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ABSTRACT

The Adult Development and Aging Branch of the National Institute of Child Health and Human Development supports research and training relevant to the biological and behavioral changes that occur in humans with increasing age from the adult years through maturity and old age. Supported are research projects, training projects, special and post-doctoral fellowships, career development awards, and contracts. This brochure describes each of the projects supported within these categories during fiscal year 1969. Project descriptions are arranged in alphabetical order according to the name of the principal investigator. Currently there are 62 projects of which seven are large multidisciplinary projects. There are 23 training grants for individuals interested in research or research training careers in aging, eight fellowships, and seven research career development awards. Contracts are used to support activities which are ancillary or supportive of research; during 1969 five contracts were supported. (EB)

ADULT DEVELOPMENT AND AGING BRANCH

EXTRAMURAL ACTIVITIES

FISCAL YEAR 1969

NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT

INTRODUCTION

The Adult Development and Aging Branch of the National Institute of Child Health and Human Development supports research and training relevant to the biological and behavioral changes that occur in humans with increasing age from the adult years through maturity and old age. The Branch is responsible for a program of research aimed at promoting increased understanding of the physical and behavioral changes and processes and the social and environmental changes which occur with increasing age.

Supported are research projects, training projects, special and post-doctoral fellowships, career development awards and contracts. This brochure describes each of the projects supported within these categories during fiscal year 1969. Project descriptions are arranged in alphabetical order according to the name of the principal investigator. Currently there are 62 research projects of which 7 are large multidisciplinary projects involving a number of investigators and designated program projects.

Training grants are awarded to stimulate and increase opportunities for advanced training for individuals interested in research or research training careers in aging. There are 23 training grants supported, 8 fellowships, and 7 research career development awards.

Contracts are used to support activities which are ancillary or supportive of research. During fiscal year 1969 five contracts were supported.

Should additional information be desired concerning any of the projects described here, contact the principal investigator named for the project. For additional information on any of the problems of support write to: Adult Development and Aging Branch
National Institute of Child Health
and Human Development
National Institutes of Health
Bethesda, Maryland 20014

TABLE OF CONTENTS

PROGRAM PROJECTS

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CELLULAR AND COMPARATIVE BIOLOGY OF AGING

This program is an interdisciplinary comparative study of the interplay of nutritional deprivation, aging and physiological and synthetic capabilities of cells. There are four studies designed to supply information on physiological and biochemical changes which occur in senescence and which lead to cell death; evaluate the analogy between "natural" aging and the post-mitotic state induced by nutritional deprivation; and offer insight into those deleterious changes associated with senescence in a variety of animal forms. Emphasis is on the biochemistry and ultrastructure of cells in all studies. Cell types under investigation range from protozoa to insect and mammalian cells (in vivo and in vitro).

The common theme that unifies the work is the belief that aging may be regarded as a progressive deterioration in the cell's ability to cope with its environment, an effect especially evident in post-mitotic tissue.

One study focuses on the investigation of alterations in the structure of Euglena cells and in their biochemical properties, with special emphasis on the protein synthetic machinery of the cell. Cytoplasmic protein synthesis and protein synthesis by isolated nuclei are studied as a function of "aging" of the culture.

Using phagocytosis ability as an index another investigator is exploring changes with aging at the cellular level. He is undertaking a comparative study between the phagocytes of insect blood and Tetrahymena.

The ultrastructure and function of villus epithelial cells may be affected by age of the animal, level of the intestine, and time elapsed (or extent of migration) since leaving the mitotic foci of the villus. A third investigator is studying the influence of these factors on lipid absorption, lysosomal structure and enzyme activity, and nuclear structure of rat villus cells.

The fourth project is concerned with post-mitotic cells in certain areas of the cuticle of giant silkworm pupae. The pupae are injected with juvenile hormone; these then molt into second papae

of pupal-adult intermediates. Thus it is possible to study the secretion of the same epidermal cells which secrete either pupal or adult cuticle and in this way study the action of the juvenile hormone.

Burnight, Robert
PO1 HD 00671
Brown University
Providence, Rhode Island

A CENTER FOR AGING RESEARCH AT BROWN UNIVERSITY

A panel of 600 married couples with husbands between the ages of 60 and 64 was formed in 1961 to provide a sample for the study of health changes and social adjustments among older men and women in Providence, Rhode Island. The sample was diverse in cultural background and social position, still socially active, but at an age where major health and activity changes could soon be expected for many.

Information has been obtained through detailed structured interviews held separately with husbands and wives in 1962, 1963 and 1965-66. Each time they were asked about health attitudes and condition, specific illness and impairments, medical services utilization, finances, personal goals and life satisfactions, religious beliefs, changing capacities to perform valued activities and social participation in family, work, friendships, organizations, community functions and leisure time activities. Supplementary information on health and medical care utilization is obtained from a questionnaire survey of physicians and available record sources. About 100 of the original panelists have died since the first interviews and many have reported the onset of serious health problems. Special interviews are conducted with surviving widows and widowers as well as with many of the panelists reporting significant health failures during the survey period.

Findings so far show important and complex socioeconomic and ethnic variations. Low-income groups show the highest rates of chronic illnesses in the first panel interview and their mortalities greatly exceed the higher income groups.

When men in the "over $15,000 group" are compared with the middle brackets the former show the higher death-rate and they approach the lowest income groups in reported heart disease, hypertension, and arthritic complaints. The importance of kinsmen for this

age group as source of companionship and also of economic aid is indicated by the interviews. It also appears that retirement from work is viewed more favorably by those who have close familial attachments, and that post-retirement adjustment correspondingly is made easier.

Busse, Ewald
PO1 HD 00668
Duke University
Durham, North Carolina

AN INTEGRATED INVESTIGATION OF AGING AND THE AGED

This large-scale interdisciplinary research program is attempting to define the changes associated with aging to determine the effects of these changes on the individual, and to seek ways of minimizing or postponing these changes. The staff represents many disciplines, ranging from biochemists and psychiatrists to sociologists and economists. Most of the research relates to the interaction of physical and behavioral changes in aging.

