Review of Literature
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That there exists a force of mortality which works constantly from post adolescence to senescence is well known. This has led to the development of the concept of a continuous decay of vitality (Loeb & Northrup, 1917; Brody, 1923; Pearl, 1928; Jones 1956). This process can also be regarded as a development of impairment of various types; it would appear that the additional impairment that is incurred at any time is proportionally related to the sum of earlier accumulation of impairments (Jones 1956). This theory indicates that death rate is a measure of physiologic age as well as of impairment of internal environment.

The term, ageing process is the genetically determined progressive and essentially irreversible diminution of the ability of the individual to adapt to its environment with the advancement of age. It means that there occurs diminution of the capacity of the individual to withstand the stressful situation which it faces, and thus culminating in the death of the organism.

Death risk however has been accepted as a gross measure of health and ageing. In order to study the effects of variations in specific environmental situations, the total death risk has been analysed into meaningful factors for population study and the variation in relation to the
age, place and time has helped the development of a concept that environmental circumstances can modify the health and ageing process.

Although the health of the individual can be assessed in terms of various mental characters and many physiological functions depending on the age, the assessment being fairly accurate, our understanding of ageing is far from realization, possibly because sample study have been too small to make a generalization of any conclusion.

It is yet to be determined whether common process like biological, psychological and social determinants of the behaviour of ageing can exist. It is possible that the ageing individual has many subsistence, and each of them has the potential to terminate the existence of the whole, but autonomous to a great extent which describe an independent time course during the life period. It is also possible that an interaction occurs between these subsistences.

One can expect that experimental studies of ageing will generate some approximate information so far the question of the degree of autonomy of age changes in the vital process and behaviour are concerned. Our knowledge is limited at the moment on the relation of behaviour or on the psychological and social subsistence of an individual to the vital subsistence that control the life span. In the healthy, normal human being a small group of factors only are possibly relevant at an instant of time, to behaviour of an individual. For example blood flow to the brain varies but
within a range of values do not influence the behaviour of an individual; but at its lower limit it may become a major factor for having a telling effect on the behaviour, leading ultimately to the deterioration and death of the organism. This indicates that in ageing process, it is likely that a threshold like quality of biological behaviour relationship does exist.

The concept of discontinuity in behaviour and adaptation are closely interrelated. If there occurs adaptation new act of behaviour develops within the individual, in that case a varied way of responding to the environment cannot be predicted from his past behaviour. Every living organism provides not only for the present but also for what is going to happen in future. Inborn diversity leads to versatility in the evolution process which were versatile enough to come to terms with the environment, only remains in the present. (Medawar 1957). One has to be aware that there exists uniqueness of the individual and that man and other organism also possesses a genetic system which is responsible for keeping the diversity permanently with the advancement of age man becomes more like himself in the sense that he manifests a particular genetic disposition and in consequence a unique set of accumulated experience. It has been proposed that older persons show reduction of inhibitory control over the behaviour (Birren, 1959). It is to be believed that all things being equal the aged persons show a reduction in the excitability of central nervous system which is manifested in the longer latency of responses and in a relative capacity to withhold the responses.
While considering some of the psychological effects of ageing it has been suggested that there occurs a reduction in the number of neurons with the advancement of age (Thompson 1945), but no appreciable change could be recorded in the conduction velocity, fibre diameter etc (Birren & Wall 1956). It was postulated that the decrease in the number of neurons are associated with the changes in simple reaction time and in choice reaction time leading to changes in performance in discrimination and recognition learning.

Some of the problems related to research on ageing need to be examined. It is time that if one can define a problem accurately he is found to find the solution of the problem. We are very much concerned with the term “ageing”. The question arises what exactly we mean by the term “ageing”. In this connection we might remember Craik had said that the value of a radio lies not in our ability to define it succinctly but in its ability to reproduce sound faithfully (Craik, 1943). We must remind ourselves while attempting to define ageing that the process of finishing can help orderly enquiry but it is not a replacement for it. Carnup has expressed that the task of explication consists in transforming a given more or less an exact concept into an exact one or rather, in replacing the first by the second (Carnup 1950). In the present case ageing cannot be defined exactly, but attempt can be made to clear the concept of it, by examples or by informal explanations.
Use of the form “ageing” reveals some core meanings but an attempt to define ageing by consideration of usual or core meanings would always leave something out. All persons would not agree that ageing is a genetically determined pattern. Scientifically the core meaning of ageing implies a chain of events that occupy a significant portion of life span of the individuals after maturity. Use of the phrase “Chain of events” indicates the notion of regularities. Research on ageing concerns with the systematic enquiry for the regularities in structure and function of an individual as they move forward and reach the later part of life span.

By “Ageing” we generally mean something closely related to chronological age but not identical with it. The term “ageing” can be used in two ways. One to explain the phenomenon and the other it is explained. So, in some studies ageing is the level of dependent variable and in other the level of independent variable.

We firmly believe in the statement that man and lower organisms have determinate life span and systematic changes occur in them with advancing chronological age. Whether there is a single mechanism or a group of mechanisms are involved with the passage of time in influencing the characteristics of living cells and cellular organisations thereby remains a question.

Attempts have been made to drop the term “ageing” and replace it by terms like longevity, senescence and antiquation but the term “ageing”
has acquired, a scientific as well as social significance, and ageing has been accepted as a broad prospect of post maturational change in the structural and functional properties of living things. Chronological age is one of the most useful information about an individual. From this knowledge alone a large number of predictions is possible about his anatomy, physiology, psychology and social behaviour. Chronological age is an index with which it is possible to classify a large number of data while attempting to establish relationships. When we consider the theory or explanations related to chronological age, it is felt that age or time may not be used in the same way, for explanation of events. This raises a question about the role of time in explanation. The regular changes in form or appearances of the organism with the advancement of age indicates that time has direction for the individual (Medawar, 1945). Medawar went far as to say that both Darwinian & Lamarkian views were appropriate depending on the level of observations “Inheritance that may be represented as Darwinian on one hand, may be represented as Lamarckian on the other “while differentiating the form of theory or explanations (Medawar 1957).

