Part II – Neurological Disorders

CHAPTER 11
DISORDERS OF PERIPHERAL NERVES

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2012

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BRIC 2012 

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NEUROLOGY IN AFRICA

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Layout: Christian Bakke, Division of Communication, University of Bergen

Printed by Bodoni, Bergen, Norway 

ISBN 978-82-7453-085-0

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CHAPTER 11

DISORDERS OF PERIPHERAL NERVES

Peripheral neuropathies are a major cause of neurological disability in Africa. They occur as a result of disease or injury and can affect nerve roots, individual nerves and peripheral branches of nerves (Fig.11.1). The main causes are HIV, leprosy, diabetes mellitus, drugs, nutrition and alcohol (Table 11.1 & 2). This chapter reviews the main clinical presentations, investigations and management of peripheral nerve disorders. The student should aim to be able to recognize the different types of neuropathies and know their main causes and management.

Pathophysiology

Peripheral nerves are made up of multiple axons surrounded by myelin, Schwann cells and their covering sheaths. Individual axons are either myelinated or nonmyelinated. In neuropathies the nerves may be damaged at three main sites: the axon, the myelin and the cell body. If the axon is damaged, it is called an axonal neuropathy. This is the most common form of peripheral neuropathy and usually affects sensation greater than power and has a mainly distal distribution. If the myelin is damaged this is called a demyelinating neuropathy. This affects power more than sensation and the weakness is usually proximal as well as distal. If the cell body is damaged then either sensory or motor nerve fibres or both may be damaged permanently depending on which cell body is involved. Recovery occurs if the basement membrane survives but is faster in demyelinating than in axonal neuropathies.

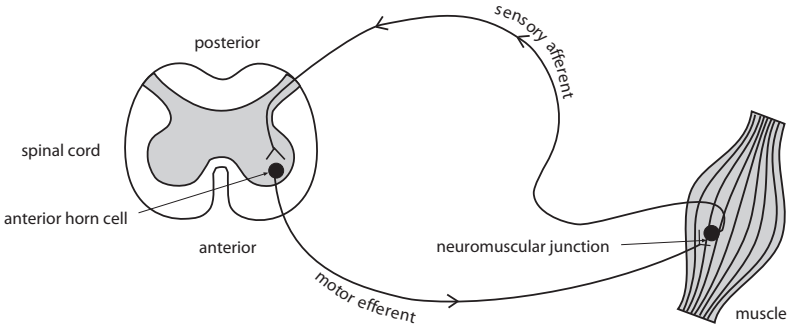


Figure 11.1 The peripheral reflex pathway

TYPES OF PERIPHERAL NERVE DISORDER (PND)

Peripheral neuropathies are divided into two main groups: mononeuropathies which involve single nerves and polyneuropathies which involve many nerves.

MONONEUROPATHY

This describes a group of focal peripheral nerve disorders (FPNDs) where individual nerves or their branches are affected. The main mechanisms are compression, entrapment, vasculitis, infiltration and infection. In the upper limbs, this happens mostly at the wrist, elbow and occasionally the upper arm. In the lower limbs, the most common sites are at the level of the inguinal ligament, the knee and the buttocks. A misplaced injection in the buttocks in young children is the main cause of sciatic nerve injury in Africa. If more than one nerve is involved, this is called multiple mononeuropathy or mononeuritis multiplex. Leprosy is a common cause of both mononeuropathy and mononeuritis multiplex in Africa. Other causes include HIV, diabetes and vasculitis. The main clinical features of the most common focal nerve lesions are outlined in Table 11.1 and illustrated in Figs 11.2-5.

Table 11.1 Common focal peripheral nerve disorders

Nerve	Main site	Mechanism	Main Cause	Clinical Features
Median	wrist	entrapment	carpal tunnel syndrome, leprosy	pain, tingling hand/wrist, arm, numbness radial 3 & 1/2 fingers, wasting thenar muscles, weakness of thumb abduction
Ulnar	elbow	compression	trauma/injury, leprosy	pain, tingling hand wrist, numbness ulnar 1 & 1/2 fingers, wasting hypothenar muscles, weakness little finger flexion, claw hand deformity
Radial	arm	compression	sleep	wrist drop, weakness wrist, dorsiflexion
Sciatic	buttock	infiltration	injection	pain buttock, leg, foot, numbness leg and foot, weakness knee flexion & muscles below knee, absent ankle jerk
Femoral	thigh	vascular	diabetes	pain thigh (severe), numbness anteromedial thigh & medial leg, weakness hip flexion & knee extension, absent knee jerk
Lateral cutaneous nerve thigh	inguinal ligament	compression	occupational, carrying baby on hip	numbness, tingling and pain over anterolateral thigh (meralgia paraesthetica)
Common peroneal	knee	compression infiltration	illness, leprosy, leg crossing	numbness dorsum foot, foot drop, weakness foot eversion

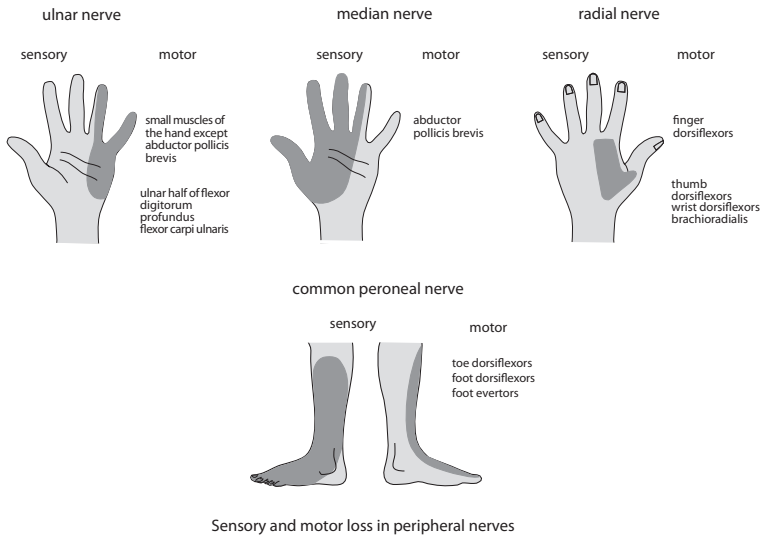
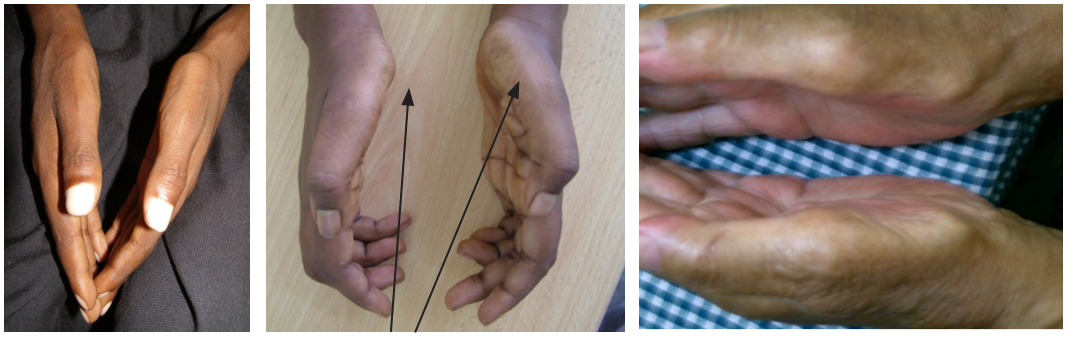


Figure 11.2 Sensory and motor loss in main mononeuropathies

Median nerve compression occurs mostly at the wrist as the median nerve passes through the carpal tunnel resulting in carpal tunnel syndrome (CTS). CTS is characterized by tingling pain in the hand or arm particularly at night. The pain and paraesthesiae are in the distribution of the median nerve and involve the thumb, index, middle and half the ring finger but may extend up the forearm and arm. It often wakes the patient from sleep at night and is relieved by hanging the arm down and shaking the hand. CTS is frequently provoked by manual tasks. Sensory loss in CTS usually affects the lateral (radial) three and a half fingers and spares the palm. Sensation to the lateral fingers and palm are lost in median nerve lesions located in the forearm (Fig. 11.2). In long standing cases there is wasting of the thenar eminence and weakness of thumb abduction and opposition (opponens pollicis) (Figs 11.2 & 3). **Tinel's sign** may be positive i.e. tapping the carpal tunnel at the distal crease of the wrist reproduces pain and tingling. Alternatively there may be tingling on extreme wrist flexion for one minute (**Phalen's sign**). However, in clinical practice these signs, although useful when present are unreliable when absent. Treatment is by local injection of steroids, wearing a night time wrist splint or by surgical decompression if necessary



