Dizziness in older adults

Rebecca Lee
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Abstract
Dizziness is a very common symptom in older adults. Its prevalence increases with age, with approximately one-third of elderly people experiencing it. It can be caused by true vertigo, of peripheral or central cause, presyncope, disequilibrium or a combination of these. A detailed history and examination are essential in distinguishing common causes. Providing there is no evidence of central vertigo or a cardiac cause, further investigation is rarely helpful in diagnosis or management. Management of the patient with dizziness should be holistic; it should not only focus on treating the underlying cause, but also include other elements such as medication and functional review, and the input of allied health professionals as appropriate.

Keywords Benign positional paroxysmal vertigo; dizziness; elderly; Hallpike test; Ménière's disease; migrainous vertigo; neurology; nystagmus; postural hypotension; vertigo; vestibular neuronitis

Key points

- Dizziness in the elderly is a common symptom and can have many different aetiologies
- A systematic approach to the history and examination will usually reveal the underlying diagnosis
- Management should be both targeted towards the underlying cause and involve other members of the multidisciplinary team as appropriate

Introduction

Dizziness is a common problem in older people, with approximately 30% of community-dwelling elderly people reporting the symptom.[1] Its prevalence increases with age, with 54% of the over-90s experiencing dizziness in the preceding 6 months. In one community study, the 1-year prevalence of elderly people presenting to their family doctor with dizziness was 8.3%.[2] The symptom is also frequently encountered among older acute medical referrals or hospital inpatients, as a primary or associated symptom.

What challenges do dizzy patients present?

- *Dizziness* is a non-specific word. When patients use it to describe their symptoms, they can be referring to true vertigo or light-headedness, presyncopal symptoms or a sensation of disequilibrium. The clinician must obtain a history to clarify what the patient means.
- The differential diagnosis of the patient with dizziness is extensive.
- In older patients presenting with dizziness, the cause is often multifactorial.
- Health professionals often hold the erroneous belief that treatment is ineffectual.

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Clinical approach to the dizzy patient

History

A good history is paramount in assessing a patient with dizziness and can identify the diagnosis in around 70% of patients.[3] The initial challenge is to determine what the patient means when they say they are 'dizzy', as the precise sensation experienced gives clues as to the underlying cause(s):

- **Vertigo** refers to an illusion of movement. The patient may feel as if objects in their surroundings are moving or that they are moving in relation to their environment.
- **Presyncope** refers to a feeling of light-headedness, sometimes associated with nausea or sweating and 'clamminess'. Positive responses to questions such as 'Does it feel as if you are about to faint?' and 'Does it feel similar to how you feel when you stand up too quickly?' suggest presyncope.
- **Disequilibrium** refers to a feeling of unsteadiness or 'veering' to one side, primarily when walking. It is typically worsened when vision is simultaneously impaired, for example in the dark or if the patient closes their eyes.

If the symptom described can be classified into one of these three broad sensations, the causes shown in Figure 1 can be considered. Precipitating and aggravating factors can provide important clues to the underlying cause.

Vertigo that is provoked by head movements such as turning over in bed or looking upwards is suggestive of benign paroxysmal positional vertigo (BPPV). An antecedent upper respiratory tract infection suggests acute vestibular neuronitis or, less commonly, viral labyrinthitis. Symptoms associated with Ménière's disease and perilymphatic fistulas can be provoked by loud noise. Perilymphatic fistulas can also be aggravated by sneezing or coughing. Stress can trigger psychogenic vertigo. Acute vestibular neuronitis, stroke and Ménière's disease can present spontaneously without any cause.

Presyncope preceded by a sudden change in posture can be caused by postural hypotension; if preceded by more prolonged standing, it can be due to a malignant vasovagal syndrome.

The time-course is useful in differentiating causation, as are the presence or absence of associated features (Table 1).

As with all common presentations in the elderly, a drug history is essential. Common drugs that cause vestibulotoxicity resulting in vertigo include gentamicin, non-steroidal anti-inflammatory agents, furosemide and quinine. Drugs that

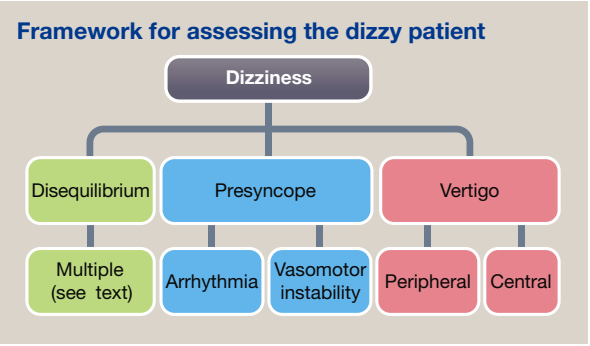

Figure 1

commonly induce postural hypotension include antihypertensive agents, tricyclic antidepressants, diuretics and levodopa.

