Recent Advances In Aging Research

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There are two aspects of aging with which one can deal when approaching gerontology from a research point of view - that of the biological process, and aging as the phenomenon observed in old people. We are concerned here with the former, and the basis of this biological process of aging is the passage of time. As noted by Hunt (1), "...it is sometimes difficult to distinguish the effects of illness from the biological aging process, but conceptually I think it can be done." Throughout the basic research laboratories of the world this differentiation has been accomplished, and it is because of this that we are able to understand much of the underlying principles governing the many physiological and tanalomical facts presented to us over the years.

The physiological manifestations of aging, as stated in the usual treatment of the subject, are the qualities most familiar to us: a decrease in the range of accomodation of the human eye with age; the very slow but obvious fall in the BMR; a decline in cardiac efficiency; alterations in carbohydrate metabolism (made obvious by glucose tolerance tests) (2). Then one is confronted with the less obvious of problems: the fall of activity in intracellular enzymes; the EM studies showing defective collagen networks of exposed areas of skin; the increase in cholesterol concentrations in the lens and arterial wall without a concomittant increase in blood cholestrerol levels; the increasing frequency of osteoporosis (3).

One more often than not, can notice the wince of the unknowing when he hears one speak of 'basic research' , yet herein lie the answers to the majority of geriatric problems. Researchers appear not so much to be concerned with that ultimate - the ageless society—but more so with facts which might eventually affect the parameters with which we are measuring our aged society. The cultural, sociological, and economical effects of these measurements are all too obvious to us: old age homes, social security, disability payments and last, but not least, the jobless...these are dealt with elsewhere in this symposium.

In Mohler's study of "Aging and Pilot Performance" (4), many parameters were used or suggested to determine the rate and extent of aging. Mohler advocates the use of the Conway and Smith Test, which utilizes the inhalation of amyl nitrate, during which time the blood pressure alterations are determined while the pulse rate remains constant - this might be a quick test to determine the elastic properties of the arterial reservoir.

With aging goes a decrease in total available hemogoblin and red cell mass, however, these implications need further evaluation. Also noted was the phenomenon of the lens which might provide another parameter in regard to estimating the "rate" of aging in an individual. As a result of this phenomenon there is a decrease in the amount of light reaching the retina for a given pupillary diameter, and the compensatory dilation of the pupil results in a loss of visual depth of field.

Another indicator of functional age is the relative importance of each of three factors in regard to hearing: pure-tone threshold, frequency difference limen, and comprehension of normal speech patterns. Pitch discrimination rapidly deteriorates after 50 years of age, especially the higher frequencies.

These are just a few of the more immediately applicable functional tests suggested, yet one is motivated to speculate their applicability and accuracy in the subdued light of our scanty knowledge of the cellular and biochemical aspects of aging.

Pulmonary.

Many studies are presently being carried out in regard to the pulmonary function status of the aged (5,6). It is generally agreed that the pulmonary function status of the individual gradually declines with age; the anatomical dead space increases, the apparent reason being non-uniform ventilation. Also noted was a tendency for the residual volume to increase and the vital capacity to decrease. The latter has been interpreted as a result of diminished mobility of the thoracic cage and a decrease in the elasticity of the lung parenchyma. The diminished mobility has arisen by anatomical changes, such as a decrease in the elasticity of costal cartilages. The changes in functional residual capacity is attributed to diminished elastic recoil of the lung.

Studies mentioned in the VA PROSPECTUS (7) seem to support the above theories. It has been found that elastic fibrils of lung fragment deteriorate progressively with age. The fragmentation of the elastic fibrils is accompanied by proliferation of fibres that stain similarly to elastic tissue, but are metacollagen rather than true elastin. There was an increased aging of elastin in such a pathological state as emphysema. A differential rate of aging was noted for the vascular bed of the lung and larger vessels and the pulmonary parenchyma, the former being some what slower. The connective tissue about large blood vessels in the lung were also tested for their swelling capacity in human lung acid; it was found that connective tissue from young individuals swalled far more than the connective tissue from aged individuals.

Bone, Cartilage and Collagen:

Chung (8), in his study of 250 joints of separate individuals, found a decrease in the pliability of the matrix of articulating cartilage with increase in age. Noticed first was an alteration in the staining characteristics of the matrix, and with increased age a secondary clumping together of cartilage. There was an apparent increase in the density of collagen fibres in the fibrous capsule with hyalinization.

Anderson (9) found that the sulfated mucopolysaccharide concentration of rat cartilage decreased with age.

Research into the changes of collagen has shown that thermal denaturation and a chemical reaction may be of significance in the aging of human collagen (10), probably of a tanning type. Kohn and Rollerson also noticed that when old collagen was treated with an alkali, it assumed the digesting characteristics of young material.