Typical wasting of thenar muscles

Figure 11.3 Median neuropathy (bilateral)

Ulnar nerve is prone to compression along its path. The main site of pressure or stretching is at the elbow within the cubital tunnel or the ulnar groove. This results in dyasthesia/paraesthesia and sensory impairment/loss in the distribution of the little finger and adjacent half of the ring finger and ulnar aspect of the hand front and back. There is wasting and weakness of the intrinsic muscles of the hand and the deep flexors of the 4th and 5th finger with sparing of the thenar muscles (Figs. 11.2 & 4). This gives rise to the characteristic claw hand deformity seen in chronic ulnar lesions.

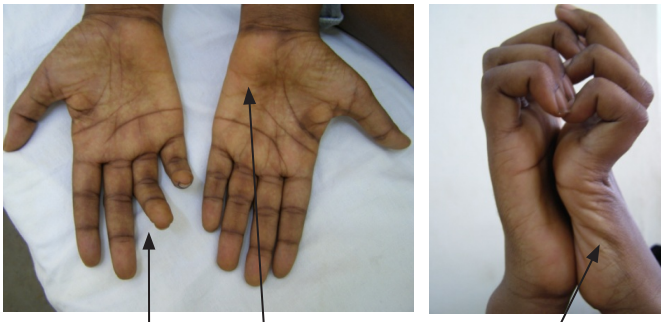


Figure 11.4 Ulnar neuropathy

Radial nerve compression arises mostly from prolonged abnormal posture with resulting compression of the radial nerve in the radial groove above the elbow e.g. drunkard's palsy. It can also arise from compression in the axilla, e.g. using crutches, and from fracture of the shaft of the humerus. Compression results in wrist drop with weakness of the finger and wrist extension and sometimes a small patch of sensory loss on the dorsum of the hand and web of the thumb (Fig. 11.2).

Lateral cutaneous nerve of thigh travels under the lateral part of the inguinal ligament. Compression results in a patch of sensory loss over the anterolateral aspect of the thigh of variable size ranging from a palm sized patch to an area extending from the hip to the knee but never crossing the midline of the axis of the thigh **(meralgia paraesthetica)**. This is one of the most common mononeuropathies and its onset is associated with weight gain e.g. pregnancy and also occupational e.g. chronic abnormal posture, bending (e.g. plumber). It is usually self-limiting.

Sciatic nerve injury most commonly occurs as a result of a misplaced injection in the buttocks in early childhood. The sciatic nerve (tibial & common peroneal nerves, L4,5,S1,2) is responsible for sensation below the knee involving the entire anterolateral aspect of leg and the sole and dorsum of the foot. It is responsible for the following movements, hip extension, knee flexion and ankle plantar and dorsiflexion. Injury results in loss of sensation and power in these distributions along with a decreased or absent ankle jerk.

Common peroneal nerve compression at the fibular head results in foot drop and sensory loss on the dorsum of foot and lateral leg (Figs 11.2 & 5). The main causes are trauma and pressure. It occurs more commonly in immobile patients who are prone to compression.

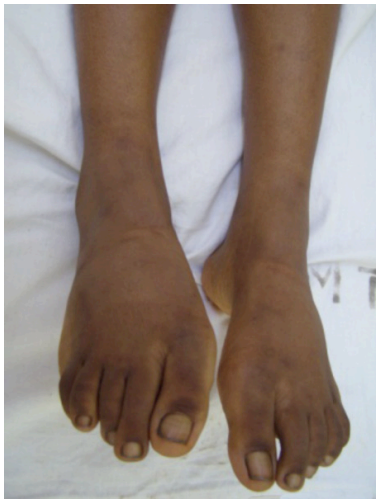


Figure 11.5 Common peroneal nerve neuropathy. Bilateral foot drop (left > right)

Femoral neuropathy most commonly occurs in association with diabetes mellitus. The main symptoms are thigh pain, weakness of hip flexion and decreased or absent knee jerk. Treatment is pain relief and treating the underlying cause.

Key points

- mononeuropathies are recognised by their clinical setting & pattern of sensory & motor loss
- include CTS: ulnar injury, peroneal palsy, meralgia paraesthetica, sciatic injury & femoral ischaemia
- main mechanisms: trauma, entrapment, compression, infection & inflammation
- leprosy is a major cause of mononeuropathies
- a misplaced injection is main cause of sciatic nerve injury

POLYNEUROPATHIES

Polyneuropathies are diffuse, symmetrical disorders usually affecting the limbs distally to a greater extent than proximally. Clinically, they are classified as acute or chronic, motor or sensory or mixed and also autonomic. Patients presenting with polyneuropathies typically present with impairment or loss of sensation in a distal or peripheral glove and stocking distribution. Distal weakness may occur later in the feet and legs followed by the hands and arms. Neurological examination usually reveals wasting, fasciculation, distal weakness with absent reflexes and loss of light touch. Vibration and joint position sense may also be involved. The sphincters involving bowel and bladder are typically spared. The main causes of polyneuropathy are outlined in Table 11.2.

Table 11.2 Main causes of polyneuropathies in Africa

Classification	Cause	Crude frequency
Infection	HIV, leprosy	very common
Metabolic	diabetes, (renal failure)	common
Drugs	ARTs (stavudine, didanosine), isoniazid, dapsone, vincristine	common
Toxic	alcohol, (chronic cassava consumption)	common
Deficiency	vitamin B-1 (alcoholics), B-6 (isoniazid), B-12 (pernicious anaemia)	uncommon
Inflammatory	Guillain-Barre Syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)	very uncommon
Vasculitis	rheumatoid arthritis, systemic lupus erythematosus (SLE), polyarteritis nodosa (PAN)	uncommon
Hereditary	Charcot-Marie-Tooth disease, others	uncommon
Neoplastic paraproteinaemia paraneoplastic	monoclonal gammopathy, carcinoma lung, breast, ovary	very uncommon
Idiopathic (>50% of all peripheral neuropathies)	unknown	most common

Main causes of polyneuropathy in Africa

- HIV
- diabetes
- leprosy
- drugs
- alcohol
- nutrition

Clinical features

The history may provide the first clue as to the aetiology of a neuropathy. There may be a history of a known risk factor for neuropathy, e.g. HIV, use of antiretroviral drugs (ART) in particular stavudine, diabetes, alcohol abuse, renal failure or very rarely a family history. The history provides essential information concerning the mode of onset, time course, distribution, character and pattern of symptoms.

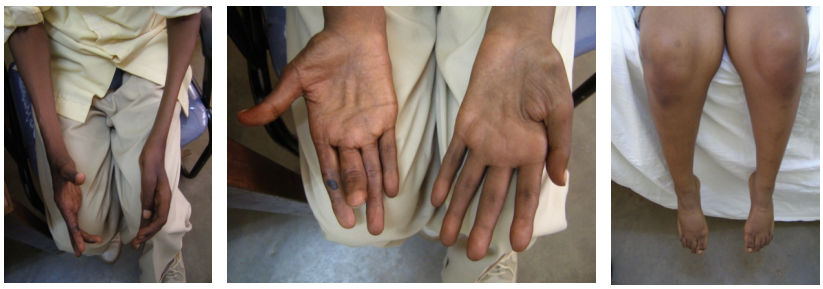
The clinical distribution will indicate whether it is confined to just one nerve or is more generalised affecting all peripheral nerves. An acute onset over days with both proximal and distal weakness suggests a demyelinating disorder like GBS, whereas a more chronic onset over months suggests a distal sensory motor axonal neuropathy as occurs in DM or HIV. Burning or pain in the feet is very characteristic of the neuropathy in HIV, diabetes, vitamin deficiencies and alcoholism. Additional clinical findings may also indicate the cause; the peripheral nerves may be thickened in leprosy, or clawing of the feet or pes cavus is seen in hereditary neuropathies or the low blood pressure on standing characteristic of autonomic neuropathies. The predominance of either sensory or motor findings is also helpful.

