

TABLE 3.1. Major changes in system.

Endocrine system

Impaired glucose tolerance (fasting glucose increased 1 mg/dl/decade; postprandial increased 10 mg/dl/decade)
 Increased serum insulin and increased HgbA1C nocturnal growth hormone peaks lost, decreased 1GF-1
 Marked decrease in dehydroepiandrosterone (DHEA)
 Decreased free and bioavailable testosterone
 Decreased T3
 Increased parathyroid hormone (PTH)
 Decreased production of vitamin D by skin
 Ovarian failure, decreased ovarian hormones
 Increased serum homocysteine levels

Cardiovascular

Unchanged resting heart rate (HR), decreased maximum HR
 Impaired left ventricular filling
 Marked dropout of pacemaker cells in SA node
 Increased contribution of atrial systole to ventricular filling
 Left atrial hypertrophy
 Prolonged contraction and relaxation of left ventricle
 Decreased inotropic, chronotropic, lusitropic response to beta-adrenergic stimulation
 Decreased maximum cardiac output
 Decreased hypertrophy in response to volume or pressure overload
 Increased serum atrial natriuretic peptide (ANP)
 Large arteries increase in wall thickness, lumen, and length, become less distensible, and compliance decreases
 Subendothelial layer thickened with connective tissue
 Irregularities in size and shape of endothelial cells
 Fragmentation of elastin in media of arterial wall
 Peripheral vascular resistance increases

Blood pressure

Increased systolic blood pressure (BP), unchanged diastolic BP
 Beta-adrenergic-mediated vasodilatation decreased
 Alpha-adrenergic-mediated vasoconstriction unchanged
 Brain autoregulation of perfusion impaired

Pulmonary

Decreased FEV₁ and FVC
 Increased residual volume
 Cough less effective
 Ciliary action less effective
 Ventilation-perfusion mismatching causes PaO₂ to decrease with age: $100 - (0.32 * \text{age})$
 Trachea and central airways increase in diameter
 Enlarged alveolar ducts due to lost elastic lung parenchyma structural support result in decreased surface area
 Decreased lung mass
 Expansion of thorax
 Maximum inspiratory and expiratory pressures decrease
 Decreased respiratory muscle strength
 Chest wall stiffens
 Diffusion of CO decreased
 Decreased ventilatory response to hypercapnia

Hematologic

Bone marrow reserves decreased in response to high demand
 Attenuated reticulocytosis to erythropoietin administration

Renal

Decreased creatinine clearance and GFR 10 ml/decade
 Decrease of 25% in renal mass, mostly from cortex with a relative increased perfusion of juxtamedullary nephrons
 Decreased sodium excretion and conservation
 Decreased potassium excretion and conservation
 Decreased concentrating and diluting capacity
 Impaired secretion of acid load
 Decreased serum renin and aldosterone
 Accentuated ADH release in response to dehydration
 Decreased nitric oxide production
 Increased dependence of renal prostaglandins to maintain perfusion
 Decreased vitamin D activation

(Continued)

TABLE 3.1. *Continued*

Genitourinary (GU)

- Prolonged refractory period for erections for men
- Reduced intensity of orgasm for men and women
- Incomplete bladder emptying and increased postvoid residuals
- Decreased prostatic secretions in urine
- Decreased concentrations of antiadherence factor Tamm–Horsfall protein

Temperature

- Impaired shivering

Regulation

- Decreased cutaneous vasoconstriction and vasodilation
- Decreased sweat production
- Increased core temperature to start sweating

Muscle

- Marked decrease in muscle mass (sarcopenia) due to loss of muscle fibers
- Aging effects smallest in diaphragm (role of activity), more in legs than arms
- Decreased myosin heavy chain synthesis
- Small if any decrease in specific force
- Decreased innervation, increased number of myofibrils per motor unit
- Infiltration of fat into muscle bundles
- Increased fatigability
- Decrease in basal metabolic rate (decrease 4%/decade after age 50) parallels loss of muscle

