# Peripheral Nerve Injury and Repair Options

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# Disclosures

- Synthes, Arthrex

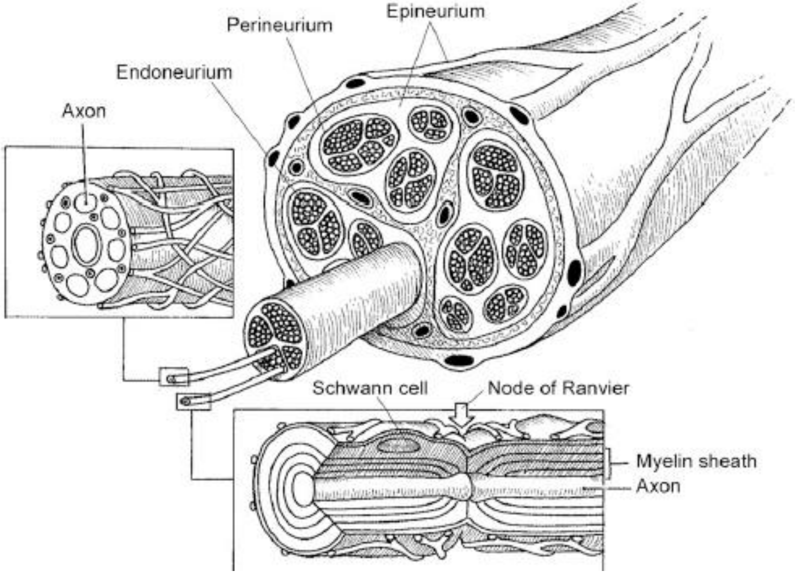
# Introduction

- Wide Spectrum of Disability
- Types of Injuries
  - Stretch/Traction
    - **Most common**
  - Crush
  - Laceration
  - Ischemic
  - Blast
  - Iatrogenic
- 75% Upper Extremity
- Prognosis
  - <50% regain useful function
- **Tremendous amount of ongoing research…….**

# Anatomy – Cellular Level

- Axons
  - Transmit signals
- Schwann Cells
  - **Supporting Cell of PNS**
    - **Produces Myelin**
    - Secrete Neurotrophic Factors
  - **Guides regrowth of axons**
    - Cylindrical Orientation (Endoneurial Tubes)
    - Myelination of regenerating axons

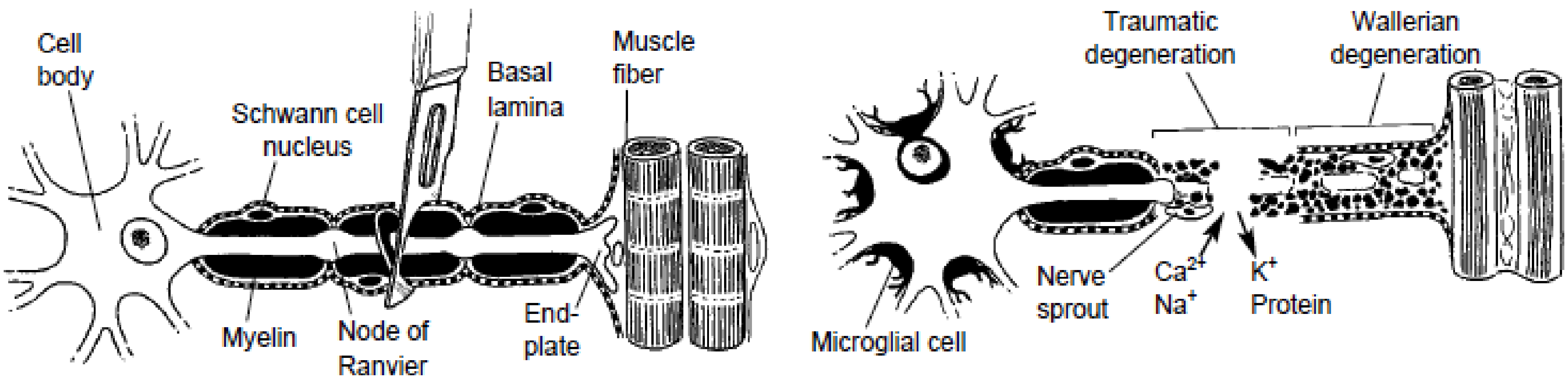
# Anatomy




- 3 Layers of a Nerve
- Epineurium
  - External Supportive Barrier
- Perineurium
  - Surrounds individual fascicles
  - **High Tensile Strength**
- Endoneurium
  - Loose Collagenous Matrix
  - Surrounds individual nerve fibers

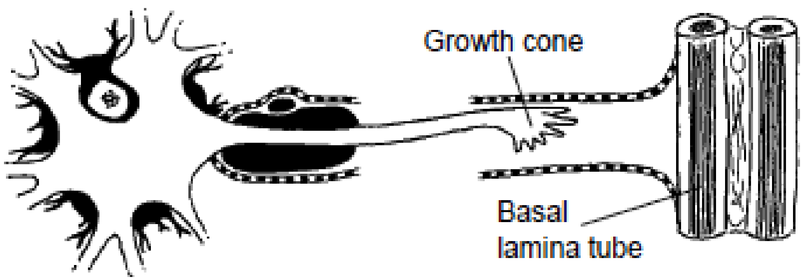

Kato H, Minami A, Kobayashi M, Takahara M, Ogino T. Functional results of low median and ulnar nerve repair with intraneural fascicular dissection and electrical fascicular orientation. J Hand Surg Am. 1998 May;23(3):471-82.
Ganel A, Farine I, Aharonson Z, Horoszowski H, Melamed R, Rimon S. Intraoperativenerve fascicle identification using choline acetyltransferase: a preliminary report. Clin Orthop Relat Res. 1982 May;(165):228-32.