Examination

A complete examination should be performed (Figure 2) in all patients presenting with dizziness, focusing on the following:

- **Erect and supine blood pressures** – if the patient's symptoms do not occur in association with a fall in blood pressure, it should not be assumed that the observed postural hypotension is the cause of recurrent symptoms.
- **Pulse** – sustained or paroxysmal tachy- and brady-arrhythmias can cause presyncopal symptoms.
- **Nystagmus** – this can help in differentiating between central and peripheral causes of vertigo. In peripheral vertigo, nystagmus is horizontal and unidirectional, with the fast phase away from the lesion; visual fixation inhibits the nystagmus. Tinnitus and deafness can be present. In central vertigo, nystagmus can be in any direction. Vertical and purely torsional nystagmus are classically associated with central lesions, often with associated focal neurological signs.
- **Neurological examination** – this should include the cranial nerves. It will identify focal neurology that might suggest a central cause of vertigo such as stroke or multiple sclerosis. It can also identify factors that may contribute to disequilibrium such as peripheral neuropathy and reduced visual acuity.
- **Examination of gait** – this identifies features contributing to disequilibrium, such as a wide-based gait, and can provide evidence of focal neurological disease.
- **Bedside hearing tests** – hearing can be assessed simply at the bedside by gently whispering into each ear and asking the patient to repeat what was said. Weber's and Rinne's tests are used to differentiate between conductive and sensorineural hearing loss.
- **Provocation tests** – the Dix–Hallpike manoeuvre can be useful in patients who do not have vertigo and nystagmus at rest (Figure 3). It has a sensitivity of 50–88% in patients with BPPV. In patients with BPPV, there is a latent period of between a few seconds and 20 seconds before the onset of the nystagmus, which lasts <1 minute. The nystagmus is unidirectional and usually horizontal or rotational. It is also fatigable with repetition. In central disorders, there is no be a latent period before the onset of nystagmus, and it

Classification of dizziness

Type of dizziness		Associated symptoms	Episode duration	Possible aetiology
Vertigo	Central	Headache	Several minutes to 1 hour	Posterior circulation transient ischaemic attack
		Vomiting	Several hours	Migraine
		Double vision	Days	Posterior circulation stroke
		Staggering gait		Multiple sclerosis
		Clumsiness		Migraine
		Dysarthria		
		Numbness of the face or body		
	Peripheral	Hearing loss	Few seconds	Acute vestibular neuronitis
		Tinnitus	Few seconds to a few minutes	BPPV
		Feeling of fullness in the ear		Perilymphatic fistula
		Nausea and vomiting	Several minutes to 1 hour	Perilymphatic fistula
			Several hours	Acoustic neuroma
				Ménière's disease
				Perilymphatic fistula
Presyncope		Sweating	Few seconds to a few minutes	Orthostatic hypotension
		Blurred or tunnel vision		Situational syncope (e.g. post-micturition, post-cough)
		Palpitations		Vasovagal – mediated by emotional distress
		Breathlessness		Arrhythmia
		Fatigue		
Disequilibrium		Numbness of the feet	Weeks to months	Cerebellar disease
		Impaired vision		Parkinson's disease
		Gait disturbance		Gait disorders
				Peripheral neuropathy
				Reduced visual acuity
Other			Weeks to months	Psychogenic

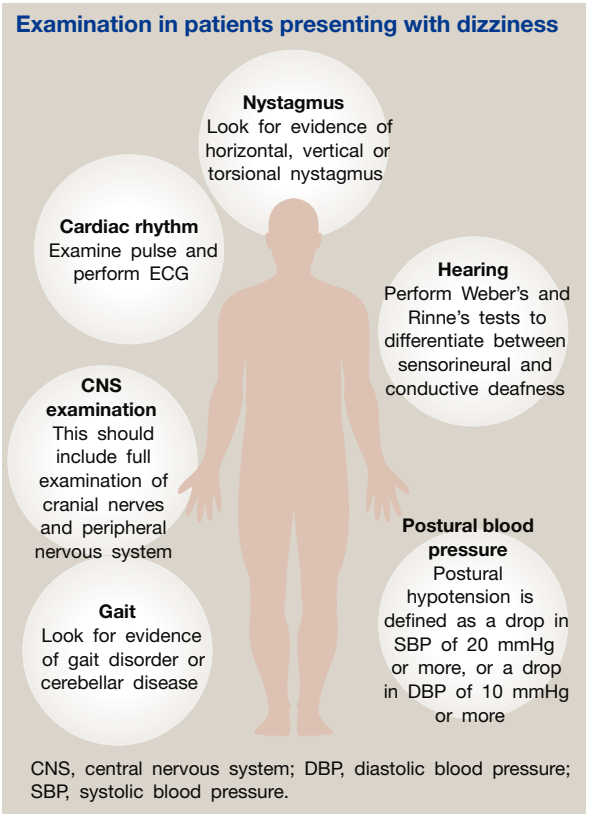

Figure 2

lasts >1 minute. There is no fatigability. The intensity of the vertigo is usually less than with peripheral disorders.

