UNIT 1 BIOLOGICAL CHANGES

Structure

1.0 OBJECTIVES

After reading this unit, you will be able to:

- describe what is aging;
- enumerate the biological changes in aging; and
- discuss the cellular mechanism of aging.

1.1 INTRODUCTION

In the previous block you have learnt about the detailed demographic history and epidemiology of aging.

In this unit you will get aquainted with the various definitions of aging. As such there are different groups of thoughts regarding the idea of aging process and exactly what is aging. It is generally defined as a process of deterioration in the functional capacity of a person occurring after maturity and resulting from structural changes related to the process in chronological order.

Subsequent to this discussion the changes in different physiological systems and regulatory processes that occur in relation to the advancement of the age have been described in detail. You will also learn the cellular and molecular mechanism of aging process at the end of this unit.

1.2 WHAT IS AGING

Aging means predictable, progressive, universal deterioration in various physiological systems, mental and physical, behavioural and biomedical. Fig. 1.1 shows the decline in the various

physiological parameteres in aging humans. There is no universal definition of aging. Aging is a gradual and steady process which takes place over the entire life span of an organism. Aging is generally defined as a process of deterioration in the functional capacity of organism that occurs after maturity resulting from structural changes and it is a consequence of the inability of the organism to restore homeostasis when given a challenge. Any alteration in homeostasis must be non-reversible, independent of pathological condition and contribute significantly to general loss in function or death. But at the same time, aging can also involve psychological growth in capacities for strategy, sagacity, prudence, wisdom, reasoning and experience. One should thus distinguish between aging of the population and individual aging.

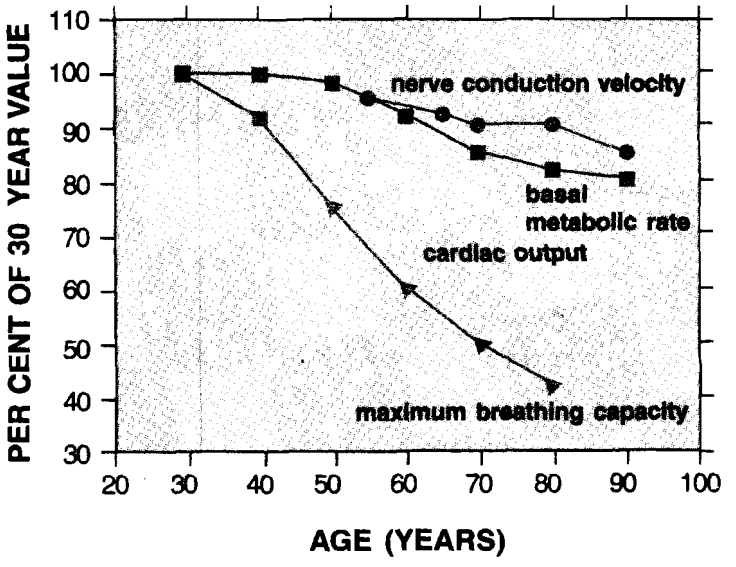

Fig. 1.1: Decline in physiological parameters in aging humans

In describing the aging of working aged people, one should take into consideration at least three factors besides biological aging viz., health, life style and work. These factors interact strongly and it must therefore be emphasized that preventive strategies to help older workers should be multifactorial.

1.3 BIOLOGICAL CHANGES IN AGING

The aging human experiences a gradual decline in almost all body functions, mainly in the cardiac performances, respiratory and renal functions, sensory faculties, nerve impulse conduction, muscle strength, endurance, agility and ability to maintain coordinated muscular effort, which may be due to structural and functional changes resulting in inability to restore homeostasis.

The process of aging also results in reduced ability to maintain an internal environment in the face of external environmental stresses. Since, the aging process affects the various factors regulating heat loss and metabolic heat production of the body, the thermoregulatory efficiency is also impaired to a certain extent. Further, age also affects the capacity of work – both physical as well as mental, and is also accompanied by deterioration of most psychophysiological functions as age advances. Thus, a need is always felt to understand the various physiological and psychological correlates responsible for functional alteration with the advancement of age. Table1.1 shows schematically how the different physiological functions are altered with advancement of age.

