Nerve Injury

2

Robert I.S. Winterton and Simon P.J. Kay

Keywords
Nerve injury • Peripheral nerve • Denervation • Reinnervation • Motor neuron • Sensory function • Motor function • Nerve repair • Traction injury • Nerve graft • Nerve conduit • Nerve transfer

Introduction

The first known reference to the central nervous system is found in the Edwin Smith Medical Papyrus, a manuscript originating in approximately 3500BC which contains the word "brain" along with a description of the coverings of the brain [1]. Early physicians, such as Hippocrates, did not distinguish peripheral nerves from tendons, and even when Galen made the distinction in the second century AD, nerve repairs were not attempted. Surgeons worried that manipulating the nerve stumps would cause convulsions, or assumed that function would recover regardless of whether repair was attempted. The development of the science of neurophysiology between 1830 and 1870 led surgeons to attempt to repair nerves, and by World War I primary neurosynthesis was accepted practice.

The management of peripheral nerve injuries advanced significantly as a result of the clinical experience gained during each World War. In the latter twentieth century the evolution of microsurgical techniques, improvements in surgical equipment, and the consistently advancing field of neuroscience also contributed. In the 1970s, work by Millesi [2] and Terzis [3], amongst others, showed both clinically and experimentally that tension across a neurosynthesis inhibits nerve regeneration, and as a result many surgeons adopted the use of nerve grafts to bridge defects.

Nerve injury is common. One study from Canada reported that 2.8 % of trauma patients had an injury to at least one major peripheral nerve [4]. Estimates from the US suggest that 200,000 peripheral nerve lacerations are sustained nationally every year.

This chapter discusses the management of nerve injury, and its basis in neuroscience. Normal nerve anatomy and microanatomy will be considered, as will the science of nerve division and repair. The pathophysiology of nerve

R.I.S. Winterton, BMedSci, MBBS, MRCS, MPhil FRCS (Plast)
Department of Plastic Surgery, Wythenshawe Hospital, Southmoor Road, Manchester M23 9LT, UK
e-mail: wintertonris@hotmail.com

S.P.J. Kay, FRCS, FRCSE(hon) FRCS (Plas Surg) (✉)
Department of Plastic Surgery, Leeds General Infirmary, Great George Street, Leeds LS1 3EX, UK
e-mail: spjkay@gmail.com

I.A. Trail, A.N.M. Fleming (eds.), *Disorders of the Hand: Volume 1: Hand Injuries*,
DOI 10.1007/978-1-4471-6554-5_2,

crush or traction will also be discussed and developments in the fields of nerve grafting, nerve conduits and neuroprotection will be reviewed.

Nerve Anatomy and Microanatomy

Nerve Micro-Anatomy

The basic cellular component of a nerve is a neuron, consisting of a cell body and an axon. The cell body of a motor neuron lies in the anterior horn of the spinal cord whilst sensory neuron cell bodies reside in the dorsal root ganglion. Axons lie in continuity from the cell body to distal target organs, and may be myelinated or unmyelinated. Myelinated axons are wrapped in the bilayer basement membrane of an accompanying Schwann cell. Manufacturing and energy exchange occur in the cell body and nucleus and include the enzymes required for neurotransmitter synthesis. Some intracellular components may travel along the length of an axon at speeds of 410 mm per day, whilst other components such as structural proteins move at a maximal rate of 1–6 mm per day [5]. It is this slower transport mechanism that limits the rate of nerve regeneration.

An axon and its associated Schwann cell sheath is called a nerve fibre, and each nerve fibre is surrounded by a sheath (the endoneurium). A bundle of nerve fibres (which is surrounded by collagen and elastin) is called a nerve fascicle. A fascicle is invested with perineurium, composed of concentric layers of flat cells with prominent basement membranes that fit together and are linked by "tight junctions". The perineurium serves to resist traction, and also acts as an extension to the blood brain barrier by controlling the intraneural environment via active diffusion control (Fig. 2.1).

A fascicle is the smallest subunit of a nerve that can be surgically manipulated. Fascicles are not separate cables that run in parallel throughout a length of nerve, but instead have numerous interconnections that result in the formation of a complex intraneural plexus. The plexus complexity varies over the length of a nerve. Generally, interconnections are most numerous in the proximal part of major nerves, indeed by the time a nerve had reached the forearm, fascicles may be dissected over long distances before they fuse with adjacent fascicles [6]. Identification and mapping of fascicles and fascicular groups has an impact on the management

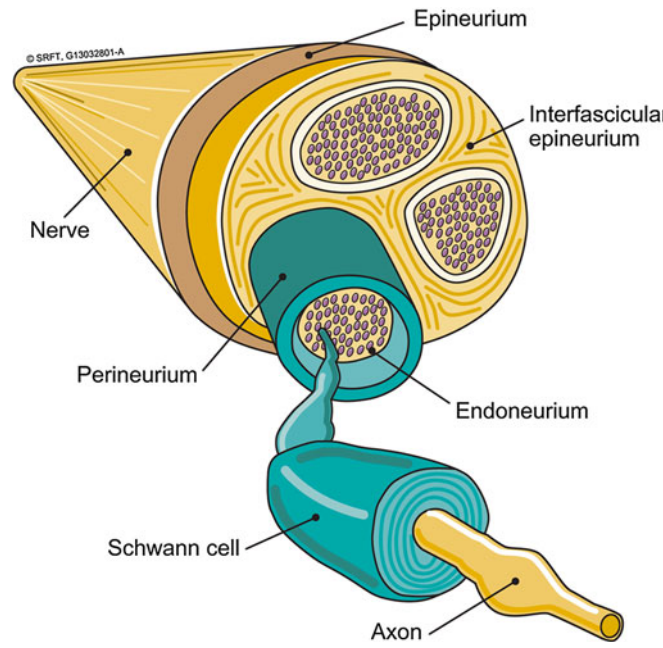

Fig. 2.1 Diagram showing the internal anatomy of a peripheral nerve

of peripheral nerve injuries. Fascicular groups may be isolated over greater distances than individual fascicles and connections are fewer between fascicular groups [6, 7]. Corresponding fascicular groups can be identified in distal and proximal segments, and should be used to orientate the divided nerve before repair, optimising sensory and motor recovery.

A collection of fascicles is a nerve. It is ensheathed by epineurium, a loose connective tissue composed mostly of collagen, which adheres to nutrient vessels as they enter the nerve. This epineurium is usually haemorrhagic after contusion or traction injury, and it is the epineurium which thickens after chronic nerve compression [8]. It is the epineurium that is dissected during intraneural neurolysis. The percentage of nerve cross sectional area that is occupied by epineurium differs along each nerve, from nerve to nerve, and between individuals. Higher amounts of epineurium are often found around joints, and the proportion of epineurium may vary widely from 25 to 75 % of the cross sectional composition of a nerve [9].

Epineurium may reach 2–3 mm thickness in chronic inflammation and much of the scar formed after nerve traction results from proliferation of epineural fibroblasts. It is the epineurium that is sutured in most nerve repairs.

Blood Supply and Surgical Anatomy

Peripheral nerves have a rich segmental blood supply. Nerves are supplied by longitudinal vessels in the epineurium, which in turn supply a segmental plexus that lies within the perineurium. This segmental plexus gives rise to capillary sized vessels that spread uniformly throughout the fascicles. There are no lymphatics within the endoneurium. Because of this longitudinal interconnections between arterioles and venules, an in tact peripheral nerve may survive extensive mobilization from its bed, although this property is proportionally lost if the nerve is transected, as this disrupts the blood supply as well as the axons.

Peripheral nerves rarely cross a joint at its axis of motion. Consequently a nerve moves relative to its surrounding tissue and changes in length as a consequence of joint motion. The mesoneurium is loose areolar tissue around the outside of a nerve that allows for this translation, and the segmental blood supply enters through this layer. The changes in nerve length can be dramatic, for instance the median nerve must elongate by 4.5 % on arm extension and shorten by 4.5 % during full flexion from a resting position [10]. Surgery can create fibrosis within the mesoneurium that leads to tethering and, as a consequence, traction with normal joint motion.

Nerves have viscoelastic properties such as stress relaxation (decreasing tension when pulled to a fixed length) and creep (elongation with constant tension). Normally nerves are elastic and under little tension, although towards the end of joint excursion, increased strain raises intraneural pressure and hence decreases perfusion. An injured nerve has altered biomechanics and therefore is more susceptible to the reduced perfusion caused by joint motion, and also has higher perfusion requirements at the site of repair. Increased neural ischaemia, scar formation and subsequent reduced axon regeneration, may lead to impaired recovery of nerve function. Prevention of this chain of events may require avoidance of tension by nerve grafting, or other manoeuvres such as anterior transposition of the ulnar nerve at the elbow.

