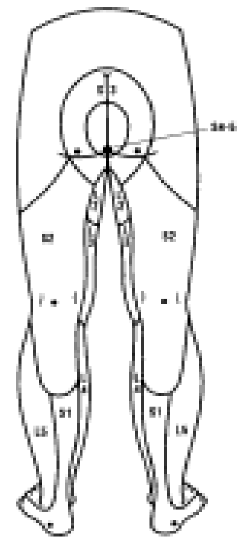
(MAXIMUM) (50) (50) (100)

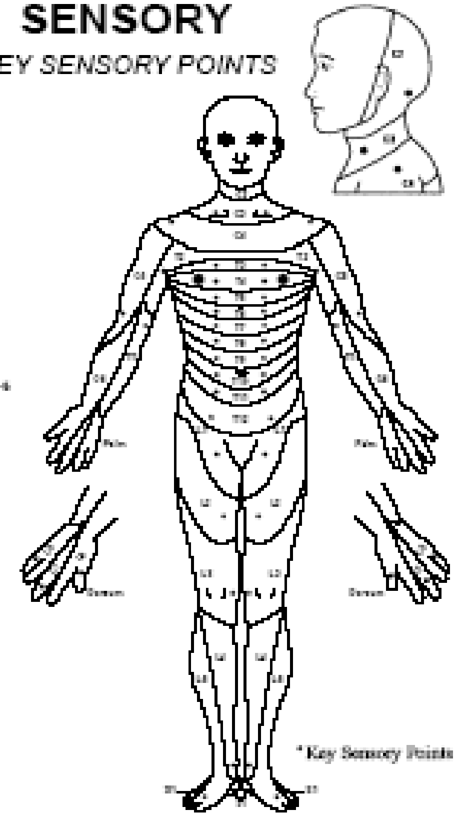
SENSORY

KEY SENSORY POINTS

	LIGHT TOUCH R	LIGHT TOUCH L	PIN PRICK R	PIN PRICK L
C2				
C3				
C4				
C5				
C6				
C7				
C8				
T1				
T2				
T3				
T4				
T5				
T6				
T7				
T8				
T9				
T10				
T11				
T12				
L1				
L2				
L3				
L4				
L5				
S1				
S2				
S3				
S4-5				

0 = absent
1 = impaired
2 = normal
NT = not testable





☐ Any anal sensation (Yes/No)

TOTALS { ☐ + ☐ = ☐ **PIN PRICK SCORE** (max: 112)

☐ + ☐ = ☐ **LIGHT TOUCH SCORE** (max: 112)

(MAXIMUM) (56) (56) (56) (56)

NEUROLOGICAL LEVEL *The most caudal segment with normal function*		R	L
	SENSORY		
	MOTOR		

COMPLETE OR INCOMPLETE? ☐

Incomplete = Any sensory or motor function in S4-S5

ASIA IMPAIRMENT SCALE ☐

ZONE OF PARTIAL PRESERVATION *Caudal extent of partially innervated segments*		R	L
	SENSORY		
	MOTOR		

This form may be copied freely but should not be altered without permission from the American Spinal Injury Association.

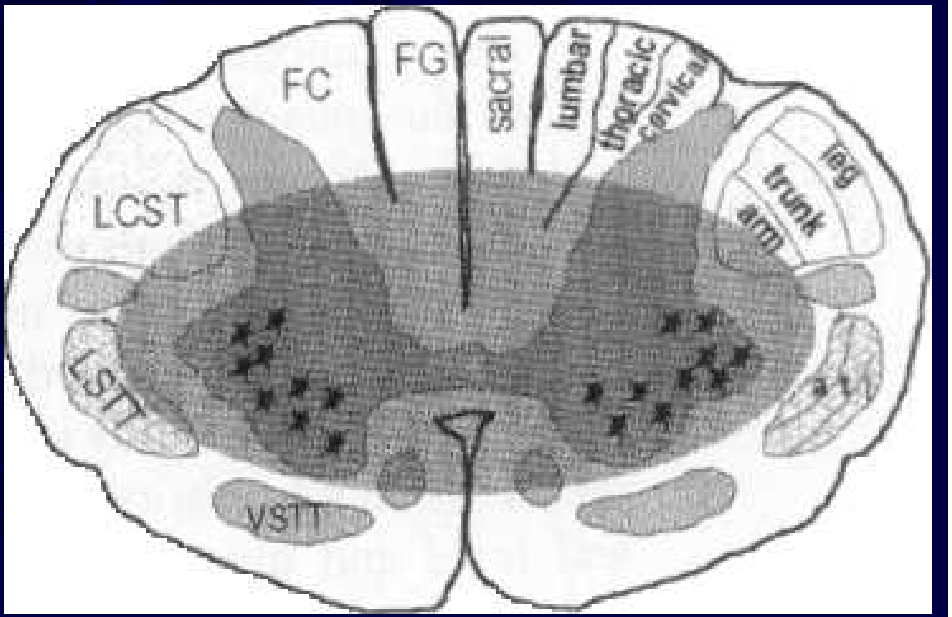
2000 Rev.

Classification

Incomplete SCI syndromes

Central Cord Syndrome

- Motor loss UE>LE
- Hands affected
- Common in elderly w/ pre-existing spondylosis and cervical stenosis.
- Substantial recovery can be expected.

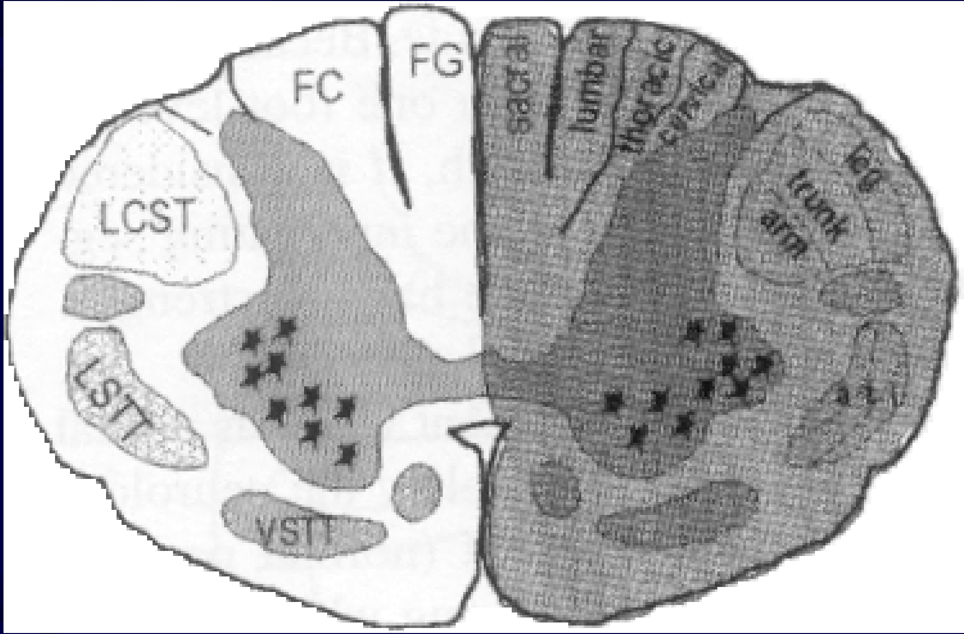


Classification

Incomplete SCI syndromes

Brown Sequard

- Ipsilateral motor, proprioception loss.
- Contralateral pain, temperature loss.
- Penetrating injuries.
- Good prognosis for ambulation.

