

Spinal Cord Injury

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Spinal Cord Injury

“An ailment not to be treated”

Edwin Smith Papyrus – 2500 BC (Imhotep)

Case Thirty-Three: Instructions concerning a crushed vertebra in his neck.

Examination: If thou examinest a man having a crushed vertebra in his neck (and) thou findest that one vertebra has fallen into the next one, while he is voiceless and cannot speak, his falling head downward has caused that one vertebra crush into the next one; (and) shouldst thou find that he is unconscious of his two arms and his two legs because of it...

Diagnosis: Thou shouldst say concerning him: "One having a crushed vertebra in his neck; he is unconscious of his two arms (and) his two legs, (and) he is speechless. An ailment not to be treated."

Edwin Smith Papyrus – 2500 BC (Imhotep)

SCI: Evolution of Treatment

- 2500 BC “an ailment not to be treated”
- 1930’s – SCI units – medical care
- 1940’s – rehabilitation of remaining axons
- 1950’s – closed reduction, realignment, instrumentation
- Improved medical care: pulmonary, nutrition, bladder management (decreased renal failure) (specialized SCI units)
- Innovations in rehabilitation
- Strategies for regrowth and axon replacement

Spinal Injury Statistics

- 28-55 per million population
- 10,000 per year in USA
 - 4,000 die before hospital
 - 1,000 die in hospital
 - (50% mortality)
- 5,000 Survivors
 - 45-65% paraplegics & quadriplegics
- *Males 15-34 years (males ~ 4x women)*
- *Average lifetime cost \$0.5-2 Million*

SCI: Incidence

- Etiology
 - MVA 50.4%
 - Fall 23.8%
 - Violence (guns) 11.2%
 - Sports 9%
- Changes 1979-2003
 - Increasing age
 - Increasing incidence of falls
 - Increasing cervical injuries
 - Increasing incomplete lesions (52%)

Ho Arch Phys Med Rehab 88:S49, 2007

SCI: Mortality

- Predictors early survival
 - Loss of consciousness
 - Level and severity neurological injury
 - Need for ventilatory assistance
 - Multiple associated injuries
 - Age, psychological, social and vocational factors
- Long term causes mortality
 - Pneumonia, ventilatory failure
 - Cardiac failure
 - Sepsis
 - Pulmonary embolus
 - Suicide
 - [Renal Failure]

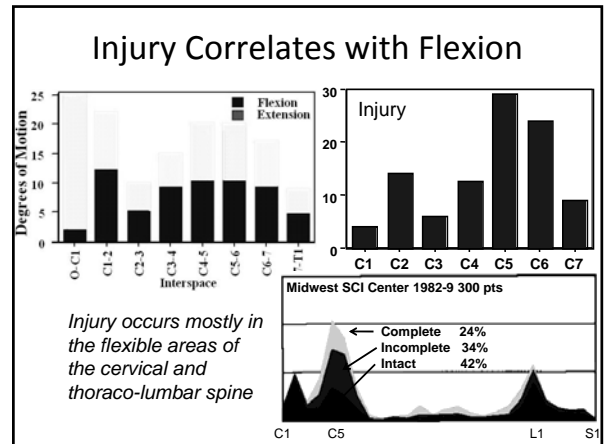
Ho Arch Phys Med Rehab 88:S49, 2007

SCI: Sports Injuries

Acute Spine Injuries in Skiers and Snowboarders

Joel M. Kary
St. Vincent Sports Medicine, Indianapolis, IN Current Sports Medicine Reports 7:35, 2008

- 3rd most common injury in skiers and snowboarders
- Flexible spine: T12-L1 burst Fx, C7 Fx
- Increased with increase snowboarding 3x
- Skiers: falls and collisions (forward fall, loss of control)
- Snowboarders: failed jumps (fall backwards)
- Poor judgment: fatigue and alcohol
- High speeds, poor equipment (no helmet)
- Poorly groomed & crowded slopes
Sloan's rule: "Fall down early and often"



SCI: Mechanisms of Injury

- *• **Flexion-Extension-Blunt** trauma: (shifting of vertebral bone in flexible spine areas) (mid-lower C spine, Thoraco-Lumbar region)
- **Distraction**: Head motion away from body (hanging, hyperextension, head forces)
- **Axial Compression/ Burst Fx**: (Thoracic injury)
- **Torsion**: rotation injury (falls, MVA)
- **Penetrating** injury: (gunshot, knife)
- **SCIWORA** (lax ligaments – elderly, child)

