Nerve Grafting

History

- Philipeaux and Vulpian
  - experimental nerve grafting
  - Hypoglossal nerve function in dogs, 2cm defect with a lingual nerve
- First Clinical Nerve Graft 1876
  - Albert outcome not known
- Clinically Successful
  - Mayo-Robinson in 1888
  - "sensation returns within 36 hours of operation"
  - Outcome at 3 years "nearly perfect in every respect"

History

- W W I
  - Much opportunity – overwhelming failure
  - ‘Nerve graft … should be considered usless’

- 1920 Huber
  - reported on 21 series -- 219 cases – concluded autogenous nerve graft was superior to homo or heterograft

- 1927 Bunnell
  - started in 1927 -- by 1939 reported on 32 successful nerve autografts in the forearm and hand
  - emphasized the use of cable grafts for median and ulnar nerve grafting
  - experiments on cat sciatic nerve revealing central necrosis in a trunk graft

- W W II
  - Sanders and Young – autograft
  - Uniform means of reporting outcomes

- Seddon 1954
  - 67 patients 68% useful recovery “autologous grafting is worthwhile and reliable procedure in peripheral nerve surgery”
  - Poor outcomes -- sepsis, scarred beds with poor vascularity

  - No microvascular techniques

- Millesi et al
  - Now established techniques
  - Tension and tension free comparison
    - Proliferation of connective tissue
    - Secondary loss regenerating axons from distal stump
    - Replaced cable grafting with inter-fascicular grafting

Reasons for poor outcomes

- Length of nerve graft regarded as important factor
  - i.e. longer the graft the worse the expected results
  - Shorten the defect
    - Flexion of adjacent joints
    - Mobilization of nerve stumps
    - 2 sites of coaptation under tension
- Significance of schwann cells for neurotization of nerve graft not recognized
    - Ciliate preserved allograft
    - Deep frozen allograft
    - Lyophilized and radium treated cadaver nerve grafts
- DEAD TISSUE

Successful Nerve Graft

- No tension at site of coaptation
- Preservation of fascicular pattern
- Survival of schwann cell
- Length (with-in reason) of graft is of no significance

Neurotization

- Axon sprouts
  - Basis of nerve regeneration is the ability of axons to produce axon sprouts
  - Sprouts from neuroma if they do not meet a distal stump
  - Neuroma contains minifascicles
    - Fibroblasts
    - Axon sprouts
    - Schwann Cells
    - Capillaries
  - Minifascicle – favorable structure – Neurotization

  - Neuromatous vs Nerve to Nerve
    - No need to bring schwann cell in N. to N.
    - Dead grafts <4cm minifascicles advance

Types of nerve graft

- Trunk
- Cable
- Pedicle
- Interfascicular
- Free vascularized
- Allograft

Trunk Graft

- Full thickness segment of a major nerve trunk
- Problem – poor revascularity
  - Central necrosis
  - Total graft dissolution

- May be considered in salavage of combined median and ulnar n. transection
  - Pedicle grafting is preferred