Verbal learning deficit in the aged and the associated autonomic and cardiovascular events is being studied by one of the investigators. Emphasis is focused on the role of internal arousal and subjective anxiety on performance during the learning situation. In addition, the effect of available time and those factors which inhibit or facilitate responsivity in aged individuals are being considered. Attempts are made to modify central nervous system or autonomic nervous system status with the use of pharmacologic agents.

The aging process has an effect upon the central nervous system and one component of this research project is observing and studying this effect through means of a longitudinal study which began in 1954. The subjects are elderly individuals who when entering the study were healthy and socially well adjusted.

Scalp-evoked potential elicited by visual stimulation is looked at in relation to age, background EEG activity, and digital reaction time. Attempts are being made to correlate senescent changes in the "average" evoked response with deviations in the resting EEG, particularly focal disturbances and observations of whether such changes parallel age-related increases in reaction time.

Results of one project have shown that aged subjects in comparison to young subjects show less change in adrenalin levels in the urine, less lability of beat-to-beat variation in the heart rate with respiration and more fast low voltage EEG activity. The differences in peripheral sympathetic neurogenic and adrenalin activity and in electrocortical activity may reflect age determined differences in hypothalamic function.

Adaptation to retirement among a sample of white and blue collar workers show that satisfaction with work predicts life satisfaction in retirement. Short and long term adaptations to retirement are different for white and blue collar workers. The white collar worker brings personal and social resources to retirement which increase the probability of life satisfaction in the long run. The blue collar worker in retirement is in the short run likely to indicate a sense of relief from extrinsically valued work, but in the long run, the absence of work as a regulator and stabilizer of life leads to life dissatisfaction.

Deming, Quentin
P01 HD 00674
Albert Einstein College of Medicine
Bronx, New York

COMPREHENSIVE PROGRAM OF RESEARCH IN AGING

The program has as its objective the understanding of the aging process at all biological levels, from the subcellular particle to man and his social structure. The emphasis is on chemical, physiological and pathological attributes of development and degeneration in living systems. Research is carried out on both nonclinical and clinical levels. Some of the specific areas under investigation are protein chemistry and the chemistry of connective tissue; growth and aging of single cells; the control of the size and growth of the whole organism; genetic bases of disease states; pathogenesis of disease in aging including atherosclerosis, chronic obstructive pulmonary disease, degenerative renal disease and osteoporosis. In addition to the research effort the program serves as a stimulus to the development of new research programs and the training of scientific investigators.

Green, James
P01 HD 04334
Rutgers University
New Brunswick, New Jersey

MULTIDISCIPLINARY APPROACH TO AGING IN RATS

This is a multidisciplinary investigation of changes occuring simultaneously in the rat over time. Physiological parameters such as muscle lysosomes, intestinal absorption, liver metabolism, red cell metabolism and endocrine function are being investigated along with onset and progression of pathological lesions in the same strain of animals at different ages. By following these parameters, it is believed that the changes observed over time in one system relative to another can be established and that the resulting data on physiological deterioration will serve as a basis for identifying cause and effect in the process of aging.

In investigation of the changes in the distribution and properties of lysosomes in aging, tissues examined include liver, kidney, heart and skeletal muscle. Analysis is based on tissue fractionation including differential centrifugation and enzyme analysis.

One portion of the project is considering age dependent changes in the intestinal absorption pattern of sugars, amino acids and fatty acids in portions of the jejunum and ileum taken from one- to three-year-old rats. Rates of absorption and transport are determined by measuring the radioactivity of labeled carbohydrates, amino acids and fatty acids. Changes in potential difference across the intestinal wall of rats at different ages is monitored.

Information is obtained on liver metabolism in aging rats in order to define specifically the aspect of glycolytic and oxidative pathways that is affected in the aging animal. After the establishment of baseline for various metabolic pathways attempts are made to determine the existence of possible alterations in metabolic pathways as well as in the ability to alter such pathways in relation to aging.

It has been reported that with aging the erythrocyte changes its chemical composition, becomes more dense, less osmotically resistant, decreases in glycolytic capacity, and increases its methemoglobin content, along with some alteration in its enzyme activity. The degree to which the aging of individual rats may be associated with changes in function of their erythrocytes is being examined.

Functional changes in endocrine glands during aging and their possible connection with metabolic changes are also examined. A wide variety of organs are surveyed for histological appearance to establish "normalcy" of the animals used in the experiments.

Proper, Robert
PO1 HD 00518
Lovelace Foundation for Medical
Education and Research
Albuquerque, New Mexico

STUDY OF PHYSIOLOGICAL AND PSYCHOLOGICAL AGING

The study is concerned with the effect of aging on the functional capacity of various body systems in a group of professional aircraft pilots, individuals of a profession requiring high standards of bodily and mental health. The areas of study are anthropolmetric and physical competence, pulmonary function, cardiovascular-renal function and psychological capacities. Repeated examinations are conducted in these areas in pilots 20 to 60 years old to assess differences in functional capacity in different age groups and to follow changes in individual subjects over a period of years. In addition to the special tests of function, each subject is given a thorough medical examination comprising history, physical examination and conventional laboratory measurements. A major effort is made to correlate the data from many measurements of many physiological and psychological systems to produce an overall evaluation of the aging process and the interrelations between various body systems.

Robbins, Frederick
PO1 HD 00669
Case Western
Reserve University
Cleveland, Ohio

AN INTERDISCIPLINARY PROGRAM OF RESEARCH IN AGING

The multidisciplinary study of aging was reorganized and reoriented in 1969 into an interdisciplinary approach to the study of aging of macromolecules at different levels of biological organization. As a result of the federation of Western Reserve University with Case Institute of Technology, members of the faculties of the School of Medicine and the Division of Macromolecular Science in the School of Engineering have coordinated

their resources for studies on the mechanisms and consequences of aging. The purpose of the coordinated studies is to characterize the metabolic, physical, and chemical properties of non-renewable macromolecules like collagen and elastin as a function of age at the molecular and supra-molecular levels.