Nerve Division

Physiology of Peripheral Nerves Following Injury

Augustus Volney Waller, an English neurophysiologist, originally described the changes that occur in a nerve following a transection or crush injury. Wallerian degeneration (also known as anterograde or orthograde degeneration) is a process in which the part of the axon separated from the neuron's cell body as a result of the injury, degenerates. The length of the proximal segment that degenerates is proportional to the nature of the injury and the amount of force that is absorbed by the nerve. A nerve that is transected by a sharp division has less proximal injury than one that is

avulsed in a heavy machinery accident. Within 24 h after transection, each single axon begins regenerating by sending out multiple axon sprouts. At the tip of each sprout is a "growth cone" that consists of tentacularfilopodia rich in actin. The tips of these filopodia explore the distal environment in search of fibronectin and laminin, which are found in the basal lamina of the distal endoneurial tubes.

In the absence of any mechanical barrier, the growth cones are guided by neurotropic factors that are present in the surrounding environment. Once the regenerating filopodia encounter the appropriate substrate, they adhere to the structure and draw the entire growth cone distally. This process of contact guidance causes the axon to grow further towards the distal nerve segment.

In the distal nerve segment, anterograde Wallerian degeneration occurs along the entire length of the nerve. After transection, Schwann cells proliferate and phagocytose the degenerating myelin and axonal components. Endoneurial tubes collapse, and the proliferating Schwann cells organise themselves along channels. As the axon sprouts from the proximal nerve stump regenerate into the distal nerve remnant, they find the fibronectin and laminin in the basal lamina and are drawn distally.

The preference of a nerve fiber to grow toward a nerve instead of other tissue depends on a critical gap across which the fibre responds to the influences of the distal nerve. Current research suggests that the expression of various Schwann cell and myelin-associated glycoproteins may facilitate or impede the regeneration of damaged axons to their correct targets.

The axon continues to grow until it reaches an end organ or a mechanical barrier. If an appropriate end organ is reached, as when a motor axon that reaches a motor end plate, neurotrophic hormones signal the cell nucleus and the surrounding tissues and the axon is allowed to mature. If an inappropriate connection has been made, such as a motor axon to a Meissner's corpuscle, the errant axon involutes.

The end organ itself, whether a motor end plate or a sensory receptor, also undergoes atrophy. Unlike the motor system in which functional recovery is limited after a period of 12–18 months, recovery of Meissner's corpuscles, Pacinian corpuscles, and Merkel cells is possible years after nerve injury. Functional recovery depends on the number of motor fibers correctly matched with motor endplates and the number of sensory fibers correctly matched with sensory receptors, in a timely fashion.

Morphology of Peripheral Nerves Following Injury

The microscopic appearance of peripheral nerves following injury was described by Terenghi in 1998 [11].

The proximal stump of a divided nerve shows regenerating clusters of unmyelinated and myelinated axons as one moves proximo-distally. This is succeeded by an outgrowth zone of minifascicles of myelinated and unmyelinated axons, and their associated Schwann cells, all lying within a well vascularised collagen-rich matrix, as the neuroma is approached. There is a corresponding change in the perineural sheath over the same length of nerve. The perineurium becomes disorganised at the distal tip of the proximal stump and disappears in the outgrowth zones. However there are perineural-like cells present which may migrate with the regenerating axons and Schwann cells.

The neuroma of the nerve consists of masses of irregular minifascicles, each one enclosed by a layer of perineural-like cells. These axons are associated with Schwann cells positive for the S-100 stain and these in turn are associated with a basal lamina.

In the distal stumps, collagen deposition and endoneurial tube shrinkage are uniformly present. The level to which evidence of re-innervation is seen varies. However, all stumps contain PGP-9.5 positive axons, which are co-localised with S-100 positive Schwann cells, with some containing variable amounts of myelinated axons. There appears to be fewer immunoreactive fibres present in the distal stumps than in the proximal stumps.

Schwann cells were demonstrated to be present within these stumps at a period of 53 months post injury. There was no Wallerian degeneration

seen and no evidence of fragmentation of the basal laminae.

This study by Terenghi et al. [11] confirmed that the morphology following injury is similar in humans to that described in animal models. It was noted that even a neuroma in continuity seemed to provide a rich source of regenerating axons, although few of these entered the distal stump, which conformed to the view that a chronically denervated stump provides a less conducive microenvironment for axon regeneration.

If one accepts that the morphology within injured peripheral nerves is similar in mammalian animal models and humans, then given the findings in rat studies on axon-Schwann cell interactions, one might presume that human axon-Schwann cell interactions in chronically denervated nerves are also inadequate, which may contribute to the poor outcome after nerve reconstruction.

Giannini and Dyck [12] has described the appearance of the basement membrane in Schwann cells following denervation. Electron micrographic studies (in rat peroneal nerves) showed that as time progressed following denervation, the basement membrane became discontinuous and eventually dispersed. It is suggested that this alteration in the scaffold by which axons are able to reinnervate distal nerve stumps, may partially explain why it takes longer for distal nerve stumps to recovery if they have been denervated for a prolonged period.

Furthermore, it has been shown experimentally that chronically denervated Schwann cells down-regulate expression of receptors for axonally derived ligands, specifically c-erbB4 or c-erbB-2 [13], such that axonal growth cone chemotaxis is reduced, as there is a close correlation between levels of receptor expression by denervated Schwann cells and the extent to which distal stumps are reinnervated.

How Does the Response of Denervated Schwann Cells to Reinnervation Relate to Time?

When a peripheral nerve fibre is divided and the two ends retract, the axons within the distal stump degenerate. If the nerve ends can be sutured, or bridged with a short cable graft then regenerating axons typically penetrate the distal stump within a few weeks of injury. However, if the repair is delayed or the graft length is long, few axons will penetrate the distal stump and recovery will be severely compromised [14].

It has been supposed that physical changes in the microenvironment of a chronically denervated distal nerve stump, such as endoneural fibrosis or atrophy, block axonal regeneration. Conversely, we also know that despite this atrophy, they rarely lose all of their Schwann cells, even after 12–18 months [15]. However, despite the presence of Schwann cells, their functionality remains to be defined fully. Any impairment of axon-Schwann cell signaling could contribute significantly to the failure of nerve repair.

Protection of Motor Neurons and Sensory Neurons Following Injury

When considering reconstruction of major nerve function following injury, the principle aim remains motor recovery. However, sensory recovery is also important if a satisfactory functional outcome is to be achieved.

In recent years it has been established that central loss of neurons contributes to poor nerve recovery [16–18], and this is time and site dependent. Approximately 50 % of ventral horn spinal motor neurons die following ventral root transection, and this figure rises to 80–90 % following root avulsion [19, 20]. Neurons can die by passive necrosis, or active cell death (apoptosis). Necrosis is rapid and cannot practically be prevented, although the period of active cellular death lasts some weeks. There is evidence that adjuvant pharmacotherapy with N-acetyl cysteine (NAC) is able to prevent cellular death in sensory neurons following distal axotomy [21] and in motor neurons following ventral rhizotomy [22]. Though surgical intervention may also benefit neuronal survival, it is often less practical in vivo for a variety of reasons.

Protection of the proximal motor neurons from active cell death may in future allow a

potentially delayed and refined intervention to be applied to the injured nerve, which subsequently may allow improved recovery.

Clinical Assessment of the Injured Nerve

History

Trauma to the upper limb that results in a wound, a crush or traction, should raise the suspicion of an injury to a peripheral nerve. The mechanism of injury determines how much degeneration occurs in the proximal nerve segment, and also indicates whether one should anticipate a nerve deficit. It is important to determine the sharpness and width of the cutting object, the degree of traction or crushing, together with an estimate of the force that was involved and its duration of application.

The time elapsed since the injury is also important. Most nerve injuries are seen within the first 24 h, although injuries may not present until much later. Delayed presentation implies scar tissue at the nerve stumps and the possibility of intractable nerve retraction. In addition, following repair, return of motor function may be poor depending on the level of injury and the length of time that the muscle has been denervated, as a result of motor endplate decay.

Symptoms of numbness, paraesthesia or weakness should be elicited. It is also important to determine preoperatively whether there was any history of nerve injury or neuropathy prior to the accident. Specific elements of the patient's general condition, age and occupation will also guide planning to appropriately reconstruct the deficit.

General Assessment

In the emergency setting, where life or limb is at risk, making a diagnosis of peripheral nerve injury and treating the injured nerve may be low on the list of priorities. Once the acute phase is over, however, the loss of function of an injured nerve or the pain related to a nerve injury often dominates the subsequent clinical picture.

If there are wounds, a peripheral nerve in the region of the injury may be injured. If there are no open wounds, a peripheral nerve may be injured in proximity to a closed fracture or dislocation. Detailed, repeated neurological examination, along with the recording of examination findings, is important in identifying and defining the injury.

Assessment of Sensory Function

Sensibility on the hand may be examined with a blunt object such as a paper clip, and testing with a needle is discouraged. It is worth remembering that in the patient already in pain, this stimulus might not be as readily perceived as it would in a non-trauma setting.

The extent of sensory nerve injury is best determined by moving and static two-point discrimination, which are measurements of innervation density and the number of fibers innervating sensory end organs. Light moving touch, for example, evaluates the innervation of large A-β fibers and can be quickly screened with the valid and reliable "ten test" [23] (see below). Vibration instruments and Semmes-Weinstein monofilaments are used as threshold tests to evaluate the performance level of nerve fibers and are more useful in evaluating chronic compressive neuropathies. Testing is also performed after nerve repair to assess the quality of nerve repair, determine the need for revision, and monitor recovery.

