CHAPTER 3

Neurological Presentations

Neurological presentations are more common in the tropics than in the developed industrial world. Infectious diseases make a major contribution, but non-infectious causes are also important (Table 3.1). A complex mixture of socioeconomic and environmental factors contribute to the increased incidence.

Reasons for increased incidence of neurological disorders in the tropics

• Non-infectious neurological disorders—trauma is more common in the tropics, especially road traffic accidents. Patterns of vascular disease are catching up with those in the developed world, but the usage of drugs to control them lags behind.

• Infectious neurological diseases—the climate supports transmission of insect-borne pathogens (malaria, trypanosomiasis, arthropod-borne viruses). Environmental factors include the close proximity of homes to zoonotic infections. Vaccine-preventable diseases are more common (e.g. measles, tetanus, diphtheria, polio). There is also unregulated use of over-the-counter antibiotics, leading to the partial pretreatment of central nervous system (CNS) infections, which hampers diagnosis and therapy, and promotes the development of antibiotic resistance.

• Poverty, overcrowding, poor sanitation and lack of education about disease risk factors and prevention are important. These may lead, for example, to cysticercosis and typhoid.

• Immunosuppression, particularly as a result of HIV, allows many other infections such as cryptococcal and tuberculous meningitis.

Neurological syndromes

Neurological diseases—particularly infections—can present with a range of syndromes.

• *Encephalopathy*—a reduced level of consciousness from any cause (infectious, metabolic, vascular, traumatic).

• *Meningism*—clinical signs of meningeal irritation (headache, neck stiffness, Kernig's sign; see below).

• *Paralysis*—weakness of one or more limb, respiratory or bulbar muscles, which may be a result of damaged upper motor neurones, lower motor neurones, peripheral nerves, or muscles.

• *Chronic neurological presentations*—insidious presentation over weeks or months, often with changes in personality, behaviour or other psychiatric illness. Fever may not be prominent, even with an infectious cause (Table 3.2).

• *Headache*—may be the only symptom (e.g. in cryptococcal meningitis).

• *Other focal neurological signs*—including hemispheric signs, brainstem signs, seizures and movement disorders.

CAUSES OF NEUROLOGICAL DISEASE

Vascular
Ischaemia/infarct
Subarachnoid/subdural/extradural/intracerebral haemorrhage
Hypertension/hypotension

Infectious
Direct effect on CNS
Bacteria
- Meningococcus, streptococci, *Haemophilus influenzae*, tuberculosis, leprosy

Viruses
- Arboviruses, herpes viruses, enteroviruses, rabies

Parasites
- Protozoans
  - malaria *(Plasmodium falciparum)*
  - African trypanosomiasis (*Trypanosoma gambiense* and *T. rhodesiense*)
  - toxoplasmosis (*Toxoplasma gondii*)
  - amoebiasis *(Entamoeba histolytica)*
- Trematodes (flukes)
  - paragonimiasis
  - schistosomiasis (especially *Schistosoma japonicum*)
- Cestodes (tapeworms)
  - cysticercosis (*Taenia solium*)
  - hydatidosis (*Echinococcus granulosus*)
- Nematodes (roundworms)
  - ascariasis (*Ascaris lumbricoides*)
  - parastrongyliasis (*Parastrongylus cantonensis*)
  - gnathostomiasis
  - trichinosis (*Trichinella spiralis*)

Spirochetes
- Neurosyphilis (*Treponema pallidum*)
- Lyme disease (*Borrelia burgdorferi*)
- Leptospirosis (*Leptospira* species)
- Louse-borne/epidemic relapsing fever (*B. recurrentis*)
- Tick-borne/endemic relasing fever (*B. duttonii*)

Rickettsiae
- Epidemic/louse-borne typhus (*Rickettsia prowazekii*)
- Endemic/murine/flea-borne typhus (*R. typhi/R. mooseri*)
- Scrub typhus (*O. tsutsugamushi*)
- Rocky Mountain spotted fever (*R. rickettsii*)

Fungi
- Cryptococcosis
- Histoplasmosis
- Aspergillosis
- Coccidioidomycosis
- Candidiasis
- Paracoccidiomycosis
- Blastomycosis
- Nocardiasis*