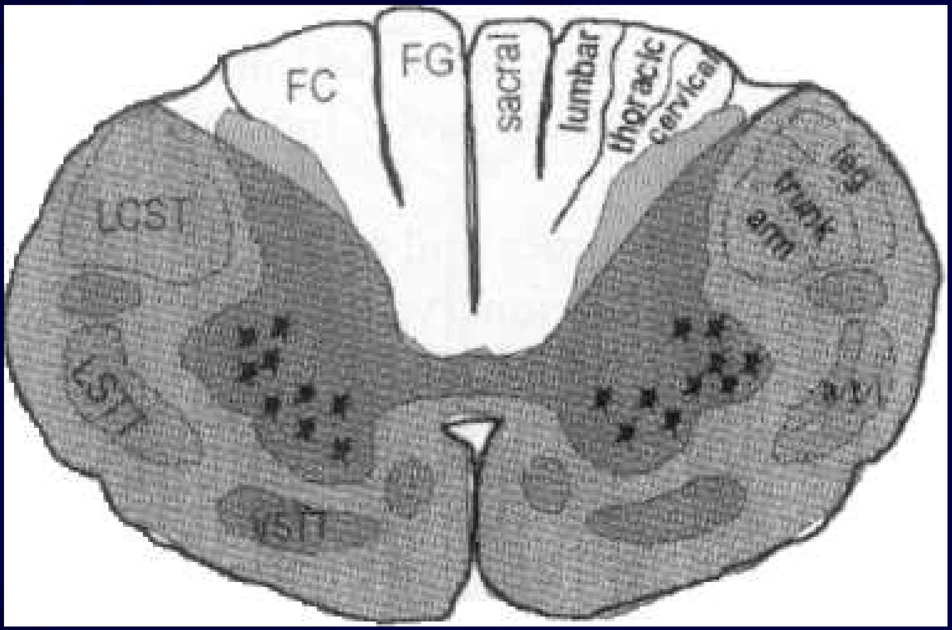


Classification

Incomplete SCI syndromes

Anterior Cord Syndrome

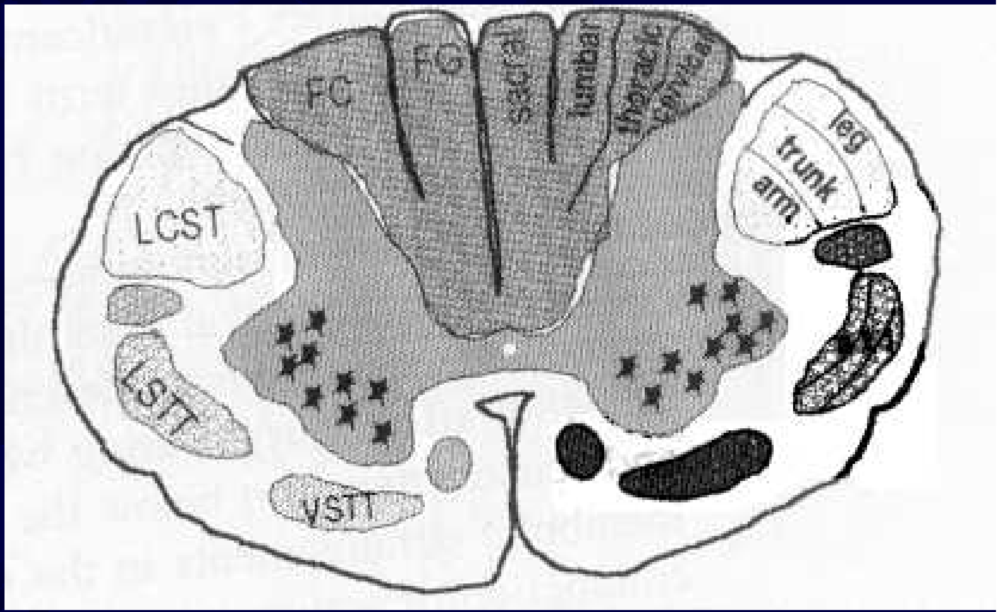
- Motor loss
- Vibration/position spared
- Flexion injuries
- Poor prognosis for recovery



Classification
Incomplete SCI syndromes

Posterior Cord Syndrome

- **Profound sensory loss.**
- **Pain/temperature less affected.**
- **Rare.**



Classification

Other SCI syndromes

Conus Medullaris Syndrome

- Loss of bowel or bladder function
- Saddle anaesthesia
- Looks like cauda equina
- Skeletal injuries T11-L2

Expected Neurorecovery

Complete Tetraplegia

- **Little chance for functional motor recovery in LE's**

- **extent of neurorecovery in UE's determines functional independence**

Expected Neurorecovery

Complete Tetraplegia

- **70-85% chance of gaining at least one additional level**
- **Motor grade 2/5 for a given level @1 week, all gained functional strength at next level**

Ditunno, Arch Phys Med Rehabil, 2000

Expected Neurorecovery

Incomplete Tetraplegia

- **>90% gain at least one UE motor level**
- **If pinprick spared in same dermatome, 92% chance of recovery to ≥ 3/5 motor strength**

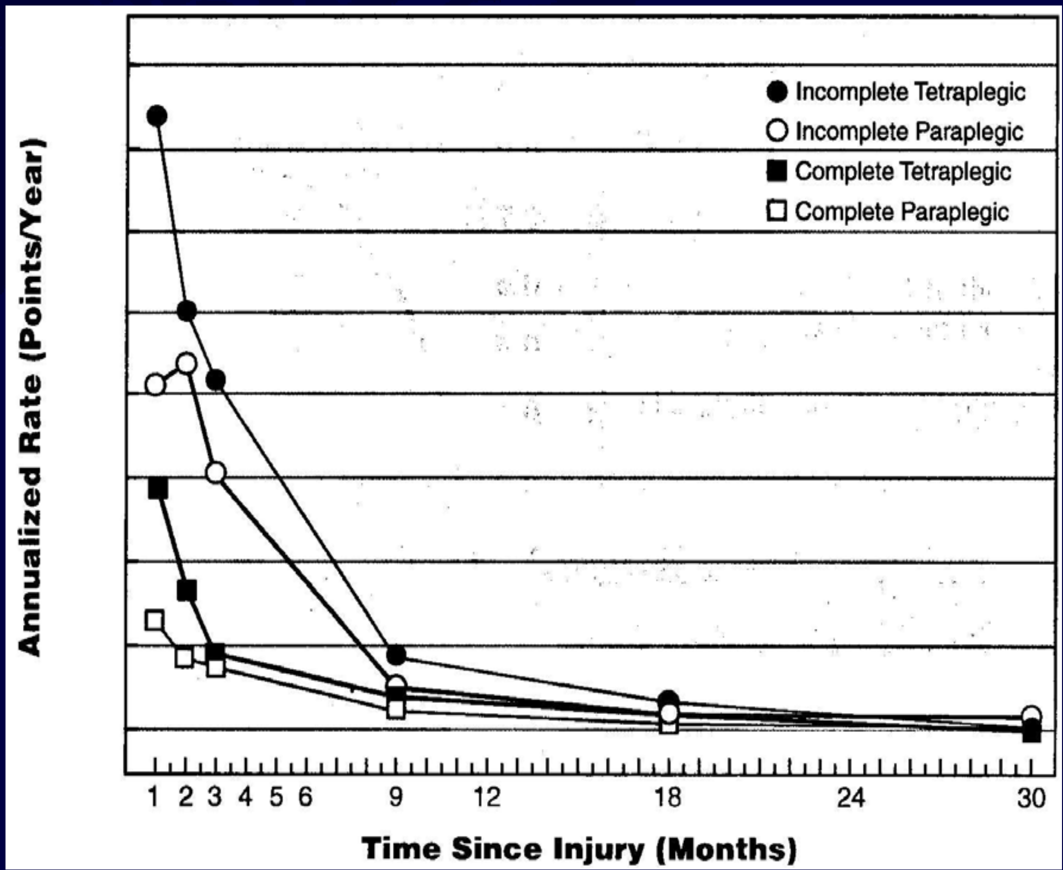
Ditunno, Arch Phys Med Rehabil, 2000

Poynton, JBJS-Br, 1997

Expected Neurorecovery

Incomplete Tetraplegia

- Majority of improvement in first 6-9 months.