Division of the median, ulnar, or radial nerves should not be a diagnostic dilemma in the cooperative patient. In the acute setting, the examiner will elicit the presence or absence of gross sensation in the following areas (Fig. 2.2):

- Volar, proximal third of the distal phalanx of the index or long finger for the median nerve
- Volar, proximal third of the distal phalanx of the little finger for the ulnar nerve
- Dorsum of the thumb index web space for the radial nerve
- Proximal ulnar aspect of the thenar eminence for the palmar cutaneous branch of the median nerve
- Dorsal metacarpal of the little finger for the dorsal cutaneous branch of the ulnar nerve

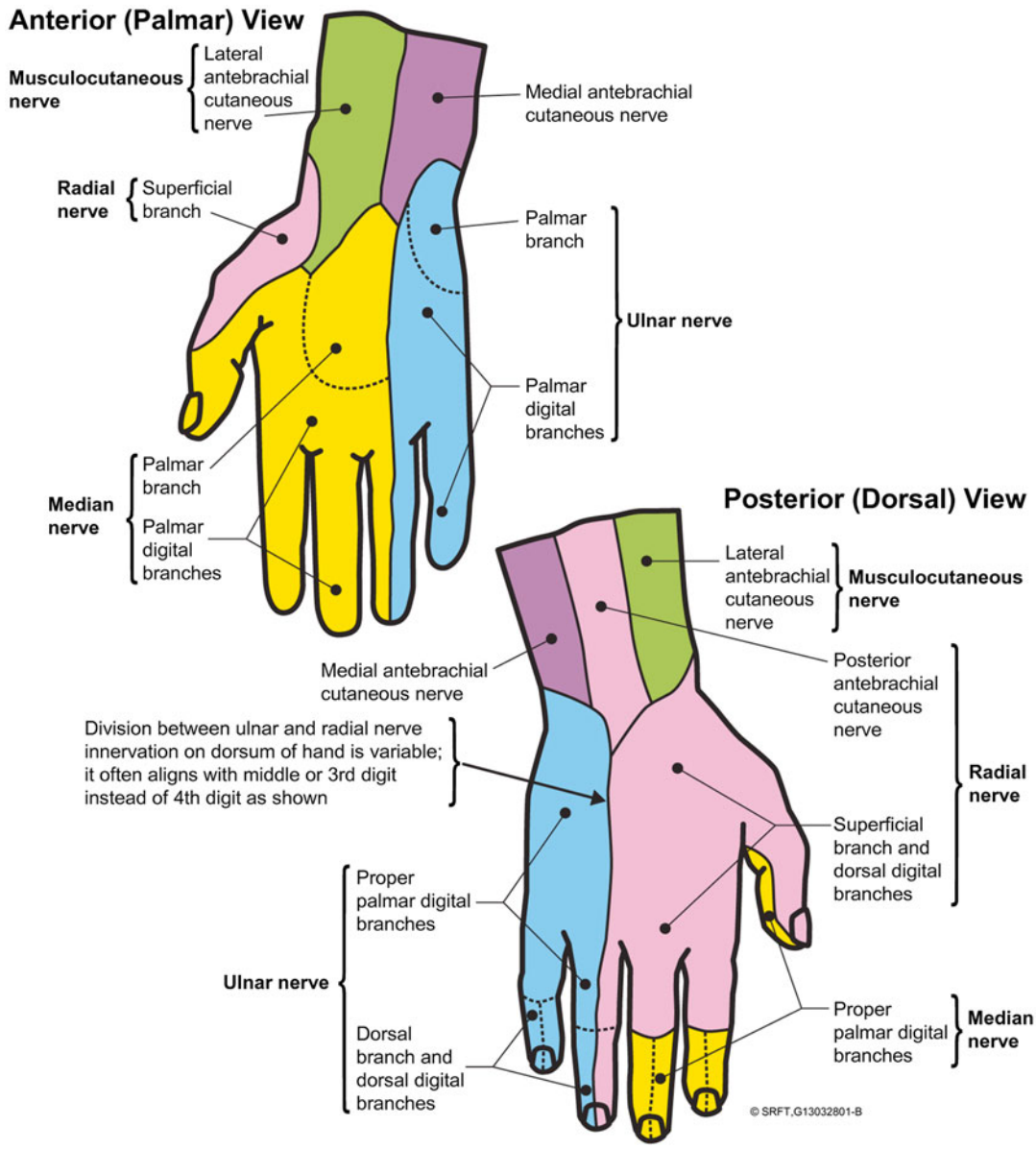

Fig. 2.2 Diagram showing distribution of sensory supply to the hand

When examining digital nerves patients may be asked to grade their appreciation of sensibility from 1 to 10 [23]. By establishing a "normal" score of 10 on an uninjured digit, patients will often record 8–9 out of 10 where no nerve injury is seen but the digit is generally swollen, 6–7 out of ten where the digital nerve is contused and 2–3 out of ten where the nerve is divided. These guides are less reliable in the patient presenting several days after their injury.

More proximal or brachial plexus injuries are better assessed by dermatome assessment. Knowledge regarding the distribution of the sensory dermatomes in the upper limb allows sharp and light touch, together with vibration, to be assessed in each area, thus guiding the examiner

towards the correct identification of the injured nerve root or brachial plexus element.

When assessing hand sensibility following severe proximal injuries it may not be practical to carry out a detailed assessment, and the clinical situation is often best defined by the answer to questions such as:

- Can you feel me touching you?
- Can you tell which side of the hand I am touching?
- Can you tell which finger I am touching?

Assessment of Motor Function

The extent of a motor nerve injury is determined by an evaluation of weakness, loss of function, and muscle atrophy. Evaluation of motor function is generally easier than evaluation of sensibility. If a motor nerve is completely divided then the muscle that is innervated by that nerve does not voluntarily contract. To test a given muscle, the examiner first asks the patient to make active movement. To determine power, the examiner places the patient into the position to which they would be moved if the muscle were functioning, then asks the patient to maintain that position against a force directed in the opposite direction.

For example, to evaluate median nerve motor function at the wrist the abductor pollicisbrevis muscle is tested. The patient's thumb is placed into palmar abduction, while the examiner's finger is placed on the thenar muscles. The patient is then asked to resist as the examiner attempts to push the thumb into adduction. The examiner then notes any contraction or fullness in the thenar eminence. Other examples of muscles that can be tested for nerve injury in the forearm are the flexor pollicis longus and the flexor digitorum superficialis for the median nerve, the abductor digiti minimi and the flexor carpi ulnaris for the ulnar nerve and the extensor pollicislongus, the extensor carpi radialis longus, and extensor carpi radialis brevis for the radial nerve.

The Medical Research Council (MRC) grading of muscle power is widely used to assess muscle function. The patient's effort is graded on a scale 0–5:

- Grade 5: Muscle contracts normally against full resistance
- Grade 4: Muscle strength is reduced but muscle contraction can still move joint against resistance
- Grade 3: Muscle strength is further reduced such that the joint can be moved only against gravity with the examiner's resistance completely removed. As an example, the elbow can be moved from full extension to full flexion starting with the arm hanging down at the side
- Grade 2: Muscle can move only if the resistance of gravity is removed. As an example, the elbow can be fully flexed only if the arm is maintained in a horizontal plane
- Grade 1: Only a trace or flicker of movement is seen or felt in the muscle or fasciculations are observed in the muscle
- Grade 0: No movement is observed

The value of this grading system in the upper limb is, however, limited to the large proximal joints. Gravity has little influence over the posture and movement of the intrinsic muscles of the hand or the supinators/pronators of the wrist. When recording the power of these movements it is more useful to use descriptive terms such as:

- Flicker of movement
- Movement, but not against resistance
- Limited ability to overcome resistance
- Strong movement against resistance
- Normal power

In cases of delayed presentation, muscle fibers lose trophic stimulation and decrease in bulk. Clinically this is apparent as muscle wasting which implies prolonged loss of innervation.

Clinical Pearl

An accurate knowledge of dermatome and sensory distribution is essential to accurately assess nerve injury.

Similarly, a thorough knowledge of muscle innervation and action is important to detect motor deficit.

Other Techniques

In the child or unconscious patient, a rarely used but helpful test for nerve division is the water immersion test. A normally innervated fingertip wrinkles within 4 min when placed in 40 °C water [24]. The absence of wrinkling of a finger when it is immersed indicates that the peripheral nerve that innervates that fingertip is not in continuity.

A more straightforward assessment may be made of sweating within the dermatome of the nerve in question. If the nerve is not functioning, the skin will feel characteristically dry to touch as it loses the ability to excrete sweat. If nerve function returns, the skin will once again be able to excrete sweat and the normal tactile qualities of the skin will be restored.

Nerve Recovery After Direct Repair Following Division

Terms

Although individual nerve fibres support axoplasmic flow, nerves are not hollow tubes. Therefore joining two ends of nerves is best termed a nerve repair or neurosynthesis, not an anastomosis. When sutures are placed through the epineurium, any neurosynthesis is an epineurial neurosynthesis. When the sutures are placed through the epineurium and perineurium, joining individual fascicles, the repair is called a fascicular neurosynthesis or epineural repair. When several groups of fascicles are joined, the repair is termed a grouped-fascicular neurosynthesis. A nerve may be fixed by a direct nerve repair, which is also called an end-to-end, abutment, or coaptation neurosynthesis. The term "nerve reconstruction" is used more commonly when referring to the use of a conduit or nerve graft.