Table 1.1: Physiological Changes in Aging

Cardiovascular	**Special senses**
Total cell mass↓	Reaction speed ↓
Fat storage up to 65-70 ↑	Acuity ↑
Central and Peripheral	
Neural network ↓	**Thermo-regulation**
Myocardial cells ↓	Tolerance to heat ↓
Tissue compliance/dispensability ↓	Sweating ↓
	Vasodilation ↓
	Skinfold thickness ↑
Respiratory	**Aerobic Power**
Bronchial cilliary function ↓	Decline
Dyspnoea ↑	Self paced : Machine paced
Mucous accumulation ↑	Compliance ↓
Alveolar exchange surface ↓	
Dead space ↑	
Nervous system	**Muscle strength**
Cell and fibre loss ↑	Muscle mass ↓
Neuro-axonal degeneration ↑	Muscle diameter ↓
Central conduction ↓	Speed of contraction ↓
Catecholamine synthesis↓	Max. voluntary strength ↓
Catecholamine disposal ↑	Control of movements ↓
Bone	**Musculoskeletal disorders**
Mass and Mineralization ↓	Tendon elasticity ↓
Osteoporosis ↑	Joint flexibility ↓

Now we will discuss the structural and functional changes in different systems in detail in the following sub-section.

1.3.1 Cardiovascular System

The predominant structural alteration in aging humans is the gradual decline of total cell mass associated with increased fat storage, up to age 65-70 year, with a subsequent decline in body fat. This reduction in metabolic tissue mass and still more of body water has obvious influences on the demands for blood supply and thereby also on the design, filling, functional performance and overall control of the cardiovascular system. There are at least four general manifestations of normal aging that have important consequences for cardiovascular performance:

i) A slowly progressive reduction of both central and peripheral neuronal networks is a normal consequence of aging. This affects not only psychomotor mechanism but also the central integration of the neurohormonal systems controlling cardiovascular performance.

ii) The number of myocardial cells decline with age, although compensating hypertrophy may regenerate ventricular mass.

iii) There is a slow decline in tissue compliance or distensibility and this importantly affects the cardiovascular system.

iv) A modest decline in BMR and oxygen consumption per unit body weight occurs with aging. In addition, the common age related decline of physical activity leads to a lowered cardiovascular performance.

Changes in life style occur concomitantly with advancing age. These changes include an individual's "habits" of physical activity, eating, drinking, smoking, thinking, etc. It is likely that many changes in cardiovascular function that have been attributed to aging process are in part due to the sedentary life style or the presence of occult coronary disease that accompanies aging. With advancing age, because the prevalence of disease increases sharply and major changes in life style occur, the effect of aging, disease, and life style on cardiovascular system are intertwined. This is described in Fig. 1.2, interactions among these factors can alter the nature of each factor.

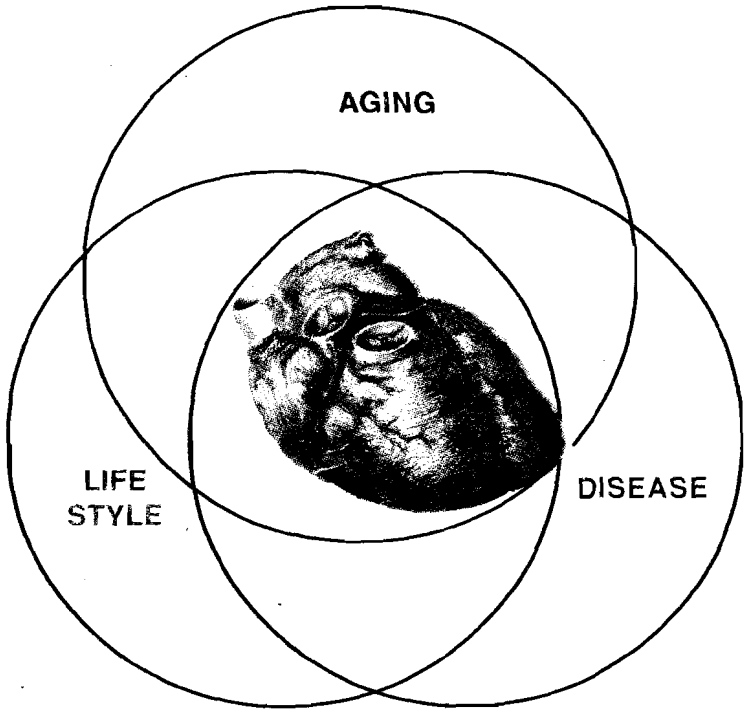

Fig. 1.2: Changes in life style and diseases occur with advancing age. Interactions among these factors and aging that makes it difficult to identify or characterise the presence of an aging process in the heart.