Waters, J Spinal Cord Med, 1998

Despite the Medical Advances of the last 50 years,

Prediction of Functional Capacity Based on Neurologic Level is still similar to that described in:

Long, Lawton, Arch Phys Med Rehab, 1955

Functional Capacity

C1-C4

- C1-C3 need mechanical ventilation (portable vent or phrenic nerve stimulator)
- C4 may need CPAP or Bi-PAP for nocturnal hypoventilation

Functional Capacity

C1-C4

- Dependent for self-care and transfers.
- Motorized wheelchair with special controls
  - mouthsticks (C3-C4)
  - infrared
  - sip-and-puff

Functional Capacity

C5

- Active elbow flexion present
- Capable of some simple ADL's with appropriate setup:
  - -Eat with balanced forearm orthosis.
  - -Write and type with opponens splint.
- Still dependent for transfers % bed positioning

Functional Capacity

C6

- Added shoulder stability due to rotator cuff innervation.
- Active wrist extension (extensor carpi radialis).
- Tenodesis grip: passive finger flexion and thumb opposition with wrist extension.
- Tenodesis grip strengthened with flexor-hinge orthosis.

Functional Capacity

C6

- Improved capability for self -feeding.
- Self-catheterization (males), bowel programs required.
- Upper body dressing possible.
- Lower body dressing difficult.
- Assistance for transfers, bed mobility.
- Manual wheelchair for short distances.

Functional Capacity

C7

- Functional strength in triceps.
- Can roll over, move in seated position, transfer.
- Can eat independently (except cutting).
- Long distance manual wheelchair propulsion.

Functional Capacity

C8-T1

- Intrinsic hand function.
- Improved grasp and dexterity.
- Independent bed mobility & transfers.
- Independent for ADL's.

Functional Capacity

Thoracic Paraplegia

- Abdominal strength beginning at T6.
- Sitting balance improved.
- Bipedal ambulation with KAFO & walker (swing-to gait pattern).
- Energy consuming, difficult for community use.

Ambulation after SCI

Motor Requirements

- **Grade ≥ 3/5 strength in hip flexors on one side**
- **Grade ≥ 3/5 strength in quadriceps on other side**

Ambulation after SCI

Incomplete Injuries

<u>Community ambulators @ 1 year:</u>

46% of incomplete tetraplegics

76% of incomplete paraplegics

Waters, Arch Phys Med Rehabil, 1994

Treatment Strategies

(current & future)

Acute Stage Therapies:

- Optimize critical care management
- Modulate the secondary injury cascade
- Includes steroids, Sygen, hypothermia

Treatment Strategies

(current & future)

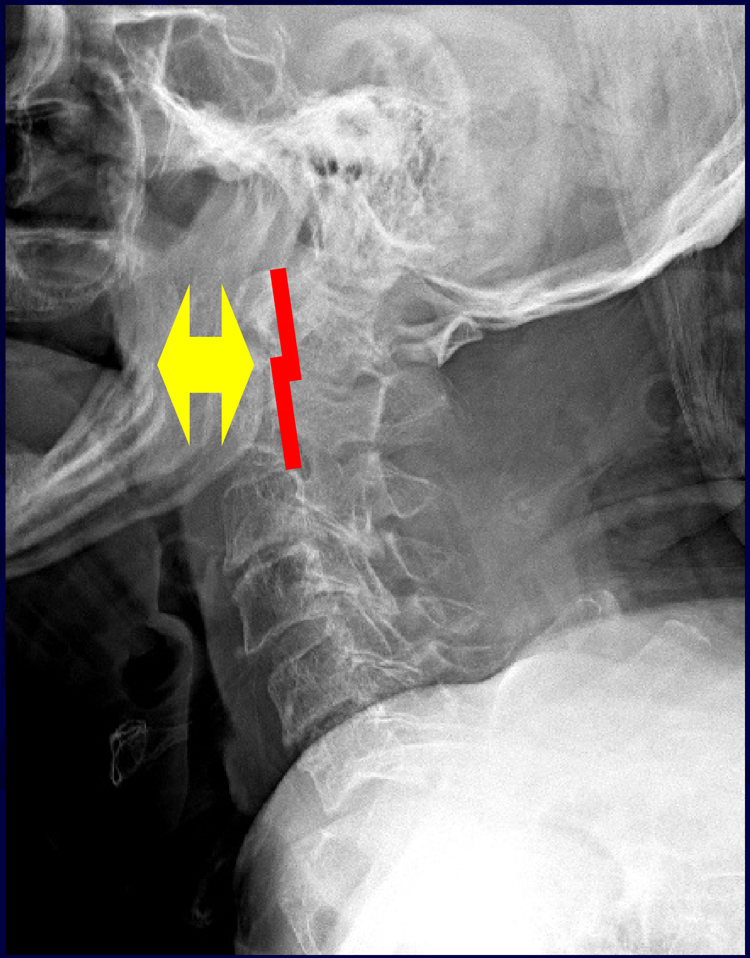
Subacute Stage Therapies

- **Modify the environment of adult CNS which inhibits neural tissue recovery.**
- **Includes peripheral nerve grafts, olfactory ensheathing cells, activated macrophages.**

Optimize Critical Care Management

- Acute respiratory failure has been observed in patients after external immobilization for displaced odontoid fractures.
- 32 patients with posteriorly displaced fractures, 13 experienced acute respiratory compromise, whereas only one of 21 patients with anteriorly displaced fractures had respiratory difficulties ($p = 0.0032$).
  - All 13 were initially managed using flexion traction for reduction of these fractures.
- Two of these patients died because of failure to emergently secure an airway during closed treatment of the fracture.
- Frequent respiratory deterioration during acute closed reduction of posteriorly displaced Type II odontoid fractures was observed, whereas respiratory failure in patients with anteriorly displaced fractures was rare.
- **Manage the airway!**

Closed management of displaced Type II odontoid fractures: more frequent respiratory compromise with posteriorly displaced fractures.



Przybylski GJ, Harrop JS, Vaccaro AR. Neurosurg Focus. 2000 Jun 15;8(6):e5.