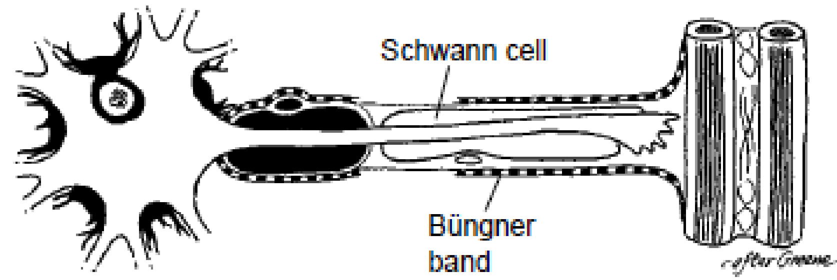
# Pathophysiology of Injury and Regeneration




- Axon transected with traumatic degeneration in zone of injury
- **Wallerian Degeneration** of distal nerve
  - Breakdown of neural and glial elements
  - Moderated by Schwann cells and macrophages
  - Only occurs with axon disruption
  - Starts 24-96 hours post injury
  - Completes by 6-8 weeks

# Pathophysiology of Injury and Regeneration



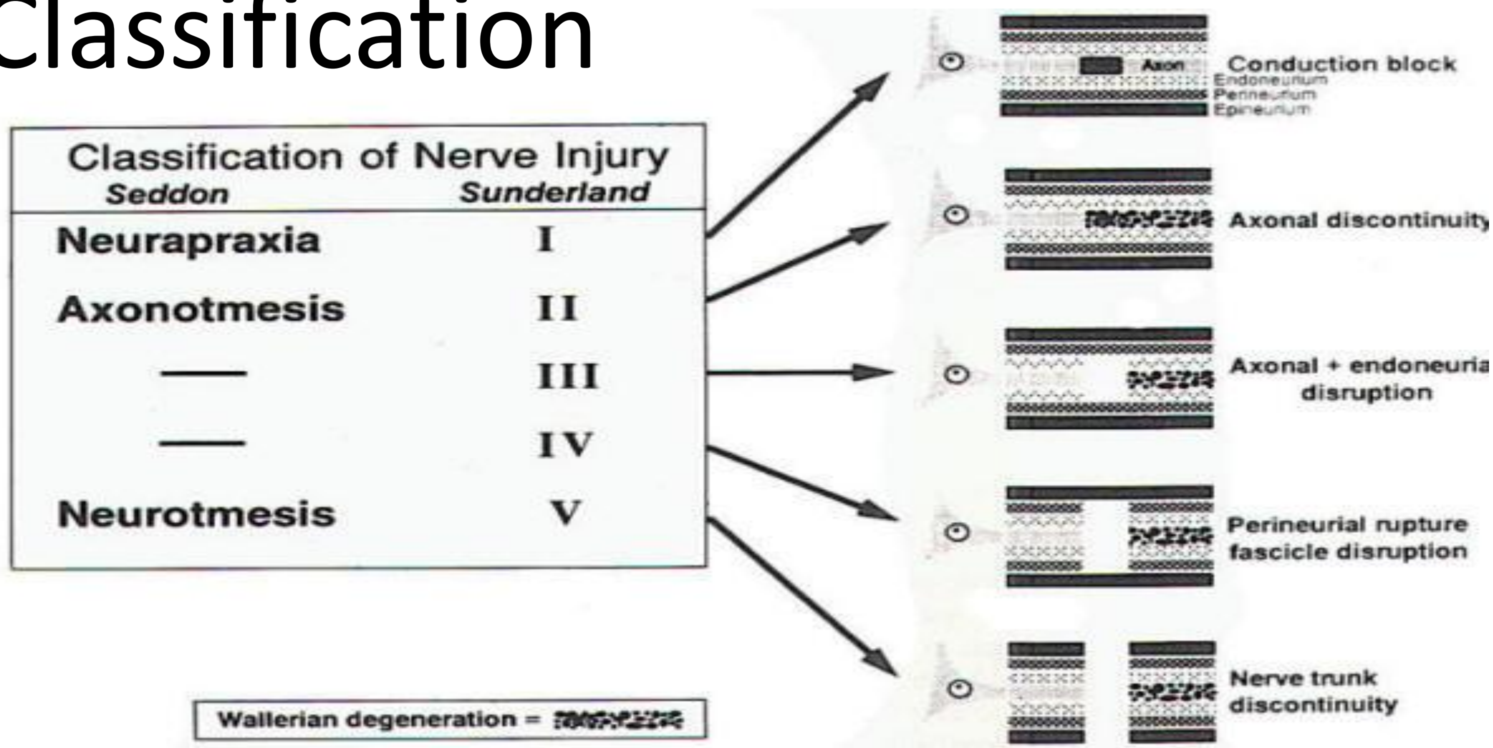

- Growth cone regenerates
  - 1 mm/day, 1 inch/month
  - Basal lamina guides

- Schwann cells align to form Buengner bands

Adapted from Seckel BR: Enhancement of peripheral nerve regeneration. Muscle Nerve 1990;13:785-800.

