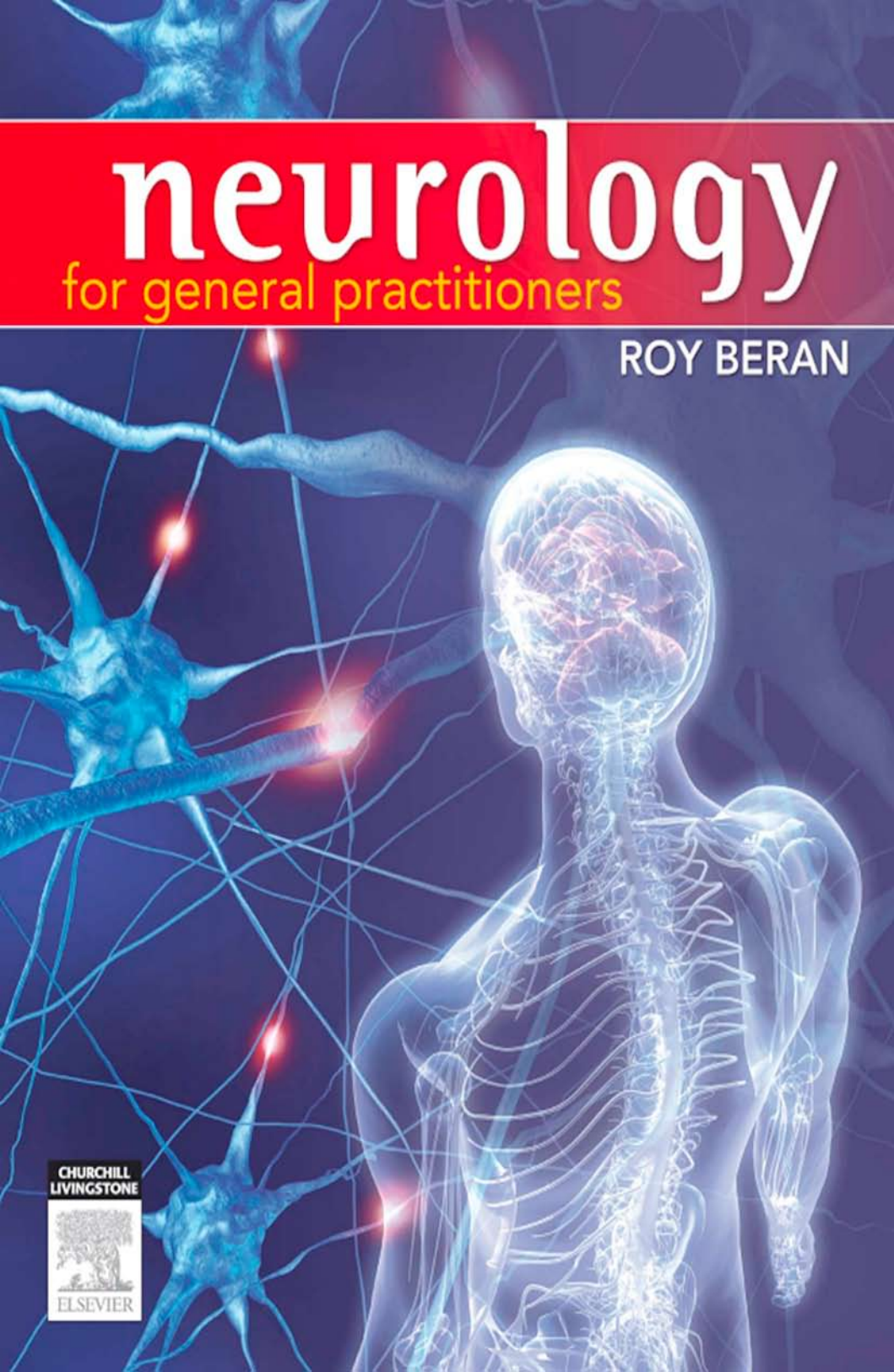
neurology

for general practitioners

ROY BERAN



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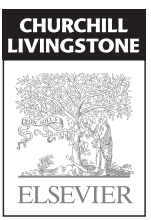

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Contents

Foreword

In this creative book, *Neurology for General Practitioners*, written by the eminent neurologist and educator, Roy Beran, we have a text presented at a most appropriate level for general practitioners. The author's stated objective was to demystify a complex discipline and avoid 'an overly complicated and patronising cookbook of neurological conditions'. He has certainly achieved this, yet at the same time presents a scholarly text with the imprimatur of an authoritative specialist.

This back-to-basics approach has undoubtedly been influenced by the author's past experience as a coalface general practitioner in suburban Sydney. This surprising fact would certainly allow the author to identify with and understand the general practice perspective, and it shows! During my long term as medical editor of *Australian Family Physician* I came to know and admire Roy for his ability to swathe through the esoteric verbiage and get to the core issues. Practitioners will be familiar with his neurology series in *Medical Observer*. He is committed to general practice education. I was subsequently delighted with his positive response to my request to act as a reviewer and mentor for the neurological component of *Murtagh's General Practice*.

In this text Roy Beran has simplified many of the complexities without sacrificing excellence.

The choice of content is particularly pleasing to the general practitioner. Many of the recognisable brain-teasing issues are addressed and this includes the common presenting problems of headache, vertigo, seizures, peripheral neuropathy and muscular disorders; not in great detail but in an economy of words and concepts. As one would expect, the author challenges the practitioner to achieve excellence in diagnostic methodology by adhering to the traditional values of good history taking and physical examination. This emphasis is reflected in the excellent chapters on neurological examination

of higher centres, cranial nerves and the peripheral nervous system. To facilitate our understanding the text is enhanced with first-class simplified illustrations. We are also challenged to think laterally as exemplified by the chapter on 'non-organic neurological disease' and other relevant nuances throughout the text, including sections on pain, sleep and lifestyle.

At last we have a commendable, user friendly, but subtly scholarly, text for the general practitioner, who is treated with respect and understanding by an experienced author. The book would be equally appropriate and valuable for students, registrars and other clinicians. It has been my privilege to be invited to write the Foreword, and I can recommend this book with sincere enthusiasm to my colleagues.

Professor John Murtagh AM, MBBS, MD, BSc, BEd, FRACGP, DipObstRCOG
Emeritus Professor, Monash University; Professorial Fellow, Department of General Practice, University of Melbourne, Victoria; Guest Professor, Peking University, Beijing; Adjunct Clinical Professor, Graduate School of Medicine, University of Notre Dame, Western Australia; Senior Examiner-Australian Medical Council and Patron of General Practitioners Registrars Association

Preface

The writing of this book was a labour of love. It began with my writing an article for the medical broadsheet, *The Medical Observer*. This led from article to article to result in a compilation that reflects my overview of neurology for General Practitioners (GPs).

The last thing GPs needed was an overly complicated and patronising 'cookbook' of neurological conditions. They did not need another set of meaningless lists, which included minutiae they would never encounter. Some of my happiest time in medicine was when I was working as a GP in the inner western suburbs of Sydney. It was then that I learnt to respect the role played by GPs in the delivery of healthcare. I learnt to understand that GPs were the vanguard in medicine.

My objective in writing *Neurology for General Practitioners* was to offer these frontline doctors some insight into my approach to neurology. I am reminded of the saying that if one gives a man a meal he is fed for a short time, but if one teaches him how to feed himself he might be fed for life.

This book was conceived as a way of repaying some of the debt that I owe to general practice. I believe it was my FRACGP that allowed me to enter neurological training more than 30 years ago. General practice taught me to accept my responsibility as a doctor, to think laterally and to deal with medicine from first principles rather than from a 'recipe book'. Lists are necessary to pass exams but medicine is more than rote learning of mindless lists. It is an intellectual challenge, which should be enriching and invigorating.

My hope is that *Neurology for General Practitioners* provides food for thought. My goal is to encourage colleagues to think for themselves. My ambition was to open a few windows or doors for others to pass through so that they may be equally affected by the joy that medicine has to offer.

Throughout my writings I reiterated that this book reflects the idiosyncratic approach of a single doctor. Not everyone will agree with some of my

dogmatic concepts. All I can say in my defence is that these concepts have served me well throughout my years as a clinician. I offer them to those who choose to read this book to accept, reject or modify. If I encourage just a few colleagues to renew their love of learning, which motivated them to be coal-face clinicians, then I have written a successful book.

I thank you for taking the time to read my offering and sincerely ask for feedback. I truly hope that at least some of you find this book worthwhile and that I can benefit from your insights to improve it into the future.

Roy G Beran

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This book has been many years in evolution, dating back to my time in general practice with Ewen Loxton and Roger Davidson in Enmore, Sydney. Ewen and Roger had a well-established practice that taught me to appreciate family medicine. During this time Ric Day and Don Frommer from St Vincent's Hospital, Sydney tutored me, for which I will be eternally grateful.

I moved to Adelaide where people like Dick Rischbeith, Andrew Black, Paul Hicks, Jim Manson and Jeremy Hallpike helped train me in neurology. Graham Schapel introduced me to clinical pharmacology, which led into clinical trials. I returned to Sydney to undertake my doctorate with Professor Ian Webster, the founding Professor of Community Medicine at the University of New South Wales (UNSW), and Professor James W Lance, the first UNSW Professor of Neurology. Having a combined appointment in community medicine and neurology is a very rare opportunity, which should not be undervalued. Professor Lance taught me never to accept anything unless its rationale made sense, and Professor Webster taught me that a commitment to community service was mandatory. I hope this book reinforces those views, although my teachers may not endorse all my hypotheses. An enduring friend from this time is Paul Spira, with our latest collaboration published in 2011. Another friend from this time is Rod Mackenzie, who introduced me to sleep medicine.

I was an intern at Liverpool Hospital, Sydney in 1973, and I am still there almost four decades later. From one neurologist, Tony Broe, who came as needed and later became a foundation Professor of Geriatrics, it grew to two, namely David Rail and myself. David always questioned what others took for granted, with most interest in chaos theory. What could be more chaotic than the road I have travelled in preparation for this book? The Department expanded, with some good friends moving on, to now claim eleven neurologists. I thank all these colleagues for their encouragement and collegial

friendship. I was dubbed ‘Uncle Roy’ and I hope this book reflects the views of an elderly uncle for my friends in general practice. One person who has been like an ‘uncle’ to me is Frank Vajda, who was always ready to advise and criticise. I know that I have omitted names of very important friends and colleagues who helped my career and I beg their forgiveness for the oversight.

The most important recognition must go to my beautiful, devoted, intelligent and wonderful wife, Maureen, who steadfastly stood by me since my last year as a medical student. She supported me as a GP, while preparing for the RACP exams, during my neurological training, while working for my doctorate and later as my practice manager. Her intellect, enthusiasm and support are unique, and without her I could not have achieved half of what I consider a very proud and worthwhile career. I must also acknowledge my four beautiful children, their partners and my grandchildren, who helped make all of this worthwhile.

Having acknowledged those doctors and family members who contributed to my career, an acknowledgement also must go to the wonderful team who has worked with me, be it in my private rooms or within the hospital. They are like family to me.

Final acknowledgement must go to the thousands of patients who allowed me to be their doctor—be it as a GP, in my younger years, or as a neurologist.

1

The neurological diagnostic consultation

INTRODUCTION

The neurological examination is really no different to any other medical examination except that it appears more impressive for the novice. There is a formula that allows maximal yield from the process.

This chapter will offer discussion of more than just the examination and will cover how to conduct the neurological diagnostic consultation.

HISTORY

The most important component of the neurological consultation is a detailed history. Many neurological illnesses lack absolute diagnostic tests and may rely exclusively on the history. It follows that the history must be as comprehensive and searching as possible.

While it is important to listen to what the patient offers as the main presenting complaint, it is equally important not to take this at 'face value'. Patients can believe all bad headaches are migraines, all disequilibrium is vertigo and all loss of consciousness is a seizure. Nothing could be further from the truth. Patients should be advised to avoid jargon and diagnostic terminology, as far as possible. Severe tension-type headache is far more common than is migraine; loss of balance due to upper respiratory tract infection and blocked Eustachian tube is more common than is true vertigo; and syncope is far more common than is seizure.

Concurrent with overuse of jargon is the use of ambiguous and ill-defined terminology, such as dizziness, giddiness, numbness, blackout or even double vision. It is imperative to ensure that message sent is the same as message received. It follows that if a term can have multiple meanings, both the patient

and clinician must agree on the meaning to be adopted. An example of this may be 'dizziness', which may mean true vertigo but could also mean light-headedness, loss of balance, disequilibrium, failure to think clearly, or even having a 'flu-like' heavy headedness. 'Numbness' can mean loss of sensation, a feeling of heaviness of a limb, pins and needles dysaesthesia, impaired movement of a limb or digits with loss of dexterity, or something quite different. It follows that the doctor must interrogate the patient to be sure that both are 'reading from the same text'. Patients may complain that the doctor doesn't believe them so it is important to be reassuring. It helps to explain the need for clarity and for avoidance of ambiguity.

Patients often misinterpret symptoms, such as reporting loss of vision in one eye, when what has happened is loss of vision in a visual field, such as homonymous hemianopia. The distinction is very important as monocular loss of vision may be amaurosis fugax, caused by impaired vascular supply to the eye as may occur with temporal (giant cell) arteritis. Monocular loss of vision is rostral, distal to the optic chiasm, while hemianopia is caudal, proximal to the chiasm. When a patient reports loss of vision in one eye it is important to ask if they have tested each eye individually, namely if covering one eye caused total loss of vision while covering the other eye allowed clear vision. This implies that covering the good eye caused binocular loss of vision, while uncovering it allowed the unaffected eye to see normally. Many patients believe left vision comes from the left eye and right vision from the right. With hemianopia it doesn't matter which eye is covered as the visual loss is the same.

With any symptom, it is important to get a clear description of what actually happened without any ambiguity. Much of this is covered in individual chapters on specific topics. Once one understands the true nature of the actual symptom, 'What is the problem' (the first 'W'), it is time to explore the other three 'W's—Where, When and Why. 'Where' is 'where in the body' (such as focal, unilateral or bilateral) and whether the demarcation is anatomically sound. 'When' asks in what situations does the symptom occur; for instance, provocative factors. An example of this is the use of alcohol, which differentiates between tension-type headaches that may be relieved by alcohol, and migraines, which may be provoked or exacerbated by alcohol. It seeks causes, such as stress, which is also important in tension-type headaches and other conditions such as benign essential tremors. 'Flashing lights' are a hallmark of photically induced seizures, and benign paroxysmal positional vertigo is provoked by rolling over in bed. 'Why' may include auxillary factors that might be important, such as exposure to toxic agents, trauma or genetic predisposition with positive family history.

Diagnosis is much easier if one knows which questions to ask. The first symptoms of Parkinson's disease may be difficulty getting out of a low chair or a low car seat, such as a sports car, or trouble turning over in bed at night. Much of this subtlety in history taking comes with experience but just asking the patient 'What did you first notice wrong?' or 'When did you first notice

TABLE 1.1 The formal approach to taking a history

History	Area covered
Presenting symptom	What caused the patient to seek medical attention?
History of present illness (the 4 'W's)	Detailed history of events leading up to the presenting symptom i **What** (presenting complaint) is causing the patient to go to the doctor? (description of the symptoms and their evaluation) ii **Where** in the body? • focal, generalised, unilateral or bilateral • radiation • is it anatomically sound? iii **When?** • provocative factors • possible causes • situations in which symptoms occur iv **Why?** • auxiliary factors often found in past and personal history
Personal history	i History of smoking ii Alcohol consumption iii Medications: name, strength, dosage iv Medical past history v Surgical past history vi Psychosocial history as may be relevant to the complaint
Symptom review	History covering symptoms relevant to other organs

things were not right?' will help. Given a chance and forced to describe symptoms in simple words rather than using jargon, which is often misunderstood by the patient, the description in plain language will greatly improve the diagnostic process.

Before leaving the discussion of history, it is important to set out the formal approach to the taking of an adequate history (see Table 1.1).

EXAMINATION

The examination starts long before the patient reaches the consultation room. An observant receptionist may diagnose sleep apnoea, with excessive daytime sleepiness, before the patient has seen the doctor. An experienced receptionist will usually identify patients with behaviour disorder in the waiting room. A good receptionist will share these thoughts with the doctor.

As already stated, difficulty getting out of a chair may alert the doctor for Parkinson's disease. A wide-based gait, looking like a drunken sailor, may suggest cerebellar disease. A white stick is self-evident for visual impairment and a hearing aid may be important for the patient complaining of 'vertigo'. There are many diagnostic gaits, such as the stooped, shuffling, unsteady gait of the Parkinsonian; the hemiparetic gait of the stroke patient; or even the flamboyant, brazen gait of the patient with a psychological disorder.

Similarly language, facial expression or facial asymmetry, ptosis, dystonic posturing or the way in which a walking aid is used (which should be different for balance problems or pain support) all provide diagnostic tools. These provide direction for the consultation. They should alert the doctor if the patient fails to mention something that is important. An example of this is the patient who complains of an unprovoked fall but shows Parkinsonian gait, expressionless face, softly spoken voice, appears younger than the stated age and is moving slowly. The astute doctor will have made the diagnosis before the consultation has commenced: the cause of the fall probably will be 'failed righting reflexes'. The consultation will then focus on this diagnosis and try to exclude the potential differential diagnoses.

In the majority of neurological cases the diagnosis is obvious once the history has been taken. This is especially so if the clinician has been observant both before the consultation (as the patient moves from the waiting area to the consultation room) and during history taking. In most cases the physical examination is largely unnecessary other than to reassure the patient that the doctor is both competent and diligent. If there is not a strong suspicion of the provisional diagnosis prior to commencing physical examination, it is unlikely that the examination will provide the answer and the missing clue. The examination should confirm the expected findings. The competent neurologist will have anticipated the findings before examining the patient. This translates into students being very impressed because the doctor can afford to be flamboyant in demonstrating the signs and even suggesting additional techniques that the doctor knows will be positive. Concurrently, patients are impressed when the doctor can predict clinical findings, thereby reassuring patients that they are in good hands.

Despite dismissing the need for physical examination, only a foolish doctor would not carry it out. It is part of patient expectation and, hence, part of the mystique that is medicine. It may also uncover other problems unrelated to the presenting complaints, such as goitre, cardiac murmur or skin lesions.

2

The neurological examination: higher centres

The neurological examination is broken down into three components:

1 higher centres
2 cranial nerves
3 peripheral neurological examination.

Each comes with its own tricks and shortcuts, and each will be explored in separate following chapters.

HIGHER CENTRE FUNCTION TESTING

Many people use tools such as the Mini Mental State Examination (MMSE) or a variety of other tests such as The Rowland Universal Dementia Assessment Scale (RUDAS) developed by a team at Liverpool Hospital in Sydney. Over the years I have developed my own tool, which I will now share. This tool takes less than ten minutes to administer and offers fairly specific answers as discussed below. Higher centre function testing is usually only necessary if cognitive impairment is the presenting complaint.

As a general rule, higher centre function testing is adequately tested in the routine consultation, taking the history and assessing patient participation and cooperation. Clinicians will form a fairly accurate assessment of higher centre function by this alone.

Where further testing of cognition is needed, as with assessment of dementia, the MMSE is mandated by the government to underwrite appropriate medication. Personally, I believe that the MMSE is an extremely blunt instrument and should only be used if so mandated to allow prescription. My alternative tool is as follows.

1 The patient is given a six-item name and address (for example, William Bourke, 61 Griffith Avenue, Waverley) and asked to repeat it correctly on three consecutive attempts and until it is correctly repeated three times. The number of times the initial material needs to be offered should be scored. The average person should not require more than ten repetitions of the data to repeat it three times correctly. This tests immediate recall and allows transfer from the metaphoric RAM (random accessed memory) to hard drive. Once the material is correctly repeated three times, the patient is advised that an alarm has been set and they will be asked why it was set when it goes off in five minutes. The reason will be to see if the patient can remember that the alarm was set for a reason, what that reason was, and then repeat the six-item name and address. Most people can remember why the alarm was set, and personal experience suggests the average patient will recall three or four out of the six items. This tests immediate memory, five-minute recall, compliance and cooperation. It does contain a cultural element as the name and address is Australian based, but the recall of why the alarm was set does not reflect cultural bias.

2 Once Step 1 has been completed and the backwards timer is set, the remainder of the higher centre function testing can take place. This distracts the patient to allow proper five-minute recall rather than the patient practising and thus only testing immediate recall rather than five-minute recall.

3 Within the Australian context the patient is asked the name of the prime minister, state premier, day and date. This tests orientation in time and place as well as awareness of current affairs with an element of memory testing. Most will know at least day and date, and many will offer politicians' family names if prompted with given names.

4 The next test is 'Serial 7s'. Patients are asked to sequentially deduct 7 from 100, 7 from the response (i.e. 93) and 7 from that—until asked to stop. Once the patient reaches '30' the sequence recurs, thus if the patient correctly states 100, 93, 86, 79, 72, 65, 58, 51, 44, 37, 30, it is my practice to stop at 30. The average person loses concentration when the answer is '44'. The most common error is 100, 93, 84 but this still shows good arithmetic skills: (a) the patient correctly subtracts 100 – 7 to achieve 93; (b) then subtracts 3 from 93 to achieve the 80s; (c) then subtracts 3 from 7 to get 4; (d) but rather than subtracting 4 from 90 the patient adds 4 to 80, hence the answer 84. This demonstrates anxiety rather than dyscalculia. Serial 7s test calculation (eloquent dominant hemisphere function), visual spatial orientation (spatial non-dominant hemisphere function) and the connections between the hemispheres to coordinate both hemispheres (corpus callosum). It also assesses concentration and anxiety levels. It is important to determine which of these factors has provoked an error if one occurs, as demonstrated above with the '84' response.

5 The patient is then asked to manipulate 29×3 to achieve 87. Once the correct answer is given the patient is asked for the method used. The intelligent, sophisticated calculation is $30 \times 3 = 90 - 3 = 87$. This demonstrates capacity for lateral thinking and equates to proverb testing. The traditional method of long multiplication $9 \times 3 = 27$; $20 \times 3 = 60$; $60 + 27 = 87$ demonstrates a degree of concrete thinking.

6 Next in higher centre testing is 5-digit repeat and reverse. The patient is given a 5-digit number and asked to repeat the number in the sequence given and then to recite it in reverse order. As part of the instructions the patient is provided the example of 1, 2, 3, 4, 5 followed by 5, 4, 3, 2, 1 to demonstrate what is expected. The average patient should be able to complete the process with no more than ten attempts. Should the patient have trouble giving the number in its correct forward order, the number should be repeated for the patient before the next attempt. The failure to perform the task is recorded as one of the attempts, and the attempt after the repetition of the number constitutes the next attempt. The number of times the base number is provided should also be recorded but does not constitute one of the ten attempts. This tests immediate recall, visual spatial orientation, concentration and may also provide the best indicator of organic pathology if there is a perseverative error; for example, the reverse of 1, 2, 3, 4, 5 is repeatedly given incorrectly as 4, 3, 5, 2, 1 despite being advised that this was incorrect. If the patient successfully completes the 5-digit repeat and reverse sequence then a 7-digit number is provided. The average patient can repeat the 7-digit number but cannot correctly reverse it, even after ten attempts.

7 The next step is to test dominant parietal lobe function by asking the patient to name: a watch, strap, clasp and hands of a wristwatch. Other questions include the lapel of a jacket and the cuff of a sleeve. These test for nominal dysphasia, but such items as the lapel of a jacket may be culturally and socio-economically reflective so this needs to be considered.

8 Receptive dysphasia and right/left dissociation is tested by asking the patient to place the right hand over the left ear and then the left hand over the right eye.

9 Finger agnosia and right/left dissociation is tested by asking the patient to indicate the right index finger, the left middle finger and so on. This also further tests receptive dysphasia.

10 Constructional dyspraxia and visual/spatial orientation is tested by asking the patient to draw a clock face (analogue) with the hands set at 10:45 hours (Fig 2.1). The reason for selecting this time is because it further tests receptive dysphasia as it is somewhat more complex and further it requires both the hands to be set on the left-hand half of the clock face, thereby further testing non-dominant hemisphere function due to the

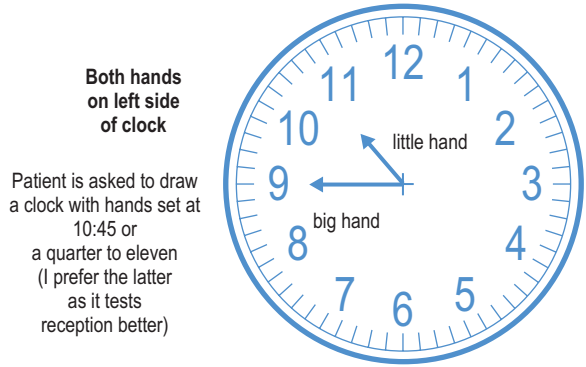


FIGURE 2.1 Clock.

potential for left-sided neglect. Clock drawing tests constructional dyspraxia as well as left-sided neglect.

11 Within the Australian context, the final test is to ask the patient to draw a map of Australia with a capital letter identifying each capital city at an appropriate spot on the map. This tests educational standard, visual/spatial orientation and constructional dyspraxia (Fig 2.2).

Dressing and undressing, as part of the physical examination, is also part of higher centre function testing. Inability to dress is known as dressing dyspraxia and is further evidence of non-dominant hemisphere dysfunction.

It is not enough to know which tests to perform as it is equally important to appreciate what is being tested and what the results mean. The above tool describes both the test and the modality tested. It also offers suggested limits of normality based on experience of the average patient (see Box 2.1 on p. 10). A patient achieving below average for a test has demonstrated a localised problem, such as memory problem with possible temporal lobe dysfunction. This helps direct further investigations.

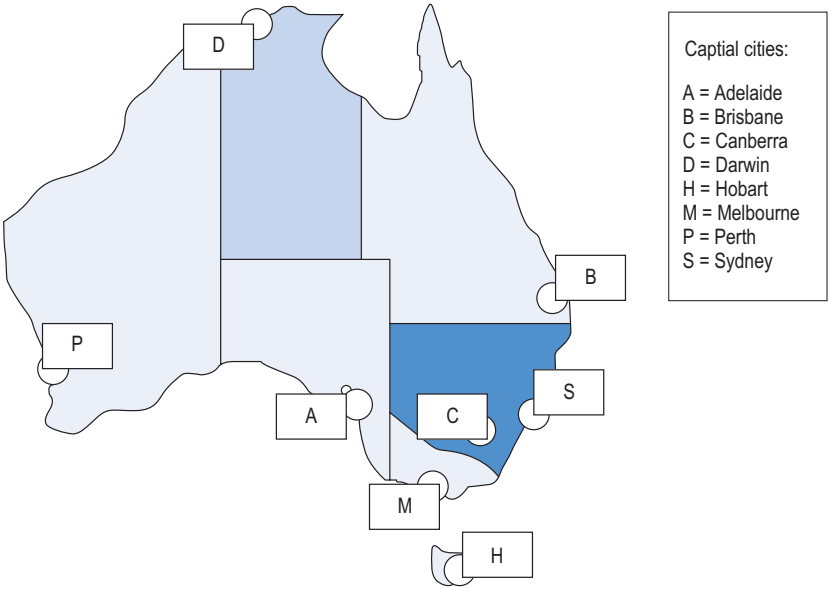


FIGURE 2.2 Map of Australia.

BOX 2.1 Testing cognition: summary

A Memory testing (a) immediate recall and (b) five-minute recall

a The patient is given a six-item name and address and asked to repeat it correctly three times without error.

Abnormal: Most can do this with less than ten repetitions of the six items.

b After three correct repetitions, an alarm is set to sound in five minutes, and the patient told to remember:

i why the alarm was set

ii to recall the six-item name and address.

Abnormal: Most know:

i why the alarm was set

ii can recall at least three of the six items.

B Orientation in time and place and current affairs

Patients are asked to name the prime minister, state premier, day and date.

Abnormal: Most will know:

i day and date

ii only politically aware will know politicians.

C Calculation, visual spatial orientation, concentration and interhemispheric connections

Serial sevens: 100 – 7 = 93 – 7 = 86 – 7 = 79 …

Abnormal: Most people retain concentration to 44.

D Calculation and lateral thinking

29 × 3 = 87. The method adopted to achieve the result tests lateral versus concrete thinking, which is important.

8 × 3 = 27, 20 × 3 = 60, 60 + 27 = 87 (concrete/traditional thinking)

30 × 3 = 90 – 3 = 87 (lateral thinking)

Abnormal: Most can do this but how it is done is important.

E Immediate recall, visual spatial orientation concentration and perseveration

i Patients are asked to repeat and reverse the sequence of a five-digit number.

Abnormal: Most can do this within ten attempts.

ii Once achieved (i), repeat with a seven-digit number.

Abnormal: Most cannot do this even after ten attempts.

F Dominant hemisphere function

The patient is asked to: name common objects (looking for nominal dysphasia); perform complex tasks (place right hand over left eye—looking for receptive dysphasia plus right/left dissociation); and name fingers on right or left hand (looking for finger agnosia and right/left dissociation).

G Non-dominant hemisphere function

The patient is asked to draw common objects (such as a clock face) to test for constructional ability.

3

The neurological examination: cranial nerves

CN I (OLFACTORY NERVE)

Smell, if tested, requires soft musks, floral and ketone smells rather than astringents, such as ammonia or cloves. The reason for this is that astringents are also noxious. They may stimulate trigeminal (CN V) nerve endings in the nose, causing perception of the stimulus even with completely severed CN 1. Each nostril is tested individually and not necessarily with a different scent, so that the patient is asked if the test scent is the same or different in each nostril. Often the patient will say they are different when they are the same, making interpretation difficult.

A CN 1 palsy should alert the GP to the possibility of a meningioma of the olfactory groove. This is a slow growing tumour that may be ignored because its effects come on slowly. The patient may not be aware that they have lost the sense of smell. Loss of smell, associated with the flu, may be permanent. Sensation of smell and taste are intertwined so a patient complaining of altered taste may be identifying problems with smell.

CN II (OPTIC NERVE)

This requires four separate tests: field, fundi, acuity and pupils.

Fields are tested by confrontation, by standing in front of the patient and randomly wiggling fingers in each of the four quadrants of the visual fields (Fig 3.1).

The patient is asked to point at the wiggling fingers, and at times it is worth wiggling fingers in more than one quadrant to encourage the patient to pay extra attention. If this test suggests abnormality, then each eye should be tested individually by covering the other eye. The crude test has the doctor

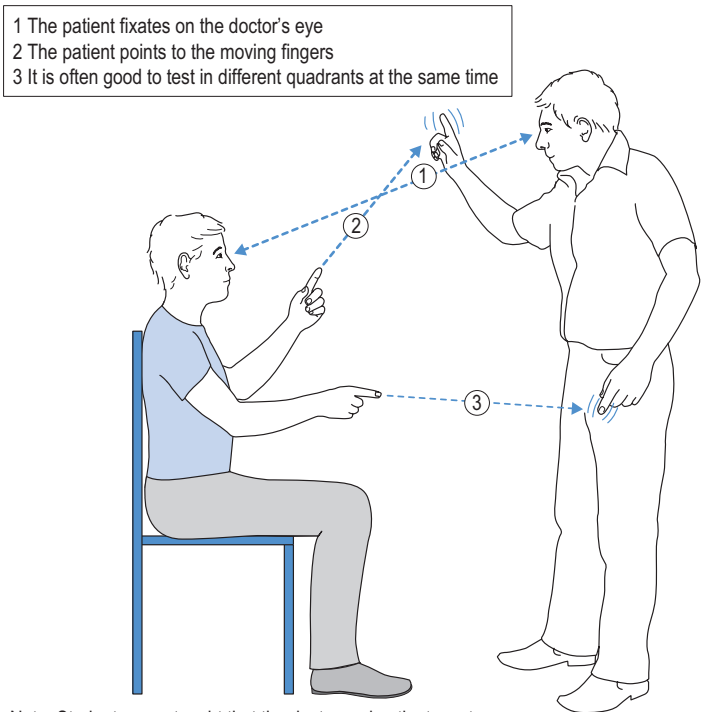


FIGURE 3.1 Testing visual fields.

wiggle the finger in each of the four quadrants of the visual field and the patient must identify the wiggling finger. More sophisticated testing has the doctor move the fingers in on the diagonal in each quadrant (see Fig 3.2).

The patient is asked to indicate as soon as the finger is seen, and the doctor compares this to their own perception of the finger to see if there is parity between doctor and patient. Use of a red object, such as a red pin, produces a more precise definition of the field of vision. The patient is asked to nominate when the pin is clearly perceived as red, thereby relying on colour vision, rather than a relatively large moving object. Loss of vision must respect the horizontal and vertical meridians to be anatomically sound (see Fig 3.2).

When the patient is uncooperative and will not point to the moving finger or object, an alternative method for testing visual fields is to use 'menace'. Menace employs a motion as if the examiner is going to poke the patient in the eye, either with a fist or flattened hand, stopping just short of the point of contact. If the patient has preserved vision within the quadrant being tested,

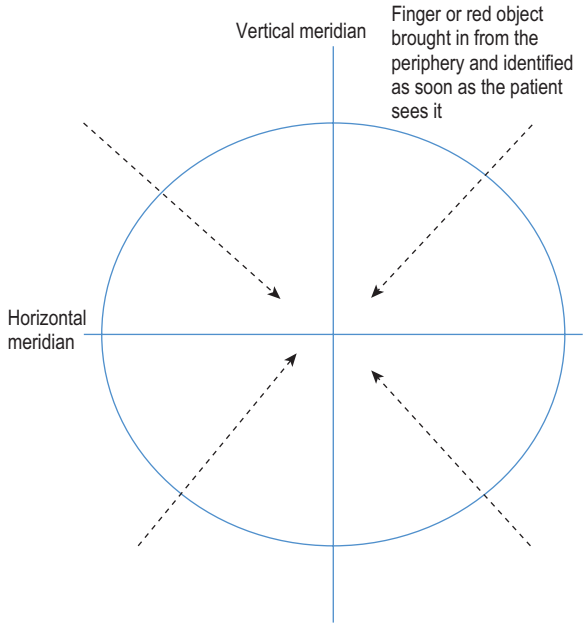


FIGURE 3.2 Testing visual fields.

it is almost impossible for the patient to avoid blinking. This is an innate, self-protective reflex evoked by the patient seeing the menacing object, such as a fist, approach. Failure to blink in the face of such menace suggests blindness in the fields being tested. It is not absolute but it is very suggestive.

Fundi are tested using an ophthalmoscope. It is important to use the right eye to examine the right eye, to approach the patient from directly in front to avoid the forehead covering the line of vision of the other eye (the one not being examined) and to place the disc (that is, optic nerve) where it is most convenient to view it, rather than looking for it. The way to do this is to ask the patient to look at a convenient object that allows the examiner to approach using that line which follows an imaginary line drawn between the object and the eye (Fig 3.3).

Once the optic nerve has been identified the doctor needs to examine it for colour, contour and for signs of raised intracranial pressure. Asking someone who has little experience of ophthalmoscopy to note colour changes is often difficult but if it looks very white, rather than golden yellow, it suggests optic atrophy. If it is very pink it may reflect increased pressure. These are value judgments that may be too hard to call.

The optic disc contains within it an internal ‘cup’. If this is very obvious it may simply be a variant of normal but it may also herald the first sign of

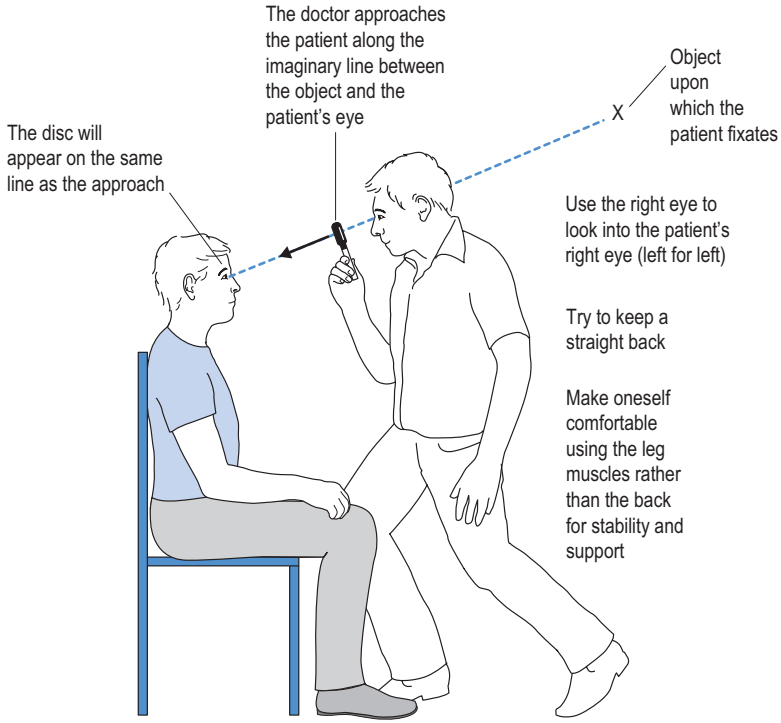


FIGURE 3.3 Ophthalmoscopic examination.

glaucoma and, hence, if noted, should alert the examiner to seek measurement of intraocular pressure from either the optometrist or ophthalmologist.

If the disc margins are 'blurred', this may reflect any number of normal conditions, such as medullated nerve fibres (fibres with myelin still in place) but it may also reflect papilloedema. Papilloedema is usually accompanied by haemorrhages and an angry looking disc (see Fig 3.6). Perhaps the first sign of papilloedema is a loss of venous pulsations, which can be seen in 90% of normal people. To seek out venous pulsations, the operator must identify the disc and focus upon it. The relative ratio of arteries to veins is 2:3, with the veins being the wider and darker vessels. The doctor selects the end of the vein before it disappears into the nerve, and focuses on that end. If venous pulsations are present then the vein will fill and empty while being observed. Alternatively, the vein may change from fatter to thinner in

rhythmic fashion while pulsating. The presence of venous pulsations automatically excludes the presence of raised intracranial pressure but, as already stated, up to 10% of the normal population do not demonstrate such pulsations. Thus, absence of venous pulsations need not reflect raised intracranial pressure, while their presence excludes it (see Figs 3.4 and 3.5).

If, after numerous attempts, it is impossible to gain access to the disc through the lens, the doctor must question if there is opacity of the lens and, hence, presence of cataracts. This too should result in referral to the ophthalmologist. Often doctors were taught to look for the 'red reflex' but most will not know exactly what this is nor how to identify it. It follows that it is not a helpful tool.

While not directly part of CN II testing, when examining the eyes it makes sense also to look for ptosis (droopy eyelid). Ptosis may obscure the pupil from fundoscopy. If it is necessary to hold the eyelid up while performing fundoscopy, then ptosis should be considered. Equally, pupillary examination is part of CN II examination and pupil size helps to differentiate causes of ptosis. It follows that this is the time to remember to look for ptosis, even though the only cranial nerve palsy to actually cause ptosis is CN III, discussed below.

There are basically only four causes of ptosis:

1 Horner's syndrome: small pupil, droopy eyelid, loss of sweating on forehead and an impression of sunken eye
2 CN III palsy: larger pupil, droopy eyelid and eye possibly deviated down and out

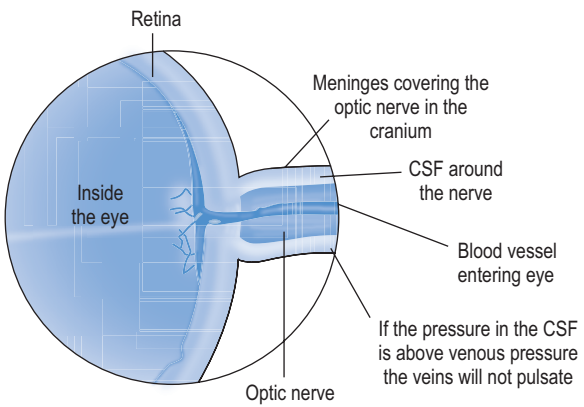


FIGURE 3.4 The basis of venous pulsations.

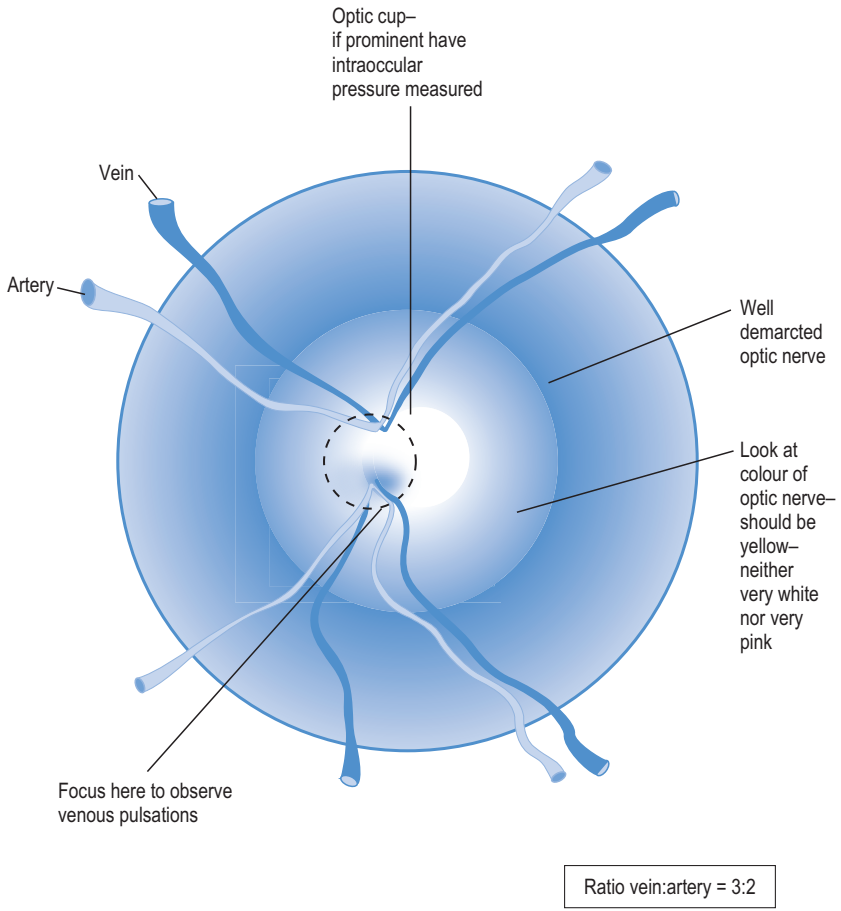


FIGURE 3.5 Ophthalmoscopic disc examination.

3 mysasthenia gravis: fatiguable droopy eyelid, pupils should be equal
4 mitochondrial myopathy: pupils are equal and the ptosis is longstanding and can be confirmed by old photographs.

Acuity can be tested using either or both Schnellan charts and/or near chart tests, and pupils are tested for direct and consensual response using a shielded light source directed at one and then the other pupil.

Shining the light into the right pupil and shielding that light from the left eye should evoke constriction of both pupils. The right eye constricts because

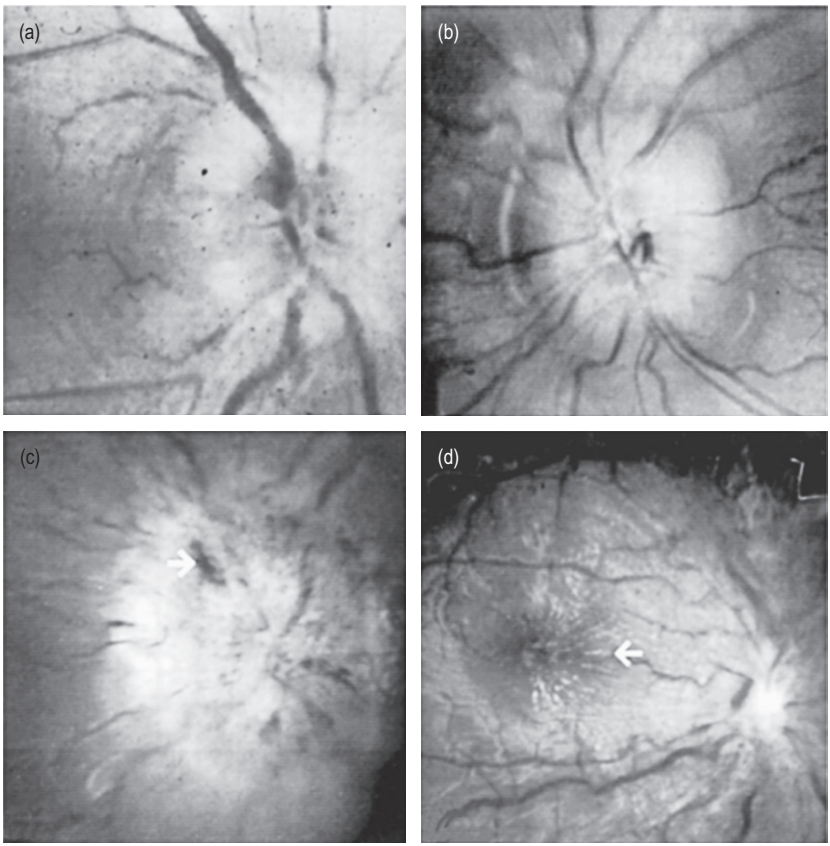


FIGURE 3.6 Papilloedema. *(Kliegman. Nelson Textbook of Pediatrics, 18th edn. 2007 Saunders; Figure 591-1 (a) Mild papilloedema. Blurred disc margins and venous congestion. (b) Moderate papilloedema. Disc oedematous and raised. Vessels buried within substance of nerve tissue. (c) Severe papilloedema. Haemorrhages are evident within disc (arrow), and there are microinfarcts (soft exudates) in the nerve fibre layer. (d) Macular star (arrow) with oedema residues distributed within the Henle layer of the macula.)*

of direct response of the light onto the right optic nerve. The left pupil constricts because that message from the right CN II is transmitted consensually to the left pupil via CN III and parasympathetic fibres. Thus blindness in the right eye will prevent the process happening, and damage to the transmission via CN III, assuming functioning right eye, will result in no pupillary response on the left.

Having evoked the response from the right pupil, the shielded light is focused onto the left eye. This should result in a repetition of the above

response. If the left eye is blind and does not constrict, then both pupils may dilate as a relaxation of the previous constriction. This does not imply the dilatation is evoked by the left eye, but rather that the left eye cannot perceive the light and does not prevent the dilatation consequent to the earlier constriction. This is known as the 'swinging lantern sign'.

CN III, IV, VI (OCULO-MOTOR, TROCHLEAR AND ABDUSCENS NERVES)

Eye movement is tested formally using an 'H' manoeuvre (see Fig 3.7).

The distant object, namely the image that is furthest away, is generated from the affected eye because the image of the object falls furthest away from central vision on the retina. The distant object is lost by covering the affected eye, and the muscle involved is determined by the 'H' manoeuvre.

Where there is loss of distant object, irrespective of which eye is covered, it is unlikely to be due to individual muscle or cranial nerve damage. While testing eye movement, the examiner should also look for nystagmus. As a simple rule of thumb, horizontal nystagmus suggests peripheral deficit and vertical nystagmus suggests central damage. This is not an absolute as

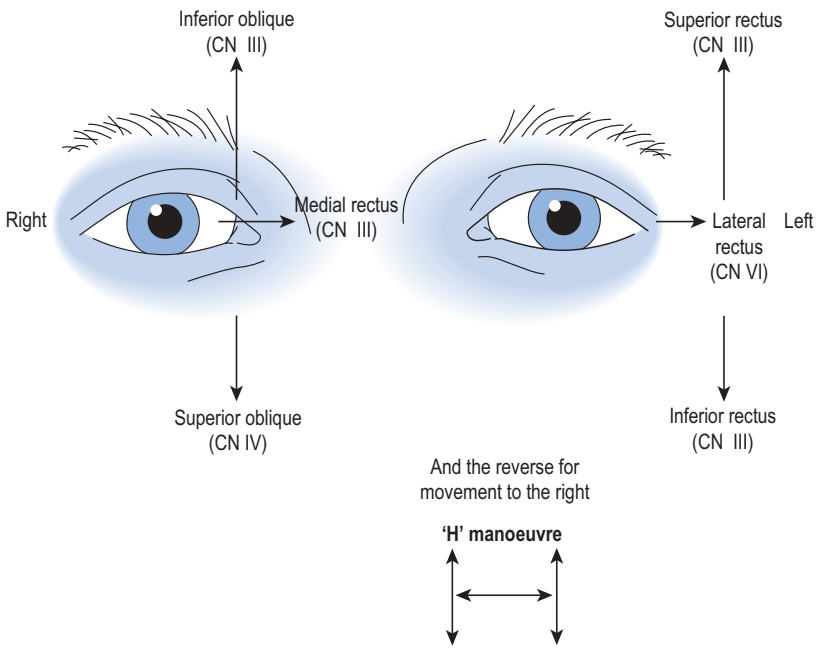


FIGURE 3.7 Muscles and cranial nerves.

cerebellar damage may cause horizontal nystagmus and drug toxicity may cause nystagmus in all directions.