Previous metabolic studies have indicated the need for studying aging of non-renewable macromolecules at supramolecular levels as well as molecular levels. Until the present, most studies of aging have centered on a molecular level. This research program is concerned with the metabolic activity and fate of non-renewable macromolecules as well as the amount and kind of cross-linkages involved. The consequences of non-renewability and cross-linking of macromolecules is being evaluated in terms of its mechanical properties at a macroscopic level and its dynamic mechanical properties at the ultramicroscopic levels. Research projects on the aging of macromolecules are carried out within three broad categories.

Physiological and metabolic studies are conducted on prelabled intact animals to determine the relationship between non-destructive and destructive turnover of collagen during aging.

Physical properties of connective tissues are studied to determine the effect of aging on their mechanical behavior. This is done at the macroscopic level by measuring the stress-strain and elastic properties of normal bone, cartilage and tendons, and at the ultramicroscopic level by measuring the structure-mechanical property relationships of collagen in response to various types of stress. This project involves both electron microscopic and x-ray diffraction studies of collagen fibrils.

Chemical studies of macromolecules are done to isolate and determine the nature of the intermolecular cross-linkages that develop with the aging of collagen.

RESEARCH GRANTS

Adams, Frank
RO1 HD 03238
Oregon State University
Corvallis, Oregon

ENVIRONMENTAL FLUORIDE INFLUENCE ON CALCINOSIS

This research is based on the observation that aorta calcification in residents of high fluoride drinking water areas was lower than those in low fluoride areas of North Dakota. The hypothesis is that calcium removal from bone concurrent with the onset of osteoporosis may be deposited in the dorsal aorta but such calcification is prevented in man by naturally occurring fluoride concentrations of 4-5 ppm in the drinking water. This hypothesis is being tested under experimental conditions with cotton rats and hamsters which are given diets to intensify aorta and cardiac calcification and the administration of appropriate amounts of fluoride to the animals. Being used are the basal diets, casein and Torula yeast with and without 5 ppm of fluoride in the drinking water. Four groups of 20 animals each are used with cardiac calcification expected to develop in 10 weeks. At this time the animals are sacrificed. Measuring criteria are gross and histological examination of heart and aorta for calcification, heart content of mineral (dry ashing) and x-ray examination of bone to determine differences in state of calcification, if other results of the research so warrant.

Adams Mary
RO1 HD 02416
Case Western Reserve University
Cleveland, Ohio

EXPLORATION OF ILLNESS CRISIS IN FAMILY OF THE AGED

This is an exploratory study of the process by which the family of the aged counteracts the disruptive aspects of an illness crisis which physically immobilizes the aged member. The plan is to describe the reorganization of roles and values which occur within the family of the aged person, extent of family aid given and received by the disabled member during adaptation to crisis, transactions of family members with compensatory services during the process, relationship between family response to crisis and family socio-economic status, and predictive value of selected variables from previous family crisis studies for explaining family response to illness crisis of the aged.

Data collection includes at least five "panel interview schedules" undertaken with the patient and a family informant. These evaluations

occur at time of intake, four to six weeks, four months, and twelve months after intake. The sample of 150 includes two groups, those with private resources to meet their hospital costs and those dependent upon other resources for hospitalization. Physical immobilization is to have occurred within one month of hospitalization, the patient having been discharged to home, and no nursing home placement having been made for at least three months past discharge.

Anderson, Robert
R01 HD 02194
University of New Mexico
Albuquerque, New Mexico

THE PATHOLOGY OF AGING IN GERMFREE MICE

Bacterial and viral infections and symbotic pressure contribute to the evolution of the late effects of ionizing radiation in mice. Determinations are being made as to whether apparent and inapparent infections are related to the decreased longevity associated with the post-irradiation state. There is suggestive evidence that the presence of bacteria and viruses may greatly modify the direct effects of the radiation. If the life-shortening effect of radiation of equal dose is significantly diminished in germfree as compared with conventional laboratory animals, that would constitute strong evidence that radiation does not in fact induce an acceleration of physiological aging.

Bergman, Moe
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Hunter College
City University
New York, New York

HEARING AND AGING: DESCRIPTION AND IMPLICATIONS

Changes in auditory abilities and behavior that occur with aging, and the effect of these changes on the activities of daily living pose a problem for consideration. A battery of tests which detect differences in hearing between younger and older adults was developed and is being administered. The tests are designed to reveal deterioration in suprathreshold hearing for speech under a variety of conditions. Equal numbers of subjects are included in each decade from 20-29 through 70-79, for a total of 240 subjects, all of whom have relatively normal hearing audiometrically.

The results thus far indicate that whereas there is only a small change with aging in the understanding of everyday speech heard under favorable conditions, performance under more difficult listening conditions declines with advancing age very dramatically under certain conditions. Among the older subjects it has been found that if a person's original language was not English, even though English may have been used daily for many years, his hearing performance under difficult listening conditions tends to be markedly worse than that of persons of comparable age for whom English is the native tongue.

Botwinick, Jack
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Washington University
St. Louis, Missouri

PSYCHOPHYSIOLOGICAL ASPECTS OF AGING

As people grow older there is usually an associated general slowing of behavior. The problem of loss of speed with age and role of set or expectancy in this slowing down are the research concerns of this project. Simple auditory reaction time (RT) is compared in young and old adults while electroencephalogram (EEG) and electromyogram (EMG) recordings are being made. The data collected should aid in an understanding of the relation between electrocortical activity and reaction time, and between set and slowing with age. Set is being veried by manipulating the preparatory interval and context is varied by the use of regular and irregular series of preparatory intervals.

Results show that anticipatory RT as manipulated experimentally by variation of both preparatory interval duration and context of preparatory interval is a premotor phenomenon. Premotor time, but not motor, is in functional relation with preparatory interval and this relation is almost identical to that of total RT. The results indicate that for meaningful measurement of RT in relation to age, and for meaningful theories of the loss of speed with age, the role of practice in relation to both age and sex must be considered in the context of preparatory set.