Anatomic Changes in the Aging Human Heart

A number of different changes have been observed in the aging human heart which includes alterations in size and geometric contour. The left ventricular cavity tends to become smaller because of the reduced physical demands and activity in old age. Enlargement of the left atrium, widening of the aorta as a result of the lost of elasticity, shifting of the aorta to the right, and great rigidity and thickening of heart valves place the aged human heart at a mechanical work disadvantage that may impair heart function. The atrioventricular valves demonstrate marked disruption of architecture, progressive loss of cellularity, elastosis of the spongiosa and fibrosa, and a marked increasing endocardial hypertrophy. These changes are listed in detail in Table 1.2.

Table 1.2: Anatomic Changes in the Aging Human Heart

• Heart size same or smaller
• Smaller left ventricular cavity, larger left atrium, dilation of aorta as a result of loss of elasticity and rightward shift of aorta
• Greater rigidity and thickening of valves
• Aging aorta and great vessels due to increased collagen-elastin ratio

Coronary artery atherosclerosis can modify myocardial function by reducing myocardial blood flow. Although coronary atherosclerosis is usually perceived as a problem of advanced age, this perception is somewhat incorrect. This vascular disease begins at a young age, its severity increases progressively over the entire adult age span, and when threshold severity is reached symptoms or signs of its presence become evident. Fig. 1.3 illustrates the prevalence of fibrous plaques, calcific lesions, and stenosis in coronary arteries in a subset of the sample. A major point of interest here is that between the age of 15 and 24 years the early manifestations of this disease, i.e. fibrous plaques, are present in 30 per cent of hearts. By age 35 to 44, coronary arteries from more than 85 per cent of hearts demonstrated this finding. Calicification also increased with age by age 55 to 64, more than 60 per cent of hearts exhibited vascular endothelial calcification. However you should know that the most important vascular abnormality to consider regarding myocardial function is not the presence of fibrous or calcific lesions but, rather, vessel narrowing or stenosis, by age 55 to 64 half of all hearts studied have 50 per cent or more occlusion of atleast one of the three major coronary arteries.

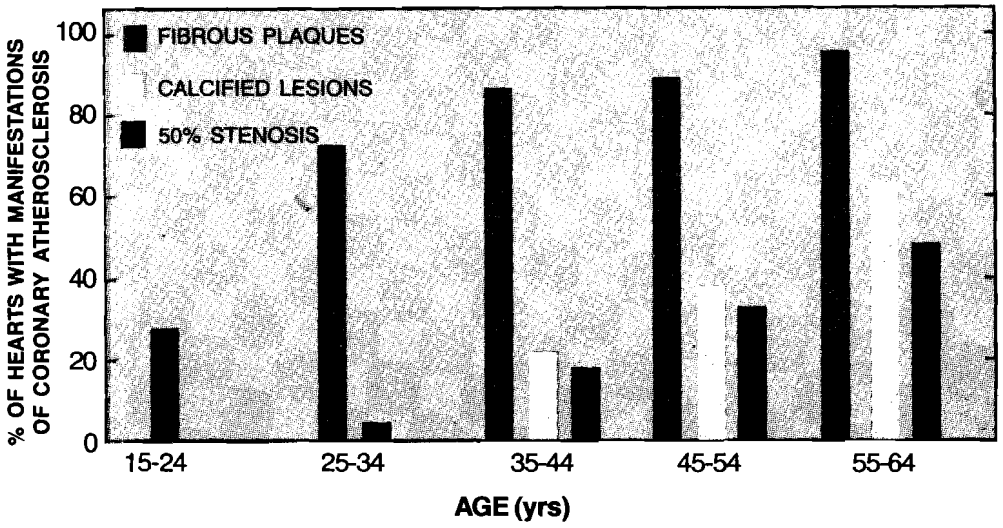

Fig. 1.3: Manifestations of atherosclerosis in coronary arteries from hearts of individuals of a New Orleans Caucasian population. The data for fibrosis and calcifications were derived from those individuals who died from accidents, infections and miscellaneous causes other than heart disease. Data for stenotic lesions were derived from individuals of this population who died from any cause.