When a nerve has a segment of neural tissue missing, there is a nerve defect. However, simple transection of a nerve can result in a gap between the two ends, even if no neural tissue is missing. The difference between a 1 cm gap and a 1 cm defect is that the repair of a gap is not usually under any excess tension. In addition, in a gap, the fascicular anatomy is mirrored at the proximal and distal faces. In the case of a nerve defect, increased tension is required to bring the nerve ends together, occasionally making end-to-end repair impossible. Furthermore, because of the ever changing internal topography of the nerve trunks, axons at the proximal and distal faces of the nerve are usually arranged differently. This can have an adverse effect on regeneration.

Principles of Nerve Repair

We know that once a nerve has been divided it cannot be repaired in such a manner that sensory and motor end organ function will be restored to the pre-injury state [25].

The basic principles of nerve repair include the use of meticulous microsurgical techniques using adequate magnification, instruments, and sutures. Ideally a primary nerve repair is performed in a tension-free manner. To facilitate repair the injured ends of the nerve may be mobilized (or, in the case of the ulnar nerve at the elbow, transposed) to obtain length. Peripheral nerves intrinsically afford a limited degree of excursion, on account of the nerve fibres following an undulating or zig-zag course at a microscopic level. This property gives peripheral nerves a banded appearance, known as the bands of Fontana, which disappear when the nerve is compressed or stretched. If a tension-free repair cannot be achieved, an interposition nerve graft with the limb held in a neutral position is preferred to a primary repair with the limb in an extreme position for a prolonged period of time.

Clinical studies have not shown fascicular repair to be superior to epineural repair. If the internal topography of the nerve is known to be segregated into discrete motor/sensory groups, as is more likely the closer to a branch of the nerve one travels (as the fascicles become designated to end organ territories), a grouped fascicular repair should be better than an epineural repair. If there is not such an arrangement, then the additional

manipulation and increased suture material may hinder functional recovery. For this reason epineural repair is standard.

Bleeding from epineural vessels should be controlled with gentle pressure or fine bipolar coagulation under microscopic guidance. After transection of a nerve the individual fascicles tend to mushroom out from the epineural sheath because of the endoneurial fluid pressure. At the time of epineural repair fascicles may not lie smoothly, causing a misdirection of the regenerating fibers. Appropriate trimming of the fascicles allows them to lie end to end within the epineural sheath. The epineural sutures should be placed so as not to cause additional bunching of fascicles so the nerve can be realigned appropriately.

Postoperative motor and sensory re-education maximizes the surgical result.

Timing of Nerve Repair

Optimum results are obtained after immediate repair of a sharply divided nerve. Fascicular patterning and vascular landmarks are present to guide the proper orientation of the nerve ends. Retraction and neuroma formation, which may result in the need for grafting, are avoided. Within the first 72 h following nerve transection, motor nerves in the distal nerve segment still respond to direct electrical stimulation because of the presence of residual neurotransmitters within the nerve terminals.

When a nerve is injured by crush, avulsion or blast, the surgeon must consider nerve injury proximal and distal to the site of transection. In the acute setting the extent of injury may be difficult to determine even using the operating microscope. In this situation, the nerve ends should be tacked together to prevent retraction and repair delayed until the local area permits. At re-exploration the extent of injury will be defined by neuroma and scar formation. The neuroma must be excised until a healthy fascicular pattern is seen proximally and distally and the resultant defect usually requires nerve grafting.

Clinical Pearl

If a repair without tension cannot be achieved, an interposition nerve graft with the limb in a neutral position is preferred to a primary repair with the limb held in an extreme position for a prolonged period of time.

Clinical studies have shown no difference in outcome between a fascicular or epineural repair.

Surgical Technique for Nerve Repair

General Considerations

Surgical nerve repair may be classified as immediate or delayed based on the time between injury and repair. An immediate repair is one that is performed within the first 24 h after injury. A primary repair is one that is performed within the first week after injury. A delayed primary repair is performed after 1 week following the original injury.

In most instances, transected nerves should be repaired at the time of exploration. An alternative, however, particularly if there is inadequate surgical expertise or equipment, or where the patient condition precludes a long surgical procedure, it is appropriate to simply tag the nerve ends with a marker suture, returning later to do a formal nerve repair. Nerve repair may also be delayed in cases of gross contamination, or where a nerve graft is required and soft tissue cover is inadequate.

Delayed exploration and repair of a nerve may be indicated where a nerve is injured by traction or crush. In these cases, surgical exploration may reveal the nerve to be in continuity. In such circumstances (especially with the common peroneal nerve at the knee) it may be apparent that there is a considerable redundancy in the stretched nerve, although it is still in continuity. In such instances, the redundant nerve should be excised back to healthy nerve ends and a graft used to reconstruct the defect.

Such clinical findings are most easily evaluated in the first few days following trauma,

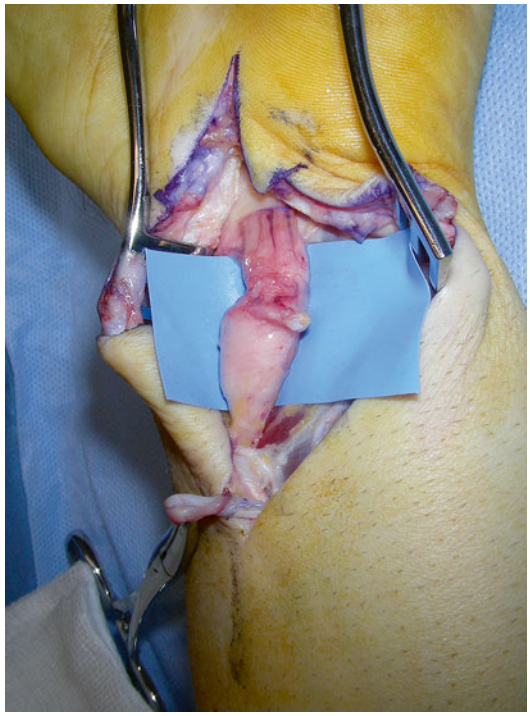

Fig. 2.3 "Mushrooming" seen at the transected end of the median nerve in the forearm after excision of a neuroma (Image kindly provided by Norbert Kang (Royal Free Hospital))

although even then doubt can exist and a "wait and see" policy adopted. If the wound is closed over a lesion in continuity, meticulous attention to the anticipated signs of recovery is needed, and early re-operation is indicated if this recovery fails to appear.

Prior to immediate or primary repair of a peripheral nerve, the cut ends of the nerve should be trimmed, under magnification, until axonal mushrooming is seen (Fig. 2.3). In delayed or secondary repair, the nerve should be trimmed so that there is no intra-fascicular scarring present and fresh, viable nerve fascicles are visible. Some surgeons employ frozen section microscopy to decide the extent of resection, although this requires a skilled specialist histopathologist to be present during the operation. If this preparatory procedure results in a nerve defect then strategies to reconstruct the gap should be employed.

Suitable anaesthesia and (usually) a pneumatic tourniquet are used as appropriate.

Epineural Repair

The aim of nerve repair is to direct regenerating axons in such a way as to allow sensory and motor axons make optimal end organ connections. The technique most commonly used is end to end epineural repair.

Longitudinal vessels on the extrinsic epineurium may be used as landmarks to align fascicles. Along with the varying cross-sectional areas of fascicles, these landmarks can be used to line up the nerve prior to repair. The first suture will provide rotational realignment and the stitch perforates only the epineurium. Most neurosyntheses are performed with a 9-0 (or smaller) non-absorbable suture. The epineurium should be closed loosely. As a guide, if the nerve ends cannot be held in approximation with a single 8.0 suture, then the nerve is under too much tension for a satisfactory repair.

Subsequent sutures are placed to align other anatomic landmarks, each time ensuring that the internal fascicular alignment is correct. The sutures should not violate the fascicles, and the nerve should not gap. It is worth remembering that this technique provides a physiologic tube for nerve regeneration, although the axons themselves are not mechanically reattached. Of the available techniques this is the simplest and quickest, and is most applicable to pure motor or sensory nerves or nerve repairs with indeterminate internal topography.

One suture is usually required for each peripheral fascicle, and the closure should be loose, rather than watertight, to avoid the development of a haematoma. The use of tissue glue around the neurosynthesis is a useful adjunct to prevent movement around the repair, which may otherwise dislodge or disorientate the aligned fascicles (Fig. 2.4).