The idea behind the prediction and explanation rest upon the assumption of the general regularities and certain antecedent conditions. Few researchers have specified the kind of regularities, they have in mind when they talk of ageing and the concept of ageing has remained the most illusive one and they cannot approach the subject with experimental
techniques. It is also true of the concept of the development in the biological and social science as well (Anderson 1957; Hamburger 1957; Spencer 1957; Wernet 1957). The concept of ageing appears to be ambiguous, whereas development implies a positive direction of the organism and the use of the term “ageing” is suspiciously viewed implying a belief in a systematic degradation of the organism.

Lavelling a phenomenon of “ageing” as positive or negative as evolutionary or involuntary, as expression or differentiation or as integration or degradation depends on the kinds of prediction we wish to make.

If irreversitility is a key issue at all levels of biological, psychological and sociological analysis then we must direct our attention to these mechanisms in the individual and in society. Young organisms grow rapidly at first and slow as they approach the characteristic limit of form, size and function of species (Carmicheal 1954). The developing organism grow at characteristic rate, toward some limit in size, form and function with the final state or limit representing a relatively steady state of forces (Medawar 1945).

A series and sincere attempt at analysis of the phenomenon involved in the process of growing old in order to find out the differences that exist between the young and the old in the early years of the last century. The research activities of there individuals. Minot, Metchnikoff and Child in
widely dispersed areas published in fairly quick succession gave rise to the field of gerontology. The work of Minot (1908) was based on cytological investigation, that of Metchnikoff (1908) was based on combination of biological and medical observations and Child (1915) was based an experimental data collected by him on studies of regeneration and senescence of invertebrates.

Now that gerontology has been a subject on its own, communications between the investigators will be meaningful if the terms like ageing, senescence and sensibility is effectively distinguished. To some ageing refers to the process of change in the organism from the time of fertilization of the ovum till the death of the individual and to them the study of ageing is equivalent to the study of time in the life history of the organism. Analysis of growth and involution of some organs like thymus and uterus are included in the study. Senescence appears to be a more specific designation of the process that we refer to ageing that leads to the gradual deterioration of the adult organism (Lansng 1952). Senescence was described by him as a process of unfavourable progressive change usually correlated with time which becoming apparent after maturity and terminating invariably in the death of the individual.

According to gerontological society (1959) gerontology is that branch of knowledge that is concerned with situation and changes inherent in increments of time, with particular reference to post maturational stages.
It would follow from this that the end product of the process of senescence is the state of being aged or decrepit which is termed as senility.

The place of genetic principle has been recognised in medical and behavioral sciences as well as in gerontology. A gradual convergence of psychodynamic and physiodynamic theories of health, growth and ageing has occurred resulting in a greater realization of the imperative need for collection of detailed information about all kinds and at all levels of genetics (Medical Research Council 1956, Kalmann & Rainer 1959). It has been accepted that the process of senescence are just as much a part of the normal development pattern as are growth and organ formation (Dobzhansky 1957). According to him what we inherit are not characters or traits but genes & what genes determine are not states or particular stage but processes according to him. To be more precise it has been said that "the genes bring about the development as a whole, both the ascending portion in the youth and the descending part of the trajectory known as ageing and senility".

Within the general idea of life span differences of apparent genetic origin, the understanding of sex specific longevity variation in man has been greatly enhanced by animal studies. It is well established that in human population the life expectancy of the female exceeds that of the male in almost all national and ethnic group at birth as well as at later
ages. In a white population of the United States, male and female life expectancies varied from 67.4 to 73.6 yrs at birth; from 31.8 - 36.7 at the age of 40 yrs and from 10.5 - 12.4 yrs at 70 yrs of age. Even in those few countries (India & Ceylon) where the male enjoys a slight advantage in life expectancy at birth, he begins to confirm to the universal pattern as he grows older. (United National Statistical office 1957). These findings indicate that the basic reasons for the relatively greater vulnerability of the male population are biological, rather than social in origin regardless of this phenomenon is ascribed to male’s andric components (Draper et al, 1944), to an androgenically condition, acceleration of the metabolic rate (Hamilton 1948), to increased susceptibility to degenerative disorder (Madigan 1957; Madigan & Vance 1957) or perhaps even to the lack of some genes on the dimunitive Ychromosome. These findings also indicate that ageing process needs separate analysis for males and females.

The striking fact about the development of organism whether the embryology of the individual or the evolution of the phylum, is the increase in organised complexities which necessarily involves a series of regulated and interacting processes occurring in a sequential manner, quantity and locus wise. A number of processes are involved in producing an intricate organisation. Inspite of the best homocostatic control, a small variation is possible in view of exposure of the same to the vicissitude of environmental accidents.
It means therefore that each organism is the product of its particular past and the more are the complexities, the more does it carry an individuality based upon its built in history. It is possible that in the evolution of species, a completely accidental event may be decisive (Wright 1948). It is certain that the more elaborate the development of the individual, the more it is dependent on its own past.

In the complexities of the organism, differentiation also occurs in the parts or subsistence of it. Differentiation can occur in various directions and by virtue of the past cells can be laid to form liver or limbs, they cannot become gut or brain. The progressive specialisation with the differentiation of the units and their consequent integration and coordination in the whole is the basis of the organic development.

It is obvious that ageing occurs only in the material system. There is no such thing as an old nerve impulse, what happens is only a new impulse in an old nerve even in old organisation which differs from a young one in the lines of communication, depends on the material objects or on individual who have acquired behavioural pattern and accepted certain roles dependent on the material change in the nervous system.

A system might be considered as a built-up by its population of its units - a community built up man, men of cells and cells of molecules. The old entity differs from young ones in the populations of the units of various types. An old society will have a larger proportion of the kind of
individual we call "old" than a young society. This also holds good for a cell and its molecules, where old molecules are those which appear in larger population with the passage of time. Ageing of connective tissue similarly relate to an increase in dicarboxylic acid, in protein, their combination with calcium etc (Lansing 1955).

In every change of state of systems with time, there is some sort of change in its components but not all these are called ageing. The changes of ageing will involve a decrease in reactivity of the system. There is ageing of cells that attribute alteration of certain components with attendant changes in rates of change in metabolism, in diffusion, in contraction or secretion, in irritability and speed of response and the like. Organs age, as a cell type, and number that compose them are altered and as the connections and channels between these change so that vascular tubes become rigid and narrow and the neural pathways become fixed and unalterable. The old individuals as a result exhibit rigidity of performance with repetitiveness and slowing, and a group with well grooved roles and communication channels similarly falls into habitual performance pattern.