Motor

Muscle weakness suggests motor neuropathy. Motor symptoms include mild to severe weakness in the limbs, problems with walking or running, and difficulties manipulating or using fingers and hands. The main causes of motor neuropathy are GBS, polio and very rarely lead poisoning. Main findings on neurological examination include wasting, weakness and loss of reflexes in the limbs (Fig.11.6).

Sensory

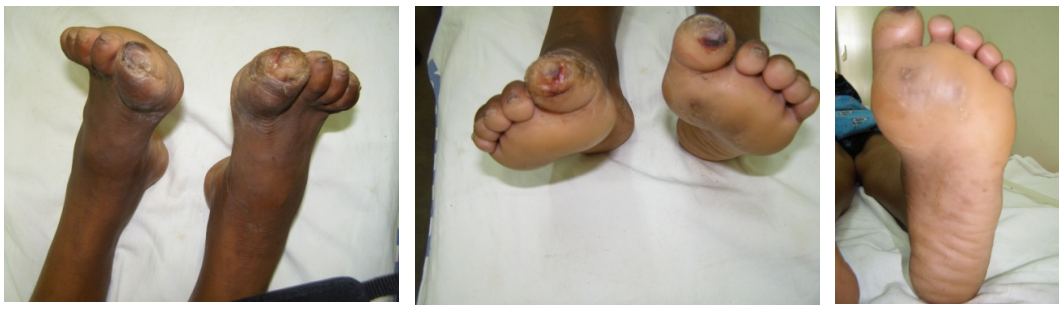
Numbness, tingling or pain in a glove and stocking distribution suggest a mainly sensory neuropathy. Terms used to describe the superficial sensory symptoms include: paraesthesia, meaning abnormal tingling sensation; hyperaesthesia, meaning increased sensitivity to a stimulus and dysaesthesia, meaning unpleasant tingling. The term allodynia means painful sensation from light non painful stimulus e.g. stroking. Sensory symptoms tend to occur before motor symptoms and typically involve the feet earlier than hands. Findings on neurological examination include loss of light touch, pain and joint position sense distally in the limbs mostly the feet. A sensory polyneuropathy may also cause poor balance and unsteady gait due to a loss of position sense in the feet. This is called sensory ataxic neuropathy. When the neuropathy involves loss of pain then trophic changes and digital loss can occur (Fig. 11.7)



Wasting forearms & small hand muscles

Distal wasting & foot drop

Figure 11.6 Motor and sensory neuropathy



Loss of terminal digits, ulcers & trophic changes

Figure 11.7 Sensory neuropathy

Differential Diagnosis

The differential diagnosis of neuropathies includes diseases affecting muscle, neuromuscular junction and occasionally myelopathy and rarely motor neurone disease. Polymyositis and myopathy may sometimes mimic a neuropathy but skin involvement and the mainly proximal pattern of weakness should suggest underlying muscle disease. Fatigability after exercise, a mainly truncal-axial pattern of weakness, ptosis and intact reflexes all point to myasthenia gravis. While myelopathy symptoms may sometimes mimic neuropathy, the predominantly upper motor neurone signs, the sphincteric involvement and pattern of sensory loss or alteration should all suggest spinal cord involvement. Exclusive motor involvement with weakness and

fasciculation are pointers towards progressive muscular atrophy (PMA), a form of motor neurone disease, although this is uncommon.

Diagnosis

The diagnosis of peripheral neuropathy relies mainly on the clinical findings and in as many as half the cases no underlying cause is found. Investigations should include laboratory screening tests for the common causes as outlined in Table 11.3. Simple blood tests exclude causes such as HIV, diabetes and B-12 deficiency. CSF examination may show an elevated protein in GBS and CIDP. Nerve conduction studies and electromyography are very helpful if available.

Nerve conduction studies (NCS) and Electromyography (EMG)

These are used mainly to determine whether there is a disease of the peripheral nerves, neuromuscular junction or muscle and to distinguish between them. NCS can also determine whether the neuropathy is purely sensory or also affects the motor fibres and whether the primary disease is axonal (causing death of axons) or demyelinating (affecting Schwann cells and myelin sheaths) or a mixture of both.

NCS involve stimulating a nerve with an electrical impulse and measuring the speed of conduction at two points along the nerve. This is called the conduction velocity. NCS also involves recording and measuring the amplitude of muscle action potential (MAP). NCS can distinguish demyelinating from axonal neuropathies. In general, a reduction in conduction velocity and normal MAP favours demyelination whereas normal conduction velocity and reduced MAP favours axonal neuropathies. Most neuropathies are axonal in type and largely untreatable. The most common type is termed distal symmetrical polyneuropathy (DM and HIV). In contrast demyelinating neuropathies (GBS) are uncommon but are largely treatable.

EMG involves insertion of a needle electrode into muscle and measures electrical activity in muscles. The patterns of electrical recordings at rest and during activity can determine the likely origin of the disorder.

Table 11.3 Laboratory investigations in peripheral neuropathy

Type	Investigation	Disorder
Haematology	FBC, B-12, folate, HIV, VDRL, ESR	vit deficiency, HIV, syphilis infection, vasculitis
Biochemistry	glucose, renal, liver, thyroid function tests, protein electrophoresis	diabetes, renal failure, myxoedema, paraproteinaemia
Urine	cells, protein casts	
Immunology	auto antibodies: ANCA, rheumatoid factor, antinuclear antibody	RA, SLE, PAN
X-ray	chest, bones	malignancy, myeloma
Lumbar puncture	protein	GBS, CIDP
Electrical	NCS	axonal versus demyelinating
Skin slit smears/biopsy	acid fast bacilli	leprosy

Management of neuropathy

The first principle of management is to diagnose and treat the underlying cause of neuropathy. High dose corticosteroids are used in neuropathies complicating vasculitis and chronic inflammation. Other forms of immunosuppression include intravenous immunoglobulin (IVIG) and plasma exchange (PE). These are used in GBS but these are unavailable to all

but the largest medical centres in Africa. Pain is controlled by local and general measures. Local measures include application of heat, and topical anaesthetics. General measures include analgesics, anti inflammatories, tricyclics, the antiepileptic drugs carbamazepine, pregabalin and gabapentin and also opiates (Chapter 20). Weak or paralysed limbs may be assisted with orthoses. General advice is given to prevent ulcers by wearing protective foot wear and avoiding injury. The most common or important individual neuropathies are presented below.

Key points

- main causes of neuropathy are HIV, diabetes, leprosy & ART
- history and examination provide clues to diagnosis & aetiology
- neuropathies are either sensory or motor or a mixture of both
- investigations involves bloods, csf examination and X-rays
- main aim is treat the underlying cause & to control symptoms

INDIVIDUAL NEUROPATHIES

HIV

HIV frequently affects peripheral nerves. The main mechanisms are direct HIV infection and autoimmunity (Chapter 8). The most common neuropathy in HIV is a distal sensory neuropathy (DSN) secondary to HIV infection itself and to ART. Less common neuropathies include Bell's palsy and inflammatory neuropathies including Guillain-Barre syndrome.

Distal sensory neuropathy (DSN)

DSN is the main HIV related neuropathy and occurs as a result of direct HIV infection triggered immune activation affecting peripheral nerves (Fig.11.8). It affects about one quarter of AIDS patients, occurring mostly but not exclusively in more advanced HIV disease with CD4 counts <200/cm^3.