In the unconscious patient, these three cranial nerves can be tested by holding the eyelids up and moving the head in the 'H' pattern. The eyes will move by actually remaining in the same position, hence moving within the socket. For example, when the head is moved quickly to the left, the horizontal of the 'H', the eyes will move to the right within the socket. This tests the right abduscens (CN VI) and the left oculmotor (CN III) or, alternatively, right lateral rectus and left medial rectus. This tests the equivalent of passive movement of these muscles and hence the competence of the brainstem connections. Where the brainstem is damaged, the eyes will move with the head rather than in the opposite direction—namely, just continue to look 'straight ahead' in whatever direction the face is pointing.

A CN III palsy allows the competing muscles (those muscles not innervated by CN III) to dominate eye movement. This causes the eye to be turned down and out. The levator palpebrae (eyelid elevator) is weak, causing ptosis. The parasympathetic innervation of the pupil is weak, allowing the sympathetic autonomic function to dominate, causing an enlarged pupil. The parasympathetic fibres travel on the outside of the nerve so pressure from the outside will affect those fibres first, causing midriosis. Partial ptosis with midriosis should raise suspicion of a partial CN III palsy. This may be caused when the CN III nerve passes between the posterior cerebral artery and the posterior communicated artery of the circle of Willis. Thus, partial CN III palsy may result from an aneurysm of the posterior communicating artery. This should alert the doctor to order a computer tomography (CT angiogram), which is not invasive and available to most GPs. It is important to advise the radiologist what to look for.

A CN IV lesion is often overlooked. It innervates the superior oblique muscle of the eye, causing the eye to turn down and in (see Fig 3.7). It is not the only muscle doing this as CN III turns the eye in (medial rectus) and pulls the eye down (inferior rectus). Thus competing muscles may obscure a CN IV palsy presentation. What should alert the doctor is the patient who complains of diplopia and presents with the head held in a tilted position. The tilt is to overcome the diplopia. Remember that full adduction of the eye switches off most of the inferior rectus function (see Fig 3.7). Downward movement in this position is reliant on the superior oblique (innervated by CN IV). This two-step testing helps to identify the CN IV palsy on clinical testing.

CN VI abducts the eye on the horizontal plane. A CN VI palsy prevents the eye from full lateral movement. Such palsy allows there to be sclera between the iris and the margins of the palpebral fissure. If there is still 'eye white' lateral to the iris in the fully abducted eye, then a CN VI palsy should be considered. The CN VI has the longest, and hence most precarious, passage through the cranial vault. It follows that a partial CN VI palsy (incomplete abduction) may be a false localising sign of raised intracranial pressure. It should alert the GP to the possible need for repeat examination of the fundus,

looking for papilloedema (see Figs 3.5 and 3.6), the first sign of which is loss of venous pulsations. It should also alert to the need for cerebral CT scanning looking for a space occupying lesion causing raised intracranial pressure. Unlike CN IV, where competing muscles produce some of the same eye movement functions, the competitors to the lateral rectus, the only muscle innervated by CN VI, is the medial rectus which adducts the eye. Hence a complete CN VI palsy will cause the eye to be turned in on the horizontal plane.

CN V (TRIGEMINAL NERVE)

CN V is tested with respect to its three divisions, namely, first, ophthalmic branch, second, maxillary branch, and third, mandibular branch (Figs 3.8 and 3.9). It is important to note that sensory changes, which do not respect these anatomical demarcations, provide positive evidence of psychological, non-organic disease.

While motor testing of CN V is said to be important, motor function is rarely affected without sensory loss. Testing sensation with a motor response is performed via the corneal reflex, which is a useful way to test trigeminal

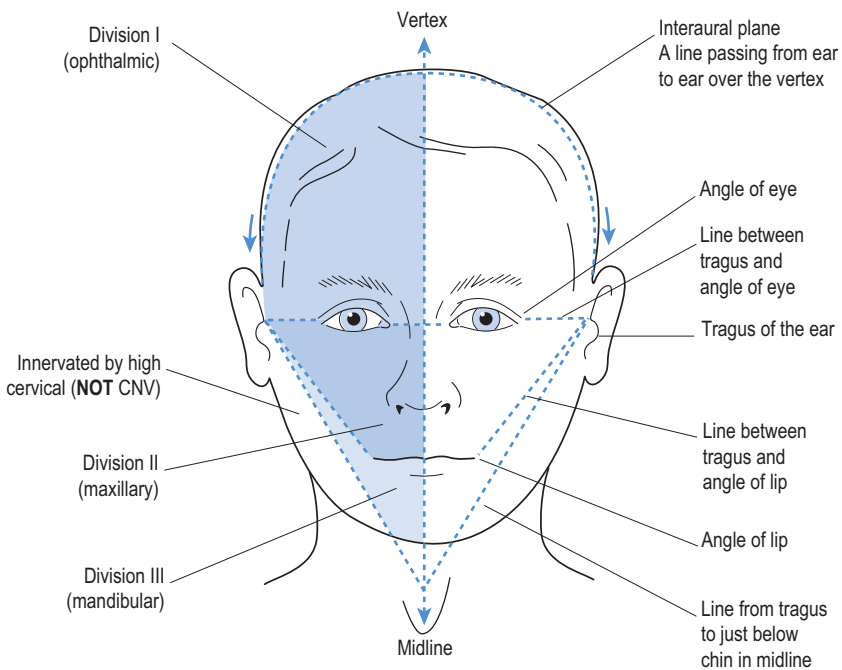


FIGURE 3.8 Trigeminal nerve (I).

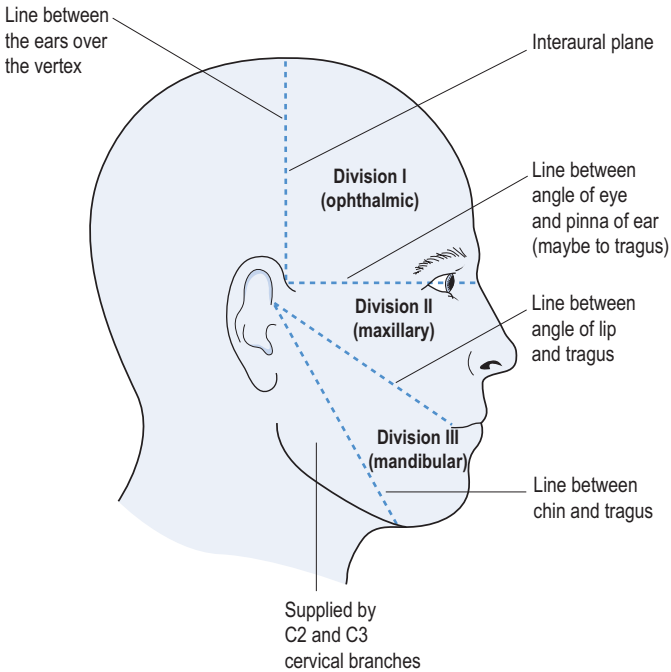


FIGURE 3.9 Trigeminal nerve (CN V).

sensation in the unconscious patient. It is not my chosen route, because if tested using cotton wool on the cornea, it is theoretically possible to leave a wisp of cotton wool on the cornea and thereby provoke a corneal ulcer. My chosen route, in unconscious patients, is to approach from the side with a rolled up tip of tissue and stimulate inside the nostril. This will usually evoke twitching of the nose due to an unpleasant sensory stimulation inside the nose. If the patient is conscious but uncooperative, it is best to stimulate surreptitiously so that the patient does not see the tissue approach, thereby evoking an unconscious response that truly reflects sensation of an unpleasant nature, rather than anticipation of that stimulus.

Testing eye closure can be achieved without the need to try to prise the eyes open. The eyelashes provide a natural 'manometer' of eye closure. Strong eye closure will result in burying of the eyelashes. If the lashes are evident on one side but hidden on the other with strong eye closure, it is evidence of weak eye closure on the side where the lashes are seen. The crow's-feet wrinkles at the side of the eye with tight closure offer an alternative manometer of strength.

CN VII (FACIAL NERVE)

The maxim 'lower is upper and upper is lower' is important when considering the CN VII. Involvement of the lower face, below the eye, suggests upper motor lesion. Involvement of the forehead is indicative of lower motor neurone, namely CN VII involvement. Failure to close the affected eye, with the eye rolling upwards to place the pupil behind the partially closed upper eyelid, is termed Bell's phenomenon. The easiest way to test spontaneous facial movement is to get the patient to smile or chuckle. This may be achieved by asking if the patient is ticklish or, alternatively, asking if the patient knows any jokes, particularly 'dirty jokes'. It is important not to ask about 'dirty jokes' if it is felt this might offend the patient. Asking about jokes, especially 'dirty jokes' where appropriate, almost universally evokes at least a hesitant or self-conscious smile, even in the depressed patient. This is usually more useful in discerning subtle upper motor neurone weakness with the affected cheek moving less quickly than the unaffected side. The naso-labial groove may also be less pronounced on the affected side.

Taste, which travels via the chorda tympani, is affected in CN VII palsy, especially in Bell's palsy. It joins the CN VII late in its passage, thus more distal involvement of CN VII in Bell's palsy will affect taste. Testing taste is both difficult and usually unreliable. It will suffice in most cases to question sense of taste when taking a history and where testing is required to leave it to others. Taste involvement has localising value rather than therapeutic implication. It is important, as stated earlier, to remember that taste and smell sensation are interrelated.

The CN VII also sends a small branch to innervate the muscle to the stapedius in the middle ear. If this is affected the patient with Bell's palsy may complain of hyperacusis. Hence if a patient with Bell's palsy says that things sound louder, this does not suggest non-organic disease. The symptom has no therapeutic value but is also helpful in localising the lesion affecting the CN VII.

CN VIII (VESTIBULAR COCHLEAR NERVE)

CN VIII is usually tested by covering the patient's vision (to exclude lip reading), rubbing the hair on the side opposite to the ear being tested (to confound hearing in that ear) and asking the patient to repeat numbers that are whispered. This tests lower frequency hearing. More formal testing may be achieved by using the same approach for low tones and a ticking wrist watch for high tones. A tuning fork adds additional sophistication with a 256 Hz frequency (middle C) tuning fork being preferred.

Weber's test involves placing the vibrating fork in the middle of the forehead. It should be perceived in the midline, at the place it is positioned. Should it be perceived lateralised to one ear, that implies either middle ear problems in that ear (enhanced conduction to that side) or neurosensory deafness in the opposite ear. If the patient has difficulty with the tuning fork placed in the

midline of the forehead, the same test can be repeated by placing the same vibrating tuning fork at the vertex on the top of the head. Some patients find this easier to perceive.

This testing can be further refined by placing the vibrating tuning fork next to the ear in the air (position 1) and then on the mastoid behind the ear (position 2). Normal hearing conducted via the cochlear nerve (VIII cranial nerve) will perceive air conduction (position 1) louder than bone conduction (position 2). The reverse implies middle ear pathology. This is known as Rinne's test.

A simple confirmation of hearing deficit is to lightly tap the tuning fork, place it in the air next to the patient's ear, and ask the patient to identify when it stops emitting a sound. If the doctor can still hear it when the patient cannot, the simple implication is that the patient has less preserved hearing than does the doctor. This is known as Schwabach's test.

The final test of the ears is direct otoscopy. An ear full of wax provides less clear hearing than an ear without wax. Likewise, it is important to recognise an inflamed ear, or the presence of herpes zoster in the ear of someone with Bell's palsy (lower motor neurone facial weakness) as it requires antiviral treatment in addition to steroids to treat the Bell's palsy.

CN IX, X, XI (HYPOGLOSSAL, VAGUS AND ACCESSORY NERVES)

The pharyngeal plexus is tested by shining a bright light into the pharynx and asking the patient to say 'AHHHH!'. This should result in the midline elevation of the uvular and soft palate. Weakness will deviate these structures to the contralateral side. I rarely, if ever, perform the gag reflex as it is most unpleasant and one should be able to predict its response by observing the palatal movement and listening to the patient's speech.

A lower motor neurone, palatal speech will sound as if air is escaping while the patient is trying to enunciate. Such deficit should cause paucity of gag response. Conversely, a spastic, tight, higher pitch speech should be accompanied by exaggerated gag reflex. A pointer to upper motor neurone 'pseudobulbar palsy' is emotional incontinence. This is different to emotional lability in which mood fluctuates apparently from highs and lows without obvious cause. With emotional incontinence, the patient reflects an over-expression of appropriate emotions. Examples of this may be the reflection of sadness with sobbing and crying rather than dull affect. Alternatively the patient may laugh uncontrollably, when the appropriate response may be a polite smile.

Further evidence of 'pseudobulbar palsy' will be bilateral representation of frontal lobe signs, such as grasp reflexes as discussed below.

The accessory component of the CN XI is not really a cranial nerve but rather high cervical roots travelling up into the cranium and then out to supply the sternocleidomastoid muscles, which turn the head and elevators of the shoulders, the trapezius muscles. Pushing the chin against a hand will activate

the sternocleidomastoid muscle opposite to the direction of the force; that is, pushing to the right with the chin will activate the left sternocleidomastoid muscle (and vice versa).

CN XII (GLOSSOPHARYNGEAL NERVE)

CN XII innervates the tongue and is best tested by first looking at the tongue and then asking the patient to protrude the tongue in the midline. The tongue will deviate to the affected side, being pushed over. Suspicion of tongue deviation must be balanced by observing facial movement. If the patient has unilateral facial weakness, as occurs in Bell's palsy, there may be the perception of the tongue deviating to the side of weakness, but this is almost universally wrong, namely the tongue protrudes in the centre of where the lips should have been were it not for the facial weakness.

The tongue is the only place in the body where the observer can see fibrillations with the naked eye. By definition a fibrillation is the spontaneous firing of a single muscle fibre (rather than a motor unit which produces fasciculations and reflects numerous muscle fibres spontaneously firing). The tongue is the only place in the body where single muscle fibres can be seen in the natural setting, and the presence of fibrillations is a most worrying sign suggestive of amyotrophic lateral sclerosis, a form of motor neurone disease.

TABLE 3.1 Summary of cranial nerves

Cranial nerve	Features
I	Sensation of smell—need to test with 'soft' scents as astringents may stimulate CN V endings in the nose
II	Fields, fundi, acuity, pupils Ptosis is often first noted while testing CN II
III, IV, VI	Tests eye movement: • III palsy causes the eye to deviate down and out, incomplete adduction, dilated pupil and ptosis • IV palsy impairs looking down and in, so the head is often held tilted • VI palsy prevents complete abduction—think of false localisation
V	Facial sensation and facial muscle power. Non-anatomical sensory changes herald non-organic disease Eyelid closure is tested by comparing burying of eyelashes **not** forcing closed eyes open Testing corneal reflex has the risk of causing corneal ulcer in the unconscious patient—testing intranasal sensation achieves the same outcome
VII	Facial movement rather than power 'Upper is lower and lower is upper' Asking about jokes usually provokes spontaneous smile—akin to testing facial muscle reflexes
VIII	Hearing—crudely tested with whisper Whisper tests low frequencies Ticking watch tests high frequencies Air conduction perceived softer than bone conduction sound suggests middle ear problems Always perform otoscopy in hearing impaired as wax may block sound
IX, X, XI	Pharyngeal movement—look and listen Air escaping during talking suggests palatal weakness—lower motor neurone High pitched tight voice suggests upper motor neurone weakness Remember pseudobulbar palsy causes emotional incontinence The accessory nerve (CN XI) is not really a cranial nerve but innervates muscles of neck and shoulder movement
XII	Movement of the tongue Tongue fibrillation raises concern for motor neurone disease Facial asymmetry may falsely suggest tongue deviation

4

The neurological examination: peripheral nervous system

Examination of the peripheral nervous system assumes a stylised approach when adopting the traditional method. This means following a set pattern of: observation and inspection; tone; power; reflexes; sensation; coordination; and gait. This ignores what was stated earlier, namely that the consultation starts long before the patient enters the consultation room.

The first part of testing of the peripheral nervous system is observation, namely observing how the patient gets out of the chair and walks into the room. Difficulty rising from the chair may suggest Parkinson's disease. Not swinging one arm when walking may suggest either pyramidal disease, such as a stroke, or may also suggest Parkinson's disease. Spastic posturing (flexed upper limb and extended lower limb) with circumduction of affected lower limb suggests upper motor neurone damage, such as stroke. Stooped posture, shuffling gait with festination, hesitancy and inertia of gait initiation are almost diagnostic of Parkinson's disease, and are apparent long before the consultation formally commences.

Ataxic, wide-based gait is suggestive of cerebellar disease. Wide-based gait is far less common than one would think. The width between the feet is usually wider than the shoulders of the patient and gives the impression that the patient is drunk—hence the statement that the patient walks like a drunken sailor. Wide-based gait provides stability of stance, and sailors used to moving ships often walk with such wide-based gait to maintain stability on a ship.

Before undergoing the formal peripheral assessment it is worth testing for grasp reflexes. This is done by distracting the patient, possibly by engaging in 'small talk', and while doing so sliding the hand out, pushing up against the patient's palm and fingers. Grasp reflex may be as subtle as feeling the fingers of the patient flexing downwards towards the examiner's sliding fingers. A positive grasp reflex is indicative of contralateral frontal lobe (upper

motor neurone) damage. Other frontal lobe signs may include palmar–mental response. This is evoked by applying a noxious stimulus (such as scratching) to the palm of the patient's hand and observing the movement of the chin (mentalis muscle) on the same side as the scratched hand. This again suggests contralateral frontal lobe damage.

The glabellar tap is elicited by tapping the index finger on the patient's forehead. It is best achieved by holding the hand above the forehead and tapping the forehead without coming front-on as this movement, equivocal to menace (as described when testing visual fields in Ch 2), may itself evoke a blink response. When testing the glabellar tap the normal response allows up to three blinks. More than three blinks represent a positive response. When testing glabellar tap it is worth reappraising the patient for ptosis, as attention is focused on the eyelids.

Much of the above actually tests central nervous system function, but it is best examined at this point in patient assessment. This uses the peripheral to test central competence.

While the approach adopted has been compartmentalised, this has been done for ease of understanding. An additional consideration has been to instil time-efficient consultation methods: all busy doctors are 'time poor' and anything that can improve clinical acumen and save time is of value.

OBSERVATION AND INSPECTION

Before testing tone it is important to examine the patient closely, looking for fasciculations (brief muscle twitches), focal wasting in isolated muscle groups, skin lesions (such as café au lait patches which go with neurofibromatosis) and other scars or lesions that may be obvious but overlooked during a rushed examination. Fasciculations, which indicate lower motor neurone disease, may provide the first clue to the presence of motor neurone disease but may be detected only because they were specifically sought.

Much of what should be observed has already been addressed in the opening few paragraphs of this chapter. They dealt with broad overview, namely observing the 'whole' patient. In this section on observation, the aim is to look for specific markers of various diseases, which may only become apparent after years of self discipline and being aware of the need to look for them.

TONE

Tone is tested by a number of different methods. Initial resistance, followed by a feeling of giving way, is called 'clasp knife' as it is similar to opening the blade of a pocketknife. This is found with spasticity in upper motor neurone damage.

If Parkinson's disease is considered, then the initial testing of tone by moving the hand up and down at the wrist should be normal early in the disease process. The patient is asked to move their head from side to side,

pushing the ear into the shoulder with each turn, at which time the tone increases with 'cogwheeling' and 'lead pipe' rigidity. This is pathognomic of early Parkinson's disease.

If the patient is examined soon after the onset of a stroke, the hemiplegic limbs may be totally flaccid and floppy. After longstanding upper motor neurone damage, the hyper-tonicity may progress to clonus. This is evoked by short, sharp joint movement, such as sudden sharp dorsiflexion of the foot, similar to the initial provocative jerking movement. The same may be caused by jerking the patella bone towards the foot in the extended knee. This may evoke repeated movement of the knee bone up and down in a similar fashion to that seen at the foot. Clonus may be evoked at other joints, such as the wrist, but lower limb clonus is more common.

Cerebellar damage does not cause increased tone which is often decreased, causing pendular movements on testing. This is often difficult for the inexperienced to discern. While increased or decreased tone is relatively easy to identify, often the subtleties of tone are not that easy to identify for the doctor not attuned to the neurological examination.

POWER

Various conditions affect different muscles. Upper motor neurone weakness, as with stroke, affects the antigravity muscles. Most inexperienced doctors have difficulty remembering which muscles constitute the antigravity muscles (see Fig 4.1).

It is because of weakness of the antigravity muscles that the patient with upper motor neurone damage presents with flexion of the upper limbs and extension of the lower limbs. With weakness of the antigravity muscles, the opposing muscles exert their effect causing posturing without counter effect by opposing muscles (see Fig 4.2).

To make it simpler for the doctor, it is easier to remember just one group of muscles, such as the extensors in the upper limbs. It is even easier to remember just one upper limb muscle, such as the triceps, which is an extensor muscle. This will reinforce extensors in the upper limbs and the opposite, namely the flexors with lower limbs. Alternatively, the doctor may choose to remember just a single flexor in the lower limb, such as the hip flexor, the iliopsoas.

It is obvious that a 60 kg female may have trouble overcoming the strength of a 100 kg male who is engaged in very physical work. One way to overcome this is to use mechanical advantage to test power. An example of this might be to test triceps power by flexing the elbow much more than the traditional 90° (see Fig 4.3).

Power is graded on a five-point scale:

(0/5) 0 = No movement
(1/5) 1 = Flicker of movement
(2/5) 2 = Some movement

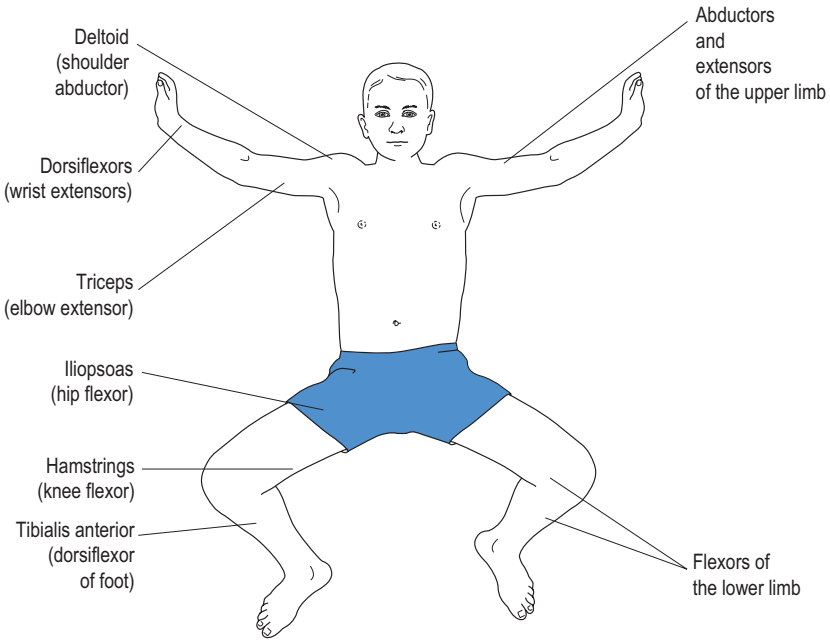


FIGURE 4.1 Antigravity muscles.

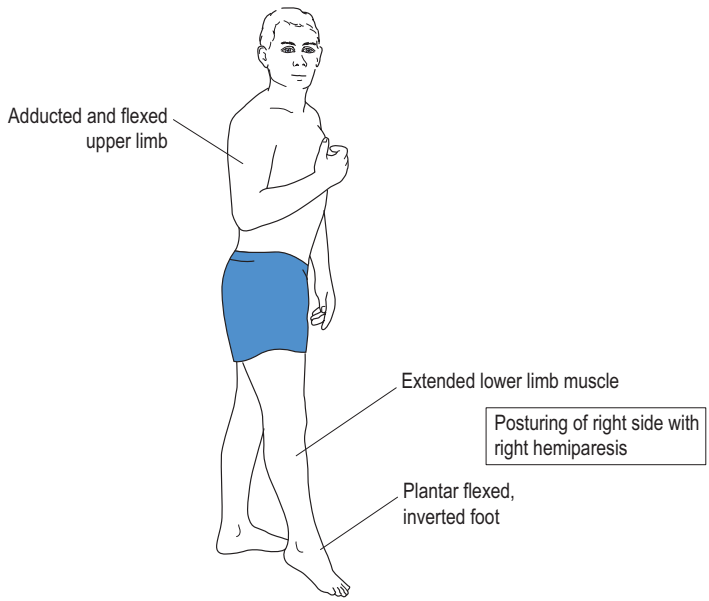


FIGURE 4.2 Spastic posture—non-antigravity muscles.

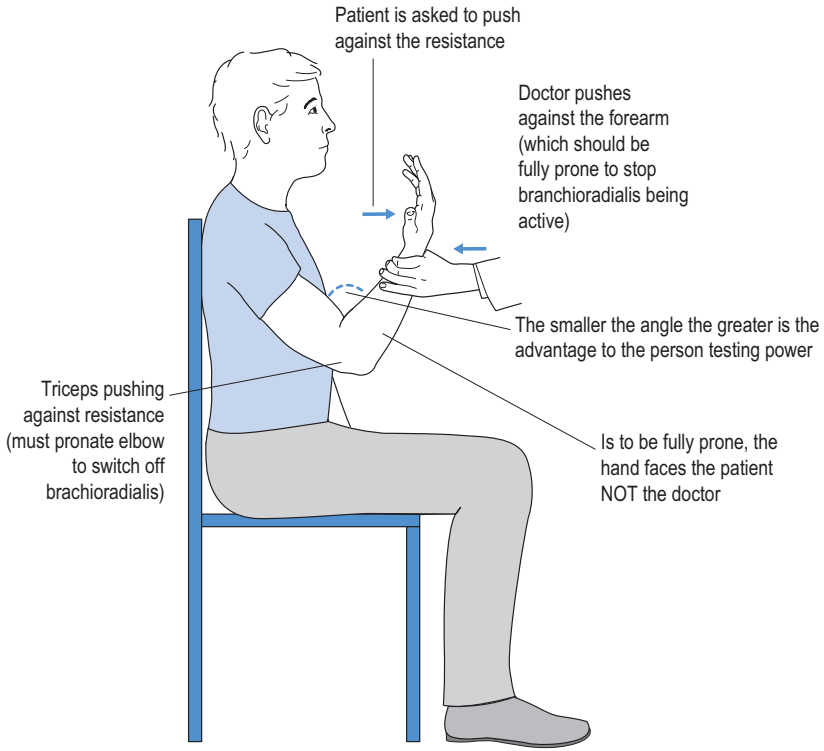


FIGURE 4.3 Testing triceps power.

(3/5) 3 = Movement against gravity
(4/5) 4 = Power against resistance
(5/5) 5 = Full power

Some examiners try to add further sophistication (for example 4+ or 4–) but this is less universally accepted.

Endocrine disorders, such as excessive exposure to steroids, may cause proximal weakness. Some myopathies specifically target certain muscles, such as facio-scapular humerus muscles. Other diseases, like Charcot-Marie-Tooth, may cause wasting of calf muscles, giving the appearance of inverted champagne bottles in the lower limbs. It helps to remember some of these patterns when performing the neurological examination.

Weakness may be restricted to particular innervated muscles with mononeuritic disease. An example of this is specific weakness of abductor pollicis

brevis (APB), flexor pollicis brevis (FPB), opponens pollicis and the lateral two lumbricals with median nerve entrapment and carpal tunnel disease.

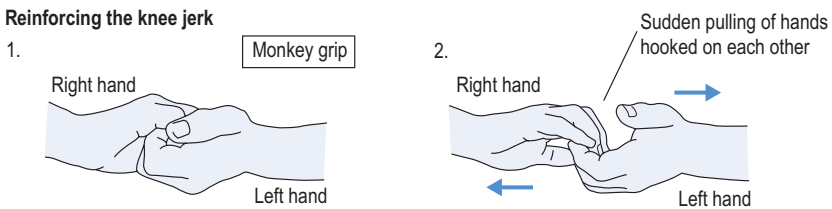
REFLEXES

Upper motor neurone weakness causes hyperreflexia. By far the most common cause of hyperreflexia is anxiety with excess adrenaline. When reflexes are particularly brisk, the tapping of a reflex with a tendon hammer may be sufficient to provoke clonus, as described above.

The basis of the deep tendon reflex is to stretch receptors within the muscle. This causes the muscle to contract, thereby resulting in the jerk of the joint being tested. The way that clonus is provoked is as a consequence of increased tone within the muscle. The single jerk that normally occurs when tapping a reflex is enough to cause another jerk to happen because of the hypertonicity of the tight muscle. This is repeated until the size of the resultant movement is too small to evoke a further jerk response.

Some anxious patients are too 'uptight' to allow the free movement/jerk of the muscle. The patient needs to relax, and the best way to encourage this is to distract the patient. Ask the patient to adopt the finger clasp known as a 'monkey grip' (see Fig 4.4). The patient is asked to close the eyes and relax, and to only pull on the grip when told to do so. This instruction is given as the reflex is tapped. Some neurologists ask the patient to clench the teeth at the exact same time as tapping the reflex. This is another method of distraction.

It is more difficult to test upper limb deep tendon reflexes in a patient who is stressed (and uptight) and who is 'splinting' their muscles. To test the right upper limb deep tendon reflexes, the patient is given an object to hold in the



1 Hands hooked to stop the movement of one on other
2 Patient is asked to relax until told to pull one on the other
3 Instruct the patient to pull at exactly the same time as tapping the knee jerk

Pull one hand on the other upon instruction followed by relaxation

FIGURE 4.4 Distraction for testing reflexes.

left hand. The patient is asked to squeeze the object at exactly the same time as the deep tendon is tapped with the hammer, or more correctly just as the swing of the hammer starts. The sides are reversed when testing left upper limb reflexes. Again, clenching the teeth tightly at the same time as swinging the tendon hammer to tap the reflex is an alternative method of distraction. This is often best achieved with the patient's eyes closed so they cannot anticipate the tap of the hammer.

Deep tendon reflexes represent specific spinal root levels:

Supernator (radial) jerk = C5,**6**
Biceps jerk = C**5**,6
Triceps jerk = C6,**7**
Knee jerk = L**3,4**
Ankle jerk = S1

It is difficult to be sure that the tendon hammer can be appropriately targeted at the biceps jerk. To assist with this and ensure that the focus of stimulus is correctly directed at the biceps tendon in the elbow, the doctor places a thumb over the biceps tendon at the elbow and hits their thumb, thereby ensuring that the immediate jerk is evoked over the tendon.

Ankle jerks are difficult to elicit if one is not sure how to do it. If the patient is lying down then the foot is drawn across the opposite shin and the Achilles tendon is tapped (see Fig 4.5).

An alternative method is to dorsiflex the ankle joint and then tap the sole of the foot (see Fig 4.6).

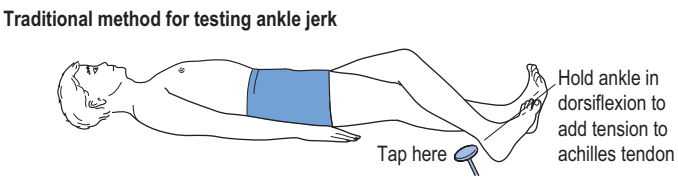


FIGURE 4.5 Ankle jerk testing.

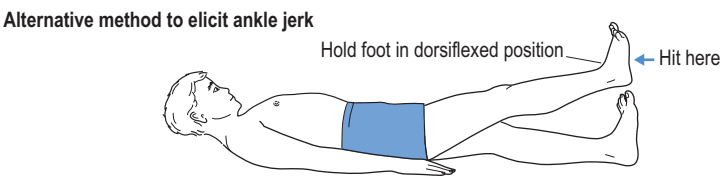


FIGURE 4.6 Dorsiflex ankle joint testing.

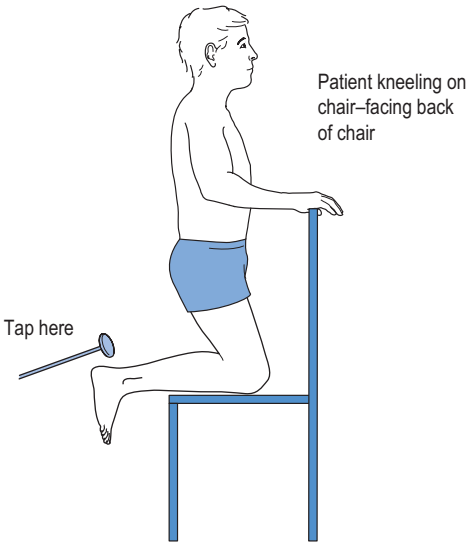


FIGURE 4.7 Achilles tendon testing.

If both these methods fail, then the patient may be asked to kneel on a chair while the Achilles tendon is tapped (see Fig 4.7). This way the patient is distracted by kneeling on the chair and cannot predict when the ankle jerk will be tested, thus reducing the propensity of 'splinting'.

The Babinski response is often misunderstood. Most people focus on the great toe, but for subtle response the examiner should focus on the little toe. Rather than scratch the sole of the foot, my preference is to stimulate the lateral border of the foot and see if the little toe moves medially (joining the other toes as they all move in a downward direction) or moves laterally (away from the other toes) in a splaying motion as the great toe moves up. Upper motor neurone lesions cause the toes to splay, followed by upward movement of the great toe if it is sufficiently positive. The easiest way to understand this is to consider that the Babinski response is the foot either opening or closing, the equivalent of a fist. When a hand closes to make a fist all the fingers come together and the last action is the thumb wrapping around the front of the fist. Equating the thumb with the great toe, the thumb is the last digit of the hand to move—as is the great toe with the Babinski response.

The role of other reflexes, such as the cremasteric reflex (L1), abdominal reflexes (T6–T12) or adductor reflexes of the lower limb (L2), are all relevant to the neurological examination but they are subtle tests generally extraneous to the needs or role of the general practitioner.

SENSATION

While neurologists test light touch, temperature, pain, position (proprioception) sense, vibration sense and two-point discrimination, the routine neurological examination by the general practitioner may be limited to light touch (which travels together with pain and temperature) in the lateral spinothalamic tracts of the spinal cord and joint position (which travels with vibration sense) in the posterior columns of the cord.

It is easier to work from the area of impaired sensation towards the area of increased sensation. As sensory loss usually starts in the periphery, it follows that light touch stimulation should start at the feet or hands and move centrally up the limbs to the torso until the patient reports increased perception of the stimulus.

Fingers are as useful as cotton wool to test light touch as we know how heavily we place our fingers, and hence we can better gauge the stimulus applied when testing light touch. If there is greater need for subtlety when testing light touch, then personal preference is to use a small paintbrush because the handle of the small brush lends itself to tighter manipulation and control than does holding a wisp of cotton wool.

While many advocate using a pin or needle to test pain, it is difficult to apply consistent pressure with a pin to be sure that the patient is responding to the same stimulus each time. A simple tool that allows consistent and acceptable stimulation is a serrated edge haberdashery tracing wheel rolled from the foot, or hand, up the limb until a change in perception is recognised. As stated earlier, pain travels a similar pathway to light touch and hence it needs to be tested only if the history dictates a need for more accurate sensory demarcation, which may be better defined with painful stimulation.

Similarly, temperature perception accompanies light touch and pain pathways, and thus only needs testing in more subtle cases. Use of a cold metal object, such as a tuning fork, may be adequate for the crude testing of temperature perception and follows a similar pattern, moving from the periphery, centrally. The patient may report the cold metal suddenly feels colder, thereby establishing a level if there is ‘glove and stocking’ hyposensitivity as occurs with peripheral neuropathy.

For vibration sense testing, the tuning fork should vibrate more slowly than is the case for testing hearing. A 128 Hz cycle frequency, the C note one octave below middle C on the piano, is the ideal tuning fork to test vibration sense. Vibration sense accompanies joint position sense (proprioception) in the posterior columns of the spinal cord. Testing vibration sense is a comparative test in which the patient compares perception of vibration to areas thought to be normal. Again it behoves the examiner to move from the periphery. Obviously the doctor needs to have an appropriate tuning fork to test vibration sense and this is not always the case. Joint position testing also evaluates posterior column integrity.

Joint position should be tested moving from the periphery centrally, namely the great toe before the ankle, before the knee, before the hip or, in

the upper limb, finger, before the wrist, before the elbow, before the shoulder. The great toe is held between index finger and thumb (held on the sides of the toe rather than the top and bottom). The reason for holding the sides is to avoid additional position sense cues, as may be provided by pushing up and down with pressure on the top or bottom of the toe. A similar approach can be adopted with other joints if the patient cannot identify upward/downward movement of the joint, starting at the periphery, namely great toe or little finger.

It is important to remember that spinothalamic sensation (pain, light touch and temperature) travels up two to three segments above where clinical examination suggests the level to be. It then crosses to the other side of the spinal cord at this level two to three segments above where sensory changes are detected. This means a right-sided spinal cord lesion at this level will result in altered pain, light touch and temperature perception on the left from about two to three segments below the lesion. Thus, a level at T10, the umbilicus, on clinical testing suggests a spinal cord lesion at T7 or T8.

Alternatively, posterior column sensation (such as joint position sense, vibration sense and possibly two-point discrimination) travels up the posterior columns of the spinal cord to the brainstem where they cross over in the medullar oblongata. It follows that spinal cord lesion on the right side of the cord, affecting the right side posterior columns, will result in loss of joint position sense and vibration sense on the right side (the same side as the lesion). Appreciation of these points is important when evaluating hemicord lesions, as may occur with Brown-Séquard's syndrome.

COORDINATION

Cerebellar dysfunction is identified with the testing of coordination. The examiner will already have clues from the wide-based gait, which should be noted as the patient entered the room. Other features include horizontal beating nystagmus to the side of the lesion, incoordinated slurred speech and general ataxia, not restricted to gait but including ipsilateral hand.

Finger–nose ataxia can easily be tested by asking the patient to place their index finger on their nose while extending the contralateral index finger to the side and swapping the positions repeatedly, seeking exact movements (Fig 4.8).

Repetitive movements are tested by having the patient tap a rapid rhythm on one hand with the other, and then repeat the process using opposite hands. Similar testing can be directed to the feet tapping out a rhythm.

Heel–shin ataxia is tested by asking the patient to run the heel of one foot down the opposite shin and vice versa.

It is important to appreciate that upper motor neurone lesions are reflected with deficits on the contralateral side of the body, while cerebellar signs are reflected on the ipsilateral side to the lesion.

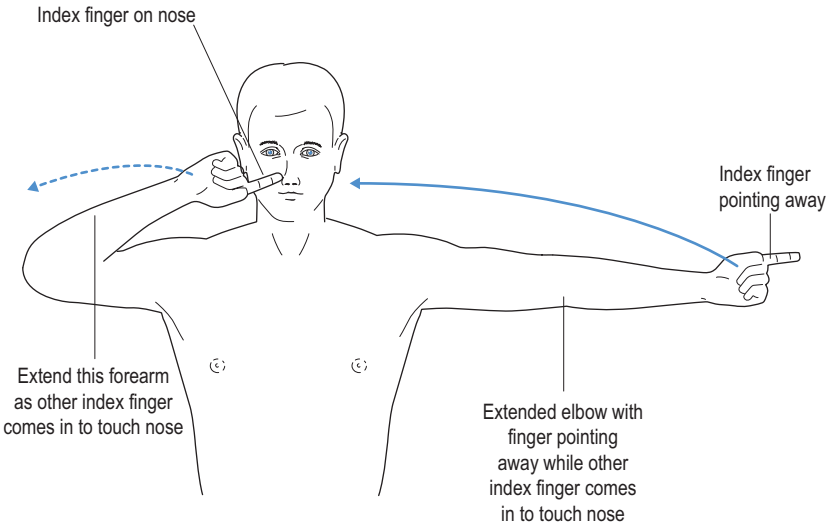


FIGURE 4.8 Finger–nose ataxia testing.

GAIT

Under normal consultation conditions, gait already will have been observed as the patient entered the consultation room. If the neurological examination is part of a formal test, it may be necessary to ask the patient to walk again and to observe gait at the end of the consultation. Much of this has been covered in the opening paragraphs but it is worth revisiting some important points.

Often the inexperienced observer will focus all the attention while assessing gait at the feet, looking for features such as wide-based gait. It can be more productive to look at arm swing. Patients with upper motor neurone damage will not swing the contralateral arm as much as the other side. Patients with Parkinson's disease don't swing both or, at times, either arm when walking.

Those with upper motor neurone disease will have difficulty walking on their heels due to weakness of foot dorsiflexion. Posture (stooped), ataxia (clumsy) and dystonia (unusual hand positioning or movements) may all be noted while observing gait.

5

Non-organic neurological diseases

INTRODUCTION

Many believe that the diagnosis of functional, and for that read non-organic or psychological, disease should be a diagnosis of last resort. Those advocating this approach adopt the view that one should never have functional illness as the number one diagnosis. They believe one should only entertain the possibility after all other potential diagnoses have been excluded. The problem with this concept is that it has the capacity to encourage 'sick' behaviour. It reinforces that there is something seriously wrong.

The need for an exhaustive list of investigations before broaching the topic of psychological illness suggests that the true diagnosis is beyond the doctor's capacity to discern. It suggests that the label of 'functional illness' is a euphemism for medical ignorance or incompetence. This may be more worrying to the anxious patient than would be an early identification of the probable diagnosis of psychological illness.

It does not mean that the provisional diagnosis of non-organic disease should exclude investigation for alternative differential diagnoses. While a provisional diagnosis is the most likely answer, it is not the only possibility. The same applies to the provisional diagnosis of functional illness. Nevertheless, an early acknowledgement that the most likely diagnosis is non-organic serves to reinforce that the doctor retains clinical acumen, assuming that there are valid reasons for placing the 'functional' label as the most likely diagnosis.

To consider what some claim a diagnosis of last resort necessitates the clinician appreciating those features of non-organic diseases that justify placing them at the top of the diagnostic ladder. What follows in this chapter is the evidence upon which a diagnosis of non-organic disease can be suspected as the principal diagnosis.

OBSERVATION

In earlier chapters it was proposed that an astute receptionist may be invaluable in suspecting psychological illness. A patient may display a range of behaviours that lead to the suspicion of non-organic disease. A receptionist may note how the behaviour changes when the attending doctor is, or is not, in the waiting room. The way the patient walks into the room or excessive complaint of pain without attendant signs may raise suspicion. These features suggest malingering and patient complicity in the claim of symptoms and signs. The patient may benefit from a fraudulent claim, as might occur following an accident. An experienced general practitioner will be atuned to such behaviour, which will not be discussed further in this chapter.

HISTORY

As was stated earlier, the taking of an accurate medical history remains a fundamental tool of the neurological consultation. Within the context of functional illness, other than the case of a malingerer who wilfully aims to confound the picture, the patient usually is unaware of the possibility of a non-organic diagnosis. As with so many neurological diagnoses, including non-organic neurological presentations, the doctor must maintain a high index of suspicion. This is imperative if the diagnosis is to be identified as early as possible. Often the diagnosis of non-organic disease emerges because the history in these cases makes little sense, does not suggest a diagnostic label and confuses, rather than assists, the clinician.

Whenever the history fails to offer clinical diagnostic direction, the possibility of functional illness should arise. In these circumstances functional illness should not climb the diagnostic ladder, but merely be included among the potential diagnoses. It is part of the differential options but lacks credibility to be a principal choice. The provisional diagnosis should be based on positive factors, and confusion is far from positive, but may provide an important clue.

Having made the distinction, history is the tool that differentiates tension-type headache from migraine. Tension-type headache may well be a ‘front’ for non-organic disease. Particularly in societies in which physical fitness is a primary requirement, as is the case for members of the armed forces, patients often find it unacceptable to present with complaints of a psychological nature. Once tension-type headache becomes apparent, then the general practitioner is in an ideal position to seek and deal with the cause of the tension. The same applies to various complaints of pain. An example of this is the chest pain that accompanies da Costa’s syndrome, which is a left inframammary pain attached to stressful situations. It is unlike the pain that reflects ischaemic heart disease or chest infection. This should raise the red flag of probable psychological illness but this warning does not negate the need to investigate for both cardiac and pulmonary disease. An early suggestion that the primary diagnosis is most likely non-organic, allows a strengthening of

the doctor–patient relationship and potential for mutual respect while the auxiliary investigations proceed.

The differentiation between epileptic seizures and non-organic, so-called pseudo-seizures, also referred to as 'non-epileptic' seizures, is based on meticulous history taking. There are some features that assist in the differentiation, including: whether the eyes were open or shut during the seizure (eyes are usually open during an epileptic seizure); what post-ictal features existed (people after a seizure are often confused, disoriented, fatigued and may complain of headache while those with non-organic seizures may not experience these symptoms); if there was tongue biting or biting of the buccal mucosa; as well as possible incontinence of urine and/or faeces. While none of these are pathognomic of true epileptic seizures, they add to the weight of evidence, which may differentiate between the two. Absence of features associated with epileptic seizures offers the doctor the opportunity to explore causes of functional illness. Raising this with the patient demonstrates an understanding of the subject matter and encourages trust and respect.

Within these scenarios the doctor can both reassure the patient that there is probably nothing organically wrong, while concurrently conducting the tests to prove this to be the case. Unlike the situation in which non-organic diagnosis is the diagnosis of last resort, early identification and intervention reduces the risk of the patient adopting the 'sick' role.

The doctor needs to explain the reason, based on the available evidence, as to why functional illness is at the top of the list of diagnoses. While the initial response may be disagreement, it reinforces the integrity of the doctor; as will be reinforced if later findings support the earlier supposition of non-organic disease. This allows the doctor and patient to build a relationship on trust, in which the intimacy of the relationship may permit the doctor to explore issues that might otherwise be off-limits. It may provide the portal to introduce psychological or psychiatric support.

EXAMINATION

Neurology is a delightful speciality because the signs must fit the anatomical dictates. If these fail to match what is expected, then they provide unequivocal evidence of non-organicity. In previous chapters the approach to neurological examination was dissected to allow the doctor to complete the process in a formalised, traditional fashion. What follows will use this approach to demonstrate features that are anatomically unsound. Where there is incongruity between clinical findings and anatomical parameters, there is unequivocal evidence of functional illness.

A claim of monocular diplopia, in the absence of nystagmus, lenticular dislocation as occurs in Marfan's syndrome or other obvious pathology, indicates that the final diagnosis is most likely non-organic. Nevertheless, the patient requires proper cranial nerve testing. The claim of monocular diplopia should be a red flag for non-organic disease. Further investigation is

dependent upon what other features have emerged, either during the history taking or other examination. Recently, a patient complaining of monocular diplopia was shown on MRI to have her lens dislocated to the back of the globe. This confirmed the potential, thereby dispelling the diagnosis of functional illness. Suspicion of non-organic disease does not suggest the general practitioner should not fully investigate for organic diseases. It allows the doctor to reassure the patient that the investigations are expected to be negative and thus reduce fear of probable devastating findings. This in turn serves to reduce the risk of 'sick' role-play by the patient.