Further investigations

Routine investigations for all patients presenting with dizziness are rarely helpful, and the cause of dizziness can usually be elicited from a thorough history and examination.[4]

If neurological examination reveals previously unrecognized focal neurological signs suggestive of central nervous system disease, neuroimaging is indicated. If an arrhythmia is suspected, perhaps because of clearly paroxysmal episodes of presyncope without a clear cause, further cardiac investigations such as Holter monitoring are warranted.

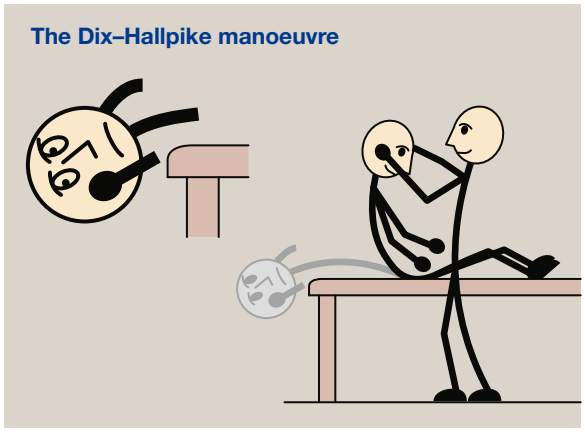

Figure 3

Management

Management depends on the underlying cause. Any contributing drugs should be stopped. It is useful to refer the patient to an optician if they have reduced visual acuity. Assessment by a physiotherapist is useful.

Postural hypotension

The first priority should be the withdrawal of any offending medications. Patients should be taught to stand up slowly and in stages. Thigh-high thromboembolic deterrent stockings can be useful. However, many elderly patients have difficulties in getting them on and off, and they are not suitable for patients with peripheral vascular disease.

Fludrocortisone, a synthetic mineralocorticoid, is often used in patients who do not respond to conservative measures. Treatment with fludrocortisone is started at 100 micrograms daily and can be gradually titrated up to a maximum of 400 micrograms daily. Discontinuation as a result of adverse effects is common. Adverse effects include peripheral oedema, cardiac failure, hypokalaemia and supine hypertension. Midodrine, a peripheral selective α_1-adrenergic agonist, acts by increasing arterial resistance, resulting in an increase in blood pressure, There is limited evidence that midodrine improves some symptoms of orthostatic hypotension. Adverse effects include supine hypertension, piloerection, scalp pruritis and urinary retention. It should initially be started at 2.5 mg three times daily and can be titrated up at weekly intervals to reach a maximum dose of 10 mg three times daily. The last daily dose should be taken at least 4 hours before bed. Supine hypertension often limits therapeutic use.

Benign paroxysmal positional vertigo

Particle-repositioning exercises such as the Epley manoeuvre are the mainstay of treatment in BPPV. In a meta-analysis, 74% of patients who used the Epley manoeuvre had clinical resolution of their symptoms within 1 month, compared with only 33% of controls. Brandt–Daroff exercises can be performed at home and can be useful for patients with recurrent episodes, although the response rates for these exercises are less than those obtained with the Epley manoeuvre.

Ménière's disease

A low-salt intake is recommended. Nicotine, alcohol and caffeine, which can result in vasoconstriction and impaired microvascular flow within the labyrinthine system, should also be restricted. There is little evidence for any of the drug therapies commonly used in Ménière's disease: two systematic reviews concluded that there was insufficient evidence to determine whether either betahistine or diuretics, both believed to act by reducing the volume of fluid in the inner ear, had any effect on Ménière's disease.[1] Vestibular rehabilitation can be useful for patients with residual balance problems after their vertigo has settled. For the minority of patients who do not respond to lifestyle interventions and medical management, interventional treatment such as intratympanic gentamicin or vestibular neurectomy can be used.

Migrainous vertigo

The treatment of acute episodes should include standard treatments for acute episodes of migraine, including analgesia, antiemetics and 5-hydroxytryptamine-1-receptor agonists such as sumatriptan. Known migraine triggers should be avoided, and prophylactic medications (e.g. tricyclic antidepressants, β-adrenoceptor blockers) can also help patients with recurrent episodes of migrainous vertigo.

Vestibular neuronitis

Symptomatic treatment in the form of antiemetics and vestibular sedatives (e.g. prochlorperazine, cyclizine) is often required in the first few days of an acute episode.[5] These treatments should not be used for more than a few days as they delay compensation mechanisms, and therefore long-term recovery.

A recent review found that, compared with placebo, corticosteroids improved the rate of complete caloric recovery after 1 month but not at 12 months. However, corticosteroids did not appear to improve symptoms of vertigo at 24 hours compared with placebo, and there is currently insufficient evidence to support the routine use of corticosteroids in acute vestibular neuritis.

Central causes of vertigo

These are generally best managed in a specialist environment by either a neurologist or a neurosurgeon. ◆

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Ten principles of good psychiatric prescribing

Peter M Haddad

Abstract

Psychopharmacology is not the sole province of psychiatrists. General practitioners (GPs) should be familiar with the management of common psychiatric disorders, especially depressive and anxiety disorders, as most people with these disorders are treated in primary care. Hospital physicians encounter many patients for whom psychiatric drugs have been prescribed, partly due to the increased prevalence of anxiety and depressive disorders in individuals with chronic medical disorders and the increased prevalence of diabetes mellitus and cardiovascular disease in people with schizophrenia and bipolar disorder. Psychiatric drugs can cause a wide range of adverse effects that can present to GPs and physicians. This article describes 10 principles of good psychiatric prescribing for the non-specialist.

