Physiology of ageing

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Abstract

The impact that ageing has on organisms is a complex interaction between the processes of ageing at a cellular, organ and integrated systems level, and the effects of environmental factors such as nutrition, infection and trauma. Recovery from an insult that triggers a pathological response is never complete. The incremental fall in possible performance is part of the progressive diversity in 'physiology' that is the true hallmark of ageing. In this article we will outline some of the physiological changes, particularly cardiorespiratory, associated with the ageing process that will be of relevance to anaesthesia.

Keywords Ageing; anaesthesia; cardiorespiratory; exercise; physiology; temperature

Royal College of Anaesthetists CPD Matrix: 1A01

Learning objectives

After reading this article, you should be able to:
- explain why PaO_2 reduces with age
- discuss why blood pressure is more prone to fluctuations with advancing age
- understand the importance of perioperative temperature regulation in the elderly

Theories of ageing

Ageing is a progressive physiological degeneration resulting in decline in function of organ systems and diminution of physiological reserve. It can be thought of as 'primary ageing,' the inevitable deterioration of cellular structure and function, independent of the disease and environment, and 'secondary ageing' caused by disease and environmental factors, such as smoking.[1]

The biological basis of ageing is incompletely understood with the many theories being divided into two main categories: programmed theories and damage theories. Theories of primary ageing tend to belong to the former category, where ageing follows a programmed biological timetable. Damage theories explain ageing in terms of accrued damage at a cellular or molecular level as a result of environmental insults or accumulation of toxic by-products of metabolism.

As our understanding of the ageing process deepens, the crossover between the groups of theories becomes apparent. 'Shortening of telomere theory' is considered a programmed theory of ageing. Telomeres, the DNA–protein complexes at chromosomal ends, shorten with each DNA replication, with cells undergoing apoptosis/senescence when telomere length reaches a critical limit acting as a 'biological clock'. However, evidence has linked lifestyle factors such as smoking and obesity with accelerated telomere shortening. The purported mechanism is via elevated levels of reactive oxygen species, itself a damage theory of ageing thus bridging the gap between theories and hinting at the true complexity of the underlying mechanisms.

Cognitive function

Ageing leads to a loss of cognitive function primarily via neuronal loss, decrease in neurotransmitter function and reduction in neurogenesis. In the ageing brain there are fewer synapses and synaptic plasticity is impaired. These changes result in slower thought processing, impaired higher understanding and increased vulnerability to delirium. These changes are independent of dementia, the prevalence of which is significantly increased in the older population.[2]

Physiological rhythms including the sleep cycle and the endocrine axis are also disrupted by the ageing process and deterioration in sensory functions such as sight loss or hearing impairment can also contribute to disruption in cognition.

Respiratory system

The structure of the upper airway changes little with ageing providing dentition is maintained. There are, however, age-related structural lung changes including decreased elastic recoil of the lung, increased chest wall rigidity and decreased force generating capacity of the respiratory muscles. These changes lead to a reduction in forced vital capacity, forced expiratory volume in 1 second (FEV_1) and vital capacity, and an increase in functional residual capacity (FRC).

The loss of some of the elastic recoil of the ageing lung causes the intrapleural pressures to become less negative allowing airway closure in the lowermost areas of the lung at higher volumes. Indeed, closing capacity reaches FRC by the age of 44 when supine and by 66 when upright. Lung base closure leads to a redistribution of inspired gas to apical areas of the lung which are underperfused (increased physiological dead space). It also leads to underventilation of the dependent areas of the lung (shunt). This is known as ventilation–perfusion mismatch and is clinically manifest as a reduced arterial oxygen tension with consequent increased risk of perioperative hypoxia in the elderly.

A further factor which contributes to the increase in the alveolar–arterial oxygen gradient $(PA-a)O_2$ seen with ageing is the decline in the lung diffusion capacity. This is commonly measured as the diffusion capacity of carbon monoxide (DLCO) which declines by 2–3 ml/minute/mmHg per decade of life.