The main symptoms of DSN are a painful, hot, burning, numbness or paraesthesia like sensation occurring symmetrically in a foot and stocking distribution, developing slowly over weeks and months. Power is usually maintained but may very occasionally be decreased around the ankle joint. The ankle and infrequently the knee reflexes are absent or decreased and this may be the only sign to indicate the presence of DSN. Sensation involving touch is mostly intact but touch is characteristically perceived by the patient as painful or dysaesthetic, particularly when touched crudely on the soles of the feet and the palms of the hands. Vibration and pinprick may be impaired distally in the feet in advanced disease. The upper limbs are typically unaffected apart from the dyaesthesia in the palms.

The mainstay of management is to start ART as soon as possible. Symptomatic relief of pain may be obtained using simple analgesics and/or amitriptyline; however opiates may be necessary in severe cases.

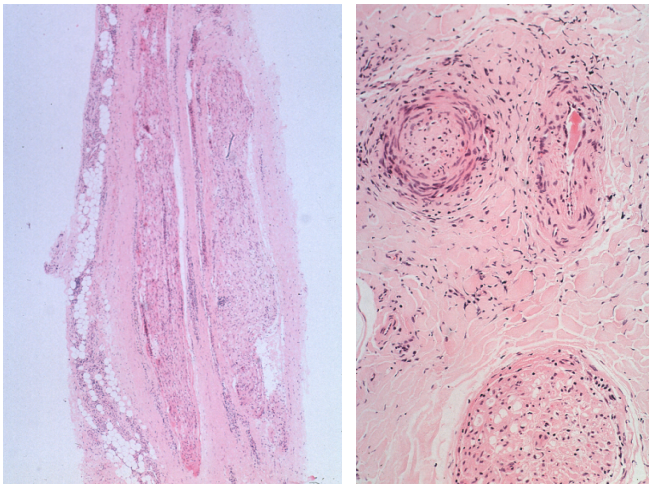


Figure 11.8 DSN in HIV, histopathology. Perineural inflammation.

ART associated neuropathy

Peripheral neuropathy may also occur as an adverse effect of antiretroviral therapy. The symptoms and signs are very similar to HIV related neuropathy, although the sensory signs may be more marked in ART neuropathy. Both HIV and ART related neuropathy are termed DSN. In Sub-Saharan Africa, DSN is one of the main limiting side effects of first line ART. In particular this occurs with the use of the nucleoside reverse transcriptase inhibitor, stavudine (d4T). The incidence of DSN in HIV has been shown to increase with the use of d4T, in particular with 40 mg dosage and its duration of use. DSN may affect up to 20% of patients who have been on dT4 for 6 months or more and this increases the overall rate of DSN in HIV to >40%.

Management involves either reducing the standard dose of d4T from 40 to 30 mg (as recommended by WHO) or stopping and replacing d4T or the likely causal ART drug. Two thirds of patients may improve if switched to a non d4T regime. Other ART drugs associated with peripheral neuropathy include didanosine (ddl), lamivudine (3TC) and zalcitibine (ddC). Known risk factors for DSN include a history of previous or active antituberculous therapy, older age, alcohol use and malnutrition. Care should be taken to ensure that pyridoxine 20 mg/po/daily has been prescribed in all patients taking isoniazid, and that thiamine 100 mg/po/daily should be given in suspected cases of B-1 vitamin deficiency. Otherwise symptomatic management is the same as in HIV disease.

Bell's palsy

Bell's palsy or facial nerve palsy is the most frequent presentation of mononeuritis in HIV infection (Chapter 8). On screening during the acute phase of the HIV epidemic in some areas in Africa as many as 50% of patients presenting with Bell's palsy tested positive for HIV. Bell's palsy occurs typically during the asymptomatic phase of HIV infection when the patient feels otherwise well and is still relatively immunocompetent. The facial weakness develops over 24 hours and the clinical course is similar to that in non HIV associated Bell's palsy, however it may occasionally be bilateral. Facial nerve palsy onsets during the later stages of

HIV infection occur mostly in association with opportunistic infections involving the CNS, mainly meningitis.

Inflammatory neuropathies

Guillain Barre Syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy may also occur in association with HIV infection. These occur during the otherwise asymptomatic phase of HIV infection when immunity is relatively intact. They are both relatively uncommon forms of neuropathy but may be the first clinical indication of underlying HIV infection. Their mechanism is considered to be autoimmune based. Clinically GBS in HIV is indistinguishable from non HIV associated GBS apart from the presence of a number of lymphocytes in the CSF possibly due to the concurrent HIV infection. The management and the prognosis is the same as in non HIV associated demyelinating neuropathies.

Key Points

- neuropathy in very common in HIV disease
- most common is DSN in 40% of patients
- mechanisms are direct HIV infection, ART toxicity & autoimmunity
- management includes starting ART & reducing/stopping offending drug
- frequency of GBS & Bell's palsy are increased in HIV infection

LEPROSY

Leprosy is a chronic progressive potentially disabling granulomatous disease of the skin, and or peripheral nerves caused by *Mycobacterium leprae*. It causes damage to nerves which results in characteristic deformity and disability. It used to be the commonest cause of neuropathy worldwide but since the introduction of multi drug therapy (MDT) in the late 1980s over 15 million cases of leprosy worldwide have been treated successfully. Despite a reported decline in the incidence of leprosy, there are still a quarter to half a million new cases reported worldwide each year with most occurring in India. Africa accounts for over 40,000 newly reported cases annually. The countries with the highest incidence in Africa are the DRC and Mozambique.

Transmission

Leprosy is transmitted by inhalation of aerosolized nasal secretions from an infected person. Effective transmission requires regular prolonged close household or community contact with an infected person. The incubation period from infection to clinical disease varies from months to up to 30 years. The average incubation of contracting the disease from contact household cases is estimated to be about 5 years. Touching does not spread the disease.

Clinical features

The clinical features are determined by the host immune response. The main clinical presentations are anaesthetic skin lesions and peripheral neuropathy.

Host response

The majority of persons infected with *M. leprae* never develop clinical disease and this represents an effective host response. When disease does develop the clinical spectrum corresponds with the degree of T cell mediated immunity of the patient. Leprosy has a wide range of clinical presentations ranging from polar tuberculoid (TT) through borderline to polar lepromatous

(LL) (Figs. 11.9-10). While TT leprosy represents a good but still ineffective cell mediated immunity, LL represents little or no cell mediated immunity.

In TT at histology there are high levels of cell mediated immunity with granuloma formation and very few if any bacilli seen on histology, which limits the disease to a single or few well defined anaesthetic skin patches or palpable nerve trunks. This is in contrast to LL where there are no granuloma and many bacilli which result in multiple, bilateral, symmetrical skin and nerve lesions which are consequently more extensive and slowly progressive (Fig. 11.10).

In between, there are borderline states ranging from paucibacillary disease in borderline tuberculoid (BT) with 3-5 skin lesions with local palpable enlarged nerves to multibacillary disease in borderline lepromatous (BL) with multiple skin lesions with variable sensory loss and symmetrical nerve enlargement.