Hyperflexion Hyperextension Compression Burst Fx

Acute SCI: Pathophysiology

Primary Injury
initial mechanical or vascular destruction

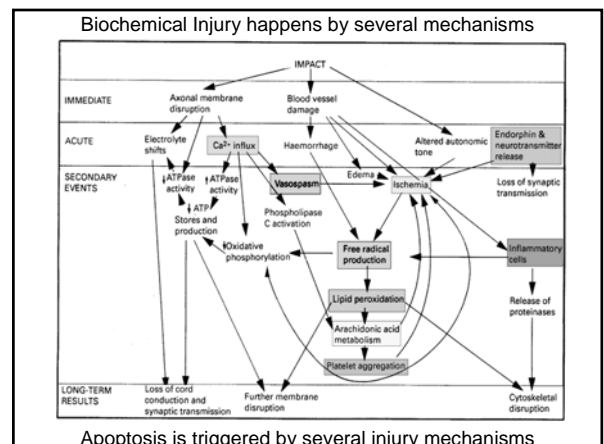
Secondary Injury
delayed injury from initial derangement (e.g... compression)
delayed mechanical injury (e.g... unstable spine)
biochemical injury

Apoptosis
Motor recovery may allow function with only 5% of axons remaining

SCI: Pathophysiology

Acute	<ul style="list-style-type: none"> • Mechanical injury 15-30 minutes • Ischemia, hemorrhages 1-2 hours • Temporary conduction in white matter, EDEMA 30 min - 3 hours
Sub-acute	<ul style="list-style-type: none"> • Vascular destruction 3-4 hours • White matter injury several hrs - several days • Cessation of cord changes 2-3 months
Chronic	<ul style="list-style-type: none"> • Function of reflexes below injury 6- 8 months

Injury progresses from central grey to axonal elements



Pharmacological Treatment SCI

- **Accepted Benefit**
 - Avoid hyperglycemia
 - Methyl prednisolone?
- **Potential Benefit**
 - 21 amino steroids, (tirilazad)
 - G_{M1} gangliosides,
 - prostacyclin analogs
 - NMDA receptor antagonists,
 - hypertonic saline,
 - platelet-activating factor antagonists,
 - neurite growth inhibitor antibodies,
 - antioxidants and free radical scavengers

SCI: National Acute Spinal Cord Injury Study (NASCIS II)

Glucocorticoids

- 30 mg/kg load methylprednisolone
- 5.4 mg/kg/hr for 24 Hr if started < 3 Hr
- 48 Hr if started > 3 and < 8 Hr

- Neurological “scores” improved but not clinical function
- Postulated decreased edema, inflammation, excitatory transmitter mediated injury
- Study challenged on statistical grounds, cannot replicate
- Numerous risks: hyperglycemia, delayed wound healing, infection, GI Hemorrhage

Currently a “standard under question”

Gomes Crit Care Med 33:1214, 2005
Wuermser Arch Phys Med Rehabil 88:S55, 2007

Acute Spinal Cord Injury

extremes of age – SCI without bony injury


Children

- 5-10% all SCI
- C-spine most common, esp. occipitoatlantoaxial
- Large head, lax ligaments, elasticity of spinal column, horizontal alignment facets.
- Common SCIWORA
- Traction especially concerning

Elderly

- SC is at greater risk:
- Narrowed spinal canal,
- Poor vascular supply

SCIWORA Best seen on MRI



Management of Spinal Cord Injury

ATLS

American College of Surgeons
Committee on Trauma
April 1996

- Immobilize
- Airway
- Breathing (adequate O₂, CO₂)
- Circulation (adequate Blood Pressure)
- Neurological
 - Consciousness (Glasgow Coma Scale)
 - Spinal cord function (sensory, motor, reflex)
- Associated injuries
- Medical Examination, management
- [Rehabilitation, Chronic management]

Medical Management I

Pulmonary Function

- Normal Tidal volume requires diaphragm (C3-5) (65% vital capacity)
- Accessory muscles key for cough and handling atelectasis and infection
- Associated chest injuries, PE, pulmonary edema, aspiration aggravate neural compromise
- Supine position and abdominal binders help push the diaphragm up to help breathing (late abdominal wall spasticity)
- Gastric distention can impede breathing
- Pulmonary complications leading cause of death in cervical and upper thoracic injuries (75%)
- Vital Capacity can be used to follow evolution of SCI (< 1 liter, <15 ml/Kg needs intubation)