# Injury Classification

- Seddon (1942)
- Sunderland (1951)




**Neurapraxia**: injury without physical disruption of axon or supporting structures *** No Wallerian Degeneration ***

**Axonotmesis**: disruption of axon but nerve in continuity (further subdivided by Sunderland based on structures disrupted)

**Neurotmesis**: complete transection of nerve

# Prognosis

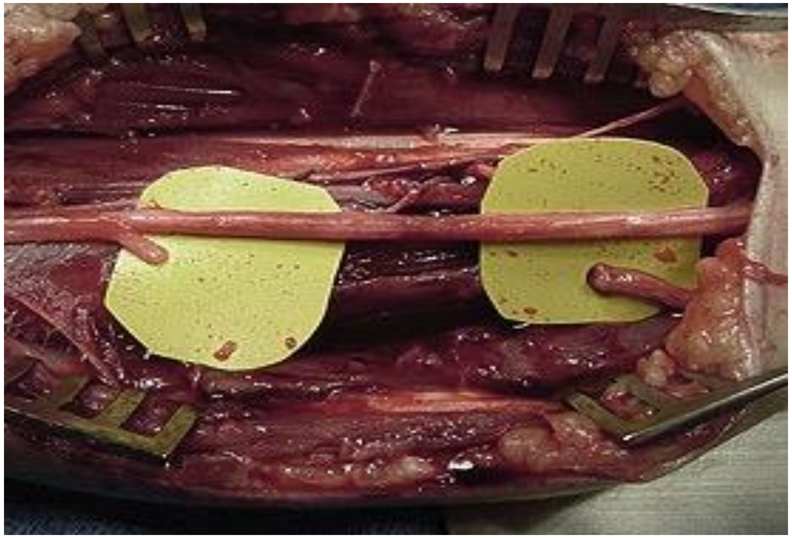
- **<u>Classification important for prognosis</u>**
- Neuropraxia - Full Recovery
- Neurotmesis - No Recovery
- Axonotmesis - Variable Recovery

# Other Prognostic Factors

- **Age**
  - **Younger do better**
    - **3rd Decade**
- **Level of the Lesion**
  - **Distal better than proximal**
- Nature of the Nerve Injured
  - Sensory recovers better than motor
- Cause of the Injury
- Zone of Injury (soft tissue)
- Delay From Injury to Repair
  - Surgeon has some control

# Clinical Exam

- Careful documentation of neuro deficits
  - Define level and degree of injury
  - Baseline to compare for recovery
- Open injuries
  - Wound Evaluation
    - Clean/dirty
    - Zone of injury
  - Associated Injuries
    - Musculoskeletal
    - Vascular



# Imaging

- Ultrasound
  - Reliable, cheap, available
  - Assess for continuity, neuroma, scar
- MRI
  - Nerves not accessible to ultrasound
  - Assess surrounding structures
    - Muscle atrophy, other soft tissues

Toros T, Karabay N, Ozaksar K, Sugun TS, Kayalar M, Bal E. Evaluation of peripheral nerves of the upper limb with ultrasonography: a comparison of ultrasonographic examination and the intra-operative findings. J Bone Joint Surg Br. 2009Jun;91(6):762-5.
Grant GA, Britz GW, Goodkin R, Jarvik JG, Maravilla K, Kliot M. The utility of magnetic resonance imaging in evaluating peripheral nerve disorders. Muscle Nerve. 2002 Mar;25(3):314-31.
McDonald CM, Carter GT, Fritz RC, Anderson MW, Abresch RT, Kilmer DD. Magnetic resonance imaging of denervated muscle: comparison to electromyography. Muscle Nerve. 2000 Sep;23(9):1431-4.

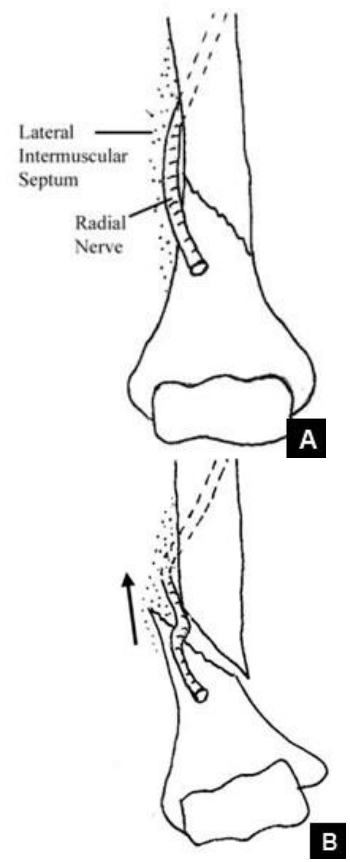
# Nerve Conduction Studies Electromyography (NCS/EMG)

- Determine the site of injury
- Estimate severity of injury
- Follow and predict recovery

- NCS can localize the injury acutely

- EMG not useful acutely
  - becomes abnormal 3-6 wks after injury
  - ⦰ **acutely** distinguish neuropraxia from axonotmesis/neurotmesis

- Indications
  - Closed Injuries/Fractures with Nerve Injury
    - e.g. Humeral Shaft Fractures, Knee Dislocations
  - Elective Procedures with Neuropraxia
    - e.g. Sciatic N after THA