The trigeminal nerve provides a most fertile ground for the definition of functional illness. As demonstrated in Chapter 3, the trigeminal nerve has defined anatomical demarcation of its boundaries of sensory representation (see Figs 5.1 and 5.2).

As the interaural plane defines the limit of the ophthalmic branch of the CN V, it follows that sensory change occurring at other than this plane is anatomically unsound. Many patients with non-organic disease will identify sensory change at the start of the hairline on the forehead. This provides unequivocal evidence of functional illness. The same applies when the patient claims the angle of the jaw as the site of sensory change. The angle of the

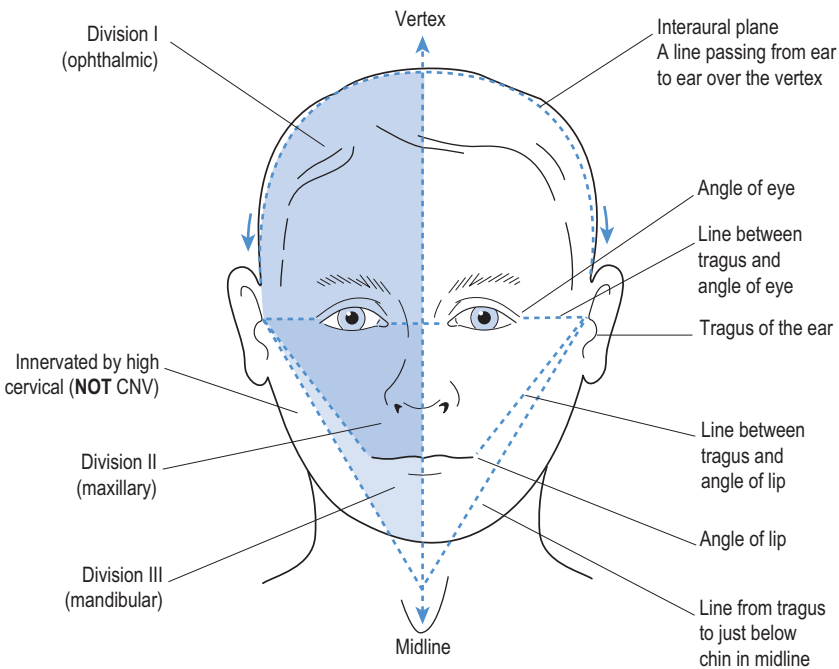


FIGURE 5.1 Trigeminal nerve (I).

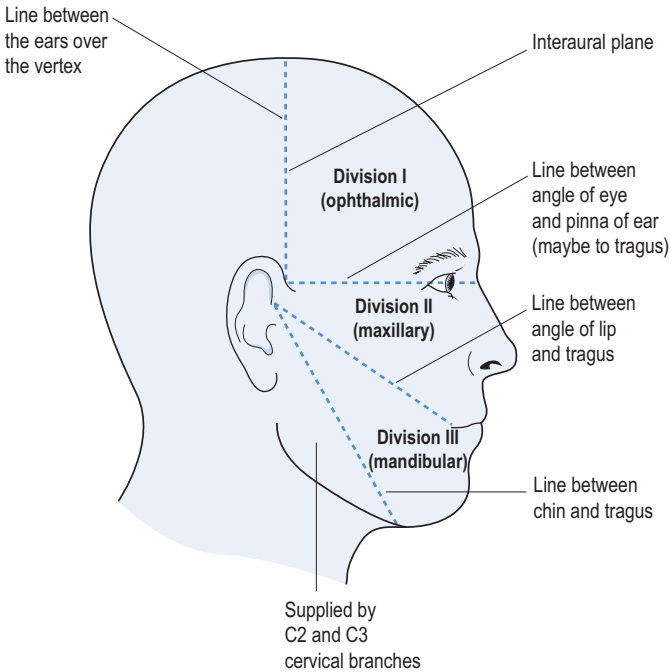


FIGURE 5.2 Trigeminal nerve (CN V).

jaw, below the line from the tragus of the ear to the midline (just below the jaw), is innervated by high cervical roots (especially C2 and C3) (see Figs 5.1 and 5.2). A patient identifying sensory change at the angle of the jaw offers unequivocal evidence of functional illness.

Predetermined sensory maps are not restricted to the cranial nerves. The torso is also divided into dermatomes that establish expected, affected areas according to anatomic landmarks. All sensation in the body, be it head or torso, changes at the midline. If a patient reports altered sensation which does not respect the midline, be it on the face (with sensory change over the cheeks rather than the midline) or on the body (be it the nipple line rather than the midline), this is further unequivocal support for the diagnosis of functional illness. Similarly, the midline posteriorly (head and torso) defines the anatomical landmark for dermatomal separation of right and left, and failure to respect this is tantamount to non-organicity.

Every clinical practice should have the dermatomal map available for scrutiny. An invaluable reference is *Aids to the examination of the peripheral nervous system* (O'Brien 2010), which is a MUST for all serious clinicians interested in the nervous system. There are some useful landmarks to

remember that will allow the examiner to localise lesions with ease (see Box 5.1). A more complete dermatomal map has not been provided here as the above reference is both cheap and invaluable.

The cranial nerves are not the only source of definition of non-organicity. Patients who complain of weakness of muscles, when asked to exert maximal effort from a specific muscle or muscle group, may show activation of antagonistic muscle groups. An example of this might be the patient claiming weakness of the triceps muscle, but when strength in this muscle is tested there is clear evidence of biceps involvement (see Fig 5.3).

Activation of antagonistic muscle(s), within the context of testing 'maximal' power of a specific muscle or muscle group, offers unequivocal evidence of

BOX 5.1 Anatomical landmarks re sensation

Anatomy (anterior)	Dermatome
Root of neck and shoulders	**C3, C4**
Level of nipple	**T4**
Level of costochondral margin	**T6**
Umbilicus	**T10**
Pelvis	**T12**

(NB: midline differentiates sensation from right and left.)

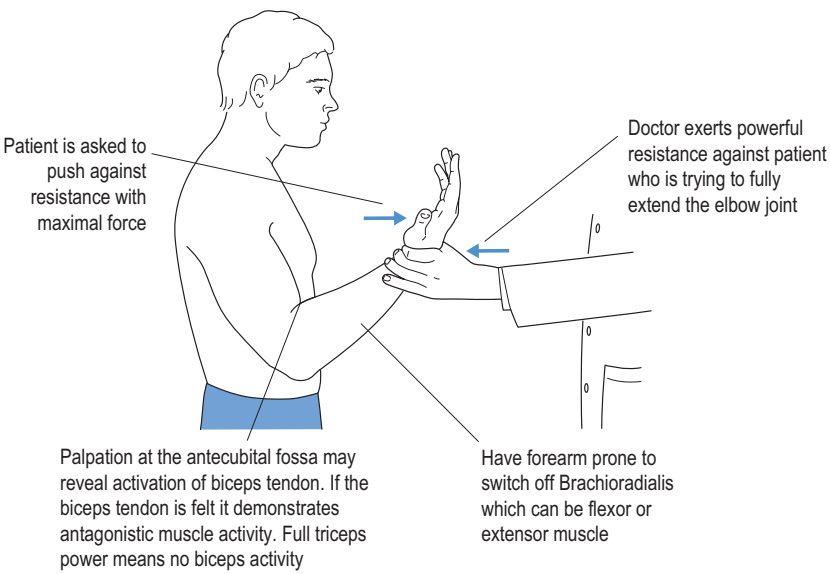


FIGURE 5.3 Use of antagonistic muscles.

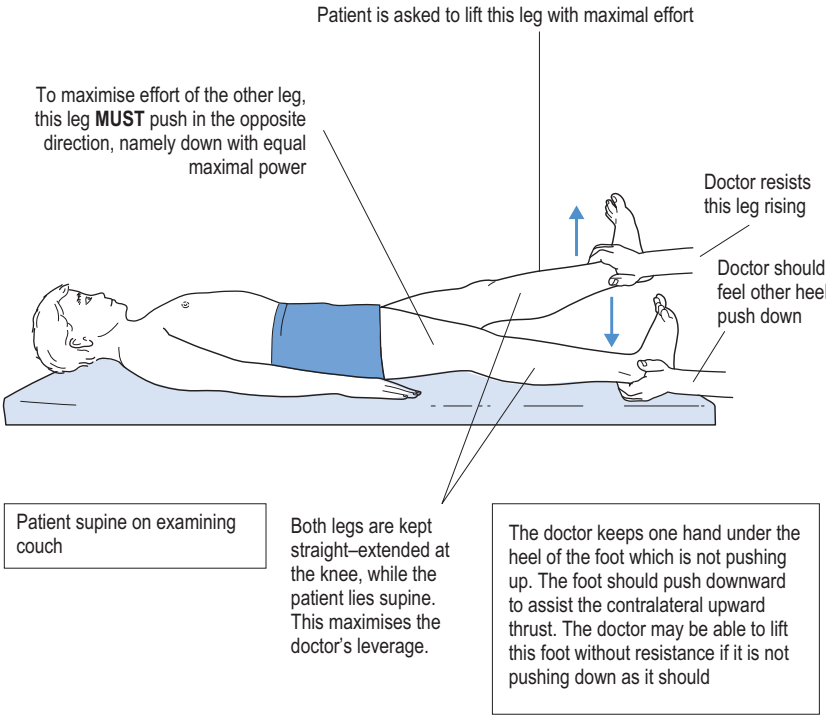


FIGURE 5.4 Hoover's sign.

suboptimal effort. This does not mean the patient is aware of so acting on a conscious level, but does offer clear evidence of functional illness.

Another region in which weakness may reveal functional illness is in the examination of lower limb power in a patient who is lying down (see Fig 5.4).

Hoover's sign relies on Newton's third law—namely, 'for every action there is an equal and opposite reaction'. The patient is asked to lift up one leg with maximal power against resistance while lying flat. The doctor resists the effort to lift this leg while placing their other hand under the heel of the other foot. Based on Newton's third law this foot must push down to maximise the upward effort of the opposite leg. In the patient who is not pushing up with maximal effort, the doctor will not feel the downward thrust of the heel, a positive Hoover's sign. The doctor may even be able to lift the heel effortlessly because of the lack of downward force. This further emphasises non-organicity. A positive Hoover's sign provides unequivocal support for the

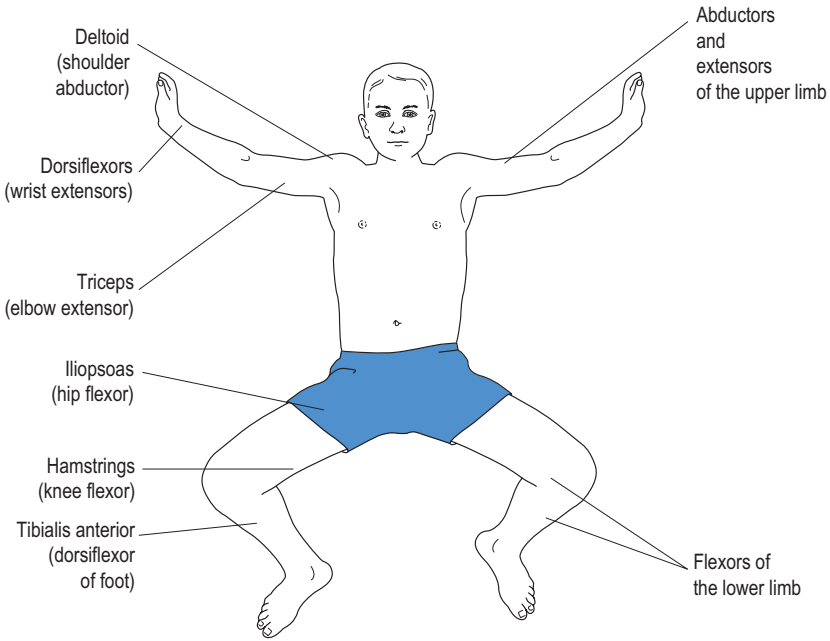


FIGURE 5.5 Antigravity muscles.

diagnosis of functional illness. Such finding opens the way to explore the underlying cause for such behaviour.

As demonstrated in Chapter 4, neurological diseases assume a set pattern of presentation. This is particularly so for upper motor neurone deficit which affects antigravity muscles (Fig 5.5). Damage, as evidenced by hemiparesis, causes a set pattern of weakness, with resultant unequal power in the muscles that oppose the antigravity muscles (Fig 5.6).

A patient presenting with one-sided weakness suggestive of hemiparesis, who does not have weakness in the distribution of the antigravity muscles and who has downward plantar responses, provides clear evidence of functional illness. This demonstrates the need for further investigation and may suggest the need to involve either a clinical psychologist or psychiatrist.

CONCLUSION

As stated earlier, a detailed neurological history and examination arms the doctor with an appreciation of what to expect. When the findings fail to live up to expectation, then the doctor should consider ‘functional illness’ among the differential diagnoses. Just because ‘functional illness’ appears on the list

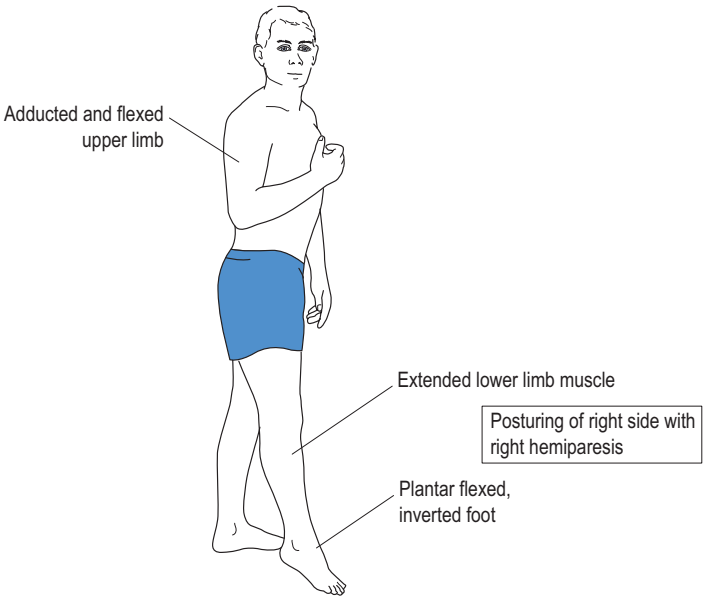


FIGURE 5.6 Spastic posture—non-antigravity muscles.

of potential diagnoses, it does not stop the doctor fully investigating other possibilities.

Some findings, such as: non-anatomical sensory deficit on the face; activation of antagonistic muscles when exerting 'maximal' power; inappropriate pattern of weakness; or a positive Hoover's sign, provide unequivocal evidence of functional illness. In these circumstances functional illness may climb to the top of the diagnostic ladder, in which case it may be appropriate to discuss this with the patient early in the clinical course. It would also be appropriate to involve a psychologist or psychiatrist early in the process. In this context it may be a positive move to reassure the patient that subsequent investigations are not being conducted to find an alternative, as yet unsuspected, diagnosis but rather to protect the patient from any possible omission. Such early acknowledgement of suspected non-organic cause for the presentation may serve to obviate chronic 'sick behaviour' and allow early intervention, as well as protecting against subsequent investigation to exclude differential diagnoses.

FURTHER READING

O'Brien M. Aids to the examination of the peripheral nervous system. 5th edn. London: Saunders; 2010.

6 Headache

INTRODUCTION

Headache is the most common neurological condition for which consultation is sought.[1] The approach adopted in this review offers a clinical strategy to guide the family doctor without need to resort to the International Headache Society (IHS) classification.[2]

This should not be interpreted as undervaluing that classification,[2] which is pivotal in allowing international consensus necessary for clinical research and trials, but clinical trials do not necessarily reflect everyday practice. The IHS criteria[2] allow researchers around the world to recruit patients with rare headache diagnoses to trial novel treatments with the ability to recruit sufficient patients to achieve statistical power. While this is fundamental for scientific progress, it does little to assist the general practitioner who sees very few cases of such conditions; for example, cluster headache. Cluster headache was not randomly chosen for this example, but rather because it is diagnosed more often by family doctors than neurologists, and affects less than 1% of those with headaches.[3]

What follows is an idiosyncratic approach to headache management developed over years of clinical experience, rather than based purely on evidence-based medicine.

BROAD-BRUSHED CLINICAL APPROACH

A practical, if unscientific, approach to headache is to consider that primary headaches lie on a continuum (see Fig 6.1). At one end of this continuum lies tension-type headaches, while at the other is migraine (with or without aura). In the middle is what might be called tension-vascular headache with features of both, a term excluded from the IHS classification.[2]

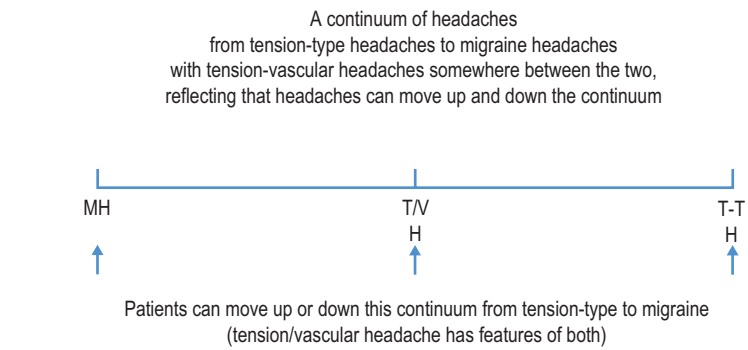


FIGURE 6.1 Headache continuum.

Differentiating tension-type headache from migraine

Most patients who present to the neurologist with 'bad headaches' automatically assume these are migraines. Migraine and 'bad headache' have become synonymous for patients, but doctors need to determine the type of headache to select the appropriate treatment.

This starts with a concise history dating from the onset of the headaches. The doctor needs to know: how long the patient has had headaches; where they occur in the head (unilateral, bilateral, frontal, occipital, vertex or completely generalised); the nature of the pain (be it constant and gripping, throbbing and pulsating, or stabbing and lancinating); associated features (visual symptoms, gastrointestinal (GI) symptoms of nausea and/or vomiting, photophobia, phonophobia or osmophobia); the frequency and duration; and precipitating and relieving factors. This will assist in differentiating migraine from tension-type headache (see Table 6.1).

Detailed physical examination is warranted for all headache patients, particularly fundoscopy and searching for focal neurological signs, which should alert the doctor to more serious illness and the need for investigation. It is most important to look for venous pulsations on fundoscopy, which, if present, exclude raised intra-cranial pressure (see Fig 6.2).

While migraine (with and without aura) and tension-type headaches make up the vast bulk of primary headaches encountered, the doctor should not ignore the possibility of other headache types. For the majority of patients, the above approach to history and examination will be sufficient to provide a firm diagnosis, thereby obviating the need to order expensive tests.

TABLE 6.1 Differentiation between migraine and tension-type headaches

Migraine	Tension headache
Unilateral—often in the temple	Bilateral—like a band or in both temples
Throbbing pain—pulsating	Tight, gripping pain—constant
May be provoked by: • often occurs once stress has passed (let-down phase) • smells • foods (e.g. chocolate) • hormonal changes	May be provoked by times of maximal stress
May have: • teichopsia (zigzag bright shimmering colours) • fortification spectra (like seeing the top of a cowboy fortress) • see rainbow effects • see photons of light (bright flashes)	Either no visual symptoms or simply some blurring of vision
Nausea and vomiting is common	Nausea may be present but rarely vomiting
Commonly have: • photophobia • phonophobia • osmophobia • positive family history	Usually do NOT have: • photophobia • phonophobia • osmophobia • positive family history
Acute intervention: • triptans • ergots • occasionally early use of analgesics	Acute intervention: • rest • simple analgesia
Prophylaxis: • pizotifen offers effective prophylaxis	Prophylaxis: • tricyclic antidepressants (amitriptyline and imipramine offer effective prophylaxis)
May be provoked by alcohol	May be eased by alcohol

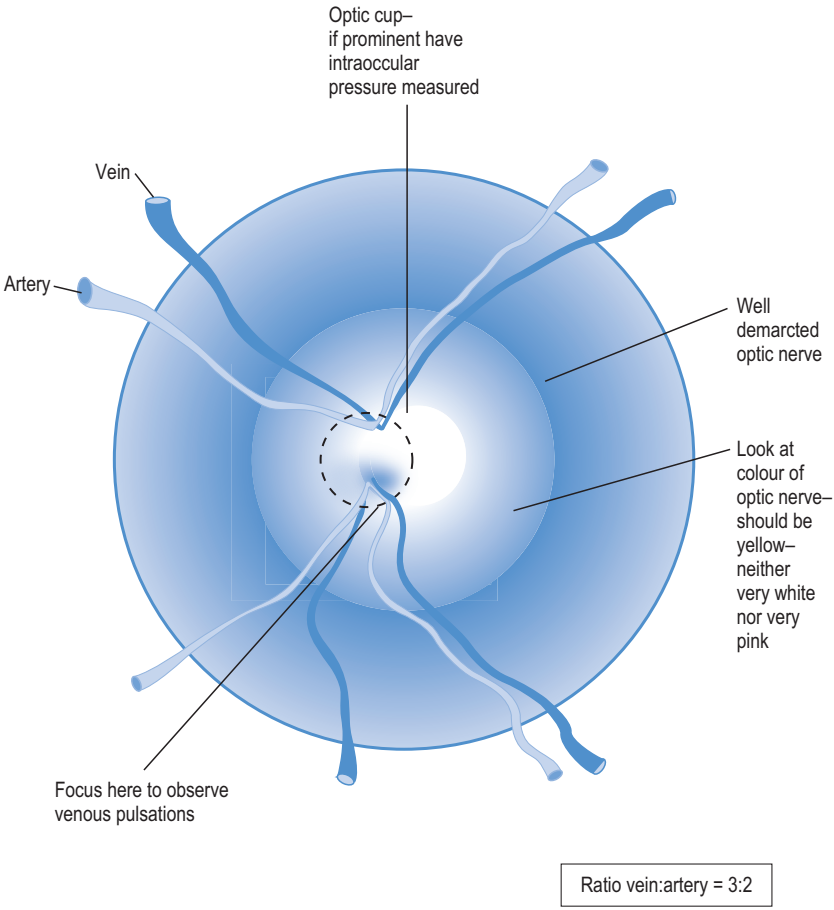


FIGURE 6.2 Ophthalmoscopic disc examination.

RED FLAGS FOR THE NEED FOR FURTHER INVESTIGATION

Some symptoms should alert the doctor to the need for further testing (see Box 6.1).

These 'red flags' include marked exacerbation of headaches with coughing, straining or sneezing.[4] If the headaches are provoked by stooping or postural changes, the doctor should order cerebral imaging. Associated neurological symptoms, such as sensory changes or weakness, demand further testing. Headache associated with eye movement and impaired vision suggests

BOX 6.1 Need for further investigation

- Headaches exacerbated by coughing, sneezing or straining
- Headaches exacerbated by postural change (stooping or bending over)
- Headaches associated with eye movement and blurred vision
- Sudden onset severe headaches worse than previously experienced
- Headaches associated with focal neurological signs (be aware of neurological signs consistent with non-organic disease (Ch 5))
- Headaches not responding to appropriate treatment
- Significant change in quality, nature or site of headache
- Headaches associated with stiff neck, symptoms of infection, generalised aches and pains and skin rash (need not have all these symptoms)

retrobulbar neuritis. Headache with enlarged blind spot may suggest papilloedema or raised intracranial pressure. Headache with stiff neck, nausea and vomiting should be sent to the hospital for consideration for lumbar puncture.

When in doubt, the general practitioner faced with a 'red flag' should involve a consultant early in the clinical picture. If the provisional diagnosis was that of a simple primary headache for which response to treatment was unexpectedly poor, there is need to revisit that diagnosis and reconsider investigations.

A change in the nature, quality or site of the headache should also raise suspicion. It is easy to become complacent when treating a patient with long-standing headaches and thus an index of suspicion is vital for good patient care.

DIAGNOSTIC CRITERIA

a Tension-type headache

This is the most common type of headache in which attacks are usually mild to moderate but can be quite intrusive and severe.[5] They are classified within the IHS classification[2] as episodic or chronic, for which the underlying cause is often presumed to be emotional but is uncertain with a variety of aetiologies considered.[5] It is said to be most common in the fifth decade with females affected somewhat more than males.[5]

Infrequent headaches do not usually cause medical presentation unless the pain is significant. Those who present may complain of frontal, occipital or band-like pain that usually has tight and gripping quality (see Table 6.1). It may involve the neck, causing concern of neck pathology that may or may not be found. The finding of neck pathology, such as osteoarthritis, does not necessarily have any relevance to the headache as both conditions are very common and may co-exist.

A similar picture can emerge from excessive use of analgesics, and medication-overuse headache can be overlooked unless the doctor has a high index of suspicion.

The physical examination in these patients should be normal, both generally and neurologically. It cannot be overemphasised that the examination of the patient with headache necessitates a fundoscopic examination with ophthalmoscope, as this remains the closest the doctor will get to actually look at the brain to exclude raised intracranial pressure.

b Migraine

While migraine is often perceived as the most common headache type, the relative prevalence is approximately 5% for migraine as compared to approximately 27% for tension-type headache in an adult population.[6] This is important because the correct diagnosis dictates the appropriate treatment.

Migraine is classified into those with and without aura,[7] which replaces the older terms of 'common' and 'classical' migraine. Unlike tension-type headaches, migraines are usually unilateral, throbbing in quality and often associated with nausea, maybe vomiting, and visual symptoms such as teichopsia (zigzag shimmering lights), fortification spectra (like the pointed top of a cowboy fortress), photons of light or a rainbow effect (Table 6.1). Patients may describe coloured lights (as if looking through a prism). The patient may experience photophobia, phonophobia and/or osmophobia.[7]

The relationship between headaches and alcohol is helpful as alcohol relaxes muscles and hence can relieve tension-type headaches, while it exacerbates migraines (see Table 6.1). Other provocateurs for migraines include: low blood sugar; hormonal changes (such as catamenial); odours (such as perfumes); allergies; excess or insufficient sleep; and transformation from other headache types.

People who have migraines often report a positive family history of headaches, suggesting a genetic propensity. It must be remembered that tension-type headaches are also very common, thereby possibly giving a false impression regarding the relevance of family history, which may be coincidental.

c Symptomatic headaches

The community cannot afford to investigate every headache when tension-type headaches are so common. Conversely, one cannot ignore headaches that are symptomatic of underlying illness. Some of the 'red flags' have already been discussed (Box 6.1). Headaches exacerbated by coughing, sneezing or stooping justify urgent cerebral imaging. Absence of venous pulsations on fundoscopy or evidence of raised intracranial pressure with stiff neck call for more detailed assessment and referral. It must be remembered that 10% of the normal population do not have venous pulsations.

Sudden onset of severe headaches with nausea, vomiting, stiff neck and visual obscuration may suggest subarachnoid haemorrhage. Skin rash, symptoms of upper respiratory tract infection, generalised aches and pains, photophobia and possible exposure to infected individuals may suggest meningoencephalitis. Lumbar puncture is warranted in these patients, usually preceded by cerebral imaging and definitely by fundoscopy, to exclude raised intracranial pressure (see Fig 6.2).

Headaches associated with neurological signs, such as weakness, sensory changes and/or a history of seizures, may suggest a space-occupying lesion. Cerebral imaging, such as magnetic resonance imaging, is mandatory in such cases.

It must be remembered that weakness and sensory changes follow set patterns within neurological evaluation (see Chs 4 and 5). Similarly, headaches associated with such symptoms and signs that do not conform to anatomically defined patterns, suggest psychological illness and may justify an alternative approach to management.

d Other headache types

While there are many headache types included within the IHS classification[2] only the most common forms, referable to general practice, will be discussed in this section.

i Cluster headache has already been identified as over-diagnosed by family doctors. These headaches often occur on 'the-morning-after-the-night-before', are generally unilateral with suffused red eye, lacrimation and stuffy nose. The headaches usually occur at the same time each day, frequently in the early hours of the morning (often waking the patient), and are more common in males. The IHS classification requires patients to have at least five attacks occurring from one every other day to eight per day without other cause. They are associated with unilateral, orbital, supraorbital or temporal pain lasting 15–180 minutes (if untreated) and are associated with one or more of the following: ipsilateral conjunctival injection or lacrimation; ipsilateral nasal congestion or rhinorrhea; ipsilateral eyelid oedema; ipsilateral forehead and facial swelling; ipsilateral miosis or ptosis; or a sense of restlessness or agitation.[8]

ii Cervicogenic headache is another common family practice diagnosis characterised by chronic hemicranial pain said to be referred from bony or soft tissues in the neck. This is thought to be generated from the spinal trigeminal nucleus[9] but is often indistinguishable from other headache types, such as tension-type headache,[9] and thus is treated within the spectrum of those headache types.

iii Thunderclap headache[10] presents with a sudden onset of frightening head pain that may occur during sexual intercourse, often at the climax. It is

thought to relate to a sudden rise in blood pressure that may accompany coitus, and requires sensitive management and reassurance to avoid emotional consequences. It is usually self-limiting. Thunderclap headache may be the first sign of a variety of other conditions, such as subarachnoid haemorrhage, unruptured intracranial aneurysm, cerebral venous sinus thrombosis, cervical artery dissection, acute hypertensive crisis, spontaneous intracranial hypotension, ischaemic stroke, pituitary apoplexy or intracranial infection. It follows that these need to be excluded before reassuring the patient.

iv Chronic daily headache (CDH) is a term frequently used but excluded from the IHS classification.[11,12] Rather than being a specific headache type, it defines severity. The IHS prefers terms such as chronic migraine or chronic tension-type headache. Headaches may change from one type of chronic headache to another.[12] Headaches in CDH should occur at least every other day (15 days per month) lasting a minimum of four hours per day for a period of at least six months. CDH is the most refractory form of headache and is the final common pathway for a variety of headache types.[13]

MANAGEMENT

Management encompasses both diagnosis and treatment, and the above diagnostic criteria offer better selection of treatment options. Treatment seeks immediate headache cessation and prophylaxis against recurrence.

Tension-type headaches respond to oral aspirin 500–1000 mg or non-steroidal anti-inflammatory agents.[5] Many of these are available without prescription, thereby allowing excessive use, which may itself cause headaches. Analgesia-overuse headaches always must be considered and addressed when necessary.

Prophylaxis for tension-type headaches includes tricyclic antidepressants, such as amitriptyline or imipramine, starting at 25 mg nocte and building up to a maximum of 200 mg nocte. Tricyclics offer effective intervention, with amitriptyline used if there is a poor sleep pattern and imipramine where sleep is adequate. Recently, a patient on maximal dose of tricyclic antidepressants developed sufficient bradycardia to experience congestive cardiac failure. Patients should be warned that if breathing problems or palpitations occur an urgent consultation with the doctor is required.

Side-effects include fatigue, anti-cholinergic properties with thirst (which some interpret as hunger causing excessive eating and weight gain), palpitations and GI disturbance. The medication is taken half-an-hour before retiring but if GI disturbance ensues it should be taken with the evening meal.

Headache treatment is not restricted to pharmacological intervention and should include: review of lifestyle issues; counselling; exploration of diet and alcohol consumption; work-related habits; and an holistic approach to patient

care, that transcends headache boundaries and is relevant to all headache types.

Immediate migraine intervention includes the triptans or ergot-containing compounds taken at the very onset of symptoms (either the aura or headache). The triptans include sumatriptan, zolmitriptan and naratriptan, which may cause a sensation of chest pressure, flushing, paraesthesia and drowsiness.[6] Some patients may respond to one type of triptan and not another. Many ergot-containing compounds are no longer commercially available and may require a compounding pharmacist, but should not be lightly discarded from the therapeutic options.

Pizotifen offers an effective prophylaxis against migraines but little benefit in tension-type headaches. Thus it is mandatory to differentiate between them (see Table 6.1). The dosage starts at 0.5 mg b.d. and can be increased up to 1.5 mg t.d.s. (IX per day). Side-effects may include increased appetite and fatigue.

Methysergide is still an effective prophylaxis for migraine (4–8 mg/day) but it carries too many risks to be first-line therapy. Immediate side-effects include leg swelling, muscle pain, chest pain and nausea but the long-term risks, which are attached to ergotainine-based products such as pleural and retroperitoneal fibrosis, are worrying and limit its use.

For those headaches that fall somewhere between tension-type headaches and migraines, so-called tension-vascular headaches (see Fig 6.1), propranolol offers prophylaxis. Immediate headache cessation may rely on either of the above approaches though more commonly the tension-type headache approach is favoured.

The dosage of propranolol starts with 10–20 mg b.d. and can increase up to a maximum of 160 mg q.i.d. Care must be taken to avoid exacerbating cardiac disease or failure, asthma or provoking excessive hypotension. A history to identify these conditions is mandatory before prescribing medication and the patient must be warned to seek immediate medical attention if breathing problems or lightheadedness occurs.

Recently use of antiepileptic medications, such as valproate, topiramate, gabapentin,[12] pregabalin and even levetiracetam,[13] have been used for headache therapy but it is wise to involve a consultant before embarking on their use. Similar caution should apply to the use of botulinum toxin that also has received recent acclaim following clinical trial.[14]

While cluster headache is rare, its features are classical, thereby making diagnosis easier. Immediate headache treatment may be offered by oxygen inhalation by a non-rebreathing mask at 6.10 L/min for 15 minutes. Subacute triptan administration (for example, 6 mg sumatriptan) or intranasal triptan (such as sumatriptan or 10 mg zolmitriptan) is efficacious. Prophylaxis is given early in an attack and maintained for a couple of weeks after it. Virapamil, a calcium channel blocker given 80–160 mg t.d.s. or 240 mg sustained release daily, is currently accepted treatment. Lithium is also used, as are steroids.[8]

CONCLUSION

Headache is a very common condition for which most patients respond to the above paradigm. **Primary headaches must be differentiated from secondary headaches, and doctors need to be cognisant of the 'red flags' alerting the need for extra vigilance. Where patients fail to respond, or there is reason for concern, the early involvement of a consultant specialist is advised.**

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7 Epilepsy

INTRODUCTION

Epilepsy is a diagnosis that evokes fear and stigma, as evidenced by the commonly used phrase, 'I wouldn't do it in a fit!'. The definition of epilepsy is a tendency to recurrence of seizures, which is as broad a definition as are the variety of seizures.

Extrapolating from this, epilepsy is not a satisfactory diagnosis. It represents a symptom of another underlying diagnosis that has provoked the seizures. This has translated into an internationally accepted classification of seizures (see Fig 7.1),[1] which offers the road map to provide treatment options.

There is also an internationally accepted classification of the epilepsies[2] (note the plural) provided to allow the clinician to acknowledge that one type of epilepsy may incorporate numerous seizure types (see Box 7.1).

The classification of the epilepsies also permits prediction of prognosis, thereby making both classifications part and parcel of a better understanding of the condition. An easier way to describe this is that the description of seizures offers phenomenology of the event, and description of the epilepsies provides a syndromal approach. As these classifications should mirror current knowledge, the leaders in the field are constantly trying to improve their content and suggesting enhanced pedagogy.[3]

It can be seen that the study and management of epilepsy is a vibrant and complex endeavour. It encompasses many other illnesses that can themselves provoke seizures, fits, turns or any other such term that may be in vogue. The aim of this chapter is not to turn the family physician into an 'epileptologist' but rather to offer epilepsy's 'travel guide' to better understanding and an appreciation of the pitfalls.

Classification of seizures		
Partial (focal)	**Generalised**	**Unclassified**
Simple partial (SPS ↓ Complex partial (CPS) ↓ Secondarily generalised (2° gen'd) Can move from one to the other Starting SPS and moving to other (ie: SPS→CPS→2° gen'd) Starting CPS→2° gen'd (not in the opposite direction)	-Typical absence -Atypical absence -Tonic -Myoclonic -Tonic clonic Can have combinations of generalised seizures	

FIGURE 7.1 Classification of seizures.

DIAGNOSIS OF EPILEPSY

The diagnosis of epilepsy rests completely on a convincing history. If the patient satisfies the above definition, then the diagnosis is confirmed even in the absence of any positive tests. The tests provide an adjunct to clinical skill rather than a substitute.

A comprehensive history is the principal tool of all neurology. The patient often is unable to report exactly what happened during the seizure due to loss of consciousness, but the doctor should not capitulate at this point. The patient should be able to describe what they were doing just before the seizure and any preliminary symptoms, such as the perception of bad smell (e.g. burning rubber), bad taste (e.g. metallic taste), or a feeling that the unfamiliar is familiar (déjà vu—I have seen it before) or the opposite (jamais vu—the familiar is unfamiliar—I have not seen it before). The patient may be able to identify flashing lights as a photic stimulation that provoked the seizure, but this only occurs in approximately 10% of people with epilepsy.[4] Stress, fatigue, sleep deprivation, drugs, alcohol or even sleep itself can provoke seizures. Menstruation and hormonal changes may cause seizures. Most of this information is readily available from the patient if the right questions are asked (see Table 7.1).

The patient will know if they bit their tongue, buccal mucosa or injured themselves in a seizure. Similarly, they can report if they were incontinent of urine or faeces. The patient will also know how they felt in the post-ictal period, whether they were confused, disoriented, exhausted and had to sleep, or if they had a headache. Thus the history from the patient is very helpful (see Table 7.1).

In addition, a history from any eyewitness will help the doctor to ascertain a word picture of what occurred during the seizure. Questions should include:

BOX 7.1 Some typical syndromes

Lennox-Gastaut syndrome

- tonic seizures
- tonic clonic seizures
- myoclonic seizures
- slow spike and wave EEG
- intellectually handicapped
- difficult to control with AEMs.

Juvenile myoclonic epilepsy

- early morning myoclonic jerks
- tonic clonic seizures
- generalised EEG abnormality
- may have photic sensitivity with spike and wave on EEG
- responds well to VPA
- exacerbated with fatigue, alcohol and stress, so need lifestyle changes
- may need lifelong treatment once started.

Temporal lobe epilepsy

- may have simple partial seizures
- may have complex partial seizures
- may have secondarily generalised seizures
- focal EEG abnormality
- often shows mesotemporal sclerosis on MRI
- may respond to CBZ
- if refractory may respond to epilepsy surgery
- may consider stopping medications after 2–5 years seizure freedom (with 60% change of seizure freedom).

(NB: each example above includes more than one possible seizure type.)

did the patient appear absent; were there automatisms (automatic behaviour such as smacking lips, fiddling with clothing, involuntary behaviour or apparently purposeful activity for which the patient has no recall); did the patient turn the head to one or the other side; where, if identified, did the seizure start (such as in one hand or in the face to then move throughout the body); were the eyes open or shut (often used to differentiate non-epileptic, pseudo-seizures from truly epileptic phenomena where eyes are open); did the patient shake, twitch, talk, writhe, flail or do anything else during the episode? (See Table 7.2.)

After spending considerable effort to define the seizure the next step is to determine if there are precipitating factors, such as illness, genetic influences

TABLE 7.1 Questions and answers that help diagnose epilepsy

Question	Answers pointing to epilepsy
When and where did the seizure occur?	• when asleep • when sleep deprived • with excess alcohol • with alcohol withdrawal • at times of stress • related to menstrual cycle • at time of flashing lights (e.g. at a dance or while playing video games)
Were there any warning symptoms or signs that occurred before the seizure?	• abnormal sensations: – smell of burning rubber – abnormal taste – rising sensation – strange focal features • twitching of limb: – tremor of hand or foot • false memory (déjà vu) • failure to recognise (jamais vu)
What do you recall from the seizure?	• loss of consciousness or awareness • bit tongue/buccal mucosa • injured self • incontinent (urine/faeces)
What have others told you about your seizure?	• eyes open during seizure • eyes rolled up • stiff before shaking • shaking (*not* thrashing) • head turned to one side • movement started on one side • automatisms: still acting while appearing unconscious • unresponsive to stimuli (be it talking or to pain)
How did you feel after the seizure?	• post-ictal confusion: – disorientation – fatigue – exhaustion and sleep – headache – muscle aches and pains
Is there a family history?	• especially with primary generalised epilepsy there may well be positive family history
Were there febrile convulsions?	• prolonged febrile convulsions may have been seizures provoked by fever rather than true febrile convulsions
Is there a history of brain trauma?	• birth trauma • accidental trauma (e.g. motor vehicle accident) • head injuries (e.g. fall from a horse) • sporting injury with loss of consciousness • hospitalisation with or without coma

TABLE 7.2 Description of seizures

Seizure type	Description
Simple partial seizure (SPS)	Consciousness retained but focal features determined by site of seizure, such as perception of a smell, a sound or a vision. Uncontrolled movement or twitching of a part of the body, such as a thumb or hand, without loss of consciousness, which may spread (such as Jacksonian march in focal motor seizure).
Complex partial seizure (CPS)	Differentiated from SPS by altered state of consciousness. Patient may be unaware or poorly relate to the surrounding environment as with déjà vu (false memory) or jamais vu (blocked real memory). The patient, while non-responsive, may have automatisms—automatic behaviour that can be quite complex—such as driving a car. The appearance may be of a patient on automatic pilot. The patient has post-ictal features of fatigue, headache or confusion. 'Absence' with post-ictal features may be CPS rather than generalised absence.
Secondarily generalised seizure	This is a convulsive seizure that follows focal onset. A convulsion in which the patient reports an aura (representing a focal seizure) is experiencing secondary generalisation (2° gen[d]) throughout the brain.
Typical absence	The patient has generalised absence that is short lived and often multiple, possibly provoked by hyperventilation. There is often no post-ictal feature.
Atypical absence	Similar to typical absence but may have automatisms. Differentiation from CPS may be difficult. EEG with typical 3 Hz spike and wave pattern may be necessary to differentiate from CPS, which will have more focal, often temporal lobe abnormality.
Tonic seizure	Drop attacks with hands and arms often coming up in front of the body and the head dropping forward as the patient becomes stiff and falls down, usually forward.
Myoclonic seizure	Sudden jerking of limbs and head—often first thing in the morning after waking. A form of generalised seizure without focal features.
Tonic clonic seizure	Primarily generalised convulsive seizure starting abruptly without focal features. Similar features to 2° gen[d] but without focality—no aura at onset.

(with family history), or exposure to toxins. An obstetric history looking for birth trauma is important, as is any other history of brain damage from accidents, assaults or trauma. An educational history gives a clue regarding poor cognition and possible impaired function. A past history of febrile convulsions is worth seeking as is the detailed past medical and surgical history.

After history taking the patient should undergo a full medical examination, particularly a neurological assessment. In general, the patient with only epilepsy and an otherwise unremarkable history will have no focal neurological signs. If signs are found then further questions seeking cause for focal cerebral damage must be asked. The doctor must accept that seizures, and hence epilepsy, are the physical manifestation of what is occurring in the brain and must question what that might be, such as a space-occupying lesion, congenital abnormality, ischaemic lesion, cerebral bleed or site of infection, such as an abscess.

INVESTIGATION OF THE PATIENT WITH EPILEPSY

a Electroencephalograph

One of the first tests is an electroencephalograph (EEG). It is imperative for the family doctor to appreciate that 10% of 'normal' patients can have an abnormal EEG and, at the same time, a person with epilepsy can have a normal EEG.[5] If ten interictal EEGs are performed in a person with diagnosed epilepsy, 25% will all be abnormal, 60% will have at least one abnormal study and 15% will have all ten studies being normal. A typical epileptiform EEG is helpful when making the diagnosis, but a vaguely abnormal or completely normal EEG is neither helpful nor unhelpful.

If the first EEG is normal but the suspicion of epilepsy is high, then a repeat study with sleep deprivation may prove helpful. Where the diagnosis of epilepsy is suspicious and the question of non-epileptic seizure (pseudoseizure) is raised, video EEG may clarify the situation and may be enhanced with sleep deprivation. Invasive EEG, relevant to more aggressive intervention, such as epilepsy surgery, will not be further discussed. Interpretation of EEG is the domain of the neurologist but it is helpful when requesting an EEG to state the reason for ordering it. Concurrent with the EEG there is usually a modified lead-2 electrocardiograph (ECG) rhythm strip. A normal EEG may still provide a diagnosis by identifying cardiac pathology, such as dysrhythmia, asystole or aberrant conduction (e.g. Wolff-Parkinson-White syndrome)[6] which gives a possible reason for the episodes—such as cardiac-caused syncope.

b Cerebral imaging

Should the examination or EEG identify focal abnormality then cerebral imaging is mandatory. If the patient has not been referred to a neurologist then this would be a good time to seek further opinion.

Magnetic resonance imaging (MRI) is far superior to computer tomography (CT), and a normal CT may not exclude cerebral pathology. MRI is usually accompanied by MRA (angiography), which may reveal aberrant vessels or increased vascularity to an area of the brain. Gadolinium enhancement may reveal tumours or abscesses.

Other cerebral imaging includes single-photon emission computed tomography (SPECT), used to assess perfusion across the blood–brain barrier, and positron emission tomography (PET), which maps cerebral metabolism. Both perfusion and metabolism is reduced in the epileptic focus interictally and enhanced during a seizure. Neither of these is within the domain of the family physician but are offered to whet the appetite to read on.

c Additional tests

As previously stated, no test is definitive for epilepsy, but as epilepsy represents underlying illnesses the clinician needs to find any identifiable diagnoses that may be treatable. Blood tests may identify electrolyte imbalances, connective tissue diseases, organ failures, infections, drug toxicities or exposure to other external agents that may be treatable. Testing urine or stools may expose causative factors, such as drug metabolites.

The history and examination may reveal causes, such as stroke in the elderly, that demand secondary prevention measures in addition to seizure management. Imaging, especially diffusion-weighted MRI, will identify new onset strokes. Intracerebral space-occupying lesions, suggestive of malignancy, demand the seeking of a primary source, thus necessitating chest and abdominal CT.

It can be seen that there is an extensive list of investigations, but by this stage most patients with epilepsy would have been referred to a consultant. Having said that, it is also envisaged that the consultant would be partnering the primary care doctor within the management team. It should never be ignored that the team captain is the general practitioner with the consultant providing expertise in the area of specialisation. For example, where neoplasia is the root cause for seizures, the oncologist plus the possibility of additional cancer specialists will manage the neoplasia-related issues, and the neurologist will advise on seizure control. Other specialists may need to be involved, such as palliative care specialists or possibly endocrinologists (for para-neoplastic accompaniments). At all times the family doctor remains the doctor of first call, the coordinator of the team, to ensure holistic medicine and, most important of all, the supervisor of wellbeing, counsellor and family ‘friend’.

DIFFERENTIAL DIAGNOSIS

Epilepsy is itself not a stand-alone diagnosis. In many cases it is secondary to some other underlining condition, so the doctor must be acutely aware of alternative diagnoses (see Table 7.3).

TABLE 7.3 Differential diagnoses

Syncope	Cardiac causes: • dysrhythmia • prolonged QT • valvular heart disease • cardiomyopathy Situational causes: • micturition • defecation syncope • cough syncope • carotid sinus hypersensitivity • valsalva manoeuvre
Orthostatic hypotension	Dysautonomia
Cerebrovascular disease	Vertebrobasilar insufficiency Subclavian steal Transient ischaemic attack Migraine Transient global amnesia
Brainstem compression	Chiari malformation Hydrocephalus
Nocturnal parasomnias	Somnambulism Obstructive sleep apnoea PLMS REM behaviour disorder
Psychiatric disorders	Non-epileptic seizures or pseudoseizures Conversion reactions Panic attacks Hysterical fugue Malingering

These may also exclude epilepsy altogether. The most common 'mimic' of a seizure is syncope. Syncope will be accompanied by negative 'epilepsy' tests, although it may reveal abnormal lead-2 rhythm ECG tracing during the EEG. Syncope will usually start abruptly, arrest spontaneously and be devoid of para-ictal features, such as confusion, fatigue or incontinence. There may be some epileptiform twitches due to cerebral hypoxia, which may create a diagnostic dilemma.[7]

Nocturnal parasomnias may mimic epilepsy. Somnambulism may be confused with ictal automatisms. Conversely, frontal lobe epilepsy, often with bizarre writhing and even mastibatory movements, particularly in female patients who are shown to rhythmically gyrate their pelvis in epilepsy telemetry, may be considered non-epileptic phenomena until the diagnosis is confirmed by the neurologist.[8] Concurrent with this recognition that sleep-related phenomena may be confused with epilepsy, it is also important to respect that such phenomena may also provoke seizures due to sleep disturbance

and possible additional hypoxaemia affecting the brain. Obstructive sleep apnoea (OSA) with twitching, jerking and gasping for air may be confused with epilepsy. OSA was first diagnosed as a consequence of epilepsy with overnight video monitoring. It should not be ignored that sleep is a neurological state and it is only with the advent of therapeutic interventions, such as continuous positive air pressure (CPAP), that respiratory physicians have claimed sleep medicine. Judicious use of CPAP, averting hypoxaemia and sleep deprivation in cases of OSA, has proven efficacious in seizure control, thereby recognising that epilepsy and OSA can co-exist, necessitating proper management of both.[9]

Transient global amnesia (TGA) in which the patient lacks recall of recent events may be confused with epilepsy.[10] Even if the diagnosis of TGA is suspected, many clinicians will still investigate the patient for epilepsy.