Brand, Gerhard
RO1 HD 00146
University of Minnesota
Minneapolis, Minnesota

STUDIES ON AGING IN SKIN

The research objective of this study aims for an understanding of the process of aging as exemplified in the skin. Investigations are carried out at the organ and at the cellular level. Materials used include young, adult, old, and super-aged (serially transplanted) skin, and tumors induced by implanting plastic or glass cover slips. Methods of procedure include histological and histochemical investigations; karyological investigations, antigenic analysis, investigations on the response to infection with dermotropic viruses, investigation on the influence of sex and sex hormones, investigations on the hair growth cycles and hair regenerating capacity.

Brandes, David
RO1 HD 00042
Baltimore City Hospitals
Baltimore, Maryland

FUNCTION OF LYSOSOMES IN RELATION TO AGING

The aim of this study is to investigate changes in functional properties of acid hydrolytic enzymes in the course of cellular aging, and to establish their possible role in the genesis of age pigment. There is evidence which indicates that these enzymes are involved in the digestion of foreign material ingested by endocytosis and in the breakdown of worn-out obsolete cytoplasmic constituents. Incomplete digestion of these materials and loss of the ability of cells of higher organisms to expel such residues may represent one of the mechanisms responsible for the intracytoplasmic deposition of age pigment. These assumptions are tested experimentally in laboratory animals. An attempt is made to elucidate whether this is due to a loss or deficiency of required intracellular enzymes; or whether chemical transformation of the altered material, particularly due to the process of auto-oxidation, is responsible for incomplete digestion and accumulation of unwanted cellular debris.

A congenital deficiency in lysosomal enzymes has been implicated in the pathogenesis of many of the storage diseases, including some of the glycogen storage anomalies. It is possible to establish an analogy by considering age pigment deposition as a chronic form of storage disease related to the aging process. The functional significance of this deposition of pigment in cells of the reproductive

tract in the course of aging, and the analogy with similar pigment deposition in vital organs such as heart, liver, and brain are also being investigated. Because age pigment deposition in cells of the reproductive tract can be readily influenced by experimentally-induced hormonal and other chemical and nutritional manipulations, it is hoped that this will serve as a model for establishing valid correlations between cellular alterations and the aging process.

Carp, Frances
RO1 HD 03643
Langley Porter Neuro-
psychiatric Institute
San Francisco, California

ADULT DEVELOPMENT: AGING IN THE COMMUNITY

This project supports the investigation of age-related characteristics of behavior and attitude by studying (1) effects of change in environment for older persons, (2) changes over time in community-resident old people, (3) correlates of chronological age in later maturity, and (4) differences between elderly and younger people (one pair of groups similar on I.Q. score, the other on socio-economic status).

Other purposes are to predict the adjustment of older persons to a different physical and social environment, and to trace the processes by which older people, originally strangers, form friendships and other social relationships. Earlier findings are being validated by obtaining and analyzing data over a longer period of time on survivors of the original group, and on a different sample of subjects in a different setting.

Carrow, Rexford
RO1 HD 03918
Michigan State University
East Lansing, Michigan

HISTOCHEMICAL STUDY OF CHRONICALLY EXERCISED MUSCLE

Histochemical techniques which identify levels of enzyme activity in the oxidative and glycolytic pathways clearly indicate that large differences in energy metabolism exist within, as well as between, muscle fiber types. Numerous investigations have been directed toward understanding the enzymatic changes that occur with various myopathies while others have used surgical alterations in attempting to clarify the fundamental metabolic processes of skeletal muscle and to determine the extent to which these processes can be modified.

If the "condition" of skeletal muscle is seen as falling along a continuum between the extremes symbolized by severe degeneration on the one hand and high work capacity on the other, with "normal" somewhere in between, the myopathic and neural innervation studies take on new perspective. Collectively, they encompass that portion of the continuum from "normal" to "degenerate," however, histochemical investigations of the other end of the continuum are absent.

The purpose of this project is to study the extent to which various types, intensities and durations of physical exercise affect the distribution of selected histologic and histochemical characteristics of individual skeletal muscle fibers as identified in serial sections. An integral part of this study will be the establishment of enzyme profiles for a large number of muscle fibers from animals subjected to a variety of controlled regimens of chronic exercise.

Chang, Robert
RO1 HD 04144
University of California
Davis, California

MICROBIOLOGICAL STUDY ON HUMAN CELLS IN VITRO

This project is the continuation of a long-term study of the phenomenon of senescence of human cells in tissue culture. Primary cultures of amnion cells are used for study because they divide very slowly. Findings have established the fact that aging is accompanied by an increase in the incorporation of cholesterol and fatty acids into all lipids and a decrease in their oxidation to carbon dioxide. Hydrocortisone at a concentration of 0.1 ug per ml has been found to prolong significantly the postmitotic lifespan of primary human amnion cells in vitro. It has also been repeatedly confirmed that the transformation of primary human amnion cells by the virus SV 40 occurs more readily in aged culture than in younger culture.

Clark, Margaret M.
RO1 HD 02656
Langley Porter Neuropsychiatric Institute
San Francisco, California

STUDY OF SUBCULTURAL FACTORS IN AGING

Through various means cultural factors shape the nature of aging adaptation, influencing some characteristics so that they are very similar among cultures and causing other characteristics to be very

dissimilar. Three subcultural communities in San Francisco, Mexican-American, Japanese-American, and Anglo-American are being studied in terms of characteristics of and adaptation to aging. Three generation families compose the sample interviewed. Special attention is being given to value-shifts resulting from acculturation or historical change from one generation to another and the influence of these on aging adaptation; to the social provisions made for the care of the aged in the three subcultures, the range of behavioral variation permitted the elderly and the status, power, and prerogatives accorded the elderly in each group.