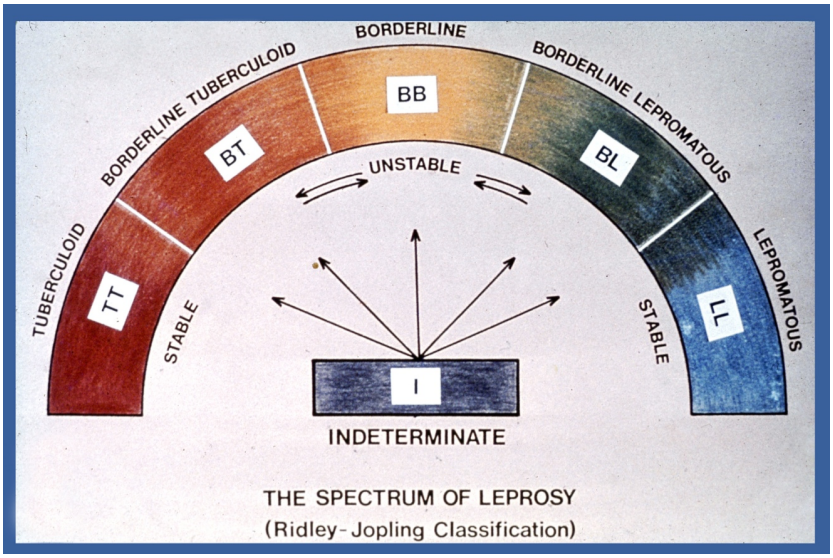


Figure 11.9 Immunological spectrum of leprosy

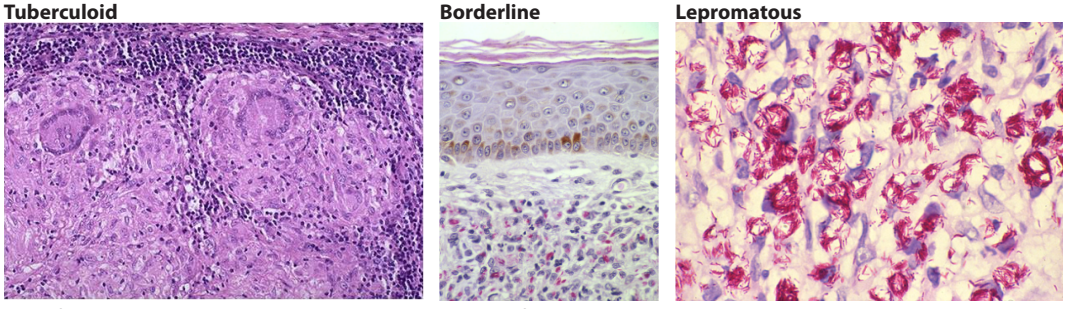
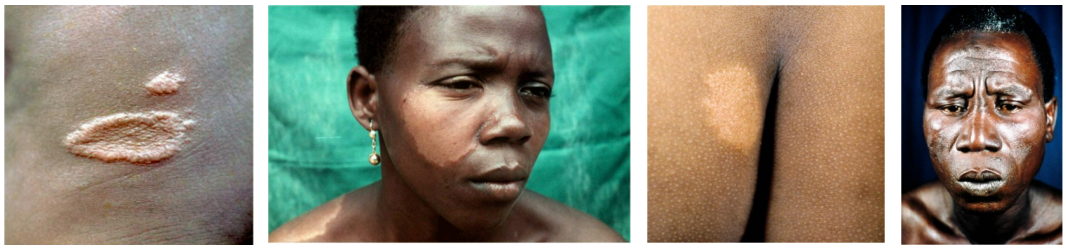


Figure 11.10 Histopathology leprosy

Skin

The skin lesions in leprosy vary with type, stage and immunity. The most common are plaques and macules but papules and nodules also occur. In tuberculoid leprosy there are single or few well circumscribed hypopigmented lesions with sharp borders. These are macular or plaque-like hypoanaesthetic patches often with loss of sweating and occurring usually on the trunk (Fig. 11.11). In lepromatous leprosy there are multiple, widespread, symmetrical, hypopigmented lesions with mostly intact sensation and/or infiltrated patches, papules and nodules. Widespread skin infiltration of the face results in the classical "leonine facies" of lepromatous leprosy (Fig. 11.11). All suspected skin lesions should be tested carefully for light touch, pain, temperature and for sweating.



TT BT Indeterminate LL

Figure 11.11 Skin in leprosy

Nerves

The main sequela of untreated leprosy is chronic disability secondary to nerve damage. Patients with leprosy present with skin lesions, muscle wasting, weakness or numbness in a peripheral nerve distribution or a burn or an ulcer in an anaesthetic hand or foot (Fig. 11.19). Nerve damage in leprosy occurs at two main levels; at the level of peripheral nerves and their main branches in TT and at the level of the small nerve twigs in skin and subcutaneous tissues in LL.

In TT, there is localized and asymmetrical involvement of the peripheral nerves. This occurs near the surface of the skin, where they present with palpable, thickened sometimes tender nerves and loss of neurological function in the distribution of the nerve. The common sites are the greater auricular in the neck, the ulnar at the elbow, median at the wrist, radial cutaneous at the wrist, common peroneal at the knee and posterior tibial behind the medial malleolus (Figs. 11.12-13).

In LL the dermal nerves are destroyed and there is a symmetrical peripheral neuropathy with a peripheral glove and stocking sensory loss.

Borderline leprosy produces most nerve damage as multiple nerves are involved earlier and more rapidly than in LL. Patients typically present with new skin lesions, nerve pain and sudden nerve palsies.

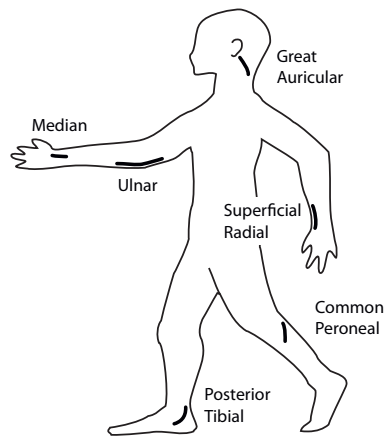


Figure 11.12 Sites to examine for enlarged nerves in leprosy

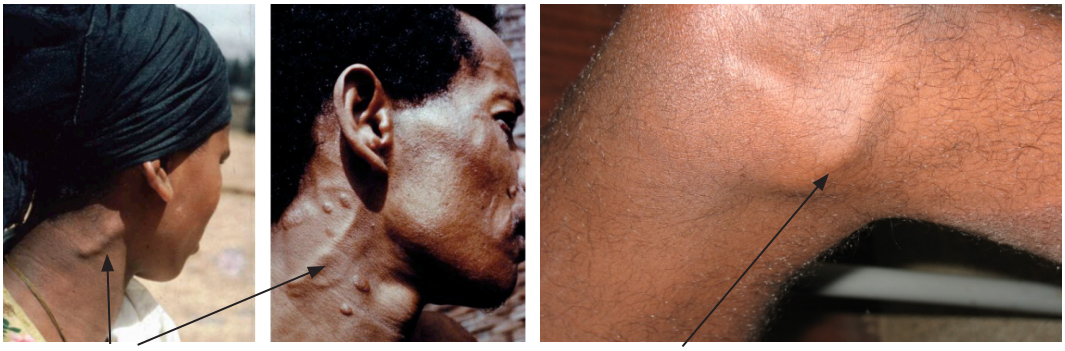


Figure 11.13 Nerve enlargement in leprosy

Neurological findings

There is a wide spectrum of sensory and motor neurological findings in leprosy. The sensory findings range from a subtle loss or decrease of temperature, pain, touch and sweating in a single skin patch in TT to a widespread peripheral neuropathy with evidence of sensory loss in the cooler extremities in LL. The sensory loss in LL may involve the extensor surface of the legs, feet, forearms and hands, nose, cheeks, breasts, abdomen and buttocks with sparing of the palms soles and scalp. An abrupt transition to normal sensation on the scalp is called the "hairline sign". Marked single or multiple peripheral nerve damage can occur in TT leprosy resulting in wrist drop, claw hand, dropped foot or failure to close an eye (lagophthalmos) (Figs.11.14-15). Motor findings in LL present as distal weakness of the intrinsic muscles of hands and feet. Loss of peripheral reflexes, joint position and vibration sense are typically late findings in leprosy being preserved early on in the disease.