At the molecular level changes in macromolecules and their water and ion-binding properties seem to be of special importance. The resultant changes in collagen and elastic tissues are critical at cellular level, those involving fibroblast are most important as they lead to key changes at the
organ level in the cardiovascular system. Performance of the individual depends more critically on the changes in the nervous system and almost certainly on the patterns of neuronal interaction rather than on the changes in the neuronal entities. The problem of the ageing man is that of a loss of a functioning place or role in the ongoing business of his community - the aged survive better in primitive societies than in our society which shelves them (Comfort 1956). In all cases, however ageing leads to a loss of speed and flexibility, the establishment of more rigid pattern of structure and performance and the breakdown of integration of homeostatic process.

Comfort (1956) has condensed the theories of senescence dividing them into fundamentalist theory which regards it as some inherent properties of living matter or cells and epiphenomenalist theory which attribute it to a particular system or conditions. In the first group he places cellular wear and tear, colloid deterioration and inherent running down of tissue - nervous, endocrine, vascular or connective. In the second group toxin production metaplasma accumulation, cumulative damage of radiation, running down of a fixed energy store, depletion of material and cessation of growth. He summarised mechanisms under the heading 1) Senescence in cells including irreplaceable enzymes, cellular turnover, somatic mutations and specificities and 2) endocrine senescence including general, gonad-pituitary system and hormonal regulation of growth in vertibrates. In order to account for certain facts associated with
chronological age investigators have made large number of predictions about one individual's anatomy, physiology, psychology and social behaviour. Chronological age is possibly a powerful index with which we can classify large amount of data while seeking relationship. But there are certain difficulties to take chronological age as sole criteria for assuming one individual for disordered state of senescence. Actually senescence will probably be a better term for what we mean by ageing. When there occurs a decline in power of self renewal in some or all of the tissues in the divergent processes inside the body, the tissues no longer coordinate to maintain the function, because senescence would be matter of progressive disorganization. Actually, senescence is a change in the behaviour of the organism with age leading to a decrease in power of survival and adjustment which means that the organism progresses from an efficient state in order, to a disordered chaotic state with advancement of age (Comfort 1956). The attainment of senescence may vary greatly depending on various factors like nutrition, social circumstances, disease processes, satisfaction or frustration in life. An individual can attain age of senescence at any period between fifty to eighty years if not earlier or later. It has been admitted that the concept of biological, psychological and social age are abstract, since the length of life if taken as specific criteria for measuring age is less pertinent so far psychological and social age is concerned. The psychological age is closely related to the measures of adaptive capacity while social age depends on social output
or performance of the individuals in relation to others. On the other hand, biological age relates to longevity and chronological age of the individuals.

When we look towards demography of ageing it is noted that graying of the population referred to as geriatric or demographic imperative is the most significant demographic changes of the twentieth and 20th century (Current population report 1982)

The older population is increasing at a rate, much more than the rest of the population and the trend is likely to continue into the next century. Decline in birth rates along with a progressive increase in longevity is responsible for this trend. The increase in older population is likely to occur in two stages. The proportion of persons of fifty five years of age and above is likely to remain stable in twenty percent of total population, because of maturation of persons born during the “baby - born”. Conversion of older persons to younger ones is likely to rise. It is expected that in 2010, 25% of the total population would be at least 55% old and one seventh of the total population would be 65 years and over, and by the year 2050 33% of the population is expected to be over 55 years of age and one out of four would reach the age of 65 and over. If we look into the statistical figures it is to be noted that process has started to distinguish the older population (55-64 yrs) the elderly (65-74 yrs of age), the aged (75-84 yrs of age) and the very old (85 yrs of age and older).
The number of individuals in the group beginning with 75 years of age is extremely important because it is at this age, chronic diseases and disabilities rise steeply (Current population reports, US. Bureau of the census 1982).

In order to explain the phenomenon of ageing, various theories have been put forward which fall primarily into two basic groups 1) Programmed or genetic clock theory and 2) Accumulated or acquired damage theory. Both are concerned with functioning at cellular level with a scope to interact. Although it is not known where exactly the genetic clock is located but it appears that genetically determined characteristics predict whether one will withstand or fall prey to environmental situations which in turn can directly influence the genetic blue prints. It is interesting to note that each species of the organisms has its own maximum life expectancy and some correlation has been drawn between the length of this life expectancy period and overall metabolic activities. Studies of twins have indicated concordance of life span for mono twins but not for dizygotic types, the monozygotic dying within 5 yrs. of each other usually.

Although there exists many genetic theories which attribute to cellular ageing a number of questions on methodologies and interpretation and significance have been raised due to varied and indirect nature of evidences. Theory that links acquired progressive damage at cellular level is “Error catastrophe hypothesis”. This is based on errors in synthesis of
proteins due to chance coding inaccuracies or environmental factors resulting in abnormalities resulting in the enzymes that are concerned with catalysing the genetic information process leading to multiplication of original error. Sufficient abnormal proteins accumulation leads to failure of functioning of cells causing a threat to survival of the cell.

It is possible that abnormal proteins or dysfunctional enzymes accumulate and contribute to the manifestations of cellular ageing process and it is also possible that these changes originate from programmed genetic sources or acquired cellular damage. This is the unifying point between the two major theories of ageing process.

Free radical-induced oxidation of cytoplasmic or nuclear components has been demonstrated in vitro experiment. Hydrogen peroxide which can cause damage to several components of human cell is likely to be the primary, cause, (Halliwell 1981). In animal experiments, when large amounts of antioxidants is added to the diet it seems there is prolongation of life span although experimental design has not been christened.

Lipofuscin, a yellowish brown granular substance in found to be present in many species and the concentration of the same increases with advancement of age which was first observed by a pathologist about sixty years ago. Histochemical and biochemical analysis of this substance reveals numerous molecules which include protein, lipids, carbohydrates, RNA and possibly lysosomes. Ultrastructurally lipofucin is comprised of
very high electron dense particles with a banded structure. Disruption of
cytomicrostructure is possibly related to reduction in functional status of
tissues having inflamation (Sohal 1981).