The lung volume changes in the elderly are demonstrated in Figure 1.[3]

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Cardiovascular system

There are myriad structural, functional and molecular changes seen with ageing which are summarized in Table 1.[3]

Ageing is associated with stiffening of the large elastic arteries, i.e. the aorta and the carotid arteries. Enhanced pulse wave velocity (increases 40–50%) and prolonged ejection augment antegrade and retrograde arterial waves, elevating systolic and pulse pressures, cardiac work and oxygen demand.[4] Left ventricular hypertrophy ensues, as does tissue damage as a result of the increase in pulsatile flow, especially in high-flow organs, resulting in cerebrovascular events and renal impairment. Interestingly, occult diastolic dysfunction is common (50% of elderly patients with heart failure) with reduced early diastolic filling compensated by increased end-diastolic filling and consequent reduction of the echocardiographic early wave/atrial wave (E/A) velocity ratio.

Delayed or impaired baroreceptor response causes blood pressure lability, postural and postprandial hypotension and loss of sinus arrhythmia. This can exacerbate the arterial hypotension which is the most frequent haemodynamic complication of anaesthesia. In addition, with ageing there is a reduction in β-adrenoceptor sensitivity with a reduced response to exogenous β-agonists. This baroreflex deterioration is multifactorial: reduced arteriole compliance, blunted transduction of stretch signals, altered central neural processing, altered baseline efferent autonomic outflows, and dampened end-organ responsiveness. Pacemaker cell attrition (>50%) predisposes to atrial arrhythmias.

Exercise

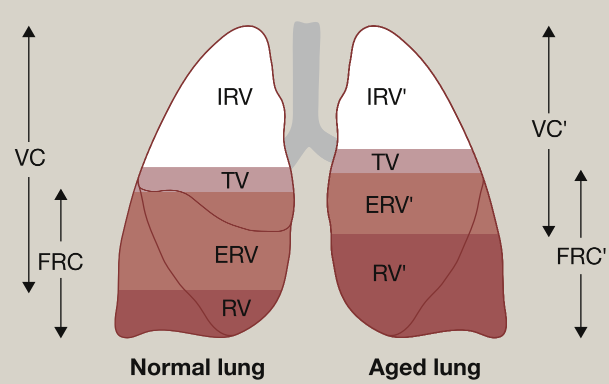
Physiological functional capacity (PFC) abruptly decreases after age 60–70 years, due to reduced maximal oxygen consumption (VO_2 max) and exercise velocity at lactate threshold.

Habitual aerobic exercise improves many physiological parameters including: PFC, VO_2 max, aerobic capacity, arterial compliance and endothelium dependent dilatation. In addition it raises total oxyradical scavenging capacity, fibrinolytic capacity (maintaining endothelial tPA levels), regenerates endothelium (maintains endothelial progenitor cell numbers) and reduces intima-media wall thickness. Resistance training particularly improves leg blood flow.

Energy and temperature regulation

Reduced total energy expenditure and physical activity reduce basal metabolic rate by 20%. Diminished gluconeogenesis, fat oxidation, Na^+/K^+ ATP-ase activity, and altered mitochondrial membrane proton permeability also contribute.[5] Age-related anorexia occurs due to impaired taste and smell, faster antral filling and early satiation (elevated cholecystokinin and reduced ghrelin levels). Multiple anorexic cytokines are implicated, for example, IL-1, IL-2 and IL-6, TNF-alpha and ciliary neutrotrophic factor. The consequent weight loss, linked to elevated leptin, is associated with pressure ulcers, hip fractures and cognitive impairment. Of note, negative energy balance in the context of longstanding cardiopulmonary disease likely reflects inadequate intake rather than hypermetabolism as traditionally taught, highlighting the importance of early feeding.

Lung volume changes associated with ageing



Note that with senescence, there is a decrease in the inspiratory reserve volume (IRV′), the expiratory reserve volume (ERV′), and the vital capacity (VC′). There is a corresponding increase in residual volume (RV′) and functional residual capacity (FRC′) such that the total lung capacity (TLC) remains about the same. Tidal volume (TV′) is unchanged.

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Figure 1

Effects of ageing on major structural and functional characteristics of the cardiovascular system

Cardiac changes		Vascular changes	
Heart weight	↑	Arterial wall thickness (intima-media)	↑
Cardiomyocyte dimensions	↑	Subendothelial collagen	↑
Cardiomyocyte number	↓	Elastin	↓
Collagen in cross-linking	↑	Elastin fragmentation	↑
Ejection Fraction	=	Proteoglycans	↑
Stroke volume	=	MMP activity	↑
Cardiac output	=	Intimal migration/ proliferation of VSMC	↑
Early diastolic filling	↓	Arterial distensibility	↓
End-diastolic filling	↑	Pulse wave velocity	↑
Chronotropic responsiveness to β-adrenergic stimuli/ catecholamines	↓	Total peripheral resistance	↑
Intropic responsiveness to β-adrenergic stimuli/ catecholamines	↓	Endothelial permeability	↑
Intropic response to digitalis glycosides	↓	Endothelial nitric oxide release	↓
Peak cardiac output to maximal effort	↓	Inflammatory markers/ mediators	↑
Lusitropic function	↓	SOD activity	↓
Release of natriuretic peptides	↑	β-Adrenergic-mediated vasodilation	↓