Transient ischaemic attack (TIA),[11] due to short-lived cerebral ischaemia, may be confused with epilepsy because of potentially short duration with possible post-ictal features and general good recovery. Acute index of suspicion is needed for such diagnoses.

Migraine is also within the differential and was discussed in an earlier review of headache (see Ch 6).

Briefly, anything that results in short-lived, altered cerebral function may resemble a seizure. Some events that are devoid of organicity, so called 'non-epileptic seizures' or 'pseudo-seizures', may resemble epilepsy. Some of the features have been discussed but the differentiation often requires involvement of a neurologist. Even the neurologist may be confused and misdiagnose non-epileptic seizures as the real thing. Two important features should be sought, namely, the potential gain for the patient and the source of the model for the featured behaviour. Even competent psychiatrists may have difficulty teasing these out, thereby making treatment difficult. One must remember that the same patient may demonstrate both real seizures and hence epilepsy, as well as non-epileptic phenomena, thus truly confounding the picture.[12]

TREATING THE SEIZURES

As already discussed, seizures are divided into those with focal or generalised onset. This differentiation determines the choice of optimal anti-epileptic medication (AEM). Carbamazepine (CBZ) [Tegretol®] is the choice for focal seizures, also known as partial seizures, and valproate (VPA) [Epilim®] is the choice for generalised seizures. These belong to the older generation of AEM, with both being first published in the 1960s. Phenytoin (PHT) [Dilantin®] is no longer a first-line agent because of saturable metabolism, which causes potential for a large increase in blood levels with minor dosage adjustment and a wide range of unwanted effects[13] that can affect all bodily functions from pseudolymphoma to cardiac dysrhythmia and heart block. The reason for favouring the older AEMs is that none of the newer AEMs has surpassed them in head-to-head trials and they are far cheaper.[14] There is

evidence suggesting newer AEMs have a better side-effect profile[15] but their cost precludes their initial use.[14]

It would be remiss not to mention generic AEMs. Many specialists argue against generics in epilepsy because one cannot be certain of absolute bioequivalence. Allowing the pharmacist to switch from standard AEM to generics, recognising there may be more than one generic per AEM, could result in the patient continuously changing AEM, thus placing seizure control in jeopardy.[16]

Over the last few decades there has been an explosion of newer AEMs. Some, like vigabatrin, felbamate or tiagabine, have already largely fallen out of favour due to unacceptable adverse effects. They are only used in niche markets, such as vigabatrin for West's syndrome.

If the patient does not respond to the initial AEM, be it CBZ or VPA, the likelihood of responding to subsequent AEM is less favourable.[17] This does not exclude trying other AEM but this is probably the time to call in reinforcements (if the general practitioner initiated treatment without consultant input). Seizure control has become more complicated with respect to choosing AEM or combinations thereof. Competition between monotherapy (preferred) and rational polypharmacy, where certain combinations (such as VPA with lamotrigine (LTG)) have a mutually beneficial pharmacokinetic and pharmacodynamic interaction,[18] is a hot topic.

AEM thought efficacious for generalised epilepsies include VPA, LTG, levetiracetam (LVT), topiramate (TPM) and maybe gabapentin (GBP) (see Table 7.4). These are 'broad-spectrum' AEM that can also be used for partial onset (focal) seizures.

Less broad spectrum AEM can usually only be used to treat focal seizures (see Table 7.4). They are either ineffective for generalised seizures or they may exacerbate some forms, such as CBZ exacerbating myoclonic seizures. Ethosuximide (Zarontin®) is an AEM only suitable for generalised absences but may exacerbate tonic–clonic seizures and largely has been replaced with VPA.

Other AEM within the newer generation available for focal seizures include oxcarbazepine (similar efficacy to CBZ with less central nervous system unwanted effects). Pregabalin, a new AEM developed after GBP, may have good efficacy although personal experience has not been encouraging (see Table 7.4). It is advisable to involve an epilepsy specialist if CBZ and VPA fail to achieve seizure control. Personal preference would advocate involvement of a neurologist to validate the diagnosis even before prescribing the first AEM, to choose the best AEM.

Prescribing Tegretol® or Epilim®

The above offered a broad overview of AEM treatment of seizures. What follows will focus specifically upon Epilim® (VPA) and Tegretol® (CBZ), acknowledging the use of trade rather than generic names. Ticking the

TABLE 7.4 Selection of medications

Generalised seizures	Partial seizures [focal]
Epilim® (valproate [VPA])	Tegretol® (carbamazepine [CBZ])
Lamictal® (lamotrigine [LTG])	Epilim® (valproate [VPA])
Keppra® (levetiracetam [LVT])	Dilantin® (phenytoin [PHT])
Topamax® (topiramate [TPM])	Trileptil® (oxcarbazepine [OXC])
Maybe Neurontin® (gabapentin [GBP])	Lamictal® (lamotrigine [LTG])
Zarontin® (ethosuximide [ETX]) • only for absence seizures	Keppra® (levetiracetam [LVT])
Phenobarb (phenobarbital [Pb]) • rarely used	Topamax® (topiramate [TPM])
Mysoline® (primidone [Pm]) • rarely used	Neurontin® (gabapentin [GBP])
	Lyrica® (pregabalin [PGB])
	Phenobarb (phenobarbital [Pb]) • rarely used
	Mysoline® (primidone [Pm]) • rarely used
	Vimpat® (lacosamide [LCM]) • In Australia can only be started if patient is on one old AEM and one new AEM with refractory epilepsy (see Pharmaceutical Benefits Scheme)

appropriate box on the prescription that precludes brand substitution by the pharmacist obviates the risks of generic substitution. Unfortunately some pharmacists will substitute generics even if the box is ticked.

There is a caveat that must be appreciated which reflects a relatively unique attitude to epilepsy therapeutics, based on years of experience that include both general practice and consultative neurology. It contradicts what purists incorporate into textbooks about epilepsy. Such tomes are usually written by consultants who believe patients comply with the doctor's advice. This may be true in the beginning when the fear of further seizures is pervasive, but as this fear relaxes so does compliance.

General practitioners recognise that patients are a law unto themselves: they do what is simple and rarely fully comply with the doctor's advice. Thus it is imperative to provide options that accommodate the modern pace of living. The goal is to achieve seizure control with minimal disruption to quality of life, avoiding unwanted treatment effects, such as sedation. Before prescribing AEM, the doctor needs to warn the patient that unwanted effects

may occur, to read the package insert and avoid dangerous situations, including driving.

Most patients, once they have accepted a more relaxed routine, cannot be relied upon to take a midday dose of medication. Prescription of a three times per day dosage is largely impracticable as what will eventuate is a twice per day consumption. Where compliance remains questionable, the use of a diary in which the patient records the taking of medications at the time thereof provides a written record available to the doctor.

Both Tegretol® and Epilim® are offered in enteric coated, slow release format making 'twice per day' dosing possible. CBZ is offered as a 400 mg controlled release (CR) tablet, starting with half a tablet at night and increasing by half a tablet on every fourth day until the dosage is a full tablet twice per day. The patient should be warned about toxicity, including fatigue, nausea, vomiting, confusion, ataxia or incoordination. CBZ evokes autoinduction of liver enzymes that may lower the steady state level, so blood levels should be measured in approximately six weeks. The dosage is then adjusted to achieve a total blood level of 25–50 μmol/L or a free (unbound) level of 6–13 μmol/L.

Unlike CBZ, which is scored and can be broken in half, VPA is not scored and should not be divided because this will disrupt the enteric coating. VPA should be started with 500 mg nocte and on day 3 or 4 increased to a full tablet twice per day. As seizures are more common during sleep it is always wise to initiate CBZ and VPA at night, and when increasing the dose to give the larger of the two doses before retiring at night. Blood levels of VPA are more rapidly achieved and hence the levels can be measured in approximately two weeks, aiming for a total level of 300–750 μmol/L or a free level of 30–75 μmol/L.

Blood level monitoring has largely fallen out of favour, possibly because it was measured too frequently without proper appreciation of how best to use the results. Personal preference is to use them where doubts exist about doses in individual patients, especially when initiating treatment. Blood levels are not a substitute for clinical judgment and if levels do not reflect expectation, such as very low levels in patients prescribed large doses, questions regarding compliance need to be addressed. If patients appear toxic, despite therapeutic total blood levels, then unbound, free-fraction may need measurement. Where levels suggest toxicity but the patient has no such symptoms—treat the patient, not the levels—monitor levels more closely.

TREATING THE EPILEPSY

Epilepsy is more than seizures. It is a condition with stigma, social implications and potential lifelong impact even if seizures are controlled. No-one is better placed to deal with these issues than is the general practitioner.

People have an established self-image, and adult or even adolescent onset epilepsy may threaten that image. Epilepsy invokes a lack of predictability—

there is always the threat of another seizure without knowing exactly when, or even if, it will occur. The person who has had a first seizure has approximately 35–70% chance of a second seizure, and after a second seizure the risk is approximately 80% continuing to rise with each subsequent seizure.[19,20]

The patient must deal with a reliance on medications, which reduces independence. There is reliance both on pills and the doctor who prescribes them. The doctor must supervise compliance with treatment and adjust lifestyle issues to accommodate the epilepsy.

Seizures and driving are incompatible, such that the patient must be seizure free for predetermined periods of time to be permitted to drive. While the doctor advises the licensing authority on 'fitness to drive', the licensing authority is responsible for the final decision established within the Austroads Guidelines.[21] This is not absolute and the doctor needs to acknowledge a duty of care both to the patient and the wider community. If a doctor does not stop a person with uncontrolled epilepsy from driving, there is potential for an injured third party to litigate against that doctor.

PSYCHOSOCIAL ISSUES

Driving is not the only psychosocial issue requiring the general practitioner's attention. Recreational activities, such as swimming, surfing and sporting activities, dictate that the person with epilepsy should not swim alone. Someone present should be aware of the epilepsy and be capable of rendering assistance if necessary.

Social interaction in school and even special schooling needs may require general practitioner involvement. A letter seeking special consideration from the Department of Education and the school principal may determine the difference between achieving optimal results or failing. Generalised epilepsy may hinder concentration, while focal epilepsy may impact on recall. Once teachers are aware of this, they might tailor teaching to the student's idiosyncratic needs.

Juvenile myoclonic epilepsy (JME) is exacerbated by alcohol, lack of sleep, stress and poor compliance. The general practitioner should assist the patient to adopt a lifestyle that accommodates the epilepsy (with ample sleep and avoiding alcohol) while also encouraging the patient to strive to achieve maximal potential. Quality of life demands realistic expectations. Some career choices are impracticable, such as airline pilot, bus driver, soldier, working at heights or with dangerous equipment. The general practitioner needs to ensure that the patient's aspirations are compatible with their epilepsy. Self-employment avoids potential for discrimination but is not always practicable for the person with epilepsy.

Teratogenicity needs to be considered, and folate may protect the neural axis during development. High doses of some AEM, such as VPA, are to be avoided if possible. Should pregnancy be planned then it is advisable, where possible, to wean out AEM prior to the pregnancy. It is generally too late to wean out medications after the pregnancy has been confirmed, as this is

usually well into the first trimester. By this time potential teratogenicity, if it is to occur, will have happened and removal of AEM increases the risk of seizures.

Blood levels of AEM may change dramatically during pregnancy and should be monitored. This is very much the case with LTG where levels fall dramatically during pregnancy and doses need to be increased during the pregnancy and reduced thereafter.

Oral contraception may be affected by AEM, especially those metabolised by the liver. It is important to advise the patient accordingly to obviate the traumas of an unwanted pregnancy. If liver metabolism is increased then so is metabolism of the contraceptive pill, which may render it ineffective. If contraception is important then one of the newer AEM may be better to avoid interaction with contraceptive metabolism.

Recurrence of seizures in previously controlled epilepsy should alert the doctor to possible infection. This is especially important for women with possible urinary tract infection. By far the most common reason for recurrence of seizures in previously controlled epilepsy is lack of compliance or, more correctly, lapse of compliance. This can be confirmed by determining blood levels of the prescribed AEM.

Therapeutic drug monitoring

AEM can interfere with other medications, such as antibiotics or anticoagulants, and patients need to adjust for this. The combination of erythromycin with CBZ can lead to CBZ toxicity. Warfarin may need adjustment with more frequent INRs in combination with AEM.

The time to measure AEM blood levels is when doses have been changed, compliance is doubtful or the epilepsy has inexplicably altered. Highly protein-bound AEM such as PHT, CBZ or VPA may have altered protein binding, especially with polypharmacy, renal disease, liver disease or pregnancy, and both total and free blood levels can assist treatment. Most of the newer AEM do not have a proven therapeutic range with the exception of LTG, for which measuring levels may allow a larger dosage than is usually adopted.

Blood level measurement can also improve treatment of status epilepticus (SE), but SE falls into emergency medicine rather than routine care and won't be further discussed. It is imperative that carers be taught how to give emergency buccal or nasal midazolam to abort a prolonged seizure. This needs to be discussed between the general practitioner and consultant, and between the doctor and patient or patient's carer, and will not be further addressed here.

Reflex epilepsy

Some forms of epilepsy are provoked by special situations, such as flashing lights as encountered in discotheques or night clubs or with a faulty television, and the patient with photosensitive response during EEG should be advised to avoid such circumstances.

Should seizures only occur in the catamenial period then the addition of clobazam (Frisium®) during the period just before (say 1–2 days) and into (also about 1–2 days) the mensis may be all that is required.

If seizures occur at times of stress then judicious use of a short-acting benzodiazepine, such as lorazepam (Ativan®), may obviate seizures.

CONCLUSION

Management of epilepsy requires both the correct diagnosis and appropriate choice of treatment—both pharmacological and psychosocial. The most important diagnostic tool is the taking of an accurate and comprehensive history, which is complemented by suitable investigations, all of which may be normal without disturbing a history-based diagnosis. The early involvement of a consultant assists both diagnosis and treatment, but there is little reason to bypass the established AEM of CBZ for focal epilepsy and VPA for generalised epilepsy as first-line agents. The general practitioner is by far the best placed to address the psychosocial issues.

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8 Vertigo

INTRODUCTION

All too often the patient presents to the doctor complaining of 'dizziness', which is a 'non-word' as it is ambiguous and means different things to different people. 'Dizziness' can mean 'true vertigo' but it can also mean confusion, tiredness, light-headedness, loss of balance, headache, hunger or any other variety of words idiosyncratic to any particular patient. It follows that there can be no correct approach until the definition relevant to that patient has been established.

Patients will often get angry when asked to define 'dizziness' and, all too often, the doctor will accept 'dizziness' to mean something different to what the patient is trying to report. The doctor will translate 'dizziness' to mean 'vertigo' when in many cases it does not. As with all neurology, it is the history that is so important. The word 'giddy' is not a substitute for 'dizzy', and likewise is ambiguous and a 'non-word' meaning different things to different people.

Vertigo is a very specific word derived from two words, namely 'vertere', to turn and 'igo', a condition.[1] It implies an unreal sensation of motion, meaning that the patient perceives the sensation of movement when, in fact, the patient is stationary. Thus history taking when exploring what might prove to be true vertigo *must* explore the question of unreal motion, which can be objective, implying the external environment is perceived as moving, or subjective, in which the patient feels as if they are moving while the surroundings are stationary. Both equate to vertigo.

Perhaps the most common cause for vertigo to be referred to a neurologist is that of benign positional paroxysmal vertigo (BPPV), which can and should be successfully treated by the family doctor, although more often than not it

does result in referral to either a neurologist or ear, nose and throat (ENT) surgeon.

What follows is a discussion of vertigo that will allow the general practitioner to take control in most instances. It aims to demystify vertigo and empower the general practitioner.

TAKING THE HISTORY

The most important part of history taking has already been discussed. It is absolutely imperative for both patient and doctor to read from the same text. Message sent must equate to message received. Causes for loss of balance can be quite different to those for vertigo. Differentiation will dictate appropriate management, namely diagnosis and its treatment.

Having confirmed that the basis for presentation is vertigo, the doctor needs to clarify its cause. The type and nature of the vertigo will help with diagnosis. Vertigo that occurs in bed, particularly after turning over in bed either right to left (or the converse), is more likely than not, going to be BPPV (see Table 8.1). Vertigo that follows an upper respiratory tract infection will probably be caused by labyrinthitis or vestibular neuronitis (see Table 8.1). Vestibular neuronitis (labyrinthitis) is usually of acute or subacute onset, causing rotatory vertigo together with nausea and postural loss of balance.

Vertigo associated with profound vomiting and deafness may be a case of Ménière's disease (see Table 8.1). Ménière's disease often has a greater problem with tinnitus, which may precede the complaint of loss of hearing. Other peripheral causes of vertigo are fairly rare (see Table 8.1).[2]

TABLE 8.1 Peripheral causes of vertigo

Cause	Symptoms
Labyrinthitis (also called vestibular or peripheral neuronitis)	Follows an upper respiratory tract infection with acute or subacute onset
Benign positional paroxysmal vertigo	Occurs when turning in bed or with positional changes
Ménière's disease	May precede or follow hearing loss associated with increased vomiting, tinnitus, debilitating vertigo
Barotrauma	History of diving
Otosclerosis	Difficulty hearing with background noise
Herpes zoster oticus	Often associated with Bell's palsy (Ramsay Hunt syndrome) Often very painful
Perilymphatic fistula	Painful
Cholestatoma erosion	Rare and often only diagnosed with imaging

TABLE 8.2 Central causes of vertigo

Cause	Symptoms
Ingestion of substances such as alcohol or medications	History of ingestion More widespread incoordination ataxia
Transient ischaemic attacks and strokes	Sudden onset in patients with history of vasculopathy (possibly diabetes and hypertension) and often smokers
Trauma affecting the brainstem (pons) with possible haemorrhage	History of trauma, assault or accident prior to onset
Acoustic neuroma	Slow onset and associated with hearing loss
Multiple sclerosis	Symptoms divorced in time and place
Migraines	Headache may be a significant feature but need not be so
Psychogenic causes	Psychogenic true vertigo is exceedingly rare but possible

When considering vertigo, one should not overlook motion-induced vertigo that may relate to either peripheral vestibulitis or BPPV. Psychogenic causes of vertigo, as are reported in the patient who claims seasickness even when watching the ocean from dry land, may need desensitising and referral is warranted. Psychogenic vertigo may also occur in conjunction with panic disorders or hyperventilation.

There are also central causes of vertigo (Table 8.2),[3] acknowledging that vertigo may be provoked by dysfunction anywhere along the vestibulo-cochlear pathway. This travels from the receptors in the ears, which record motion and position within the environment, and travel along the 8th cranial nerve to the pontine, brainstem connections. Hearing is also dependent upon competence of the 8th cranial nerve and, with mutual passage, both can be 'interrupted' by common aetiologies.

Perhaps the most common central cause of vertigo, often associated with ataxia, incoordination and other definitive symptoms, is the ingestion of toxic amounts of substances such as alcohol or medications; for example, anti-epileptic medications. These causes will often have other associated histories that make their diagnosis quite straightforward (see Table 8.2).

Damage to the pontine or cerebellar connections, as may occur with trauma, ischaemia (be it transient ischaemic attack or stroke), tumours of the cerebello-pontine angle (such as acoustic neuromas or pontine tumours like gliomas) or vascular anomalies, can all provoke true vertigo.[4] Lesions in the brainstem may also have other cranial nerve abnormalities.

Tumours located in the cerebellopontine angle, such as acoustic neuromas or schwannomas, may evoke vertigo. The onset of symptoms may be slower

TABLE 8.3 Vertigo-associated symptoms that may assist with localisation

Location	Symptom
Inner ear	Impaired hearing Tinnitus
Internal auditory canal	Impaired hearing Tinnitus Facial weakness
Cerebello-pontine angle	Impaired hearing Tinnitus Facial weakness Altered facial sensation (dysaesthesia) Limb ataxia/incoordination
Brainstem	Cranial nerve symptoms: • diplopia • facial weakness/dysaesthesia • dysarthria • dysphagia Limb weakness/ataxia/dysaesthesia
Cerebellum	Limb ataxia Generalised incoordination

than is the case with other causes. Less common causes of central vertigo may include migraines or multiple sclerosis, but the history should be self-explanatory. Vascular malformations may cause centrally-induced vertigo.

From the above it is established that vertigo can result from lesions anywhere along the vestibulo-cochlear pathway. Knowing the symptoms that attach to each location may enhance diagnostic acumen (see Table 8.3).

EXAMINATION

Examination starts at the time of calling the patient into the consultation. Coordination and gait ataxia should have been noted even before talking to the patient. How the patient stands up from the chair or whether they heard their name being called are all valuable signs.

The history will direct attention in the appropriate direction. Cranial nerve examination is the usual formal starting point. The ophthalmoscope is particularly useful. It may allow the definition of nystagmus even in the primary position, as patients often have difficulty focusing on a distant object with the bright light of the ophthalmoscope. Evidence of raised intracranial pressure may suggest a brainstem or cerebellar pontine angle space-occupying lesion if vertigo is the initial complaint. Ophthalmoplegia may suggest multiple sclerosis; while 6th or 7th cranial nerve deficit may imply pontine

lesion; and deafness suggests vestibulo–cochlear damage, either centrally or peripherally.

Having used the ophthalmoscope it is wise to also examine the ears with an otoscope. The tympanic membrane should be viewed for inflammation. Signs of previous damage with perforation of the drum may be seen. There may be associated pus. Pressing on the tragus of the ear may provoke vertigo, suggestive of perilymphatic fistula (Hennebert's sign).

Central subtle nystagmus, provoked during ophthalmoscopic examination and possibly not seen otherwise, has already been alluded to. Horizontal nystagmus may be either central or peripheral but if it always presents as the fast component moving to the same unilateral direction irrespective of eye position, it suggests peripheral cause for nystagmus. Vertical nystagmus, especially down-beat nystagmus, suggests a central cause.

One of the best-known tests, used specifically for BPPV, is Hallpike's manoeuvre. In this the patient sits upright on the examination couch, is drawn back quickly and advised to keep the eyes open. The head is turned such that the ear is lowermost and the head is held at an angle of 45° to the horizontal. The patient is asked to keep the eyes open and to look down to the floor. This evokes a torsional affect on the calcium carbonate laden hairs in the inner ear, causing a sensation of rotation towards the lowermost ear, which occurs after a brief latent period. This is repeated so that both sides are tested (see Fig 8.1).[5] Absence of the latent period is more indicative of a central cause for the vertigo.

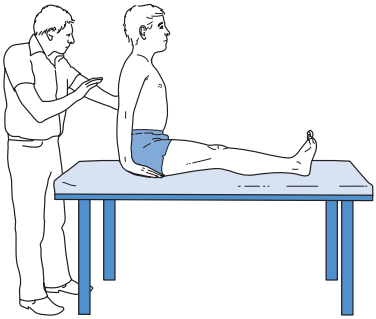
Other useful tests include the 'head impulse test' and the Fukuda-Unterberger test.[6] The 'head impulse test' assesses acute vestibulopathy with head turn to the affected ear evoking a delayed response with the need for a corrective saccade, eye movement, to maintain focus on an object. The Fukuda-Unterberger test causes the patient to deviate to the affected side when 'marking time', namely stepping or marching on the spot.

Romberg's test has the patient standing to attention in military fashion, closing their eyes. This will evoke enhanced dysequilibrium rather than vertigo. The navy has refined this test to have the patient stand with one foot in front of the other (heel touching toe) with arms crossed over the chest, known as Heightened Romberg's test. If the patient is already unsteady this test will add nothing: its original use was for testing proprioception in patients with tabes dorsalis rather than vertigo. Personal preference dismisses use of Romberg's test when assessing vertigo, but its discussion was thought necessary as most general practitioners insist on its inclusion in the assessment of patients with vertigo.

INVESTIGATIONS

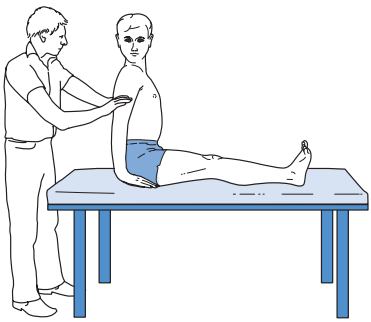
Most investigations, such as vestibular function studies, brainstem-evoked responses or even MRI, are beyond general practitioner involvement but are not usually routinely indicated in the assessment of vertigo.

Position 1



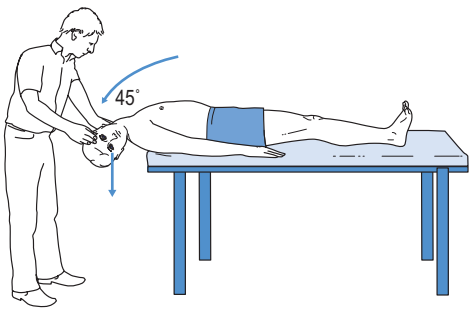
Patient sitting on bed–doctor standing behind patient

Position 2



Patient brought rapidly backwards with head turned to side

Position 3



Head down at 45 degrees to horizontal, eyes kept open and looking down to the floor. The procedure is then repeated with the head turned to the opposite side

Note: Positive Hallpike's manoeuvre has latent period in position 3 before onset of symptoms +/– nystagmus, when in the vulnerable position with the affected ear lowermost

FIGURE 8.1 Hallpike's manoeuvre.

The majority of patients with vertigo do not need sophisticated testing and the symptoms will be self-limiting. If this is not the case then specialist referral is appropriate.

TREATMENT

As already stated, the majority of cases of vertigo, especially those of peripheral aetiology—such as labyrinthitis—are self-limiting and will only require symptomatic assistance. Such treatment may adopt Maxolon® (metoclopramide hydrochloride) given as 5–10 mg t.d.s. for adults or Stemetil® (prochlorperazine maleate) 5 mg t.d.s., as may be needed. In severe cases parenteral administration may be necessary.

If these fail, Serc® (betahistine dihydrochloride) given as 8–16 mg t.d.s. may give symptomatic relief. Avomine® (promethazine theoclate) is used especially in motion sickness but may also be helpful with vertigo in a dosage of 25 mg up to q.i.d.

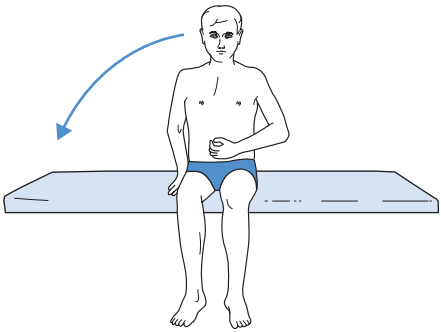
Treatment of BPPV does not usually require pharmacologic intervention unless the vertigo is so intrusive as to preclude quality of life. The most effective intervention is to use fatiguing exercises (see Fig 8.2) and the BPPV is also usually self-limiting, although it may recur. The best-known manoeuvre is the Epley manoeuvre, but it is not the one personally favoured. The one favoured is self-administered by the patient and is a variant of the Semont manoeuvre. The patient sits on the edge of the bed and drops to one side, waits for the vertigo and associated symptoms to improve, and then sits up again before performing the identical drop to the opposite side (see Fig 8.2). The patient does this, dropping to each side five to ten times in the morning upon waking and before getting up from bed, and at night before going to sleep.

This allows the deposits of calcium carbonate that attach to the hairs in the inner ear to be dislodged and thence reabsorbed. The described procedure is usually very effective and will empower the general practitioner to treat BPPV without need to refer the patient to a specialist, once a positive Hallpike's manoeuvre has confirmed the diagnosis. It should be remembered that the procedure may evoke nausea and vomiting, so it is wise to advise the patient to have a receptacle, such as a bucket, available by the bed when performing the manoeuvre.

Ménière's disease requires specific intervention and usually requires specialist involvement both for diagnosis and treatment. It is caused by dilatation of the endolymphatic organ, which causes the vertigo, tinnitus, feeling of fullness in the ears and impaired hearing. This is the most debilitating form of vertigo, often necessitating bed rest and antiemetics such as Maxolon®, Stemetil® or Serc®. Patients are prescribed a low salt diet limited to less than 3 g per day and may require use of a diuretic, such as hydrochlorthiazide at a dosage of 25 mg per day.

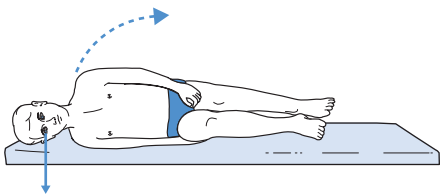
Position 1

Drop rapidly to side



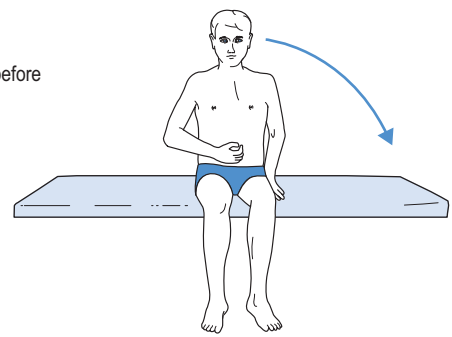
Position 2

Wait for symptoms to settle before rising



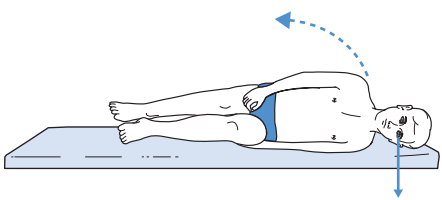
Position 3

Wait for symptoms to settle before dropping to other side



Position 4

Wait for symptoms to settle before sitting up



Note: Personal preference is to ask the patient to perform this procedure 5 times to each side before rising from bed in the morning and 5 time to each side before going to sleep at night

FIGURE 8.2 Fatiguing exercises in benign paroxysmal positional vertigo.

Serc® (betahistamine) acts as a vasodilator thought to increase vascular supply to the inner ear, although it may also have other benefits for Ménière's disease, at a dosage of 8–16 mg b.i.d.

Other treatments, such as surgical intervention (with endolymphatic sac decompression or nerve section) are beyond general practitioner involvement, as is intra-tympanic gentamicin in those with deafness.

The remaining treatments of vertigo are dependent upon the underlying diagnoses, which demand primary attention. Symptomatic intervention, as discussed above, remains relevant but is secondary to treating the condition that provoked the vertigo. The most important message is to remain within one's comfort zone and, if in doubt, it is time to involve a specialist when that comfort zone is breached.

CONCLUSION

This chapter has aimed to demystify vertigo and to show that **the bulk of vertigo remains within the domain of the general practitioner to manage.** Exact history is imperative to ensure that the patient truly is complaining of vertigo rather than many other conditions also covered by the word 'dizziness'. Once that is confirmed then the majority of causes are self-limiting and peripheral, such as vestibular neuronitis or BPPV. Both of these are properly managed by the general practitioner, but when in doubt the involvement of a specialist is warranted.

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9 Parkinson's disease

INTRODUCTION

Parkinson's disease (PD) was first described by James Parkinson, the English physician after whom it was named, in his monograph on the 'Shaking Palsy' in 1817.[1] While it occurs in 0.3% of the general population this climbs to 1% of those 60+ years old[2] and up to 3% in patients aged at least 80 years.[3]

It is a progressive degenerative neurological disorder characterised by a tetralogy of symptoms, including tremor, rigidity, bradykinesia and postural instability.[4] The pathological features are loss of dopamine-producing neurons from the substantia nigra in the brainstem and other brainstem nuclei,[5] together with Lewy bodies (ubiquinated protein deposits in the cytoplasm of neurons) and Lewy neurites (thread-like proteinaceous inclusions in neurites).[6,7]

Most general practitioners are less concerned with pathophysiology of the illness and much more concerned with diagnosis and treatment. What follows is a coalface clinician's approach to diagnosing and treating PD. While the above provides a scientific backdrop to PD, the purpose of this chapter is to alert the general practitioner to proper management.

PD is diagnosed on the basis of history and examination, rather than any specific blood test.[8] The 2006 United Kingdom clinical guidelines suggest that PD requires specialist confirmation of diagnosis and subsequent follow-up.[9] While there is good argument for the involvement of a neurologist, PD is a chronic illness with a predictably progressive decline so optimal care dictates a partnership between the specialist and general practitioner. As with all chronic illnesses, ideal care must accommodate lifestyle factors, careers and demonstrate an empathic approach, which is the forte of the general practitioner who is often more closely aligned with the patient and the home environment.

While the exact cause is unknown, a variety of genes have been identified from PARK1 at locus 4 q21[10] through to PARK13 at locus 2 p12[11] and the

list is continuing to expand. This has special relevance when PD occurs in young patients, especially those younger than 50 years. It is hard to organise the tests in Australia but any condition with a potential genetic basis mandates discussion. The majority of cases of PD are sporadic and hence counselling will probably not alter the prevalence.

There was a major outbreak of Parkinsonism after the influenza epidemic (with encephalitis lethargica) in the early twentieth century, when lesions in the substantia nigra became apparent.[12] Nevertheless the role of environmental factors was not fully appreciated until the 1980s when MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine), a by-product of synthetic opiate MPPP, a meperidine analogue designer drug, was reported to cause acute Parkinsonism in drug addicts in California.[13] Since then it has been acknowledged that pesticides may cause Parkinsonism,[14,15] thus various potential toxins can be avoided.

One may also consider lifestyle issues thought to protect against PD, such as smoking or taking of Chinese green tea,[16,17] although smoking has sufficient other reasons to be avoided.

What follows is an idiosyncratic approach to the diagnosis and treatment of PD. It does not follow some of the rules endorsed by many 'Parkinsonologists' but after considerable clinical experience it has proven effective and is provided as one possible way to manage the disease.

MAKING THE DIAGNOSIS

As with all diagnoses in neurology, the diagnosis starts with a high index of suspicion and a detailed history. Often 'the penny drops' when calling the patient to come into the consultation. The patient is slow to respond to the call; has difficulty rising from the chair, especially if that chair is low; and will be slow to walk into the consultation room.

Critical observation will reveal that the patient has a paucity of movement, is somewhat bent forward rather than standing erect, and may take smaller steps than is usual for their age group. The face is often expressionless, looks younger than that of chronological peers, and there is reduced blinking. The patient often doesn't swing both arms when walking (but may swing one arm) and appears to be shuffling along rather than taking discrete steps. The alternative may be the patient about to be called into the consultation room, seen sitting in the waiting room appearing to be somewhat bored, with a slow 'pill rolling' tremor of one hand. This seems to stop as soon as the patient realises it is their turn to see the doctor, and they may use that 'shaking' hand to push up from the chair to walk into the room and in so doing the 'shaking' stops.

It can be seen that in the classical case the diagnosis has been offered on a platter, even before the patient has entered the consultation room when the formal process is supposed to start. The corollary of this is that one has to be acutely aware of what is on the platter to realise that the diagnosis is being

offered, otherwise it may be missed and rely on someone else to show superior clinical acumen.

TAKING A HISTORY

Patients with PD will present with a number of initial complaints, which may be as vague as a feeling of 'slowing down' to a complaint of falling without cause, or of shaking. There are no prizes for diagnosing the classical case with the patient having the obvious Parkinsonian tremor and those features described above. Skill is required to tease out early cases, especially if one believes in early treatment, something that remains quite controversial but is a personal preference.

Once suspicion has been aroused, there is a series of mandatory questions to seek out the early symptoms that even the patient may not have identified without prompting. Patients with early PD may have trouble turning over in bed at night; they may have difficulty rising from a low sofa; or getting in or out of a car, especially a low-slung car such as a convertible. They may complain of difficulty initiating gait because they are afraid of falling over. Some may report falling when they turn quickly or losing their balance and being unable to regain stability, although they were able to do so previously. Symptoms of feeling stiff, which may translate as 'feeling funny or heavy in the limbs', may be confirmed if actively sought.

PD has been staged by Hoehn and Yahr[4] (see Table 9.1) as starting with unilateral symptoms and signs through to serious disability. As the condition progresses a patient may report speech changes with softer, monotonous speech, possibly complicated by excessive dribbling or drooling. Patients may have problems initiating gait, having what is called 'inertia'. These patients may report that they cannot get started when they want to walk but once they get going they seem to gain speed, even starting to run without wanting to, and may have difficulty stopping. They might develop techniques to stop, such as selecting a fixed object like a wall and walking into it to slow down their centre of gravity that they have been chasing.

TABLE 9.1 The Hoehn and Yahr staging of Parkinson's disease

Stage 1	Unilateral symptoms and signs
Stage 2	Bilateral symptoms and signs
Stage 3	Bilateral features with impaired postural reflexes causing disability
Stage 4	Severe gait disturbance though still able to stand and walk without aids
Stage 5	Inability to stand or walk without aids, wheelchair or bed-bound

TABLE 9.2 Differentiating Parkinsonian tremor from essential tremor

Characteristic	Parkinson's disease	Benign essential tremor
Tremor location	Hands, legs, circumoral	Hands, head (titubation), voice
Laterality	Usually unilateral at onset	Usually bilateral
Bradykinesia	+	–
Rigidity	+	–
Family history	Usually –	+ in ≥ 50%
Effect of alcohol	–	+ (reduces tremor)
Age of onset	Usually > 60 years	Younger, ~40 years
Timing of tremor	At rest (when distracted)	With activity (rarely at rest)

Posture, being bent in the middle and unable to stand up straight, may be a major symptom. Writing may be difficult, either due to the imposition of the tremor or patients may report their handwriting has become smaller, veering up and off the horizontal, hence becoming difficult to read even without tremor.

Often the patient will present with the complaint of tremor and will suspect the diagnosis of PD. Benign essential tremor is far more common than is PD, and the patient will be greatly relieved if given this diagnosis. It is therefore important to have simple tools with which to compare the two most common causes of tremor (see Table 9.2). A patient with PD may have both an essential and a PD tremor.

More recently there has been a realisation that PD may be associated with symptoms that transcend the motor features. These include neuropsychiatric symptoms, sleep disorders (such as REM sleep behaviour disorder), autonomic symptoms and sensory symptoms.[18] Impulsivity, increased gambling and antisocial behaviour have been associated with PD and its treatment.[19] The term 'punding' with associated compulsive sequenced behaviour is associated with PD. Impotence is reported by up to 60% of men with PD.[20]

It can be seen that there are many questions needing to be asked, both to assist with the diagnosis and with defining the extent of the illness and its impact on the patient's life.

EXAMINATION

In the section above 'Making the diagnosis', many of the early features have already been described and should be apparent even before starting the formal consultation. From these findings and corroboration based on the history, the doctor can steer directly towards the signs to be displayed.

BOX 9.1 Tetralogy of principal features of Parkinson's disease

1 Tremor
2 Rigidity
3 Bradykinesia
4 Postural instability

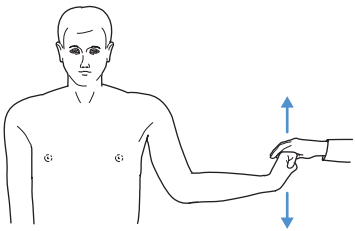
The tetralogy of principal features is well accepted (see Box 9.1) and available for examination. Working from the head downwards, the features include: positive glabellar tap (tapping the patient over the forehead above the bridge of the nose should only illicit three blinks—more than this is considered positive); paucity of blinking; difficulty with upward gaze; cogwheeling of saccadic eye movements; decreased facial wrinkling with increased sebum in the skin, giving an oily appearance and looking younger than actual age; increased drooling; soft voice devoid of intonation; expressionless face; and possibly a posture with the head somewhat flexed forward. The patient may well have a positive palmar mental response (scratching the patient's palm may elicit movement of the ipsilateral jaw, via the mentalis muscle) and is concurrent with other frontal lobe signs such as grasp reflexes.

In the early stages of the disease tone may seem superficially normal. Once the patient is distracted, such as asking the patient to turn the head from side to side, it will exacerbate the increased tone, feeling like a lead pipe. With the superimposed tremor, this may feel like a cogwheel going over the cogs. To elicit this response the doctor flexes and extends the hand at the wrist while asking the patient to turn their head from side to side. This increases the tone as it allows the expression of resting tone. Without distraction the patient often tries to help, even without being aware of it (see Fig 9.1). In some cases there may be the need for further distraction, such as waving the contralateral arm.

The patient may adopt a stooped posture and have failure of righting reflexes in which they are incapable of correcting for propulsion or retropulsion. This is explained by an inability to spread the centre of gravity once balance has been disrupted, due to stiffness of the joints, especially the hips. Hence, following loss of balance, the patient will often fall down. The patient may have inertia of gait, again due to fear of falling once the centre of gravity has been disturbed. A 'trick' to initiate walking is to ask the patient to step over a dropped object, such as a pen or piece of paper. Performing the task of stepping over the pen automatically moves the patient forward and they can then continue in the same direction because the centre of gravity has likewise moved forward.

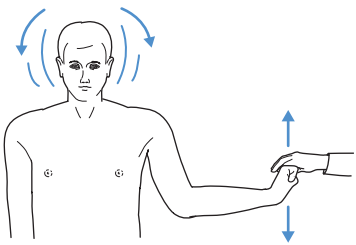
Festinating gait is a further expression of the fear of moving forward with the patient stepping on the spot, thereby retaining the position of the centre of gravity. Having moved forward, the patient may have a shuffling gait with small steps and have difficulty turning, such that the turn is made by small steps, called 'turning by numbers'.

Step 1



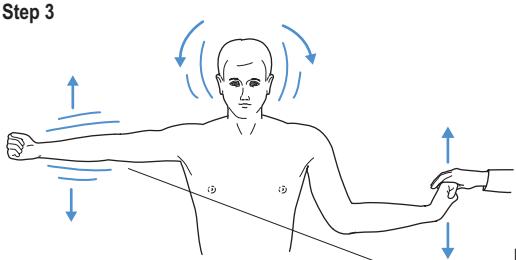
First move patient's hand up and down without the patient turning the head.
Often the tone will be normal

Step 2



Repeat the same manoeuvre with the patient pushing his/her head from side to side. (from shoulder to shoulder). This should produce leadpipe and cogwheeling

Step 3



If PD is really expected but Step 2 did not produce significant rigidity and cogwheeling, repeat it but ask the patient to also wave the contralateral arm up and down

If further distraction is needed the patient is asked to wave the extended contralateral arm up and down

FIGURE 9.1 Provoking leadpipe and cogwheel rigidity in a patient with Parkinson's Disease.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of PD includes a variety of other neurodegenerative diseases, such as atypical Parkinsonisms, including progressive supranuclear palsy; multiple system atrophy; autonomic type (Shy-Drager syndrome); olivopontocerebellar atrophy; and corticobasal degeneration. Other conditions to be considered include Alzheimer's disease with extrapyramidal signs; Lewy body dementia (LBD); Huntington's disease; Wilson's disease; calcification of basal ganglia and Creutzfeldt-Jakob disease.

A number of acquired diseases also need to be considered, such as carbon monoxide poisoning, carbon disulfide poisoning and methanol intoxication. Other conditions, such as subcortical vascular disease, tumours, subdural haematomas and anoxic brain injury are included in the differential. Drug effects, as may accompany psychotropic antipsychotic neuroleptic medications, such as phenothiazine, can evoke the extrapyramidal features seen in PD.

Features that favour illnesses other than PD include: symmetric onset; early gait disturbance or falling; non-responsiveness to agents such as L-dopa; severe disability within five years; and stepwise progressive disorder or sustained remission. Some clinical signs, such as cerebellar signs, lower motor neurone features, and features typical of the above-cited differential diagnoses, also make PD less likely.

In his initial description of PD, Parkinson felt that cognition remained unimpaired but this is not accurate, although early onset dementia makes PD less likely and favours LBD.

One of the simplest diagnostic tools for PD, as compared with Parkinsonism, is a trial of therapy with L-dopa. The response with PD is excellent while that for 'Parkinsonism' is poor.

TREATMENT

The approach to treatment of PD that follows reflects an idiosyncratic approach, as explained earlier. It may be at odds with what many advocate but has proven efficacious, at least from the view of the author.

a Levodopa

Since the 1960s when levodopa (L-dopa) benefits were first recognised,[21] L-dopa has become the gold standard of PD therapy.[22] There is a dichotomy as to whether one starts this early or waits. Many experts prefer to wait until the condition is fully apparent, arguing that L-dopa may have a finite period of possible effect after which the potency is diminished. This is contrary to personal view and is not the course personally adopted. The patient is referred because symptoms are affecting quality of life, which should improve with treatment. This translates into a personal choice to start therapy early after diagnosis.

L-dopa is provided either in combination with carbidopa or benserazide (Sinemet® or Madopar® respectively). Both carbidopa and benserazide are peripheral dopa decarboxylase inhibitors (DDI). They act by reducing the peripheral metabolism of L-dopa, which translates into more L-dopa crossing the blood–brain barrier (BBB). This, in turn, means that less L-dopa need be administered. L-dopa is used because dopamine does not cross the BBB and L-dopa is metabolised to dopamine after crossing it, replacing failing dopamine stores.

Personal preference is to start low and go slow (SLGS), starting with a 100 : 25 combination of either Sinemet® or Madopar® with half b.d. as the initial dose. This often produces significant benefit and can be maintained at this low level for a period of years. Early in the disease process the response to L-dopa lasts longer than later in the disease, thereby allowing small doses to give prolonged benefit.

To properly use the carbidopa or benserazide there has to be enough of it to make a difference. Initially Sinemet® was produced in a 1 : 10 ratio of carbdopia:L-dopa (while Madopar® adopted 1 : 4 ratio (of benserazide:L-dopa). Subsequently it was realised that the 1 : 4 ratio was more effective and hence it was adopted for Sinemet®, while still offering the 1 : 10 ratio as an alternative. Unfortunately some still use the 250 : 25 formulation, often to the patient's detriment.

The best tools to judge efficacy are the patients themselves. It is important to note their ability to get out of the chair in the waiting room, the gait while walking to the consultation room and their facial expression (namely, the ability to smile). The primary 'quality of life' question, 'How are you?', will clinch it, as patients become acutely aware when things start deteriorating.

Once symptoms progress, the dosage of Sinemet® or Madopar® can be increased to one b.d. but, if symptoms progress to the point of requiring more than one b.d., personal preference is to add a second agent rather than chase L-dopa dosages.

L-dopa is not without side-effects and is known to activate malignant melanoma. It can react with other agents, such as antihypertensives, causing postural hypotension but can also do this in its own right. One of the reasons to SLGS is the potential to cause dyskinetic movements, and one may be forced to reduce dosages of L-dopa because of this troublesome side-effect. This is less common when using the low doses as recommended above, until one is forced to chase symptoms as the condition deteriorates.

Other than involuntary movements, other adverse effects include nausea, vomiting, diarrhoea, constipation and rash, which attach to every medication. Mental changes may be experienced, including paranoia, psychotic hallucinations and delusions, and can be of sufficient intensity to preclude its use. Cardiac irregularities and orthostatic hypotension can also be quite intrusive, dictating cessation of use, especially if given in combination with selegiline (discussed below). Special precautions are also advised in patients known to have glaucoma.

b Selegiline

Selegiline has largely fallen out of favour. It is a selective monoamine oxidase-B inhibitor (MAOBI). Rasagiline is another within this family but it is not available in Australia. Examination of 'MIMS Annual' states that '… Monamine oxidase inhibitors (MAOIs) and Sinemet® should not be given concomitantly'. It is accepted that the combination of L-dopa and Eldepryl® 'may be accompanied by orthostatic hypotension of a severity, which precludes their combined use…'. Again, adopting the SLGS approach minimises this potential but it still does occur and must be anticipated.