Indirect effect of infection
Toxin-mediated infectious diseases (tetanus, diphtheria, shigellosis)
Immune-mediated postinfectious inflammatory (GBS, acute disseminated encephalomyelitis)

Metabolic
Hypoglycaemia
Diabetic ketoacidosis
Hepatic encephalopathy
Uraemia
Hyponatraemia
Hypothyroidism/hyperthyroidism
Addison's disease

Tumours/trauma/toxins
Alcohol
Drugs (medical, recreational, traditional)
Pesticides
Poisons

Other
Hydrocephalus
Epilepsy
Psychiatric disease (hysteria)
Inflammatory
Nutritional
Degenerative

Abbreviations: CNS, central nervous system; GBS, Guillain–Barré syndrome.
*Nocardia are actinomycete bacteria which are grouped with fungi because of their morphology and behaviour.

Table 3.1 Causes of neurological disease (VIMTO).

CHRONIC NEUROLOGICAL PRESENTATIONS

Infectious	Other
Sleeping sickness (especially *Trypanosoma rhodesiense*, *T. gambiense*)	Tumours
Tuberculous meningitis	Chronic subdural haemorrhages
HIV encephalopathy	Lead, other heavy metal poisoning
Toxoplasma gondii and other parasitic space-occupying lesions	Dementia
Bacterial abscesses	Vitamin deficiencies
Partially treated bacterial meningitis	Drugs
Neurosyphilis	Toxins
Cryptococcal meningitis and other fungi	
Subacute sclerosing panencephalitis	

Table 3.2 Causes of chronic neurological presentations in the tropics.

Pathological processes

These neurological syndromes are explained by a range of pathological processes.

- *Encephalitis* — inflammation of the brain substance, usually in response to viral infection, but also in response to other pathogens.
- *Meningitis* — inflammation of the meningeal membranes covering the brain, in response to bacterial, viral or fungal infection.
- *Myelitis* — inflammation of the spinal cord. This may occur across the whole cord (causing transverse myelitis, which is often postinfectious) or be confined to the anterior horn cells.
- *Neuropathy* — damage to peripheral nerves (e.g. Guillain–Barré syndrome, diphtheria, leprosy, rabies, vitamin deficiencies).
- *Space-occupying lesions* (Table 3.3) — these cause pathology in the brain or spinal cord directly (by interrupting neuronal pathways), and indirectly (by causing localized swelling, raised intracranial pressure and brainstem herniation syndromes). Typically, they present with focal signs or a chronic insidious deterioration.

CNS SPACE-OCCUPYING LESIONS

- Tumours and metastases
- Haemorrhage
- Bacterial abscesses
- Tuberculomas
- Parasites
  - Protozoa (toxoplasmosis, amoebiasis)
  - Trematodes (paragonimiasis, schistosomiasis)
  - Cestodes (cysticercosis, hydatidosis)
  - Nematodes (ascariasis)
- Fungi
  - Aspergillosis, blastomycosis, nocardiasis

Table 3.3 Causes of central nervous system space-occupying lesions in the tropics.

Rapid assessment of patient with coma in the tropics

1 Stabilize the patient, and treat any immediately life-threatening conditions.

- Airways.
- Breathing — give oxygen; intubate if breathing is inadequate or gag reflex impaired.
- Circulation — establish venous access.

Obtain blood for immediate bedside blood glucose test (hypoglycaemia?).

Malaria film (look for parasites and pigment of partially treated malaria).

FBC, U&E, blood cultures, arterial blood gases.

- Disability.

Give intravenous (i.v.) glucose (e.g. 10% glucose 50 mL in adults, 5 mL/kg in children), irrespective of blood glucose.

Give adults 100 mg thiamine i.v., especially if alcohol abuse is suspected.

Immobilize cervical spinal cord if neck trauma is suspected.

• Rapidly assess AVPU scale (alert, responds to voice, to pain, or unresponsive).

If patient responds to pain or is unresponsive, examine the pupils, eye movements, respiratory pattern, tone and posture for signs of cerebral herniation (see below).

If herniation is suspected start treatment for this.

• If purpuric rash is present give penicillin or chloramphenicol (or third generation cephalosporin) for presumed meningococcal meningitis (after taking blood cultures).