Keywords Adherence; adverse effects; antidepressants; antipsychotics; drug interactions; drug safety; prescribing; psychopharmacology; SSRIs; teratogenic

Introduction

Pharmacological treatment is an important component of the management of many psychiatric disorders. A meta-analysis concluded that psychiatric drugs were not generally less efficacious than drugs used in treating physical disorders.[1] This article covers key principles in prescribing psychiatric drugs and is aimed at non-psychiatrists, in particular general practitioners and hospital physicians.

Key prescribing principles

Keep prescribing within licence

The non-specialist should ensure that psychiatric drugs are prescribed for licensed indications and within the licensed dose range. Prescribing for unlicensed indications or at above licensed dosages is not necessarily inappropriate, but there needs to be a sensible rationale to support such use and it should usually be recommended by a psychiatrist. Off-licence prescribing should be fully discussed with the patient, who should give informed consent that is documented in the notes.

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Key points

- Keep prescribing within licence
- Ensure the benefit of a medication outweighs the risks
- Start at a low therapeutic dosage and increase gradually
- Ensure a therapeutic trial of sufficient duration
- Avoid unnecessary polypharmacy
- Ensure prescribing is part of a wider treatment plan
- Involve the patient in treatment decisions
- Discuss adverse effects before and during treatment
- Explore adherence regularly
- When terminating treatment, consider withdrawing the drug gradually

Ensure the benefit of a medication outweighs the risks

If a drug is to be prescribed, the likelihood of it leading to improvement, and the clinical benefit of that improvement, should outweigh the risk of any adverse effects. The overall risk—benefit balance for the drug should be more favourable than that expected from no treatment/watchful waiting or alternative drug or psychological treatments. Assessing the risk—benefit balance involves clinical judgement and a knowledge of the evidence base for different treatments, and should take account of the patient's views. Table 1 summarizes some factors that should be considered when selecting a drug.

Start at a low therapeutic dosage and increase gradually

Most psychotropic drugs have a therapeutic dosage range, and it is impossible to predict the dose at which an individual patient will respond. Conversely, most adverse effects become more frequent and severe as the dosage is increased. Doses should be increased gradually, especially in elderly individuals. It is important, however, that following this principle does not inadvertently result in a patient being left permanently on a subtherapeutic dose of medication.

Ensure a therapeutic trial of sufficient duration

Improvement with antidepressant treatment in depressive and anxiety disorders tends to be gradual, and it can take several weeks before a clinically meaningful response occurs. Consequently, treatment should not be stopped prematurely because it is assumed that the drug is ineffective. Conversely, however, if there has been no detectable improvement after 4 weeks of treatment with a therapeutic dosage of an antidepressant, the likelihood of future improvement is low and treatment should be changed.[2]

Factors to consider in choosing the most appropriate medication for an individual

Patient age

- Elderly patients and children/adolescents are more vulnerable to many adverse effects
- In these groups, use lower dosages and slower titrations

Is the patient pregnant or likely to become pregnant? If yes:

- Obtain expert advice
- Avoid drugs that are known teratogens (e.g. lithium, valproate, carbamazepine)
- Choose a drug for which there is evidence of safety in pregnancy
- Consider adverse effects on the fetus and newborn other than teratogenesis
- Consider risk to the newborn if the mother plans to breastfeed while prescribing continues
- Consider risks to the mother and unborn child if psychiatric illness is not treated pharmacologically

Are there coexisting medical disorders?

Consider whether these increase the risk of specific drug adverse effects. In particular, consider:

- Cardiovascular disease
- Epilepsy
- Renal impairment
- Hepatic impairment
- Respiratory problems
- Gastrointestinal disorders including ulcers
- Dementia and cerebrovascular disease

Is there a potential for drug interactions?

- With other prescribed medication
- With over-the-counter medication
- With alcohol
- With illicit drugs

Is the patient at risk of overdose? If yes, consider:

- Prescribing a less toxic drug
- Dispensing in limited quantities
- Asking a relative to give out medication (if the patient agrees)

Is there a history of drug allergies or serious drug adverse effects?

- If yes, avoid these or similar drugs

What are the patient's views about drug treatment?

- In particular, are there specific adverse effects the patient wishes to avoid?

NB: The current Summary of Product Characteristics should be consulted to ensure prescribing is within licence.

Table 1

Avoid unnecessary polypharmacy

The simultaneous use of more than one psychiatric drug from the same British National Formulary class (e.g. two hypnotics, two antidepressants, two antipsychotics) is often termed 'polypharmacy' and should be avoided. In general, polypharmacy does not increase effectiveness but does increase the risk of adverse effects and can lead to drug–drug interactions. The complementary pharmacology of drugs within the same class, and the needs of the patient, occasionally make polypharmacy appropriate (e.g. prescribing a second antipsychotic in a patient with treatment-resistant schizophrenia who has only partially responded to clozapine at an optimal dosage), but these cases are relatively few and will usually be the province of a psychiatrist. A brief period of polypharmacy is appropriate when a cross-taper is used to switch between two drugs in the same class.