Cardiovascular Performance and Maximum Work Capacity

There is ample evidence to suggest that cardiac output during exercise fail to supply the required flow for the aged people.

1.3.2 Respiratory System

Shortness of breaths (dyspnoea) can be a perfect normal consequence of aging but can also be an important symptom of cardiovascular or lung disease. Bronchial ciliary function declines with age and dependent mucous accumulation may reduce ventilation in lower parts of the lungs in the elderly. Pulmonary distensibility and total alveolar exchange surface reduce but 'parallel coupled' dead space increases with age. With aging the lungs lose elasticity, but functional residual capacity increases, which at age of 60 years is approximately 60 per cent of the total lung capacity. It is difficult to judge to what extent such effects are a consequence of environmental and life style factors like smoking, rather than due to aging *per se*.

The major changes are seen in the vital capacity (VC), which decreases with age after 20-35, and the residual volume (RV), which increases with age. Total lung capacity (TLC) which is the sum of the VC and RV, changes little with age. The forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1) decrease with age, as do the flow rates. The functional residual capacity increases with age. Lung elastic recoil decreases with age as the lung becomes more dispensable. Chest wall compliance decreases with age and expiratory muscles

become weaker, both leading to the increase in RV. The total volume remains almost unchanged or slightly reduced. However there is a significant decrease in the maximum voluntary ventilation (MVV) with age.

The ultimate function of respiratory system is gas exchange, and arterial oxygen pressures (PaO_2) are reduced with age. Fibrosis of small pulmonary artery intima is common, increasing vascular resistance. The vascular response to hypoxia becomes blunted.

It has been observed that there is a definite change in the host defence mechanisms with aging, leading to increases in the pathogenicity and virulence of microbiological organisms. Pneumonia and influenza are significant infections in the elderly and produce high mortality rates that increase with age. The mucociliary clearance mechanisms affected in aging by loss of cilia, reduced ciliary activity, and atrophy of mucosa and nasal secretory glands. Reactivation of granulomatous diseases, e.g., tuberculosis, occurs more frequently in the elderly as well.

Check Your Progress 1

1) Define aging.

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2) What are the salient changes in aging human heart?

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3) In which part of the lung ventilation reduces in the elderly and why?

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4) What happens to the functional residual capacity in the aged people?

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5) What happens to the following parameters with age like, vital capacity, total lung capacity, forced vital capacity, maximum voluntary ventilation and tidal volume?

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1.3.3 Nervous System

The weight of the brain reaches its peak of approximately 1.4 kg in the early 20s and then undergoes a slow decline. By age 80, the loss reaches 7 per cent or about 100 g. During the aging process the ratio of grey to white matter changes, indicating that there is some differential loss of cells and fibers. Cells are lost from the cerebral cortex. The Golgi type II cells and pyramidal cells are particularly affected. Significant changes occur in both neurons and supporting cells. There occurs neuroaxonal degeneration. The perfusion of young adult brain occurs at 50 to 60 ml/min/100 g of tissues which reduces to 40 ml/min/100 g tissues in very old age. Typical of aging is the slowing of many neural processes. Most of this slowing occurs in central processes, where conduction over multisynaptic pathways is substantially delayed. A limited number of studies in humans have shown that the level of enzymes concerned with catecholamine synthesis decreases with age, while the major enzymes involved in the disposal of the catacholamines, monoamines oxidase, increases in concentration in several parts of the brain. At the segmental level of spinal organization, the simple stretch reflexes are often depressed.

EEG and Sleep

A slowing of alpha rhythm is typical of the healthy older person. Sleep studies of young and elderly persons have revealed the following findings:

1) **Older persons take longer to fall asleep than do the young.**
2) **Total time spent asleep is not different between groups.**
3) **Old persons wake-up more frequently during the night and spend a longer time awake on each occasion. The older persons thus spend longer total time in bed.**
4) **The transition between sleep and wakefulness is abrupt in old people and considered 'light sleepers'.**

1.3.4 Endocrine System

Apart from the hormonal changes that accompany female menopause, however, functional alterations in aging endocrine glands tend to be subtle and frequently can be revealed only by challenges to the regulatory and feedback systems of the hypothalamus and pituitary.