# Nerve Repair

- Indications
  - Open injuries
    - Neurotmesis (complete transection)
    - Acute repair
  - Closed injuries
    - Neuropraxia or Axonotmesis
    - Observe 3-6 wks
    - EMG
      - Baseline reinnervation, repeat in ~ 6wks
    - Imaging
      - Assess for continuity of nerve
      - US or MRI

    - Delayed repair if discontinuous or no recovery in 3-6 months

# Primary Repair

- **Best results: Immediate Primary Repair**

- Intraneural scarring with delay
- Earlier exploration provides easier diagnosis
  - Less scar tissue
  - Increased chance of matching fascicular arrangement

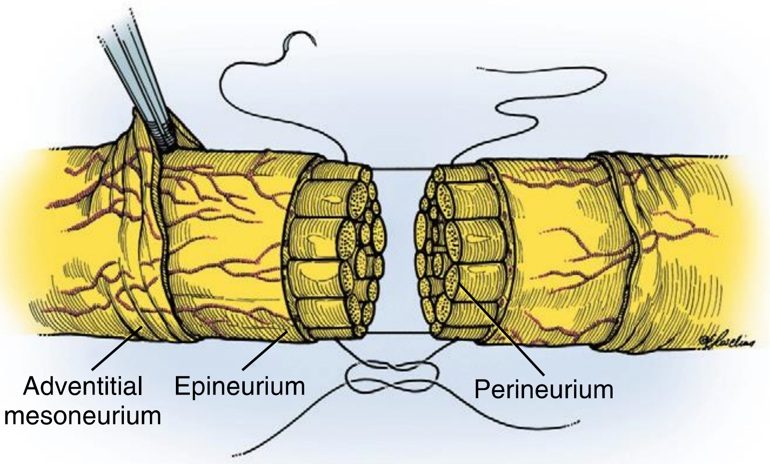
- Prerequisites:
  - Clean wound
  - Good vascular supply
  - No crush component
  - Adequate soft-tissue coverage
  - Skeletal stability

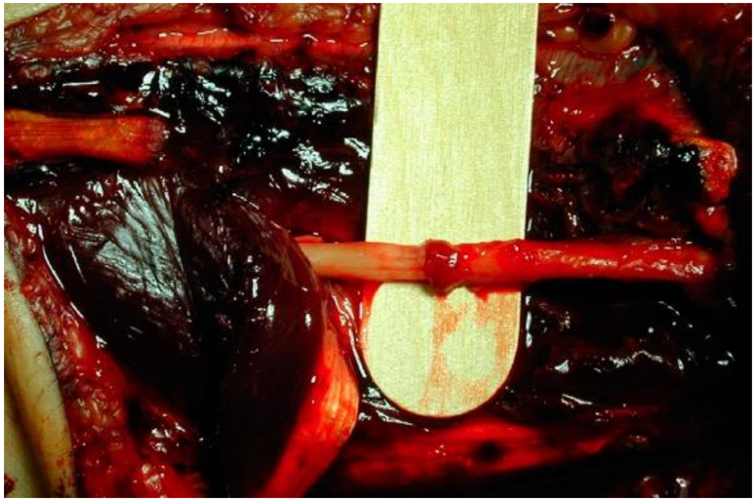
# Primary Repair

- Goal = Tension-free repair
  - Tension causes
    - Gapping
    - Scar formation
    - Ischemia of nerve
- Mobilization of nerve
  - decrease tension
    - Transposition of Ulnar/Radial → 3 cm

# Primary Repair

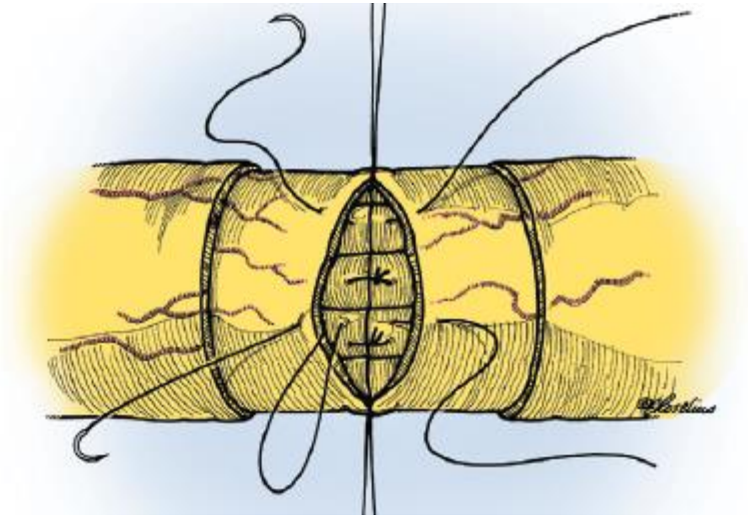
- Technical Considerations
  - Neurolysis
    - **Decrease tension**
  - Resect to "healthy" nerve
    - **Common cause of failure**
  - Secondary Repair
    - Resect proximal neuroma and distal glioma
  - Gentle tissue handling
  - Microscope very helpful