Ensure prescribing is part of a wider treatment plan

Pharmacological treatment should be accompanied by social and psychological treatment approaches, although the complexity of these can vary greatly. At its simplest, this can include assisting the patient to identify and manage stressors and reduce excess alcohol consumption. Psychological treatment includes the supporting and trusting professional relationship with the treating doctor and other clinicians, and extends to cognitive behavioural treatment and other psychological therapies.

Involve the patient in treatment decisions

Where possible, the patient should be involved in selecting a medication and given several options. Clinicians have an important role in providing information, and it is important that they dispel any misconceptions the patient has. Depending on the psychiatric disorder and its severity, patient choice can also include psychological treatment as an alternative, or adjunct, to drug treatment, or the option of no drug treatment and a period of watchful waiting. Adherence and patient satisfaction tend to be better when patients are involved in treatment decisions.

Discuss adverse effects before and during treatment

Psychotropic drugs can cause a wide range of adverse effects encompassing all bodily systems.[3] Adverse effects are clinically important as they can cause suffering, impair quality of life, stigmatize patients and lead to non-adherence with medication that can result in relapse of the underlying psychiatric disorder.[3] Common adverse effects, as well as rare but serious ones, should be discussed with a patient before starting a medication.

At subsequent consultations, it is important that the clinician enquires about adverse effects rather than simply waiting for the patient to volunteer information. For antipsychotics, which can cause a wide range of adverse effects, the use of an adverse effect checklist can help to ensure a systematic approach to monitoring. Depending on the prescribed medication, symptom enquiry may need to be supplemented by examination and blood tests. For example, monitoring body mass index and blood glucose and lipid levels is recommended during treatment with antipsychotics. If adverse effects are detected, their impact on the patient should be explored and options for treatment discussed. Some can be managed by simple lifestyle changes (e.g. sipping water if a drug causes a dry mouth), but others may require a dosage reduction or a switch to an alternative medication with less propensity to cause the particular adverse effect. Some adverse effects may require treatment in their own right (e.g. a statin may be used to treat raised cholesterol).

Explore adherence regularly

Poor adherence with psychotropic drugs, as with drugs used in general medicine, is common but often covert and a frequent reason for apparent non-response.[4] In addition to discussing adverse effects with patients and involving the patient in treatment decisions, the clinician should try to understand the patient's beliefs and concerns about their illness and

medication so that potential barriers to adherence can be identified and tackled.[4]

When terminating treatment, consider withdrawing the drug gradually

When psychiatric drugs have been prescribed for 4 weeks or longer and are to be stopped, with no plan to switch to another drug in that class, it is best to taper the drug down over several weeks rather than to stop it abruptly. This is to decrease the likelihood of discontinuation or withdrawal symptoms. These terms refer to a wide variety of symptoms that can occur within a few days of stopping a drug and can be understood in terms of pharmacological 'rebound'.[5] Withdrawal symptoms are well recognized with benzodiazepines, antipsychotics and antidepressants. If a patient is switching from one drug to another in the same class (e.g. from one selective serotonin reuptake inhibitor to another), it is usually possible to switch directly without tapering the first drug as the common pharmacology of the two drugs makes the occurrence of withdrawal symptoms unlikely.[5] ◆

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The physiology of ageing

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Abstract
Britain's ageing population is growing at its fastest rate to date, making it increasingly important for clinicians to understand the physiological changes associated with ageing and recognize the difference between changes secondary to ageing and changes that occur as a result of disease. Ageing is characterized by a progressive and heterogeneous decline in physiological reserve of all organ systems, albeit at different rates, which vary in different individuals. Cellular senescence, although beneficial early in life, is likely to contribute. An age-related decline in reserve and compromise of homeostasis have important clinical implications for the interpretation of physiological findings and for understanding the atypical presentations of illnesses in older patients.

Keywords Ageing; frailty; physiology; senescence

Key points

- All organ systems undergo physiological ageing albeit at different rates
- Age associated decline in renal excretory function is arguably the most clinically relevant change
- Cardiovascular ageing causes increased vascular stiffness associated with increasing pulse pressure; postural fall in systolic BP is another feature
- Reduction in muscle bulk and strength is an important physiological change that underlies the increasing fall rate in old age

Introduction

Individuals age at different rates and there is significant heterogeneity in physiological response. The hallmark of ageing is the progressive reliance on homeostatic reserves. Most organ systems show a physiological reduction in function with age, although the rate varies between systems within an individual as well as between individuals. There is reduced redundancy of function and ability to repair. The increased risk from loss of functional reserve is worsened by the increased prevalence of coexisting disease. An understanding of the relationship between physiological ageing and disease is often helpful in interpreting physical signs and investigation results. It is sometimes difficult to differentiate between physiological ageing and disease states. This article focuses on the physiological changes of ageing that have most clinical relevance.