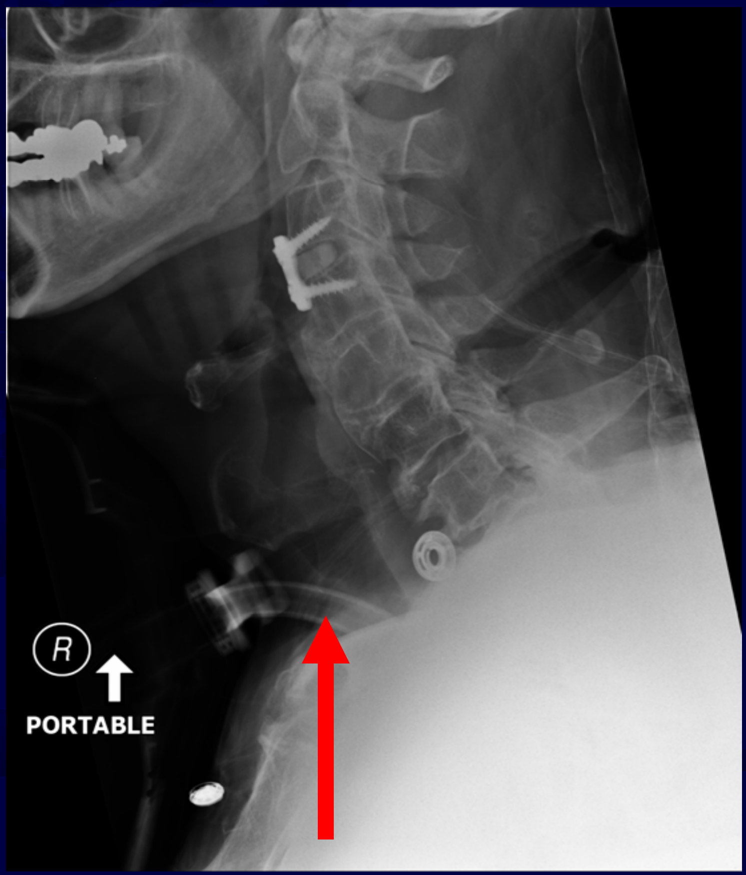
Myth of Myelopathy

- No clear case of spinal cord injury after direct laryngoscopy in English language literature
  - McLeod and Calder Criteria
- All airway maneuvers cause some motion at fracture site
  - Lessened with manual in line immobilization
  - Increased with increasing instability
- Fiberoptic intubation minimizes displacements
  - May still require direct laryngoscopy
  - May require surgical airway

Crosby, E. Airway Management in Adults After Cervical Spine Trauma. *Anaesthesiology*. 2006

Incidence and Clinical Predictors For Tracheostomy After Cervical Spinal Cord Injury: A National Trauma Databank Review.

- After CSCI, a fifth of patients will require tracheostomy.
- Intubation on scene or ED, complete CSCI at C1-C4 or C5-C7 levels, ISS >/=16, facial fracture, and thoracic trauma were independently associated with the need for tracheostomy.
- Patients requiring tracheostomy had a higher Injury Severity Score (ISS) and required intubation more frequently on scene and Emergency Department (ED)
- Patients requiring tracheostomy had higher rates of complete CSCI at C1-C4 and C5-C7 levels
- Patients requiring tracheostomy had more ventilation days, longer intensive care unit and hospital lengths of stay, but lower mortality.



Branco BC, Plurad D, Green DJ, Inaba K, Lam L, Cestero R, Bukur M, Demetriades D.J Trauma. 2010 Jun 3. [Epub ahead of print]

Breathing

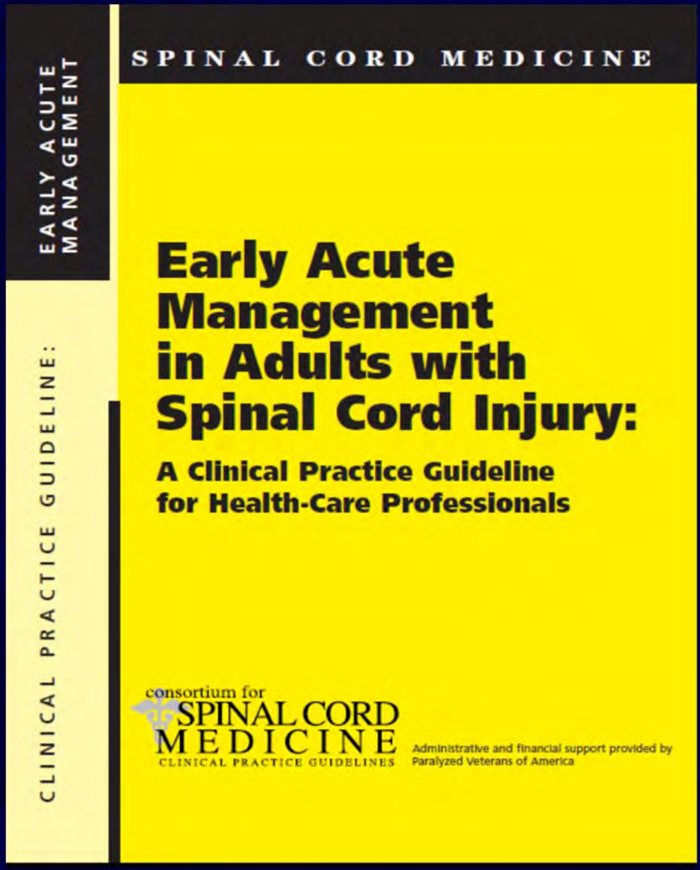
- Of patients with CSCI above C5, 87.5 per cent required intubation compared with 61 per cent of patients with CSCI at C5-C8 (P = 0.026).
- Similarly, of patients with complete quadriplegia, 90 per cent required intubation compared to 48.5 per cent of patients with incomplete quadriplegia or paraplegia (P < 0.001).
- There were 3 independent risk factors for the need of intubation:
  - Injury Severity Score > 16
  - CSCI higher than C5
  - complete quadriplegia.
- The combination of the 2 latter risk factors resulted in intubation in 21 of 22 patients (95%).
- The majority of patients with CSCI require intubation.
- In patients with CSCI above C5 and complete quadriplegia, intubation should be offered routinely and early because delays may cause preventable morbidity.

Intubation after cervical spinal cord injury: to be done selectively or routinely?

Velmahos GC, Toutouzas K, Chan L, Tillou A, Rhee P, Murray J, Demetriades D. Am Surg. 2003 Oct;69(10):891-4.

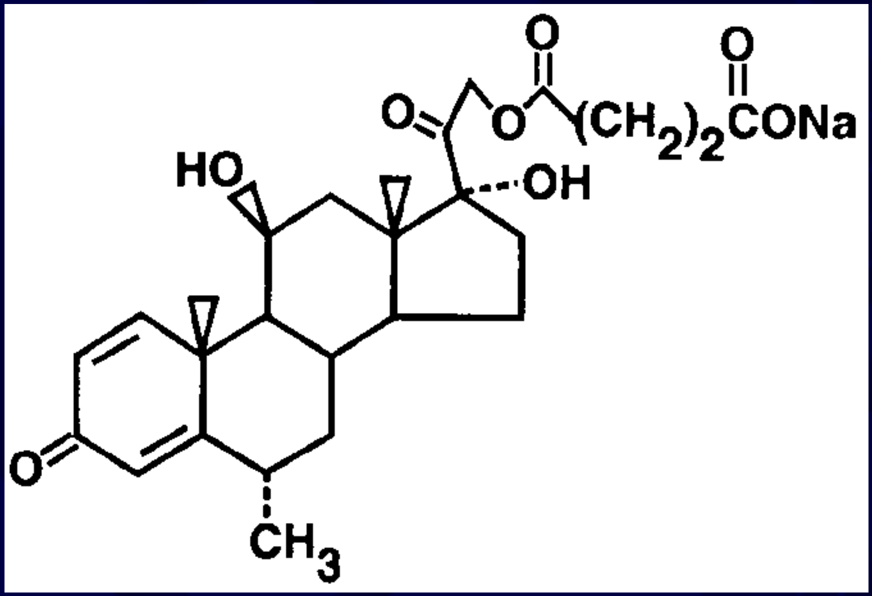
Circulation

- Early appropriate fluid resuscitation is necessary to maintain tissue perfusion
  - Avoid fluid overload!
- Appropriate resuscitation endpoint and optimal mean arterial blood pressure for maintenance of spinal cord perfusion are not known
  - Uncontrolled studies using vasopressin to maintain a MAP of 85 for 7 days have shown improved outcomes