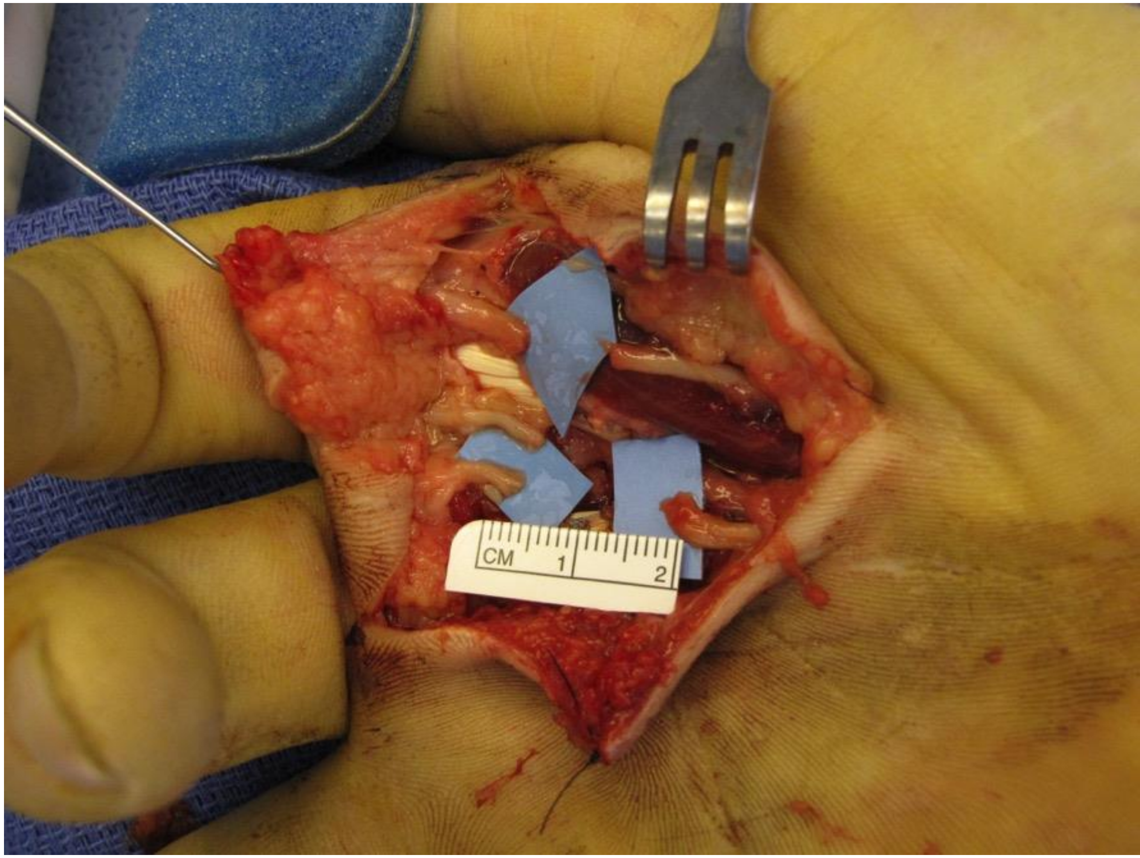
# Epineurial vs Fascicular Repair

- Equivalent results in most studies
- Exception is ulnar nerve near wrist
  - Motor fascicles definable
    - Ulnar side of nerve
- Epineurial Repair
  - 7-0, 8-0, 9-0 Nylon Suture
- Intra-fascicular Repair
  - 8-0, 9-0, 10-0



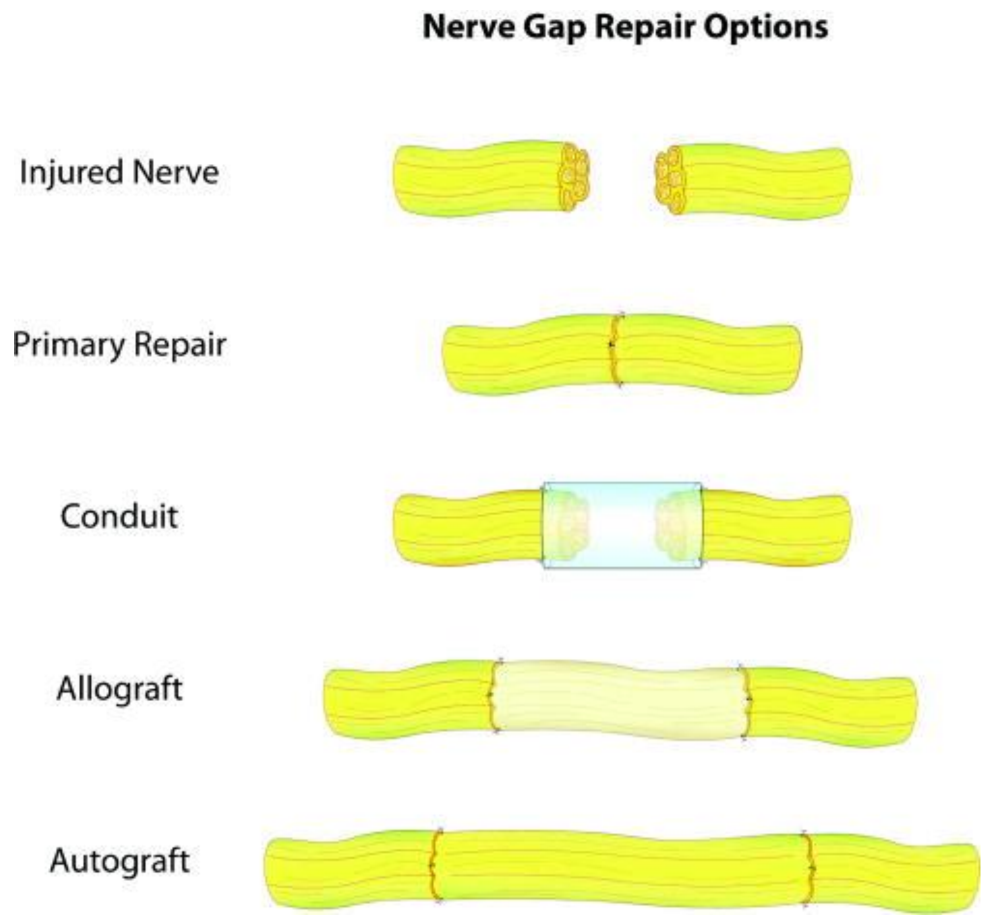
# Nerve gap

- Precludes tension-free repair
- Occur with
  - Wide zone of injury
  - Delay in repair
    - Retraction
    - Scarring
  - Excision of neuroma or tumor