SCI: Ventilatory Factors

- Airway injury
- Head injury abnormal ventilatory drive
- Lung
 - Aspiration, pneumonia, secretion retention
- Chest wall trauma
 - rib fracture, pneumothorax
- Lung parenchymal injury
- C3-5 Loss phrenic nerve function
- Thoracic muscle loss
- Abdominal muscles
 - expiration and effective cough

Ventilatory Dysfunction Changes

- **Decreased:**
 - vital capacity
 - total lung capacity
 - expiratory reserve volume

All volumes decreased except RV
- **Increased:**
 - residual volume
 - work of breathing

Vital Capacity is the best indicator of adequate function

Medical Management II

Cardiovascular Function

- **Initial HTN** 2-5 minutes (catecholamine release with SCI)
- **Hypotension** (loss tonic vasoconstriction)
 - MAP > 85 mmHg x 7 days has improved outcome*
- Functional **sympathectomy** (above T1-T4)
 - **bradycardia** (resolve 3-5 weeks) and
- “**Spinal Shock**” hypotension, motor loss, sensory loss, sympathetic loss
- **Pulmonary edema** (unable to compensate for volume loads)
- **Fat embolus** (subacute) *Volume and contractility management may be essential in quadriplegia (pulmonary artery catheter)*
- **Pulmonary embolus** (late)
- Treatment: fluids vs. vasoconstrictors (beta agonists, dopamine before afterload increases)

Vale J Neurosurg 87:239, 1997

Spinal Shock

- Injury **above T6** (celiac plexus)
- **Hypotension** (loss sympathetic activity with pooling of blood in extremities)
- Loss of **temperature regulation** (loss of control of vasomotor tone) - hypothermia
- Small bowel **ileus**
- Loss of colonic and bladder **reflexes**
- Absence of sensory and motor function

Differentiated from hemorrhagic shock by slow heart rate (tachycardia usually seen with hemorrhagic shock)

Medical Management III

- **Gastrointestinal (11%)**
 - Ileus, gastric distention, peptic ulcer, pancreatitis
- **Genitourinary**
 - Flaccid bladder (early), Spastic (late), recurrent infections, stones, urosepsis, renal failure
- **Temperature Control**
 - Poikilothermia – loss sympathetic control
- **Coagulation**
 - **DVT 40-100%** with 4-13% PE
- **Infections**
 - **Leading cause of death** (pneumonia, urosepsis)
- **Immobilization**
 - Decubitus ulcers, heterotopic ossification (**pain**), calcium stones

SCI: Surgery?

- **Acute:**
 - Re-align a spine – “locked facets”
 - Remove pressure on SC
 - hematoma, bone fragments
 - **Improved outcome decompression 4-6 hours**
 - Associated Trauma
- **Subacute:**
 - **Improved outcome in incomplete injury (<24 Hr)**
 - Stabilize a spine to improve nursing care and mobilization
 - Greenfield filter
- **Chronic:**
 - Consequences of Chronic SCI (e.g. decubitus, renal stones)
 - Incidental surgery (e.g. appendectomy)

Anesthesia for SCI

Acute

- **Intubation**
- **Succinylcholine** (<24 hrs)
- Maintain MAP, CO₂
- Fluid Status
- Position
- Methyl prednisolone
- Associated Problems
- E.P. Monitoring
- Post-op Vent Support

Chronic

- Airway ?
- **Succinylcholine** (> 8-12 mo)
- **Autonomic HTN**
- Positioning
- Substance Dependence
- Renal Function

Intubation

Triad of Injuries above the clavicle

- Head Injury (5% have SCI)
- Basilar Skull Fracture (nasal intubation?)
- Spinal Cord Injury

Clearing the C-spine

Methods of Intubation

SCI: Clearing the C Spine?

- If clear consciousness (pt can contribute to the examination) and no preexisting deficits (to mask assessment)
 - No Pain to preclude ligamentous injury by lack of pain
 - No new neurological deficits
 - No tenderness to palpation
 - Full range of motion
Easier to clear if cooperative
- If clouded consciousness (ETOH, drugs, HI)
 - Lateral, AP, and “open mouth” odontoid plain X-Rays
 - CT Scan
 - MRI? – SCIWORA
If patient can't cooperate, need anatomic evaluation