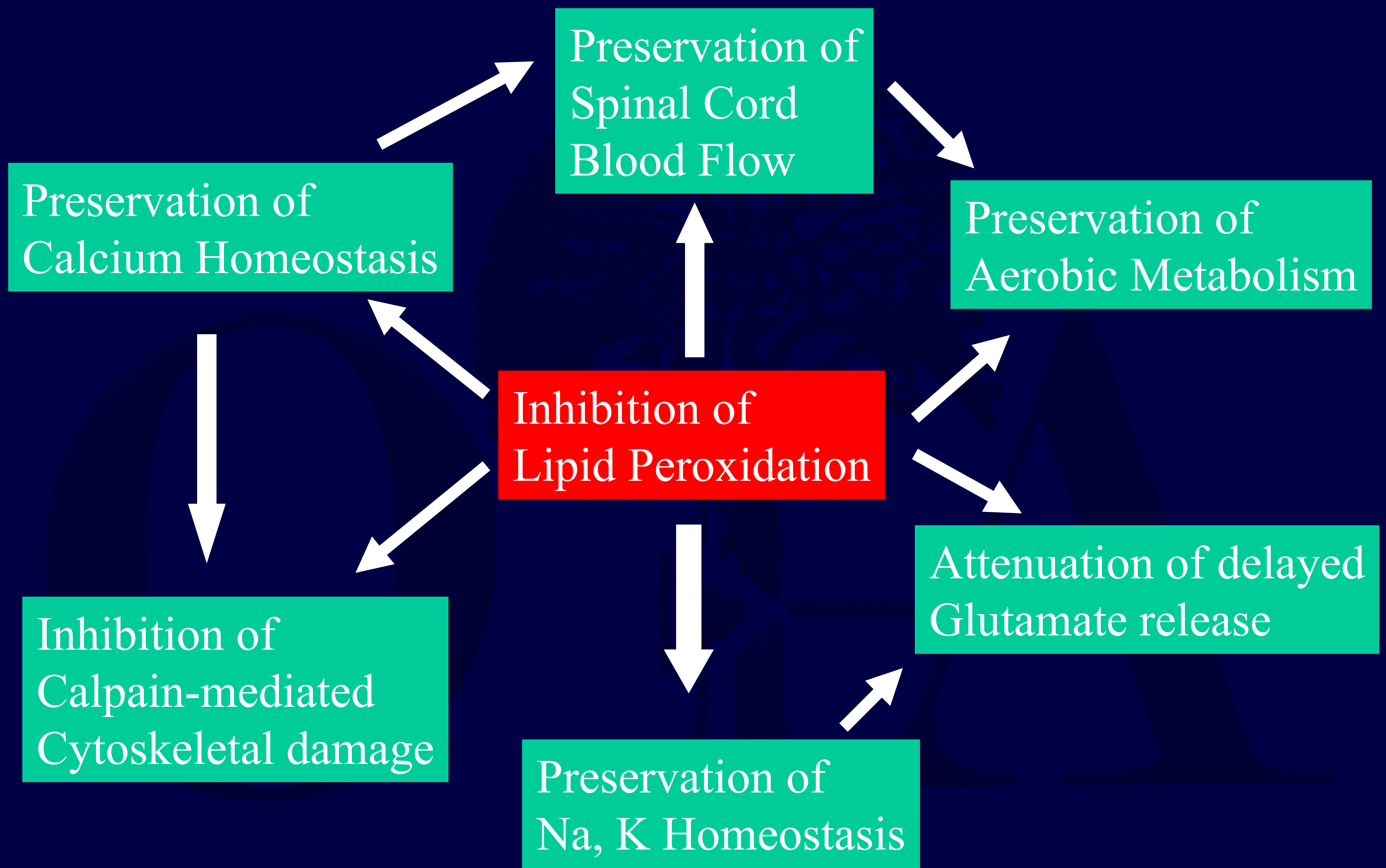
Steroids

methylprednisolone sodium succinate



- Large body of animal studies
- Various neuroprotective mechanisms postulated

Neuroprotection w/ MPSS



National Acute Spinal Cord Injury Studies

NASCIS II

- 10 hospitals, 487 patients
- Compared:

  MPSS (30 mg/kg bolus + 5.4 mg/kg x 23°)

  Naloxone (5.4 mg/kg bolus + 4.5mg/kg x 23°)

  Placebo
- ≤ 8 hours, steroids ⇒neurologic improvement
- Infections, PE ↑ but not significant

Bracken, N Engl J Med, 1990
Bracken, N Engl J Med, 1992

NASCIS III

- 16 hospitals, 499 patients
- 3 treatment arms (all got MPSS bolus)

  MPSS 5.4 mg/kg 24 hrs

  MPSS 5.4 mg/kg 48 hrs

  Tirilazad 2.5 mg/kg Q6 hr for 48 hrs
- 48 hr protocol better than 24 hr protocol *(if treated between 3 and 8 hours)*
- 2x incidence of pneumonia, sepsis in 48 hr group (NS)

Bracken, JAMA, 1997
Bracken, J Neurosurg, 1998

Criticism of NASCIS II

- **All primary outcomes (-)**

(no diff in neuro improvement between grps)

- **(+) findings only in post-hoc analyses**

(arbitrary stratification to before or after 8hrs)

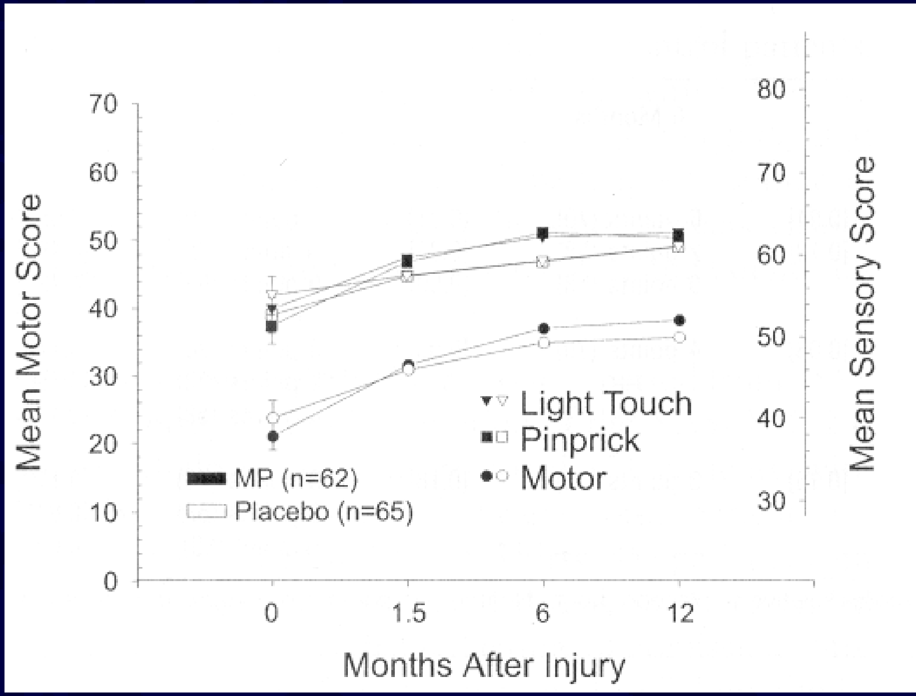
- **Only 38% of original enrollment included**
- **<8 hr control group poor results**
- **Treatment effect small**
- **Inappropriate statistics**

60 t-tests

no correction

Parametric

- **6 mo results reported in media**
- **Prior to peer-review publication**
- **1 yr results less encouraging**