Studies of circulating hormone play an important role in understanding the age-related changes in hormone secretion. Most hormones do not circulate at constant levels but fluctuates considerably. The largest age-related difference occurs at night when testosterone levels are highest in the young. Similarly, growth hormone levels are considerably lower in the elderly than in the young. But this difference cannot be detected if measurements are made only during the day. In young adults, growth hormone secretion occurs at night in association with deep slow-wave sleep. It is this aspect of growth hormone secretion that is specifically lost in the elderly.

Altered responsiveness to hormone actions may contribute to a number of age related changes in physiological regulations. Hormone action at cellular level initially involves interaction with a specific hormone receptor. As a result of these interactions, a signal(s) is generated that activates mechanisms ultimately leading to the cellular response. Diminished cardiac beta-adrenergic receptor function has been suggested by studies that demonstrate decreased heart rate responses to beta-adrenergic agonist stimulation in the elderly. Studies have indicated impaired insulin mediated glucose disposal in the elderly. Recent work suggests that the age-related defect in insulin action is due to impaired ability of insulin to increase the number of glucose transport units in the cell membrane.

1.3.5 Excretory System

Kidney weight remains stable from maturity until 40 years of age and then progressively decreases so that at age 80, the renal mass is only 70 per cent of the adult value. Renal perfusion in late adolescence receives 25 per cent of the cardiac output, which remains stable until age 40, when a major linear decline begins. At age 80, perfusion is only 50 per cent of

that in the young adult. The glomerular filtration rate follows a similar course of decline. A major problem of the aged kidney is its inability to handle either an acid or a base load. This is the consequence of the reduced glomerular delivery of adequate amounts of bicarbonate and other buffers.

Check Your Progress 2

1) How much percentage of the original weight is lost by the brain at the age of 80 years.?

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2) What changes take place in the brain cells in the aged?

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3) What happens to the sleep function of the aged ?

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4) How the distribution of cardiac output is changed in kidney at different ages of life?

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1.3.6 Digestive System

Most important change in the aging alimentary tract is the loss of teeth. The turn over rate of lining epithelial cells of the gut diminishes with age. After age 50, there is a reduction in salivary secretion and a reduction in the ptyalin content, which slows the early stages of digestion of complex carbohydrates. The volume of gastric secretion in response to a test meal diminishes after age 40. Resting acid secretion and secretion in response to a test meal decreases after 50 years. Pepsin secretion diminishes between 40 and 60 years of age. However there is no evidence that aging impairs absorption of the major nutrients.

1.3.7 Thermoregulation

Aging reduces the tolerance of work at hot environment because the rate of sweating is reduced and vasodilation is less well coordinated. The rise in core body temperature when working in a hot environment depends on the relative rather than the absolute intensity of effort. Elderly employees are handicapped because their maximal oxygen intake is low. Problems of heat dissipation are greater in older workers because skin fold thickness increase by an average of 4-5 mm over the course of working life. Older workers are usually more vulnerable to heat-stoke than younger ones.

1.3.8 Aerobic Capacity

Aerobic capacity declines from around 50 ml/kg/min in a young man and 40 ml/kg/min a young woman to 25-30 ml/kg/min in 65 years old of either sex. A corresponding decrease of productivity might be anticipated in tasks with a high aerobic demands. In self paced heavy work, energy expenditure is held to a level where lactate accumulation is minimised; around 50% of aerobic capacity under favourable working conditions, droppoing to around 35% if the environment is difficult, the posture is awkward, small muscles are used or there are intermittent peaks of intensive physical activity. In madchine paced tasks, the standard rate of working is commonly set at a pace which demands 80% of oxygen consumption tolerated for 8 hours. Given a 10 per cent loss of aerobic power per decade, the average 65 years old man will work at 105 per cent and the 65 years old female at 140 per cent of the 8 hours standard rate of working. But in practice, complain of fatigue are relatively infrequent. The response of VO_2, ventilation heart rate and lactic acid in different age groups during a standard sub-maximal exercise is given in Table 1.3.

Table 1.3 : Physiological responses during a standard submaximal exercise in the various age groups. Value are given in mean ± SD.