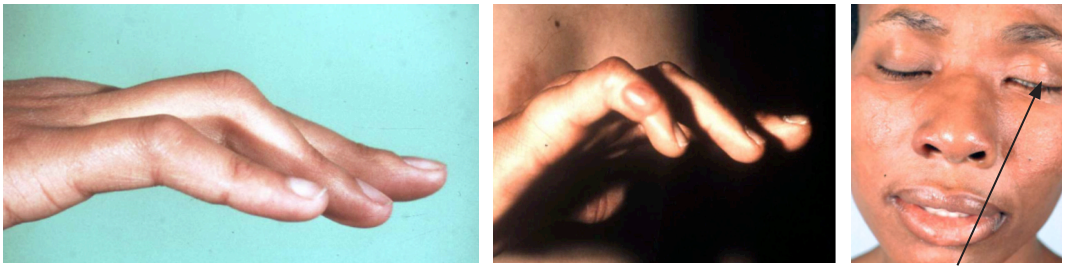
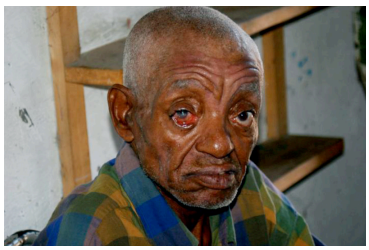


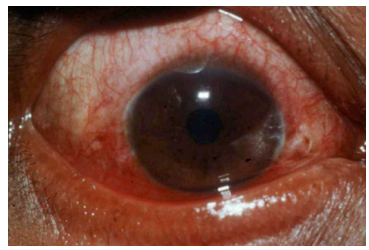
Figure 11.14 Nerve damage in leprosy

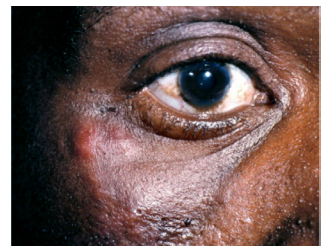
Eyes

Damage to the eye results from involvement of both trigeminal and facial nerves. This results in a loss of sensation on the cornea and inability to close and protect the eye (Fig. 11.14). A minor injury may result in corneal scarring and blindness. Direct massive invasion of the cornea can occur mainly in LL causing conjunctivitis, iritis and eventually blindness (Fig. 11.15).



Ectropion & blindness





Iritis & blindness

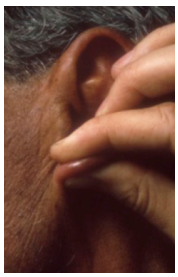
Figure 11.15 Eye damage in leprosy

Diagnosis

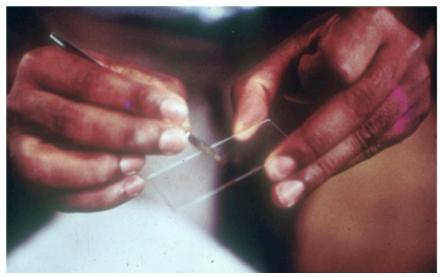
The diagnosis of leprosy is above all a clinical one and early diagnosis is crucial to management. The diagnostic features are hypopigmented patches with definite loss of sensation (Fig. 11.11) (however skin lesions in BL/LL may not have sensory loss), palpably thickened peripheral nerves (Figs. 11.12-13) and the presence of acid fast bacilli in slit skin smears or biopsy. Samples are taken from the ear lobes (Fig. 11.16), eye brows and the edges of active lesions. The density of bacilli on slit skin smears is called the bacterial index (BI). WHO classifies leprosy as paucibacillary (PC) when no bacilli are seen and multibacillary (MB) when bacilli are seen. If more than five skin lesions are seen, this is also classified as MB disease regardless of the absence of bacilli on skin smear. This method is used when slit skin smears are not available.

Diagnostic features of leprosy

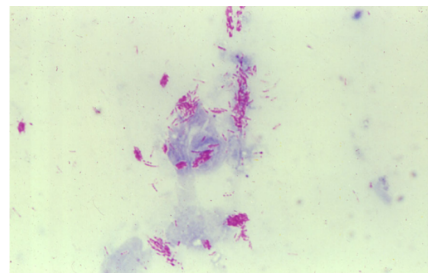
- skin lesions with sensory loss
- thickened peripheral nerves
- acid-fast bacilli on slit skin smears or biopsy



Slit ear lobe



Scrape & smear evenly on glass slide



AFB+++

Figure 11.16 Slit skin smear

Differential diagnosis

The differential diagnosis for neuropathy in leprosy includes mononeuropathies, sensorimotor polyneuropathies, hereditary neuropathies and syringomyelia. Amyloid and neurofibromatosis also can cause nerve thickening mimicking leprosy. While the typical pattern of skin and neurological involvement help to establish the diagnosis in leprosy particularly in endemic areas, a keen index of suspicion is always necessary especially in non endemic areas.

Key points

- leprosy is chronic infection of skin and nerves caused by M. leprae
- a major cause of disabling peripheral neuropathy in Africa
- findings explained by variation in degree of cell mediated immunity
- neurological features: numbness or weakness in individual nerves & polyneuropathy
- diagnosis: anaesthetic skin lesions, thickened peripheral nerves & AFBs in skin snips

Treatment

Education of the patient about their disease has been identified as the most important strategy in successful management of leprosy. The key areas are an understanding of its low infectivity, importance of drug compliance, an awareness of reversal reactions, the critical need for care of anaesthetic feet and hands and social issues.

The main aim of treatment is to cure the patient without residual permanent disability. The treatment of leprosy depends on whether it is lepromatous or tuberculoid in type. All patients should receive multiple drug treatment (MDT); for 6 months in TL or paucibacillary disease and for 12-24 months in LL or multibacillary disease. The treatments include dapsone, clofazamine and rifampicin and are outlined in Table 11.4. Patients are no longer infectious after 72 hours of treatment. Relapse rates range from 0 to 2.5% in paucibacillary disease to 0-8% in multibacillary disease. The main side effects of MDT include red urine discolouration with rifampicin, red-brown discolouration of the skin with clofazamine and haemolysis with dapsone, particularly in patients with G6PD deficiency. Nerve damage in leprosy can occur before, during and after MDT. The main mechanism of nerve damage after starting MDT is by reactions (Table 11.5).

Table 11.4 MDT regimes (WHO)

Type of Leprosy	Drug Treatment				
	Daily (self administered)		**Monthly** (supervised)	**Length, months**	**Side effects**
Paucibacillary	dapsone 100 mg	and	rifampicin 600 mg	6	haemolysis (G6PD), allergy, hepatitis, red urine
Multibacillary	clofazimine 50 mg dapsone 100 mg	and	rifampicin 600 mg clofazimine 300 mg	12-24	red skin, ichthyosis

Reactions

The clinical course of leprosy can be made acutely worse by reversal reactions. These can be precipitated by drug therapy (MDT), pregnancy and other illnesses. These are two main types of reactions, type 1 reversal reactions and type 2 erythema nodosum leprosum (ENL) reactions (Table 11.5). Type 1 reactions tend to occur in immunologically unstable borderline patients, (BT, BB and BL) upgrading towards tuberculoid leprosy during the first or second year of

MDT or after treatment. It occurs in about 30% of BL patients. The peak time is within the first 2 months of treatment. They present with acute inflammation, erythema, oedema and tender nerves, sometimes with dramatic loss of nerve function (Fig.11.17). Short course steroids are used for 3-4 months in BT and 6 months in BL patients. Erythema nodosum leprosum (ENL) type 2 reaction occurs in about 20% of LL and in 10% of BL patients (Fig.11.18). Patients with a high bacterial load are more at risk. It presents with fever and crops of small pink nodules mainly over the extensor surfaces. Systemic and nerve involvement are also common. To suppress the inflammation repeated short courses of steroids may be necessary and clofazamine is also used. Thalidomide has been successfully used in young men. However, it is relatively contraindicated in young females because of the high risk of teratogenesis mainly phocomelia and has not therefore been licensed in the majority of centres.

Table 11.5 Reversal reactions on treatment

Classification	Leprosy risk group	Frequency	Clinical features	Occurrence	Management
Type 1 (reversal)	borderline leprosy	30%	**skin:** erythema, oedema hands and face mainly **nerves:** tender & loss of function in nerve distribution	1) within the first 2 months of treatment 2) within 12/12 or after Rx 3) puerperium	prednisolone 40-60 mgs daily decreasing by 5 mg every 2-4 weeks for 3-6 months
Type 2 (ENL)	lepromatous borderline lepromatous	20% 10%	**skin**: crops of painful pink nodules **others:** fever uveitis/iritis, arthritis neuritis orchitis	1) within the first or second year of treatment 2) may occur years after treatment 3) pregnancy, lactation	prednisolone 1mg/kg/day/2-3/52 weeks only clofazimine 300 mg daily for 2/12, followed by 200 mg daily for 2/12 thalidomide 400 mg daily (use in men) for months

Complications

The complications of leprosy arise as a result of nerve damage leading to deformity and disability. This occurs through loss of pain sensation leading to trauma, burns, tissue damage, injury and secondary infection. The main complications are ulceration, osteomyelitis, foot and wrist drop, contractures, loss of digits and blindness (Fig. 11.19). Prevention is by patient education about the early recognition of the disease, reactions, complications and the initiation of appropriate treatment. Teaching patients about their disease is most important. The patient needs to be particularly aware of risk and guard an anaesthetic limb by protective measures including special footwear and routine daily inspection for signs of trauma. Ulcers should be treated with rest, surgical debridement and antibiotics if infected. Reconstructive surgery is helpful in contractures and in eye complications.