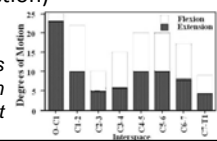
Radiographic Evaluation of C Spine

- **Cross-table lateral x-ray**
 - Need to see down to C₇ (7-14% fractures)
 - Cross-table lateral misses 15-20%*
 - **Antero-posterior film**
 - **Odontoid (open-mouth) view**
Reduced to 4-7% with A-P and odontoid views
 - **CT scan – better C1, C2**
Reduced to <1% with CT Scan
 - * **MRI – see spinal cord tissue** * Required in symptomatic patients
 - * **Flexion-extension films**
- Likely can't really clear the spine in most acute injuries*

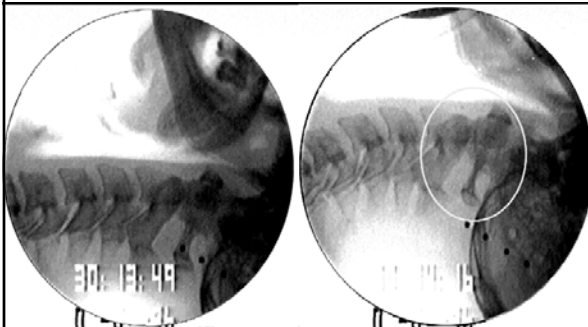
Airway Acquisition

- **Awake Fiberoptic**
 - Best, but often not possible (alcohol, drugs, head injury, “bloody mess”)
- **Blind** and other techniques with minimal movement
 - Not always minimal spine movement!
- **Asleep** intubation using midline stabilization (MILS) (not traction)
- **Surgical airway**

Extension correlates with intubation movement

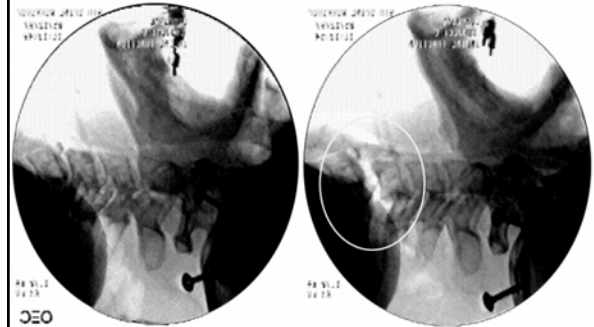


Normal - Intubation

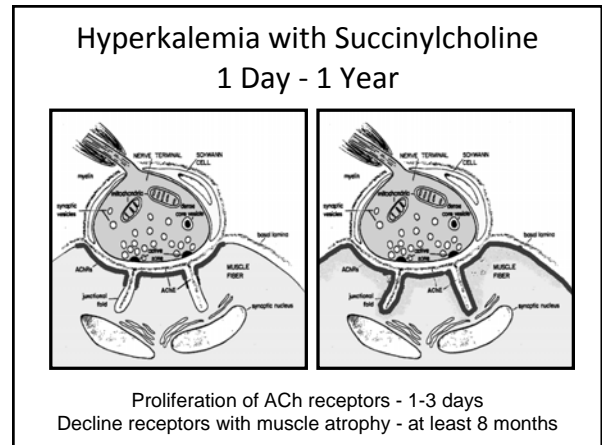
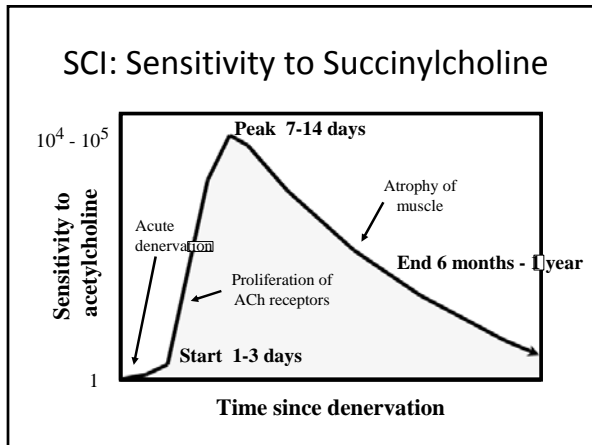
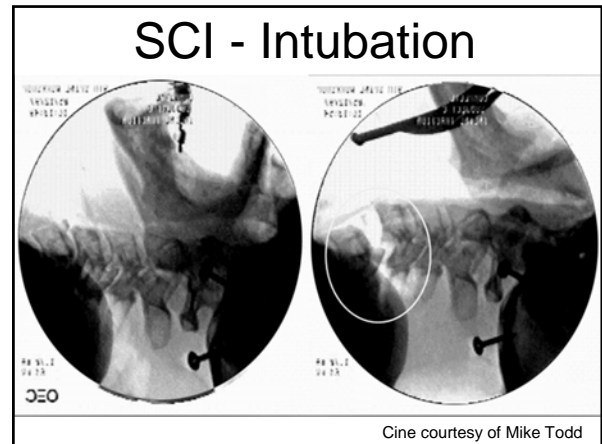
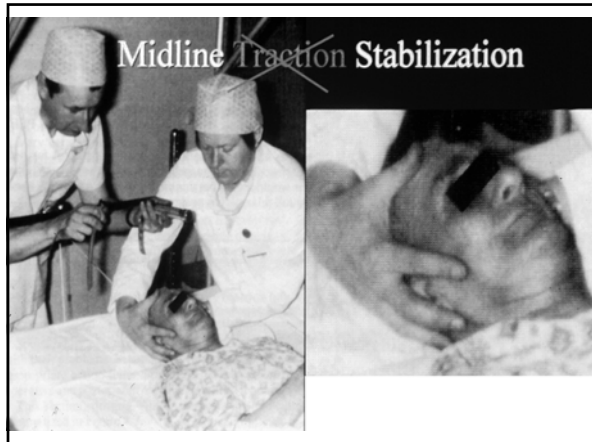