Acquired cellular changes are also thought to result in release of
antigenic cellular components that stimulate long continued low grade
histocompatibility reactions. Evidences in favour of this theory indicate
possibility of increased concentration of autoantibodies with advancement
of age but this is not universally accepted. Autoantibodies may reflect time
related pathologic conditions occurring in genetically determined sub-set of
individuals and thus need not be associated with ageing process. So
alternative theories have been put forward to relate changes in immune
functions and associated lower immune surveillance to the ageing process
(Hoopir et al 1972).

The pathological changes that occur ageing individuals may be related
to different disease processes common among the elderly or may be due
to truly universal progressive changes that constitute the wearing out of
human organism. The numerous structural and functional changes that
appear to occur uniformly with advancement of age progress steadily, in a
linear fashion although rate of this progress varies greatly for different
individuals and may be quite different for different organs for the same
individuals. The majority of individuals attaining the age of seventyfive
years or more, however have a limited functional reserve capacity when
subjected to stressful situations and hence are susceptible to both acute life threatening illness as well as to more common chronic problems that affect them (Lambert and Reid, 1970).

It has been said that “A man is only as old as his arteries”. In fact the pathology of vascular disease is interestingly important so far the pathology of old age is concerned. The importance of the problem related to cardiovascular system is further evident from the fact that the cardiovascular diseases and in many countries arteriosclerosis alone are associated with more deaths than any other diseases including cancer (Chronicle of WHO 1957). It has been reported that life span of man in developing communities mainly depend on the ability to prevent and control the development of arteriosclerosis and the associated complication in the heart and brain. It is heartening to note that a significant decline in coronary heart disease and stroke mortality has been recorded in the U.S.A. (Lancet Editorial 1980), possibly due to health education programmes -oriented changes in the life style with alterations in various risk factors like smoking, blood pressure, exercise, habit, nature of the diet etc which means consequent prolongation of life.

It is to be stated that the plasma lipids in the form of cholesterol, triglycercide and phospholipids being virtually water soluble are not circulated in the free state but are bound to proteins as lipoproteins. Since the HDL does not vary much in health or disease, increase of total low
density lipoproteins (TLDL), which is the component of primary importance in atherogenesis because of the retention of lipids in the vessel wall depends on the nature of vehicles of serum lipids rather than the nature of lipids being carried.

Lipid deposits occur not only in the muscular arteries but also in the mitral and aortic valves, which are devoid of muscles. It has been demonstrated that lipid in atherosclerotic lesions at all stages of development from the fatty streak to the raised atheromatous plaques in the form of total low density lipoprotein (TLDL) (Walton and William 1968; Walton 1970).

It is evident that TLDL is concerned with the formation of not only arterial but also extra vascular lesion associated with atherosclerosis. The rate of elevation of serum TLDL correlates well the rate of progress of atherosclerosis. Epidemiological findings indicate that in developing countries healthy males begin to from atherosclerotic lesions soon after puberty and these increase in number with the advancement of age. In healthy females the onset of this lesion is delayed but by the time of menopause the distribution and number of lesions increase in them and in later years much of difference is not observed between males and females of corresponding age (Glazier et al 1954). The accelerated rate of progression of atherosclerosis in primary hyperlipidaimia occurring in association with extravascular deposits of lipids has been well documented
(Kachadurian, 1964). In secondary hyperlipidemia too, as occurs in hypothyroidism, diabetes mellitus, and nephritic syndrome, increase in incidence of atherosclerosis has been recorded (Walton 1969). Miller & Miller (1975) Gordon et al (1977) has observed a consistent and independent negative association of HDL and coronary vascular diseases. That HDL predicts against cardiovascular diseases has been confirmed by lipid research clinic programme prevalence study (Heiss et al 1980). Although it is evident that TLDL can be accorded as positively atherogenic and HDL may be protective and reducing the risk of cardiovascular disease (Miller and Miller 1975) and of peripheral vascular disease (Bradby et al 1978), the mechanism by which such an affect is brought about is not very clear. It has been suggested that a reverse chylomicron transport for HDL which is thought to carry chylomicron derived from deposited LDL from peripheral tissues back to the liver is the process that involves the transformation of free cholesterol in HDL to cholesterol esters through the action of lecithin cholesterol acyl transferase (Glomset 1968). It has now been suggested that HDL might exert a protective effect by reducing the cellular uptake of LDL cholesterol at the binding site (Carew et al 1976) or HDL might act as a scavenger molecules accepting lipids derived from chylomicrons & VLDL during intravascular lipolysis (Levy and Rifkind 1980). Because of postulated roles of HDL, current interest search for diet, drugs or other regimens which can bring about an elevation of HDL levels in order to have beneficial effect of such a change.
Evidences of contradictory findings on the size of thyroid gland with advancement of age has been recorded. That thyroid sizes increases with age has been demonstrated (Mortensen et al 1955), on the other hand record exists to show that there was no relationship between thyroid gland weight and age (Denkam and Wills 1980), but considerable evidence exist which indicate the functional activity of thyroid gland decrease with age (Pittman, 1962; Gregorman 1967; Ingbar 1978). From thyroxine turnover studies, it was estimated that the rate of production of thyroid hormone decrease by 50% between the age of twenty and eighty. This finding was confirmed by Oddie et al 1966 in Australia and by Nielson and Friss in 1973 in Denmark. With the advent of general availability of direct hormone measurements like radioactive iodine uptake or estimation of protein bound iodine are now only of historical interest. The recent measurements indicate that both $T_4$ and $T_3$ are lower in the elderly in comparison to the younger patients (Ratcliffe et al 1974; Seth et al 1975; Lee et al 1964; Caplax et al 1981).

Physiologic systems have substantial reserve in young individuals. The process of ageing and intercurrent pathologic process gradually eliminate these reserves in the form of androgen deficiency in men, loss of skeletal mass, decrease in growth hormone concentration in serum and increased incidence of Type II Diabetes. Maintenance of lipid profile protects against cardiovascular events, maintenance of skeletal muscle mass, decreased fracture risk and risk for loss of mobility and independence.
Testosterone replacement in hypogonadal older men improves strength and presumably function and independence. Growth hormone therapy is reported to have similar effects (Perry 1999).

It is not unusual to encounter male patients in their fifties or older who report having loss of libido, erectile dysfunction, fatigue and depression which signal an age related decline at the androgen levels although psychologic problem and medical illness often confound the diagnosis of andropause (Tan and Pu 2004).