Personal preference is to introduce Eldepryl® 5 mg at half b.d. and review the patient in a month. Depending on efficacy, the dosage can then be increased to one b.d. The patient will be on combination therapy with both L-dopa and MAOBI at one b.d. and may remain on this for a period of years before requiring further adjustment.

The most supportive evidence favouring the use of Eldepryl® emerged from the DATATOP study[23] that suggested Eldepryl® delayed disease progression, although it was less clear as to its direct symptomatic effects.

One of the reasons Eldepryl® fell out of favour was the 1995 United Kingdom report that identified increased mortality from the combination of Eldepryl® and Sinemet®.[24] This has subsequently been criticised[25,26] and 'MIMS Annual' states 'No other clinical trial to date has shown an increase in mortality associated with the use of selegiline'.

MAOIs have been associated with hypertensive crises when administered with cheese and red wine, but this is not a problem with the selective MAOBI, such as Eldepryl®, especially at the low dosages recommended. Nevertheless the potential should not be ignored. Similarly the possibility of postural hypotension with L-dopa combination cannot be dismissed, but personal experience indicates that it is sufficiently rare not to obviate its use. It may exacerbate other L-dopa side effects set out earlier, including dyskinesia, hallucinations, agitation and confusion, and possibly the sleeping disorders already recognised as part of PD. Thankfully the SLGS policy minimises these troublesome issues that surface in a few patients.

c Dopamine agonists

The role of dopamine agonists is changing with the introduction of non-ergot derivative dopamine agonists. These should eliminate the current risks of fibrosis associated with ergot-based agents, which can cause cardiac valvular disease, pulmonary and retroperitoneal fibrosis. Some advocate repeated echocardiography and routine ESR monitoring of patients on the ergot-derived agonists, which may become superseded as non-ergot derivatives become more popular.

Once the patient has shown progression on the combination of low dose L-dopa and selegiline (Sinemet® or Madopar®) in 100 : 25 combination one b.d. (maximum one t.d.s.) plus Eldepryl® 5 mg one b.d., personal preference

advocates addition of low dose dopamine agonist to the cocktail. Previous personal preference was for cabergoline (Cabaser®), a long-acting ergoline-8-carbamoxide dopamine agonist. Such is the changing face of therapeutics that a whole different genre of dopamine agonists is currently available.

The first of these is pramipexole (known as Mirapex® overseas and Sifrol® in Australia). It will probably be the first to achieve Pharmaceutical Benefits Scheme (PBS) listing for its 125 µg, 250 µg and 1 mg scored tablets. The company literature advocates slow introduction starting at 125 µg t.d.s. and titrating to need and efficacy or a rapid overnight conversion from the previously used dopamine agonist. Slow introduction and caution are advocated in patients with renal impairment. More recently, this has been superseded by the extended release formulation that allows a once-a-day dosing. Most patients can be transferred from standard Sifrol® to Sifrol ER® without skipping a beat. Again, the SLGS approach has seen personal preference start Sifrol ER® at 0.375 µg one mane. Many patients can be maintained at this very low dosage with them reporting very satisfactory efficacy. This has caused some difficulty because the dosage is so low that the PBS will only allow a single prescription without repeats. This translates into the patient being compelled to visit the doctor once a month to get a prescription. Personal preference is to maintain this low dosage while the patient reports adequate efficacy, even if the PBS insists the dosage is too low thereby necessitating monthly visits. As a consequence, personal approach is for the patient to attend the general practitioner once a month and to visit the consultant as needs be.

Pramipexole is not the only non-ergot dopamine agonist with other agents, such as rotigotine, to be offered as a transdermal patch. It may possibly have beneficial compliance considerations on the basis of an alternative mode of delivery but it is far too early, at least within the Australian context, to know what will be the place of these 'newer' agents. The use of patches as an alternative to oral administration may have particular relevance for patients with PD who undergo surgery and are on 'nil orally'.

It is argued that dopamine agonists are particularly useful for PD patients experiencing the on–off fluctuations and dyskinesias associated with L-dopa. It seems reasonable to assume adopting the SLGS policy will dictate that by the time the patient is on a dopamine agonist, the partnership between consultant and general practitioner will have been well established. Thus the role of the general practitioner will be to monitor patient progression and help determine when it is time to add further anti-PD agents to improve quality of life, which remains the ultimate goal.

One must consider the role of dopamine agonists in the evolution of 'punding' and discontrol syndromes, such as compulsive gambling and impulsivity. Punding is a constellation of complex sterile and stereotyped behaviours, including absorption in use of technical equipment, almost obsessional behaviour (including handling, examining, sorting, grooming, hoarding, fidgeting while rearranging) and purposeless behaviour.[19] While

first noted in amphetamine and cocaine addicts in the 1970s, it was described with PD therapy in 1994.[19] Excessive gambling and impulsivity are other considerations thought to be exacerbated by dopamine agonists, as is hypersexuality.

d COMT inhibitors

Stalevo®, essentially a combination of Sinemet® with entacapone (Comtan®) in a single tablet (100 mg L-dopa, 25 mg carbidopa, 200 mg Entacapone® with other combinations also available), allows the addition of a catechol-O-methyl transferase (COMT) inhibitor without increasing the number of pills required. When adding Stalevo® there is no need to also take Sinemet® or Madopar®.

Entacapone® is a reversible, specific and mainly peripherally acting COMT inhibitor, which slows the clearance of L-dopa from the blood, thereby enhancing and prolonging its efficacy. Thus, once the benefits of combination L-dopa (Sinemet® or Madopar®), Eldepryl® and dopamine agonist, such as Sifrol ER®, start to wear off, personal preference is to substitute Stalevo® for the L-dopa. Adverse effects of L-dopa may be enhanced and the amount of L-dopa may need to be reduced.

OTHER MEDICATIONS

By the time the patient is on a combination of four anti-PD drugs the partnership between general practitioner and consultant has been fully developed. This translates into the consultant advising changes in medications and the general practitioner supervising ongoing care. The above four types of medications provide the framework for treatment of PD but do not exhaust it.

Should tremor be the major complaint then the above combination may seriously fail the patient. Personal preference is to rely on anticholinergic agents, such as benzhexol (Artane®), starting with a dosage of 2 mg half b.d. and titrating to need but rarely exceeding one t.d.s. Anticholinergic effects, such as dry mouth and constipation, may limit its use. Some doctors suggest these agents exacerbate psychotic behaviour or depression, but this is contrary to personal experience.

Tremor may not be restricted to PD 'pill rolling' tremor and may also include physiological, so-called benign essential type tremor, for which β-blockers, such as propranolol, provide additional benefit. Starting dosage is 40 mg half b.d. and titrating to need may relieve this additional tremor.

Should tremor persist despite Artane® then apomorphine, delivered by way of a pump, may help. This requires in-hospital titration to determine dosage plus domperidone (Motilium®) to counteract troublesome gastrointestinal side-effects. If this still doesn't give adequate relief of intrusive tremors then deep brain stimulation and neurosurgery, directed at the subthalamic nucleus, may offer a viable alternative.

Should there be need for greater dopamine effect the use of amantadine (Symmetrel®), starting at a dosage of 100 mg per day and again titrating to efficacy, may offer additional gain. Psychiatric side-effects with Symmetrel® may limit its use.

Pain, depression, sleep disturbance and vague aches may be addressed with tricyclic antidepressants such as imipramine (Tofranil®) or amitriptyline (Endep®), starting at 25 mg nocte and titrating to need. They may also reduce the problem of enuresis that can accompany PD. The tricyclic antidepressants also produce anticholinergic effects leading to the same criticisms mentioned above with Artane®. Personal experience has not encountered significant problems in this area.

No antipsychotic agent is totally without Parkinsonian side-effects, but personal preference favours use of olanzepine (Zyprexa®). The SLGS rule applies if one wishes to achieve maximal benefit, namely improvement in control of schizophreniform features without exacerbation of PD. Some advocate quetiapine fumarate (Seroquel®) as superior to Zyprexa® but personal preference is for Zyprexa®, starting at 2.5 mg nocte and titrating to need.

CONCLUSION

PD is a complex and chronic illness that may evade early detection unless one maintains vigilance and closely observes patients as they come into the consultation. Personal preference is to start treatment early upon the diagnosis, but this is not universally accepted.

The SLGS policy underpins introduction of anti-PD agents with **preferential choice favouring sequential and additive introduction of L-dopa, selegiline, dopamine agonist, COMT inhibitor and additional agents for specific symptomatic relief as the symptoms increase and the patient continues on the inevitable downward slide**. The aim of treatment is to flatten the slope of the slide, as it is virtually impossible to totally arrest progression.

This chapter has not discussed physical intervention with mobilisation training and rehabilitation with physiotherapy. This does not diminish their role but the focus is on pharmacological treatment. Having said that, the general practitioner is ideally placed to observe the patient and recommend mobilisation training as the condition progresses. The use of a walking stick or later a walking frame may greatly reduce the propensity to falls, as a consequence of 'failed' 'righting reflexes'. The use of these aids is somewhat different to their use in painful situations, as their purpose is to spread the centre of gravity (rather than function as a splint). **The addition of a walking aid in PD is to widen the area of stance, thereby enhancing stability. This is often a foreign concept for patients and hence requires training.** This may dictate referral to an experienced physiotherapist, possibly within a rehabilitation service. These concepts are definitely the role of the general practitioner, who is best equipped to approach each individual patient's needs

and expectations. This confirms the ongoing need for a strong, working partnership between the general practitioner and consultant.

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10 Multiple sclerosis

INTRODUCTION

Multiple sclerosis (MS) is one of the most dreaded diagnoses in neurology. Patients visualise a fit and healthy person, such as the Olympic athlete Betty Cuthbert, reduced to a wheelchair existence. Patients told the diagnosis of MS are often reduced to tears in much the same way as the diagnosis of cancer causes patients to jettison hope. This should no longer be the case in the light of recent advances in the treatment of MS. In the past, the neurologist's waiting room was crowded with the wheelchairs of patients with MS but, thankfully, this has now become the exception rather than the rule.

Even the understanding of the basic pathophysiology of MS has changed enormously over the last decade. It used to be thought that MS was purely a white T-cell autoimmune demyelinating central nervous system (CNS) disease. More recently, the immunological role of B-lymphocytes in the evolution of MS has been appreciated, as has the major contribution of the associated axonal degeneration that causes shrinkage of the brain volume. To better understand the concept of demyelination contrasted with axonal degeneration, the reader is referred to Chapter 11 on peripheral neuropathy in which the issues are discussed in depth. The basic concepts remain the same although the location is the central rather than the peripheral nervous system.

One reason MS is feared is that it is an unpredictable disease with exacerbations and remissions. It is a disease in which lesions occur within the CNS that are 'separated in time and place'. The diagnostic criteria for MS have also been modified with the international acceptance of the 'McDonald criteria' (see Table 10.1).

These criteria acknowledge the role of magnetic resonance imaging (MRI) in the diagnosis of MS. The criteria, formulated by a panel of experts chaired

TABLE 10.1 McDonald criteria

Clinical attacks	Objective lesions	Additional evidence needed for MS diagnosis: dissemination in space	Additional evidence needed for MS diagnosis: dissemination in time	Diagnosis of MS
2 or more	2 or more	Not required	Not required	Yes
2 or more	1	Positive MRI *or* Two or more MRI-detected lesions consistent with MS plus positive CSF *or* Await further clinical attack implicating a different site	Not required	Yes
1	2 or more	Not required	Positive MRI *or* Await a second clinical attack	Yes
1	1	Positive MRI *or* Two or more MRI-detected lesions consistent with MS plus positive CSF	Positive MRI *or* Second clinical attack	Yes
0	1 or more	One year of disease progression *and* Two or more of the following: a positive brain MRI (nine T2 lesions or four or more T2 lesions with positive VEP) b positive spinal cord MRI (two focal T2 lesions) c positive CSF		Yes

by McDonald, recognised that MS may be identified by clinical symptoms and signs, MRI detected lesions (that may occur without associated clinical features) and the presence of oligoclonal bands in the cerebral spinal fluid (CSF) that herald CSF immunological insult.[1]

The easier access to MRI has produced a practical recognition that for every clinically identified 'attack' of MS, there may be as many as six to ten

sub-clinical 'attacks' that would remain silent were it not for the MRI trademark of the MS plaque.

While the treatment of MS remains largely the precinct of the consultant neurologist, there should exist an effective partnership between the neurologist and the general practitioner to maximise patient wellbeing. The role of the general practitioner within this partnership should not be underrated, and is mandatory for an optimal outcome. This chapter maps out the clinical features of MS so that the diagnosis is appropriately made, without which this partnership cannot operate to the patient's advantage.

There is a variety of types of MS, and it is accepted that not all types respond equally to accepted MS treatment. Use of disease modifying agents, such as the interferons or glatiramer acetate, requires a diagnosis of MS confirmed by MRI[2] (the date of that MRI being part of the prescription approval process), but these agents are not available to patients with advanced disability (unable to walk more than 100 metres without assistance). This is equivalent to the disability rating of 6.0 on the Expanded Disability Status Scale (EDSS)[3] (see Table 10.2).

These agents are likewise denied to patients with MS who do not have relapsing remitting MS (RRMS). Patients with progressive disease are at a distinct disadvantage and, in many instances, symptomatic relief as provided by the general practitioner is the only therapeutic option available on the Pharmaceutical Benefits Scheme (PBS).

DIAGNOSING MS

A repeated mantra in this book is that 'without heightened index of suspicion the diagnosis will often be missed'. This is equally true and important when diagnosing MS.

MS occurs more commonly in females than males (ratio 2 : 1), usually between the ages of 20 and 40 years, although childhood and geriatric onset are now becoming more widely diagnosed because of MRI. The diagnosis of MS is becoming more common, but it is suspected that this reflects better diagnostic tools and heightened index of suspicion rather than an increased prevalence.

If the place of birth is further from the equator, migration after the age of 15 years means one brings the prevalence of MS of the place of origin to the destination rather than assuming the prevalence appropriate to the destination. Within the Australian context, the incidence of MS is sixfold greater in Tasmania than in northern Queensland. Some argue that this relates to an increased exposure to sunlight and vitamin D, which occurs closer to the equator, but the absolute answer remains unclear. If one parent has MS there is a 1–2% chance of the child having MS and, if a monozygotic twin has MS, then the chance of the sibling twin developing MS is of the order of 35%. There is a suspicion of an association between MS and previous infection with the

TABLE 10.2 Expanded disability status scale

EDSS score	Description	Summary
0.0	Normal neurological functioning	Able to partake in regular activities
1.0	Minimal impairment in one functional system but essentially normal	
1.5	Minimal impairment in more than one functional system but essentially normal	
2.0	One functional system with minimal disability	
2.5	Two functional systems with minimal disability	
3.0	One functional system with moderate disability *or* minimal disability in three or four	
3.5	No problems walking but with moderate disability in one functional system plus mild disability in two or more functional systems	Moderate impairment in daily functions
4.0	No problems walking without aid for 500 m but severe impairment in one functional system or combinations of mild to moderate impairments in multiple functional systems	
4.5	No problems walking without aid for 300 m but severe impairment in one functional system or combinations of mild to moderate impairments in multiple functional systems	
5.0	Cannot walk more than 200 m without aid and unable to complete a full day of activities without impairment	Unable to complete all daily activities
5.5	Cannot walk more than 100 m without aid and unable to complete a full day of activities without impairment	
6.0	Requires unilateral assistance to walk 100 m	Needs ambulatory assistance
6.5	Requires bilateral assistance to walk 100 m	
7.0	Unable to walk 5 m even with bilateral assistance, restricted to a wheelchair	Mostly restricted to a wheelchair
7.5	Unable to take two steps even with bilateral assistance, restricted to a wheelchair	
8.0	Arms still effective, confined to wheelchair or bed	
8.5	Arms have some functioning, confined to bed	Bedridden
9.0	Arms not functional, can communicate and eat	
9.5	Cannot communicate or eat effectively	
10.0	Death due to MS	Death

Epstein-Barr (EB) virus. It follows that there is a variety of red flags that should alert the general practitioner to the possibility of MS.[4]

Because the presentation of MS can be so varied, it is most important, especially when assessing young women, not to dismiss symptoms that are difficult to understand. If it is possible for the symptoms to emanate from the CNS, then the diagnosis of MS should be entertained. As a rule of thumb, the diagnosis of MS is beyond the scope of the average general practitioner. It requires lumbar puncture, looking for oligoclonal bands; evoked potential studies (including visual, somatosensory and possibly brainstem) looking for lesions that are separated in place (located within the CNS); as well as the MRI. Despite general practitioners now having greater access to MRI, in reality, to diagnose MS most general practitioners will refer the patient to a consultant before ordering an MRI. Another reason for early referral is that there is good evidence to suggest that the earlier treatment is instigated, the better is the outcome.[2] A number of companies are now offering special compassionate access to disease modifying drugs for patients with Clinically Isolated Syndrome (CIS)—for patients having experienced a single attack without meeting the criteria for a definitive diagnosis of MS—to ensure the earliest possible availability of treatment. This further recognises the merit of early intervention on long-term prognosis.

As stated in other chapters, it is far more intellectually rewarding for the general practitioner to refer the patient to the consultant with a confirmed and correct provisional diagnosis, so the family doctor needs to be aware of the symptoms of MS to take an appropriate history (see Table 10.3).

TABLE 10.3 Symptoms of MS

	Symptoms	Signs
Optic neuritis	Unilateral loss of central vision Pain on moving the eye Blurred vision	Swelling of single nerve head (papillitis)
Motor involvement	Limb weakness Possible incoordination Twitching	UMN signs Cerebellar signs
Sensory involvement	Diffuse numbness (decreased sensation) Tingling paraesthesia Pain	Sensory changes on testing
Spinal cord involvement	L'hermittes phenomenon (reporting shock sensation on bending neck) Urgency of micturition	Bending neck causes electric shock sensation down spine
Psychological factors	Anxiety or depression Fatigue	

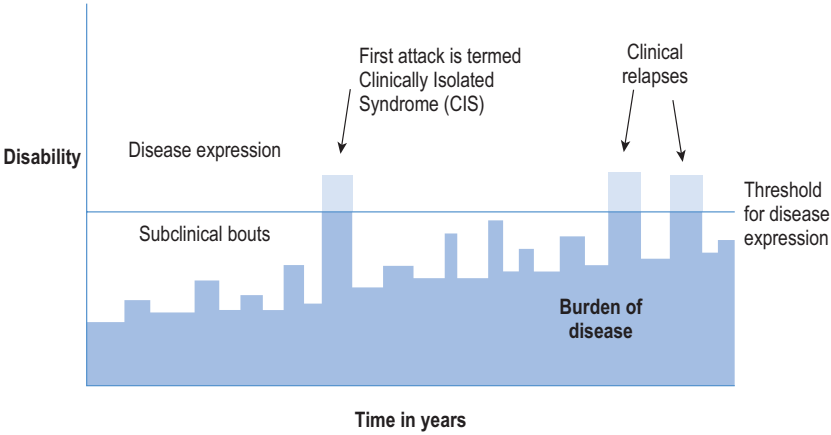

FIGURE 10.1 Relapsing remitting MS.

TYPES OF MS

Of the variety of types of MS, the most common is relapsing remitting MS (RRMS) that occurs in approximately 85% of MS at the onset of the disease and about 60% of the total MS population.[4] Patients with RRMS may have subclinical episodes preceding and following a clinical 'attack' (see Fig 10.1).

The first clinically identified attack is termed CIS, because at this stage there is no history of repeated episodes. While the disease may remain subclinical, at the time of CIS it does not prevent the accumulation of the burden of disease with possible decreased volume of the brain.

Once the relapses combined with the burden of disease surpass the threshold for clinical disease expression on a more permanent basis, the RRMS enters the secondary progressive phase, known as secondary progressive MS (SPMS). The patient never returns to a subclinical status (see Fig 10.2). This accounts for approximately 20% of all people with MS.

About 5% of all MS patients are said to have progressive relapsing MS (PRMS) in which they never really return to a subclinical status below the threshold of a disease expression, and the disease continues relentlessly. They do have bouts of increased disease expression, which constitute relapses, from which they do improve, but the burden of disease increases and is cumulative (see Fig 10.3).

In one form of primary progressive MS (PPMS) there appears to be a linear progression of disease from the outset, without apparent relapses and remissions, without the patient returning to a subclinical state, with constant expression of disease (above the threshold of disease expression). PPMS more commonly includes spinal involvement and appears to affect a somewhat

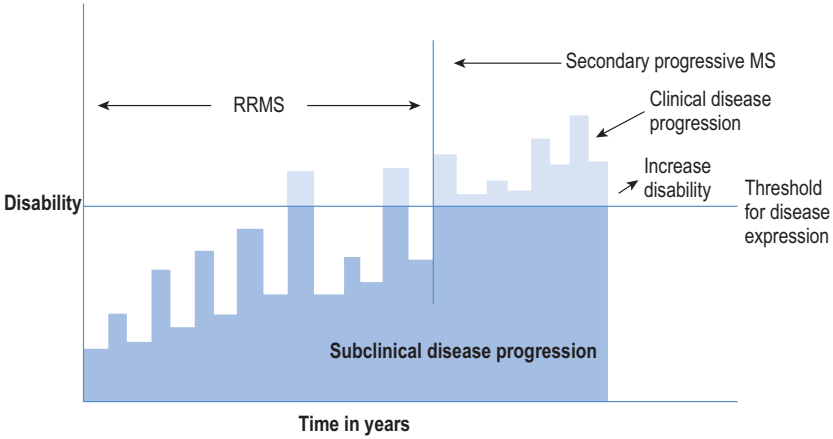

FIGURE 10.2 Secondary progressive MS.

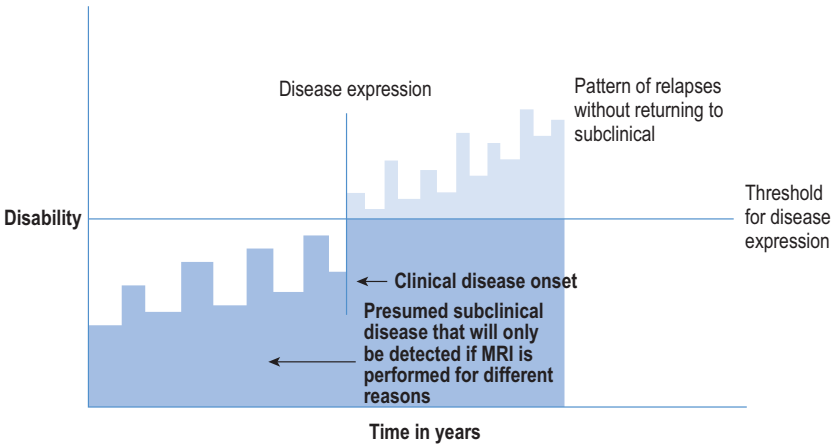

FIGURE 10.3 Progressive relapsing MS.

older population at onset (30s and 40s at onset). This is also said to occur in approximately 5% of all MS patients and 10% at the onset of disease.

Some 10–30% of MS is said to be benign as the diagnostic criteria are met yet there is minimal or no disability after 15 years and the attacks, if they are recognised as such, may be very minor, infrequent and with excellent recovery. Conversely, there is also a malignant and severe form of MS with rapid progression that may result in death or marked disability within two years.

A form of possible MS known as Devic's disease, also known as neuro myelitis optica (NMO), appears to affect a somewhat different population,

being more common among Occidental people. It is less responsive to currently available remedies. There remains an argument as to whether NMO is actually part of the MS spectrum or is a completely different disease entity with specific involvement of the spinal cord and optic pathway.[5] For the purpose of this discussion such debate is irrelevant and remains the precinct of specialists, as the patient will have been referred for a consultative opinion prior to diagnosis of NMO. What is worth noting is that there is an NMO antibody, also called aquaporin[3], that is measurable in NMO patients.

The reason for delineating the various patterns of MS is to help the general practitioner better understand how MS expresses itself. It empowers the general practitioner to better understand the disease, and therefore assists in trying to support patients with MS. Patient reassurance, support, rehabilitation and symptomatic relief often rely more heavily on the family doctor with whom the patient generally has a closer relationship.

SYMPTOMS AND SIGNS OF MS

As MS is a disease of relapses and remissions, it is important to appreciate that a relapse is classically defined as the onset of new symptoms or the exacerbation of existing symptoms that last for at least 48 hours, and are often called 'attacks'. Such exacerbations represent an episode of demyelination: what occurs within the relapse is defined by the site, be it in the cerebral hemispheres (affecting cognition, emotions, motor activity or sensation); brainstem (possibly affecting cranial nerves or their interconnections); or the cerebellum (affecting coordination). It is accepted that MS can also cause demyelination within the spinal cord and, again, its expression is determined by the site within the cord and the pathways affected (see Tables 10.2 and 10.3). As touched upon above, in the condition known as NMO demyelination is restricted to the optic pathways and the spinal cord. One of the hallmark features of NMO is that the spinal cord involvement is much longer, covering a number of vertebral segments, than is usually encountered in other forms of MS. As indicated above, aquaporin[3], also called NMO-antibody, can be measured in the blood and/or CSF of the patient with NMO.[6]

Often the first presentation of MS is optic neuritis, with demyelination and inflammation of the optic nerve. This causes obscuration of vision, usually restricted to one eye, with pain that is often exacerbated by eye movement. Ophthalmoscopic examination of the optic fundus should provide the diagnosis of optic neuritis (also called retrobulbar neuritis or papillitis) with the appearance of what looks like papilloedema that is usually restricted to one eye, while papilloedema is usually bilateral.

A lesion in the brainstem may cause internuclear ophthalmoplegia (INO) with involvement of the medial longitudinal bundle that connects the midbrain with the pons, and hence coordinates the movements of the eye muscles. An INO lesion in the midbrain may result in failure to adduct the affected eye due to poor communication between the third cranial nerve and sixth cranial nerve, when looking laterally, with nystagmus in the abducted eye

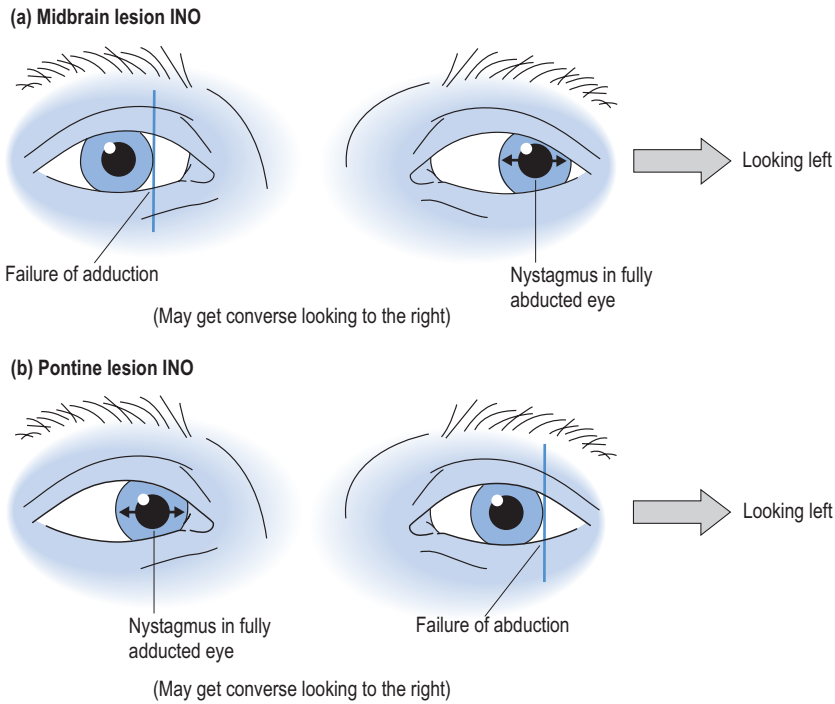

FIGURE 10.4 Brainstem lesion.

(see Fig 10.4). The converse may be the case with a lesion in the pons (see Fig 10.4).

Discussion so far has focused upon the major symptoms and signs that attach to MS, but there remains a host of MS-related symptoms and signs for which the general practitioner plays the principal role in treatment. These include help with rehabilitation in the advanced case, and assistance with bowel and bladder problems, such as urgency, urinary retention or constipation. Counselling, particularly in the area of potential sexual dysfunction, with possible erectile impotence, or the consequences of emotional problems, are often best addressed by the family doctor with whom the patient usually has a more intimate relationship.

Fatigue is often a major concern for people with MS. A recent pilot study showed the potential for sleep disorders, such as periodic leg or limb movement in sleep with arousal (PLMS with PLMA) and possibly even obstructive sleep apnoea to be contributing factors to this symptom.[7] It follows that referral to a sleep physician and polysomnography may provide additional insight into the associated fatigue with the potential for intervention, such as continuous positive air pressure (CPAP).

Emotional factors may play a significant role within the evolution of MS, both for the affected patient and their relatives and loved ones. Anxiety and depression are often associated with MS. The general practitioner is ideally placed to identify the needs, provide counselling and, when necessary, medication to alleviate these symptoms.

TREATMENT OF MS

The treatment of MS is divided into the treatment of relapses and the provision of more long-term disease modifying therapies, together with symptom relief and counselling.

Treating relapses

Patients presenting with a relapse of MS are treated with a five-day course of intravenous infusion of 1 g of methylprednisone, administered over an hour for five consecutive days. Some doctors will also prescribe a tapering course of oral prednisolone after the five-day course of infusions.

The course of infusions is usually offered within the local hospital on the basis of the patient presenting to the ambulatory care facility, thus allowing the patient to remain at home while the treatment is provided on a daily basis.

Long-term disease modification

Disease modification is very much the domain of the specialist, and the earlier such treatment is initiated the better is the prognosis.[8,9] The most widely used disease modifying agents include: Avonex® (interferon beta 1A) administered intramuscularly weekly; Rebif® (interferon beta 1A) injected subcutaneously on Mondays, Wednesdays and Fridays; Betaferon® (interferon beta 1B) injected subcutaneously second daily (on a two-weekly cycle of Monday, Wednesday, Friday, Sunday, Tuesday, Thursday and Saturday); or Copaxone® (glatiramer acetate) given subcutaneously every day. Despite the various claims from the different companies, the pivotal trials have confirmed relative equality between all four of these modifying agents with respect to reduction in relapses. Hence the choice of which agent to use remains the province of agreement between the specialist and the patient involved.

Tysabri® (natalizumab) is a monoclonal antibody, given monthly via intravenous infusion, usually within the ambulatory care ward of the local hospital under the auspices of a specialist. Patients need to appreciate the potential of deaths on Tysabri® consequent to the emergence of progressive multifocal leukodystrophy (PML), which is a progressive disease of the brain related to JC viral infection, secondary to depressed immunocompetence. Those on Tysabri® with previous exposure to immunomodulating agents have a significantly increased risk of PML, as do those who have been on it for more than two years.

Another treatment of the immune system includes mitoxantrone, which is reserved for the difficult cases and can be given to a maximum of 140 mg/m^2 of body surface area with the potential for significant adverse effects, such as heart disease. Other immunosuppressive agents, such as methotrexate or azathioprine, have been used to treat MS as has plasmapheresis, but these definitely remain within the ambit of the specialist.

Perhaps the most exciting area in the long-term disease modification for MS has been the explosion of experimental agents, currently undergoing clinical trialling, which may one day replace the current injectable therapies. Fingolimod (Gilenya®) is a once daily oral agent that binds to sphingsine-1 phosphate receptors in the lymph nodes, thereby sequestrating lymphocytes in the lymph nodes. It has been internationally approved in Australia, the United States, Canada and Europe as an effective agent in MS. It is not yet on the PBS, but widespread familiarising programs are in place. Another oral agent is cladribine (Movectro®), an anti-cancer treatment given in two short courses that acts against MS for up to a year. It has been approved in Australia and Russia for MS but refused in Europe twice by the European Medical Agency. It is also not yet PBS approved, but familiarisation programs are in place. Other agents, such as BG12 (a fumaric acid derivative used in Europe to treat psoriasis) and teriflunomide, have been trialled in RRMS. None of these agents are available to general practitioners but they, and others, herald a new era in the treatment of MS. Further discussion of these agents is definitely beyond the scope of this chapter, although patients with MS, particularly those who refuse to self inject or who have had unacceptable consequences from the current agents, should be offered a referral to a specialist involved with these agents and the ongoing trials.

Symptomatic relief

The area in which the general practitioner dominates in the treatment of MS is symptom relief. Spasticity may be treated with baclofen (Lioresal®) 10–25 mg nocte, diazepam (Valium®) 2–10 mg t.d.s. or dantrolene (Dantrium®) 25 mg/D to 50 mg q.i.d., supplemented with physiotherapy and a possible exercise program. Botulinum toxin also has been used for MS spasticity, but is definitely the domain of the specialist.

Pain and dysaesthesia may be treated using some of the antiepileptic medications, such as carbamazepine (Tegretol®) building up to 400 mg CR b.d. or even gabapentin (Neurontin®) building up to a dose of the order of 800 mg t.d.s. or higher. Again, use of botulinum toxin may be considered.

Amantadine (Symmetrel®) given in the dosage of 100 mg per day has been used to treat MS-related fatigue. As described earlier, sleep disorders, especially PLMS with PLMA, may be a provocateur for fatigue,[7] as may obstructive sleep apnoea. A trial of pramipexole (Sifrol®) 250 µg nocte or even L-dopa (Sinemet® 100/25) one nocte may offer symptomatic relief. The

possible role of CPAP is also worthy of consideration, but further studies are required.

Urgency may respond to the use of tricyclic antidepressants, such as amitriptyline (Endep®) 25–75 mg nocte or imipramine (Tofranil®) at the same dosage. A choice between these two will be based upon the history of the patient's sleeping pattern, with Endep® favoured if the patient has a poor sleep pattern. Constipation is a recognised anticholinergic adverse event caused by the tricyclic antidepressants, and may be problematic in patients with MS who are already experiencing constipation. This may require a balancing act on the part of the therapist and could necessitate use of cathartics, either to treat the constipation in the absence of the use of tricyclic antidepressants or in conjunction with their use.

Counselling

The general practitioner is pivotal in counselling patients with MS on a variety of concerns. Patients may often perceive the consultant as being too busy to discuss some of the mundane issues that deeply affect their life. One of these concerns could relate to pregnancy, which is not contraindicated in MS, and may be accompanied by significant improvement in the patient's wellbeing—at least during the second and third trimester. It may deteriorate significantly in the immediate postpartum period due to a combination of sleep deprivation, postpartum depression and possibly changes in hormonal balance, especially regarding steroids. It is advisable to stop the disease modifying agents some months before a planned pregnancy and to restart them postpartum. They are not contraindicated for breastfeeding, but the inherent sleep deprivation that attaches to night-time feeds may be counterproductive for the patient with MS. Family planning, using the contraceptive pill, is also not contraindicated in the presence of disease modifying medications.

The psychological and potentially intrusive sexual problems that might affect the person with MS have already been alluded to. There is no absolute contraindication to the use of psychotropic medications, and the general practitioner should complement their use with patient counselling. There is a belief that stress is a provocateur for MS relapses, and the general practitioner is best placed to help with the management of stressful situations for the patient. Excess heat also may adversely affect patients with MS, so the patient should be counselled against undue exposure to heat, be it in the form of excessively hot showers, steam baths or saunas, or travel to very hot climates.

One final consideration must also include addressing the social needs of the disabled patient with MS. General practitioners have a real contribution to make in helping patients find suitable accommodation and, when necessary, appropriate placement for which social worker intervention may be necessary. It is not the role of the consultant only to involve the self-help groups, such as the MS Society, as the general practitioner may be better attuned to the

patient's needs. The MS Society may be ideally placed to assist. Some hospitals, such as Liverpool Hospital in Sydney, have MS nurses who are specifically trained in the care of patients with MS and provide an invaluable resource for the family doctor to ensure access to all available treatment.

Some of the most important areas for treatment in MS relate to symptomatic relief and counselling—they are unequivocally areas in which the general practitioner should have a more intimate relationship with the patient. Patients may identify problems in these areas with the general practitioner and be more accepting of the general practitioner's involvement in their treatment.

CONCLUSION

MS is a disease that carries with it a great amount of fear and negative connotations. The diagnosis often produces similar patient responses as a diagnosis of cancer, but it is an exciting time for those treating patients with MS.

The condition is easier to diagnose with the benefit of MR, and there are treatments available even before the diagnosis of clinically definite MS has been established. **In addition to the traditional disease modifying injectable agents, such as the interferons and glatiramer acetate, treatment of MS is at the dawn of new age oral treatments with medications such as fingolimod and cladribine** currently undergoing international regulatory review, and other agents being trialled or just completing clinical trialling.

These remedies are complemented by Tysabri® or Mitoxantrone®, and brave new world use of stem cells is on the horizon. All of these treatments remain the precinct of the consultant specialist but the true hands-on, direct patient care, day-to-day management of intrusive symptoms and psychosocial issues, and relief of fear and assistance with rehabilitation or even habilitation, remain the domain of the primary care general practitioner.

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11

Peripheral neuropathy

INTRODUCTION

Peripheral neuropathy (PN) represents nerve damage outside the central nervous system. It includes lower motor neurone (LMN) damage as well as sensory neuropathies. Radiculopathy (nerve root damage) is also part of PN.

Ability to differentiate between upper motor neurone (UMN) and LMN damage is fundamental to understanding PN (see Table 11.1). Cranial nerves represent a special type of peripheral nerve emanating from the brainstem. This raises an 'old chestnut', namely facial weakness of either UMN or LMN origin.

All too often patients are diagnosed with 'UMN facial palsy' and by definition 'palsy' is of LMN origin (as is the case with bulbar palsy and pseudobulbar palsy, the latter being of UMN origin and hence not really a palsy—thus the use of the term 'pseudo'). It follows that 'UMN facial palsy' is stating 'UMN LMN weakness' which is inappropriate. The word 'palsy' is a corruption of the French word 'paralysie', meaning paralysis but usually implying LMN lesion.

A LMN facial nerve lesion (cranial nerve VII palsy) affects both upper face (forehead) and lower face—hence the saying 'lower is upper', while an UMN facial weakness affects only the lower part of the face justifying the statement 'upper is lower'. To be correct one should refer to either facial palsy, implying LMN deficit, or UMN facial weakness, implying involvement of only lower face.

There are some conditions that may affect both UMN and LMN,[1] such as motor neurone disease (often referred to as amyotrophic lateral sclerosis) or subacute combined degeneration, as may occur with vitamin B_{12} deficiency.[2]

TABLE 11.1 Differentiation between upper motor neurone and lower motor neurone damage

	UMN	LMN
Inspection	Limited or no loss of muscle bulk No fasciculations	Localised or generalised muscle wasting Fasciculations may be present
Tone	Increased muscle tone (clasp knife)	Decreased tone consistent with loss of bulk
Power	Decreased power in distribution of UMN (antigravity muscles)	Weakness of muscles innervated by damaged nerves
Reflexes	Increased (brisk) reflexes below level of damage Up going or splaying of toes	Decreased or absent reflexes in muscles denervated Toes down going
Sensation	Generally not affected	Decreased if sensory nerves also involved

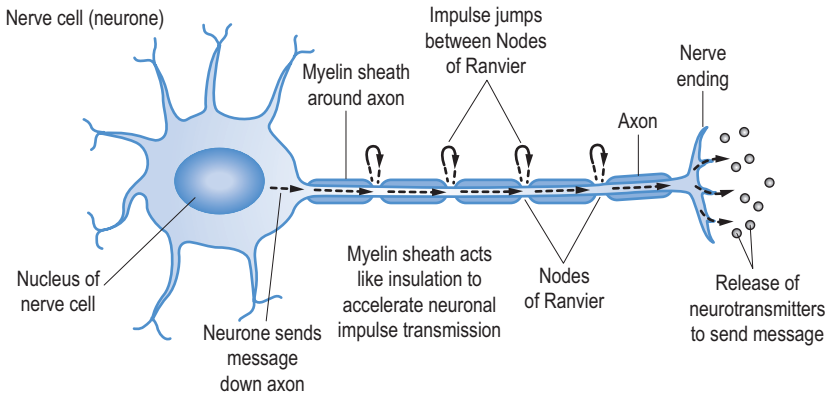
What follows in this chapter is a discussion of the nature of nerve damage, causes of PN, diagnosis thereof, a look at some focal neuropathies, nutritionally induced neuropathies and some illnesses associated with PN. The aim is to help general practitioners become more involved in patient care and, hence, better enjoy the therapeutic partnerships with the consultant.

THE NATURE OF NERVE DAMAGE

Nerves transmit their messages via an electrical impulse from the nerve cell (the cell of the neurone) down the length of the 'arm' of the cell (the axon) to pass the message either to another nerve or the end target organ. The message is sent via the impulse causing release of the neurotransmitters that produce the desired effect, be it to stimulate or suppress a subsequent response, such as causing a muscle to contract or to stimulate another nerve (see Fig 11.1).

To speed up transmission the axons of the nerves are usually coated with myelin, which acts in a similar fashion to the plastic coating that insulates and allows unimpeded passage of electrical current down an electrical wire (see Fig 11.1). Along the myelinated nerve fibre the impulse 'jumps' between Nodes of Ranvier, breaks in the myelin.

In the same way the wire within the plastic transmits the electrical current, so too does the axon send the neuronal impulse. It follows that damage to the axon (analogous to the electrical wire) will reduce the amount of message able to be transmitted. In neurophysiological terms, axonal damage will reduce the amplitude of the impulse and hence the amplitude of the action



(NB: A nerve may have more than one axon.)

FIGURE 11.1 Schematic of neural transmission.

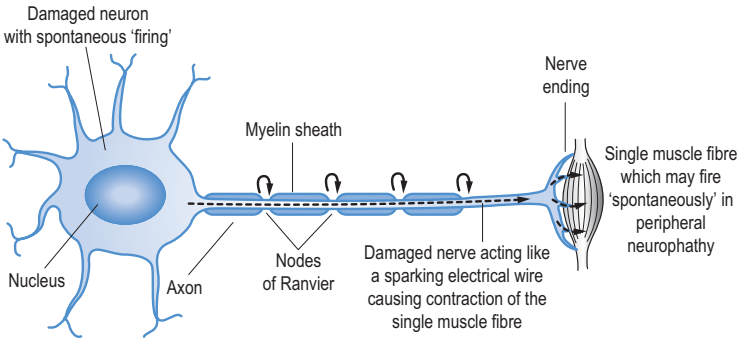
potential generated,[3] namely the size and strength of the message received rather than the speed of the transmission.

Transmission speed (or conduction time) is facilitated by the myelin sheath. It follows that damage to myelin, as occurs in demyelinating illnesses (such as Landry-Guillain-Barré syndrome, often referred to as GBS—omitting the name Landry, or multifocal motor neuropathy) will slow conduction time.[4] In the same way damage to the plastic coating of the electrical wire will ultimately allow the wire to corrode and be damaged, so too will established demyelination allow subsequent axonal damage.[5]

From the above it can be seen that nerve damage will occur if there is a disease process that will remove myelin from nerves (demyelination causing slowing of conduction); axonal damage causing less impulse to be transmitted; or a combination of both. Understanding of this will enhance appreciation of the results from neurophysiological testing.

When nerves are damaged it may be akin to a short circuit, to continue the electrical wire analogy. Thus nerves may 'fire' spontaneously. This may result in the activation of a single muscle fibre (called fibrillation, see Fig 11.2) or a group of muscle fibres known as a motor unit, which is limited to muscle fibres innervation by a single motor nerve (called fasciculation, see Fig 11.3).

Both fibrillations and fasciculations are recorded using needle electromyography to record spontaneous firing. Fibrillations are not generally visible with the exception of the tongue, which may be wasted and show fibrillations in motor neurone disease. Fasciculations can be seen as small muscle twitches as they involve more than a single muscle fibre. Fasciculations may be completely benign as can occur in marathon runners, or may reflect significant PN and often accompany motor neurone disease.



Fibrillations are recorded using needle electromyography–they can not be seen with the naked eye except if the fibrillation is in the tongue

FIGURE 11.2 Fibrillation.

CAUSES OF NERVE DAMAGE

PN can be the result of either local damage or a more generalised process affecting a wider target (see Box 11.1).

The most common cause of local damage is consequent to pressure, which causes a 'neurapraxia' that damages the nerve at the site of the pressure. An example of this process is damage to the lateral popliteal nerve with resultant foot drop. The lateral popliteal nerve activates the tibialis anterior muscle that dorsiflexes the foot.[6] Similarly, direct damage to the radial nerve as it transverses the humeral groove in the humerus bone will result in wrist drop due to deficits of wrist extension.[7]

Perhaps the best-known local nerve damage is carpal tunnel syndrome (CTS), which affects the median nerve. This causes weakness of the muscles innervated by the nerve plus specific sensory deficit referable to local median nerve damage (see Fig 11.4).

Only four intrinsic hand muscles are innervated by the median nerve.[8] The remainder are innervated by the ulnar nerve. There is a mnemonic to remember these four muscles: LOAF (**L**ateral two lumbricals, **O**pponens pollicis, **A**bductor pollicis brevis and **F**lexor pollicis brevis).

Generalised PN results from a systemic problem that can be the result of a variety of toxins, for example drugs (e.g. vincristine)[9] or infections, which may be the precipitant for conditions such as motor neuropathy (as may occur with infectious hepatitis)[10]. A variety of other environmental toxins, such as lead and other heavy metals,[11] can also cause pure motor neuropathy.

Conditions such as Landry-Guillain-Barré syndrome (GBS, also known as idiopathic ascending inflammatory polyradiculopathy)[12] and chronic inflammatory demyelinating neuropathy[13] (CIDP) represent allergic responses to reputed infective agents causing demyelinating radiculopathy or neuropathy.[12,13]

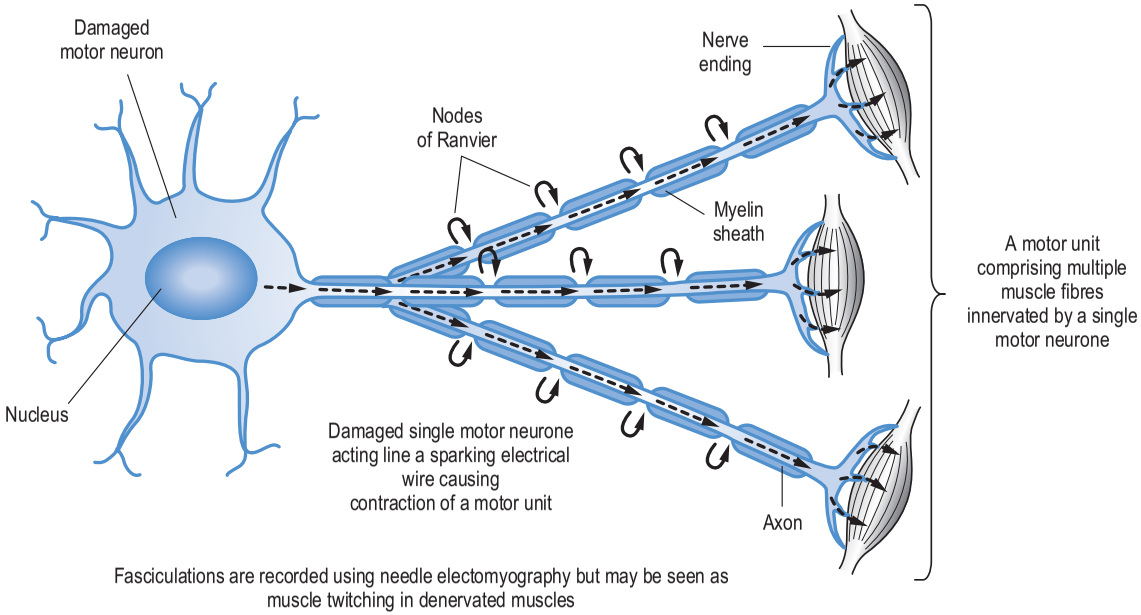


FIGURE 11.3 Fasciculation.