Cine courtesy of Mike Todd

Traction

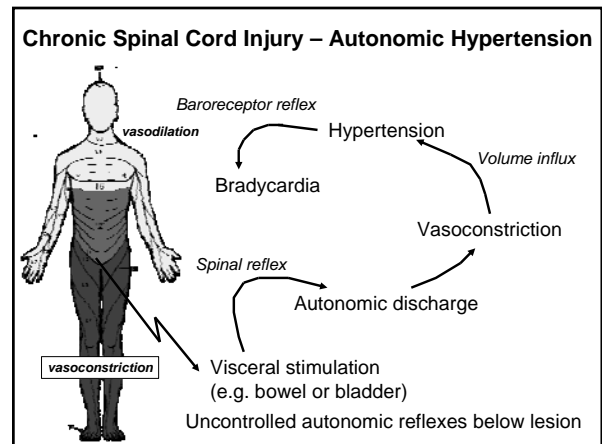


Cine courtesy of Mike Todd



Autonomic Dysreflexia
Autonomic Hypertension

- 60-85 % in chronic, complete lesions above T6
- Any stimulus below lesion:
 - Vasoconstriction below
 - Vasodilation above the lesion
- Hypertension, headache, diaphoresis, piloerection, chills w/o fever, nasal congestion, blurred vision, anxiety, bronchospasm
- Reflex bradycardia, except in high lesions where cardiac accelerators (T1-T4) part of reflex

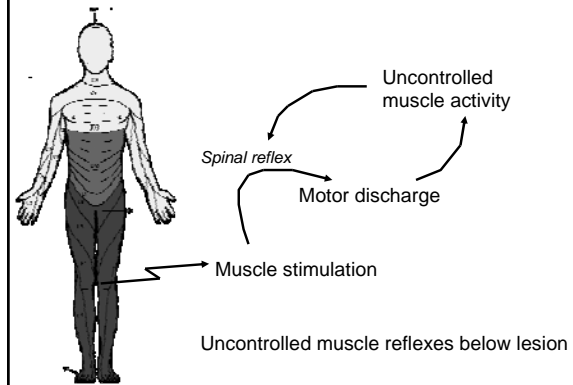


SCI & Pregnant Patient

Autonomic dysreflexia is life-threatening in labor and delivery

- Physiology
 - severe HTN, CVA, ICH, death
 - utero-placental vasoconstriction, fetal hypoxemia, fetal bradycardia
- Confused with pre-eclampsia
- Institute lumbar epidural anesthesia early
- Good bowel and bladder management

Chronic Spinal Cord Injury – Mass Reflex



SCI Improving Outcome

- Acute
 - Realign bony elements
 - Remove objects impinging on sc (e.g. bone fragments)
 - Basic optimal medical environment
 - Improve cellular environment (Neuroprotection, block EAA, free radicals, inflammation)
 - Block apoptosis?
- Chronic
 - Rehabilitation strategies to maximize or augment function
 - Regrowth of axonal neural elements

*Only 1.4 – 12% of neurons surviving will support function
1-2 dermatomes can be difference in function*