Fascicular Repair

A Group of fascicles may on occasion be repaired in a manner similar to an epineural repair. The external epineurium is incised, while protecting the internal epineurium and perineurium. The

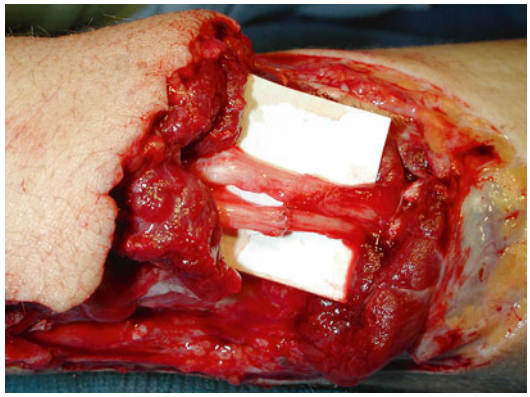

Fig. 2.4 Direct neurosynthesis performed in divided ulnar nerve and dorsal sensory branch of the ulnar nerve in the forearm (Image kindly provided by Norbert Kang (Mount Vernon Hospital))

largest identifiable group is repaired first, using two or three 9.0 or 10.0 non-absorbable sutures for each group.

This technique is most appropriate for repairing nerves with easily identifiable fascicles, such as the common digital nerve in the palm or the ulnar and median nerves at the wrist. It requires considerable effort and manipulation of the nerve compared to an epineural repair. It is especially important that this technique is not performed under tension because tension at this level is transmitted directly to individual fascicles, thus leading to ischemia at the repair site. For this reason, further sutures may be placed in the epineurium to take the tension away from the internal epineurium.

Single fascicles can also be repaired, but indications are limited. The external and internal epineurium must be incised, while the perineurium is preserved. The suture material should be 10-0 or 11-0 material, with few sutures per fascicle. This type of repair is usually only indicated in partially transected nerves.

Many *in vitro* and *in vivo* studies have compared whether fascicular repairs or epineural repairs result in better outcomes [26–28]. To date, evidence is insufficient to suggest one technique is superior to the other. If it were possible to align the fascicles perfectly with minimum surgical disruption, it is theoretically likely that fascicular repair would produce better clinical results than an epineural repair. However as fascicular repairs almost certainly (but unintentionally) result in misalignment of some fascicles, and cause additional intraneural damage to an already traumatised nerve, this theoretical improvement is not seen. Despite an epineural repair being inexact, it does allow neurotropic factors to exert their influence on the direction of nerve fiber growth and this is probably why this less exact technique produces the same clinical results as fascicular repair.

Results of End to End Neurosynthesis

The results of end to end neurosynthesis of acute nerve transection varies widely from patient to patient. Motor and sensory return have been found to correlate closely with four factors:

- Age (the single most important factor): young patients have better results than older patients.
- Level of transection: the more distal the transection, the more functional return can be expected. This is due to the shorter time to reinnervate end organs, and the more discrete fascicular anatomy leading to better fascicular alignment.
- Mechanism of injury: sharp transection has a better outcome than crush, traction or avulsion injuries. Blunt injuries have a longer section of injured nerve so precise axonal matching is more difficult.
- Pre-surgical delay to exploration.

Usually, none of these factors is within the control of the surgeon. Sensory end organs may be reinnervated several years after injury but motor end plates appear to become refractory to reinnervation after approximately 15–18 months. Since axons only regenerate at a rate of 1.0–1.5 mm per day, in brachial plexus injuries, even where primary repair or grafting is carried out promptly, there is such a delay before reinnervation reaches the hand, that good motor recovery of the intrinsic muscles rarely occurs.

Post-operative Care and Complications

Postoperative care is usually straightforward. The soft tissue envelope is closed and the limb is

splinted in a manner that is appropriate for the nature of the surgery. Because the neurosynthesis is not under tension, prolonged protection of range of motion is not necessary for the nerve itself, but may be indicated following repair of other injured structures. For isolated nerve injuries, movement should be started within 3 weeks of surgery to prevent joint contractures and to promote sliding of the nerve relative to the surrounding tissue.

In patients with a nerve injury that results in a motor deficit, the limb should be splinted in a safe position. Concurrently the strength of the functioning muscle is maintained with an exercise program, which also helps to prevent contracture of the denervated muscle.

Oral antibiotics may be given, depending on the amount of wound contamination. Unlike bone or cartilage, nerve is well vascularised and so is not at a greater risk of infection than other soft tissues. Pain control is important, as decreased pain leads to decreased inflammation and swelling. The patient should take enough oral analgesia to eliminate sharp or burning pain and to permit participation in postoperative therapy.

The most common complications of nerve repair or reconstruction are failure to achieve the desired functional outcome, painful neuroma in continuity, or both. Some patients present with adequate distal nerve recovery, but complain of having painful scars. This may be due to scarring between the nerve and the skin (or surrounding tissues), which produces traction. Scar massage and desensitisation therapy are indicated in these patients.

Occasionally nerve repair or reconstruction may result in complex regional pain syndrome. The detailed treatment of this disorder is beyond scope of this chapter, but early recognition and intervention are essential. Hand therapy, TENS, medications including corticosteroids, and regional indwelling anaesthesia all have a role to play.

Clinical Pearl

A blunt or traction injury and delay to surgery all have negative effects on the clinical outcome.

Complex Injury

Traction Injury

Peripheral nerves may be stretched approximately 10 % without losing function and approximately 15–20 % with temporary loss of function (neurapraxia) [29, 30]. Stretch of greater than 20 % results in the elastic limits of the perineurium being exceeded and therefore creates at least an axonotmesis and sometimes a neurotmesis or complete rupture.

The most common causes of traction injuries in the UK are motor vehicle collisions, sports and birth related trauma. Such injuries may recover over a period of months if a neurapraxia has been sustained, or may result in permanent loss of function if there has been extensive disruption of axons with secondary intraneural fibrosis.

The diagnosis of traction injury requires clinical suspicion based on the mechanism of injury and knowledge of other injuries sustained. If the injury has resulted in an open wound, the relevant nerves should be explored at the same time as any vascular/bony/soft tissue repair. If the wound is closed, immediate surgical exploration is not usually carried out solely for the purpose of evaluation of the nerve. With a closed wound diagnosis is based on repeated physical examinations, and electrophysiology studies.

Classification

The classification of nerve injuries was first described by Seddon in 1947 (three classes of injury) and expanded by Sunderland in 1951 (five classes of injury). This classification system remained unchallenged until Mackinnon added a sixth category representing a mixed injury pattern.

- *First-degree injury* (*neurapraxia*) – a localised conduction block in a nerve segment that remains structurally in tact, with normal conduction proximal and distal to the segment, and trophic activity maintained. Axons are not

injured therefore regeneration is not required and complete recovery should occur.

- *Second-degree injury* (*axonotmesis*) – axonal disruption in which the distal segment undergoes Wallerian degeneration. By definition connective tissue layers are uninjured. Recovery is complete unless the distance of the injury from the motor endplate results in such prolonged denervation of the receptor muscle that motor recovery is adversely affected.
- *Third-degree injury* – Wallerian degeneration is combined with endoneurial fibrosis. Recovery is incomplete because scar within the endoneurium may block axonal regeneration or cause mismatching of regenerating fibers with the appropriate end organs.
- *Fourth-degree injury* – the nerve is in continuity, but only the epineurium remains in continuity. Thus a complete scar block (neuroma in continuity) means regeneration will not occur unless the block is removed and the nerve is repaired or grafted.
- *Fifth-degree injury* (*neurotmesis*) – nerve is completely divided and must be repaired before any regeneration can occur.
- *Sixth-degree injury* – a combination of any of the previous five levels of injury. Because of the longitudinal nature of crush injuries, different levels of nerve injury can be seen at various locations along an injured nerve. This is the most challenging nerve injury for the surgeon, as some fascicles will need to be protected and not "downgraded," whereas others will require surgical reconstruction.

The degree of injury is important in determining treatment. First, second, and third degree injuries have the potential for recovery and generally do not require surgical intervention. A first degree injury recovers complete function within 3 months. A second degree injury recovers completely but slowly (somewhat less than 1 mm per day from proximal to distal), whereas recovery after third degree injuries is slow and incomplete. Fourth and fifth degree injuries will not recover without surgical intervention. A sixth degree injury shows a variable recovery.

Neurapraxia

Neurapraxia is a localised conduction block in a nerve segment that remains structurally in tact, with normal conduction proximal and distal to the segment, and trophic activity maintained. Axons are not injured, regeneration is not required and complete recovery should occur. It is therefore very important to be able to recognize neurapraxia, as surgery is not indicated in such cases.

Factors within the history and examination suggest when a neurapraxia has occurred:

- History of minor or low energy trauma, or prolonger low pressure crush
- Often not all function modalities are lost (motor and proprioception is lost preferentially, while vibration, pain and hot versus cold discrimination are often preserved)
- No Tinel's sign on examination, and no muscular fibrillation
- No trophic changes are seen, and minimal muscle atrophy occurs
- Sensory recovery occurs ahead of motor recovery (sensorimotor dissociation)
- Sudden, sporadic, non-sequential recovery of motor function occurs

If a neurapraxia is suspected, then regular and repeated examinations should be undertaken to monitor recovery and confirm the diagnosis. EMG studies may also be of value to demonstrate preservation of distal action potentials which lends weight to the diagnosis.

Gun Shot Wound

Gunshot wounds are severe, high energy and unique. They are capable of dividing a nerve (grade V injury) but most often their damage is due to blast effect (grades I-IV injury). The former requires exploration and direct repair, the latter should be observed and managed as a traction injury.