The cardiovascular system

Cardiovascular ageing results in attenuated mechanical and contractile efficiency. Specific changes include arterial wall thickening, changes in vascular matrix composition with increased elastolytic and collagenolytic activity, and an increase in smooth muscle tone. Ultimately, vessels 'stiffen' with age, resulting in elevated systolic arterial pressures, increased systemic vascular resistance and increased cardiac afterload. These changes account for the common finding of isolated systolic hypertension, and, as the left ventricle has to work harder to eject blood into the stiffer aorta, the increased workload can eventually lead to left ventricular hypertrophy. Coupled with these changes, plasma renin activity (PRA) and aldosterone concentration both fall with age. In addition, the PRA response to upright posture is reduced or even absent, and the aldosterone response to sodium restriction is also markedly reduced.

Hypertrophy of myocytes in response to elevated afterload lengthens contraction time, with subsequent effects on the remainder of the cardiac cycle. Ventricular relaxation is delayed at the time of mitral valve opening, contributing to diastolic dysfunction. Early diastolic filling rate decreases with age and is partly compensated for by an increase in the rate of late diastolic filling, which is dependent on atrial contractile activity. This contributes to the positive correlation between left atrial size and age, the increased likelihood of lone atrial fibrillation and the greater effect of a change from sinus rhythm to atrial fibrillation on cardiac output.

Cardiac output is dependent on heart rate and stroke volume. Stroke volume falls, resulting in a fall in cardiac output. With exercise, the heart rate response falls, exaggerating the effect on cardiac output. In addition, there is progressive decline in the number of atrial pacemaker cells resulting in a decrease in intrinsic automaticity, which can predispose to the development of conduction defects and rhythm disturbances. Resting cardiac output remains stable with age, but the increase in cardiac output that is associated with exercise is attenuated, even in healthy ageing.

The venous system acts as a reservoir, holding 70% of circulating blood volume. Veins also stiffen progressively with age, reducing their compliance. The elderly patient is therefore particularly susceptible to abrupt changes in intravascular volume, as the venous capacitance system is less well equipped to buffer marked changes. Thus, physiological changes such as those associated with micturition, assuming an upright posture and following a meal are associated with more significant falls in blood pressure with increasing age.

These changes contribute to the reduced efficiency of the baroreflex – the extent to which heart rate rises in response to falls in blood pressure. Thus, ageing is associated with less

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efficient maintenance of cardiac output in the face of falls in blood pressure.

The nervous system

Central nervous system

Ageing produces a decrease in neural density. An estimated 30% loss of brain mass occurs by the age of 80 years, primarily involving grey matter. There is reduced production of important central neurotransmitters, including catecholamines, serotonin and acetylcholine, with secondary effects on mood, memory and motor function. There is an age-related deficiency of dopamine uptake sites and transporters, in addition to depletion of cortical serotonergic, α_2-adrenergic, β-adrenergic and γ-aminobutyric acid binding sites. These changes result in age-associated reduction in speed of processing and memory.

Peripheral nervous system

Motor, sensory and autonomic fibres are lost. There is a significant reduction in afferent and efferent conduction velocities, with a progressive decline in signal transduction rate within the brainstem and spinal cord. The number of muscle cells innervated by each axon falls, leading to denervation and muscle atrophy.

Autonomic nervous system

In youth, baseline autonomic tone is largely regulated by the parasympathetic division. With increasing age, tonic parasympathetic outflow decreases and sympathetic tone increases. Increased sympathetic nervous system activity contributes to increased systemic vascular resistance. Despite this increase in sympathetic activity, ageing is associated with a blunted response to β-adrenergic stimulation.

There is reduced ability of aortic arch and carotid sinus baroreceptors to transduce changes in arterial pressure, resulting in an attenuated heart rate response to changes in arterial pressure.

This combination of age-related autonomic and baroreflex dysfunction compromises haemodynamic homeostasis, as is evident in elderly patients who are taking diuretics or have a reduced fluid intake. This dysfunction is also associated with increased postural and postprandial hypotension. Diminished baroreceptor reflex activity also contributes to sinus node depression, carotid sinus syndrome and syncope in otherwise healthy elderly people.

The kidneys

Renal mass is approximately 50 g at birth, peaks at 400 g during the fourth decade and then gradually decreases to about 300 g by the ninth decade. Loss of renal mass is primarily cortical with relative sparing of the medulla, and correlates with the reduction in body surface area. With diminished glomerular lobulation and sclerosis of the glomeruli, there is reduced surface area available for filtration, contributing to an age-related decline in glomerular filtration rate (GFR). Glomerular basement membrane permeability increases, with a secondary increase in microalbuminuria and proteinuria. This occurs even in the absence of diabetes mellitus, hypertension and chronic kidney disease.