Cable Graft

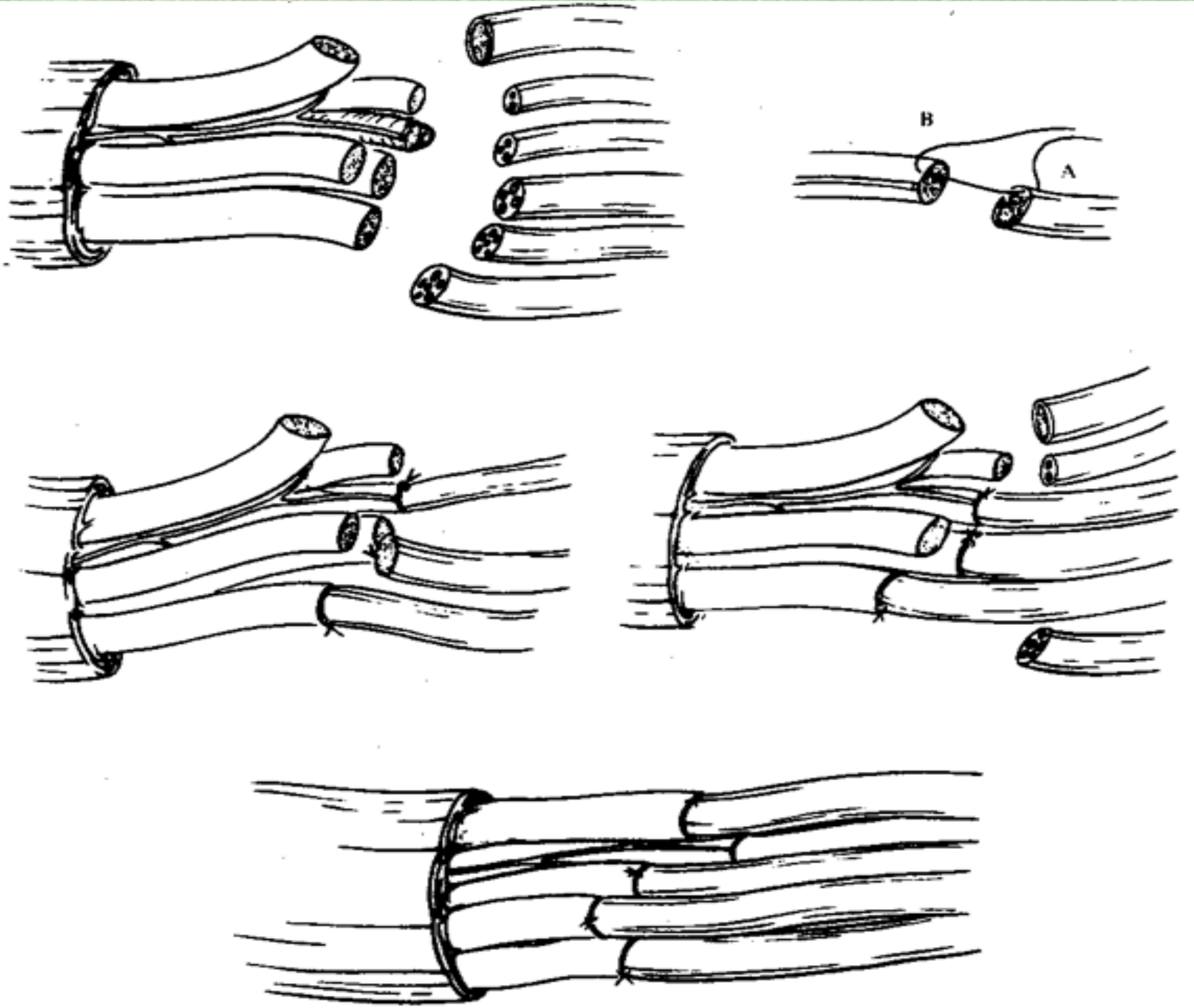
- Replaced trunk after WWI
- Strands of cutaneous nerves sewn together at both ends trimmed to form a flat surface
- facilitated revascularization by increasing surface area
- Wastes Axons
  - Axons opposed to epineurium
  - Replaced by interfascicular grafting

Pedicle Nerve graft

- With median and ulna damage ulna n may be used as a pedicle graft
- St. Clair Strange
- Two stage procedure
  - Stage 1: U with proximal stumps
  - Stage 2: Ulnar nerve swung down
- Protective sensibility restored
- 2pd and intrinsic function not achieved

Interfascicular Nerve Graft

- Aka: group fascicular grafting
- Fascicular groups are defined by the application of gentle force perpendicular to the long axis of the nerve
- Fascicular groups of different length
- Graft and host fascicles are matched
- One or two 10-0 sutures
- Graft length with wrist neutral, elbow extended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Free Vascularized