With regard to tendon, Kao et al (11) found that an ester of cholesterol increased in concentration with age, yet there was a significant decrease in total cholesterol, phospholipids and triglycerides.

Probably the most universally occuring disease of man is osteoarthritis, and is one of the most clearly related to increase in age. Fortunately, researchers have found this degenerative joint disease in laboratory animals which has provided an excellent opportunity to study the disease under controlled conditions. Silverstein (12) did just this in mice and found that osteoarthritis here closely resembles the human counterpart in morphology. It appeared to be localized, increased with age and seemed to be genetically determined. Hormones, diet and mechanical factors affected development of the lesion. As far as obesity is concerned, (a definite problem of the aged), its effect appears to be a metabolic one rather than the increase in weight on joints. His observation was that a high fat diet, modified by hormones increased degenerative joint disease in mice.

Silberberg et al (13) has studied the human sternoclavicular joint with respect to osteoarthritis and aging. The incidence and severity increased to age 80 but thereafter declined. There appeared to be a positive correlation between osteoarthritis, diabetes, and chronic renal disease. Silberberg's evidence tends to support research in mice, where the relationship between arthritis and obesity was not a mechanical factor. Hyperplasia and hypertrophy of the articulating cartilage cells was observed and it is postulated that this occurred early in the aging process.

Electron Microscopy and Cytochemistry:..

The basement membrane has long been of great interest to cellular physiologists, microanatomists and biochemists. "The location of this structure between parenchymal cells and blood vessels leads to the conviction that they have considerable physiologic significance, constituting a layer across which fluids, solutes, and macromolecules must pass" (14). Ashworth et al (15) has shown that a significant alteration in the basement membrane of renal glomeruli and capillaries occurs in the process of aging. His EM studies of the basement membrane in rat kidney show a definite thickening of the B.M. of glomeruli and tubules with advance in age. It is postulated that this alteration might be related to the development of hypertension, or an alteration in the quantity of glomerular filtrate, or to the abnoral deposition of macromolecular particles in walls of blood vessels.

Lansing (16) is presently studying the properties of fibroblasts, especially those in relation to developing and their effect on aging of connective tissue.

Arcadi has looked into the cytochemical changes occuring in the prostote of rats (17). Supranuclear granules in the prostatic acinar cells of aged white rats were stined with periodic acid- leuchofuchsin No such granules are seen in younger animals. This finding appears to suggest a biochemical difference in the prostate between the two age groups. This was the first attempt to do a cyochemical study of aging in the prostate.

An interesting study was done by Allen et al (18) to determine body potassium and gross body composition in relation to age. It was found that the ratio of K to total body mass (minus water) decreased with increase in age. A correlation was noted between body K and BMR, but further study is required to explain the exact relationship.

Theory:

Often, in research there are some who are capable of fundamentalizing varied concepts. Szilard and Smith (19) have presented a theory which points a way to the genetic factors which control longevity, which more or less revolves about the number of faults one has inherited. An individual of inbred strain might be homozygous for a greater number of 'weak alleles' and "... it may be maldeveloped in the sense that it may have a much smaller reserve at birth than a more wild type of individual, with respect to a number of physiological functions."

Harman (20) has postulated that aging is in part a result of side effects of free radicals normally produced in the course of metabolism, or by the interaction of o_2 with oxidate catalysts in the intracellular spaces.

Johan Biorksten has taken review of all accumulated data and has come about with a possible common denominator which is

not at all incompatible with other findings presented thus far, clinically or experimentally (21). It is supposed that there is a progressive insolubilization of large molecules of protein brought about by potential cross-linking agents normally present in the human bloodstream. Future research projects are outlined which may be of inestimable value if a 're-mobilization' molecule can be isolated.

Mental Status:

Thus far, I have attempted to present some of the more resent investigations which might be more relevant to a complete geriatric study. The psychological manifestations related to the aging process are extreme, in severity and incidence, yet one finds a certain lack of positive results in this area of research. The lack is not in the so-called 'basic-states' but in the complexilites of psychological evaluations and therapeutics. True, with the invention of tranquillizing pharmaceuticals many of the clinical geriatric problems (eg. depression, loneliness, anxitiey, a sense of uselessnes) were 'solved', however, they have proven to be of temporary value only. Much more must be done if our aged society is to once more be a dynamic and a productive one.

Conclusion:

Many doubt that research in the biological aging process is going to solve the problems of old age, but believe that it will further the understanding of basic life processes; the factors which lead to death; but most of all those that contribute to the disabling infirmities of old age, ((22). It is of necessity that this research continues, but what of these patients in the meanwhile—often this fact is overlooked—'the forest is forgotten.'

It is the family physician who must resolve these final moments " . . . of calm, and peaceful existence, the rounding-out of a well-balanced life" (23).

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