RACGP
Royal Australian College *of* General Practitioners

RACGP aged care clinical guide (Silver Book)

5th edition

Part B. Physiology of ageing

General principles

- Ageing can be defined as a failure to maintain homeostasis under conditions of physiological stress.
- Normal physiological changes occur due to ageing that are not a result of disease states.
- Normal physiological changes can affect an older person's reserves in times of stress and illness.
- Aged-related decline varies between individuals.
- All organ systems undergo physiological ageing but at different rates.

Introduction

The biology of ageing refers to the progressive accumulation of random molecular defects that accumulate in tissue and cells, which eventually result in age-related functional impairment of tissues and organs.

Genetic factors account for around 25% of the variance in human lifespan, and nutritional and environmental factors determine the rest.

A major accumulation of molecular damage is due to reactive oxygen species produced during the metabolism of oxygen to produce cellular energy. Oxidative damage results in:

- damage to nuclear chromosomal deoxyribonucleic acid (DNA)
- shortening of telomeres – ageing is associated with shortening of telomeres
- mitochondrial DNA and lipid peroxidation – this results in reduced cellular energy production, eventually causing cell death.

The rate at which damage occurs is variable, and the environment and nutrition have a role in oxidative damage in the ageing body. Insulin signalling pathways are important, and chronic inflammation is also important because it drives the production of reactive oxygen species.

Below is a list of the age-related physiological changes and associated clinical manifestations in various body systems. All information has been compiled from major physiology textbooks.[1,2,3]

Cardiovascular system

Age-related physiological changes

- Attenuated contractile and mechanical efficiency
- Arterial wall thickening
- Increased elastolytic and collagenolytic activity
- Increased smooth muscle tone
- Vessels stiffen with age – this increases systemic vascular resistance and cardiac afterload, which leads to increased workload
- Reduced plasma renin activity (PRA) and response to upright posture reduced or absent
- Reduced aldosterone concentration and response to sodium restriction
- Hypertrophy of myocytes lengthens contraction time
- Ventricular relaxation delayed at the time of mitral valve opening, which results in diastolic dysfunction
- Early diastolic filling rate decreases
- Late diastolic filling rate increases
- Left atrial size increases
- Left ventricle stiffens
- Aortic and mitral valves stiffen and develop calcific deposits
- Cardiac output falls
- Decreased responsiveness to catecholamines
- Reduced baroreceptor sensitivity
- Decline in atrial pacemaker cells leading to reduced intrinsic automaticity
- Resting cardiac output stable with age, but increase in cardiac output in response to exercise decreases
- Veins stiffen progressively with age, leading to reduced compliance, which results in the venous system having less capacity to buffer changes in intravascular volume
- Reduced maximum heart rate
- Dilatation of the aorta
- Reduced elasticity of conduit or capacitance vessels
- Reduced number of pacing myocytes in the sinoatrial node
- Endothelial dysfunction

Associated clinical manifestations

- Isolated systolic hypertension
- Higher resting blood pressure (BP)
- Left ventricular hypertrophy
- Diastolic dysfunction
- Increased risk of postural hypotension
- Slowing of intrinsic heart rate – falls of five to six beats per minute per decade
- Decline in maximum heart rate
- Reduction in maximum heart rate during exercise or stress (not modified by exercise training)
- Reduced heart rate variability
- Loss of sinus arrhythmia
- Increased likelihood of atrial fibrillation
- Increased risk of conduction defects
- Reduced cardiac rate response to exercise and stressors
- Reduced maximal oxygen consumption – aerobic capacity, cardiovascular fitness
- Reduced response to parasympathetic antagonists (atropine)
- Reduced response to β-adrenergic agonists
- Slowed heart rate response at exercise onset
- Reduced exercise tolerance
- Widening of aortic arch on X-ray
- Widened pulse pressure
- Increased venous stasis

Nervous system

Age-related physiological changes

Central nervous system:

- Neuronal loss
- Brain volume decreases after 65 years of age – greater amount of white matter than grey
- Cerebral blood flow decreases with deterioration of mechanisms that can maintain cerebral blood flow with fluctuation in blood pressure
- Reduction in neurotransmitter production, especially catecholamines, serotonin and acetylcholine
- Slowing of central processing
- Reduced dopamine uptake sites and transporters
- Reduced cortical α2-adrenergic, β-adrenergic and γ-aminobutyric acid (GABA) binding sites
- Neurofibrillary tangles and senile plaques (amyloid deposition) occur in normal ageing
- Anterior horn cell loss
- Dorsal column loss
- Slowed conduction times
- Increased ocular lens rigidity
- Increased ocular lens opacity
- Cochlear degeneration

Peripheral nervous system:

- Loss of motor, sensory and autonomic fibres
- Reduction in afferent and efferent conduction velocities
- Reduction in signal transduction rates within brain stem and spinal cord
- Number of muscle cells innervated by each axon decreases

Autonomic nervous system:

- Parasympathetic outflow decreases
- Sympathetic tone increases
- Increased sympathetic activity increases systemic vascular resistance
- Blunting of response to β-adrenergic stimulation
- Reduced ability of aortic arch and carotid sinus baroreceptors to transduce changes in arterial pressure

Associated clinical manifestations

- Cerebral atrophy
- Reduction in speed of processing, episodic and working memory, attention, and executive function
- Reduced mood
- Learning capacity and problem solving slows
- Benefits of exercise
- Increased risk of delirium
- Muscle weakness and wasting
- Reduced vibration sense, proprioception relatively preserved
- Increased risk of falls
- Reduced visual accommodation
- Presbyopia, abnormal near vision
- Reduced clarity of vision
- Reduced contrast sensitivity
- Impaired dark adaptation
- Presbycusis or high-tone hearing loss
- Increased sway during standing
- Reduced capacity to compensate for destabilising forces
- Reduced speed of simple and repetitive movements
- Altered control of precision movements
- Reduced gait velocity
- Reduced stride length
- Reduced time tolerated on single leg stand
- Slowed processing and reaction times
- Muscle atrophy and denervation

- Attenuated heart rate response to changes in arterial pressure
- Compromised hemodynamic homeostasis – care must be taken with the effects of diuretics and reduced fluid intake
- Increased postural and postprandial hypotension
- Sinus node depression
- Carotid sinus syncope
- Syncope

Renal system

Age-related physiological changes

- Reduction in renal mass or loss of nephrons
- Increased renal fat and fibrosis
- Increased glomerular membrane permeability
- Renal blood flow decreases from the age of 30 years
- Creatinine clearance reduces by about 10 ml/min every decade – creatinine clearance is influenced by nutritional status, protein intake, muscle mass and body weight
- Reduced creatinine production increases tubular secretion of creatinine, leading to stable creatinine
- Impaired fluid balance and regulation
- Impaired sodium and potassium acid excretion and conservation
- Reduced concentrating and diluting capacity
- Reduced serum renin and aldosterone
- Reduced vitamin D activation
- Decrease in the rate of urine flow and increase in urinary retention (benign prostatic hyperplasia [BPH] in men, but a decrease is also noted in women)
- Changes in urogenital mucosa
- Reduced tone in sphincters

Associated clinical manifestations

- Reduction in glomerular filtration rate (GFR)
- May overestimate creatine clearance despite decreased GFR
- Declining GFR in older people is accompanied by lower rises in serum creatinine, compared with younger populations
- Microalbuminuria and proteinuria
- Increased susceptibility to acute kidney injury
- Reduced capacity to adapt to acute ischaemia
- Increased vulnerability to contrast dye
- Compromised volume regulation under conditions of stress
- Increased risk of dehydration or overload
- Impaired drug metabolism and excretion
- Increased risk of urinary tract infections (UTIs)