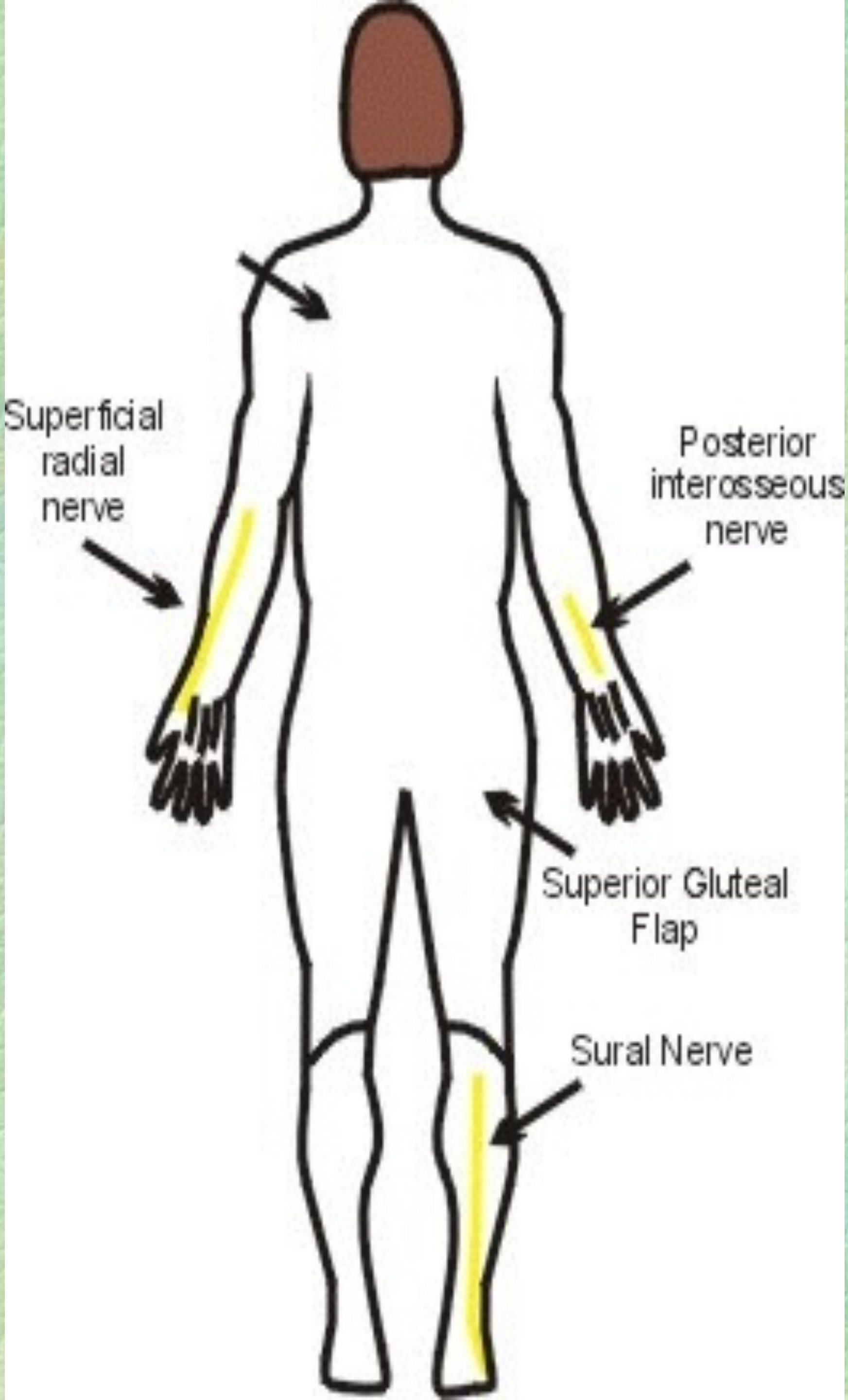
- Taylor and Ham (1976) to prevent ischemic graft failure
- Gilbert, Merel et al – no superiority
- Largely investigational
- May be for extremity salvage when graft is available from amputated parts

Graft Criteria

- Sunderland and Ray Criteria
- Large fascicles with little interfascicular connective tissue
- Separate parallel fascicle or few interfascicular connections
- Overall large diameter
- Large-caliber axons
- Accessible location without variation
- Long unbranched segments
- Minimal sensory deficits
- No scars on pressure bearing areas