The major question asked of the research is whether there are particular dominant value orientations that if strongly held and firmly sanctioned in a culture pose serious problems in the adaptation of individuals to later life. Such problems might arise if society prohibits the aging individual from acquiring or retaining the means to manifest the desirable qualities of if the values of the culture require activities that are inconsistent with biological changes common to old age. On the other hand, there may well be other value-orientations characteristic of different societies that pose no significant adaptive problems for the elderly and that ease the transition from middle to later life. It is hoped that the findings of this investigation will contribute to the development of crosscultural theories of the psychosocial aspects of the aging process.

Comings, David
RO1 HD 03637
City of Hope Medical Center
Duarte, California

AGING AND DNA: IN VITRO STUDIES

Relatively little is known about the phenomena of aging. The data available suggest that aging is an intrinsic and hereditable change which takes place in each cell. This strongly implies a change in the informational macromolecules of the cells. Recent studies have indicated that changes in the properties and rate of synthesis of DNA, RNA, and protein occur in aging cells. The purpose of this research is the use of an in vitro cell culture system to study the effect of aging on the informational macromolecules of the cells, especially DNA. These include the many advantages for superior control of environmental conditions offered by an in vitro system, the use of non-aging heteroploid cells as controls, and the advantages of the use of pure cells for biochemical studies. Some of

the specific questions considered deal with the following: It has been shown that the DNA of aging rats has a higher melting point than younger rats, is this also true of diploid cells grown in tissue culture? If so, is this increase in DNA Tm secondary to changes in the base composition of DNA, secondary to increased binding by nuclear proteins, or due to other factors? Is there a change in the rate of DNA, RNA, or protein synthesis in aging fibroblasts? Does chromatin become progressively less able to support DNA dependent RNA synthesis? Does the electrophoretic pattern of proteins change as cells age? Can the addition of specific compounds to the media alter the development of these biochemical changes and does this also result in a prolongation of the lifespan of the cells?

Cristofalo, Vincent
RO1 HD 02721
The Wistar Institute of
Anatomy and Biology
Philadelphia, Pennsylvania

CARBOHYDRATE METABOLISM AND AGING IN VITRO

Certain populations of normal diploid cells, e.g., human fibroblasts, will survive only a limited number of generations in tissue culture. The process that kills them may be cellular senescence. If so, these cells provide a much simpler system for studying cellular senescence than does the whole organism.

In contrast to diploid cells, populations of cells whose chromosomes have been altered from the normal may survive indefinitely.

This study uses both normal diploid fibroblasts in culture for various periods of time and fibroblasts that have been transformed by SV40 virus so that they have an abnormal chromosomal pattern and indefinite survival.

The hexose monophosphate shunt pathway of glucose to pentoses and eventually to the nucleic acids is being studied. The hexose monophosphate shunt provides ribose and deoxyribose for nucleic acid synthesis and also provides reduced nicotinamide adenine dinucleotide phosphate (NADPH) for use in a number of synthetic reactions.

The incorporation of labeled glucose into deoxyribonucleic acid and ribonucleic acid and the relative contribution of oxidative and non-oxidative pathways of pentose synthesis are being evaluated.

Measurements are being made of NADPH/NADP ratios, e.g., hexokinase G-6-PO4 dehydrogenase, transaldolase, and transketolase.

Daniel, Charles
RO1 HD 04164
University of California
Santa Cruz, California

AGING OF MOUSE MAMMARY GLAND

This project is aimed at investigating aging processes in mouse mammary tissue under conditions of serial propagation in vivo. While it is well known that several types of cells are able to propagate for only a finite period of time in tissue culture without undergoing degenerative changes in morphology and growth rate, similar evidence has been difficult to obtain in living animals because of various technical difficulties.

Through use of a technique of serial transplantation of mammary gland into "cleared" fat pads, it has been recently shown that mouse mammary epithelium has a limited lifespan when propagated serially in vivo even under conditions which are optimal for survival, growth and function. This investigation is being pursued at present by varying a variety of experimental parameters such as time, host age, and endocrine status. Several criteria are being used to describe and measure the aging process, including morphological, physiological, functional (secretory) and kinetic.

Davis, Roger
RO1 HD 03949
University of South Dakota
Vermillion, South Dakota

AGING IN MONKEYS

The effects of aging on performance of rhesus monkeys are being investigated through a continuation of research begun in 1952 with a group of 16 monkeys ranging in age from 18 to 30 months. Seven of that group, now 18 years old, survive and form an aged group. Four of the offspring of these animals provide a comparison group of mature adults. Six aspects of performance are being investigated, manipulatory behavior, memory, motivation, time estimation, vigilance, and assessment of activity.

Results compiled to date show that old animals perform more poorly on tasks which involve memory and are more susceptible to interfering effects of shifting set than middle aged animals although the old animals perform as well or better than middle aged monkeys on many familiar laboratory tasks. The deficit in short-term memory can be overcome to some extent with over-training on the particular kind of task. Short-term memory tasks will be explored further and distracting elements will be introduced. Experiments aimed at determining whether short-term memory losses in old animals are related to interference at the onset of the stimulus pattern, during the memory interval or to a decay of the signal during short-term memory. Since it is known that short-term memory effects can be compensated for to some extent by overlearning the additional information might lead to further understanding as to the order, temporal spacing, and context of signals that favor remembering by old subjects.

Donahue, Wilma
RO1 HD 01274
University of Michigan
Ann Arbor, Michigan

MILIEU TREATMENT OF OLDER MENTAL PATIENTS

Certain of the environmental characteristics used in therapeutic treatments are being varied in this project in order to determine their effects. There are two clearly distinguished kinds of orientation for milieu therapy. One is directed towards the establishment of social and work relationships within the institutional setting and the other toward the community. The first is represented by such activities as institutional work programs, recreation, and other designed to help the patient effect a better adjustment in the institutional community. The second attempts to develop a more active relationship between the patient and the outside community. These two factors are varied in the treatment of four separate wards in order to be able to assess the effectiveness of institutional-oriented versus community oriented milieu therapy and at the same time assess the effectiveness of these two types of treatment with the regular staff of the institution and with a staff augmented by specially trained personnel.