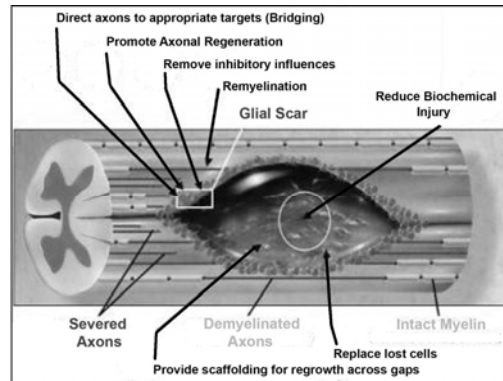
SCI: Rehabilitation

- Maximize function of remaining neurons (only a fraction of total needed for function)
- Relearning the use of available neurons
- “Plasticity” use of remaining neurons to do other tasks (central pattern generators)
- Electrical stimulation to assist function
- Reduce interfering spasticity (clonidine, cyproheptadine, baclofen)

SCI: Adjuncts to Function

- Tendon Transfer to improve hand grasp
- Transcutaneous or direct stimulation of muscle (requires intact LMN, muscle)
- Prothesis & others: phrenic n. pacemakers
- Functional electrical stimulation of the Bowel and bladder
- Sensory rhizotomy (S2-5) to reduce reflex contraction and improve bladder compliance

Strategy: Repair axonal elements in injury



SCI: Repair Strategy I
Reduce Inhibitors to Neuron Re-Growth

With injury an inhibitory environment is present to prevent neural regrowth

- Inflammatory process (T cell autoimmune response directed at myelin)
 - RX glucocorticoids?, T cell regulation (+/-)
 - Bind T cells with synthetic myelin basic protein
- Myelin (destruction) growth inhibitors (oligodendroglia, microglia): Nogo-A, myelin-associated glycoprotein (MAG), oligodendocyte-myelin glycoprotein (Omgp), Tenascin-R (TN-R)
 - RX: antibodies to myelin and factors
 - RX: enzymatic destruction of inhibitors
 - RX: genetic manipulation of inhibitor expression

Ang Clin Exp Pharm Physiol 33:541, 2006
Willerth Adv Drug Del Rev 60:263, 2008

SCI: Vaccination?

Clinical and Experimental Pharmacology and Physiology (2006) 33, 541-545

Frontiers in Research Review: Cutting-Edge Molecular Approaches to Therapeutics

THERAPEUTIC VACCINATION FOR CENTRAL NERVOUS SYSTEM REPAIR

Beng Ti Ang,^{1*} Gang Xu² and Zhi Cheng Xiao^{1RS}

¹Department of Neurosurgery, National Neuroscience Institute, ²Center for Molecular Medicine, ³Department of Clinical Research, Singapore General Hospital, ⁴Institute of Molecular and Cell Biology and ⁵Department of Anatomy, National University of Singapore, Singapore

Can we use the body's immune system to remove inhibitors to neuron regrowth?

SCI: Repair Strategy II
Develop Framework for Regrowth

After injury the architecture is unfavorable for neural regrowth

- Reduce formation of glial scar (reactive astrocytes)
 - RX transplanted cells
- Bridging a cystic infarct area
 - Polyglycolic acid-chitosan conduit coated with adhesion molecule L1
 - Lecithinized brain derived neurotrophic factor (BDNF)

Ang Clin Exp Pharm Physiol 33:541, 2006
Willerth Adv Drug Del Rev 60:263, 2008

SCI: Repair Strategy III
Providing Neural cells

Providing cells to form "bridging" neural tissue (axons)

- Neurotrophins to promote inherent cell growth
- Transplanted cells can secrete extracellular matrix and cytokines to promote cell migration
- Promote Vascular support to repair area
 - Embryonic & Neural stem cells
 - Bone marrow Stromal cells\Mature cells: Schwann, olfactory ensheathing cells, fibroblasts

Ang Clin Exp Pharm Physiol 33:541, 2006
Coutts Exp Neurol 209:368, 2008

SCI State of the Art

Standard
Works in humans

Unclear in animals

Beginning to learn in cells

Experimenting in animals

Acute Care

- ABC's
- Realign bony elements & remove objects impinging on sc
- Basic optimal medical environment
- Improve cellular environment (Neuroprotection , block injury mechanisms)
- Block apoptosis?

Rehabilitation

- Rehabilitation strategies to maximize or augment function
- Adjuncts

Repair strategy

- Block inhibitors and glial scar formation
- Developing bridge strategies in spinal cord
- Regrowth of axonal neural elements
- Transplantation of neural elements