Criticism of NASCIS III

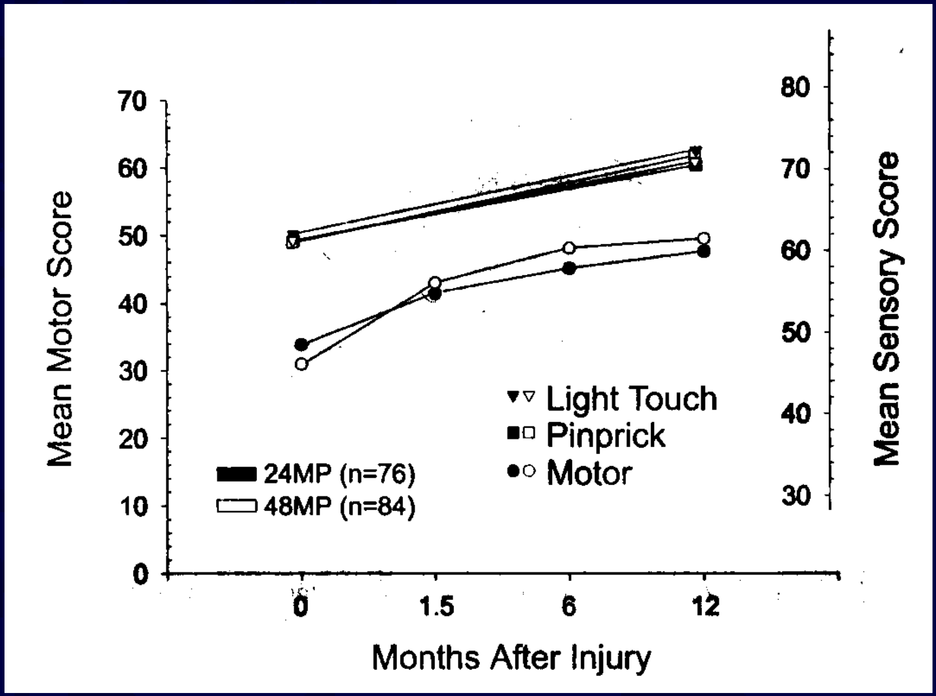
- Primary outcomes negative

(no diff in treatment among groups)

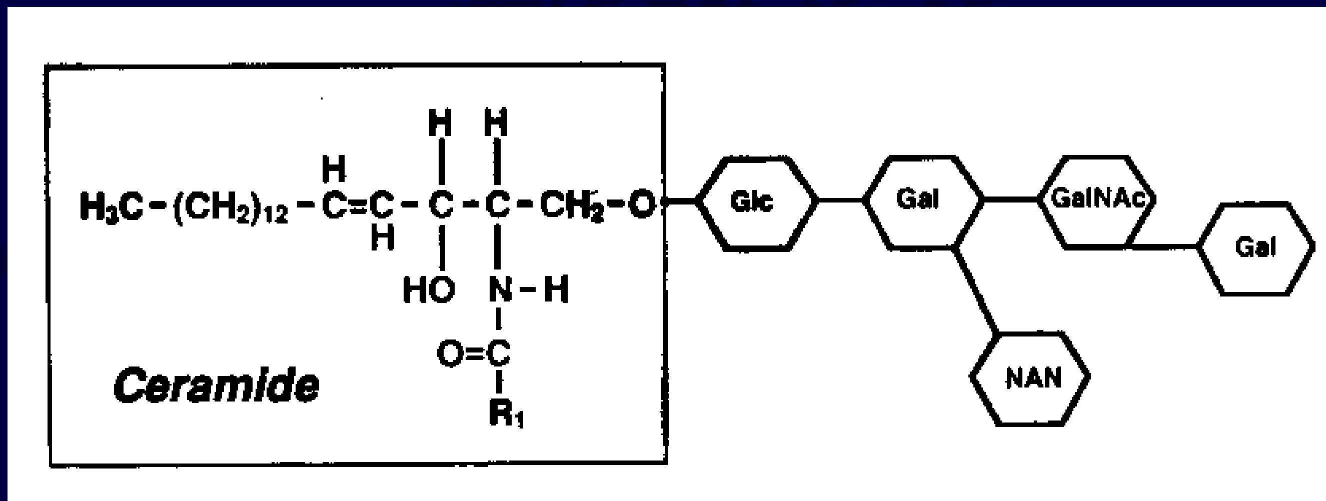
- all positive findings in post hoc analyses

(when arbitrarily divided into <3hr/ >3 hr)

- Treatment effects small
- Effect NS @ 1yr
- ? Inappropriate statistics



SYGEN®



- Monosialotetrahexosylganglioside GM1 sodium salt
- Found in CNS cell membranes

SYGEN®

experimental models

- Acute neuroprotection
- Anti-excitotoxic
- Potentiates neuritic sprouting

Roisen, 1981
Agnati, 1983
Toffano, 1983
Fass, 1984
Schneider, 1998

- Single center trial, 37 pts: promising
- Multicenter trial, 800 pts: disappointing

Geisler, N Engl J Med, 1991
Geisler, Spine, 2001

Acute Neuroprotective Agents

new areas of interest in household drugs

minocycline

DOI: 10.1093/brain/awg178 Advanced Access publication June 4, 2003 *Brain* (2003), **126,** 1628–1637

Neuroprotection by minocycline facilitates significant recovery from spinal cord injury in mice

Jennifer E. A. Wells,[1] R. John Hurlbert,[1] Michael G. Fehlings[2] and V. Wee Yong[1]

erythropoietin

PNAS | July 9, 2002 | vol. 99 | no. 14

Recombinant human erythropoietin counteracts secondary injury and markedly enhances neurological recovery from experimental spinal cord trauma

Alfredo Gorio*†, Necati Gokmen†‡, Serhat Erbayraktar§, Osman Yilmaz¶, Laura Madaschi*, Cinzia Cichetti*, Anna Maria Di Giulio*, Enver Vardar‖, Anthony Cerami**, and Michael Brines**††

Lipitor

Journal of Neuroscience Research 79:340–350 (2005)

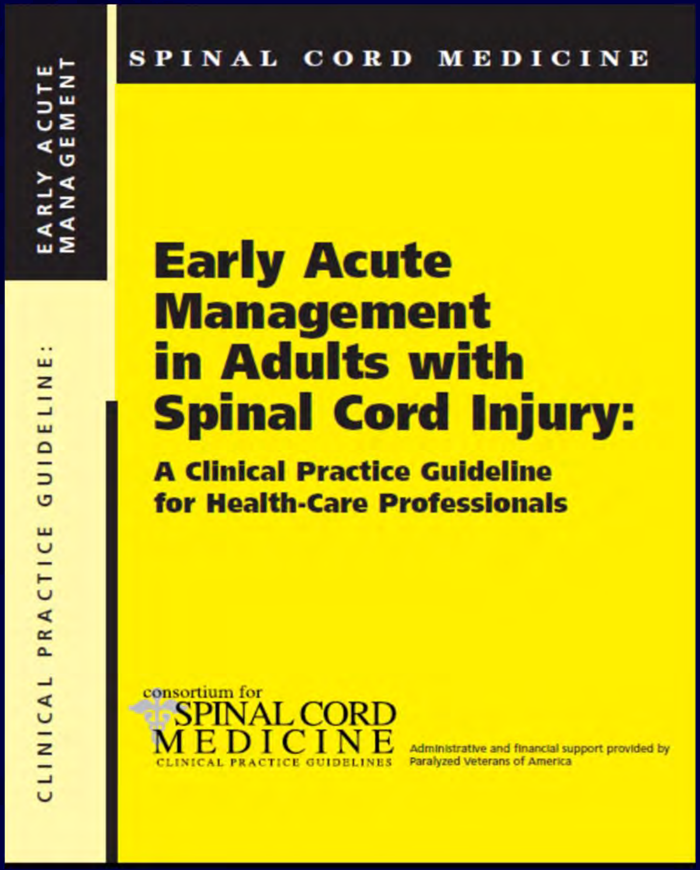
Attenuation of Acute Inflammatory Response by Atorvastatin After Spinal Cord Injury in Rats

Ravinder Pannu,[1] Ernest Barbosa,[1,2] Avtar K. Singh,[1,3,4] and Inderjit Singh[1]*