• Look for and treat generalized seizures, focal seizures and subtle motor seizures (mouth or finger twitching, or tonic eye deviation).

2 Take a history, while preliminary assessment and resuscitation proceeds. This is the single most useful tool in determining the cause of coma. In particular:

• Duration of onset of coma.

Rapid onset (minutes–hours) suggests a vascular cause, especially brainstem cerebrovascular accidents or subarachnoid haemorrhage. If preceded by hemispheric signs, then consider intracerebral haemorrhage. Coma caused by some infections (e.g. malaria, encephalitis) can also develop rapidly, especially when precipitated by convulsions.

Intermediate onset (hours–days) suggests diffuse encephalopathy (metabolic or, if febrile, infectious).

Prolonged onset (days–weeks) suggests tumours, abscess or chronic subdural haematoma (see Table 3.2).

• Any drugs?

• Any trauma?

• Important past medical history (e.g. hypertension)?

• Family history (e.g. tuberculosis)?

• Known epidemic area (e.g. viral encephalitis)?

3 Perform a rapid general medical examination, and in particular:

• Check pockets for drugs.

• Note temperature (febrile or hypothermia) and blood pressure (hypo- or hypertensive).

• Examine for signs of trauma (check ears and nose for blood or cerebrospinal fluid (CSF) leak).

• Smell the breath for alcohol or ketones (diabetes?).

• Examine the skin for:

rash (meningococcal rash, dengue or other haemorrhagic fever, typhus, relapsing fever);

needle marks of drug abuse;

recent tick bite or eschar (tick-borne encephalitis, tick paralysis, tick-borne typhus or relapsing fever);

chancre, with or without circinate rash (trypanosomiasis, especially *Trypanosoma rhodesiense*);

healed dog bite (rabies); or

snake bite.

• Examine for lymphadenopathy (e.g. Winterbottom's sign of posterior cervical lymphadenopathy in African trypanosomiasis).

• Examine the fundi for papilloedema (long-standing raised intracranial pressure) or signs of hypertension.

4 Determine the coma score to allow subsequent changes to be accurately monitored. The scale in Box 3.1 is for adults and children over 5 years of age and in Box 3.2 for young children.

5 Neurological examination. A detailed description of the neurological examination is beyond the scope of this chapter. For most practical purposes the ability to recognize the following four clinical patterns (and combinations of them) will allow appropriate classification and subsequent investigation and treatment.

• *Meningism* — with or without encephalopathy.

• *Diffuse encephalopathies* — usually metabolic or infectious.

• *Supratentorial focal damage* (above the cerebellar tentorium) — usually manifests as hemispheric signs.

• *Damage in the diencephalon or brainstem* (midbrain, pons or medulla) — may indicate a syndrome of cerebral herniation through the