↓, diminished; ↑, augmented; = , unchanged; VSMC, vascular smooth muscle cells; SOD, superoxide dismutase; MMP, matrix metallo-proteinases.
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Table 1

Evidence describing the relationship between age and baseline core body temperature is inconsistent. However, the vasconstrictor response to cold and thermogenesis are attenuated. The physiological response to heat stress also fails with impaired sweating (reduced output per gland rather than loss of gland numbers) and inadequate skin blood flow response due to poor splanchnic redistribution and cardiac output.

Frailty

Frailty often describes a process of ageing that leads to a reduction in physiological reserve and in the ability to cope with stress, illness or injury. It occurs as part of physiological ageing independent of comorbidity, but can be exacerbated by environmental exposure, disease and poor nutrition.

Frailty is more common in women, its prevalence increasing with age. It can be summarized in the phenotype model, encompassing sarcopenia, reduced exercise tolerance, weight loss, weakness and fatigue. Alternatively, it can be described by the deficit accumulation model that characterizes frailty according to collective deficits that the patient has accrued in domains such as activities of daily living, concurrent illness and sensory loss, amongst others.[6]

A plethora of clinical assessment tools have emerged to identify and score frailty. The majority of scoring systems include objective tests such as the 6 minute walk test, hand grip strength, CPEX and cognitive assessment, although as of yet there is no consensus for a standard measurement of frailty.[7]

The relevance of frailty to the anaesthetist is reflected in the ability to identify and treat modifiable features and to risk stratify in order to improve outcomes and resource planning.

Drug handling

In the elderly, drug handling is altered, the cause being multifactorial. Reduced muscle mass and a greater ratio of fat to muscle alters drug pharmacokinetics. A reduction in hepatic function, and both hepatic and renal blood flow reduction leads to slower metabolism and excretion of drugs. This is frequently demonstrated in the older population by increased opioid sensitivity and vulnerability to opioid toxicity. Reduced cardiac output leads to slower drug onset; however, a reduction in circulating volume necessitates lower drug dosing to achieve similar blood concentration levels to those in the younger population. This accounts for the requirement for lower doses of propofol in older patients for the induction of anaesthesia.[8]

Avoiding anaesthesia-induced cognitive dysfunction in the elderly is becoming increasingly important. However, a recent Cochrane comparing TIVA with inhalational anaesthesia failed to show superiority of either technique despite TIVA exhibiting more rapid recovery and less postoperative nausea and vomiting. Research in this area is ongoing.

Summary

Age-related changes occur at a structural, functional and molecular level throughout the body systems precipitating an abrupt decline, aged around 60–70 years, in physiological functional capacity, aerobic performance, cardiovascular responsiveness and autonomic homeostasis. Perioperatively these changes will be further compounded by the stress associated with anaesthesia and surgery.

Reduced respiratory reserve in the elderly patient in the context of surgical stress, anaesthesia and/or systemic inflammation contributes to basal atelectasis, sputum retention and pneumonia. Baroreceptor and diastolic dysfunction together with loss of pacemaker function predispose to blood pressure lability, unforeseen pulmonary oedema and atrial fibrillation, respectively. Transient decline in renal function and cognitive function are commonplace and should be anticipated. Optimizing volaemic status, calorific intake, environment and avoiding triggers of delirium (e.g. short anaesthesia, good analgesia) are measures that should be employed routinely. Moreover, elderly patients are in particular risk of perioperative hypothermia with dampened responses to heat and cold stress.

Habitual exercise (e.g. brisk daily walking) and adequate (but not excessive) calorific intake appear to decelerate most detrimental cardiopulmonary and metabolic processes and undoubtedly contribute to a survival advantage in the setting of major surgery and critical illness. Preoperative assessment, with cardiopulmonary exercise testing can help identify those elderly patients who would benefit most from prehabilitation and may be a useful tool within critical care follow-up clinics in assessing recovery from critical illness. ◆

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