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 FEV_1 and FVC
- Increased residual volume
- Cough less effective
- Ciliary action less effective
- Ventilation–perfusion mismatching causes PaO_2 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 erythropoeitin 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-idiotype 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 regretfully 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

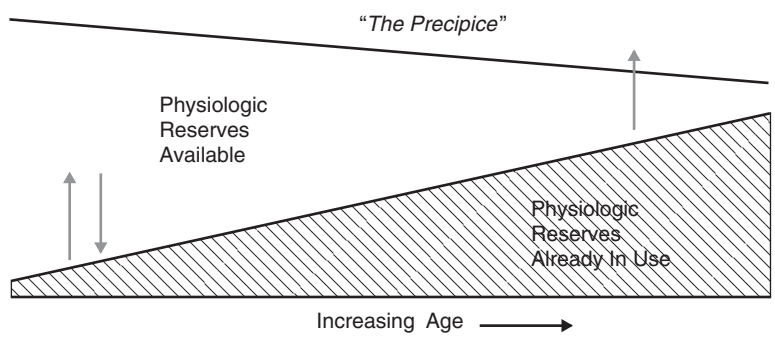

Figure 3.3. Revised schematic of homeostenosis. In comparison to Figure 3.1, this diagram shows that maintaining homeostasis is a dynamic process. The older person employs or consumes physiologic reserves just to maintain homeostasis, and therefore there are fewer reserves available for meeting new challenges.