After the age of 30 years, renal blood flow declines progressively at a rate of 10% per decade. A greater proportion of the decline in renal blood flow occurs in the cortex, with a relative increase in blood flow to the juxtamedullary region. In the ageing population, the ability to vasodilate the afferent renal artery to increase renal plasma flow and GFR is impaired. This largely results from an imbalance between vasodilatory and vasoconstrictive influences in ageing kidneys.

Age-related structural changes in the kidney

- Reduction in renal mass
- Decreased cortical thickness
- Reduction in number of glomeruli
- Diminished glomerular lobulation
- Global glomerular and vascular sclerosis
- Tubular atrophy and fibrosis

Table 1

Age-related changes in structure and renal haemodynamics (Table 1) compromise the ability of the kidney to adapt to acute ischaemia and heighten susceptibility to acute kidney injury, including normotensive ischaemic nephropathy. It also sets the stage for progressive chronic kidney disease.

Davies and Shock — in a classic cross-sectional inulin clearance study — demonstrated that GFR decreases by about 8 ml/minute/1.73 m^2 per decade from the fourth decade onwards.[1] There is wide inter-individual variability in the age-related fall in estimated GFR, further amplified by the presence of vascular and renal disease.

Creatinine clearance is influenced by nutritional status, protein intake, muscle mass, body weight, gender and ethnicity.[2] As people age, muscle mass is reduced and daily urinary creatinine excretion decreases, accompanied by an age-related reduction in creatinine clearance. This means that interpretation of estimated GFR needs to be accompanied by a clinical assessment of muscle mass.

The combined effect of these changes is that declining GFR in older patients is accompanied by lower rises in serum creatinine than would occur in younger patients.

The respiratory system

A number of key age-related changes have been described (Table 2). Loss of elastic support of the airways contributes to increased collapsibility of the alveoli and terminal conducting airways, and accounts for varying effective lung volumes.[3] The closing capacity during normal tidal ventilation gradually increases and encroaches on the tidal volume, resulting in ventilation/perfusion mismatch and reduced arterial oxygen tension.

Key age-related changes in the respiratory system

- Decline in elasticity of the bony thorax
- Loss of muscle mass, weakening of the muscles of respiration and reduced mechanical advantage
- Decrease in surface area for alveolar gas exchange
- Decrease in central nervous system responsiveness

Table 2

This age-related change is reflected in the following formula to estimate normal arterial oxygen tension:

$PaO_2 = 13.3 - (age/30)kPa$

The pressure–volume curve of an older lung is shifted upward and to the left owing to a reduction in elastic recoil.[3] This difference in compliance is not uniform across the lung, but affects different regions to different extents. Some lung regions empty normally, whereas passive exhalation is slowed in others. With increases in respiratory rate, lung expansion becomes less effective in particular areas. This worsens the maldistribution of ventilation in relation to perfusion. Notably, the ventilatory response to either a hypoxic or hypercapnic stimulus is blunted in the older patient.

The gastrointestinal system

Ageing causes a variety of physiological changes in the oropharynx, oesophagus and stomach that increase the likelihood of oesophageal and gastrointestinal disorders.[4]

Swallowing is initiated by voluntary control and involves the coordinated contraction of skeletal muscles. Whereas the first stage of swallowing is voluntary, the second stage is governed by involuntary neural control, which leads to relaxation of the sphincter between the pharynx and oesophagus. The next stage relies on reflex transport and smooth muscle peristalsis. With age, contraction and relaxation become desynchronized, leading to less efficient deglutition.

Other changes with ageing include decreased secretion of hydrochloric acid and pepsin and an associated small rise in gastric pH. There is evidence of an age-related decline in the absorption of some substances absorbed by active mechanisms (e.g. vitamin B_{12}). It is not clear whether failure to increase calcium absorption in response to a low-calcium diet is a reflection of vitamin D deficiency or a primary malabsorption process associated with ageing.

Higher levels of neural control ranging from the cortex to the spinal cord become less effective. Prolonged transit time is associated with ageing and can result in constipation.

The immune system

Immune senescence predisposes the ageing individual to infection and delayed/ineffective recovery. Both the innate and acquired forms of the immune response are affected by age-related changes. Macrophage function, essential in phagocytosis and antigen presentation, becomes impaired with age. Dendritic cells decline in number but appear functionally unaffected. The complement pathway functions via cytolysis, opsonization and activation of inflammation, and demonstrates a blunted response in the presence of infection. B- and T-cell function, which form the mainstay of adaptive immunity, is similarly affected by age. Thymic involution starts at birth and reaches 90% by age 60 years. Helper T-cell function fails to rise with maximal efficacy. There is dysregulation of differentiation and reduced ability to proliferate under threat. The humoral response mediated by B cells is similarly impaired.

Other aspects of immunity that alter with age include cytokine function and regulation. Despite more non-specific activation, there is reduced capacity to generate important mediators including tumour necrosis factor-α, interleukin-1 and nitric oxide. Such changes increase the risk of reactivation of dormant viral and mycobacterial infections and predispose to new exogenous infection. Autoimmunity becomes more pronounced in the elderly population, with an increased frequency of autoantibodies against organ-specific and non-organ specific antigens.