Both ageing and age associated neurodegenerative diseases are associated with various degrees of behavioural impairments and among the prime candidates responsible for producing the neuronal changes mediating these behavioral deficits appear to be free radicals and the oxidative stress they generate. Diets particularly rich in antioxidants such as vit A,C,E and bioflavonoids (such as flavones tannins and anthocyanins) through their synergistic effect reduce certain types of cancers and cardiovascular diseases and it appears that these types of modification may be beneficial in altering neuronal and behavioral deficits in ageing (Cantali 2000).

Most ageing individuals die from atherosclerosis cancer or dementia. In the oldest of old also loss of muscle strength resulting in frailty becomes the limiting factor for individual chances of living an independent life until death. Hormonal changes that mark the ageing process in man are a
subtle drop of testosterone activity from forty years onwards might be accompanied by more difficulty to recognise symptomatology of andropause (Lamberts 2003).

While examining the association between androgen sex hormone and depressed mood in community-dwelling older men it was observed that the level of bioavailable testosterone reduced with age but total testosterone and DHT did not. It has been suggested that testosterone treatment might improve depressed mood in old individuals who have low levels of bio available testosterone (Barett and Connor et al 1999).

In the ageing human testis particularly regressed tubules contain sertoli cells with an altered appearance and reduced number of germ cells. It has been observed that a selective breakdown in germ cell - sertoli cell interaction could lead to severe reduction in male fertility. It has been proposed that selective destruction in communication between sertoli cell and germ cell contribute to loss of germ cell in ageing (Syed and Hecht 2002).

The age has an enormous influence an gonadal function in man has been extensively studied. Large number of references in the existing literature suggest that there occurs a progressive impairment of leydig cell function with the advancement of age although the existence of hyperplasia (Kothari and Gupta 1974, Honore 1978) or an attrition (Kelar and Neaves 1978) of Leydig cell in an elderly man is still a subject of
debate, evidences exist to show that the capacity of Leydig cell to synthesise androgen and to secrete them is reduced, as age advances (Takahashi et al 1985). That with ageing process, the responsiveness of Leydig cell to Human Chronic Gonadotrophin (HCG) is reduced is also evident (Longscope 1973; Bubens et al 1974; Nawata et al 1977; Harman and Taitaurus 1980; Nankin et al 1981; Nieschlag et al 1982). However conflicting reports exist regarding plasma level of total testosterone. It has been seen that testosterone is diminished with advancement of age (Takahashi et al 1985, Hammar 1985; Morose and Verkharotsky 1985; Tanover 1987; Blackman et al 1988). On the other hand plasma testosterone level has been shown to remain unchanged in very old people (Sparrow et al 1980; Purifoi et al 1981; Nieschlag 1985; Taitaurus 1987). The sum of free testosterone and albumin bound testosterone were found to be best index for evaluation of androgen activity (Cumming and Wall 1985) and it was shown that this index decreases significantly in elderly individual in comparison to young ones (Nankin and Calkin 1988). Nahoul and Roger (1990) could demonstrate that total testosterone level in plasma decreases only to a small extent with age but there occurs a significant increase in FSH level in plasma with advancement of age, although LH and prolactin level did not alter much during this period.

The study of disease specific mortality does also indicate why there is unexpected difference between the major racial components of a given na-
tional population (Manton 1980). Studying the five disease category, which accounted for 64% of all white and black deaths, Manton has described what he calls as black/white mortality cross over.

The identification of environmental factors and life condition that are capable of influencing the rate of ageing in human population has presently become one of the major goals in human ecology. In order to achieve this goal it is necessary to have at one’s disposal, examining tools for quantitative assessment of functional changes that occur with the advancement of age. It is said that native tropical people in humid tropics are prone to age quickly than people from the temperate climate. But it has never been proved that this ageing is due to climatic condition only because weightage has not been given to the study of poor nutrition, heavy parasitic load, and tropical diseases.

It is interesting to note that in the bushmen of Kalahari desert studied by Truswell and Hansen (1976) ageing occurs in a similar fashion like that of forest pygmies, their mean blood pressure does not rise between the age of 20 and 83; nobody was found to develop hypertension in the population nor there was any evidence of coronary heart disease in them. Truswell and Hansen did not find a single case who had Angina pectoris or anybody who had sudden death their serum cholesterol level was found to be low and no significant variation between age and sex. The high percentage age of old people in the population over sixty years of age also should be taken into account (Lee 1972).
At the other extremes of climatic condition, the Eskimos do not age prematurely in spite of the stressful situation under which they live and continue the hunting activities. In them also skin fold thickness and blood pressure do not increase between the age of twenty and fifty four (Mann 1962) although a small increase occurs in individuals above fifty four years of age (Scott et al 1958), cholesterol level in serum, remaining more or less unchanged.

High altitude also did not appear to speed up the ageing process in individuals born and living permanently above 3500 meters. The Peruvian Indians did not show an increase in blood pressure between 20 and 60 years of age (Ruiz and Pennallosa 1970; Corone et al 1977). That altitude is not a serious handicap for resident is also suggested by the fact that most of the communities of centenarians (Hunzas and Abkhasians) are to be found in mountain areas.

Chronic irradiation of the whole body have been thought to cause acceleration of ageing process but an increase in mortality rate cannot be equated with an acceleration of the rate of ageing. Individuals exposed to chronic radiation die without ever displaying most of the physiological changes normally associated with the ageing process. Life expectancy of the radiologist does not appear to be reduced significantly by their day in and day out exposure to radiation (Miller 1989).
Atom bomb survivors following atomic explosion in Hiroshima, did not provide any evidence of premature ageing although the incidence of leukemia and cancer was higher in them in comparison to non irradiated population (Hollingworth et al 1969).

Even though an intense background radioactivity was found to be present in coastal Kerala in southern India people born and living there permanently do not age there quickly than others (Gruneberg 1966).

It is true that the speed of development and the rate of ageing of cold blooded animals depend to a large extent on physical factors such as temperature. On the other hand, biological adaptation of man to the extremes of heat, cold and latitude as studied by environmental physiologists show that the native tropical people in the humid conditions, age more quickly than people of temperate latitudes but the studies made were short terms ones, and that is the reason why the drastic climatic conditions could not be correlated properly with ageing process (Henry and Stephens, 1977).