In general it is unlikely that a gunshot wound would cause a transection of a major peripheral nerve without damaging the nearby artery. However, as almost all gunshot wounds (even

without major vascular injury) require debridement, then exploration of the peripheral nerves is usually indicated. A delayed primary repair of a complete or partial nerve laceration caused by a bullet is easier than management of a neuroma in continuity, and this can safely be undertaken when the wound is stable.

Management of a Nerve gap

Principles of Nerve Grafting

When end to end neurosynthesis cannot be carried out without tension, a nerve graft (or other solution) is necessary, as even minimum tension on the nerve coaptation may compromise the final result. Repairing a peripheral nerve with the extremity flexed to approximate the two nerve ends is inappropriate, as ultimately the nerve must glide as the extremity moves not only to a neutral position, but also into full extension.

There remains contention as to the critical length of nerve gap that necessitates a nerve graft. In the digit, a 1 cm gap in a digital nerve cannot be overcome. In the arm and forearm Millesi [31] supports mobilisation and end to end repair for defects of 6 cm or less, if they are easily approximated without flexion of the adjacent joints. Our experience is that a 6 cm nerve gap would be difficult to overcome without nerve graft, with the exception of the ulnar nerve where anterior transposition gains some length.

Placement of the nerve graft into a healthy bed is important for graft survival. The grafted nerve, much like a skin graft, requires ingrowth of blood vessels from the surrounding tissue to survive. Thin cutaneous nerve grafts are more easily vascularised than trunk or cable grafts [32]. If neovascularisation of the nerve graft has not occurred by the third day, the special components of the nerve, such as the endoneurial Schwann cells, involute and are replaced by fibrous tissue [32].

Nerve grafts heal by ingrowth of new vessels, and therefore require a vascularised bed capable of angioneogenesis (not seen in post irradiation tissue). They also require no barriers to ingrowth and inosculation such as infection, haematoma, fat on the nerve graft or metalwork. The nerve graft should be under no tension, repaired with sutures and minimal fibrin glue, and have a maximal surface area to volume ratio. Surgical technique is crucial in that nerve grafts should not be clumped together to form a trunk. All fat should be removed from the graft, haemostasis should be obtained and antibiotics used to minimize infection. Generally, a slightly longer graft is preferred to avoid tension. On occasion, a vascularised would bed may need to be imported (with a muscle flap), or a dry wound bed created with the use of a silicone spacer, the latter left in situ for a few weeks before grafting.

One of the technical challenges of nerve grafting is maintaining the proper fascicular alignment between the proximal and distal nerve ends. Often the internal topography of nerve will change as it traverses a gap, or the proximal stump will contain a different number of fascicles to the distal stump. When nerves contain mixed sensory and motor fascicles the problem is compounded. Correct orientation is assisted by knowledge of the internal anatomy of the nerve, distal dissection, and careful inspection of the cut ends of the nerve. When resecting a nerve associated with a tumour, if the nerve is functioning before resection then individual fascicle stimulation and marking may help orientation of the graft during reconstruction.

A further challenge is to maximize the number of axons crossing a nerve graft through both the proximal and distal neurosynthesis. Reversal of the direction of the nerve graft reduces leakage of axons through side branches, and effectively funnels regenerating axons distally. Making use of the maximum possible number of cables of nerve graft across a gap also increases the number of axons which may potentially regenerate (Fig. 2.5).

Clinical Pearl

The key to success of a nerve graft is surgical precision. Any graft should be under little or no tension and sit in a good vascular bed. It is also important that the fascicles are aligned as accurately as possible.

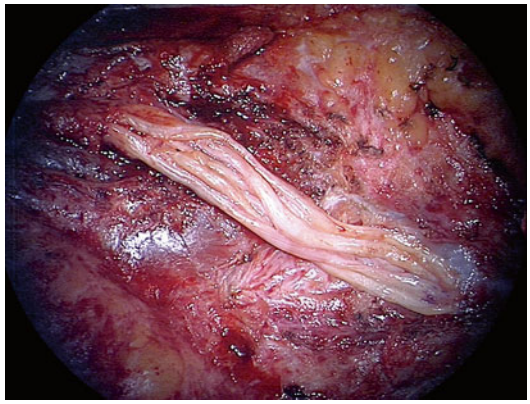

Fig. 2.5 Multiple cables of sural nerve graft crossing a 7 cm nerve gap in the common peroneal nerve, following resection of injured nerve after posterior knee dislocation

Donor Nerves

The sural nerve in adults can provide 30–40 cm of graft, with 11–12 fascicles being reliably present [33]. In 80 % of dissections it is formed by the medial sural cutaneous nerve and the peroneal communicating branch. The communicating branch can contribute an additional 10–20 cm if required. The nerve is adjacent to the lesser saphenous vein posterior to the lateral malleolus, and is usually harvested through a longitudinal incision (so as to avoid compromising the quality of the nerve graft), though some surgeons prefer multiple transverse incisions, or to harvest the nerve endoscopically. The consequent area of numbness on the lateral foot is well tolerated. The disadvantages of this donor site are the separate distal donor site, and the relatively high proportion of connective tissue to axons when compared to upper limb nerves.

When a small amount of nerve graft is required, the medial or lateral antebrachial cutaneous nerves may be harvested from an injured upper limb. The lateral antebrachial cutaneous nerve (LACN) lies adjacent to the cephalic vein along the ulnar border of brachioradialis, and 8 cm of graft can be harvested in adults. The medial antebrachial cutaneous nerve (MACN) lies in the groove between triceps and biceps alongside the basilic vein, and has an anterior and posterior division. Twenty centimeter of nerve graft may be harvested if both divisions are taken, although sensibility is lost over the elbow and resting part of the forearm if the posterior division is harvested.

For short grafts, to reconstruct digital nerve defects for instance, the posterior interosseus nerve may be used. It is most accessible where it lies in the radial part of the fourth dorsal extensor compartment at the wrist, and a short incision allows easy harvest of a 2.5 cm graft. Loss of wrist joint sensibility and proprioception is well tolerated if the anterior interosseus nerve is left undisturbed.

Surgical Technique of Nerve Grafting

The surgical technique of nerve grafting that was developed by Millesi [34–36] is similar in many ways to primary nerve repair. The surgeon prepares the proximal and distal ends of the nerve by evaluating and excising the damaged or scarred nerve. The harvested nerve is then placed across the gap between proximal and distal stumps without tension. The involved extremity is moved through a passive range of motion before setting the length of the graft. One end of the graft is sutured, the graft is positioned in the gap, and the other end trimmed to fit the defect. Two or three fine sutures are all that are required to secure each graft to the nerve stumps. It is our practice to reinforce the neurosynthesis with fibrin glue. Major nerves may require several cables of nerve graft, while a digital nerve will only require a single cable in most instances.

When insetting the nerve graft, it is important to try to achieve an appropriate sensory and motor fascicle match at the proximal and distal repair sites. Techniques to assist in the orientation of the nerves have been discussed previously. In proximal extremity grafts, the fascicles at the proximal stump are frequently mixed and so the fascicular alignment of the grafts cannot be specific. At the distal nerve stump, the alignment can usually be more specific. Occasionally it may be useful to direct all reinnervation into the restoration of a critical motor function. For example in radial nerve injuries, the proximal level of the graft is frequently a point at which the fascicles are mixed

motor and sensory. Distally, however, the sensory fibers of the superficial radial nerve can be completely excluded from the graft so that all regenerating fibers are directed into the distal motor fascicles and none into the sensory fascicles.

Vascularised Nerve Grafts and Allografts

In conventional nerve grafting, success is inversely proportional to the length of the graft. This is because the longer the graft is, the more likely it is that part of the graft will not revascularise. Vascularised nerve grafts aim to circumvent this problem, particularly where the wound bed is poor or the graft is long.

Potential donor nerves include anterior tibial, saphenous, superficial peroneal, deep peroneal, superficial radial, ulnar, and sural nerves. Although clinical series have proven the feasibility of performing vascularised nerve grafts in humans, a definite clinical role in peripheral nerve repair is yet to be defined. Currently there is little experimental evidence to demonstrate their superiority to justify the additional surgical morbidity and effort.

Rarely, a situation arises where an otherwise salvageable extremity has a peripheral nerve injury that is unreconstructable with autogenous nerve grafts because of insufficient donor sites. Mackinnon and Hudson [37] have reported obtaining protective sensation in the foot by using a 23 cm, ten cable allograft to reconstruct a sciatic nerve and Bain has used this technique in seven patients who needed major nerve reconstruction [38]. Although still experimental, this technique may provide an excellent alternative source of graft material.