Pharmacologic Neuroprotection in Patients with SCI

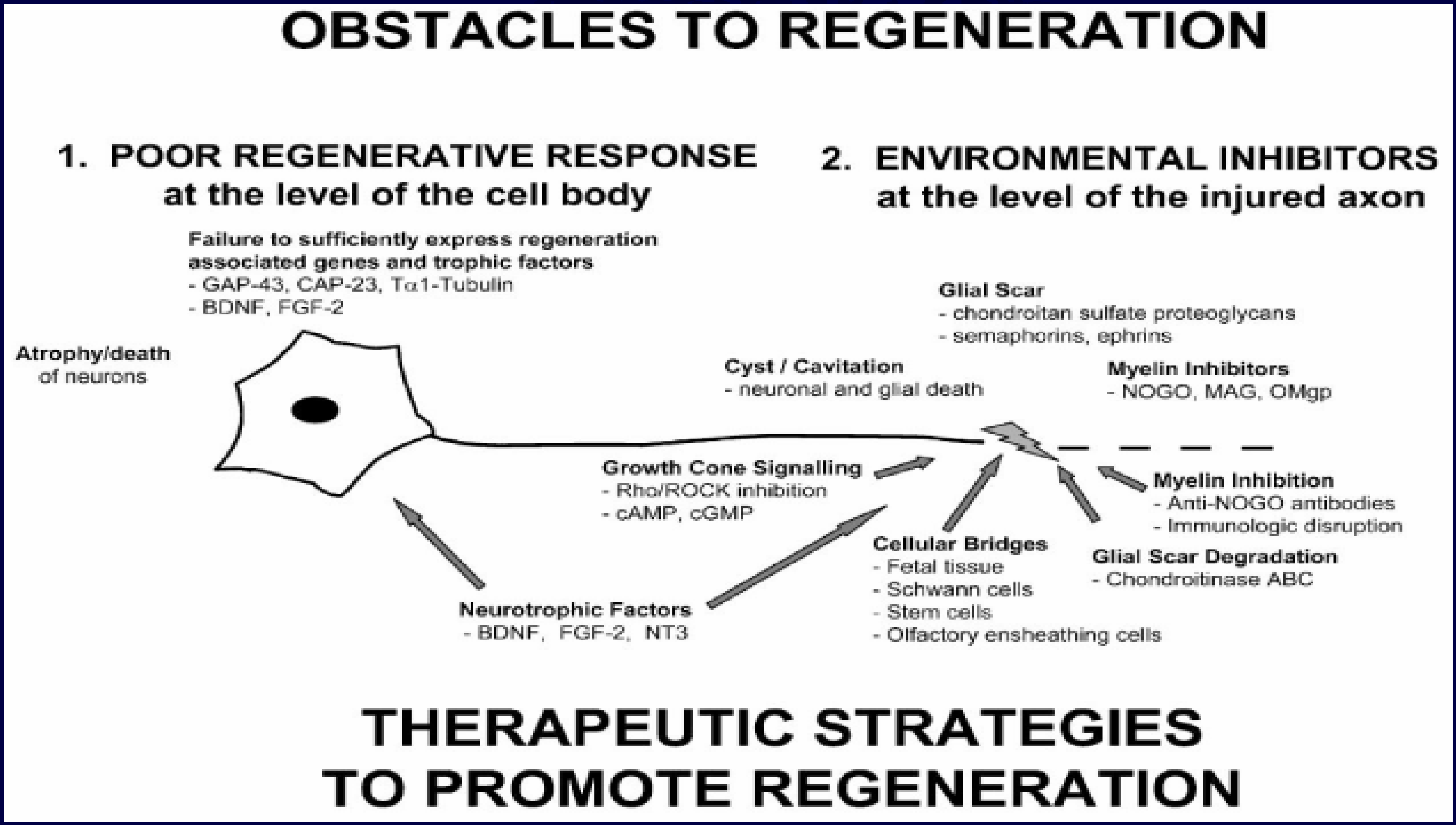
- **No clinical evidence exists to definitively recommend the use of any neuroprotective pharmacologic agent, including steroids, in the treatment of acute SCI to improve functional recovery. *(Scientific evidence–NA; Grade of recommendation–NA; Strength of panel opinion–5)***

- **If it has been started, stop administration of methylprednisolone as soon as possible in neurologically normal patients and in those whose prior neurologic symptoms have resolved to reduce deleterious side effects. *(Scientific evidence–NA; Grade of recommendation–NA; Strength of panel opinion–5)***



Subacute Stage Therapies

modify environment of adult spinal cord



Augmentation of Regenerative Ability of CNS Neurons

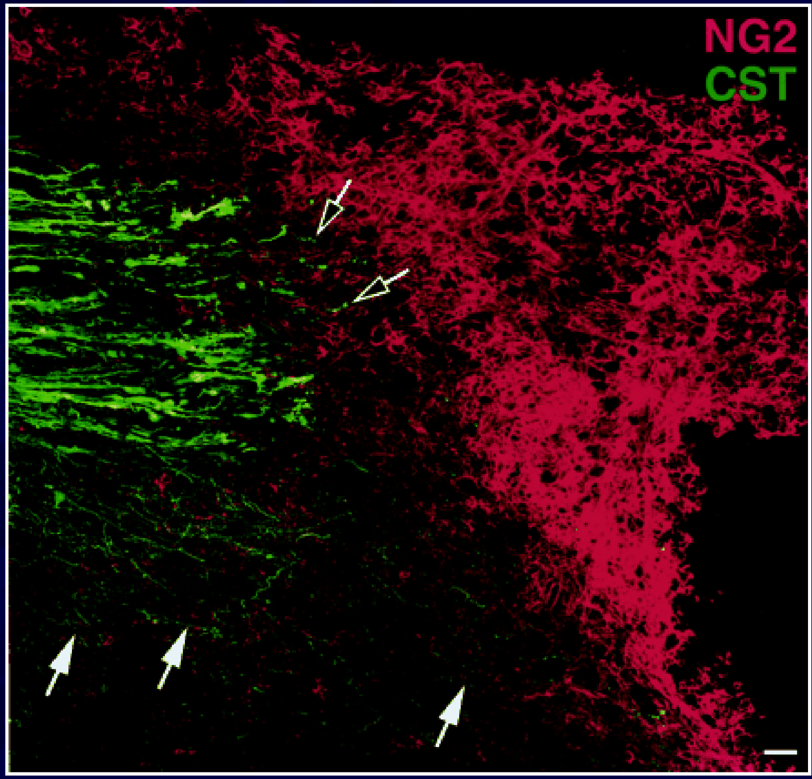
Neurotrophic Factors

- **Epidermal growth factor**
- **Fibroblast growth factor 2**
- **BDGF: brain derived growth factor**
- **Cyclic AMP**

Kojima, J Neurotrauma, 2002

Inhibitors of Neurite Outgrowth

- **ECM molecules in CNS myelin**
- **Glial scar/ cystic cavity that forms at injury site**



Jones, J Neuroscience, 2002

Cellular substrates

- Bridge the gap across cystic cavity glial scar.
- Facilitate axonal regeneration in the face of various inhibitors.