Unlike physical factors biotic factors have a definite influence over human development and ageing process. One important relationship between man and his environment is represented by his mandatory use of some plants and animals for food. The characteristic of people living on low calorie diet is the conspicuous absence of increase in body weight after the third decade of life. In industrialized population, the subcutaneous fat deposits do not increase with age. This is the case with the rural population of Algeria (Bourlierre
and Parrot 1962), the rural population around Delhi (Padmavati and Gupta 1959), the pygmies of eastern Zaire (Mann et al 1961), the Eastern African Masai (Mann et al 1964, 65) the Pappua of New Guineas (Maddocks 1967; Boyce et al 1978), the Soloman island natives (Page et al 1977), and even in some Japanese samples (Page et al 1974).

These populations living on low calorie diet have low blood pressure which do not rise with age; they also have low serum cholesterol which do not show significant variation over the years. The Kalahari bushmen are known to have low lipid contents in their blood. In all these people no chemical evidence nor any ECG indication were found for coronary heart disease. On the other hand rise of blood pressure with age has been shown to be present in affluent societies because of their life style, and is a concern for their early ageing process. High calorie diet in them have resulted in steady increase in body weight up to 50 to 60 years of age especially in women which is largely due to marked thickening of fat deposits with advancing age (Montoye et al 1965, Bourlierre et al 1966). The rise in blood pressure and high serum cholesterol in them are associated with increased prevalence of arteriosclerosis and coronary heart disease (Ho et al 1971). Vegetarian people also can have too rich a diet. In the case of Polynesians in the Vokelen island (Prior et al 1977), their diet being comprised of bread, fruit, taro and poulaco and coconut with addition of fish, chicken and pork only on different occasion, 56% of the calorie intake is made of saturated fat. The body weight of these people rise with age in both sexes with the steady increase in body fat,
rise in cholesterol level, triglyceride, blood pressure and incidence of angina pectoris, myocardial infarction and diabetes mellitus and naturally the expectancy of life. People in an area below Russia are strictly vegetarian; animal protein factor, they derive from a glass of milk everyday. Their average life expectancy has been as high as one hundred.

Very wide variation of salt consumption exist between cultures. Those taking no salt or low salt (Oliver et al 1975; Page et al 1977), blood pressure does not increase after third decade of life. On the other hand, in the population with the habit of taking more salt, high rise of blood pressure and incidence of coronary heart disease are common. The high salt intake in Japanese has also been correlated with much higher incidence of stroke among the Japanese (Komachi et al 1977, Hatano 1975).

The study comprised of massive running performance as related cardiovascular adjustment to effort and maximum oxygen consumption (Mann et al 1965) indicate that the fitness of the subjects although untrained is remarkable. They display this remarkable physical fitness despite their poor work load, frequent malnutrition, poor hygiene and living conditions. The balanced and sustained physical training, however, enable the adult to make the best use of physical abilities because sustained exercise prevents the accumulation of fatty deposits during adulthood and decreased cholesterol levels and naturally delay ageing process.
Psycho-social factors also need to be considered since the stress of life accelerates the pace of ageing, certain stimuli resulting from social mal-relationship can quicken the functional ageing or increase the prevalence of age associated diseases (Levy 1972, Henry and Stephens 1977).

Ageing has been thought to be characterized by a failure to maintain homeostasis under condition of physical stress and failure is associated with a decrease in viability and an increase in vulnerability of individuals (Comfort 1979). Naturally ageing is a function of time but development and maturation also involve changes which are age or time related. Taking physical factors, biotic factors and psychosocial factors together, it appears that an individual after the cessation of period of reproductive activity proceeds towards ageing process with the passage of time. Environmental factors, dietary factors, psychosocial factors and hereditary factors can influence the ageing process; in some, it can occur early, in some it may be late.

With a view to characterize endocrinological changes due to ageing, Fingschleidt and Nieschlag, (1989), estimated testosterone and inhibin concentration in serum of young and old men with proven fertility before and after the stimulation with HCG. While there was a significant increase of both hormones in all young men a decreased response to serum testosterone with a significant increase in inhibin could be found in the elderly individuals. It appears that with advancement of age hormonal profile of people changes to a great extent.
That the hypothalamus and the endocrine system are intimately related with the ageing process appears to be an attractive hypothesis. Deficiencies in the hypothalamic release of thyrotrophin releasing hormone or gonadotrophin releasing hormone and hypophysial hormones like thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH) and gonadal hormones often lead to changes which give the appearance of ageing. Appropriate replacement therapy may reverse the process to some extent. In the hypothalamic or hypophyseal deficiency states, it has been proposed that hormones secreted after a certain age are inactive (Seagall 1979), evidences have been forwarded to show that target organ receptors are reduced in number so that cellular responses are also diminished (Everitt 1980). Frohlikis et al (1979) has shown that Hypothalamico Hypophyseal Adrenal Axis plays an important role in the regulation of RNA synthesis and induction of some enzymes of carbohydrate and amino acid metabolism and that these functions are diminished with age. Testosterone circulates in the plasma loosely bound to albumin and firmly bound to globulin and is in equilibrium with a small amount of free testosterone.

Brands and Garcia-Bunnel (1978), while reviewing on ageing in relation to male sex hormone observed that there occurs (1) a decline in Leydig cell function, reducing testosterone levels, (2) A decrease in binding of testosterone by target cells, (3) An alteration of hormone
metabolism takes place within accessory sexual organs (4) Decreased target organ response to testosterone. That response of target tissues to hormone alter with age could be further deduced from tissue culture experiments and transplantation studies which suggest that old tissue can be rejuvenated by a young environment. It has been observed that Adrenal androgens like dehydro epiandrosterone (DHAE) and Dehydroepianandrostosterone sulphate (DHEAS) decrease with age due to decreased production which could be due to age related loss of adrenal enzymes. The DHT is possibly related to promotion of prostatic growth (Harman 1978).

In view of possible relationship between DHT and promotion of prostatic growth (Harman 1978) it appears that DHT might be associated with suppression of FSH and LH level which could account for such situations like large testis and benign prostatic hypertrophy in elderly people. The reduction in testosterone is likely to be accompanied by a reduction in sexual activity and interest in sex as age advances.