Nerve Conduits

A conduit is a tubular structure used to connect the two transected ends of nerve across a gap. The potential role of conduits in the repair and reconstruction of peripheral nerves has interested surgeons for many years. Ever since Büngner reported

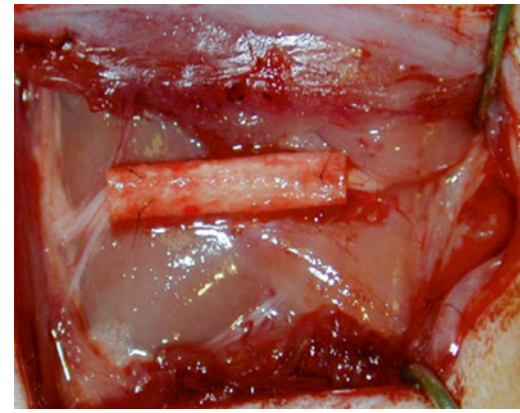

Fig. 2.6 Short segment bio-absorbable nerve conduit placed experimentally in the hind leg of a rat model

successful nerve regeneration through an arterial graft in 1891 [39], we have known that severed nerves can grow across a gap through a conduit.

The theory underpinning conduit repair of peripheral nerves is that the enclosed space allows neurotropic agents released by the distal stump to establish a uniform concentration through the conduit, thereby inducing chemotactic attraction to the proximal sprouting axons, which results in more numerous axonal reconnections.

However, there is a limit to how far a bare axon sprout can grow and various growth factors are required by the growth cone to survive. Some are provided through internal axonal transport, others are obtained from the surrounding millieu. Schwann cells begin to surround the new growth cone and provide metabolic support, and at the same time, fibroblasts begin to lay down collagen to provide structural support.

Nerve regeneration across (short defect) bio-absorbable polyglycogen tubes (Fig. 2.6) has been shown in both animal and human models, and has been comparable to a standard nerve grafts [40]. More recent work on introducing neurotrophic factors to the surface of these conduits has lead to encouraging improvements in the regeneration seen. Micro-engineering of the internal surface of conduits has also allowed the potential length of the conduit to be extended in animal models.

Commercial conduits are available for reconstruction of short defects in small and large diameter nerves, although their uptake is not

widespread. As confidence in the efficacy of these devices grows, and use increases, it may eliminate the morbidity associated with harvesting donor nerves. Currently, however, they are best considered experimental rather than clinically efficacious.

Finally, vein grafts have been used to reconstruct short, distal, sensory nerve defects, but results are not as satisfactory as using conventional nerve grafts [41].

Nerve Transfer

Indications

Nerve transfers involve using nerves with relatively less important roles, to restore function to a more useful nerve that has been injured. The use of nerve transfers has expanded as a consequence of the improved knowledge of the internal topography of peripheral nerves in the limbs.

Nerve transfers are indicated in very proximal peripheral nerve injuries or root avulsions where a proximal stump is unavailable for primary repair or grafting. Even when grafting is possible the injury may be so proximal that a nerve transfer facilitates better re-innervation of distal motor endplates than does a nerve graft. Nerve transfers are also indicated to avoid operating in regions of severe scarring, when nerve injuries present in a delayed fashion, when partial nerve injuries present with a well-defined functional deficit, or when the level of injury is unclear such as in idiopathic neuritides or radiation-induced nerve injury.

Principles

Nerve transfers are based on the same principle as tendon transfers, namely, the sacrifice of a less important function to restore a function of greater importance. An example is the attachment of the superficial branch of the radial nerve to the ulnar most palmar digital nerve to restore sensibility to that side of the hand in a patient who has an unreconstructable ulnar nerve injury.

The characteristics of an ideal donor nerve to transfer for motor function are:

- Expendable donor motor nerve with a large number of pure motor axons.
- Located in close proximity to target motor endplates, thus minimising the distance and time regenerating axons need to travel to re-innervate their target.
- Donor nerve innervates a muscle that is synergistic with its target.

Clinical Application

The most common application of motor nerve transfers is after brachial plexus injuries and includes the restoration of elbow flexion, shoulder abduction, ulnar-innervated intrinsic hand function, forearm pronation, and radial nerve function.

To restore elbow flexion, the medial pectoral, thoracodorsal, or intercostal nerves can be transferred to the musculocutaneous nerve. The flexor carpi ulnaris branch of the ulnar nerve [42] and the flexor carpi radialis branch of the median nerve can also be transferred to the biceps and brachialis branches of the musculocutaneous nerve to more specifically restore elbow flexion and limit donor nerve morbidity.

To restore shoulder abduction, the distal accessory nerve can be transferred to the suprascapular nerve, or the triceps branch of the radial nerve can be transferred to the axillary nerve. To restore intrinsic hand function, the distal anterior interosseous nerve can be transferred to the ulnar nerve. Transferring redundant fascicles of the flexor carpi ulnaris branches of the ulnar nerve to the median nerve-innervated pronator teres can restore forearm pronation. Alternatively, the flexor digitorum superficialis, or palmaris longus branches of the median nerve, can be transferred to its pronator branch. The radial nerve is most commonly reconstructed by transferring a portion of the ulnar nerve supplying flexor carpi ulnaris.

After dissecting out the functional proximal and nonfunctional distal nerves, the surgical

technique is essentially the same as a standard nerve repair. Care must be taken to ensure that, like a tendon transfer, the nerve transfer is surrounded by adequate soft tissue to provide protection from external trauma and is not obstructed or placed under compression by the anatomic structures along its course.

End to Side Neurosynthesis

End to side neurosynthesis is a technique in which the distal end of a transected nerve is coapted to the side of an intact nerve. Axons from the intact nerve theoretically sprout from the interrupted side and grow down the attached nerve to the distal end organ. End to side nerve repair was reported in patients at the turn of the century [43] after experimental work undertaken in the early 1990s [44].

Since then, a great deal of research has been published that supports the idea and refines it for clinical use. It was initially unclear where the "sprouting" axons were originating from, but double-labeling experiments demonstrated that true collateral (nodal) sprouting from the nodes of Ranvier really occurs [45]. Sensory and motor nerves are capable of collateral sprouting, and there appears to be only minimal loss of donor nerve function [46].

The technique involves mobilising the distal end of the transected nerve and aligning it next to an appropriate donor nerve. The donor nerve should be of a synergistic muscle group if it is used for motor reinnervation, or from a neighboring dermatome if it is used to reconstruct a sensory defect. Under magnification, a window that is the size of the transected nerve end is created in the epineurium, and fine sutures are used to secure the coaptation.

End to side neurosynthesis has been used in cases of facial palsy, brachial plexus injury and median, ulnar, and digital nerve injuries, all with mixed results. It appears to be more useful for sensory reconstruction when nerve grafting is not feasible, although more research is needed for this to become a reliable replacement for nerve transfers.

Investigations After Nerve Injury

Investigation

With the exception of injured nerve roots, which maybe investigated by contrast myelography or high resolution MRI, radiologic imaging is of little practical value in the diagnosis of a peripheral nerve injury. Ultrasound may be useful in a few cases to establish nerve continuity or the presence of a neuroma, although these instances are rare.

Electrophysiological diagnosis has many pitfalls. Its major limitation is that even a completely divided motor nerve may have normal findings for the first 3 weeks after the injury.

In the case of suspected peripheral motor nerve injury, serial electromyography (EMG) can demonstrate whether a muscle is innervated and beginning to undergo progressive reinnervation (nascent or polyphasic potentials) or remains denervated (spontaneous spike potentials at rest and denervation potentials). This may be useful to guide whether surgical exploration of the nerve is indicated. Measurement at 4 weeks post injury is the first occasion where the information becomes useful, and combined with clinical assessment a diagnosis of neurapraxia may be tentatively made (Fig. 2.7).

In certain circumstances, somatosensory evoked potential measurements may be a useful clinical test in the unconscious patient, as somatosensory evoked potentials can determine the integrity of the neural pathways from the fingertip to the postcentralgyrus.

Exploration

If there is still clinical doubt after a thorough history and physical examination, the diagnosis of a potential nerve injury can best be made by surgical exploration of the wound.

Summary

Nerve repair, transfer and grafting have benefited from the development of microsurgical techniques and advances in the field of

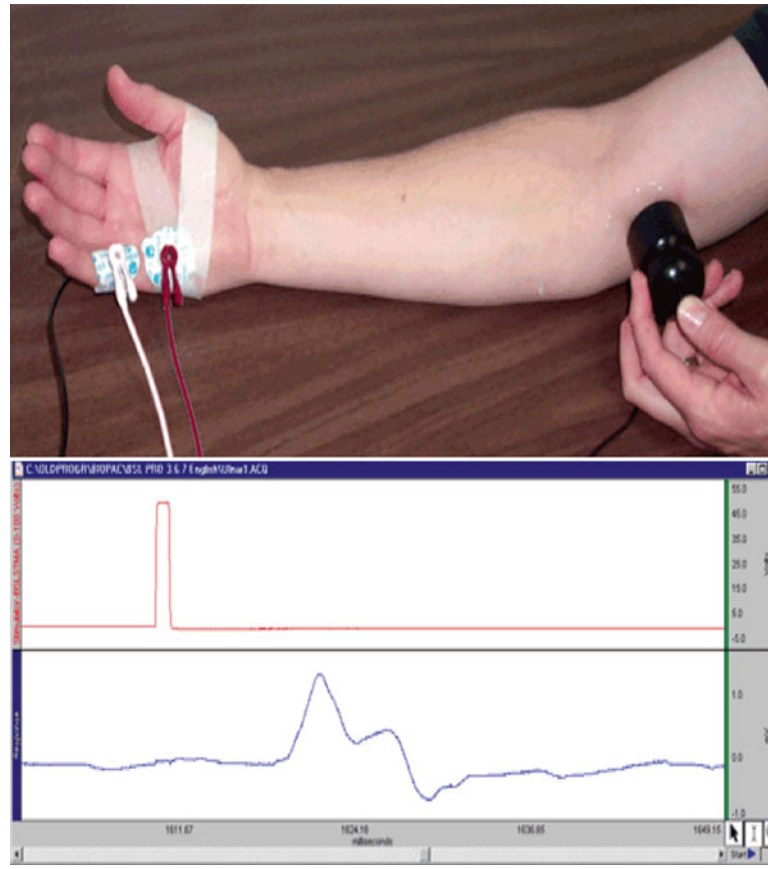

Fig. 2.7 Electromyography 4 weeks after injury may assist in decision making when combined with serial clinical assessment

neuroscience. Optimum outcomes from nerve repair not only demand precise surgical techniques, but also additional measures to direct nerve regeneration to its original function.