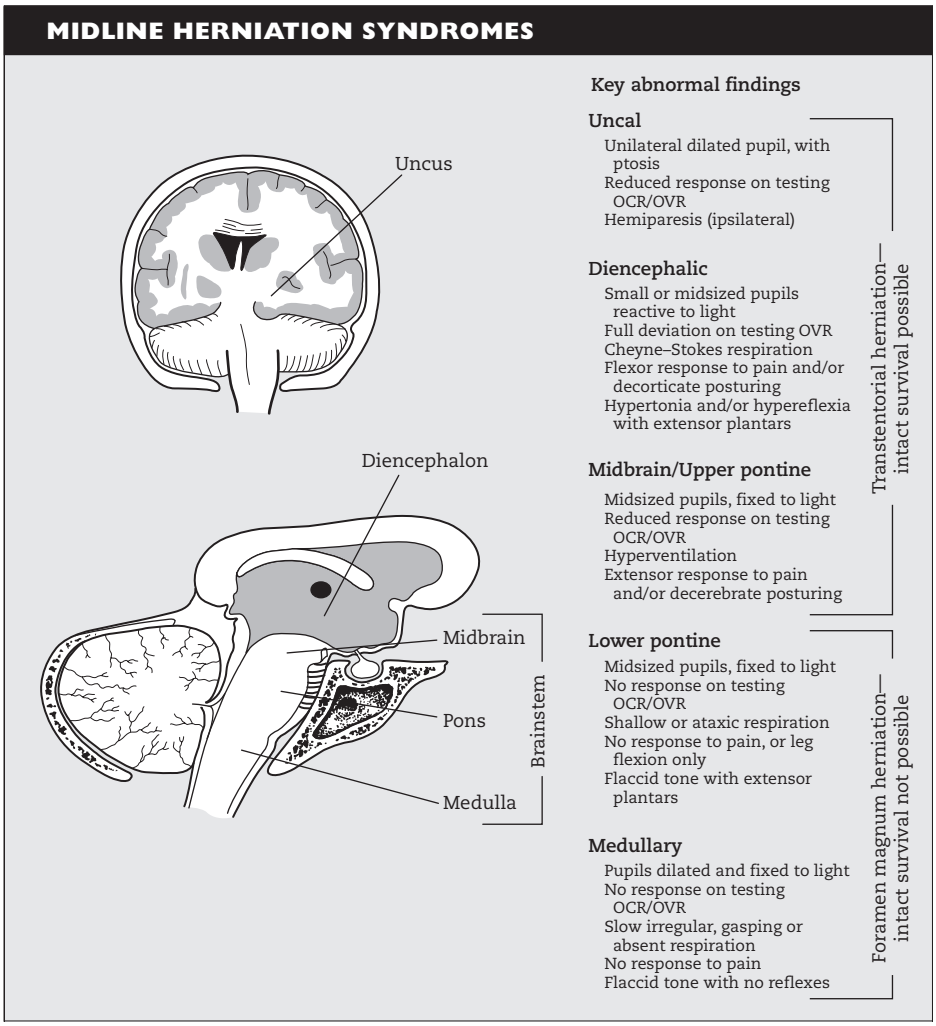

Fig. 3.1 Sagittal section of brain showing anatomy and key abnormal findings of midline herniation syndromes, and (above) coronal section showing herniation of the uncus of the temporal lobe—this compresses the ipsilateral third nerve (to cause a palsy of CNIII), and the contralateral cerebral peduncle (to cause an ipsilateral hemiparesis).

tentorial hiatus or the foramen magnum (Fig. 3.1). The importance of these syndromes is being increasingly recognized in non-traumatic coma (particularly that caused by infections). Although the level of brainstem damage is given in brackets below (and in Fig. 3.1), recognizing the presence or absence of brainstem signs, and in particular early signs of reversible damage, is usually more important than determining their exact localization.

Assessment of the following five points allows most patients to be classified.

1 Check for neck stiffness (if no trauma), and Kernig's sign (extension of knee when hip is already flexed causes pain).

COMA SCALE FOR ADULTS AND CHILDREN OVER 5 YEARS

Best motor response
6 Obeys command
5 Localizes supraorbital pain
4 Withdraws from pain on nail bed
3 Abnormal flexion response
2 Abnormal extension response
1 None

Best verbal response
5 Oriented
4 Confused
3 Inappropriate words
2 Incomprehensible sounds
1 None

Eye opening
4 Spontaneous
3 To voice
2 Pain
1 None

Box 3.1 Modified Glasgow coma scale for adults and children over 5 years. Total score is the sum of best score in each of the three categories (maximum score 15). 'Unrousable coma' reflects a score <9

BLANTYRE COMA SCALE FOR YOUNG CHILDREN

Best motor response
2 Localizes painful stimulus
1 Withdraws limb from pain
0 Non-specific or absent response

Best verbal response
2 Appropriate cry
1 Moan or inappropriate cry
0 None

Eye movements
1 Directed (e.g. follows mother's face)
0 Not directed

Box 3.2 Blantyre coma scale for young children. Total score is sum of best score in each of three categories (maximum score 5). 'Unrousable coma' reflects score <2

2 Examine pupil reaction to light (Fig. 3.1). A normal reaction (constriction) is seen in a diffuse encephalopathy. A unilateral large pupil is seen in herniation of the uncus of the temporal lobe. The pupils are reactive (small or mid-sized) in the diencephalic syndrome. Unreactive pupils occur in brainstem lesions (mid-sized in midbrain or pontine lesions; large in medullary lesions). Pinpoint pupils occur following opiate or organophosphate overdose, or in isolated pontine lesion. Other drugs can cause large unreactive pupils.