Parameters	Age (Years)							
	20-25	**26-30**	**31-35**	**36-40**	**41-45**	**46-50**	**51-55**	**56-60**
VO_2max (1/min.)	1.009 ±0.03	1.034 ±0.05	1.086 ±0.04	1.103 ±0.03	1.107 ±0.03	1.177 ±0.21	1.752 ±0.21	1.836 ±0.20
V_E (1/min.)	30.29 ±0.53	32.18 ±0.83	33.84 ±0.56	32.55 ±1.04	33.37 ±1.01	40.22 ±5.24	52.21 ±5.33	56.66 ±4.31
HR (bpm)	120.8 ±1.5	120.1 ±1.4	126.7 ±1.8	128.1 ±2.9	120.5 ±2.2	135.7 ±5.8	147.3 ±5.7	157.6 ±4.5
Lactic Acid Before Exerc.	16.15 ±1.11	17.03 ±1.45	19.41 ±1.54	18.3 ±0.78	15.25 ±0.91	16.2 ±1.08	17.3 ±1.09	19.9 ±0.94
After Exerc.	35.54 ±1.94	36.87 ±2.09	38.60 ±1.19	42.76 ±2.38	43.25 ±1.95	44.06 ±3.30	50.69 ±3.78	58.13 ±5.19

1.3.9 Muscular Strength

The growth of the physical work capacity is generally completed in man and women between 25 and 30 years. After that age, the locomotor apparatus (muscles, bones, tendons and joints) shows structural and functional deterioration. The mass of muscles and the diameter of individual muscles diminish. The speed of muscular contraction diminish. As a result of these changes, there is a drop in the maximal voluntary strength and difficulties in the control of movements. Grip strength decreases with age. The muscular changes are relatively small until 45 years, but more pronounced thereafter. Muscle changes have an effect on the bone structure. The bone mass and bone mineralisation decrease in a parallel manner, slowly till 50 years (0.10-0.15% per year). This evolution leads to osteoporosis. At 70 years of age the reduction of bone mass is about 30 per cent. Regular physical activity can maintain at a good level the bone mineralisation.

1.3.10 Musculo Skeletal Disorders

In older age, tendons lose their elasticity, which is not maintained by regular exercise. Muscle rupture can occur if excessive strength is simultaneously applied on tendons. The joint flexibility diminish in older people. When older people are subjected to the intensity of work normally carried out by young individual they suffer from different musculoskeletal problems.

Check Your Progress 3

1) Why is digestion of complex carbohydrates hampered in the aged?

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2) Why tolerance to work at hot environment is reduced in the elderly people ?

3) How can deterioration in muscular strength and bone mineralisation be prevented at old age?

1.4 CELLULAR AND MOLECULAR MECHANISM OF AGING

The most widely studied cellular model of aging is the cultured human fibroblasts. More than 25 years ago Hayflick demonstrated that normal diploid fibroblast have a limited life span in culture. Senescent fibroblasts exhibit many biochemical and morphological changes that can be interpreted as resembling aging changes in vivo. Increased number and sizes of lysosomes are common findings in fibroblasts aged in culture and in many tissues in old organisms. Chromosomal abnormalities are also increased in senescent fibroblasts, and rate of transcription, translation and protein degradation are usually reduced. Another common finding in senescent tissues is a reduced sensitivity to a variety of growth factors and hormones. An important characteristic of aged fibroblasts is the accumulation of structurally altered proteins. All proteins do not become aberrant with age. Proteins that accumulate in abnormal forms with age may impair cellular functioning e.g. the accumulation of altered DNA polymerase-alpha may be partly responsible for the failure of senescent fibroblast to proliferate. There are two major types of hypothesis that attempt to explain cellular aging. The first proposes that aging is caused by passive accumulation of errors in cellular constituents such as DNA, RNA, protein and lipid due to a variety of environmental insults coupled with imperfect repair mechanisms. The second considers aging to be an active, genetically programmed event (apoptosis). These two types of explanations for cellular aging are not mutually exclusive, since the presence of altered proteins within cells can alter gene expression.

1.5 LET US SUM UP

Aging means predictable, progressive, universal deterioration in various physiological systems, mental and physical, behavioural and biomedical. There is no universal definition of aging. Aging is a gradual and steady process which takes place over the entire life span of an organism. Aging is generally defined as a process of deterioration in the functional capacity of organism that occurs after maturity resulting from structural changes and it is a consequence of the inability of the organism to restore homeostasis when given a challenge. Any alteration in homeostasis must be non-reversible, independent of pathological condition and contribute significantly to general loss in function or death. But at the same time, aging can also involve psychological growth in capacities for strategy, sagacity, prudence, wisdom, reasoning and

experience. One should thus distinguish between aging of the population and individual aging.