# Nerve Gap Repair Options

- Operative Treatment
  - Grafting
    - Autograft
      - Cable
      - Trunk
    - Allograft
      - Transplantation
      - Decellularized
    - Conduits
      - Biologic
      - Synthetic



# Nerve Autografts

- Gold Standard
  - Nerve architecture
  - Growth factors
  - Nonimmunogenic
- Drawbacks
  - Donor site morbidity
    - Scar
    - Sensory deficit
    - Potential neuroma
  - Limited availability

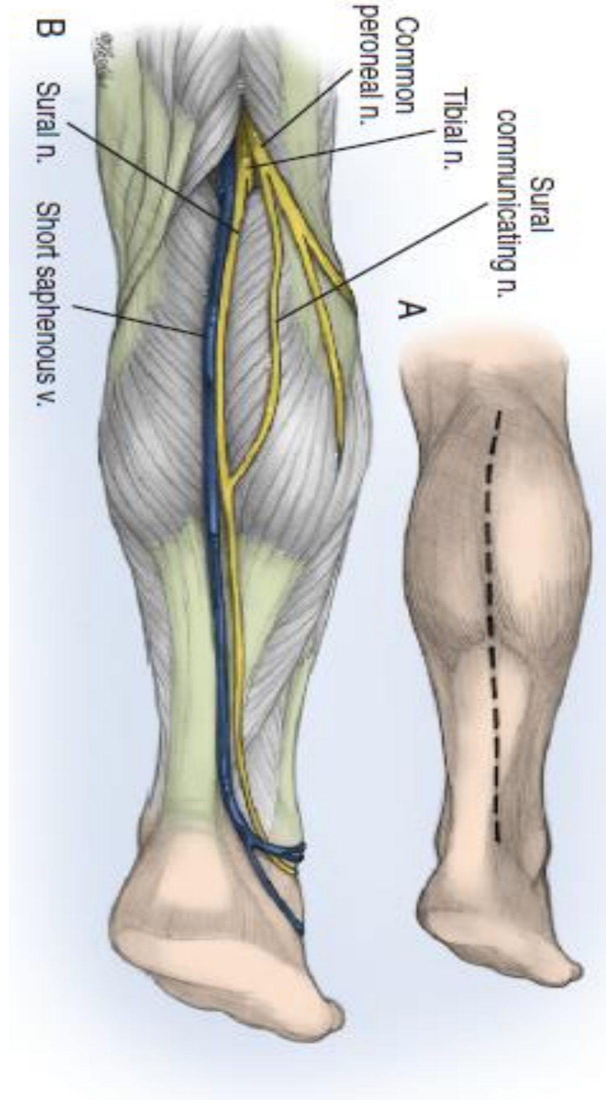
# Donor Autografts

- Requisites:
  - Tolerable donor site morbidity
  - Sufficient length
  - Appropriate caliber
  - Ease of harvest

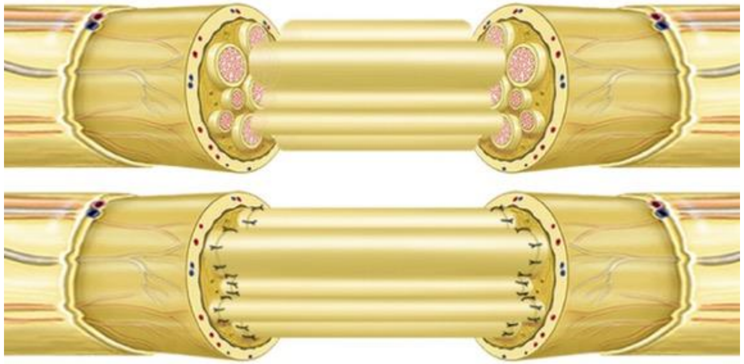
- Cutaneous Sensory nerves

- Sural Nerve most common donor
  - 40 cm length

- Multiple Other Donors
  - Upper Extremity
    - MABC, LABC, SRN, PIN, AIN
  - Lower-Extremity
    - SPN, LFCN, Saphenous



# Autograft



- Technical Considerations
  - Same principles as primary repair but 2 repair sites
  - Tension-free repair
    - Graft 10-20% longer than defect
  - Cabled Grafts
    - Injured nerve often larger than donor nerve
    - Multiple lengths of donor placed in parallel
    - Match diameter of severed nerve
    - Fascicular repair

# 4 cm Gap w/ Sural Nerve Cabled Autograft

# Nerve Allograft

- Advantages
  - No donor site morbidity
  - Unlimited Supply
  - Potential recovery near autograft
- Two Options
  - Tissue allograft
  - Decellularized allograft