The study on endocrine changes in relation to age has been reviewed on several occasions and work on this line has been gathering momentum (Gussac 1972, Gregorman and Bierman 1974, Sartin et al 1980). Documented evidences show a decline in the reproductive functions with advancement of age in both laboratory animals and humans. Although in ageing laboratory rodents, the ovaries remain
potentially functional through out the age (Meites et al 1980), in humans there has been much talk of a male menopause, the physiological basis of which is still uncertain. It is likely that decreased gonadal secretions is of major importance in senescence and accordingly it is expected that castrated subjects would show early manifestation of old age but this does not seem to be the case; Hamilton and Mestler, 1969, produced evidences to show that eunuchs live at least as long as intact males. A study on healthy aged volunteers indicate that serum levels of testosterone are not influenced by age even though the LH level in the serum significantly rises in them (Harman and Tsitauras 1980). No age related changes in the diurnal pattern of testosterone, dihydrotestosterone or estradiol could be demonstrated in the ageing Rhesus Macques monkey (Chambers and Phoenix 1981).

Extracts from different herbs have been analysed and the safety and efficacy of them have been tried on various parameters on the aged individuals the results of which have been compared with the individuals of younger age.

Geriforte a herbo mineral compound prepared from several herbs and minerals has been shown to protect the body from the damageing effects of free radicals by producing large amounts of antioxidant enzymes like superoxide dismutase and catalase (Singh et al 1994).
Triterpenoids present in African wild olive leaves, Greek olive leaves and Capetown cultivar have been found to show antihypertensive, diuretic, antiatherosclerotic, antioxidant and hypoglycaemic effects associated with ageing (Somova et al 2003).

It could be demonstrated that Moringa Olifera could lower the serum cholesterol, phospholipid, triglyceride, VLDL, LDL, cholesterol-phospholipid ratio, and atherogenic index but could increase the HDL ratio (HDL/HDL total cholesterol) as compared to the corresponding control groups showing thereby that Moringa Olifera possesses a hypolipidaemic effect (Mehta et al 2003).

A negative correlation between consumption of garlic, blood pressure and ACE activity in serum and different tissues in 2KIC rats suggest that garlic has a significant blood pressure lowering effect which could partly be mediated by reduction in ACE activity (Sharifi et al 2003).

Canned beverages containing mixed green vegetables and fruit with Broccoli and cabbage has been found to be useful beverage for lowering serum cholesterol level in hypercholesterolemic subjects (Takai et al 2003).

The herbal formulation Bouum-Myunyuk-Dan (BMD) could indicate that it has an immune enhancing effect through the production of various cytokines (Teong et al 2004).
Norsesquiterpenoid glycosides III & IV identified from the roots exhibited significant antiproliferative activities although their aglycon I and monoglycosides II did not show any inhibitory effect on the tumor cells examined (Zhang et al 2004).

A study on potential health benefits of various dietary oils in relation to cardiovascular diseases and cancer indicate the beneficial effects of Argan oil in the treatment of hyperlipidaemia and hypercholesterolemia. The effect appear to be related with the polyunsaturated fatty acids and other constituents of studied oil (Borrougui et al 2003).

Oral administration of ethanol flower extracts of Hibiscus rosa sinensis has been found to cause lowering of total cholesterol, serum triglyceride, with an increase in HDL cholesterol level. The extract is also found to have hypoglycaemic affect which is comparable to that of glibenclamide. Evidences have been produced to show that hypoglycaemic effect is not mediated through insulin release (Sachdewa and Khemani 2003).

An experiment designed to evaluate the role of endothelium mediated mechanism in vasorelaxant response of garlic in isolated aortic rings of rats showed that endothelim mediated vasorelaxation of garlic is partly mediated through EDRRS and cyclooxygenase pathway. However relaxing factor other than NO mediated through CGMP has a major role in the vasorelaxant response of garlic (Ashraf et al 2004).
Oxygen radical injury and lipid peroxidation have been suggested as a major cause of cancer, atherosclerosis and the ageing process. In an experiment with aged garlic extracts and S-allylcysteine it could be shown that they protect vascular endothelial cells from oxidative injury. It could also be shown that numerous garlic compounds could be involved in the antioxidant properties of garlic, while there could be some peroxidant compounds derived from garlic. In order to develop good herbal preparation it is important to keep an away of antioxidant compounds like aged garlic extracts (Yamasaki and Lau 1997).

While studying the effects of Yukumi (decoction of six plants) including Rehmannia, a herbal formula on liver oxidant damage induced by paraquat administered intravenously in the senescence accelerated mice it was evident that Yukmi extracts may be useful in protecting against liver oxidant damage (Kim et al 1997).

Loss of learning and memory in passive avoidance responses (PAR) failure tests through shosaikoto extracts the age induced PAR failure has been found to be improved in shosaikoto treated rats. Dopamine was increased and Noradrenaline and Vanillyl mandelic acid were decreased in brain relative to those in more treated ageing rats (Amagaya et al 1990).

While studying the effects of Qigong (Shuxinping) it could be demonstrated that Qigong may stabilise the sympathetic nervous system and is effective in modulating the levels of urinary catecholamine and
blood pressure positively and also in improving the ventilatory functions in mildly hypertensive middle aged patients (Lee et al 2003).

Ginseng (Panax Ginseng, Camare) has been a popular herbal remedy used in Eastern Asian Culture for thousands of years in norther America. The Ginseng Species indigenous to both Canada and the United State (Panax Quinquefolium) represents an important industry for both domestic and export market. Claims have been made describing the efficacy of Ginseng which can combat stress of the central and immune system and contribute towards maintaining the optimal oxidative states against chronic diseases and ageing (Kitts and Hu 2000).

An ancient system of natural medicine Maharishi-Ayurvedic prescribes certain herbal formula to enhance cognitive functioning, prevent illness and alleviate the detrimental effects of ageing process. Maharishi Amrit Kalash (MAK) has been found to enhance attentional capacity, alertness and thus reverse some of the detrimental cognitive effects of ageing (Gelderloos et al 1990).

Amongst the various herbal products the Satavari (Asparagus racemosus) and Alkushi (Mucuna pruriens) extracts have been chosen in the present experiment in order to study the efficacy on the changes associated with ageing process.

It has already been pointed out that the naturally occurring polyamines Putrescine, Cadaverine, Spermine and Spermidine are distributed throughout the eukaryotes. That cell proliferation and differentiation require their
biosynthesis has not been definitely established but the weightage of evidences was more in favour of this concern. Furthermore it was well documented that generation of these polyamines is tightly regulated (Pegg and McCam, 1982; Tabor and Tabor 1984). The metabolic reaction responsible for the formation of the polyamines and their biotransformation are known.