Respiratory system

Age-related physiological changes

- Reduced lung elasticity and alveolar support
- Increased chest wall stiffness
- Loss of elastic support of airways
- Enlargement of alveolar ducts
- Reduced alveolar gas exchange surface area
- Increased anatomic dead space
- Ventilation-perfusion mismatch
- Reduced arterial oxygen tension
- Loss of muscle mass and weakening of muscles of respiration
- Reduced pulmonary capillary blood volume
- Decrease in central nervous system responsiveness
- Pressure volume curve of an older lung is shifted upward and to the left due to reduction in elastic recoil
- Reduced cough and ciliary action
- Reduced intervertebral space – reduced height, increased anterior-posterior chest diameter
- Diaphragm flattens and becomes less efficient

Associated clinical manifestations

- Reduced forced vital capacity (FVC)
- Reduced peak expiratory flow (FEV1)
- Total lung capacity stable, but increased residual volume
- Reduced inspiratory reserve
- Limitation of expiratory airflow and dynamic hyperinflation during maximal exercise
- Reduced arterial oxygen saturation
- Maldistribution of ventilation and perfusion
- Blunted ventilation response to hypoxic or hypercapnic stimulus
- Increased risk of infection

Gastrointestinal system and nutrition

Age-related physiological changes

- Reduced production of saliva
- Oesophageal contraction and relaxation become desynchronised
- Decreased lower oesophageal sphincter tone
- Half of all older people are infected with *Helicobacter pylori* where the presence of the bacteria increases with age
- Reduced secretion of hydrochloric acid and pepsin, and a small rise in gastric pH
- Age-related decline in the absorption of vitamin B12
- Reduced efficiency of calcium absorption because of reduced vitamin D receptors and circulating 25(OH) vitamin D

- Moderate intestinal villous atrophy
- Reduced gut contractility and slowed gastric emptying
- Prolonged gastrointestinal transit time because of attenuation of higher levels of neural control
- Increased colonic sensitivity to opioids
- Reduction in serum albumin
- Reduced liver mass – reduces by 20–40%
- Reduced blood flow – reduces by 50% between third and tenth decades
- Reduced cytochrome p450
- Reduced synthesis of vitamin K-dependent clotting factors
- Reduced low-density lipoprotein (LDL) receptors, reduced metabolism of LDL
- Decreased pancreatic mass and enzyme reserves
- Reduced lactase concentration
- Reduced basal metabolic rate
- Reduced energy requirements due to reduced muscle mass and activity levels

Associated clinical manifestations

- Increased risk of periodontal disease
- Increased risk of dental decay
- Less efficient deglutition due to less effective oropharyngeal food bolus transfer
- Increased risk of gastro-oesophageal reflux
- Aspiration more likely to contain organisms
- *H. pylori* infection
- Increased rates of gastritis
- Increased sensitivity to gastric irritants (eg nonsteroidal anti-inflammatory drugs [NSAIDs], bisphosphonates)
- Reduced absorption of micronutrients (eg vitamin B12 and folic acid)
- Reduced absorption of calcium
- Constipation
- Standard liver function tests (LFTs) minimally affected by age
- Lower serum albumin levels
- Reduction in clearance of drugs metabolised in the liver
- Lower amount of vitamin K antagonists required to anti-coagulate older people
- Increased serum LDL
- Reduced appetite

Immune system

Age-related physiological changes

- Innate and acquired immunity affected by ageing
- Macrophage function impaired
- Decreased cell-mediated immunity
- Complement pathway functions, which leads to blunted response to infection
- B-cell and T-cell responses attenuated, which are the mainstay of adaptive immunity
- Thymic involution virtually complete at around 65 years of age
- Helper T-cell activity impaired
- Humoral response mediated by B-cells is impaired
- Cytokine function and regulation, which leads to reduced capacity to generate tumour necrosis factor-α, interleukin-1 (IL-1) and nitric oxide
- Autoimmunity more pronounced