3 Assess eye movements (holding eyelids open if necessary).

- *Spontaneous eye movements*—eyes spontaneously roving or eyes following indicates the brainstem is intact (a diencephalic syndrome or a diffuse encephalopathy).
- *Oculocephalic (doll's eye) reflex*—when rotating the head, the eyes normally deviate away from the direction of rotation. A normal response indicates that the brainstem is intact (diffuse encephalopathy). Reduced or absent responses occur in uncal herniation, brainstem damage or, rarely, deep metabolic coma.
- *Oculovestibular reflex*—caloric response to water should be tested if the result of the oculocephalic reflex is unclear. Check that the eardrum is not perforated, then irrigate by injecting 20 mL ice-cold water. Nystagmus is the normal response and indicates 'psychogenic coma'. Both eyes deviate towards the irrigated ear in coma with the brainstem intact. A reduced or absent response indicates an uncal syndrome or a damaged brainstem.

4 Assess breathing pattern. A normal pattern occurs in diffuse encephalopathy. Cheyne–Stokes breathing and hyperventilation occur in reversible herniation syndromes. Shallow, ataxic or apnoeic respiration occurs in more severe syndromes (Fig. 3.1). Hyperventilation also occurs in acidosis or may be caused by aspiration pneumonia, which is common in coma.

5 Assess response to pain by applying painful stimulus to the supraorbital ridge and nail bed of each limb.

- *Hemiparesis*—most often indicates supra-

tentorial hemispheric focal pathology (other signs include asymmetry of tone and focal seizures), but also occurs in uncal herniation.

• *'Decorticate posturing'*—flexion of arms with extension of legs, indicating damage in the diencephalon, and *'decerebrate posturing'* (extension of arms and legs caused by midbrain/upper pontine damage) may both be reversible. No response, or leg flexion only, are more severe.

Symmetrical posturing (decorticate or decerebrate) and hemiparetic focal signs are also occasionally seen in metabolic encephalopathies (e.g. hypoglycaemia; hepatic, uraemic or hypoxic coma; sedative drugs), cerebral malaria, and intra- or postictally. Other pointers to metabolic disease include asterixis, tremor and myoclonus preceding the onset of coma.

Classification and further investigation of patients with coma

At this stage, if the history, general examination and preliminary investigation have not made one diagnosis extremely likely, most comatose patients will fall into one of three categories, based on the presence or absence of meningism, supratentorial and brainstem signs.

1 Coma only (no hemispheric signs, brainstem signs or meningism—'sleeping beauties').

• If patient is febrile (or has a history of fever), suspect CNS infection (especially cerebral malaria) or metabolic coma plus secondary aspiration pneumonia.

• If afebrile, coma is likely to be metabolic (hypoglycaemia, drugs, alcohol, diabetic ketoacidosis, toxins), psychogenic (test caloric response to water—causes nystagmus), or, occasionally, resulting from subarachnoid haemorrhage or other cerebrovascular accident.

2 Coma with meningism, but no focal signs.

• If febrile, CNS infection (especially bacterial meningitis) is likely.

• If afebrile, subarachnoid haemorrhage is likely.

3 Coma with focal signs (with or without meningism). Decide if the signs are 'hemispheric signs', 'brainstem signs', or both.

• *Hemispheric signs only*. If febrile, consider CNS infection (especially encephalitis, bacterial meningitis, abscess, etc.). If afebrile, consider space-occupying lesion (Table 3.3), cerebrovascular accident or trauma.

• *Brainstem signs only* may be caused by either focal pathology within the brainstem (e.g. encephalitis) especially if markedly asymmetrical signs, or by herniation of the brainstem (through the foramen magnum) secondary to a diffuse process (e.g. diabetic ketoacidosis, or late bacterial meningitis) causing raised intracranial pressure.

• *Hemispheric and brainstem signs* may be a result of either a supratentorial lesion causing hemispheric signs and sufficient swelling to precipitate brainstem herniation (e.g. cerebral bleed, abscess) or patchy focal pathology in the hemispheres and brainstem (e.g. toxoplasmosis, viral encephalitis).