# Tissue Allograft Nerve

- Allotransplantation
  - Alberts 1885 -> 1st allograft transplant
  - Primary drawback – immunogenicity

  - Graft processing can decrease MHC II
    - Chemical treatment
    - Cold Preservation
    - Irradiation
    - Repetitive Freeze-Thaw
    - Lypophilization
    - University of Wisconsin Storage Solution
      - Pen G + Dexamethasone + Insulin + 5 Celsius x 7 days

  - Patients still require 24 months of immunosuppression
  - Has place for patients with very large nerve deficits to crucial nerves

# Decellularized Allografts

- Acellular - Non-immunogenic
- Highly processed
  - Detergent, Gamma Irradiation
  - Enzymatic Degradation
    - Modulate surface molecules that regulate axon ingrowth
- Structural architecture maintained
  - Microtubules, laminins
  - Support nerve regrowth

AxoGen®

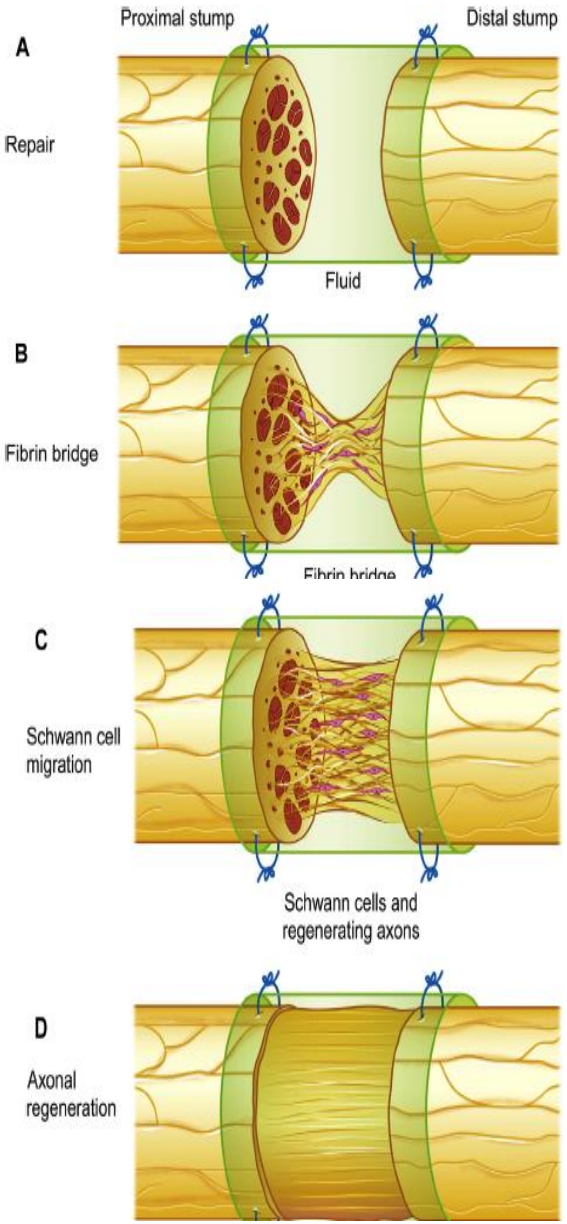
Avance® Nerve Graft

- Results equivalent to autograft for sensory nerve gaps up to 3 cm

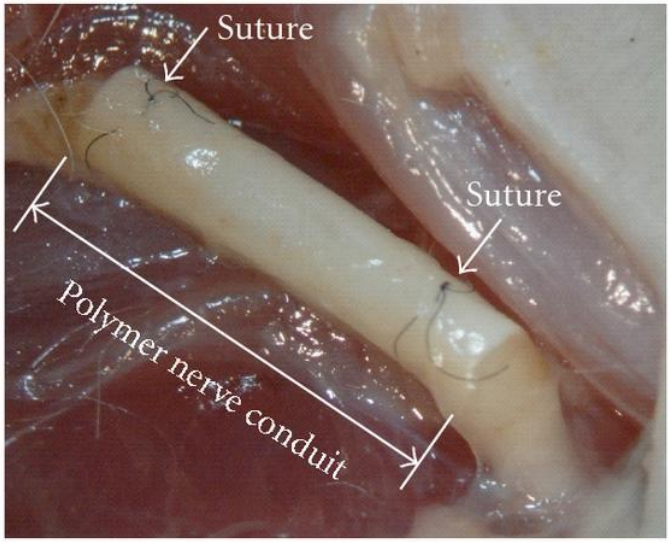
- Larger gaps or Motor or Mixed nerve
  - Less data, more mixed results in humans
  - Poorer results in animals

# Conduits

- Simple tubes to direct nerve regeneration
  - Direct axon regrowth
  - Provide barrier to fibrosis
  - Concentration of growth factors in gap
  - Lack Schwann cells, neurotrophic factors and architecture
- Biologic
  - Vein/Artery
- Synthetic
  - Collagen (NeuraGen, Integra)
  - Polyglycolic Acid (NeuroTube)
  - Caprolactone (Neurolac)



# Conduits




- Uses
  - Small sensory nerves
  - Short gaps < 3 cm
    - Inferior for larger gaps and also head to head compared to allografts and autografts in animal studies
  - Augmentation of primary repair or grafting
- Advantages
  - Directs nerve regrowth
  - Prevents fibrosis
  - Ease of use
  - Structural support for repair
- Disadvantages
  - Cost
  - No Schwann cells or nerve architecture
  - Only for small gaps in sensory nerves