**BIOSYNTHESIS OF POLYAMINES**

(From CancerMedicine, 2nd Ed. by Holland J.E. Emilfree III Philadelphia Lea and Febiger)
Ornithine has been shown to be the mother substance of polyamines, which is catalysed by ODC, the rate limiting enzyme to produce putrescine and hence other polyamines. Decarboxylated S-adenosylmethionine, catalyses decarboxylated substrate and helps in the formation of spermidine in presence of spermidine synthase. The formation of spermidine from spermine also needs an aminopropyl group derived from decarboxylated S-adenosylmethionine and presence of spermidine synthase. An interplay of both positive and negative feedback control occurs with putrescine serving as an activator and spermidine as a repressor.

It is established that polyamines are required for the formation of nucleolus, oocyte maturation, rodent embryogenesis and for appropriate embryonic development (Fozard et al. 1980). Polyamine synthesis has been found to be greatly increased in renal and cardiac hypertrophy as well as in regenerating liver (Pegg 1981). Phorbol diesters and other agents helping differentiation in human promyelocytic leukaemia cells have been found to cause an increase in putrescine and spermidine levels, suggesting thereby that polyamines play an important role in the process (Huberman et al. 1981).

It is well known that ODC is the principal enzyme concerned with biosynthesis of polyamines. The activity of ODC was however very low in cells under normal situation but the exposure of cells to different stimuli in the form of growth factors, hormones and tumor promoters lead to rapid induction of the enzyme (Selly et al., 1982). A high level of ODC activity could
be observed in skin tumours (Scalabrino et al., 1980). ODC in skin tumors was found to be functionally altered when compared to normal tissues and this functional alterations could be activated by GTP (O'Brain et al. 1986; Hietala et al., 1988). These investigators suggested that in these growths, functionally altered ODC activity is responsible for continuation of polyamine biosynthesis.

While studying tumour "Cell Biology" it was interesting to observe that one of the human ODC gene is located on chromosome 2 (Dice, 1987). In Chinese Hamster Ovary cells, deficient in ODC, it was necessary to administer putrescine for cellular growth; but these cells when transfected with human ODC gene putrescine was not necessary for the growth of these cells. In view of the increased number of cells in G2 and M phase of the cell cycle of the transfected cell in comparison to the ODC deficient cells, it was suggested that transition from S to G2 and M phase requires the presence of polyamines.

ODC is a protein, having a very high turnover rate; evidence exists to show that rise in ODC activity is associated with post transcriptional effect. It is not properly understood how the rise in ODC occurs but, certain experiments based on inducing ODC activity in mouse skin and in phorbol ester cultured keratinoocytes. Phorbol ester interacts with protein kinase C resulting in the production of some phosphorylated transducting proteins which may be responsible for increased transcription of the appropriate genes (Dice 1987).
It is more or less established that polyamine are essentially important in growing and multiplying cells and that they play an important role in many prokaryotic cells and certainly they are involved in growth stimulation in eukaryotic cells. Polyamines could be traced in important organelles such as ribosomes and it has been observed that these stimulate a number of processes involved in replication, transcription and translation which are essential for growth and multiplication. Eukaryotic cells contain spermine which is concentrated more in the nucleus and as such it appears that there exists an evolutionary development of structure, biosynthesis and function of polyamines. It has already been noted, that the regulation of polyamine biosynthesis involves ODC activity. Close on the heels of all these findings was the observation that ODC activity rapidly decline in regenerating liver following treatment with cycloheximide, indicating thereby the rapidity of the turnover rate of the enzyme.

The normal cells at various stages of development have membrane receptors that are responsive to differentiate the extracellular polyamine concentration. The more these receptors are sensitive to polyamines lower will be the intracellular ODC activity and consequently the level of intracellular polyamines. Tumour cells, rapidly growing cells and the cells of carcinomatous growths possibly have membrane receptors, that are poorly responsive and non sensitive to polyamines and that is why such cells have high intracellular ODC and polyamine levels.
Evidences exist to show that intracellular polyamine concentration is linked with increased rate of cell proliferation (Russel; 1973 and Bachrach 1973). Actively dividing mammation cells have also been shown to have a high concentration of polyamines (Calderara and Moruzzi 1970). ODC, synthesising enzyme for polyamine if stimulated by certain agents, increased polyamine levels in tissues occur (O'Brien et al 1975). Nichols and Poser 1980 however demonstrated that ODC cause only differentiation of cells and doesnot have any effect on proliferation, although it is well known that ODC is involved in polyamine synthesis.

When analysing the rapidly proliferating normal system as that in regenerating or foetal liver, a number of important enzymes involving anabolic process namely DNA polymerase was found to be present. However these enzymes could not be detected in adult liver (Potter 1982). Normal cells can reach a steady state of growth which provide a balanced economy for the body as a whole. A tight control system is manifested over the growth rate growth factor and cell loss. Physiologic stimuli can cause increase in tissue growth but cessation of growth occurs when the stimulus is taken off or a new steady is achieved. Benign inflammatory lesions at times, can grow over twenty times faster than cancer in a discrete time and place (Fakuda et al, 1990; Teodori et al, 1990). Non cancerous tissues however, cease rapid growth, unlike neoplastic tissues which continue to grow overtime.

In view of the fact that polyamines like Putrescine, Cadaverine, Spermine and Spermidine increase in growing normal cells it is natural to believe that
these fractions will be reduced with the advancement of age because proliferation and differentiation of cells were supposed to be reduced but the synthesis of polyamine may increase if there occurs stimulation of cell proliferation due to carcinogenic growth factors and such situation cause curtailment of longevity of an individual.

In the present study since no such increase in polyamine concentration in serum could be observed in individuals of both age groups it can be assumed that with *Asparagus racemosus* root and *Mucuna pruriens* seed extract treatment such episodes did not occur to curtail one's lifetime. From the result of the present analysis it appears that *Asparagus racemosus* and *Mucuna pruriens* treatment would prolong life although the study that has been conducted in its present form does not give any indication that during *Asparagus racemosus* and *Mucuna pruriens* treatment carcinogenesis will be prevented.