BOX 11.1 Treatable causes of peripheral neuropathy

Inflammatory neuropathies
Diabetic neuropathy
Dietary deficiency neuropathies:
- B_1 (thiamine) as in alcohol dependence with poor diet
- B_{12} as in pernicious anaemia or in vegans
- folate deficiency from not eating green vegetables

Mononeuropathies such as those occurring in sarcoidosis, enteritis and vasculitis (polyarteritis nodosa, lupus erythematosus):
- may be in autoimmune diseases or with specific infection or toxins

Heavy metals, such as lead or mercury poisoning
Infections, such as leprosy, hepatitis, cytomegalic virus (CMV) and Epstein-Barr virus (EBV) with glandular fever (mononucleosis)
Gammopathies
Neurotoxic drugs, such as nitrofurantoin
Porphyria
Landry-Guillain-Barré syndrome
Chronic inflammatory demyelinating polyneuropathy (CIDP)
Local neurapraxias such as:
- carpal tunnel syndrome
- ulnar neuropathy
- radial nerve neuropathy
- lateral popliteal neuropathy

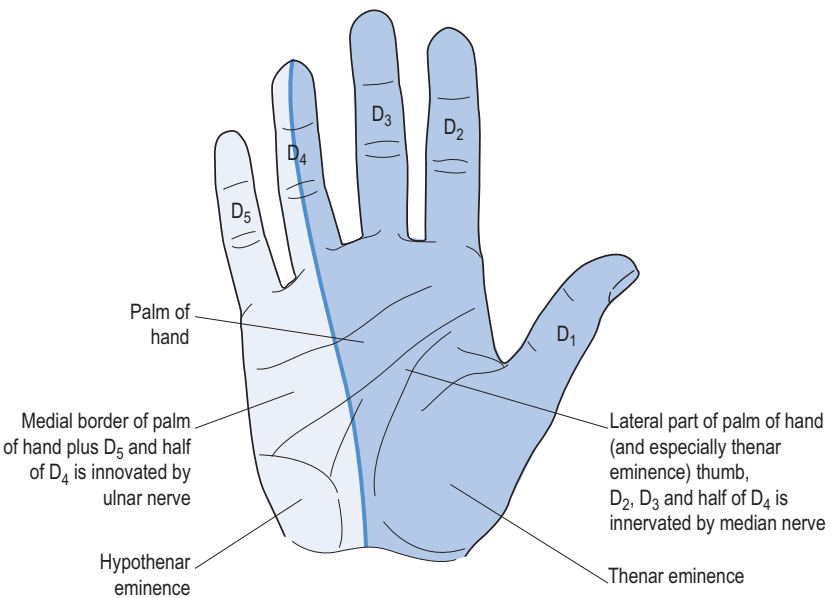


FIGURE 11.4 Sensory innervation of hand.

DIAGNOSIS OF NERVE DAMAGE

a History

As with all neurology, the fundamental building block is the history. Much of this has been covered in earlier chapters but there are specific symptoms that help diagnose PN. There are also pitfalls as provided by ambiguous 'non-words', also discussed earlier. An example of a 'non-word' re PN is the word 'numb' which may mean: loss of sensation; an unpleasant sensation (such as pins and needles); weakness; heaviness; loss of power; loss of movement; pain; or a variety of other terms specific to a particular patient, such as burning or crawling under the skin. It is imperative to be sure that the patient's meaning of 'numb' is understood rather than accepting what 'numb' should mean.

Many patients with PN will start with the complaint of numbness, so clarification **is important**. Having confirmed that both doctor and patient understand the meaning relevant to the particular patient, the next step is to define the exact distribution of the sensory change(s). Specific nerve damage should cause a typical distribution of sensory change (see Fig 11.4) but often patients find it impossible to be specific. Often patients with CTS will report waking at night and state 'my whole hand went to sleep'. They have trouble differentiating between palm and dorsum of the hand, and most will not recognise the anatomic 'splint' affecting the ring finger (see Fig 11.4). Some may report that the whole arm, meaning the whole upper limb, was affected and some may confuse the picture by stating that it started in the shoulder and passed to the hand, or started at the elbow.

It is most important to take as detailed a history as is possible. Many patients with generalised PN will not describe the classical 'glove and stocking' distribution of dysesthesia. Unless specifically questioned, patients with diabetic neuropathy may not volunteer that they have been diagnosed with diabetes mellitus even if it is well established. Some will not know they have diabetes but on history taking may report polyuria, polydipsia and fatigue that should act as red flags.

Questions to be asked must include: distribution of sensory deficit or weakness; associated symptoms; pattern of evolution of symptoms (when they started, how they started, how they affected the patient …); exposure to toxins, infections or medications; and any injuries or illnesses that either accompanied the symptoms leading to presentation or preceded them. Most doctors appreciate that flu-like symptoms may precede Bell's palsy or GBS by up to two weeks, but may have been dismissed by the patient as irrelevant. It is important not to ignore such symptoms because most are relevant and will assist with diagnosis. It is a valuable maxim to consider the taking of a comprehensive history as akin to gathering the pieces of a jigsaw puzzle. The omission of a single piece may make the difference to completing the puzzle, or not.

Some additional considerations to be included in the history taking include: any identifiable causative factors; knowledge of any pre-existing diagnoses

(such as diabetes discussed earlier); relevant family history (such Charcot-Marie-Tooth disease for hereditary neuropathies); exposure to medications; nutritional status (such as vegans not ingesting sufficient vitamin B_{12}); excessive alcohol consumption (with direct alcohol toxicity or dietary deficiencies such as vitamin B_1); and a comprehensive systems review (that may reveal conditions such as vasculitis, sarcoidosis or exposure to heavy metals such as lead or mercury, being recognised occupational hazards, or cytoxic or radiologic treatment for neoplasia).

b Examination

As suggested in Ch 5, O'Brien (2010) is an invaluable tool when evaluating the peripheral nervous system. It is highly recommended that anyone interested in the examination of the peripheral nervous system keep a copy handy, as it defines the relevant dermatomes and how to test specific radicular and nerve innervated muscles. Some examples will be provided in the discussion of classical presentations but this will not replace the value of this reference.

The 'glove and stocking' distribution of generalised PN usually starts in the distal end of the longest nerves, thus starting in the feet before involving more proximal areas such as the calf or thigh. It is easiest to start testing from the area of reduced sensation and move towards the region of increased perception. The patient finds it easier to identify when pain is first felt, rather than when it is diminished. The examiner should start testing at the periphery, be it the toes or fingers and move centrally towards the torso. If an abnormality is detected the testing should be repeated, ensuring that the patient is not watching the stimuli being applied. It is important to note if there is discrepancy between the two tests. If there is it should be repeated, marking the point at which change occurred using a pen and mapping the difference with repeated tests. If the distribution of the point of change is too great it provides 'concrete' evidence of non-organic disease (see Ch 5).

Formal testing of sensation should theoretically include: light touch; pinprick; temperature; vibration sense; joint position testing; and two-point discrimination. In reality, from the perspective of the busy general practitioner, it is worth noting that light touch, pinprick and temperature all travel via the lateral spinothalamic tracts, while vibration, joint position and two-point discrimination travel in the posterior columns of the spinal cord. Thus testing light touch, simply using a finger lightly touching the skin, and joint position testing will have evaluated both pathways. It is advisable when testing joint position sense by moving a digit, be it great toe or little finger, to hold the digit on the sides to avoid upward and downward pressures that add additional information and may confound subtle changes. Similarly, it is important to offer only slight movements up or down rather than exaggerated movements, as exaggerated movements will also allow additional stimulation that may mask subtle abnormalities.

Much of what is included within this section on examination should be combined with Chapter 4 on the peripheral nervous system for a more comprehensive overview.

c Investigations

In general terms, by the time the patient is referred for electrophysiology they have also been referred for specialist opinion. The above discussion should equip the general practitioner to better understand the report by the neurophysiologist. It should empower the general practitioner as part of the therapeutic team.

An understanding of the treatable causes of PN (see Box 11.1) will assist with appropriate tests to cast diagnostic light in some cases. These may obviate the need to refer the patient to a consultant. Most of the possible treatable causes can be explored by the general practitioner who can also prescribe appropriate treatment.

Questions of nerve biopsies, motor or sensory evoked studies or magnetic resonance imaging (MRI) of a specific nerve or plexus are all beyond consideration within this text. These tools remain the weapons of the consultant neurologist, rather than the general practitioner. As a rule of thumb, if these tests are required it is usually a complex case in which there is often no final answer.

FOCAL NEUROPATHIES

The most common focal PN is CTS,[8] which reflects damage to the median nerve due to entrapment at the level of the carpal tunnel at the wrist. There should be an appropriate history (with dysaesthesia of the hand causing waking from sleep that often responds to shaking to return sensation). There should also be weakness of the median nerve innervated muscles (remember the mnemonic LOAF, as above), especially with weakness of abductor pollicis brevis and lateral two lumbricals (see Figs 11.5 and 11.6). There may be a sensory deficit (see Fig 11.4), which may not be as anatomically distinct as shown but, as a minimum, sensation in the thenar eminence should be less than that over the hypothenar eminence.

Causes of CTS include: using vibrating equipment, such as jack hammers; repeated pressure from using tools, such as a screwdriver with the palm pushing down on it; but most commonly from sleeping in such a position as to cause marked palmar flexion of the wrist thereby impeding the blood supply to the nerve. Before contemplating either neurophysiology or surgical referral, the most common effective treatment is to organise a physiotherapist to provide a moulded night splint made specifically to meet the anatomy of the patient (see Fig 11.7).

The next most common PN is an ulnar neuropathy[14] at the elbow. This causes dysaesthesia along the ulnar border of the forearm, little finger (D5)

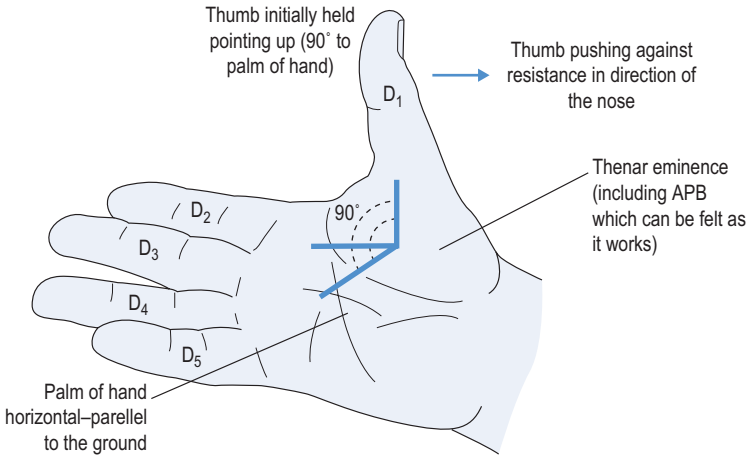


FIGURE 11.5 Testing power in abductor policis brevis.

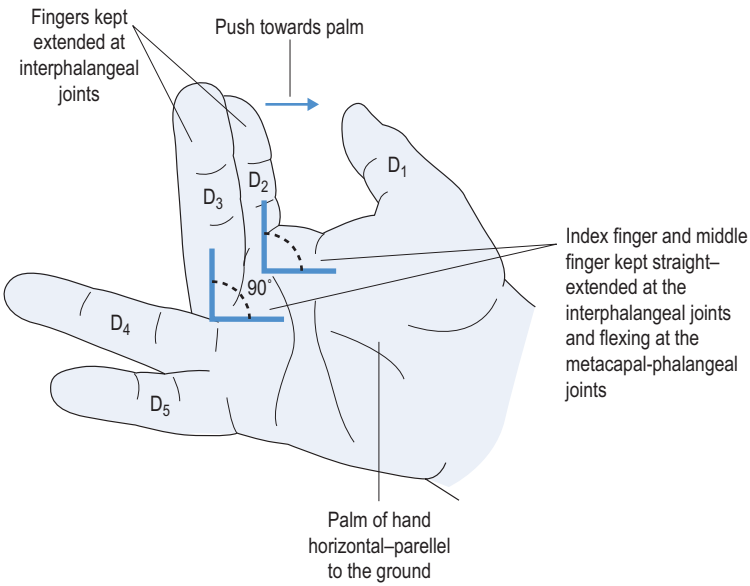


FIGURE 11.6 Testing lateral two lumbricals.

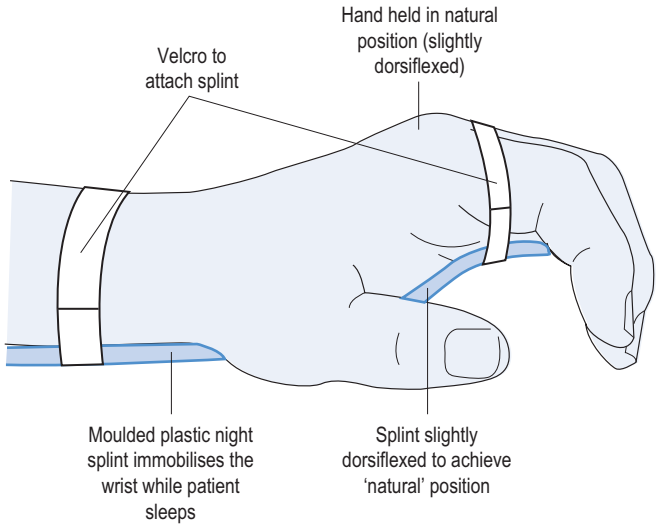


FIGURE 11.7 Night splint to immobilise at night—to treat carpal tunnel syndrome.

and medial half of the ring finger (D4) (see Fig 11.4). It causes weakness of the ulnar-innervated muscles of the hand, typified by abductor digiti minimi that forces the little finger away from the rest of the fingers and away from the palm (see Fig 11.8). It also causes weakness of the medial two lumbricals (see Fig 11.9). Long-standing ulnar neuropathy may cause wasting of the first dorsal interosseus muscle best seen in the dorsum of the hand, the muscle between the thumb and index finger (D1 and D2).

The main cause of ulnar neuropathy is direct trauma to the nerve as might occur when turning over in bed at night. This results in the whole body's weight being supported by the elbow and hence the ulnar nerve as it crosses the elbow at the ulnar groove next to the humeral epicondyle. The way to treat this is to pad the elbow over the region. This includes the medial humeral epicondyle and olecranon of the ulnar bone. The easiest way to do this is to get a piece of foam rubber, approximately 2 cm thick and about 5–10 cm in diameter. This is placed in position and held either with a bandage or more simply using a large sports sock with the toe cut out so that it can be slipped up the forearm and over the elbow (see Fig 11.10). Such padding prevents repeated pressure upon the nerve that causes nerve damage (neuropraxia) by squashing the nerve against the hard bony surfaces while rolling over. The splint only needs to be worn at night while sleeping.

Should this simple intervention fail to relieve symptoms then it is time to refer the patient for specialist opinion and to order electrophysiology.

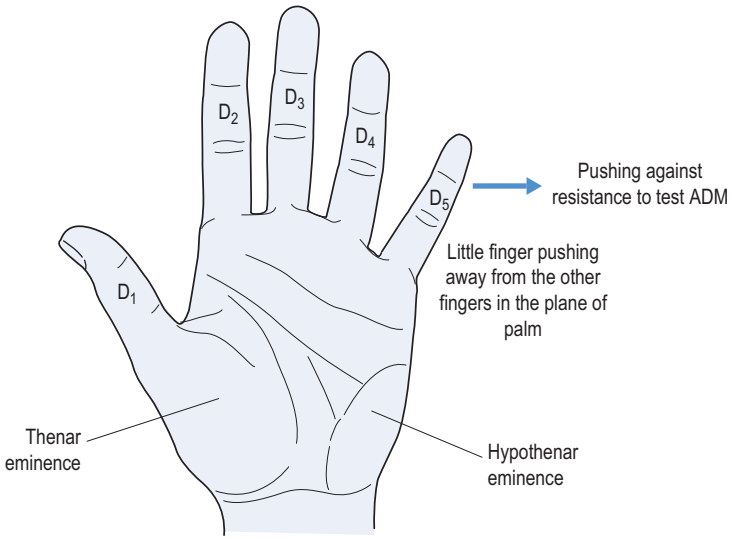


FIGURE 11.8 Testing power in abductor digiti minimi.

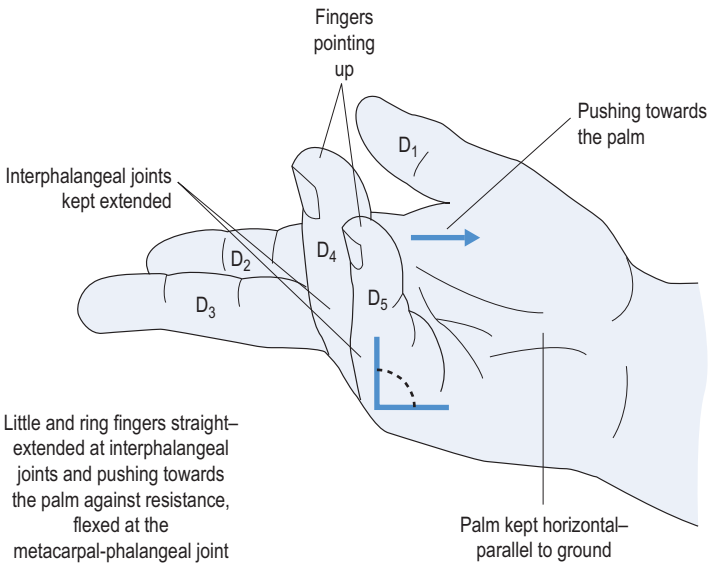


FIGURE 11.9 Testing power in medical two lumbricals.

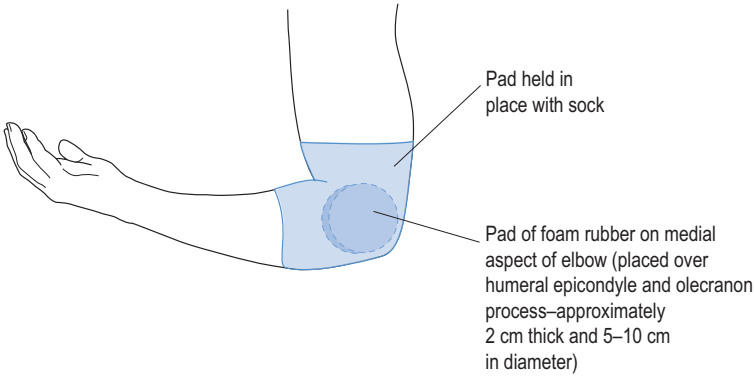


FIGURE 11.10 Padding elbow to protect ulnar nerve.

NUTRITIONALLY INDUCED NEUROPATHIES

Various vitamin deficiencies are known to cause PN, such as B-group vitamins, possibly in association with alcohol abuse.[15] The general practitioner should prescribe thiamine (B_1) to all patients with suspected alcohol dependence. A proper history, including a dietary history, should be an integral part of the diagnostic process.

The onset of PN can be slow and subtle but damage can be profound, as in the case with B_{12} deficiency that can cause CNS and PN damage.[16] Parenteral B_{12} injections may both arrest and allow some restorative benefits. Measurement of B_{12} and folate must be part of the patient assessment when considering PN. Folic acid is an essential component of B_{12} metabolism, but is often overlooked. Replacement with 5 mg folate per day is simple and effective.

Other nutritional conditions include pellagra,[17] with its triad of gastrointestinal symptoms, dementia and PN. It is caused by nicotinic acid (niacin) deficiency. Some drugs, such as penicillamine or isoniazid, may cause B_6 (pyridoxine) deficiency. B_{12} and B_6 deficiency may cause elevation of homocysteine, which is implicated in stroke evolution due to hyperviscosity. Nutritional deficiencies may reflect malabsorption rather than poor dietary intake. Without a high index of suspicion, such causes may be overlooked.

ILLNESS ASSOCIATED WITH PERIPHERAL NEUROPATHIES

The most common diagnosis associated with diffuse PN is diabetes. This should be a fundamental consideration when diagnosing PN.[18] Blood sugar level and glycosylated haemoglobin (HbA_{1c}) should be ordered early in the evaluative process. Where there are haemoglobinopathies, such as thalassemia, fructosamine measurement may be preferable to HbA_{1c}. Initial control of diet may be all that is required, but it has been personal preference to involve an endocrinologist early in the therapeutic process regarding diabetes and to advocate early introduction of insulin once PN has been confirmed. The variety of neuropathic complications with diabetes (such as painful diabetic amyotrophy) may necessitate a wider team approach and even use of immuno-modulating agents, such as IV immunoglobulin, but this is outside the scope of this review.

Any condition that may adversely affect the nerve's blood supply, as with the blocking of the vasa nervorum in diabetes, has the potential to cause PN. It follows that any cause of vasculitis (such as polyarteritis nodosa or lupus erythematosus) may cause PN, particularly mononeuritis multiplex, which may affect specific nerves rather than cause a generalised PN. Antinuclear antibody (ANA) and extractable nuclear antibody (ENA) should be included in the diagnostic process. In addition, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) should be measured in suspected cases of PN. Treatment of these vasculitites by the specialist working with the general practitioner will not be further discussed.

Sarcoidosis is also a well-recognised cause of mononeuritis multiplex (including isolated nerve damage). Angiotensin converting enzyme (ACE) should be measured as part of the evaluation.

Neoplasia can cause PN via several routes, be it direct nerve damage (due to a space-occupying or pressure effect), as a consequence of cachexia or as a paraneoplastic expression, which can cause both small-fibre or large-fibre involvement. If in doubt, the general practitioner should look for a primary source using chest imaging and possibly chest and abdominal CT. Anti-neuronal antibody screening, such as anti-Hu together with other tumour markers—alpha-feta protein (AFP) or carcino-embryonic antigen (CEA)—may assist. Agents used to treat neoplasia (such as vincristine or thalidomide) may cause PN. Other medications may be associated with PN, such as statins—now used for more than just hyperlipidaemia—in stroke prevention for vessel-wall stabilisation and even for conditions such as dementia or multiple sclerosis.[19]

The cardiac medication amiodarone, the urinary antibiotic nitrofurantoin or the antiepileptic medication phenytoin (via its anti-folate effects) may all cause PN. Unless the general practitioner is vigilant, such iatrogenic causes may be overlooked. Medications may serve as a trigger to evoke conditions known to cause PN. One such condition is porphyria, with a pure motor neuropathy that may be provoked by use of barbiturates. Being a rare

condition it is easily overlooked, but a detailed medication history may provoke its consideration.

Other illnesses to be kept in mind when considering PN include: hepatitis (particularly B and C); AIDS and HIV; mononucleosis with Epstein-Barr virus; herpes (both shingles and chicken pox); and even Lyme disease. An overview such as this cannot be exhaustive, but the general practitioner should have a list of treatable PNs to ensure patients benefit from intervention when it is available.

INFLAMMATORY NEUROPATHIES

Landry-Guillain-Barré syndrome (GBS) is a rapidly progressive and treatable cause of PN or ascending radiculopathy. While its treatment is the domain of the neurologist, its diagnosis and treatment are often delayed because it has not reached the radar screen of many general practitioners. It is easy to dismiss the early presentation of GBS. The answer is to suspect it in people with motor (and sometimes also sensory) symptoms, usually starting in the lower limbs and spreading rapidly. Initially there may be few signs, but a high index of suspicion will allow early access to IV immunoglobulin or plasmapheresis. High CSF protein, as found with lumbar puncture, is also a useful diagnostic clue with GBS.

Similarly, chronic inflammatory demyelinating polyneuropathy (CIDP) may be easily overlooked as a diagnostic entity, so the patient is denied appropriate and effective therapy. Only with a high index of suspicion, complemented by markedly slowed nerve-conduction electrophysiology, will the diagnosis be apparent and treatment with IV immunoglobulin commenced.

OTHER CONSIDERATIONS

One should not ignore the hereditary causes of PN, including inherited propensity to pressure palsies. Treatment is usually symptomatic. Heavy metals such as lead or mercury, or other toxins such as nitrous oxide can cause PN.

Multifocal motor neuropathy with conduction block or progressive muscular atrophy (part of the motor neurone disease complex) are generally neurologists' diagnoses but the general practitioner is the first port of call. With a high index of suspicion, they can dramatically reduce the time from onset to diagnosis and treatment. It follows that the general practitioner must retain an overview of PN, although early involvement of a specialist improves the therapeutic approach.

CONCLUSION

Often general practitioners exclude themselves from the management of PN, but the above demonstrates what a valuable role they can play. As with all neurology, a good history is indispensable as is a clear understanding of what

to look for and how to differentiate LMN from UMN lesions (see Table 11.1). **The general practitioner may be the person who diagnoses the treatable PNs, having a high index of suspicion and having ordered the appropriate tests (see Box 11.1).**

The most common PNs presenting to the general practitioner are CTS and ulnar neuropathy, both of which respond well to conservative treatment that might completely do away with the need for referral to a specialist (Figs 11.4–11.10). Only in those few cases that fail to respond would there be a need to seek neurophysiological diagnostic confirmation and consultant involvement. Where doubt exists as to whether the patient has CTS or ulnar neuropathy or a more widespread PN, early referral to a consultant is advisable.

Lifestyle issues, such as alcohol dependence, dietary failings (such as B_1, B_6, B_{12} or folate) and compliance with treatment for conditions like diabetes or use of inappropriate medications, are all issues that may be adequately and properly addressed by the general practitioner. With prompt diagnosis and treatment, many of these problems may not even require the consultant to become involved. It is gratifying to refer patients with unusual or complex diagnoses, which were correctly diagnosed and/or treated in general practice, and were referred simply to ensure all necessary procedures had been completed, rather than admitting failure and abrogating authority to the consultant. **PN is one such area where the general practitioner can achieve good outcomes in many patients without needing to seek outside assistance.**

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12

The neurology of sleep

INTRODUCTION

Sleep medicine is often considered the domain of respiratory medicine, rather than neurology. This reflects the fact that Colin Sullivan is credited with recognising the benefits of continuous positive air pressure (CPAP) as an effective treatment for obstructive sleep apnoea (OSA).[1] What is less known is that the identification of OSA as a diagnostic entity was consequent to video telemetric evaluation of epilepsy. Nocturnal episodes were seen and appreciated to be breathing-related abnormal behaviour rather than a seizure.[2] Until that time, the concept of OSA had not reached the radar screens of those interested in sleep.

Obstruction of the upper respiratory tract, especially in rapid eye movement (REM) sleep, is, more likely than not, the reason why sleep medicine is seen as belonging to pulmonology, especially when one realises the benefits of CPAP. What is largely overlooked is the fact that sleep is a neurological state of being with defined electroencephalographic (EEG) patterns that reflect the stages of sleep emanating from the brain.[3] It follows that sleep is an integral part of neurology rather than being of transient interest.

The purpose of this chapter is not to teach family physicians to be sleep physicians but rather to introduce general practitioners to the concepts of sleep medicine, as seen through the eyes of a neurologist. One most salient area of concern is that of the person with significant sleep disorder, be it OSA or narcolepsy, who continues to drive a motor vehicle. The general practitioner plays a vital role in advising the patient and/or the licensing authority if the patient drives contrary to advice. This responsibility exists irrespective of whether the general practitioner is conversant with sleep medicine or not.

WHAT IS SLEEP MEDICINE?

As the name implies, sleep medicine is the study of how sleep affects health or, alternatively, the interface of sleep and health. Sleep medicine is much more than OSA, although OSA represents a very important part of sleep medicine because of its impact on activities such as driving. OSA is a potentially fatal condition because it is associated with an increase in hypertension, stroke and cardiovascular disease.[4] Should death occur it is usually attributed to one of these associated conditions, thereby bypassing and camouflaging the serious implications of OSA.

Sleep medicine includes: chronobiology and the impact of shiftwork on biorhythms; insomnia (be it initial at the onset of sleep or late with early morning waking—as often associated with psychological factors such as depression); various movement disorders associated with sleep, such as periodic leg or limb movement in sleep (PLMS), which itself may cause arousal (PLMA) as well as being associated with the restless leg syndrome (RLS); narcolepsy; the sleepiness and fatigue often associated with many systemic diseases, including infections or neoplasia but also with other neurological conditions such as multiple sclerosis (MS); and altered behaviour during sleep such as REM behaviour disorder (RBD) that may be increased in Parkinson's disease. The role of the sleep physician may be as simple as to evaluate the impact of poor sleep hygiene, which itself might be highly intrusive to quality of life.

It can be seen that sleep medicine covers a magnitude of conditions in which sleep and good health are intertwined. As sleep is an integral component of the lives of all patients who attend general practitioners, it is very important that practitioners have at least a superficial understanding of sleep medicine. Without this, general practitioners are deprived of the capacity to help their patients whose complaints emanate from sleep.

WHERE TO START?

As with all neurology, the starting point necessitates the need to have a high index of suspicion, for without it, it is impossible to take an adequate history. This should be tempered with some specialised knowledge that includes an understanding of what causes sleep disturbance and the consequences of poor sleep.

Often it is the experienced receptionist who will alert the doctor to the potential for a patient to have OSA. Office staff may play a pivotal role in advising the doctor about a patient who has been nodding off in the waiting room. Once alerted to the possibility, it is much more likely that the doctor will ask the right questions to make the diagnosis.

The patient's partner is also a great source of diagnostic information, such as the history of loud and intrusive snoring, a restless sleep pattern or gasping for air during the night. The pattern of snoring punctuated by

gaps of silence in which nothing is heard, followed by violent sucking in of air to compensate for the lack of oxygen, should provide the doctor with a red flag to suspect OSA.

Sleep is often a neglected and ignored component of medical history that translates into a third of the patient's life being ignored and taken for granted. The patient's size might provide the incentive to explore sleep. The Pickwickian obese, middle-aged Caucasian male or the obese, more senior Caucasian female should herald the ringing of warning bells for OSA. It should be appreciated that OSA is associated with a particular habitus[5] that is quite different for Caucasians and Occidentals,[6] with less emphasis on obesity in Asian people who experience OSA. OSA more frequently occurs in slim Occidental people, rather than the obese, as is the case with Caucasians.

Accidents that occur while driving should alert the doctor to question the patient, and their partner, concerning a sleep-related history. Assessment of sleep, sleep hygiene and related factors, such as disturbed sleep for whatever reason, or sufficiency of sleep, both in quality and quantity of time, should become part of the routine history taking. Daytime somnolence or excessive sleepiness or fatigue need to be explored. One such question relates to the capacity to fall asleep at traffic lights. This is a most important question and, if the patient admits to this, it is grounds for serious concern both about sleep disorders and the patient continuing to drive. An overall assessment of sleep should ultimately become part of routine patient evaluation for the conscientious general practitioner.

The family doctor should have some understanding of their patient's sleep pattern to allow a more informed referral to an appropriate specialist should sleep-related issues arise. As has already been stated, sleep can impact on a host of medical conditions as diverse as headaches, Parkinson's disease, MS or epilepsy. It is not by accident that sleep-deprived EEGs are routinely ordered to enhance the diagnostic yield when assessing patients with possible epilepsy. Lack of sleep, drifting off to sleep or waking up from sleep may be sufficient to provoke an epileptic seizure in a susceptible patient. The Sleep Centre at St Luke's Hospital in Sydney will often combine a sleep deprived, full 10/20 electrode placement, prolonged EEG video telemetric recording with an all-night diagnostic polysomnograph (PSG) to assist in cases in which the differentiation between epilepsy and parasomnia is difficult to determine. This is an area where the neurologist has the advantage as the semiology of the event is important for making the diagnosis. An example of this may be found with possible rapid onset and arrest of a nocturnal episode favouring epilepsy over parasomnia.

TAKING A HISTORY

Much of the above discussion of 'where to start' covered aspects of history taking, but the following will offer a more systematic approach.

The general practitioner should specifically ask about: the sleep pattern; what time the patient retires; sleep quality; duration of sleep; possible nocturia; insomnia; snoring; time(s) of waking; and comments from sleeping partners. The patient should be asked about how restful or invigorating sleep has been and how energetic they feel the following morning.

Daytime sleepiness, clarity of thinking and daytime efficiency should be explored. A history of work-related factors, such as shiftwork, stress, responsibility and efficiency, may shed extra light on quality of sleep. A patient who is often criticised due to poor work performance may have a sleep disorder as its root cause. It is axiomatic that if one does not ask the questions one cannot expect to get the answers. Doctors need to appreciate that their patients must have enough good quality sleep so that they can recharge their batteries, to be able to function efficiently and effectively.

EXAMINATION

There is nothing specific to the examination of the patient with regards to the neurology of sleep that necessitates special consideration. Pulmonologists may well explore, endoscopically, the upper airways to seek evidence of allergies that may impact upon sleep-related breathing. This is an area in which pulmonologists have an advantage over neurologists who are generally not trained in such endoscopic techniques.

Ear, nose and throat surgeons may focus much greater attention upon the tonsils and adenoids as a source of intrusive obstruction to breathing in sleep. Routine neurological examination when assessing cranial nerves includes examination of the pharynx and mouth. This would identify enlarged tonsils that may play a role in poor sleep, especially OSA and especially in the young.

Routine neurological examination should also include cardiac and respiratory auscultation, which would identify such breathing disorders as asthma or lung infections that might adversely affect sleep. Similarly, blood pressure determination and measurement of the patient's weight are components of the assessment of the patient's vital statistics. These should be routinely recorded, acknowledging that they may have increased relevance when assessing sleep. Not infrequently one is surprised to find that a patient thought to be of average height and weight is significantly overweight, which then provides the initial focus of therapy. As with history, suspicion and a thorough approach is the key to better patient care.

SLEEP APNOEA

Sleep apnoea may be either OSA or sleep apnoea caused by a central origin, namely a brain-related cause as may occur with a lesion in the brainstem affecting the reticular formation.[7] When considering sleep apnoea, most people only consider REM-related OSA, although OSA may occur in non-REM sleep and in some patients non-REM OSA may dominate the pattern.

TABLE 12.1 Features of obstructive sleep apnoea

Patient appearance	Usually middle-aged men (can be women) Obesity (Caucasians) Need not be obese (Occidentals) Patient often has difficulty breathing, even at rest Patient will often fall asleep in the waiting room
History	Excess fatigue Daytime somnolence Loud snoring Stop breathing in sleep Nocturnal hyperhidrosis Increased symptoms with alcohol and sedation Partner may describe episodes
Associated conditions	Hypertension Cardiac dysrythmia Ischaemic heart disease Parkinson's disease Dementia Epilepsy Stroke Multiple sclerosis

In REM sleep muscles lose their intrinsic tone, which may cause the respiratory tract to collapse, blocking the upper airways. Once the respiratory pathway has collapsed, air can no longer reach the lungs. As a consequence, oxygen cannot fuel the vital organs, such as the heart and brain—thus the increased risk of myocardial infarction or stroke in patients with OSA.

A heightened awareness of the potential for OSA, particularly in overweight, middle-aged male Caucasians, will prompt the general practitioner to ask about snoring, excessive daytime sleepiness or hypersomnolence. The sleep partner is an invaluable source of history and can describe the apnoeic episodes. There are a variety of features favouring OSA (see Table 12.1).

Once suspicion of OSA has been raised, it is appropriate to refer the patient to an accredited sleep physician. This should establish a chain of events in which the physician takes an appropriate history to confirm the suspicion and refers the patient for a PSG. Should this confirm the presence of OSA the patient will be referred for further PSG, known as all-night CPAP titration PSG. This will determine the type of CPAP mask that best suits the patient's facial features and temperament, and the amount of CPAP set in centimetres of water pressure required to maintain a patent respiratory pathway, so significantly reducing the apnoea–hypopnoea index (a measure of the frequency of disturbed sleep as a consequence of altered breathing).

There is a growing industry of home assessment for OSA that bypasses the sleep physician and, while cheaper, it reinforces the maxim that 'you get

what you pay for!' There are also oral devices that resist closure of the airways, prepared by dental mould and worn at night. These too take second place to the gold standard of CPAP with proper hospital assessment. With OSA, the role of the general practitioner stops once there is a heightened suspicion of the diagnosis, as this should lead to a referral to an appropriate specialist to confirm the diagnosis and instigate treatment. It recommences once the patient has been provided with appropriate treatment, as general practitioners are vital in maintaining compliance and encouraging patients to persevere with the CPAP.

INSOMNIA

By far the most common cause for a patient to attend the general practitioner for disturbed sleep is insomnia. The most common cause for insomnia is emotional stress, such as anxiety, depression or worry for whatever reason.[8] Often the patient will present complaining of a headache, because society considers it more socially acceptable to have an organic problem rather than openly confess to having difficulty coping. The patient will often present complaining of a migraine, and a good history should exclude migraine as a realistic option with the more common type of headache being tension-type headache (see Ch 6). Once this is diagnosed, the general practitioner can take a more detailed history of potential sleep disturbance.

This is an area in sleep medicine in which a competent general practitioner will be able to solve the problem without the need to refer the patient to a consultant. The issues may resolve with appropriate counselling, although pharmaceutical intervention may also assist. A favoured medication is one of the tricyclic antidepressants, amitriptyline (Endep®), which acts as an hypnotic as well as an analgesic, as an antidepressant and anxiolytic. The dosage usually starts with 25 mg nocte and may increase to satisfy need. It is important to realise that it may take up to 10 days to 2 weeks before the response is appreciated, and possible side-effects need to be discussed with the patient. Should the patient also have nocturia contributing to a disturbed sleep pattern, the anticholinergic properties of the tricyclics may also provide symptomatic relief for this complaint. This will enhance sleep quality while relieving the headaches. The goal is to use the medication only as a 'stop-gap', to relieve symptoms while helping the patient sort out a better approach with which to deal with the issues causing concern. The general practitioner is pivotal in this relationship.

Should the insomnia be a consequence of stress or altered sleep pattern, from whatever cause, that has resulted in a pattern of inappropriate wakening through the night, it is important to investigate sleep hygiene. The patient should be questioned about timing of going to bed and whether or not they get up through the night for whatever reason. Instituting correct sleep hygiene will often go a long way to correct the insomnia provoked by its disturbance. This may be complemented by the use of hypnotics, such as benzodiazepines

in the form of diazepam (Valium®), nitrazepam (Mogadon®) or temazepam (Normison®). Such hypnotics should be taken for three nights in a row to re-establish the body-clock, while at the same time avoiding the potential for habituation and tolerance that attaches to the benzodiazepines. Some patients may complain of a feeling of being 'hung over' with the benzodiazepines, in which case zolpidam (Stilnox®) may offer a viable alternative. It must be acknowledged that there have been reports of bizarre nocturnal behaviour associated with Stilnox®, such as binge eating or somnambulism, so the patient needs to be warned.

If these simple remedies fail to achieve the desired outcome then it is time to refer the patient to a sleep physician to be assessed in greater detail, including PSG.

SOMNAMBULISM

Somnambulism (sleepwalking) is one of the parasomnias and is a condition in which the patient may execute very deliberate and, at times, very dangerous activities during sleep.[9] It is associated with an abnormality of slow wave sleep rather than REM sleep.

To highlight the potential dangers associated with somnambulism, there is the case of a sailor who walked off the stern of a battleship during his sleep, luckily while the ship was in port rather than at sea, and was aroused once underwater. He could recount the sensation of seeing lights in the distance as they passed through the water, and swimming towards them. Once he reached the surface, he had significant difficulty getting out of the water as the port was not designed for casual swimmers. Had this event occurred at sea, he would have been lost and perished.

Somnambulism is more often encountered in children, especially in the peri-pubertal period. They are often described as growing out of it, although it may resurface in later life at times of significant stress. The sleepwalking need not entail actually getting out of bed and walking; it may be as simple as talking in one's sleep, singing or just sitting up for no obvious reason. In some circumstances, the somnambulism may be confused with epilepsy and may require full investigation, thus necessitating referral to a neurologist.

The simple treatment for somnambulism is to protect the patient from the potential of causing harm to themselves or to others. Should there be an association with stress or other emotional factors, these need to be addressed, but this can usually happen at the level of the general practitioner.

NIGHT TERRORS

Night terrors[10] are also one of the parasomnias that may be confused and misdiagnosed as epilepsy. They are often very frightening for parents, who feel impotent as they are powerless to stop them and equally powerless to comfort the distressed child.

Night terrors are far more prevalent in children, particularly aged two to six, rather than adults and they are unlike bad dreams. Night terrors are associated with the feeling of apparently unprovoked fear rather than frightening imagery, as may occur in nightmares. More often than not, they occur in non-REM sleep. No specific treatment is available although ensuring that the child has adequate sleep is said by some to be beneficial, but this is debatable. Comfort, reassurance and protecting the distraught child from harm remain the mainstay of any intervention.

Referral to a specialist is advisable, and EEG is often performed if only to exclude epilepsy while at the same time reassuring the parents.

NARCOLEPSY

Narcolepsy[11] has its associated tetrad of symptoms including: excessive sleepiness (with the rapid onset of REM sleep); sleep paralysis in which the patient may actually be conscious but cannot move until stimulated by something as innocuous as a light touch; cataplexy with sudden loss of muscle tone which results in collapse that may be provoked by emotional activity (as simple as laughter associated with hearing a joke); and hypnagogic (drifting off to sleep) or hypnopompic (awakening) hallucinations, namely vivid and realistic dreams associated with REM sleep although the patient is sufficiently awake to recall the experience.

The diagnostic process requires the patient to undergo a multiple sleep latency test (MSLT) to ascertain the frequency and rapidity of the onset of REM sleep. Tests of wakefulness may also be undertaken. Both tests require referral to a sleep laboratory, and hence referral to a sleep physician or neurologist.

An introductory overview such as this, aimed at the non-neurologist, does not lend itself to the discussion of the role of genetics nor the recent finding that narcolepsy is a result of a deficiency in hypocretin, also known as orexin transmission. Orexin enhances wakefulness and inhibits REM sleep, and its deficiency may be measured in a specialised laboratory using the lumbar puncture and cerebral spinal fluid. This is offered merely to whet the appetite of any reader wishing to explore the matter further.[12]

In the past the mainstay of treatment was the use of stimulants or antidepressants, either tricyclics or serotonin reuptake inhibitors. More recently modafinil (Modavigil®) has become the drug of choice for narcolepsy, as well

BOX 12.1 Tetralogy of symptoms of narcolepsy

1 Excessive sleepiness
2 Sleep paralysis
3 Cataplexy
4 Hypnagogic or hypnopompic hallucinations

as for shiftworkers reporting excessive sleepiness. Gamma hydroxybutyrate (often called GHB), widely recognised as the 'date-rape' drug, has proven efficacy for cataplexy. Prior to these medications being prescribed, the patient will have been referred to a neurologist or sleep physician so the actual choice of medication will be at their discretion. If the diagnostic tests necessitate referral to a sleep laboratory, it is appropriate to refer the patient once the diagnosis is suspected.

REM BEHAVIOUR DISORDER (RBD)

Discussion of RBD should probably be beyond the scope of this chapter, but it also is offered to whet the appetite. RBD represents a form of behaviour that occurs in REM sleep in which the patient may act out and even become quite aggressive.[13] Sleep partners may describe all manner of strange behaviour provoked by RBD, including being physically attacked by the patient. The patient may vehemently deny it as they will have no recollection of behaving in this manner.

RBD may be confused with epilepsy, and it could take a considerable time for the correct diagnosis to be made. This may necessitate prolonged video-telemetric EEG recording coupled with all-night diagnostic PSG, so is obviously outside the domain of the average general practitioner. It is treated with low dosage clonazepam (Rivotril®) and is increased with some neurological conditions such as Parkinson's disease.

CONCLUSION

Sleep disorders are far more prevalent than might be thought if one is not actively seeking to define them while taking a history. **Sleep apnoea, particularly OSA, is often considered the hallmark of sleep medicine and clearly requires PSG, and hence referral to a consultant. Insomnia, which is frequently referred to a specialist, can often be adequately managed by the general practitioner with judicious use of counselling, instigating proper sleep hygiene, and the judicious short-term use of hypnotics. Sleep walking and night terrors are parasomnias for which the general practitioner may be able to offer sufficient support and assistance to obviate the need to involve a specialist**. Conditions, such as narcolepsy and RBD, are better treated with early referral to a specialist.

As with all such brief overviews, it is impossible to be all-inclusive, so it is hoped that this chapter offers an introduction to sleep medicine as seen through the eyes of a neurologist that will whet the appetite of the general practitioner to delve further into this fascinating area. Sleep disorders are far more prevalent than we have thought in the past. Sleep occupies a third of the patient's life, yet it is often overlooked both when taking a history and when managing patients. Awareness is the key, and it is hoped that this chapter has stimulated such awareness.

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13 Pain

Pain is a totally subjective phenomenon. It is the product of a noxious stimulus, which evokes a response in the patient. That response is predicated by the patient's pain tolerance and psychological state at the time of stimulation. What represents debilitating pain for one patient may be largely ignored by another.

More recently, there has emerged the concept of 'neuropathic pain' with an inherent grading system that allows cross-referencing for research as well as clinical purposes.[1] The working definition of neuropathic pain is pain provoked by a lesion or disease affecting the somatosensory system. The problem with such a definition is that it could, for all practical purposes, encapsulate all pain syndromes thereby making it less than specific.

Some authors have tried to differentiate chronic pain from neuropathic pain, citing prevalence rates of 20–30% for the former and 5–7% for the latter.[2] Others just divide pain into acute and chronic with claim of distinctive characteristics for each, and different approaches to management (see Table 13.1).

Acute pain provides a warning signal that something is wrong and needs attention, while chronic pain no longer serves any useful function other than to remind the sufferer that they have an irreparable complaint, or the source of the pain remains obscure.

The approach to pain management is predicated by the background of the therapist, the likely source of the pain and the long-term prognosis for the underlying condition. The approach will be quite different for the patient with a terminal condition, compared to the patient in whom the long-term prognosis is excellent.

This chapter will examine the approach to pain management and provide useful tips to help the general practitioner cope with the patient in pain. As

TABLE 13.1 Differentiating acute and chronic pain

Characteristic	Acute pain	Chronic pain
Duration	≤ 2 weeks	> 3 months
Associated features	Tachypnoea Tachycardia Sympathetic autonomic release (fright/flight)	No sympathetic features Local reaction (e.g. swelling, skin changes)
Effects on quality of life	Little to none	Significant
Altered behaviour	Little to none	Significant
Management	Primarily pharmacological	Multidisciplinary team approach (beyond pharmacological)

with so many areas of medicine, and neurology in particular, there has been a concerted effort to classify various conditions to enhance international collaboration and consensus. This is equally true for pain[3] but application of these classifications contributes little to coalface general practice and will not be further reviewed in this chapter.

HISTORY

As stated elsewhere in this book, it is sometimes easier for a patient to present with a complaint of 'physical' pain rather than 'emotional' pain. This is particularly so for people in the armed forces, who may present with tension-type headache when in reality the problem is far more deep seated. For people for whom physical fitness is a prerequisite, it is often considered inappropriate, or even a career hurdle, to present with the complaint of psychological problems. It follows that people with pain, as evidenced by tension-type headaches, need to have psychological issues also explored when taking a history.

The fact that pain may provide the presenting complaint for psychological problems does not negate the fact that the pain is still felt. Pain is a very subjective phenomenon and may follow very specific patterns that go hand-in-glove with specific complaints. The symptom constellation will provide the diagnosis (see Table 13.2).

As with all neurology, there are certain questions that need to be asked: When did the pain start? Was there a provocative incident that caused the pain? Where is the pain? Are there precipitating or relieving factors? What is the nature of the pain? Are there associated features with the pain? What is the frequency and duration of the pain? A perfect example of how these questions provide diagnostic answers is found in Chapter 6 on headache. It is these questions that differentiate tension-type headache from migraine.