Associated clinical manifestations

- Predisposition to infection
- Delayed or ineffective recovery from infections
- Increased risk of reactivation of dormant viral and mycobacterial infections
- Reduced response to vaccines
- Increased risk of malignancy
- Increased frequency of autoantibodies
- Increased autoimmune disorders
- Cytokine profile consistent with chronic-low level inflammatory state

Skin

Age-related physiological changes

- Impairment of barrier function
- Reduced epidermal cell turnover
- Decreased keratinocyte and fibroblast number
- Reduced vascular network especially around hair bulbs/glands
- Reduced vitamin D synthesis
- Immune senescence
- Decreased dermal thickness, cellularity and elastin fibres
- Photo-ageing
- Altered sweating as a result of reduced number and function of sweat glands
- Ageing of hair
- Reduced melanocytes and Langerhans cells
- Reduced nail growth
- Reduced oil and sebum production

Associated clinical manifestations

- Reduced wound healing
- Fibrosis and skin atrophy
- Stasis dermatitis
- Increased susceptibility to skin injuries, including pressure ulcers and skin tears
- Increased vulnerability to viral and fungal infections
- Increased risk of skin neoplasia
- Wrinkles, pigmentation, telangiectasia
- Altered thermoregulation
- Greying of hair
- Diffuse alopecia
- Frontotemporal balding
- Reduced photoprotection
- Dry skin

Haematological system

Age-related physiological changes

- Reduced iron stores in the body
- Impaired reticulocytosis
- Lymphocyte count reduced; other white cell indices remain stable
- Qualitative changes in white cells (eg impaired neutrophil migration response to stress)
- Increased bone marrow fat
- Reduced functional reserve of bone marrow
- Propensity for clonal expansion of cells
- Decreased stem cells
- Platelet responsiveness to thrombotic stimulators increased
- Less responsive to erythropoietin
- Reduced total blood and plasma volume

Associated clinical manifestations

- Impaired bone marrow response to acute haemorrhage
- Slight decrease in haemoglobin and haematocrit
- Slight increase mean corpuscular volume (MCV) and osmotic fragility
- Increased risk of bleeding due to anticoagulants
- Increased risk of deep vein thrombosis
- Slowed erythropoiesis

Endocrine system

Age-related physiological changes

- Reduced target organ response to hormones
- Increased carbohydrate intolerance
- Reduced dehydroepiandrosterone (DHEA), testosterone secretion in older men
- Higher serum antidiuretic hormone
- Ovarian failure in women
- Deterioration in pancreatic β-cell function

Increased levels:

- Atrial natriuretic peptide
- Insulin
- Noradrenaline
- Parathyroid hormone
- Antidiuretic hormone
- Follicle-stimulating hormone (FSH)
- Luteinising hormone (LH)

Normal levels:

- Calcitonin
- Cortisol
- Adrenaline
- Prolactin
- Thyroxine

Decreased levels:

- Adrenocorticotropic hormone (ACTH)
- Thyroid-stimulating hormone (TSH)
- Growth hormone
- Insulin-like growth factor 1 (IGF-1)
- Renin
- Aldosterone
- Triiodothyronine (T3)
- Sex hormones

Associated clinical manifestations

- Contributes to sarcopenia
- Increased incidence of hyponatremia
- Increased bone resorption
- Increased risk of insulin resistance
- Impaired glucose tolerance