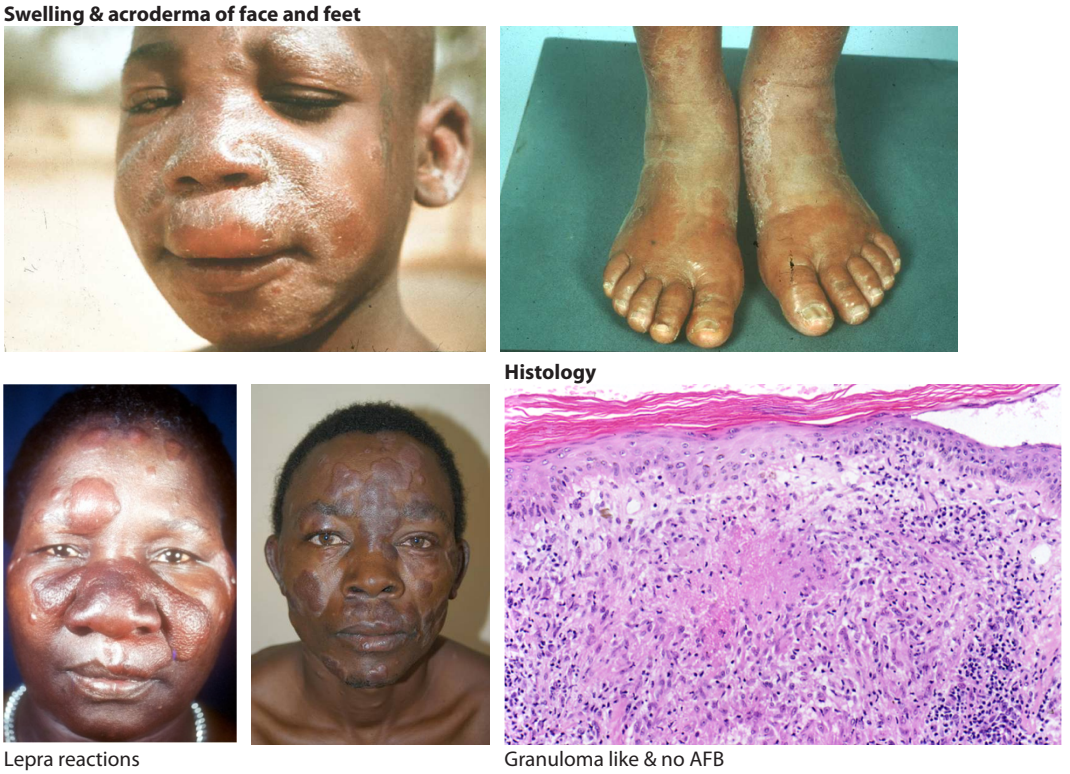


Figure 11.17 Type 1 reversal reactions

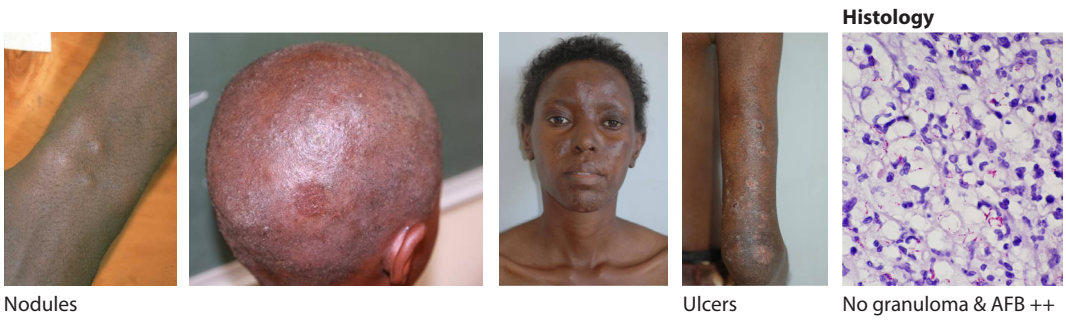
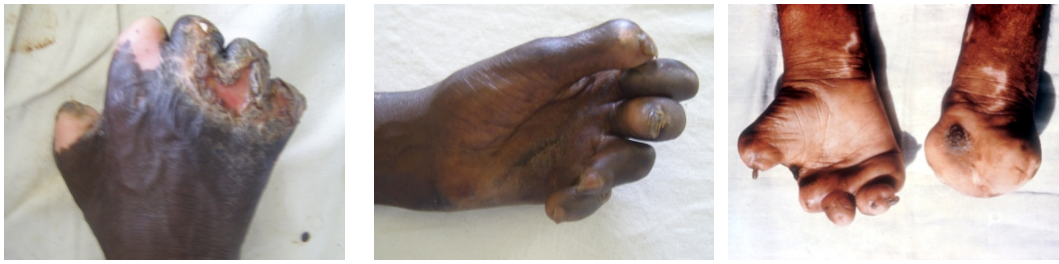


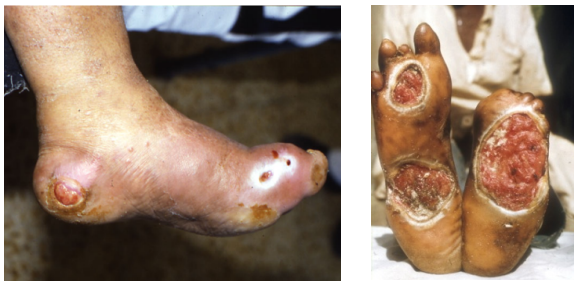
Figure 11.18 Type 2 reversal reactions, ENL

Prevention

The mainstay of the prevention of leprosy in endemic areas is by passive case finding and then directly observed treatment (DOTS) rendering the patient non-infectious to others. Chemoprophylaxis of close contacts may also be an effective strategy in the future and studies are underway to assess its role. BCG gives variable (>50%) protection against clinical leprosy.



Ulceration & loss of digits



Ulceration & osteomyelitis

Figure 11.19 Complications of leprosy

Key points

- educating the patient about their disease is best way to manage leprosy
- Rx includes MDT & compliance, awareness of reactions & prevention of disability
- complications occur as a result of nerve damage causing anaesthesia and weakness
- they include ulcers, osteomyelitis, foot/wrist drop, contractures, loss of digits & blindness
- prevention of leprosy is by passive case finding, DOTS & BCG vaccination

DIABETES

Diabetic neuropathy is the most common type of neuropathy worldwide. It is present in about one in ten diabetic patients at diagnosis and in the majority of patients 25 years later on. The main finding is a slowly progressive distal sensory neuropathy (DSN) starting in toes and gradually spreading up to knees and later to fingers and hands. It is characterized by numbness, tingling, pain, decreased sensation in the feet and legs and areflexia. Autonomic neuropathy may occur and its main clinical features include orthostatic hypotension, gastroparesis and impotence. Infrequently diabetes may cause isolated mono and multiple neuropathies. The most common ones are 6th and 3rd cranial neuropathies, femoral neuropathy and radiculopathies affecting the lumbar and sacral nerve roots. Management is by strict control of blood glucose levels, treatment of neuropathic pain and the prevention of foot and leg ulcers much in the same way as in leprosy.

Key points

- neuropathies are very common in diabetes
- DSN is the most common neuropathy
- isolated mononeuropathies may also occur
- treatment involves control of glucose, pain and prevention of complications
- blood sugar should be checked in all patients with unexplained neuropathies

VITAMIN DEFICIENCY

The main causes of neuropathy due to vitamin deficiency are B-1 (thiamine), B-6 (pyridoxine) and B-12 (cobalamin).