LUMBAR PUNCTURE GUIDELINES

All patients with suspected CNS infection should have a lumbar puncture, except those with the following contraindications:

• Obtunded state with poor peripheral perfusion or hypotension

• Deteriorating level of consciousness, or deep coma (responsive only to pain, GCS < 8)

• Focal neurological signs present:
Unequal, dilated or poorly responsive pupils
Hemiparesis/monoparesis (in patients with coma)
Decerebrate or decorticate posturing
Absent 'doll's eye' movements
Papilloedema

• Hypertension and relative bradycardia

• Within 30 min of a short convulsive seizure

• Following a prolonged convulsive seizure or tonic seizure

Abbreviation: GCS, Glasgow coma score.

Table 3.4 Guidelines for lumbar puncture in patients with suspected central nervous system (CNS) infections.

CSF FINDINGS

	Acute bacterial meningitis	Viral meningo-encephalitis	Tuberculous meningitis	Fungal	Normal
Opening pressure	Increased	Normal/increased	Increased	Increased	10–20 cm*
Colour	Cloudy	'Gin' clear	Cloudy/yellow	Clear/cloudy	Clear
Cells/mm^3	High–very high	Normal–high	Slightly increased	Normal–high	
	1000–50 000	0–1000	25–500	0–1000	<5
Differential	Neutrophils	Lymphocytes	Lymphocytes	Lymphocytes	Lymphocytes
CSF : plasma glucose ratio	Low	Normal	Low–very low (e.g. <30%)	Normal–low	66%
Protein (g/L)	High	Normal–high	High–very high	Normal–high	
	>1	0.5–1	1–5	0.2–5.0	<0.5

Normal values

Normal CSF opening pressure is <20 cm water for adults, <10 cm for children below age 8.

A normal CSF glucose is usually quoted to be 66% that of the plasma glucose, but in many tropical settings a cut-off of 40% is found to be more useful.

A bloody tap will falsely elevate the CSF white cell count and protein. To correct for a bloody tap, subtract 1 white cell for every 700 red blood cells/mm^3 in the CSF, and 0.1 g/dL of protein for every 1000 red blood cells.

Some important exceptions

In patients with acute bacterial meningitis that has been partially pretreated with antibiotics (or patients <1 year old) the CSF cell count may not be very high and may be mostly lymphocytes.

In viral CNS infections, an early lumbar puncture may give predominantly neutrophils, or there may be no cells in early or late lumbar punctures.

Tuberculous meningitis may have predominant CSF polymorphs early on.

Listeriosis can give a similar CSF picture to tuberculous meningitis, but the history is shorter.

CSF findings in bacterial abscesses range from near normal to purulent, depending on location of the abscess and whether there is associated meningitis or rupture.

An Indian ink test, and if negative a cryptococcal antigen test, should be performed on the CSF of all patients in whom cryptococcosis is possible.

Table 3.5 Cerebrospinal fluid (CSF) findings in central nervous system infections.

Indications and contraindications for lumbar puncture in suspected CNS infections (Table 3.4)

For many years lumbar puncture was performed in all patients with suspected CNS infections, in both the tropics and western industrialized nations. It has gone out of fashion in the latter, following concerns that it was being performed on patients with contraindications, and may have precipitated herniation.

In patients with a contraindication, treatment should be started and then a lumbar puncture reconsidered later. In many tropical settings in Africa and Asia, where CNS infections are very common, lumbar puncture is still considered an essential investigation. Here the benefits of accurate diagnosis and appropriate treatment may outweigh the theoretical risk of herniation, and even patients with relative contraindications

often receive lumbar punctures with no apparent harm.

Cerebrospinal fluid findings in CNS infections

Although most patients with CNS infections will have findings that are straightforward to interpret, there may be considerable overlap (Table 3.5). Ideally, the decision about starting antibiotics should await the result of the lumbar puncture (if it is available quickly). However, antibiotics should be started immediately for patients with a typical meningococcal rash, because of the speed with which meningococcal septicaemia can become fatal. In such patients, if it is certain that the rash is meningococcal it has been argued that the lumbar puncture is not necessary, because the diagnosis is already made, though others advocate always doing a lumbar puncture.

Further reading

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