A second phase of the project is the following of patients who have undergone experimental treatment after they have been returned to the community from the mental hospital. It is recognized that the effect of the treatment will interact with the type of post-hospital setting into which the individual is placed, therefore the evaluation of the post-treatment results is in terms of the dimensions of the

particular living arrangement into which the patients have been placed. The particular dimensions selected are segregate, congregate, institutional and amount of health services provided.

Eichorn, Dorothy
RO1 HD 03617
University of California
Berkeley, California

INTERGENERATIONAL STUDIES OF DEVELOPMENT AND AGING

This is a study of the relationship of early life characteristics to adult behavior and patterns of aging. It draws upon the resources of three major longitudinal studies of the Institute of Human Development (the Guidance Study; the Berkeley Growth Study, and the Oakland Growth Study). In addition to the subjects of the three studies and their spouses, two additional categories of research subjects are involved in data collection: Children of subjects and parents of subjects. Basic questions relate to continuities and discontinuities in human development. Early appearing behavior and growth characteristics are related quantitatively to late childhood and adult characteristics. Relationships over time in physical, psychological, cognitive and personality traits are examined, also such social behavior characteristics as aggression, irritability, dependency, etc.

One important area examined is the extent to which similarities can be noted between contemporary children and their parents. Comparisons are made of personality, physical and intellectual measurements of the current children and those from records on their parents at the same age. These comparisons are used to determine the levels of association between each parent and children of the same and opposite sex. An attempt is made to quantify patterns of familial resemblance in physical and intellectual growth using parameters from fitted curves of the development of individuals.

Other areas of research include development in middle and old age and intergenerational similarities and differences in family patterns. Continuity of child-rearing practices is examined across the generations. The extent to which parental attitudes toward children and child-rearing practices persist across generations is expected to contribute to the understanding of non-genetic transmission of influences in the environment.

Ewing, Larry
RO1 HD 00636
Oklahoma State University
Stillwater, Oklahoma

EFFECT OF AGING AND STRESS ON TESTICULAR METABOLISM

It has been suggested that both the endocrine and germinal elements of the testis exhibit decreased viability with advancing age in mammals. Research in progress is examining mechanisms which might be acting to cause testicular involution in the aging rabbit. Results obtained on this project to date have proven that testicular aging is accomplished by significant alterations in testis size, testis constituents, blood flow through and glucose uptake by the organ. Biosynthesis of total protein, nuclear protein, various lipid fractions, oxidation of glucose and testosterone secretion in the aging testis are being investigated.

Felts, William
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Oklahoma City, Oklahoma

CHARACTERISTICS OF DENTAL-SKELETAL AGING

There is a present lack of integrated information on age changes in any one animal form. The objective of this project is to develop an analysis of the pattern of age-related changes that occur in the dental and general skeleton of the inbred mouse. Being considered are macro- and micro-structure, physical characteristics of strength, mass volume and density and cellular activity in both the normal state and under conditions of trauma in the dental skeleton and in selected portions of the axial and appendicular skeleton. A secondary objective is the extension of critical portions of the study to the corresponding portions of the dental and general skeleton of the dog.

The quantity and mechanical organization of the dental structures are being looked at during periods of growth, maintenance and old age, above the microscopic level. One phase of the study is ascertaining age differences in the capacity of the several involved tissues in healing of dental lesions and relates alveolar healing to a parallel study of healing in fractures of limb bones.

Fozard, James
R01 HD 00340
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Boston, Massachusetts

AGING AND THE SELECTION OF INFORMATION

This project is a study of systematic changes with age in the selection, organization and short-term retention of information by human subjects. Groups of men representing each decade between 20 and 70 years are being tested for their performance on a variety of tasks developed to bring out critical features that differentiate along the age dimension. The tasks include various types of reaction time tests, short-term memory experiments, visual signal detection tests and others. Aging effects are evaluated in terms of differential or ratio scores between a subject's performance on two paired tasks that differ in complexity as well as in terms of absolute performance scores.

In most of the experiments age has produced a decrement of performance, but of more interest has been the interaction of task type with the rate of decrement. The latter findings appear to hold some promise for a general characterization of the type of decrement aging produces.

Many of the subjects in this study are also subjects in a Veterans Administration sponsored study on aging. Efforts are being made to integrate some of the information from the behavioral experiments with the extensive medical and anthropometric data available on the same subjects.

Getty, Robert
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Iowa State University
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GERONTOLOGICAL STUDIES IN THE DOG AND HOG

Tissues and organs are being collected from animals of known genetic history, age, and diet in attempts to establish a "normal" histological and cytological picture of the various systems and organs of the dog and hog from birth to senility. Because of the extensive use of the dog and hog as experimental animals in medical research it continues to be imperative that the so-called "normal" be established at both the macroscopic and microscopic levels.

The presence of atherosclerotic plaques in all the major blood vessels of the hog, including those of the brain has been observed. Spontaneously occurring atherosclerotic plaques and intimal sclerosis have been observed in the coronary arteries, the cerebral arteries, and many of the major blood vessels of the body, including the thoracic and abdominal aortas, and peripheral blood vessels.

In both animals lesions first appear in the aorta, later in the coronaries, and still later in the cerebral arteries and other major arteries. Thus both animals are similar to man as to occurrence and distribution of atherosclerotic plaques.

Gland weight to body weight ratios have been established for a number of endocrine glands in the dog and hog and these studies are continuing. Histological studies are also in progress in reference to the aging canine and porcine eye, reproductive tract, salivary glands, myocardium and nervous system. The roles of lipofuscin and amyloidosis in both the dog and hog are being evaluated and correlated with age changes in man.

Since morphologic and functional age changes can be observed in the dog and hog, it is believed that a better understanding of the normal aging processes in man and other animals should result from these comparative studies.