Bone

- Slower healing of fractures
- Decreasing bone mass in men and women, both trabecular and cortical bone
- Decreased osteoclast bone formation

Joints

- Disordered cartilage matrix
- Modified proteoglycans and glycosaminoglycans

Peripheral nervous system

- Loss of spinal motor neurons
- Decreased vibratory sensation, especially in feet
- Decreased thermal sensitivity (warm–cool)
- Decreased sensory nerve action potential amplitude
- Decreased size of large myelinated fibers
- Increased heterogeneity of axon myelin sheaths

Central nervous system

- Small decrease in brain mass
- Decreased brain blood flow and impaired autoregulation of perfusion
- Nonrandom loss of neurons to modest extents
- Proliferation of astrocytes
- Decreased density of dendritic connections
- Increased numbers of scattered neurofibrillary tangles
- Increased numbers of scattered senile plaques
- Decreased myelin and total brain lipid
- Altered neurotransmitters, including dopamine and serotonin
- Increased monoamine oxidase activity
- Decrease in hippocampal glucocorticoid receptors
- Decline in fluid intelligence
- Slowed central processing and reaction time

Gastrointestinal (GI)

- Decreased liver size and blood flow
- Impaired clearance by liver of drugs that require extensive phase I metabolism
- Reduced inducibility of liver mixed-function oxidase enzymes Mild decrease in bilirubin
- Hepatocytes accumulate secondary lysosomes, residual bodies, and lipofuscin
- Mild decrease in stomach acid production, probably due to nonautoimmune loss of parietal cells
- Impaired response to gastric mucosal injury
- Decreased pancreatic mass and enzymatic reserves
- Decrease in effective colonic contractions
- Decreased calcium absorption
- Decrease in gut-associated lymphoid tissue

TABLE 3.1. *Continued*

Vision	
	Impaired dark adaptation
	Yellowing of lens
	Inability to focus on near items (presbyopia)
	Minimal decrease in static acuity, profound decrease in dynamic acuity (moving target)
	Decreased contrast sensitivity
	Decreased lacrimation
Smell	
	Detection decreased by 50%
Thirst	
	Decreased thirst drive
	Impaired control of thirst by endorphins
Balance	
	Increased threshold vestibular responses
	Reduced number of organ of Corti hair cells
Audition	
	Bilateral loss of high-frequency tones
	Central processing deficit
	Difficulty discriminating source of sound
	Impaired discrimination of target from noise
Adipose	
	Increased aromatase activity
	Increased tendency to lipolysis
Immune system	
	Decreased cell-mediated immunity
	Lower affinity antibody production
	Increased autoantibodies
	Facilitated production of anti-idiotypic antibodies
	Increased occurrence of MGUS (monoclonal gammopathy of unknown significance)
	More nonresponders to vaccines
	Decreased delayed-type hypersensitivity
	Impaired macrophage function (Interferon-gamma, TGF-beta, TNF, IL-6, IL-1 release increased with age)
	Decreased cell proliferative response to mitogens
	Atrophy of thymus and loss of thymic hormones
	Accumulation of memory T cells (CD-45+)
	Increased circulating IL-6
	Decreased IL-2 release and IL-2 responsiveness
	Decreased production of B cells by bone marrow

$208 - (0.95 \times \text{age})$ for maximum heart rate attained with exercise. It is likely that women have lower maximum heart rates at age 30 and a more gentle fall with aging than this equation predicts. This decrease in maximum heart rate responsiveness results from a combination of factors. First, primary aging decreases the intrinsic heart

rate (the heart rate in the absence of sympathetic and parasympathetic stimulation), as well as invokes reserves just to maintain resting heart rate. Data from Jose,⁶ although regrettably including only a modest number of elders, show a decrease in intrinsic heart rate from 120–130/min to less than 80. There is no difference

FIGURE 3.3. Revised schematic of homeostenosis. In comparison to Figure 3.1, this diagram shows that maintaining homeostasis is a dynamic process. The older person employs or consumes physiologic reserves just to maintain homeostasis, and therefore there are fewer reserves available for meeting new challenges.