The aging human experiences a gradual decline in almost all body functions, mainly in the cardiac performances, respiratory and renal functions, sensory faculties, nerve impulse conduction, muscle strength, endurance, agility and ability to maintain coordinated muscular effort, which may be due to structural and functional changes resulting in inability to restore homeostasis. Since, the aging process affects the various factors regulating heat loss and metabolic heat production of the body, the thermoregulatory efficiency is also impaired to a certain extent. Further, age also affects the capacity of work, both physical as well as mental, and is also accompanied by deterioration of most psychophysiological functions as age advances.

1.6 KEYWORDS

Aerobic Capacity : Physiological responses of VO2, ventilation Heart rate and lactic acid production during a standard submaxmial exercise.

Thermo-regulation : Mechanism at which core body temperature is regulated.

1.7 ANSWERS TO CHECK YOUR PROGRESS

Check Your Progress 1

1) Aging means predictable, progressive, universal deterioration in various physiological systems, mental and physical, behavioural and biomedical in the individual. It is generally defined as a process of deterioration in the functional capacity of organism that occurs after maturity resulting from structural changes and is a consequence of the inability of the organism to restore homeostasis when given a challenge.

2) A number of different changes have been observed in the aging human heart which includes alterations in size and geomatric contour. The left ventricular cavity tends to become smaller because of the reduced physical demands and activity in old age. Enlargement of the left atrium, widening of the aorta as a result of the lost of elasticity, shifting of the aorta to the right, and great rigidity and thickening of heart valves place the aged human heart at a mechanical work disadvantage that may impair heart function.

3) Bronchial ciliary function declines with age and dependent mucous accumulation may reduce ventilation in lower parts of the lungs in the elderly. Pulmonary distensibility and total alveolar exchange surface reduce but 'parallel coupled' dead space increases with age. In addition, with aging the lungs lose elasticity also.

4) With aging the lungs lose elasticity, but functional residual capacity increases which at the age of 60 years is approximately 60 per cent of the total lung capacity. It is difficult to judge to what extent such effects are consequence of environmental and life style factors like smoking, rather than due to aging *per se.*

5) With the advancement of age, vital capacity (VC) decreases after 20-35. Total lung capacity (TLC) which is the sum of the VC and RV, changes little with age. The forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) decrease with age, as do the flow rates. There is insignificant reduction in tidal volume (V_T) but a significant decrease in maximum voluntary ventilation (MVV) has been observed with age.

Check Your Progress 2

1) By age 80 years, the human brain loses 7 per cent or about 100 g of its original weight.

2) During the aging process, the ratio of grey to white matter changes, indicating that there

is some differential loss of cells and fibers. Cells are lost from the cerebral cortex. The Golgi type II cells and pyramidal cells are manuly affected. There occurs a significant changes in both neurons and supporting cells. There occurs neuroaxonal degeneration and conduction over multisynaptic pathways is delayed. Level of enzymes concerned with catecholamine synthesis decreases with age, while the major enzymes involved in the disposal of the catacholamines, monoamines oxidase, increases in concentration in several parts of the brain.

3) Following changes occur in the sleep function of the aged people: Alpha rhythm slows down, older persons take longer to fall asleep than do the young, wake up more frequently during the night and spend a longer time awake on each occasion, thus spend longer total time in bed. The transition between sleep and wakefulness is abrupt in old people and considered 'light sleepers'

4) Renal perfusion in late adolescence receives 25 per cent of the cardiac output, which remains stable until age 40, when a major linear decline begins. At age 80, perfusion is only 50 per cent of that in the young adult.

Check Your Progress 3

1) Most important change in the aging alimentary tract is the loss of teeth. The turn over rate of lining epithelial cells of the gut diminishes with age. After age 50, there is a reduction in salivary secretion and a reduction in the ptyalin content, which slows the early stages of digestion of complex carbohydrates.

2) Aging reduces the tolerance of work at hot environment because the rate of sweating is reduced and vasodilation is less well co-ordinated. Elderly employees are handicapped because their maximal oxygen intake is low. Problems of heat dissipation are greater in older workers because skin fold thickness increase by an average of 4-5 mm over the course of working life. Older workers are usually more vulnerable to heat-stoke than younger ones.

3) Regular physical activity can maintain at a good level the bone mineralisation and muscular strength.

1.8 FURTHER READINGS

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