TABLE 13.2 Pain associated with specific diagnoses

Diagnosis	Classical symptoms
Trigeminal neuralgia (tic douloureux)	Sharp stabbing pain in the face (jabs of pain) Pain triggered by chewing, cleaning teeth, cold air Pain within the distribution of maxillary branch of CNV shooting from the jaw upwards
Glossopharyngeal neuralgia	Stabbing pain similar to trigeminal neuralgia Pain usually shoots into back of tongue Pain may shoot into ipsilateral ear
Temporomandibular (TM) joint dysfunction	Pain localised in face Pain may be in TM joint Pain provoked by chewing Aware of clicking in TM joint
Atypical facial pain	Pain in the face that does not fit other diagnoses of unilateral face pain
Post-herpetic neuralgia	History of herpes zoster infection Pain follows distribution of a cranial nerve or nerve root
Radicular pain	Pain corresponding to the distribution of a nerve root

Certain conditions, such as diabetes with peripheral neuropathy and diabetic amyotrophy, may provoke very severe pain symptoms. Pain is a particular feature of small fibre diabetic sensorimotor neuropathy. From the neurological perspective, pain in the head, neck, back and limbs may be of primary neurological origin. Pain in the thorax or abdomen is almost always a feature of a visceral disorder rather than primary neurological complaint, for instance, spinal or radicular pathology, thus dictating an alternative investigational paradigm to the diagnosis of thoraco or abdominal pain. There are some exceptions, such as herpes zoster infection with shingles (and post-herpetic pain) and diabetic radiculopathy, already identified.

Pain evokes its own set of jargon and possible confounding language, which may lead to confusion. Thankfully much of this jargon has not yet found its way into common daily language and so is largely ignored by patients (see Table 13.3).

This does not negate the need to be critical of the term ‘pain’ and to seek clarification as to what type, quality, nature and intrusion the pain causes. A dull ache is quite different to a lancinating, stabbing, throbbing pain. A ‘hot poker’ or ‘stabbing’ pain may be vastly different to ‘feeling as if my head was going to explode!’. Often the word ‘numb’ may enter the patient’s description, even of pain, and the word ‘numb’ demands clarification as it may mean different things to different people.

TABLE 13.3 Glossary of pain jargon

Term	Meaning
Allodynia	Pain perceived following non-noxious, innocuous stimulus (e.g. light touch causes burning pain)
Antalgia (antalgic)	Pain perception (noun), pain provoked action (adjective) (e.g. antalgic gait—altered gait due to the influence of pain)
Dysaesthesia	An altered perception of sensation with abnormal (often unpleasant) feeling associated with stimulation, such as touching over the affected area causes 'strange feeling'
Hypaesthesia / hypoaesthesia	Reduced perception of stimulus (both words are interchangeable)
	Decreased sensation
Hyperalgesia	Increased perception of pain
Hyperaesthesia	Increased perception of stimulus (need not be pain)
Hyperpathia	Decreased sensation to one or more modalities while concurrently having increased perception of pain (hyperalgia) or pain with innocuous stimulation (allodynia)
Hypoalgia	Reduced perception of pain
Paraesthesia	Abnormal sensations, such as 'pins and needles', tingling, pricking, reduced or even loss of sensation. It implies abnormality anywhere along the sensory pathway from peripheral nerve to sensory cortex—the epitome of 'neuropathic pain'

The concept of paraesthesia (see Table 13.3) may be short-lived with no real consequence (as in 'my foot went to sleep with pins and needles'). It may reflect altered blood supply to a target region. This produces neurological symptoms but should not dictate neurological consultation. A perfect example of this is the symptom attached to carpal tunnel syndrome with paresthesia in the fingers. This responds favourably to night splinting to obviate palmar–flexion of the wrist, which compromises blood supply to the median nerve (see Ch 11). Where paresthesia persists, it is a warning of abnormality somewhere within the sensory pathway and may dictate additional investigations, such as nerve conduction studies or sensory evoked potential studies and hence referral to a specialist.

To delve further into the understanding of pain, some specific pain complexes or syndromes will be explored.

REFLEX SYMPATHETIC DYSTROPHY OR COMPLEX REGIONAL PAIN SYNDROME

Reflex sympathetic dystrophy (RSD) or complex regional pain syndrome (CRPS) is a refractory pain syndrome in which the term RSD is being replaced with CRPS, as it is neither a true 'reflex' nor a 'dystrophy'. It is a type of limb pain characterised by: disproportional pain (both in character and distribution); allodynia (see Table 13.3); altered limb function (accompanied by antalgic movements); oedema; discolouration (often cyanotic); altered temperature; possible sweating; and maybe dystonia or spasms; or altered anatomy (with nail changes, hair loss, skin thinning or bone demineralisation).

Other terms often also included within the CRPS spectrum include: causalgia; post-traumatic pain syndrome; Sudeck's atrophy; reflex neurovascular dystrophy; post-traumatic spreading neuralgia, sympathalgia and shoulder–hand syndrome.[4] CRPS represents regional pain of uncertain pathophysiology, which usually affects the hand or foot but may also involve or spread to other parts of the body.

Mean age of onset is 35–45 years, with male to female ratio approximating 1 : 3. It can affect children with a 3 : 2 distribution of hand to foot involvement. It usually follows an injury—often a minor injury quite out of proportion to the symptoms. In up to 20% of cases the aetiology is idiopathic. It is a clinical diagnosis without implicit pain mechanism and the response to treatment is variable. It is a condition best referred to a consultant, who may investigate with: radiology to assess periarticular demineralisation; bone scan to show enhanced uptake in the affected limb; autonomic testing; and may consider sympathetic block, adrenergic block or maybe even steroids in the early stages of the disease. Additional approaches that may be adopted in general practice include use of tricyclic antidepressants, such as amitriptyline (Endep®) or imipramine (Tofranil®), starting at a dosage of 25 mg nocte and increasing up to ten times that dosage if needed. One can also consider use of antiepileptic medications, such as gabapentin (Neurontin®) starting at 100 mg t.d.s. and titrating to need or pregabalin (Lyrica®) starting at 75 mg b.d. and increasing as needed. It is important to appreciate that the use of gabapentin reflects use of the medication beyond that intended during development and is outside of the Pharmaceutical Benefits Scheme (PBS). Patients need a private prescription as gabapentin is only PBS listed for epilepsy. Pregabalin is not on the PBS. The approach to CRPS may also incorporate alternative remedies, such as a trial of acupuncture or even hypnosis. It is often a refractory form of pain complaint and usually will require specialist referral.

SPINAL PAIN

As with the classification of pain in general[3] there have also been attempts to classify spinal pain,[5] but again this has relevance to international collaboration and less application to the family physician.

What is of value is to determine where in the spine the pain is generated, the level and extent of injury. It helps to determine if the pain is of neurological (nerve) origin or musculoskeletal (bone and muscle derived). This will have direct implication on both choice of investigation and the consultant most appropriate should referral be required. In some cases, the rheumatologist may be preferred over the neurologist.

Some helpful tips for the general practitioner may include description of pain and its distribution, such as neck pain, which may be limited to the neck but have associated neurological signs, such as pain radiation specific to a given nerve root or complex. Such neurological pain includes: radicular pain with sciatica or specific finger involvement that does not respect either ulnar or median nerve distribution; muscle wasting or weakness referrable to a given nerve root; loss of deep tendon reflexes at the level of the damage and hyperreflexia below the spinal level (see Ch 4); or pain exacerbated by coughing, sneezing or straining.

From the perspective of the general practitioner the real issue with spinal pain, be it neck or lower back pain, the two most common sites, is whether to treat conservatively and offer symptomatic relief or to seek rapid referral to a specialist. Some findings will help. The nature of the pain, rather than the intensity, is important. If the pain is strictly localised without any referral, without exacerbation (either progression of symptoms or increase with coughing or straining) and devoid of associated symptoms, such as meningism, sphincter involvement or abnormal neurological signs, then the family physician can 'wait and see'. When in doubt, the involvement of a specialist may assist—rather than bypassing the consultant and ordering expensive investigations. CT scanning is relatively inexpensive and may offer considerable reassurance.

If simple analgesia or non-steroidal anti-inflammatory medications fail to provide relief, then tricyclic antidepressants often provide pain relief by generating muscle relaxation in addition to analgesia. They also provide anxiolysis and, within the context of chronic pain, the antidepressant enhances mood, sleep and a new approach to the pain by the patient. Similar doses as those suggested for CRPS apply.

One cannot ignore the need for a proper physical examination to determine the range of spinal movement, be it of the neck or the lower back. The patient is asked to touch their toes from the standing position; to slide down the lateral border of the leg with lateral flexion rather than bending forward; to sit on the couch with hands on knees and hips flexed to 90° while the doctor taps over the spine to identify localised discomfort; and to undergo straight leg raising (see Fig 13.1).

Straight leg raising is an alternative test for forward flexion in the AP plane (see Fig 13.1(i)) as is sitting on the bunk with hips at flexed at 90° (see Fig 13.1(iii)) while avoiding the tripod position. This can be administered in various guises, as shown in Figure 13.1(iv) and (v). This tests both the validity of the findings and their reliability, if producing the same results irrespective

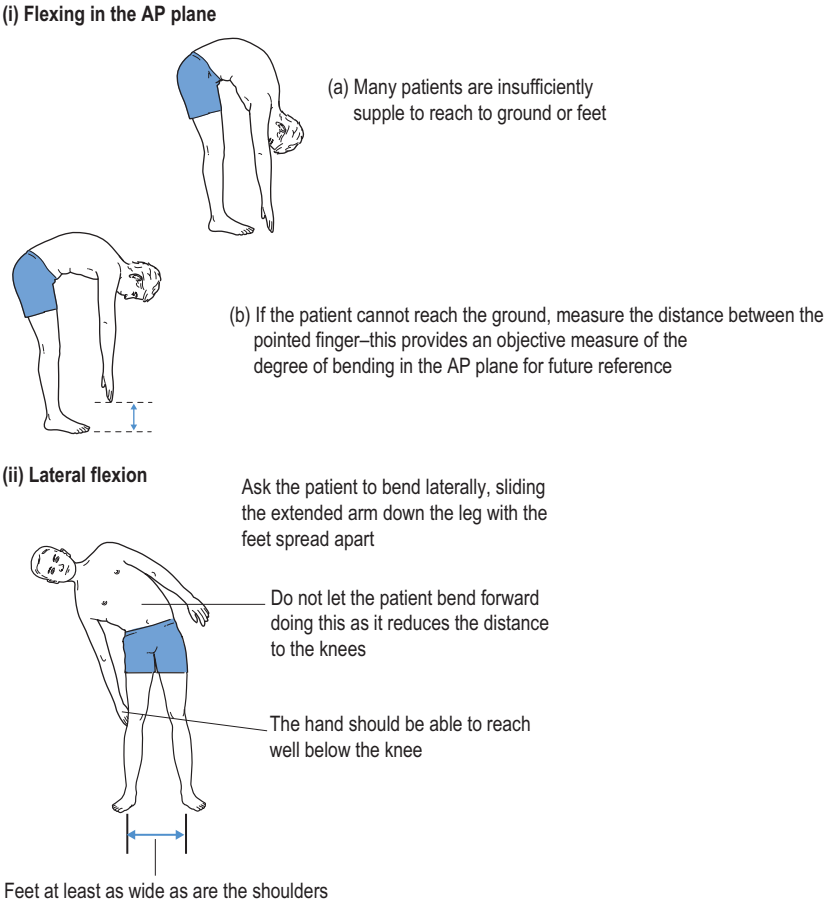


FIGURE 13.1 (i) Testing lower spinal movement—flexing in the AP plane. (ii) Testing lower spinal movement—lateral flexion.

of the method used. Where the results of various methods of testing the same modality are in conflict, it provides strong evidence of a non-organic basis for the complaint. This should alert the clinician to delve further into the psyche (see Ch 5). It may alert the doctor to question the real reason for presentation, which might be anything from a subconscious call for help to a claim for compensation.

Neck movement is tested in different planes: asking the patient to touch the ear on the ipsilateral shoulder; the chin on the shoulder (both sides); fully flex the neck in the AP plane to touch the anterior chest wall; and then to fully extend the neck. This should be objectively recorded and provides objective

(iii) Hip flexion

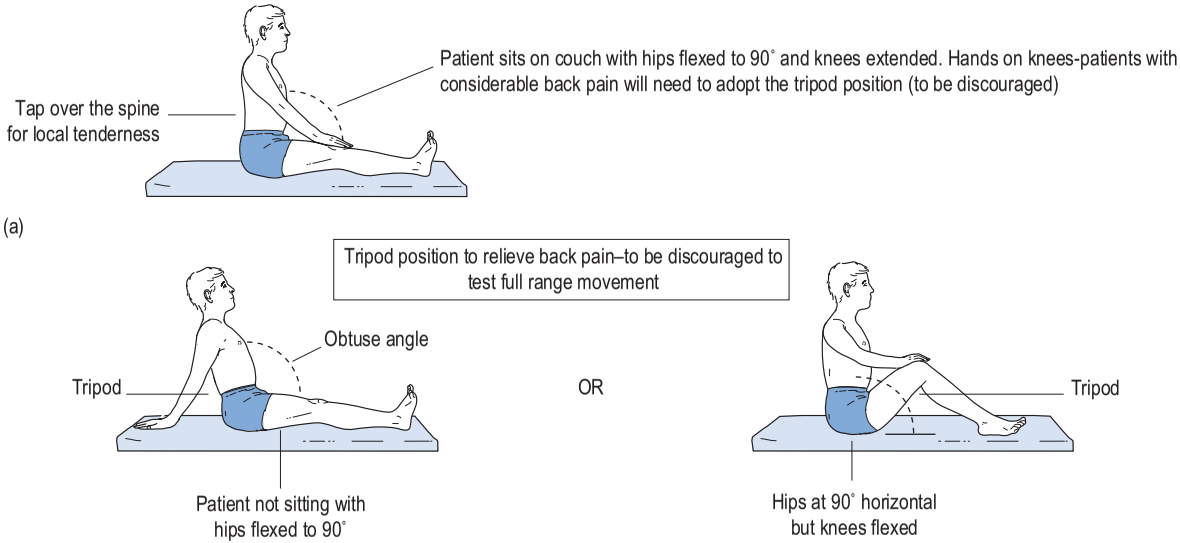


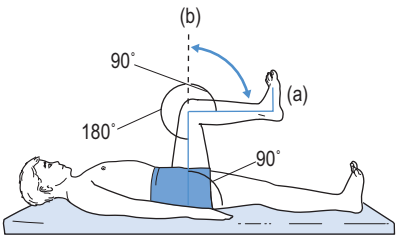
FIGURE 13.1, cont'd (iii) Testing lower spinal movement—hip flexion.

Continued

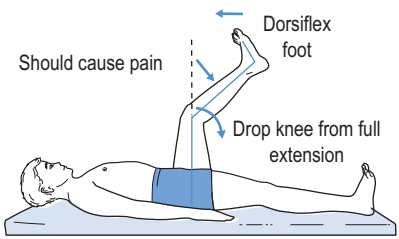
(iv) Straight leg raising

(a) First allow the knee to bend to bring the hip to 90˚
(b) Next extend knee to complete test
(c) If pain experienced in (b) flex knee slightly and then dorsiflex foot (achieves same as (b)

(a) and (b)



(c)



(v) Modified straight leg raising if in doubt

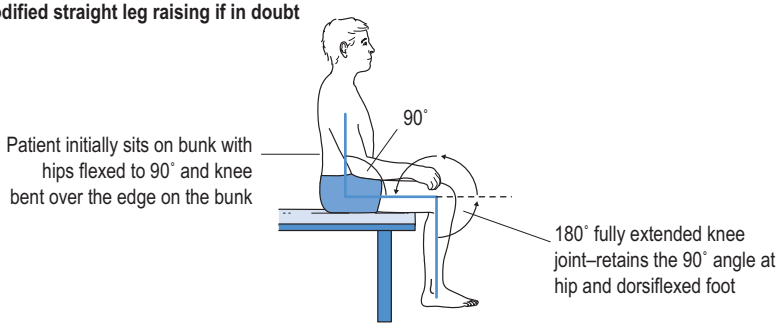


FIGURE 13.1, cont'd (iv) Testing lower spinal movement—straight leg raising. (v) Testing lower spinal movement—modified straight leg raising if in doubt.

evidence of range of neck mobility, which may give an important clue to the origin of the pain.

The examination of the spine, re pain, is not complete without a full peripheral neurological examination (see Ch 4). Completely normal upper limb examination (or even features of lower motor neurone deficit) in the upper limb, with upper motor neurone signs in the lower limb (see Ch 4) localises the lesion to either below, or at, the cervical level and above the lumbar spine. Lower motor neurone features in the lower limb also localise the damage to the lumbar spine.

If the pain does not respond to simple analgesia or even tricyclic antidepressants, then referral to a consultant is warranted. It is not advisable for the general practitioner to initiate narcotics as these are addictive and, if the pain is sufficient to require this level of intervention, further opinion is warranted to ensure a serious condition has not been overlooked. CT scanning should be considered before referral but the role of other testing, such as MRI or neurophysiological testing, remains the domain of the consultant.

TRIGEMINAL NEURALGIA

Trigeminal neuralgia[6] (tic douloureux) produces paroxysmal jabbing, unilateral facial pain provoked by innocuous stimuli, such as chewing, brushing teeth, touching the face or a gust of wind on the face. Often the cause is unknown but it may accompany multiple sclerosis, the compressive effect of a tumour or even infection, such as chronic meningitis. Current theory favours pain consequent to an aberrant blood vessel stimulating the branch of the trigeminal nerve within the skull, but this is rarely confirmed on imaging.

Generally the neurological examination of the patient with trigeminal neuralgia is normal, but if there is loss of sensation within the distribution of the nerve then cerebral imaging with MRI and MRA is warranted. Similarly, bilateral symptoms clearly justify imaging. Some would routinely image all patients, but the costs involved raise doubt about its effectiveness.

Treatment is usually provided by anti-epileptic medications (AEM), such as carbamazepine (CBZ), which remains the first-line remedy. Other AEM, such as valproate, oxcarbazepine, gabapentin, pregabalin or even lamotrigine or levetiracetam, may be considered but these are off-license uses and should entail specialist consultation. Similarly, antispasmodics, such as baclofen; tricyclic antidepressants, such as amitriptyline or imipramine; or anti-arrhythmic agents, such as mexitil, may be considered. If the patient has not responded to Tegretol CR® 400 mg 1 b.d. then the general practitioner would be wise to call for help.

The role of microvascular decompression, gamma knife surgery or ablative procedures directed at the trigeminal nerve root are definitely beyond the role of the family physician and will not be further discussed.

TEMPOROMANDIBULAR JOINT DYSFUNCTION

This is known as TM joint dysfunction[7] and includes nocturnal bruxism (so called ‘fang grinders’), TM joint malocclusion, and what some refer to as myofacial syndrome. This must be differentiated from ‘claudication of the jaw’, which may occur in the elderly with temporal arteritis.

Diagnosis depends on a high index of suspicion, and can often be enhanced by palpating over the jaw while asking the patient to perform a mimicry of chewing with large bites. During this procedure, crepitus of the TM joint may be palpated as the cartilage clicks in and out of place. This is best managed by the dentist providing a ‘bite plate’, which is specifically moulded to suit the individual patient and worn overnight.

This approach often obviates the need to involve a neurologist, who would likely follow the same approach as first-line therapy by advocating referral to a dentist. The role of the specialist emerges if this does not provide the answer, raising concerns about the diagnosis. One differential diagnosis is glossopharyngeal neuralgia, which produces a pain not dissimilar to a combination of trigeminal neuralgia and TM joint dysfunction, but often includes a lancinating pain shooting through the ipsilateral ear. Its treatment largely

mirrors that of trigeminal neuralgia but the fun, that is medicine, is the academic satisfaction of making the correct diagnosis even if it does not change treatment, especially if it also does not cause further inconvenience or cost.

ATYPICAL FACIAL PAIN

This is the final common pathway when the above differential diagnoses for pain in the face have failed to define a suitable diagnosis. When encountering this dilemma the general practitioner should involve a consultant as it is imperative to exclude occult lesions. This form of pain is often refractory to commonly used remedies and the involvement of a specialist is, of itself, often therapeutic.

POST-HERPETIC NEURALGIA

Shingles is the reactivation of herpes varicella zoster viral infection (chickenpox), which has lain dormant in the nerve root. It results in an irritating painful blistering infection that follows the anatomic path of the nerve root or cranial nerve (the dermatome). The pain generated can be severe and debilitating, but may be obviated by adding steroids to the antiviral treatment when the eruption first occurs.

Post-herpetic neuralgia has been treated with a number of approaches[8] but the principle to management remains the same. The pain needs to fit the accepted pattern: lasting in excess of three months from the bout of shingles; occurring in the route of the dermatome; possible decreased sensation within the distribution of the dermatome; and hyperaesthesia (see Table 13.3) at the transitional borders of the dermatome. The pain may be both deep and superficial with super-added tic-like lancinating pain.

First-line treatment may include application of topical remedies, such as capsaicin ointment, as a counter irritant, or even a xylocaine ointment or cream. This may be complemented with either tricyclic antidepressants (amitriptyline or imipramine) or AEM, such as CBZ, starting with a dosage of 400 mg of the controlled-release formulation b.d. and increasing the dose to mirror the therapeutic levels accepted for epilepsy treatment (see Ch 7). If first-line treatment fails, it may be worth considering a course of steroids, tapering from 75 mg prednisolone per day to nothing over a two-week period. Off-license use of some of the previously cited agents (see trigeminal neuralgia above) may be of help but would justify referral to a consultant.

CONCLUSION

Pain is a massive topic to cover in such a brief overview. It reflects the idiosyncratic nature of the individual patient, and the approach to treatment is as variable as the background of the patient and the doctor. This review has not even touched on cultural and educational influences that may impact on the

management of pain, or the use of traditional remedies, such as acupuncture or herbal treatments, which may have a place but are outside the scope of this book. Hypnosis may be an effective tool, and personal experience has taught that it is very effective when undergoing dental treatment or managing refractory head pain. If using hypnosis, it is imperative to include a protective post-hypnotic suggestion that if pain is providing a protective warning then the patient will still appreciate that warning, even if the severity of the pain is alleviated.

The principal message is that if pain does not respond to simple intervention with analgesics or non-steroidal agents, then it justifies further investigation and possible involvement of a consultant. Where the root cause for the pain is obscure, the involvement of a consultant may be warranted but **the family doctor may be the best placed to recognise non-organic causes for pain**. There may be unequivocal signs of non-organic disease (see Ch 5), which should not be overlooked because early intervention enhances prognosis. Pain is a common cause for depression and behaviour problems that may cause altered domestic dynamics, which impact negatively on quality of life. The general practitioner is by far the best placed to recognise these issues and to deal with them. As has been repeatedly stated in this book, **the best management of pain syndromes is achieved by a close working relationship between general practitioner and consultant**. Where this has proven ineffective in pain management, it may be time to involve a multidisciplinary team,[9] be that within a rehabilitative framework or a recognised pain clinic. **Pain is so intrusive that it is sometimes better to call for help early, rather than to allow the establishment of entrenched pain-provoked behaviour.**

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14

Stroke

INTRODUCTION

All too often a patient presents to hospital saying 'I thought I was having a stroke but wanted to wait to see what happened'. If not the patient, then the relative or spouse says something similar. This wouldn't happen with a suspected 'heart attack'!

It is sobering to acknowledge that one can replace a heart, or part of a heart, but it is still impossible to replace the 'motherboard' in the brain. The heart is basically a pump for which one can even offer a mechanical substitute. Conversely, the brain is a super computer that is still not fully understood. It is time to replace the nihilism and think in terms of 'brain attack', in much the same way one thinks of 'heart attack'. To do this underlines the most important message for either heart or brain, namely, 'Time is of the essence!' The catchcry for people dealing with stroke is 'Time is brain'.

What follows is an overview of stroke that offers a clinician's perspective of management. No message is more important than the need for early presentation. The previously accepted three-hour time window has been expanded to four-and-a-half hours in which to safely offer intravenous tissue-type plasminogen activator (tPA),[1] but sooner is still better.

ATHEROSCLEROSIS

'Brain attacks' and 'heart attacks' have a common pathophysiology. An embolus of thrombus dislodges from the surface of an atherosclerotic plaque and becomes lodged downstream to occlude blood flow and hence nutrition distal to the blockage. This accounts for ischaemic strokes, comprising 85% of all strokes (only 15% have haemorrhagic aetiology).[2]

Atherosclerosis increases with age, hypertension, hyperlipidemia, diabetes and cigarette smoking.[2] It follows that medical management must address these factors. The thrombus that is dislodged from the plaque was formed consequent to prothrombotic effects involving tissue factor. Activated factor VII with platelet recruitment results in formation of platelet-rich fibrin thrombus, which embolised. Thus antiplatelet agents are important in preventing thrombotic emboli and hence strokes.

CARDIAC CAUSES

One of the most common cardiac causes of strokes is atrial fibrillation (AF). It also occurs with rheumatic heart disease, increasing age, hypertension, ischaemia and thyroid disease. AF occurs in approximately 1% of those under 60 years and about 6% in those over 80 years, and the population is ageing.

While there has been an attempt to classify AF into acute and chronic,[3] this concept has less relevance to the neurologist/stroke-ologist, whose most important take-home-message concerning AF is the need to prevent emboli. Hence, one must recognise the need for anticoagulation. The actual treatment of AF is supervised by the cardiologist, but anticoagulation with Coumadin® is a high priority for stroke prevention. More recently a new class of anticoagulation drug has emerged.[4] It is still too early to be certain about the place of dabigatran, but it appears destined to replace Coumadin® as the drug of choice for patients with AF. This remains a question for consultants until there is wider experience.

There are other cardiac causes of emboli, such as micotic emboli, with growths particularly on rheumatic valves. Unless this is appreciated with an index of suspicion for bacterial endocarditis, it may be overlooked. Mercifully this is rare but echocardiography is mandatory in the stroke evaluation. Transoesophageal echocardiogram is preferable, especially in the young stroke patient. Another cause detected by echocardiogram is patent foramen ovale (PFO), which may be under-diagnosed in stroke patients. One study reported in excess of 15% in over 55-year-old cryptogenic stroke patients having PFO with atrial septal aneurysm.[5] The question of closure of PFOs in stroke patients or those with transient ischaemic attacks (TIAs) is a topic of some debate, which is not yet fully resolved. Evidence suggests an association of PFO with hypercoagulation, especially factor V leiden and prothrombin G20210A genetic mutations.[6] Often hypercoagulable states travel together to evoke symptoms, such as dehydration or antiphospholipid antibodies in association with prothrombin G20210A mutations. The take-home-message is that the stroke patient deserves a detailed assessment of their hypercoagulable profile. This should have been done while in hospital, but the general practitioner can check to make sure.

Cardiac consideration is not restricted to stroke prevention but also offers a window to predict post-stroke mortality. Conventional heart rate variability measures were not of prognostic value, but abnormal long-term heart rate

dynamics do predict post-stroke mortality. They may have value in risk stratification in stroke.[7]

CAROTID ARTERY DISEASE

Carotid vessels are a major alternative source of emboli, but management of carotid disease relies on antiplatelet agents rather than full anticoagulation (if surgery is not warranted).

The **N**orth **A**merican **S**ymptomatic **C**arotid **E**ndarterectomy **T**rial (NASCET)[8] found that stroke was reduced by 17% where carotid stenosis exceeded 70%, hence becoming the benchmark for ordering endarterectomy. Some advocate surgical intervention with stenosis as low as 60%, even in asymptomatic patients.[9] Personal preference favours the higher figure.

Stenting is a viable alternative for cardiac vasculopathy and is becoming a respected alternative to carotid endarterectomy.[10] Its exact place remains undefined with growing popularity. Furlan[11] reviewed the SAPHIRE (**S**tenting and **A**ngioplasty with Protection in **P**atients at **H**igh **R**isk for **E**ndarterectomy) trial, which showed that carotid artery stenting was safer than carotid endarterectomy in patients at high surgical risk, because of lower risk of myocardial infarction within 30 days after carotid stenting when compared to surgery. Furlan[11] reviewed the EVA-35 Study (**E**ndarterectomy **v**ersus **A**ngioplasty in patients with Symptomatic Severe Carotid Stenosis in the same issue of *The New England Journal of Medicine*), which concluded that stenting was more risky than endarterectomy for 30-day incidence of stroke or death. Carotid endarterectomy is also considered a safer option than is stenting in the elderly.[12]

This underpins the need to investigate for carotid stenosis with tools such as duplex Doppler, CTA or MRA or a combination thereof to decide upon appropriate intervention. The general practitioner may initiate both Doppler studies and CTA—and may bypass the neurologist by referring to the vascular surgeon—although most often will rely on a team, including both neurologist and surgeon.

HYPERLIPIDEMIA

The meta-analysis of 90 000 patients from studies assessing the benefits of statins in stroke prevention demonstrated that the reduced risk of stroke was particularly reflected in the lowering of low-density lipoprotein cholesterol levels.[13] Statins have become a basic component of stroke management.

The recent SPARCL (**S**troke **P**revention by **A**ggressive **R**eduction in **C**holesterol **L**evels) trial of 4731 stroke or TIA patients concluded that 80 mg of atorvastatin per day reduced the overall incidence of stroke and cardiovascular events. It was associated with an increased incidence of haemorrhagic stroke.[14] Personal preference favours starting with a lower dosage of statin and titrating to effect by monitoring cholesterol profile.

TABLE 14.1 ABCD^2 scores

Characteristic	Points
A—Age ≥ 60 years	1
B—Blood pressure > 140/90 mmHg at presentation	1
C—Clinical features: • unilateral • speech impairment without weakness	 2 1
D—Duration: • > 60 minutes • 10–59 minutes	 2 1
D—Diabetes	1
2 × Day stroke risk: • low score (< 4) = 1.0% • moderate score (4–5) = 4.1% • high score (6–7) = 8.1%	

TRANSIENT ISCHAEMIC ATTACKS (TIAs)

Perhaps the best way to consider TIAs is to equate them with mini strokes that resolve within a day. There is an even more worrying attitude to TIAs than there is to stroke. Because it has resolved by day's end and very often much sooner, the attitude to TIA is complacent. A recent study confirmed that hospital admissions of TIA patients to a specialised stroke unit has beneficial effect on short-term outcome,[15] and is preferable to home management and nihilism. Reliance on the ABCD^2 score does not necessarily increase protection by the theoretical admission of TIAs at greater risk[16,17] (see Table 14.1).

This reinforces that stroke and TIA should not be taken lightly—they demand referral to a hospital as a matter of urgency. TIA is a warning of an impending more significant 'brain attack' and should be treated with respect. TIA mimics, including syncope, seizure, migraine, vertigo and its causes, encephalopathy of non-vascular origin, multiple sclerosis or even transient global amnesia, may confound the picture. It remains far safer, where doubt exists, to have these assessed in hospital rather than expose the patient to risk of stroke. Many of the mimics are themselves worthy of admission, and there should be no shame in referring them to hospital for assessment.[18]

DIAGNOSIS OF STROKE

Correct diagnosis pre-empts appropriate treatment and, while an established stroke is easily diagnosed, the section on TIA highlights the scope of differential diagnoses. The pathophysiology and anatomical site defines the stroke's expression, be it motor or sensory deficit, loss of eloquent functions of speech,

TABLE 14.2 'Sudden Symptoms' and 'FAST' mnemonic for stroke detection

Sudden symptoms	FAST
Stroke patients may have sudden onset of: • weakness or numbness on one side • difficulty speaking or understanding • trouble seeing in one or both eyes • 'dizziness' or difficulty walking • severe headache of unknown cause	Ask patients to: • smile, • raise both arms and • repeat phrase
	F = Face—uneven movement
	A = Arm—one side drifts
	S = Speech—sounds strange
	T = Time—go to hospital ASAP

number manipulation, comprehension, orientation, consciousness or more subtle effects determined by smaller lesions.

The mnemonic 'FAST' remains a valuable tool for the general practitioner (see Table 14.2) and may be the start of the diagnostic approaches. The **C**incinnati **P**re-hospital **S**troke **S**cale (CPSS) was developed to help recognise strokes. It has since been modified to produce the 'Sudden Symptoms' and 'FAST' mnemonic to assist with early stroke recognition (see Table 14.2). Kleindorder et al[19] found that 'Suddens' would fail to detect 0.1% of strokes and 'FAST' would miss 11.1%.

One cannot over emphasise the need for early intervention should tPA for thrombolysis be appropriate. Rapid referral to a hospital capable of providing such intervention is mandatory. Before tPA can be given, within the critical four-and-a-half hour window, there must be cerebral imaging to exclude intracerebral haemorrhage, as haemorrhage and tPA are incompatible. Use of tPA is becoming more widely available and it may assist the general practitioner to understand some of the inclusion or exclusion criteria for its use (see Table 14.3). Early referral is enhanced by appreciating the process necessary to be completed by administration of tPA. Intra-arterial thrombolysis is also a valid form of intervention but it is only available in hospitals with access to interventional radiology, which restricts it to tertiary referral hospitals. This too is important for the family doctor to appreciate, as it may determine which in a selection of hospitals should be the preferred place of referral. The availability of a stroke unit is also an important deciding factor as over the last fifteen years they have been shown to improve prognosis.[20]

LIFESTYLE ISSUES

Family physicians play an absolutely fundamental and pivotal role in stroke management. As has already been demonstrated, stroke and lifestyle issues are inseparable. Risk factors, such as hypertension, AF, hyperlipidemia, diabetes, cigarette smoking, excessive consumption of alcohol, dieting

TABLE 14.3 Criteria for use of tPA for acute stroke

Inclusion	Exclusion
Ischaemic stroke causing definable neurological deficit	Resolution or clearing or improving of neurological deficits
CT imaging excluding haemorrhage	CT evidence of widespread or large infarction (e.g. hypodensity > ⅓ cerebral hemisphere)
Presentation and CT imaging available within 4.5 hours	INR > 1.7
Informed consent	Given heparin in previous 48 hours with prolonged PTT
	Platelets < 100 E9/L
	Hypertension: • systolic > 185 mmHg • diastolic > 110 mmHg or needing aggressive BP intervention
	Previous stroke or head injury within 3 months
	Major surgery within 2 weeks
	Symptoms suggestive of subarachnoid haemorrhage
	GI or UT bleed within 3 weeks

TABLE 14.4 Risk factors for stroke

Non-modifiable	Modifiable
Age	Prior stroke or TIA resulting in secondary stroke prevention—compliance
Gender	Hypertension
Race or ethnicity	Diabetes
Family history	Hyperlipidaemia
	Atrial fibrillation (AF)
	Homocysteinaemia
	Carotid stenosis
	Smoking
	Excess alcohol
	Obesity
	Lack of exercise

indiscretions, past history of stroke or vasculopathy, lack of exercise and overall disrespect of personal health, plus non-compliance with existing advice to curtail these activities and to take medications, are just as important as sophisticated intra-hospital intervention (see Table 14.4).

Addressing these lifestyle issues has far greater potential to reduce stroke rate than does anything that can be added by consultants. Failure to respect these factors renders most of the other forms of intervention suboptimal. One cannot over emphasise these when evaluating stroke treatment. Proper attention to them could obviate the need for more aggressive therapies.

PATIENT ASSESSMENT

Once the patient arrives in hospital, the initial assessment must determine that ever-important timeframe. Should a patient wake from sleep with stroke symptoms or signs then it is impossible to determine the timeframe during sleep, and IV tPA thrombolysis is usually contraindicated. Some advocate taking the midpoint of sleep duration as the commencement of the 'ticking clock', but this seems unsatisfactory.

Should the timeframe permit, non-contrast enhanced CT will allow exclusion of intracerebral bleed. Should this show a very large stroke then risk of haemorrhagic transformation also causes exclusion (see Table 14.3).

Depending on the patient's age and circumstances, blood samples should be taken for thrombophilic screening, including: ANA; ENA; cardiolipin antibodies; homocysteine; AdsDNA; lupus inhibitor; B_{12}, folate; ESR; CRP; full blood count; biochemical screen; blood sugar level (and if indicated HbA1c); T3, T4 and TSH; ACE; antithrombin III; factor V leiden; protein C and S; infective causes (such as serology for syphilis and HIV); and possibly even the prothrombin G20210A mutation.

Magnetic resonance imaging (MRI) with MRA (angiogram) of brain provides extra information, especially diffusion-weighted sequences, which differentiate newly acquired infarcts from longer established lesions. Inconsistency between perfusion and diffusion imaging (be it via CT or MR) defines the penumbra (the tissue not yet necrotic from the stroke), which surrounds the non-recoverable tissue. This indicates the potential benefit from throbolysis. This is clearly the domain of the specialist.

Carotid duplex Doppler and cardiac echocardiogram have already been discussed as important tools to discern the source of cerebral emboli.

MEDICAL TREATMENT OF STROKE

a Antiplatelet agents

There have been a multitude of trials designed to ascertain which antiplatelet agent or combination of agents is superior. Each has had the mandatory anagram such as: ESPS 1 and 2—**E**uropean **S**troke **P**revention **S**tudy

(*J Neurol Sci* 1996, 143:1–13); CAPRIE— **C**lopidogrel v **A**spirin in **P**atients at **R**isk of **I**schaemic **E**vents (*Lancet* 1996; 348:1329–1339); CURE—**C**lopidogrel in **U**nstable Angina to Prevent **R**ecurrent **E**pisodes (*N Engl J Med* 2001, 345:494–502); MATCH—**M**anagement of **A**thero-**T**hrombosis with **C**lopidogrel in **H**igh-risk Patients (*Lancet* 2004, 364:331–337); CHARISMA—**C**lopidogrel for **H**igh **A**therothrombotic **R**isk and **I**schaemic **S**tabilisation, **M**anagement and **A**voidance (*N Engl J Med* 2006, 354:1706–1717) or ESPRIT—**E**uropean/Australasian **S**troke **P**revention in **R**eversible **I**schaemia **T**rial (*Lancet* 2006, 367:1665–1673).

The number of therapeutic trials regarding antiplatelet agents has expanded exponentially: ROCKET—**R**oxifiban **O**ral **C**ompound **K**inetics **E**valuation **T**rial 1 (ROCKET—1 Platelet Substudy) Effect of roxifiban on platelet aggregation (*Am Heart J* 2003, 146:91–98); PRoFESS—**P**revention **R**egimen f**o**r **E**ffectively Avoiding **S**econdary **S**trokes: aspirin plus extended release dipyridamole versus clopidogrel and telmisartan (*Lancet Neurol* 2008, 7(10):875—884); ATHENA–A Placebo-controlled, Double-blind, Parallel-arm Trial to **A**ssess **th**e **E**fficacy of Dronedarone 400 mg BID for the Prevention of Cardiovascular Hospitalisation or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter: the inefficacy of dronedarone in AF (*Circulation* 2009, 120:1174–1180); ARISTOTLE—**A**pixaban for **R**eduction **I**n **St**roke and **O**ther **T**hromboemb**L**ic **E**vents in Atrial Fibrillation: efficacy of apixaban in AF (*Am Heart J* 2010, 159:331–339); and AVERROES—**A**pixaban **Ver**sus acetylsalicylic acid to prevent st**RO**ke in atrial fibrillation patients who have failed or are unsuitable for vitamin K antagonist treatment: efficacy of apixaban versus aspirin in AF (*Am Heart J* 2010, 159:348–353).

These suggest extended release dipyridamole in combination with aspirin (Asasantin® SR 200/25 1 b.d.) is the antiplatelet agent of choice for stroke prevention. The combination of aspirin and clopidogrel has an increased risk of intracerebral bleeds, but is favoured by cardiologists for cardiovascular disease and peripheral vascular disease. Aspirin is more effective than clopidogrel alone in stroke prevention, but clopidogrel alone is favoured for patients who are aspirin intolerant.

As already stated, Coumadin® is preferred when the emboli are of cardiac origin, at least until we fully appreciate the exact position of dabigatran[4] in our treatment algorithm.

b Statins

Statins, such as pravastatin[21] and atorvastatin,[22,23] have long been advocated to reduce strokes. As already discussed, doses of 80 mg of atorvastatin may be advocated[14] but personal preference is to start low at 10–20 mg nocte and titrate to LDL level. Statins also help stabilise vessel wall integrity, so enhancing stroke prevention. They have proven to be safe and effective agents in stroke prevention.[24]

c Antihypertensives

The HOPE (**H**eart **O**utcome **P**revention **E**valuation) study was designed to look at antihypertensives in management of cardiovascular disease using ramipril.[25] It was followed by closer examination of use of ramipril in stroke prevention.[26] The combined studies entrenched the use of angiotensin converting enzyme inhibitors (ACE inhibitors), particularly ramipril (building up to 10 mg per day), in stroke management. Use of ACE inhibitors was further reinforced with PROGRESS (**P**erindopril **Pro**tection A**g**ainst **Re**current **S**troke **S**tudy), which showed that perindopril was also effective in stroke prevention.[27]

Following the recognition of the benefits of ACE inhibitors in stroke management, use of angiotensin II receptor blockade was also explored[28] and hypertension management has become fundamental for stroke.[29] While various pharmaceutical companies espouse the virtue of their particular antihypertensive agent, the most important take-home-message is to tackle hypertension as a major focus in stroke prevention.

d Other medications

While antiplatelet agents, statins and antihypertensives are the cornerstone of stroke therapy, there has been a move to consider other neuro-protective agents. One of these agents has been the use of the semi-synthetic second-generation derivative of the tetracycline, minocycline. There is evidence suggesting better outcomes when treating acute stroke with minocycline rather than placebo.[30]

CONCLUSION

By far the most important message is to accept that 'brain attack' is a medical emergency. If intravenous thrombolysis is to be considered then there is only a four-and-a-half hour window. Arterial thrombolysis, only briefly acknowledged in this review, allows a longer timeframe but should not suggest delayed referral to hospital.

The foundation of medical treatment is antiplatelet agents (except for cardiac-origin emboli where Coumadin® or maybe dabigatran is warranted), a statin and most importantly appropriate control of hypertension. These are usually started while the patient is in hospital but compliance remains the domain of general practitioner supervision throughout.

The general practitioner has a major role in stroke prevention by supervising lifestyle issues, ensuring the patient stops smoking, eats properly, avoids excess alcohol and where indicated treats contributing conditions, such as diabetes, with the respect necessary to regain health. The general practitioner is also an important partner in the patient's rehabilitation and secondary stroke prevention.

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15 Dementia

INTRODUCTION

Dementia represents a decline in cognitive function not because of impaired level of consciousness. In other words, it reflects a lower level of mental capacity and function than had been the case for a given individual. It demonstrates a process in which intellectual level has deteriorated despite retaining consciousness, thus excluding the confounding variable of delirium. The DSM IV-R diagnosis of dementia includes memory impairment and abnormalities in at least one of the following domains: language; judgment; abstract thinking; performance of tasks; constructional capabilities; or visual recognition.[1]

What this dictates is a need to document impairment and decline of cognition, namely mental functioning, while concurrently excluding delirium. Delirium may occur consequent to a confusional state associated with interrupted vigilance, incapacity for maintenance of retained thought process, and impaired goal-directed activities.[2] Thus delirium may co-exist as a confounding factor and needs to be excluded when diagnosing dementia. Delirium may accompany a host of medical diagnoses as produced by metabolic derangement, exposure to toxins, drug effects (either licit or illicit), infections (either systemic with septicaemia or affecting the central nervous system (CNS) directly), head trauma or peri-ictal epileptic states. It follows that diagnosis of dementia should not be confounded by these concomitant illnesses, although the presence of these conditions, in the absence of any associated delirium, would not exclude dementia.[3] Cerebral pathology, resulting in dysphasia or psychiatric disorders, such as depression, also needs to be excluded. This may evoke a picture similar to dementia, resulting in pseudo-dementia.

For a diagnosis of dementia to be considered, the deficit must be of sufficient magnitude to interfere with activities of daily living, work function or

other social activities. The diagnosis of dementia does not of itself necessarily imply a specific underlying pathology. Nor does it universally suggest a progressive cause or irreversibility. The diagnosis cannot be applied unless there has been adequate assessment of mental status in the absence of confounding variables, as already defined.

As the population ages and the normal degenerative process continues to affect the population, so too the impact of dementia increases within the community. The incidence or prevalence of dementia, particularly Alzheimer's disease, increases exponentially with age—effectively doubling with each half decade[4] after the age of 60 years. It is said that Alzheimer's disease, the most common form of dementia, has an incidence of 1% per annum for those over 65 years of age with a prevalence of approximately 50% in those 85 years and older. It follows that general practitioners will be confronted with dementia in growing proportions and will need to appreciate how to best manage affected patients.[5]

This chapter will serve to assist in this process by providing a broad overview of dementia. It recognises that dementia is a final common pathway of a number of neurological conditions, which results in declining cognition without necessarily influencing level of consciousness. The general practitioner is usually the first to be consulted about evolving dementia and may be 'too close' to the patient to recognise the telltale signs.

HISTORY

The general practitioner is ideally placed to identify those individuals in whom dementia should be sought (see Box 15.1). They are the best positioned to identify changes in a patient, such as: the well dressed patient who no longer takes pride in their appearance; the patient who no longer attends to personal hygiene; the patient failing to keep routine appointments; or not requesting repeat routine prescriptions for previously stable treatment regimes. These factors should alert the general practitioner, as should repeated minor driving accidents, loss of employment or difficulty coping without an alternative cause.

Despite suggestion that general practitioners are perfectly placed to provide the initial diagnosis based on warning signs, less than 40% regularly screen for dementia.[6] Often the diagnosis is not initiated by either the doctor or patient but by a concerned family member or close friend who has observed the change in the patient. The patient may present complaining of symptoms of dementia and yet still function so well on official higher centre function tests (see Ch 2), that their complaint is dismissed. Personal experience has taught that ignoring such complaints may be at the patient's peril. An intelligent patient may be acutely aware of impaired functioning and identify this to the doctor. The doctor may not be able to confirm damage because the patient was well above the norm before noting the decline. The patient may still be above the norm, even allowing for the real decline that has occurred.

BOX 15.1 Warning signs for dementia

- Cognitive and memory decline
- Questions of competence (e.g. handling shopping, money)
- Depressed or anxious patients with cognitive complaints
- Patients appearing unable to function (without other diagnoses)
- Lack of respect for personal hygiene or appearance
- Difficulty playing games of skill
- Difficulty completing forms for business or travel
- Becoming disoriented when looking for addresses
- Difficulty keeping up-to-date with previously favoured topics (e.g. sports, politics, recreational activities)
- Difficulty with routine chores, e.g. preparing a meal
- Misplacing articles, e.g. keys, papers, mail
- Having repeated minor motor vehicle accidents
- Forgetting important dates: anniversaries or birthdays
- Not paying accounts and bills on time
- Forgetting names of people or places

Personal experience has taught that such a patient deserves a trial of therapy if reporting impaired cognition, in the absence of confounding factors discussed in this chapter. If they report improvement sufficient to justify the patient paying for medication at their own expense, then that is a reasonable option. 'Willingness to pay' is an accepted health economic measure, which has relevance within this context. The patient, at this level of functioning, retains the wherewithal to take responsibility for their wellbeing. This type of patient is also able to assess if performance has improved. This approach imposes no cost on society and may allow a patient to remain at an acceptable level of independence for longer.

What is important, especially for the general practitioner who is the family physician, is to explore questions of estate planning, organisation of personal affairs, both with respect to the patient as well as possibly other family members, and to discuss issues such as: advanced directives; enduring power of attorney; expression of wishes if in a vegetative state; and disposal of assets. This will ensure that the patient can make personal decisions while still competent to do so. While treatment of dementia is designed to delay progression of disease, it does not arrest it, so it is imperative that suspicion of dementia be accompanied by discussion of personal planning for the future. This is a necessary part of history taking and no doctor is better positioned to understand both the patient's needs and the family dynamics than the general practitioner.

Where there is doubt about the diagnosis of dementia, it is appropriate to seek the patient's permission to also interview family and possibly close

friends. Such people may be able to report on domestic circumstances, such as neglected cleanliness at home, failure to shop alone or incapacity in activities of daily living—all of which suggest advanced disease. They may also offer more subtle clues, like the attentive spouse who forgot a birthday or wedding anniversary for the first time; the loving grandparent who simply forgot the grandchild's birthday; or the bridge partner who could no longer be relied upon to make the right bid or play properly.