Vitamin B-1 deficiency

Thiamine (B-1) deficiency causes beriberi and Wernicke-Korsakoff-Syndrome (WKS). Beriberi can be dry or wet. Dry beriberi results in a sensory motor polyneuropathy while wet beriberi results in cardiac failure and generalised oedema. Beriberi in Africa is mainly caused by malnutrition arising from food shortages and also occasionally from alcoholism. WKS is an encephalopathy which can be acute or chronic. The usual cause is thiamine deficiency in alcoholism. Acute WKS is characterized by confusion, amnesia, ataxia and nystagmus and ocular paralysis. When WKS becomes chronic, it is characterized by an irreversible confabulatory type dementia with a devastating loss of short term memory. Treatment for both conditions is by thiamine replacement either intravenously or orally. The response is variable in acute or mostly none at all in chronic WKS. The dose of thiamine is 100 mg/daily. It is essential to first replace the missing thiamine before giving intravenous dextrose or treating infections or replacing other vitamins, as failure to do this can precipitate an irreversible WKS.

Vitamin B-6 deficiency

Pyridoxine (Vit B-6) deficiency causes a mainly sensory neuropathy. The main cause in Africa is isoniazid in TB treatment. It can be prevented by giving pyridoxine 20-50 mg orally daily, whenever isoniazid is used. Overdoses of vitamin B-6 may actually cause neuropathy so it is important to avoid doses greater than 100 mg daily.

Vitamin B-12 deficiency

Cobalamin (Vit B-12) deficiency causes a polyneuropathy, sub acute combined degeneration of the cord (SACD), optic atrophy, dementia and pernicious anaemia. Vitamin B-12 deficiency may be less common in Africa than in high income countries. The main clinical findings of the neuropathy are absent ankle jerks, loss of peripheral sensation (especially joint position and vibration) in combination with brisk knee reflexes and up going plantar responses. The main causes are nutritional deficiency and malabsorption of B-12. Malabsorption may be due to lack of intrinsic factor and diseases of the terminal ileum. Treatment is with hydroxycobalamin (Vit B-12) 1 mg (1000 micrograms) intramuscular injections on alternate days for a total of five injections or 5 mg. This is followed by 1 mg injections every 3 months for life. In the absence of severe malabsorption, replacement can be given orally at a dose of 1 mg daily.

ALCOHOL

Alcohol misuse is an increasingly common cause of neuropathy worldwide. Apart from malnutrition related thiamine deficiency, alcohol causes a direct effect on nerves by the toxic effect of its metabolites. It presents with a history of a slowly progressing burning dysasthesia mainly in the feet and legs over months or years in a person misusing alcohol. On examination, there are signs of a distal sensory motor neuropathy usually without significant loss of power. Treatment is to stop the alcohol and replace thiamine (Vit B-1) although painful symptoms frequently persist. Tricyclics and/or the antiepileptics may be helpful for treatment.

Key points

- Vitamin B deficiencies occur mainly because of food shortages & disease
- B-1 (thiamine) deficiency causes beriberi and WKS
- B-6 (pyridoxine) deficiency occurs with isoniazid in TB treatment
- B-12 (cobalamin) deficiency causes neuropathy treatable with B-12 injections
- chronic excessive alcohol may result in a painful persistent sensory neuropathy

GUILLAIN-BARRE SYNDROME (GBS)

GBS is an immune mediated demyelinating polyneuropathy. It is an uncommon disease affecting about 2/100,000 each year. It presents as an acute progressive usually ascending flaccid paralysis that reaches its peak usually around 10-14 days but always by definition in less than 4 weeks. This is followed by a plateau phase and eventual recovery for most patients after 3-6 months. Two thirds of cases are associated with a history of preceding febrile illness, diarrhoea, immunization or surgery during the previous 2-3 weeks. Preceding causes of fever associated with GBS include campylobacter jejuni, cytomegalovirus, and other respiratory and gastrointestinal infections. HIV infection is associated with an increased risk of GBS and patients with suspected GBS should be screened for HIV.

Clinical features

The presenting complaint is that of a rapidly developing motor weakness occurring over days and sometimes hours. Sensory symptoms, mainly paraesthesiae, often painful may accompany the weakness but these are usually mild. Motor weakness is usually marked early on both proximally and distally. Reflexes are diminished or absent. Sensation is mostly intact but may be impaired. There is no sensory loss on the trunk. Sphincters are spared. Lower motor neurone type facial weakness occurs in about half the patients but may be mild and is frequently bilateral. Other cranial nerves may be involved. Respiratory failure and autonomic symptoms occur in over a fifth of patients. The main complications and cause of death in GBS are respiratory failure, pneumonia, cardiac arrhythmias and pulmonary embolism. The differential diagnosis includes other causes of acute flaccid paralysis. These include transverse myelitis, organophosphorous poisoning, diphtheria, polio, botulinum and lead poisoning. Chronic inflammatory demyelinating polyneuropathy is a more chronic form of GBS with a slower onset, over 2-3 months and responds well to steroids.

Investigations

These include a full blood count, HIV test, blood glucose, creatinine and electrolytes. A lumbar puncture should be carried out to check for the characteristic elevation in CSF protein in

the absence of white blood cells (WBC <5/mm^3). The CSF protein may be normal during the first week of the illness and this may need repeating during the second or third week. If available, nerve conduction studies will show marked slowing of motor conduction velocities characteristic of a demyelinating polyneuropathy.

Key points

- GBS typically presents with acute rapidly progressing limb weakness over 1-2 weeks
- lower back and proximal limb pain may be an initial presenting complaint
- facial nerve palsies may be present
- approximately two thirds have a recent (2/52) history of either diarrhoea or a febrile illness
- diagnosis is supported by elevated csf protein without WBCs

General management

The outcome of GBS depends on the quality of nursing care. The patient should be initially placed in an intensive care unit. Nursing care is directed at checking for signs of increasing weakness, respiratory failure and the prevention of bedsores and contractures. The vital signs and in particular the vital capacity should be measured 4 hourly for the first few days of the illness. If the vital capacity falls to the range of 1.5-1 litre, then assisted ventilation must be considered. The heart should be monitored for arrhythmias and any surges in blood pressure treated with beta blockers. Compression stockings and low dose heparin are used to prevent deep vein thrombosis and pulmonary emboli. A nasogastric tube may need to be passed if swallowing is a concern. The patient may need analgesia for pain and psychological support. Physiotherapy should be started on admission.

Specific treatments

Steroids have no role in the treatment of GBS. Specific treatments include intravenous immunoglobulin (IVIG) or plasma exchange (PE). IVIG is the treatment of choice but both are equally beneficial. Disease progression, respiratory failure and significant disability are all indications for their use and they should be administered within the first 2 weeks of onset of the illness, as they are not of value after that time. Their main role is to halve the average period of hospital stay from about 12 to 6 weeks. However, these treatments are mostly unavailable because of their high cost and limited resources.

Prognosis

The mortality in GBS in Africa is around 10%. Recovery in the remaining 90% is good but some (10-20%) remain partially disabled at 12 months.

Key points

- acute care involves regular monitoring for respiratory failure i.e. FVC <1.5 litres
- main complications are respiratory failure, pneumonia, arrhythmia & pulmonary emboli
- specific treatments include IVIG & PE
- CFR in Africa is about 10%, with most patients recovering fully after 3-6/12

CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY (CIDP)

CIDP is similar to GBS but follows a chronic progressive course over months rather than weeks. It is very uncommon but represents a treatable neuropathy. The cause is not known. The clinical features are characterized by a mixed motor sensory peripheral neuropathy usually with proximal as well as distal weakness. Cranial nerves and autonomic system are not usually involved. The results of investigations are similar to GBS with elevated protein in CSF and evidence of demyelination on NCS.

Treatment is with high dose steroids prednisolone initially 60 mg/od for 4-6 weeks, reducing slowly over months until on a minimum maintenance dose of 5-20 mg on alternate days. IVIG or plasma exchange can also be used as in GBS. Azathioprine or methotrexate can be added as steroid sparing agents. Response to immunosuppression is good but may have to be continued in the longer term.

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