Musculoskeletal system

Age-related physiological achanges

- Decline in muscle mass – mainly type II (fast-twitch) fibres, which causes a reduction in VO2 max and force of contraction
- Type II muscle fibres are more affected than type I
- Loss of muscle mass in legs is greater than in arms
- Recovery of muscle following injury is slowed and incomplete
- Reduced oxidative capacity of muscle and greater fat mass
- Change in collagen fibres in joints – loss of elasticity
- Reduction in bone mass – cortical and trabecular bone; 3–5% loss of cortical bone per decade (10–20% during immediate post-menopausal period in women)
- Trabecular bone loss starts earlier and progresses faster
- Decreased osteoblast number and activity, but unchanged osteoclasts
- Resorption of bone exceeds formation
- Reduction in activity levels
- Weight-bearing exercise is frequently reduced in older people, which contributes to the negative calcium balance and loss of bone mineral
- Articular cartilage thins
- Joint flexibility decreases
- Decreased tensile stiffness of cartilage
- Decreased fatigue resistance of cartilage
- Reduced water content of cartilage

Associated clinical manifestations

- Progressive loss of muscle mass – 1–2% per year from the age of 40 years
- Contributes to sarcopenia and frailty
- Loss of 30–50% muscle mass by 80 years of age
- Longer and slower rehabilitation time following injury
- Rapid muscle mass loss when confined to bed
- Muscle strength declines – isometric, concentric, eccentric strength decline
- Age-related insulin resistance
- Increased risk of metabolic syndrome
- Altered volume of distribution for water-soluble drugs
- Osteopenia, osteoporosis, fracture, loss of height (1 cm per decade in those aged older than 50 years)
- Increased rate of falls and risk of fracture
- Reduced rate of repair post fracture
- Need to recommend weight-bearing exercise – increase weight-bearing time and increased loading forces
- Reduced flexion at hip, spine and ankle
- Osteoarthritis – pain, reduced joint mobility and strength

Thermoregulation

Age-related physiological changes

- Reduced thermoregulation
- Reduction of skin contribution to conserving or losing heat
- Reduced shivering threshold
- Reduced hepatic thermogenesis
- Temperature response to pro-inflammatory cytokines IL-1, tumor necrosis factor (TNF) and interleukin 6 decreases with age

Associated clinical manifestations

- Increased risk of adverse effects from hot and cold environments
- Reduced diurnal variation in body temperature
- Fever in older people is more subtle
- Oral temperature ≥37.8°C
- Persistent oral or tympanic temperature ≥37.2°C
- Rectal temperature ≥37.5°C
- Rise in temp ≥1.1°C baseline

Changes to approach to care

- Be vigilant when older patients are unwell, experience trauma or have surgery. Older people have slowed or poor recovery from stressors.
- Consider the whole person always – multiple organ systems are deteriorating; always think beyond the system of the presenting complaint and how your management will impact on other systems.
- Encourage early mobilisation and avoid prolonged periods confined to bed where possible. Older people experience rapid deconditioning.
- Recognise that signs and symptoms may be attenuated in older people – an older person may have a significant infection without manifesting a fever.
- Fluid and electrolyte homeostasis may be impaired – stress to patients and carers the importance of ensuring adequate hydration and avoiding hot environments.
- Older people are not hemodynamically robust – avoid rapid postural changes, make slow and gradual changes to blood pressure, take care with activities in the immediate postprandial period.
- Allow enough time in your consultation – to be effective, your communication will need to adjust to any cognitive and perceptual changes the patient is experiencing and examination of the patient will take longer due to reduced mobility of the older person.
- Due to poorer thermoregulation, temperature extremes should be avoided.
- Regularly review medications and consider which may be impacted by ageing physiology.
- Consider reducing the dose and increasing the interval of medication prescribing due to changes in renal function, liver function and reduced albumin.
- Avoid aggressive treatment changes and monitor the impact of treatment changes carefully.
- Regularly review the medical history and decide what remains relevant and whether the treatment or management remains appropriate.
- Actively promote healthy ageing where possible in your practice.
- Encourage older people to remain physically and socially active.
- Always consider interventions that maintain a patient's functionality.

- Recommend health and wellbeing preserving strategies including preventive activities in older age (eg immunisation, physical activity, falls, visual and hearing impairment, dementia).
- In making recommendations, take time to understand an older person – what they consider to be their problems, what is important to them and how their living circumstances can be optimised.

References

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