# Summary

| | Advantages | Disadvantages |
|---|---|---|
| Primary Repair | • **Best Outcomes** | • Must be tension free |
| Autograft | • **“Gold-Standard” for Gaps**<br>• Non-Immunogenic<br>• Bridges Long Gaps | • Donor Site Morbidity<br>• Scarring<br>• Neuroma Formation<br>• Limited Supply |
| Allograft | • Abundant Supply<br>• No Donor Site Morbidity<br>• Non-Immunogenic (Decellularized) | • Expensive $$$$ (Decellularized)<br>• Immunosuppression (Allo)<br>• Less experience |
| Conduits | • Abundant Supply<br>• No Donor Site Morbidity<br>• Less Scarring<br>• Accumulate NGF’s | • Expensive $$$<br>• No Architecture for Regrowth<br>• Only short gap, sensory |

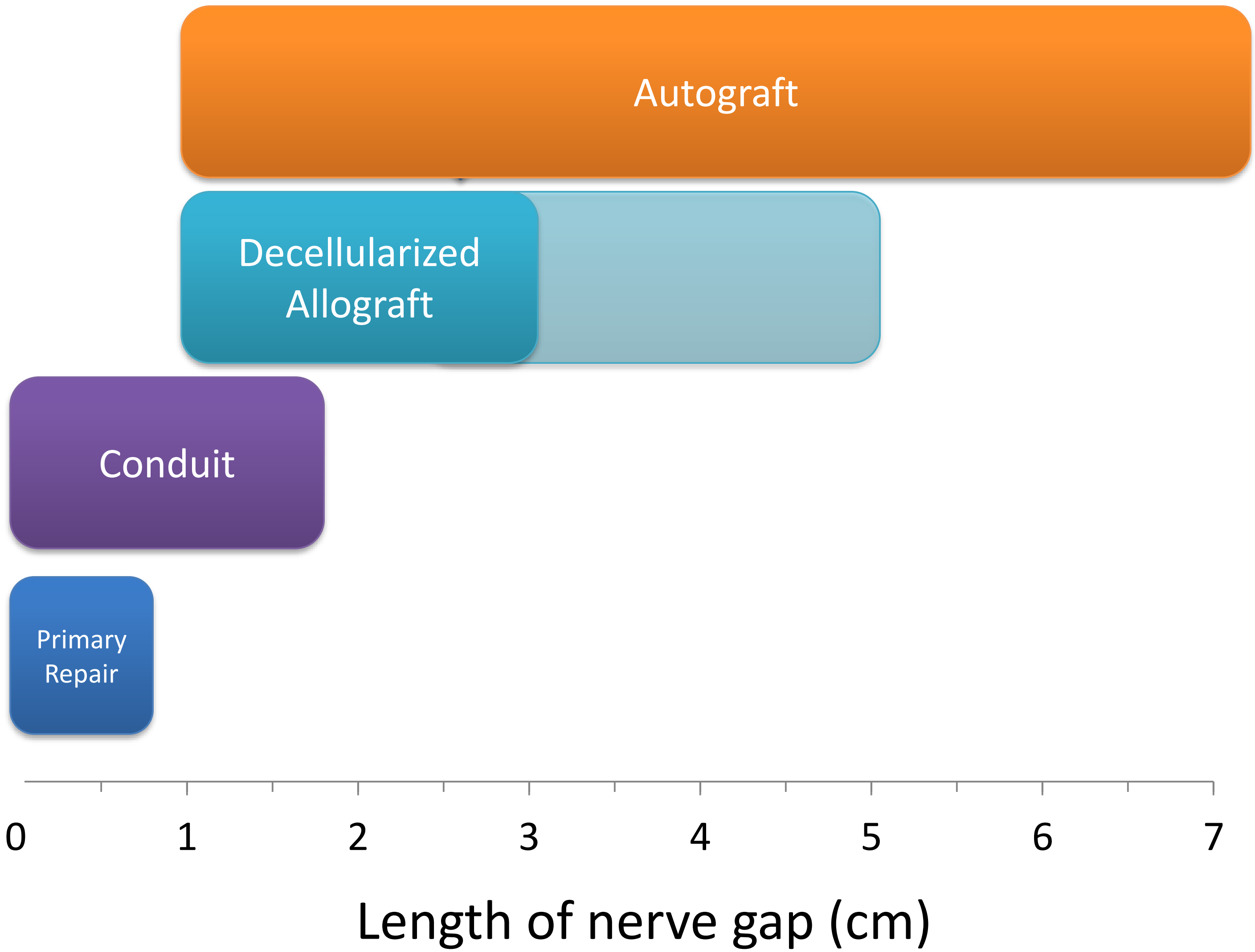
# Summary

- **Primary repair without tension always preferred**

For Gaps

- Autograft → GOLD STANDARD
  - Nothing shown better than autograft in any clinical situation
- ”Classic” Allograft with immunosuppression
  - Very large defects when autograft not available
- Decellularized Allograft
  - Gaps from 1 – 5 cm
    - Preference for sensory and < 3 cm
- Conduits
  - Sensory Nerves with gap < 1.5 cm
  - Adjunct to Direct Repair

# Summary


Autograft
Decellularized Allograft
Conduit
Primary Repair
0
1
2
3
4
5
6
7
Length of nerve gap (cm)

# Thanks!