As already stated, it is dangerous to ignore such clues because there comes a time, especially in rapidly advancing disease, when the patient passes the point of competence sufficient to be allowed to make personal decisions into the future. After this point, all future decisions may require the involvement of a guardianship board or similar protective authority. Once this point has arrived the dysfunctional family may use the patient to settle family scores, protect personal wealth at a cost to the patient, and deny the patient the right to personally direct any wishes or wants.

EXAMINATION

The critical examination of the patient with suspected dementia is the testing of higher centre function (see Ch 2). To be able to prescribe pharmacological treatments in Australia requires testing with the Mini Mental State Examination (MMSE), a tool that has been available for many years.[7]

Unlike the approach set out in Chapter 2, the MMSE is not used to assess the site of lesion but rather to give an overview of the degree of impairment. The maximal score is 30 and hence a score of 20+ is deemed 'minimal' or 'mild impairment', a score of 15–19 is classed as 'moderate', and less than 14 is considered 'severe'. The problem with this approach is that the MMSE includes asking the patient to repeat the phrase 'no ifs, ands or buts'. Even native English-speaking patients may have trouble with this and non-English-speaking patients find it impossible. Some speaking poor English have difficulty differentiating between 'country' and 'state'. Serial 7s are only conducted to 65, which fails to detect subtle change as personal normative data suggests 44 is the cut off (see Ch 2).

The team at Liverpool Hospital in Sydney, Australia, have developed an alternative tool, the Rowland Universal Dementia Assessment Scale (RUDAS),[8] which includes six items that assess multiple cognitive domains including memory, praxis, language, judgment, drawing and body orientation.[8] This instrument was not assessed by Brodaty and colleagues when recommending an alternative assessment measure, the **G**eneral **P**ractitioner Assessment of **COG**nition (GPCOG).[6] Personal preference favours the process set out in Chapter 2.

Examination should not be restricted to higher centre function testing but should also explore for other diagnoses known to be associated with dementia (see Box 15.2).

BOX 15.2 Some conditions known to be associated with dementia

- Carbon monoxide poisoning
- Cerebral trauma
- Cerebral tumours
- Cerebrovascular disease (multi-infarct dementia)
- Chronic psychiatric disease, especially depression
- Cortical atrophy from deep white matter ischaemia
- Drugs and toxins (e.g. heavy metals)
- Huntington's disease
- Hypothyroidism
- Infections (e.g. syphilis, HIV–AIDS)
- Multiple sclerosis
- Normal pressure hydrocephalus
- Parkinson's disease
- Prion disease—Creutzfeldt-Jacob disease
- Slowly progressive 'mental retardation'
- Systemic diseases:
  - lupus erythematosus
  - sarcoidosis
  - Sjogren's syndrome
- Vasculitis
- Vitamin B_{12} deficiency
- Wilson's disease

This requires full neurological examination, both cranial nerves and peripheral assessment (see Chs 3 and 4), in addition to higher centre testing. This does not exclude primary causes of dementia, such as: Alzheimer's disease (the most common primary dementia comprising 50–60% of dementias); fronto-temporal dementia (including what used to be called Pick's disease); Lewy body dementia (within the Parkinson's disease spectrum); and the combination of vascular-caused dementia in combination with Alzheimer's disease (15–20% of those with dementia). There are a number of features that help to differentiate multi-infarct dementia from Alzheimer's disease (see Table 15.1).

INVESTIGATIONS

Investigation of the patient with dementia is focused on excluding reversible causes of cognitive decline. Generally speaking, all patients with suspected dementia should have a simple battery of blood tests, including: full blood count; erythrocyte sedimentation rate (ESR) and C reactive protein (CRP); biochemical screening, including electrolytes, renal function, liver function,

TABLE 15.1 Differentiating multi-infarct dementia from Alzheimer's disease

Feature	Multi-infarct dementia	Alzheimer's disease
Onset	Rapid to abrupt onset	Slower onset
Progression	Step-wise or stuttering Fluctuating	Slowly progressive (gradual)
Concomitant features	Hypertension History of strokes Other vascular territory involvement Focal neurological symptoms and/or signs Emotional incontinence as occurs with pseudobulbar palsy Focal features on CT/MRI (e.g. deep white matter ischaemia)	Often normal blood pressure No history of strokes Less atherosclerotic symptoms No focal features Less or no emotional incontinence CT or MRI may show diffuse cortical atrophy
Personality	Relatively preserved	Often with distorted swings of emotion
Presenting feature	Depends on site of infarct	Memory disturbance

calcium, lipid profile and blood sugar level; thyroid function; B_{12} and folate levels; and anti-nuclear and extractable nuclear antibodies.

When considering some of the associated disorders there are specific tests to be considered, such as serology for syphilis, HIV screen, heavy metal screen, toxicology or copper metabolism (should Wilson's disease be sought). Neuro-imaging with CT or MRI is appropriate. Some would go further, looking at volumetric imaging, single photon emission computer tomography (SPECT) or positron emission tomography (PET), but this is definitely outside the role of the general practitioner and is unlikely to reveal treatable causes of dementia. Some neurologists would perform electroencephalography (EEG), which may show subtle changes such as an increase in theta activity (4–7 Hz frequency) or slower rhythms (less than 4 Hz). EEG may also show an excess of beta activity that is associated with exposure to a wide variety of drugs, such as benzodiazepines or barbiturates, but is also found in the presence of excess alcohol and also in anxiety states.

By this point in the evaluative process, the general practitioner will have involved the consultant and forward planning would be on the basis of a working partnership. Other tests, such as lumbar puncture (LP), would be the domain of the consultant. LP is not routinely required although it may be considered if there is suspicion of: CNS infection; neurosyphilis; neoplasia; or confusing features to the dementia that necessitate further investigation.

BOX 15.3 Reversible causes of dementia

- CNS infections (e.g. neurosyphilis or crytococcal meningitis)
- Depression
- Hydrocephalus
- Medication-induced encephalopathy
- Structural brain lesions
- Subdural haematomas
- Thyroid disease
- Tumours
- Vitamin deficiency (especially B_{12})

Generally speaking the general practitioner should look for reversible causes of cognitive decline and dementia, which comprises approximately 1% of cases but when identified and treated provide a profound effect for the patient (see Box 15.3).

SPECIFIC DEMENTIAS

a Alzheimer's disease

Alois Alzheimer in 1907[9] first described the neuropathology of the disease now identified with his eponym. The neuritic plaques and neurofibrillary tangles remain the hallmark of the disease. Originally it was thought to be a disease of the younger dementing patient, but it is now accepted that the pathology is the same for both pre-senile and senile dementing patients.

Risk factors for Alzheimer's disease include advancing age, incidence and prevalence doubling every five years between 65 and 95 years of age. Genetic factors have been recognized—if first-degree relatives have Alzheimer's disease there is a three to fourfold increased risk.[4] Early onset Alzheimer's disease is associated with the presenilin-1 (PS-1) gene on chromosome 14, the presenilin-2 (PS-2) gene on chromosome 1 and the amyloid precursor protein (APP) gene on chromosome 21. A host of mutations have been reported for early onset disease, but this information is offered to whet the appetite rather than expect the general practitioner to undertake genetic testing, which is a highly specialised process.[10]

Testing for the apolipoprotein E, especially the ε4 allele of apolipoprotein E (APOEε4), now accepted as a major risk factor for Alzheimer's disease, is beyond the scope of general practitioner expectation. Other risk factors include lack of education, head injury sufficient to cause loss of consciousness (especially in the presence of APOEε4), and women are affected twice as often as men.

The typical pattern of Alzheimer's disease is thought to be triphasic: (i) slow onset possibly with minimal cognitive impairment (MCI); (ii) accelerated progression where the diagnosis is more obvious; and (iii) severe cognitive

deficits interfering with basic activities of daily living and deteriorating to death. There is also a fulminant form of Alzheimer's disease, which may be confused with prion disease because of its rapid progression to death.[11]

The most prominent feature of Alzheimer's disease is memory disturbance, but other features include difficulties with organisational tasks and problem solving. The patient may report what is called a 'senior moment', where they have word finding difficulty, difficulty with names or dates, misplacing objects and, most worrisome, repeated minor road traffic accidents for which there is no explanation. There may be associated psychiatric features with minor depressive symptoms often associated with features of paranoia. Often the patient will accuse the spouse of theft or infidelity. Hallucinations are less common than are delusions.

Despite these defects of cognition, the patient has preserved motor and sensory skills and the personality is initially unaffected. Personal observation suggests the patient with Alzheimer's disease loses the veneer developed to function more effectively. The person who is a very gentle soul but needed to toughen up to survive in an aggressive world, returns to the gentle personage. Conversely, the aggressive person who needed to become less forthright to survive, returns to the previous aggression having lost the learned inhibitions.

Once diagnosed, the treatment of Alzheimer's disease is either an acetylcholinesterase inhibitor, such as donepezil (Aricept®), rivastigmine (Exelon®) or galantamine (Reminyl®), used for mild to moderate disease, or memantine (Ebixa®) prescribed for moderate to severe disease.

In Australia prescription of those agents requires referral to a specialist, and hence need not be further discussed. What is worth noting is that the first prescription (for two months) is given to the patient at the time of the consultation, but the second and third prescriptions will be prescribed by the specialist, sent to the central authority for approval, and mailed to the patient. The general practitioner may assist by checking that the patient received the prescription and is compliant with taking the medication.

b Fronto-temporal dementia

Fronto-temporal dementia (previously called Pick's disease) encompasses a group of degenerative conditions involving a predilection for the frontal and antero-temporal cortex.[12] They comprise approximately 10% of dementias but almost half the presenile dementias presenting below 60 years of age. In the late 1990s the fronto-temporal dementias were classified into three groups: the behavioural variant; progressive non-fluent aphasia; and the fluent aphasia–semantic dementia.[13]

The clinical features of fronto-temporal dementia include: early onset; often there is family history; change in behaviour and personality; problems with language; difficulties with planning, attention and problem solving. Fifty percent of those with fronto-temporal dementia have the behavioural variant,

with a 2:1 male to female ratio and a mean age at diagnosis of less than 60 years. Personal hygiene is often compromised with 'concrete' entrenched thinking, confounded by distractibility, stereotypic behaviour and rapid progression with less than five years' life expectancy. Approximately 20% have an autosomal dominant inheritance and 15% develop motor neurone disease.

Progressive non-fluent aphasia (dysphasia) comprise approximately 25% of fronto-temporal dementia and present with language problems affecting fluency, word finding and difficulty with speaking demonstrated by stuttering, impaired repetition and speech dyspraxia. This may be compounded by defective executive function and memory problems.

Progressive fluid aphasia comprises less than 20% of fronto-temporal dementias and progresses more slowly, although still has a life expectancy of five years. Patients may demonstrate behavioural changes with emotional withdrawal, depression, concrete thinking, receptive dysphasia, poor word recognition, nominal dysphasia and word recall. Patients may be agnostic for faces or objects, and have features of other degenerative neurological conditions including progressive supra-nuclear palsy (difficulty with vertical eye movement, Parkinsonian features and dementia), and cortico-basal syndrome (dyspraxia, sensory loss, myoclonus, Parkinsonian features and dystonia).

These are rapidly progressive disorders and refractory to treatment. They are best managed in a specialist environment and the role of the general practitioner is to be there to help family and friends.

c Dementia with Lewy bodies

Recognition of Lewy bodies as an important component of geriatric dementia is fairly recent, prior to which they were considered mainly as part of the idiopathic Parkinson's disease picture.[14] Patients with dementia with Lewy bodies present with fluctuating cognition, visual hallucinations and features of Parkinson's disease. The dementia affects executive function, with impaired visuospatial skills, memory problems and impaired verbal fluency. Visual hallucinations are common and may be exacerbated by levodopa (the drug of choice for Parkinson's disease). REM sleep behaviour disorder (see Ch 12) and autonomic problems, such as orthostatic hypotension, are more common.

Treatment is best managed by a consultant, and anti-Parkinsonian treatment is less effective in this group of patients. Anti-psychotic medications used to treat the prominent hallucinations are also often less effective and best left to the specialist.[15] There is some evidence as to the effectiveness of the acetylcholinesterase inhibitors but again this is best referred to a consultant.

d Other dementias

Vascular dementia is the collection of dementias in which there is clear evidence of diffuse small vessel disease in association with cognitive decline.

It is a heterogenous group of dementias for which the approach mirrors that for secondary stroke prevention (see Ch 14).

Other diagnoses, such as Huntington's disease and those conditions associated with dementia (see Box 15.2), will not be further discussed as the treatment of choice is determined by the underlying condition rather than the dementia per se.

ROLE OF THE GENERAL PRACTITIONER

The general practitioner is usually the first port of call for the patient with dementia, and the recognition of the symptoms and signs is a vital component of early and appropriate intervention (see Table 15.1).[16] The way to deal with the diagnosis, and the appropriate discussion of both treatment and estate planning, should be a partnership between the consultant and family physician.

Issues such as: advanced directives; power of attorney; living will; capacity to drive; need for home help or institutional placement; provision of diet; pre-packaging of medications (such as Webster pack loaded by the local pharmacist); addressing family needs; financial management; and personal safety, are all better appreciated by the general practitioner than the specialist. Organisation of support services is best arranged by a combined approach that includes both the general practitioner and specialist. Once the patient is placed in a nursing facility then the general practitioner assumes the principal managerial role.

Counselling of the patient and family may be undertaken by either the consultant or general practitioner but, as the family physician, the general practitioner may have a more intimate relationship with both the patient and relatives. The general practitioner may be better placed to provide answers in a less threatening environment.

While the Pharmaceutical Benefits Scheme (PBS) insists on specialist prescription of either acetylcholinesterase inhibitors or memantine, day-to-day patient management remains the domain of the general practitioner. The general practitioner also has a definitive role in preventative strategies, such as the management of risk factors like hypertension, hyperlipidemia or diabetes control. As repeatedly stated, the general practitioner remains the captain of the ship with specialists providing a consultative service.

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16 Muscles

INTRODUCTION

Muscle weakness is often automatically thought to reflect muscle disease, but that need not be the case. Weak or wasted muscles may result from a lesion anywhere within the nervous system. This starts from the central nervous system (CNS), which produces a typical upper motor neurone (UMN) distribution of weakness. UMN weakness results in the compensatory 'spastic' posturing (see Ch 4) consequent to weakness in the antigravity muscles. Damage to lower motor neurones (LMN) will produce weakness in those muscles innervated by the affected LMNs (see Ch 4).

It is possible to get a combination of UMN and LMN weakness that may be caused by motor neurone disease (MND) or vitamin B_{12} deficiency, as seen in subacute combined degeneration.

More peripheral involvement as evidenced by diseases affecting the neuromuscular junction, typified by myasthenia gravis, will produce muscular weakness or fatigability. Diseases affecting muscles themselves also cause muscle weakness and wasting.

Perhaps the best and most obvious example of how a lesion at different points in the 'nerve-to-muscle' relationship can result in a similar picture is reflected in the presentation of ptosis. This may be caused by nerve damage (be it 3rd cranial nerve or autonomic nerve damage), damage at the neuromuscular junction (as seen in myasthenia gravis), or long-standing muscle disease (especially with mitochondrial myopathy) (see Table 16.1).

There may even be a pseudo-ptosis produced by contralateral facial weakness, which results in a larger contralateral palpable fissure, making the contralateral eye appear larger than the eye with the 'pseudo-ptosis'. This gives a false impression of ptosis in which the wrong eye is identified as

TABLE 16.1 Identification of causes of ptosis

Cause	Features
3rd cranial nerve palsy	Ptosis Enlarged pupil (midriosis) Eye may be deviated down and out (though not always so if only affecting to outer parasympathetic fibres) May have diplopia
Horner's syndrome (sympathetic chain involvement)	Ptosis Smaller pupil (myosis) Lack of sweating (especially forehead of affected side) No limitation of eye movement No diplopia Eye may appear sunken (enophthalmos)
Myasthenia gravis	Ptosis Equal pupils Fatiguability of eye movements, may have diplopia May have other myasthenic muscles Responds to Tensilon test
Mitochondrial myopathy	Ptosis Equal pupils Usually longstanding (can be seen in old photographs) May need to do lactate levels, possibly from hair or muscle biopsy
Pseudo-ptosis from contralateral upper motor neurone (UMN) lesion	No real ptosis, the upper lid is in the same position bilaterally with respect to the top of the pupil Pupils are equal Weakness of facial muscles, especially lower face, contralateral to 'smaller' eye Weak contralateral eye closure compared to suspected eye with pseudo-ptosis

being smaller, rather than the affected eye recognised as being larger (see Table 16.1).

This chapter will not deal with muscle weakness as a consequence of either UMN or LMN lesions, as these have been discussed elsewhere (see Chs 11 and 14). The focus of this chapter will be on pathology at either the neuromuscular junction or more peripherally within the muscle itself. It will be directed to that which is relevant to general practitioners, with the aim of improving clinical acumen and the enjoyment associated with the practice of medicine.

NEUROMUSCULAR JUNCTION

a Myasthenia gravis

Myasthenia gravis[1] epitomises diseases of the neuromuscular junction, and is an autoimmune disease with antibodies directed against the acetylcholine receptors on skeletal muscles in approximately 90% of those with generalised myasthenia gravis and about half those with ocular myasthenia. Should these antibodies not be identified then the muscle-specific kinase antibodies (MuSK antibodies) are found in about half the remaining patients with myasthenia gravis. Those with MuSK antibodies tend to have a slightly atypical presentation of their myasthenic picture with more oculo-bulbar and neck extensor involvement and more respiratory symptoms.

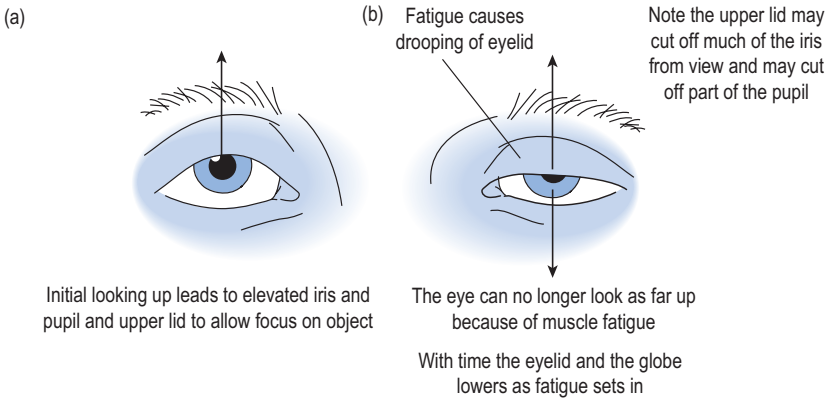
Myasthenia may occur at any age, with male to female ratio of 1 : 3 with an earlier onset in women and girls (10–40 years) as compared to men (often 50–70 years). After the age of 40 years, the male : female ratio is approximately equal. There is a neonatal form of myasthenia, thought to be secondary to placental transmission of the acetylcholine receptor antibodies. This presents with impaired sucking, weak cry and 'floppy' limbs. This presents within the first two days of life. It generally only requires supportive treatment for the lifespan of the antibodies. There is also an autosomal recessive congenital form with infantile onset, and a drug-induced form consequent to the use of D-penicillamine.

The usual presentation of myasthenia gravis is with ptosis (see Table 16.1) together with fatiguable muscle weakness, diplopia and possible dysarthria, dysphagia, dyspnoea or fatiguable proximal limb weakness. Almost any skeletal muscle may be involved, as may be respiratory muscles, and myasthenia gravis may mimic other diseases. Purely ocular myasthenia often presents with ptosis and diplopia without other muscle group involvement.

When examining the patient with suspected myasthenia gravis, fatiguability is demonstrated by asking the patient to look up at a fixed object or spot and to maintain the upward gaze (see Fig 16.1).

Alternative methods for testing for fatiguability include asking the patient to count aloud to 100, and listening to the quality of articulation to recognise the development of a dysarthric and nasal quality to enunciation as the counting proceeds. Testing muscles of mastication, the patient is asked to bite down on a wooden tongue depressor while at the same time the doctor pulls on the spatula and observes the decline in the strength of the bite. Peripheral muscle fatiguability may be tested by asking the patient to repeatedly perform a muscle task with intervening relaxation, and recording the evolving weakness over time (see Fig 16.2).

What presents as purely ocular myasthenia may often progress to become generalised myasthenia, possibly consequent to an intercurrent infection. As with all neurology, the diagnosis requires a high index of suspicion with the differential diagnosis including: brainstem lesions and other causes of ptosis (see Table 16.1); multiple sclerosis; Graves' disease (thyrotoxicosis) with



(NB: with the onset of fatigue the patient may try to increase neck extension to compensate for onset of ptosis and lowering of orbital globe. The head should be maintained in the same position to prevent increased neck extension.)

FIGURE 16.1 Testing for fatiguable ptosis.

ophthalmo-paresis; and other inflammatory myopathies, most of which causes elevation of creatine kinase (CK).

While diagnosis usually relies on specialist involvement, the suspicious general practitioner can start the ball rolling, having ordered acetylcholine receptor antibodies and a chest CT scan, looking for thymoma. Repetitive nerve stimulation or single fibre electromyography are clearly the domain of a neurophysiologist. Double-blind edrophonium (Tensilon) testing is best performed within the hospital setting with cardiac monitor and facility for resuscitation, which is rarely required. The general practitioner may perform an 'ice test' in which the application of ice produces strengthening of muscles. This is rarely, if ever, used these days as a referral to the consultant has supplanted such simple testing with Tensilon test. The 'ice' test really was only used in ocular myaesthenia.

Patients with myasthenia gravis may have concomitant other organ specific autoimmune diseases with up to 10% having associated thyroid disease, be it hyperthyroidism or hypothyroidism, that may be identified by the astute general practitioner who will treat this in their usual fashion, with possible referral.

Thymectomy is advocated in young patients with myasthenia (below the age of 50 years) and all those with thymoma. It is not usually advocated in those older than 65 years, those with pure ocular myasthenia or with MuSK antibodies.[2]

Pharmacological treatment of myasthenia is with pyridostigmine (Mestinon®) and/or the use of immunosuppression, be it with steroids or more aggressive, but this is usually the domain of the specialist.

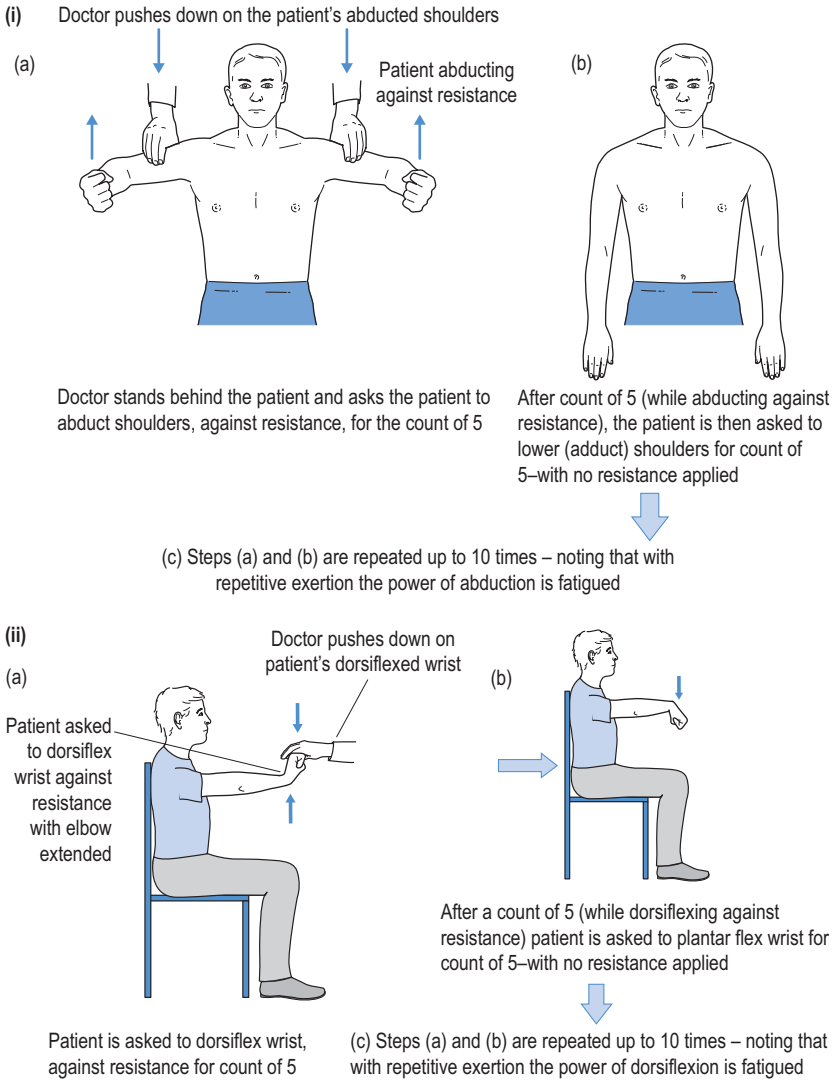


FIGURE 16.2 (i) Testing for fatiguability of shoulder abduction; (ii) Testing for fatiguability of wrist dorsiflexion.

Mestinon® is started at 60 mg b.d. or t.d.s. in mild cases, often complemented with slow release 'Time Span' (180 mg) at night. Adverse events may include excess salivation, abdominal cramping and possible diarrhoea; the latter may require anticholinergics. It should be remembered that Mestinon® may exacerbate glaucoma. A cholinergic crisis must be considered in patients with respiratory failure. These patients may also experience dilated pupils, together with the above adverse symptoms plus fasciculations. When this occurs the anticholinesterases should be withdrawn and the patient maintained in an intensive care environment with possible intubation. This represents a medical emergency, which may be provoked following the initiation of Mestinon® therapy.

Steroids, at a dosage of 1.0–1.5 mg/kg/day (usually 60–100 mg per day), may exacerbate weakness in the first one to two weeks so caution must be exercised when starting steroids, particularly in outpatients. Additional treatment with myclophenalate, azathioprine or possibly even cyclosporins has been used as steroid-sparing agents. In more severe cases plasmapheresis or IV immunoglobulin may be required, but this again is the domain of the consultant rather than the general practitioner.

b Lambert-Eaton myasthenic syndrome (LEMS)

This is usually a paraneoplastic, auto-immune, myasthenic condition.[3] It is caused by antibodies to calcium channels on the presynaptic nerve terminals of skeletal muscles and autonomic ganglia. The myasthenic syndrome usually precedes the diagnosis of the tumour, which is usually a small cell lung cancer.

The symptoms often start in the proximal leg and shoulder girdle muscles without ocular features. There may be parasympathetic symptoms of dryness, including mouth, constipation, urinary retention and impotence.

The diagnosis relies on neurophysiology with post-exercise potentiation of the compound muscle action potential, but this is definitely the precinct of the specialist. Ultimate treatment is directed towards managing the underlying malignancy, although treatment specific to myasthenia gravis may have limited efficacy.

c Botulism

The toxin produced by *Clostridium botulinum* blocks the release of acetylcholine from the autonomic and motor nerve endings, causing nausea, vomiting, anorexia, constipation, blurring of vision, diplopia, dysarthria, dysphagia, dyspnoea and limb weakness 12–36 hours after consuming contaminated food.[4]

Diagnosis requires a high index of suspicion plus identifying the toxin in serum. Treatment is the application of appropriate anti-serum, by which stage the patient will usually be in hospital.

MYOPATHIES

As the name implies, 'myo' meaning muscle and 'pathy' meaning pathology, the focus is now on the end organ, namely the muscles themselves.[5] Consideration of muscle diseases may adopt the traditional approach to classification, examining congenital and acquired causes (see Table 16.2).

This produces a long list of disorders, many of which are quite rare and either will not be encountered or will rarely be encountered by general practitioners. Even if encountered by general practitioners, many of the rarer myopathies will be incorrectly diagnosed or overlooked. In many instances

TABLE 16.2 Classification of muscle diseases

Congenital	Acquired
Muscular dystrophies: • Duchenne • Becker • Emery-Dreifuss • fascioscapulohumeral • scapuloperoneal • limb girdle	Inflammatory: • polymositis • dermatomyositis • inclusion body myositis • inflammatory and myopathies associated with connective tissue disease
Metabolic myopathies: • McArdle's disease (myophosphorylase deficiency) • acid maltase deficiency • malignant hyperthermia (central core disease carnitine palmitoyl transferase deficiency; dystrophinopathies)	Infective: • associated with HIV • trichinosis
Mitochondrial myopathies	Metabolic: • endocrine (steroid-induced, thyroid disease)
Periodic paralysis	Electrolyte disturbance: • hypokalemia • hyperkalemia • hypercalcemia • hypophosphatemia • hypomagnesemia • hypermagnesemia
Myotonias: • mytonic dystrophy • myotonia congenita	Drugs and toxins: • alcohol • diuretics • steroids • colchicine • statins and/or niacin • penicillamine

the same may be said for the general neurologist who does not practise within the super-sub-specialised area of muscle diseases.

It follows that a very detailed discussion of all these rare myopathies is unwarranted within an overview specifically for general practitioners. This should not be interpreted as being either patronising or derisive of general practitioners, but rather representing a realistic appreciation of the very great demands placed on the average general practitioner. The same might equally apply for the busy general neurologist, who will likewise rely heavily on the input of some specialised colleagues. It is thus incumbent to offer an overview to the approach, acknowledging that the list provided (see Table 16.2) is far from exhaustive.

The fundamental symptoms and signs of myopathy are muscle weakness, both reported by patients and observed when testing power, with/without pain (myalgia). Proximal muscle weakness is more common than is distal weakness, and acute myopathies are usually associated with inflammatory, systemic diseases or toxic aetiology. Slower onset myopathies include the muscular dystrophies and congenital myopathies, mitochondrial myopathies (also congenital although transmitted down the maternal line), metabolic myopathies and muscle membrane channel defects (as evidenced within periodic paralyses and myotonias) (see Table 16.2).

General practitioners faced with these presentations will have ordered CK levels, which should be elevated, and may also have ordered other simple laboratory tests such as: full blood count; biochemical screen, including calcium, phosphate and electrolyte levels plus renal function; magnesium levels; thyroid function; and other tests of systemic disease such as antinuclear antibody, extractable nuclear antibody, C-reactive protein and an erythrocyte sedimentation rate. Once the diagnostic algorithm has proceeded to electromyography (EMG), specialist involvement will have been organised.

The general practitioner may be aware of a positive family history, especially with the congenital diseases, although often other affected family members may have very subtle disease that could have avoided detection. Some diseases may have specific patterns of presentation, such as prominent finger (especially flexor) and quadriceps weakness, which is associated with inclusion body myositis, or the facioscapulohumeral distribution associated with the dystrophy of the same name.

What follows will be a brief discussion of some of the entities in Table 16.2. There will be no attempt to be exhaustive as early involvement of a consultant neurologist is almost universal. The general practitioner provides supportive measures, social interaction and day-to-day symptomatic relief, especially for longstanding disease. The astute general practitioner may offer the initial diagnostic insight, but works in partnership with the consultant. Muscle biopsy requires an even larger therapeutic team in which the physician will suggest which muscle is to be biopsied, the surgeon—usually a neurosurgeon—will conduct the procedure, and the pathologist, armed with

adequate history and clinical features, may provide the diagnostic confirmation of the relevant disease process.

CONGENITAL MYOPATHIES

a Muscular dystrophies

These are hereditary diseases[6] of which Duchenne and Becker muscular atrophies are most common. Below is a brief overview of some of the congenital myopathies (see Table 16.2).

Duchenne and Becker muscular dystrophies

Both Duchenne and Becker muscular dystrophies are X-linked recessive due to mutations in the dystrophin gene (hence sometimes referred to as dystrophinopathies). Duchenne occurs in about 1 in 3500 male births, with Becker having 10% of that incidence (prevalence 1 in 18 000 and 1 in 180 000 respectively). Males are affected while females are carriers. Becker has a similar but milder phenotype to Duchenne, presenting in young adults rather than before the age of 5 years.

Duchenne muscular dystrophy may present with proximal weakness from birth, with delayed milestones, such as walking or running, and a waddling gait. This progresses to: impaired gait; difficulty climbing stairs; problems rising from sitting or squatting (Gower's sign); exaggerated lordosis; falls; calf hypertrophy; and loss of knee and ankle jerks. Most Duchenne-affected boys are wheelchair-bound by puberty, and life expectancy is into the early third decade. Becker-affected patients survive into the fifth or sixth decade. Cardiomyopathy is common with Duchenne's (with abnormal ECG), and mental retardation occurs in a third of patients.

CK may be elevated to 20 plus times normal with a myopathic EMG. Dystrophin assay may be performed on muscle biopsy, and treatment is largely supportive and symptom directed, often provided by a multidisciplinary team from within a specialised clinic at a major teaching hospital.

Emery-Dreifuss muscular dystrophy

This is also an X-linked recessive but less common dystrophinopathy. Boys present in early childhood or adolescence with contractures at elbows, neck and ankles. There is weakness of proximal arms and peroneal leg muscles with survival into adult life. Walking is usually lost in the third decade although some patients do appear relatively unaffected. Cardiac dysrhythmias and heart block may require early pacemaker insertion. Diagnosis is by Emerin assay in mucosal cells from cheek swab, and treatment is symptomatic and supportive.

Facioscapulohumeral dystrophy and scapuloperoneal dystrophy

Both of these are autosomal dominant, the former causing scapular winging, facial weakness, arm weakness and variable peroneal weakness (affecting

about 1 in 1000). The latter causes scapular winging and peroneal weakness with relative sparing of face and upper limbs. The diseases have variable penetrance with different levels of deficit in affected family members. There are specific genetic tests on DNA analysis.

Limb girdle dystrophies

These are autosomal recessive in 90% of cases, are severe and present in early adulthood. There is an autosomal dominant variety that is less severe and presents in mid-life. There are numerous genetic mutations, which may help predict cardiac involvement and the need for pacemaking. Often legs are first affected with waddling gait, difficulty ascending stairs and rising from the sitting position. Knee jerks are often lost before ankle jerks (in contrast with peripheral neuropathy), CK is elevated almost to the levels of Duchenne's dystrophy, and treatment is largely supportive.

b Mitochondrial myopathies

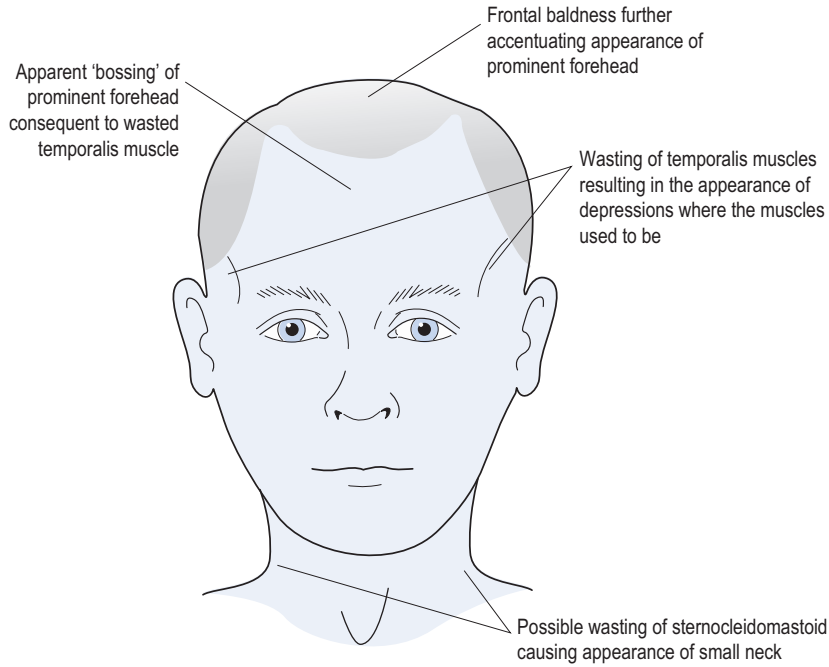
Mitochondrial myopathies[7] are inherited via the maternal line and encompass a variety of conditions, including: Kearns-Sayer syndrome (KSS); familial progressive external ophthalmoplegia (PEO); myoclonic epilepsy with ragged red fibres (MERRF); and encephalopathy, lactic acidosis and stroke-like episodes (MELAS) with overlap between the various mitochondrial syndromes. Diagnosis and treatment of the mitochondrial myopathies is usually outside the scope of general practice. They have been touched on here purely to whet the appetite, to encourage enthusiastic general practitioners to read further about a relatively new constellation of myopathies.

c Myotonias

Myotonic dystrophy[8] is the most common muscular dystrophy with autosomal dominant, multi-system presentation. It results from a protein kinase gene defect occurring in approximately 1 in 8000 adults. In advanced cases it is often an 'end-of-the-bed' diagnosis as it causes obvious wasting of the temporalis muscles, which produces a typical facial appearance (see Fig 16.3).

The disease has anticipation, meaning it presents earlier in subsequent generations. Unlike most myopathies, weakness starts more distally and patients may present following unusual accidents, such as a road traffic accident occurring at night due to a loss of night vision with blindness caused by myotonic constriction of the pupils provoked by oncoming headlights. Another classical presentation may be as a motorbike accident because of an inability to release the accelerator hand grip of a motorbike due to grip myotonia.

Features of myotonic dystrophy may include: wasting of the face and neck muscles (particularly temporalis and sternocleidomastoid muscles) (see Fig 16.3); pharyngeal weakness with dysphagia; possible aspiration; conduction cardiac problems (possibly requiring pacemaker); psychological complaints (possibly with impaired intellect, apathy or paranoia); ophthalmic problems



(NB: differential diagnosis of apparent frontal 'bossing' with very prominent forehead and frontal baldness is Paget's Disease.)

FIGURE 16.3 Facial features of myotonic dystrophy.

with specific cataract formation (in addition to senile cataracts); possible retinal or macular pigmentary degeneration; immunosuppression with low IgG; and hypogonadism (especially in males).

Physical examination may reveal the typical facies (see Fig 16.3) and grip myotonia may be evident when testing hand power—the patient having a problem releasing the tight grip. Often patients with myotonic dystrophy have learnt just how tightly to squeeze before the myotonia is provoked, and may have learned to conceal it. It behoves the clinician to encourage the patient to grip more tightly than the patient initially wants to do, and this may provoke the grip myotonia.

There is also percussion myotonia, elicited by tapping the relaxed thenar eminence with a tendon hammer. The thenar muscles contract with the thumb being kept pointing upwards with a delayed relaxation. Tongue myotonia may be provoked by tapping the protruding tongue with a tendon hammer, but personal preference is to avoid this as it should not really be necessary to make the diagnosis.

Up to a quarter of infants from affected women will have congenital myotonic dystrophy with mental retardation, respiratory distress, and poor sucking and dysphagia. It is important to warn expectant mothers with myotonic dystrophy of this possibility.

Use of anti-epileptic medications, such as phenytoin (Dilantin®) or carbamazepine (Tegretol®) may provide some symptomatic relief against the myotonia.

ACQUIRED MYOPATHIES

a Inflammatory myopathies

While uncommon (occurring in about 1 in 100 000), inflammatory myopathies[9] have the potential for reversibility so their recognition is imperative. The most common inflammatory myopathies are polymyositis, dermatomyositis and inclusion body myositis. They present with weakness, usually painless, and high CK levels. An exception to this is polymyalgia rheumatica in which there is pain, but CK is usually normal or only slightly elevated while ESR is high.

Polymyositis

Polymyositis is an inflammatory myopathy in patients usually more than 20 years old. It presents with symmetric painless proximal weakness, developing insidiously over weeks to months, although occasionally it may present acutely. It involved limb girdles, neck flexors and may be associated with dysphagia and, later, respiratory weakness and possibly myocarditis. It may be paraneoplastic and associated with anti-neuronal antibodies, such as Jo-1 nucleoprotein antibody. CK is raised, often greater than ten times normal, and EMG gives a mixed myopathic and neuropathic picture. Muscle biopsy shows muscle necrosis with inflammatory infiltrate with lymphocytes, without the vascular lesions seen in dermatomyositis or with perivascular atrophy.

Treatment is via high-dose steroids, such as prednisolone at 60–100 mg per day, roughly calculated at 1.0–1.5 mg/kilogram/day, with gradual tapering as muscle strength increases. Maintenance therapy is continued for 6 months to 2 years, adopting an alternate day regimen. Azathioprine and methotrexate may be used for steroid-sparing effect. As the patient improves so the CK recedes, but ongoing limb girdle weakness may be confounded by steroid-induced myopathy.

Should this approach with simple immunosuppression fail, then alternatives include mycophenolate, IV immunoglobulin, cyclophosphamide, chlorambucil or lymphoid irradiation. These are well beyond general practitioner involvement.

Dermatomyositis

This presents with a similar picture to polymyositis but is compounded by skin changes, including violaceous heliotrope rash of the eyelids (especially

upper eyelids) with erythematous cheeks and malar rash (possibly confused with lupus erythematosus). Knuckles may develop erythematous, scaly macules (grotons papules) with possible further involvement of elbows, knees and upper chest.

There may be an association between dermatomyositis and malignancy (such as adenocarcinoma), especially in patients older than 40 years. CK and EMG mirror polymyositis, while biopsy suggests a more vascular origin with pericapillary inflammation that is less apparent in polymyositis. Treatment mirrors that of polymyositis.

Inclusion body myositis

Inclusion body myositis is an inflammatory myopathy affecting 50+-year-old adults with insidious onset involving quadriceps and upper limb forearm flexor atrophy, causing hand involvement with weakness of finger flexors. There may be association with autoimmune diseases and a familial, autosomal recessive consanguinity factor has been recognised. CK is often normal or only mildly elevated, while EMG may show both myopathic and neuropathic features. Biopsy confirms low-grade inflammation with rimmed vacuoles, cellular inclusions and diagnostic amyloid staining, with Congo red, shows specific inclusion bodies. No treatment is really satisfactory, although it is worth trying steroids or immunosuppressive agents that occasionally are efficacious.

b Metabolic myopathies

These include the array of endocrine myopathies,[10] such as steroid-induced myopathy associated with 50–80% of patients with Cushing's disease and 2–20% of patients on long-term steroid therapy. This produces proximal weakness, more so involving the lower limbs than the upper limbs, and may be reduced by using alternate day dosage regimen.

In 25–50% of people with adrenal insufficiency (Addison's disease) there will be generalised muscle weakness, muscle cramps and fatigue, responsive to steroid replacement. This may be compounded by hyperkalemic periodic paralysis.

Thyroid disease, both thyrotoxicosis and hyperthyroidism, may cause myopathy. Both may cause proximal weakness with or without wasting and/or myalgia. Thyrotoxicosis may be associated with periodic paralysis similar to familial hypokalemic periodic paralysis, and bulbar muscles are usually spared. Hypothyroidism may cause myo-oedema with apparent muscle enlargement. While CK is usually normal with hyperthyroidism, it may be elevated in hypothyroidism.

Other endocrine diseases, such as acromegaly (with increased growth hormone), hyperparathyroidism (with elevated calcium levels) and hypoparathyroidism may be associated with various myopathies.

c Electrolyte induced myopathies

Hypokalemia may cause proximal or generalised painless weakness, which responds to potassium replacement. If hypokalemia is profound or associated with alcohol, it may produce acute necrotising myopathy with rhabdomyolysis and possible renal failure. Hyperkalemia may affect skeletal and cardiac muscle with ascending quadriparesis, respiratory failure and cardiac arrest.

Calcium and magnesium changes can also cause myopathy, as may changes in phosphate levels.

d Myopathies associated with drugs and toxins

Alcohol is the agent most recognised as being associated with myopathy for a number of reasons. Alcohol-induced obtundation, resulting in the patient lying in a single position for a long period of time with weight on certain muscles, may of itself produce rhabdomyolysis. Alcohol may possibly be a myotoxic agent or may indirectly cause problems with malnutrition, hypokalemia or hypophosphatemia.

In addition to alcohol there is a long list of medications that may cause myopathy. These include:

- Amiodarone (Cordarone®) is an anti-dysrhythmic agent which induces hypokalemia.
- Beta-blockers (such as labetalol (Presolol® or Trandate®) or sotalol (Cardol,® Solavert, ® Sotacor® or Sotalol Sandoz®)) may, on rare occasions, be myotoxic.
- Chloroquine (Chlorquin®) is an antimalarial that can cause muscle weakness due to vacuolar myopathy and a defect in neuromuscular transmission similar to myasthenia gravis.
- Colchicine (Colgout®) inhibits urate crystal deposition but may induce myoneuropathy with the myopathy being more prominent than is the axonal neuropathy.
- Diuretics may indirectly cause myopathy as a consequence of causing hypokalemia if given without potassium supplements.
- Doxorubicin (Adriamycin® or Caelyx®) is a cell cycle phase non-specific cytotoxin that may inhibit DNA synthesis and generate free radicals, both of which have the potential to damage muscle, especially cardiac muscle.
- HMG-Coa reductase inhibitors (statins) used to treat hyperlipidaemia may cause myopathy with CK elevation up to 10 times normal, and myalgia and muscle weakness, which may occur in up to 5% of patients.
- Hydroxychloroquine (Plaquenil®) is an antimalarial that is also used to treat discoid lupus erythematosus and rheumatoid arthritis. It may cause neuromyopathy, leading to progressive weakness or atrophy of the proximal muscles.

- Metronidazole (Flagyl®) is a specific bactericidal antibiotic against anaerobic bacteria and other microorganisms. It may cause both peripheral neuropathy as well as myopathy, especially cardiomyopathy.
- Niacin (nicotinic acid) is a water-soluble B complex vitamin, also used for lipid lowering, but it may exacerbate the myopathic features associated with statins or cause weakness and myalgia, even if given without the statins.
- Penicillamine (D-penamine®) is a chelating agent used for treatment for heavy metals, and also used to treat rheumatoid arthritis. It may provoke inflammatory myopathy or a myasthenic-like syndrome with increased antibodies to acetylcholine receptors.
- Vincristine (vincristine sulfate) is an antimitotic, antineoplastic agent used to treat leukaemia and lymphomas. It is neurotoxic with neuromuscular sequelae causing neuritic pain followed by irreversible motor difficulties.
- Zidovudine (Combivir+®, Retrovir® capsules and syrup and Trizvur+®) is used to treat HIV–AIDS. It may provoke a mitochondrial myopathy if a cumulative dose in excess of 250 g is given.

The above list is far from exhaustive, but has been provided to demonstrate that many of the agents encountered by general practitioners may cause myopathies. The general practitioner may be the first to recognise the association between the drug and the patient's symptoms, and thus be ideally placed to protect the patient.

CONCLUSION

Muscle weakness may reflect lesions occurring anywhere along the neuromuscular axis, from the CNS, the peripheral nervous system, the neuromuscular junction or the muscle itself. This chapter has focused specifically on the neuromuscular junction, with myasthenia gravis being the principal condition, and on muscles as end organs of the motor pathway.

Most of the conditions reviewed in this chapter dictate the early involvement of a neurologist, but this need not lead to the exclusion of the general practitioner. Many of the conditions discussed have an insidious onset, thus the general practitioner may not be attuned to note the gradual changes experienced by the patient. It follows that the general practitioner must keep an ongoing vigil, looking for patterns of disease, or be an attentive listener and acutely aware of what the patient is describing.

Even in neurology, the study of muscle diseases, for which only the surface has been scratched here, is a relatively new super subspecialty area. **The purpose of this chapter has been to identify patterns for recognition, some superficial approaches to diagnosis and treatment, and to offer a familiarisation program to further empower the general practitioner.**

Without doubt, the general practitioner will be the first port of call for the patient with muscle diseases. Once properly empowered, the joy of making the correct diagnosis of what amounts to a relatively rare medical condition cannot be overemphasised. As with the whole ethos of this book, it is hoped that such knowledge will enhance the pleasure of practising medicine. If it achieves that goal then it has benefited both the general practitioners and their patients.

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