The skin

Several structural changes in skin occur with ageing because of a combination of progressive degenerative change, intrinsic physiological change and superimposed extrinsic environmental insults. Physiological changes include impairment of barrier function, reduced epidermal cell turnover, and decreased keratinocyte and fibroblast number.[5] A reduced vascular network, particularly round hair bulbs and glands, and manifesting as fibrosis and skin atrophy, is also commonly observed. Changes in cutaneous function also occur, for example, a reduction in vitamin D synthesis. These changes, worsened by a reduced ability to effect skin repair, contribute to various pathologies including photo-ageing, vascular insufficiency that can cause stasis dermatitis, and an increased susceptibility to skin injuries, including pressure ulcers and skin tears. Parallel immune senescence renders the ageing skin vulnerable to pathology, such as viral and fungal infections, and neoplasia.

The haematological system

Although increasingly common with age, anaemia is not fundamentally related to ageing but to the presence of pathology. Although body iron stores increase, there is impaired reticulocytosis, such that the bone marrow cannot quickly respond to acute haemorrhage. Lymphocyte count reduces but total white blood cell, neutrophil and monocyte counts do not change. Although quantitatively constant, the qualitative response in response to stress is blunted, as observed from the reduced ability of neutrophils to migrate to sites of injury.

The endocrine system

The ability of target organs to respond to hormones often decreases with age. Changes in signal transduction often relate to post-receptor changes. Increasing carbohydrate intolerance occurs with ageing, but much of this is explained by other independent variables such as adiposity and fitness rather than ageing itself. The concentrations of many hormones change with age but with little demonstrable clinical relevance. In contrast, reduced testosterone secretion in older men is a contributory factor in the development of sarcopenia.

With age, there is a shift in the relationship between serum antidiuretic hormone (ADH) and serum osmolality, leading to higher serum ADH concentrations. This is probably secondary to altered baroreceptor function, and contributes to the increased occurrence of significant hyponatraemia.

The musculoskeletal system

Sarcopenia describes the loss of muscle strength that occurs with age. There is a 30% decline in muscle mass from the third to the eighth decade, and a reduced total cross-sectional fibre area. This physiological atrophy is a significant determinant of falls rate

with increasing age. The loss relates predominantly to type II fibres, resulting in a significant reduction in the maximum amount of oxygen consumed per kg per minute and force of contraction. Changes in the structure of collagen fibres within joints contribute to the loss in elasticity.

Men lose bone at a rate of 1% per year after the age of 50, and women lose bone at a rate of 2–3% per year after menopause. Loss of bone mineral density predisposes to osteopenia, osteoporosis and an increased risk of fracture. Factors including decreased activity, dietary calcium and oestrogen withdrawal also contribute. Weight-bearing and repeated strain lead to degenerative disease with a rising prevalence of symptomatic disease with age.

Thermoregulation

A variety of physiological changes give rise to reduced thermoregulation associated with ageing. The threshold for detecting changes in skin temperature rises and is associated with decreased vasomotor responses, reducing the contribution of the skin to conserving or losing heat. Two additional systems designed to increase heat production are also less effective – shivering threshold and effectiveness, and hepatic thermogenesis. The result is that older people are at increased risk of suffering adverse effects from hot and cold environments.

Physiological frailty

Frailty is a state of increased vulnerability to adverse outcomes and is dealt with elsewhere. Although the physiological changes we have described are not, by definition, evidence of pathology, they undoubtedly predispose to pathology. Interestingly, using purely physiological measures, physiological frailty has been derived in a similar way to pathological frailty; however, longitudinal studies have not yet been undertaken to determine the significance of the concept of physiological frailty.

Laboratory measures

In addition to parameters already referred to, such as creatinine and sex hormones, several laboratory parameters are known to change with age. Among these, serum albumin concentration is worthy of note; it is well known to fall in patients known to medical services – i.e., those with disease – with the rate of decline varying with disease burden. Serum albumin concentration also physiologically declines with healthy ageing at a lower rate than is seen in patients with chronic disease and with a rate that increases with age (Figure 1). The physiological change in serum albumin tends to remain within the reference range. ◆

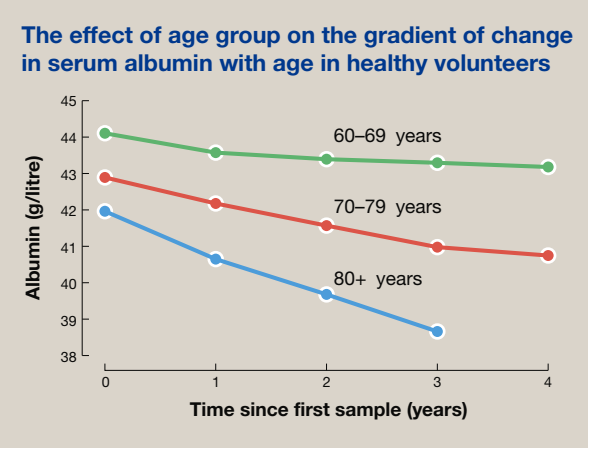

Figure 1

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