Gilmore, Charley
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Angell Memorial Hospital
Boston, Massachusetts

DISEASE IN ANIMALS RELATED TO AGING

The indentification of patterns and trends in disease processes in relation to aging animals is observed chiefly in dogs and cats in this project. The type and frequency of certain disease states may serve as indicators of the changes in the body which occur as a result of aging. Autopsies are performed on animals that die or are sacrificed during illness, or that have reached old age. The anatomic findings then are correlated with age, genetic background, sex and laboratory and clinical data which have been obtained at intervals during the lifespan of animals.

Evidence that a definite relationship exists between age and specific diseases, as well as age and diseases of particular body systems has grown out of this study. Other correlations under

study are diseases within age groups related to sex and genetic type (breed). Of particular interest among diseases having a relationship to age, breed and sex are neoplasms. The raw data from which this evidence was gained is being added to and the data are being processed by computer for critical analysis.

Studies thus far have led to the characterization and description of some disease entities in dogs and cats (Reticuloendotheliosis, Canine systemic lupus erythematosis, Thalluim poisoning, Lead poisoning) and some comparative data on diseases common to animals and man. A continuing aspect of the research is the search for additional animal models of human disease.

Goldstein, Sidney
R01 HD 01550
Brown University
Providence, Rhode Island

CHANGING CONSUMPTION PATTERNS OF THE ELDERLY

This study of consumption patterns of the aged examines the impact of aging on human adjustment. Adjustment is studied through the distribution of expenditures for health, recreation, food, housing and other basic necessities. Data from Bureau of Labor Statistics surveys on income, savings and expenditures in 1950 are compared with similar data available on the consumption patterns of the aged population for 1960-61 to ascertain changes in the situation of the aged during this ten-year period. In addition, consumer behavior patterns of the aged in 1960-61 are compared with those of younger segments of the population. This analysis of age differentials and the comparison of 1960-61 patterns of the aged with those of younger cohorts in 1950 permits evaluation of the pattern of change in consumer behavior as a given age group proceeds through the life cycle. Special consideration is given to the impact on the consumer behavior of the aged of such variables as family size, home ownership, and socio-economic status. Comparison among the aged in urban, rural-nonfarm, and rural farm places of residence permits evaluation of the extent to which place of residence affects income, expenditures, and savings.

Although the absolute amounts of funds available to the aged have increased from 1950 to 1960-61, expenditures have correspondingly increased, and there have been, relative to the rest of the population, only minimal changes in the overall patterns. The aged continue to be significantly more concentrated at low income and

low expenditure levels. Proportional expenditures for food, housing, household operations, and medical care become increasingly larger with rising age of the family head, especially after age 65.

Hausknecht, Richard
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ESTROGEN PRECURSORS IN THE POST-MENOPAUSAL FEMALE

The production rate of estrogens in postmenopausal women, using the isotope dilution technique is being studied in this project and a determination made of the important precursors of urinary estrogens in these women. Post-menopausal females produce and excrete small amounts of estrogens. Investigations have demonstrated that these females produce significant amounts of esterone, but little or no estradiol-17-beta. In view of this finding it can no longer be assumed that estradiol-17-beta is the primary precursor of urinary estrogens in the post-menopausal female, as is true in the normally menstruating female. Being administered are C^{14} and H^3 labeled estrogens, androstenedione, dehydroepiandrosterone and its sulfate, and pregnenolone. The major urinary estrogen metabolites are being identified and separated by established chromatographic techniques.

By selective inhibition and stimulation of the adrenal glands, an attempt is made to identify the role of these organs as well as the post-menopausal ovary in the secretion of such precursors. The information obtained may be of great significance in the treatment of such neoplasms as breast and endometrial carcinoma, frequently thought to be "estrogen dependent" tumors.

Hayashida, Tetsuo
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San Francisco, California

STUDIES WITH GROWTH HORMONE AND PROLACTIN

This study is concerned with the measurement of pituitary growth hormone in the pituitary and plasma of rats of all ages beginning with the foetus and postnatally up to senility. It will include the determination of the influence of other hormones upon growth hormone secretion and a reinvestigation of the effect of various types of stress upon growth hormone levels. Both bioassay and radioimmunoassay techniques will be employed. Comparative immunochemical

studies of growth hormone and prolactin among representatives of all vertebrate classes will be continued in an effort to determine evolutionary changes in the structure of these hormones. A strong emphasis will be given to the study of the relationship of growth hormone to prolactin in primates.

Hayflick, Leonard
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Stanford University
Stanford, California

PROGRAMMED SENESCENCE IN CULTURED HUMAN CELLS

It has been determined that normal human diploid cells in culture have a finite lifespan measured in population doublings. In mouse cells frequently and in cells of other species occasionally a spontaneous alteration that occurs in vitro transforms the population to one which is karyotypically abnormal and in which most usually the chromosome number varies around a mode much higher than the species of origin of the cell line. It is only these transformed cells that possess the ability to multiply indefinitely in culture.

The doubling capacity of normal cells in vitro is generally related to the age of the donor and the average lifespan of the species. Normal human fibroblasts can divide 50 $\pm$ 10 times when derived from embryonic tissue but only 20 $\pm$ 10 times when adult tissue is used. Atempts are being made to determine the uniformity of this phenomenon by studying, longitudinally and cross-sectionally, several types of tissue obtained from different animals and from man. Other age related phenomena such as effects of irradiation and limited nutritional levels of protein and carbohydrate are investigated in vitro. The induction of several enzymes and collagen production is studied at intervals during the limited in vitro lifetime of normal cells derived from man and animals.

Holloszy, John
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Washington University
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EXERCISE INDUCED BIOCHEMICAL AND ANATOMIC ADAPTATIONS

Regularly performed exercise can greatly increase the capacity for physical work. One major purpose of this project is to elucidate the biochemical and structural adaptations brought about by exercise that are responsible for this increase in work capacity. Endurance exercise used routinely is running on a motor driven treadmill.