Although nerve grafting remains the gold standard for reconstruction of a nerve gap, synthetic conduits now play a limited but important role in the peripheral nerve surgeon's armamentarium, and this role is likely to increase over the coming decades.

References

1. Elsberg C. The Edwin Smith surgical papyrus. Ann Med Hist. 1931;3:271–9.
2. Millesi H. Reappraisal of nerve repair. Surg Clin North Am. 1981;61:321–40.
3. Terzis J, Faibisoff B, Williams B. The nerve gap: suture under tension vs. graft. Plast Reconstr Surg. 1975;56:166–70.
4. Noble J, Munro CA, Prasad VS, Midha R. Analysis of upper and lower extremity peripheral nerve injuries in a population of patients with multiple injuries. J Trauma. 1998;45:116–22.
5. Dellon AL, Mackinnon SE. Basic scientific and clinical applications of peripheral nerve regeneration. Surg Annu. 1988;20:59–100.
6. Jabaley ME, Wallace WH, Heckler FR. Internal topography of major nerves of the forearm and hand: a current view. J Hand Surg. 1980;5:1–18.
7. Williams HB, Jabaley ME. The importance of internal anatomy of the peripheral nerves to nerve repair in the forearm and hand. Hand Clin. 1986;2:689–707.
8. Mackinnon SE, Dellon AL. Experimental study of chronic nerve compression. Clinical implications. Hand Clin. 1986;2:639–50.
9. Sunderland S, Bradley KC. The cross-sectional area of peripheral nerve trunks devoted to nerve fibers. Brain. 1949;72:428–49.
10. Millesi H. The nerve gap. Theory and clinical practice. Hand Clin. 1986;2:651–63.
11. Terenghi G, Calder JS, Birch R, Hall SM. A morphological study of Schwann cells and axonal regeneration in chronically transected human peripheral nerves. J Hand Surg. 1998;23:583–7.

12. Giannini C, Dyck PJ. The fate of Schwann cell basement membranes in permanently transected nerves. J Neuropathol Exp Neurol. 1990;49:550–63.
13. Li H, Terenghi G, Hall SM. Effects of delayed reinnervation on the expression of c-erbB receptors by chronically denervated rat Schwann cells in vivo. Glia. 1997;20:333–47.
14. Hems TEJ, Glasby MA. The limit of graft length in the experimental use of muscle grafts for nerve repair. J Hand Surg Br. 1993;18:165–70.
15. Calder JS, Norris RW. Repair of mixed peripheral nerves using muscle autografts: a preliminary communication. Br J Plast Surg. 1993;46:557–64.
16. Ma J, Novikov LN, Wiberg M, Kellerth JO. Delayed loss of spinal motoneurons after peripheral nerve injury in adult rats: a quantitative morphological study. Exp Brain Res. 2001;139:216–23.
17. Fu SY, Gordon T. The cellular and molecular basis of peripheral nerve regeneration. Mol Neurobiol. 1997;14:67–116.
18. McKay Hart A, Brannstrom T, Wiberg M, Terenghi G. Primary sensory neurons and satellite cells after peripheral axotomy in the adult rat: timecourse of cell death and elimination. Exp Brain Res. 2002;142:308–18.
19. Gu Y, Spasic Z, Wu W. The effects of remaining axons on motoneuron survival and NOS expression following axotomy in the adult rat. Dev Neurosci. 1997;19:255–9.
20. Novikov L, Novikova L, Kellerth JO. Brain-derived neurotrophic factor promotes axonal regeneration and long-term survival of adult rat spinal motoneurons in vivo. Neuroscience. 1997;79:765–74.
21. Hart AM, Terenghi G, Kellerth JO, Wiberg M. Sensory neuroprotection, mitochondrial preservation, and therapeutic potential of N-acetyl-cysteine after nerve injury. Neuroscience. 2004;125:91–101.
22. Zhang CG, et al. Motorneuron protection by N-acetylcysteine after ventral root avulsion and ventral rhizotomy. Br J Plast Surg. 2005;58:765–73.
23. Strauch B, et al. The ten test. Plast Reconstr Surg. 1997;99:1074–8.
24. Cales L, Weber RA. Effect of water temperature on skin wrinkling. J Hand Surg. 1997;22:747–9.
25. Lundborg G, Dahlin L, Danielsen N, Zhao Q. Trophism, tropism, and specificity in nerve regeneration. J Reconstr Microsurg. 1994;10:345–54.
26. Grabb WC, Bement SL, Koepke GH, Green RA. Comparison of methods of peripheral nerve suturing in monkeys. Plast Reconstr Surg. 1970;46:31–8.
27. Bora Jr FW, Pleasure DE, Didizian NA. A study of nerve regeneration and neuroma formation after nerve suture by various techniques. J Hand Surg. 1976;1:138–43.
28. Cabaud HE, Rodkey WG, McCarroll Jr HR, Mutz SB, Niebauer JJ. Epineurial and perineurial fascicular nerve repairs: a critical comparison. J Hand Surg. 1976;1:131–7.
29. Lundborg G, Rydevik B. Effects of stretching the tibial nerve of the rabbit. A preliminary study of the intraneural circulation and the barrier function of the perineurium. J Bone Joint Surg. 1973;55:390–401.
30. Haftek J. Stretch injury of peripheral nerve. Acute effects of stretching on rabbit nerve. J Bone Joint Surg. 1970;52:354–65.
31. Millesi H. Peripheral nerve injuries. Nerve sutures and nerve grafting. Scand J Plast Reconstr Surg Suppl. 1982;19:25–37.
32. Millesi H. Techniques for nerve grafting. Hand Clin. 2000;16:73–91, viii.
33. Brammer JP, Epker BN. Anatomic-histologic survey of the sural nerve: implications for inferior alveolar nerve grafting. J Oral Maxillofac Surg. 1988;46:111–7.
34. Millesi H, Meissl G, Berger A. Further experience with interfascicular grafting of the median, ulnar, and radial nerves. J Bone Joint Surg Am. 1976;58:209–18.
35. Millesi H, Meissl G, Berger A. The interfascicular nerve-grafting of the median and ulnar nerves. J Bone Joint Surg Am. 1972;54:727–50.
36. Millesi H. Nerve grafting. Clin Plast Surg. 1984;11:105–13.
37. Mackinnon SE, Hudson AR. Clinical application of peripheral nerve transplantation. Plast Reconstr Surg. 1992;90:695–9.
38. Bain JR. Peripheral nerve and neuromuscular allotransplantation: current status. Microsurgery. 2000;20:384–8.
39. Bungner O. Die degenerations-und regenerationvorgange am nerven verletzungen. Beitr Pathol Anal. 1891;10:321–93.
40. Lundborg G, Rosen B, Dahlin L, Danielsen N, Holmberg J. Tubular versus conventional repair of median and ulnar nerves in the human forearm: early results from a prospective, randomized, clinical study. J Hand Surg. 1997;22:99–106. doi:10.1016/S0363-5023(05)80188-1.
41. Chiu DT, Janecka I, Krizek TJ, Wolff M, Lovelace RE. Autogenous vein graft as a conduit for nerve regeneration. Surgery. 1982;91:226–33.
42. Oberlin C, et al. Nerve transfer to biceps muscle using a part of ulnar nerve for C5-C6 avulsion of the brachial plexus: anatomical study and report of four cases. J Hand Surg. 1994;19:232–7. doi:10.1016/0363-5023(94)90011-6.
43. Al-Qattan MM. Terminolateral neurorrhaphy: review of experimental and clinical studies. J Reconstr Microsurg. 2001;17:99–108.
44. Viterbo F, Trindade JC, Hoshino K, Mazzoni Neto A. End-to-side neurorrhaphy with removal of the epineurial sheath: an experimental study in rats. Plast Reconstr Surg. 1994;94:1038–47.
45. Zhang Z, Soucacos PN, Bo J, Beris AE. Evaluation of collateral sprouting after end-to-side nerve coaptation using a fluorescent double-labeling technique. Microsurgery. 1999;19:281–6.
46. Zhang Z, et al. Long-term evaluation of rat peripheral nerve repair with end-to-side neurorrhaphy. J Reconstr Microsurg.2000;16:303–11.doi:10.1055/s-2000-7338.