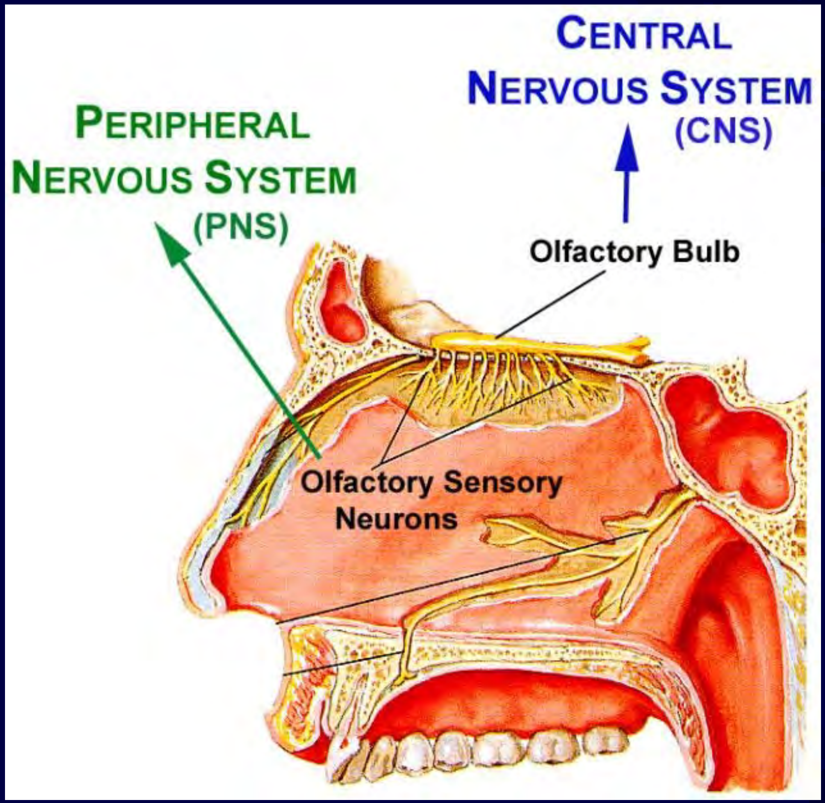
Peripheral Nerves

Rat Model

- **Multiple intercostal nerve grafts**
- **Stabilized w/ fibrin glue & FGF**
- **Redirect white matter proximal to gray matter distal**

Cheng, Olsen, Science, 1996

Olfactory-ensheathing glial cells



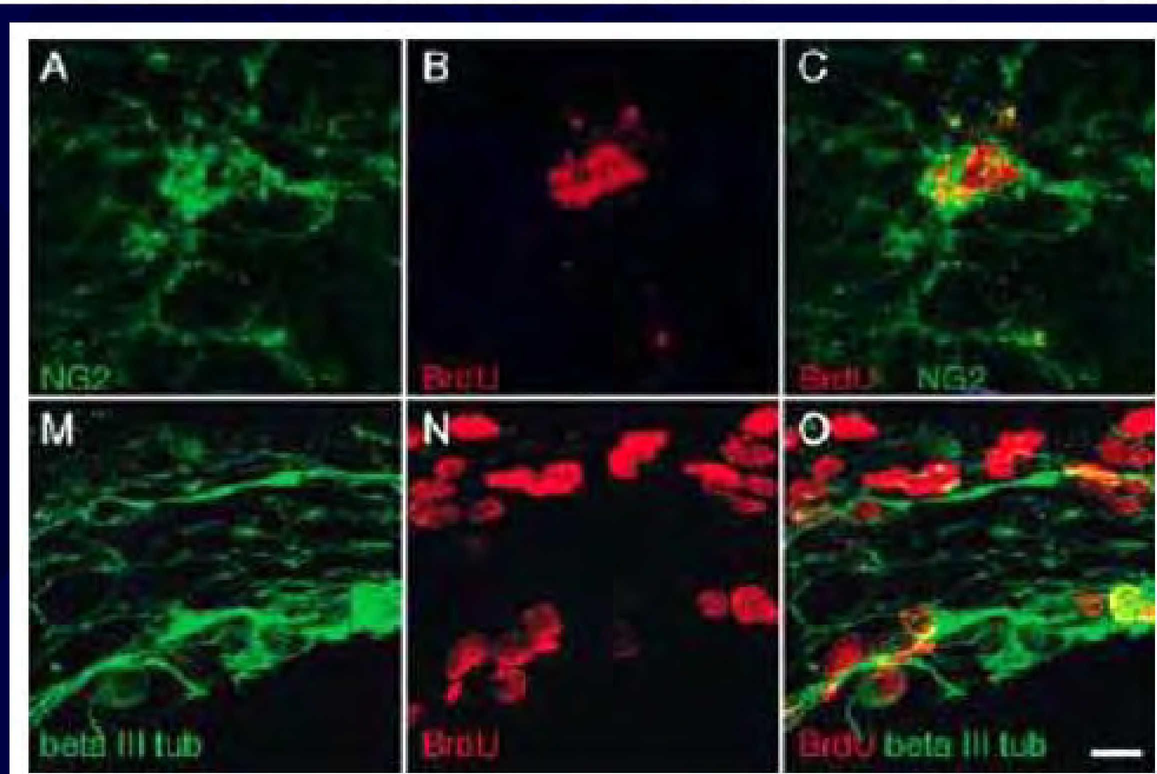
- Unique ability to regenerate in adults
- "Escort" axons across CNS-PNS boundary
- May support axonal regeneration after SCI

Stem Cell Therapy

Current Drug Targets, 2005, 6, 63-73

Adult Stem Cell Application in Spinal Cord Injury

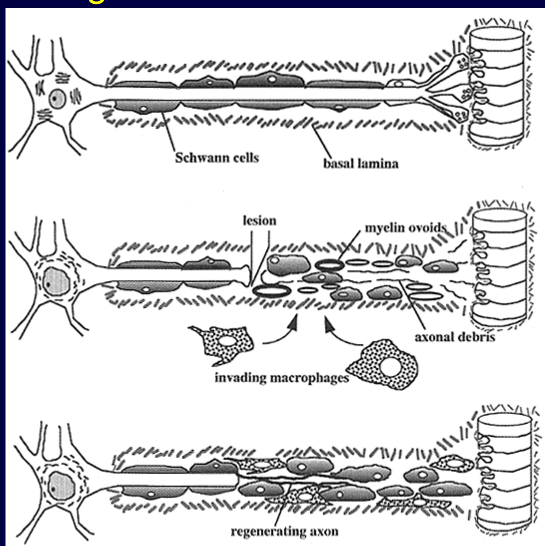
- Ongoing studies of adult mesenchymal stem cell therapy
- Animal studies are promising
- Human trials are lacking



3 weeks post-implantation, the adult neural stem cells implanted in the spinal cord.

Activated Macrophages

Macrophages play an important role in the successful regeneration of injured peripheral nerves by clearing cellular debris



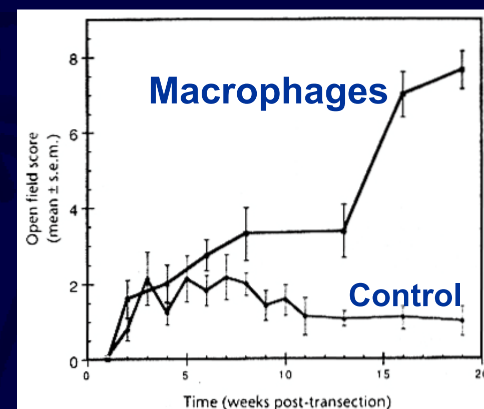
NATURE MEDICINE • VOLUME 4 • NUMBER 7 • JULY 1998

Implantation of stimulated homologous macrophages results in partial recovery of paraplegic rats

O. Rapalino[1], O. Lazarov-Spiegler[1], E. Agranov[2], G.J. Velan[3], E. Yoles[1], M. Fraidakis[4], A. Solomon[5], R. Gepstein[3], A. Katz[2], M. Belkin[5], M. Hadani[6] & M. Schwartz[1]

- Injure spinal cord of rats
- Extract macrophages from blood
- "Activate" them by exposing them to peripheral nerve
- Implant into spinal cord.

Activated macrophages result in significant functional recovery



Proneuron, activated macrophages, now in clinical trials

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