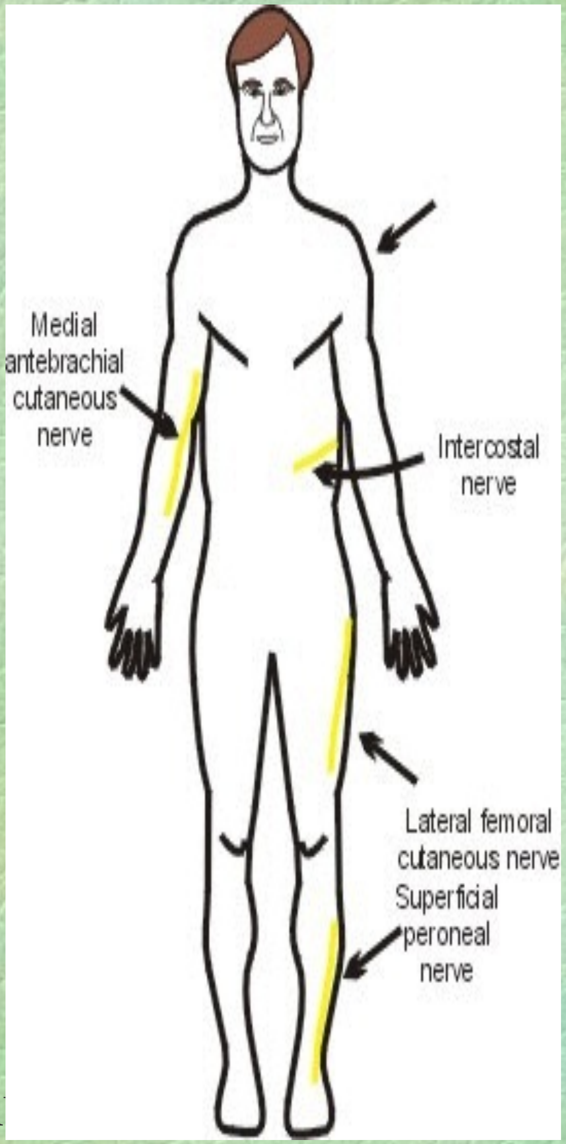
Source

- Sural
  - Standard source
  - 30-40cm length
- Lateral antebrachial cutaneous
  - Terminal branch of MC n.
  - Emerges just beneath Bicep – lateral to tendon
  - 4-5 cm through single incision
  - 20cm through multiple incisions
- Anterior branch Medial Antebrachial Cut
  - 2cm anterior 3cm distal to medial epicondyle
  - 4cm graft



Source

- PIN
  - Smaller distal digital n. grafts
  - No cutaneous sensory loss
  - 3.7cm
- Superficial branch Radial nerve
  - 25cm
  - Transect very proximal under fascia
  - Brachial plexus
- Intercostal nerves
  - 20cm
  - Inferior margin of each rib
- Saphenous Nerve
  - 40cm
  - Contralateral C7 transfer in Brachial Plex



Allograft

- Graft can be banked
- No need for sacrifice of a donor nerve
- Surgical procedures are quicker

- Immunologic host response
- Limited experience
- Sensory recovery more consistent

Gap

- Gliding tissue – accordion-like folding
- Trauma – adhesions, fibrosis
- Nerve transected
  - Two stumps spread apart – elastic forces
  - This gap is without defect
  - DEFECT
    - Loss of nerve substance
    - The fascicular pattern between the two stumps is different and the chances for successful regeneration decreases with the length of a defect
  - Length of graft not the decisive factor
  - With the same defect graft 3,4,6cm is same
- In general defecr > 2.5cm will require nerve graft

Timing graft procedures

- Best chances for motor recovery with early repair
- >6 months decreased functional recovery
- 1-1.5 years still chances for some motor function recovery
- Protective sensibility
  - Possible for several years
  - If re-exploring do it within 6 months

Indications

- Clean transection
  - Elastic retraction
  - End-to –end neurorrhaphy
- Nerve tissue loss
  - Chances of success decrease in inverse proportion to the length
- Major injury after tendons and arteries, nerve defects should be grafted as a secondary procedure
- Should be tagged and introduced into subcutaneous channels

British Medical Council Classification

MacKinnon/Dillon

- *Motor Recovery*

- M0 No contraction
- M1 Tarce: Contration without movement
- M1+ proximal muscles contract against but intrinsics paralized
- M2 Active movement with gravity eliminated, perceptable intrinsic contraction
- M2+ proximal and distal muscles all active against gravity
- M3 Fair: Active movement against gravity
- M4 Good: Active movement against resistance, some intrinsic weakness
- M5 Normal power

Hight/Sanders

- *Sensory Recovery*

- S0 Absence of sansation
- S1 Recovery of deep cutaneous pain
- S2 Return of some superficial cutaneous pain and tactile sensation (S2+ Overresponse)
- S3 Return of cutaneous pain and tactile sensation throughout the innervated area 2pd >15mm
- S3+ Recovery with some 2pd (7-15mm)
- S4 Complete recovery 2pd (2-6mm)

Functional Recovery following Nerve Grafting

Frykman and Gramyk
literature review up to 1990

- Digital Nerves
  - 6 series 151 cases
  - S3 recovery 88%
  - Delay of repair >6months
    - Limited effect, 90% recovering useful recovery
  - All patients <20yr achieved 2pd
  - Useful innervation in all patients up to 40yr
  - <5cm grafts achieved S3 sensibility 80%

Digital Nerves

- Kallio 1993
  - 4 of 26 patients with gaps >5cm – useful result
  - S3 or better
    - 9 of 12 cases with gaps 4-4.9
    - 8 patients with <2cm gaps
- Wang et al
  - Nerve grafts appeared to perform better then primary nerve repairs in mild crush (blunt, saw-type)
- MacKinnon et al
  - 86% patients achieved S3 or better
  - 33% Achieved S4

Median Nerve

- Frykman and Gramyk
  - 167 patients
  - 81% M3
  - <20yo -- better 88% useful motor return
  - > 40yo 64% success rate
  - Gap length appeared to have a more profound effect
    - <5cm 95% success
    - >10cm 66%
  - Sensory Recovery
    - 79% achieved S3
    - 98% S3 <20YO
    - 58% S3 >40YO

Ulnar Nerve

- 104 cases
  - 63% M3 or better
  - 75% S3 or better
  - Length of time and location did not correlate
  - Gap>10cm poorer results
  - <20yo 87%useful recovery (vs 70%)

Radial Nerve

- 60 patients
  - 78% useful motor function
  - 16% none at all
  - Worse results in >40, >10cm and more proximal level

On the basis of 40 years of experience Sunderland made the following conclusion:

1. Young patients generally do better
2. Early repairs do better than late repairs
3. Repair of single function nerve do better than mixed nerve
4. Distal repairs do better than proximal
5. Short nerve grafts do better than long nerve grafts

Strategies to Improve Results

- Pharmacologic agents
- Immune system modulators
- Enhancing factors
- Entubulation chambers

Pharmacologic

- Molecular level to alter nerve regeneration
  - Gangliosides
    - Neurotrophic (aid in survival and maintenance)
    - Neuritogenic (increase # and size of branching neural processes)
  - Forskolin
    - Activator of adenylate cyclase that increases nurite outgrouth
  - Polyamines
    - Increased functional recovery of rat sciatic nerve

Immune system modulator

- Decrease fibrosis and/or histiocytic response
  - Azathioprine and hydrocortisone decrease the level of antibodies
    - Gangliosides have antigens and cross the nerve blood barrier after injury
  - Cyclophamides increase motor recovery in rat sciatic nerve
  - Cyclosporin A increases nerve recovery in primate and rat models

Enhancing Factors

- Chemotrophic to regenerate neurons
  - Nerve growth factor
  - Ciliary neurotrophic factor
  - Motor nerve growth factor
  - Laminin
  - Fibronectin
  - Neural cell adhesion molecule
  - N-cadherin
  - Acidic and basic fibroblast growth factor
  - Insulinlike growth factor
  - Leupeptin
- The receptor nerve segment growth in Y tubing

Entubulization chambers

- Hollow cylindrical tubes
- Serve as condiut for loosely approximated nerve
- Decreased surgical handling/scarring
- Allow small intentional gap which allows fascicular rerouting
- May also allow local introduction of stimulating factors as described

Conduits

- Biological
  - Vein: limited use, collapse and scar, <5mm
  - Artery: not used
  - Muscle: contains collagen IV and laminin
    - Basal lamina for direct outgrowing of axons
    - 25-60mm gaps in posterior tibial and median n have be successfully treated in leprosy (Periera et al)

Conduits

- Non-bioabsorbable
  - Foreign body reactions
  - Silicone
    - Chronic nerve compression, inflammatory or fibrotic reaction
  - Polytetrafluroethylene(PTFE) (Gore-tex)
    - 4cm ulnar nerve defect 79% functional recovery
    - >4cm 13%
    - Some studies bring the gap down to 3mm
  - Polyethylene, Polyvinyl, Rubber Tubes
    - No successful studies

Conduits

- Bioabsorbable
  - Polyglycolic acid (PGA)
    - Useful technique for chronic sensory nerve lesions >2cm

- No evidence yet that nerve conduits provide a better functional outcome than autologous nerve grafting in peripheral nerve repair