The effects of physical training on the enzymatic pathways involved in the generation of ATP needed for muscle contraction are under way. Male rats of the Wistar strain are used as subjects. It has been found that the capacity of leg muscles to oxidize pyruvate doubles in rats subjected to a strenuous program of treadmill running.

A second major objective is to obtain detailed information regarding the effects of regularly performed exercise on growth and development, food intake, body composition and selected aspects of the aging process. The latter include the decline in exercise capacity, the changes in body composition, and the alterations in the levels of activity of some of the enzymes in skeletal muscle that occur with aging.

Recent studies on the effects of regularly performed exercise on body composition have shown that exercising rats are significantly leaner than sedentary animals which are food restricted so as to maintain their weights the same as those of the exercisers.

Homburger, Freddie
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AGING STUDIES IN SYRIAN HAMSTERS

These studies are aimed at determining life expectancy of the Syrian hamster and the aging changes that occur throughout the lifespan of these animals. The investigator is using several inbred strains of hamsters and is observing age-influenced strain differences. Small groups of animals are autopsied periodically with gross and histological studies performed on all organs. Attempts are being made to discover spontaneous (constitutional) disease and develop strains which have high incidences of any one disease. Disease-carrying strains may then serve as models for the study of human disease.

The mean survival time of 8 inbred strains as measured in from 38 to 79 animals surviving beyond 300 days of age was from 464 to 711 days. In the longest lived strain, the survival time was significantly longer at the 1% probability level than in all other strains studied. In the additional five strains where intercurrent disease had caused a significant mortality in animals younger than 300 days, the survival time ranged from 480 to 561 days. This information on spontaneous survival time of hamsters is new, and the dependence

of longevity upon genetic factors will enable investigators to control this variable in future studies by using inbred strains with known longevity.

In one strain a hind-leg paralysis occurs in all males relatively late in life. This is inherited by a sex-linked, recessive gene. In another strain a high incidence of adrenal cortical adenomas was found, as well as occasional pituitary tumors not statistically associated with the adrenal lesions. In the same line there is a high incidence of obesity, especially in females beyond six to nine months of age.

In two other species cystic prostatic hypertrophy occurs in all males beyond a certain age. In all strains about 25% of the animals die with enlarged hearts and nephrosclerosis. This was found tc be due to hypertension occurring quite early in life. The genetics of this phenomenon are being studied at present.

Hruza, Zdenek
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AGING MECHANISMS IN CONNECTIVE TISSUE AND VESSELS

There are three portions to this project, collagen aging in vivo, calcium turnover during aging, and cholesterol metabolism during aging. Aging of collagen in vivo can be slowed down or speeded up by a decrease or increase in the environmental and body temperature. If intact tails are sewn under the skin of rats and their environmental temperature is increased from 22 to 37 degrees C., aging of tail tendon collagen fibres is speeded up significantly. Undernutrition, which slows down aging of rat tail tendon collagen, is ineffective when the tails are kept at the body temperature. The effect of undernutrition on collagen aging can apparently be explained by limitation of blood supply to the tail. This and other experiments show that most of the experiments changing the rate of aging of collagen can be explained by physical changes dependent on the temperature and not by a change in the amount of "cross-linking agents."

Calcium turnover decreases in the bones and soft tissues during aging. It has been found that in the bones, this can be explained by a decrease of bone blood flow and in part by slower binding of new calcium in the bone mineral. Calcium turnover in the soft tissues cannot be changed by hormonal factors connected with the metabolism of calcium.

Blood level of the injected cholesterol-^{3}H decreases more slowly in old rats in comparison with young ones. This is partially caused by slower excretion of cholesterol-^{3}H in the feces, and partially by slower cholesterol uptake by the tissues. Further experiments are in progress to elucidate slower cholesterol turnover in older rats.

Jarvik, Lissy
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BEHAVIORAL AND CHROMOSOMAL CHANGES OF AGING

Alleviation of the gradual deterioration in mental functioning that characterizes so many of the aged is the long-term goal of this project. The investigator believes that age associated modifications of the biological substrate interfere significantly with the maintenance of intellectual agility in the elderly and is attempting, therefore, to unravel the intricate interplay between behavioral, physiological and chromosomal changes characteristic of advancing age. Measurements include medical examinations, psychological tests, psychiatric evaluations, clinical laboratory and chromosome analyses as well as accumulation of extensive life history information.

One group of subjects consists of survivors of a very old longitudinal study. They are all in their eighties and most continue to live in the community. Moreover, these subjects are all twins, making possible a research design whereby the co-twin is used as a control, thus minimizing effects of genetic differences, ethnic and cultural influences and to a degree socio-economic variations.

Specific psychological tests and retest performances have been examined in terms of decline. It has been found that when psychological decline meets "critical loss" criteria, biological dysfunction or pathology is indicated. Not only was there a significant correlation between such "critical loss" and five-year mortality, but among the group of twins where one partner had a "critical loss" and the other did not, it was nearly always the partner with the "critical loss" who died first.

Even the gradual memory loss characteristic of normal aging, as distinguished from the pathological changes picked up by "critical loss", may be reflected in measurable biological phenomena. Thus, a preliminary analysis of a small subsample shows a significant positive correlation between loss of memory and loss of chromosomes.

Jenkins, Marie
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Madison College
Harrisburg, Virginia

RELATIONSHIPS IN AGING AND REPRODUCTION IN PLANARIANS

Possible relationships exist between reproductive activity and aging in the planarian, Dugesia dorotocephala. Planarians are being used in this study because they are the simplest metazoans that are remotely similar in structure to higher animals. Races studied include as asexual population which reproduces only by fission, with rare exceptions, and a sexual race which deposits cocoons throughout the year. In the asexual race it appears that rejuvenation follows fission, and there is no evidence thus far that aging occurs. In the sexual race an attempt is being made to establish two lines of descent: one in which fission precedes onset of sexuality, and one in which fission does not occur during the life-time of the individual. Planarians which have become sexual do not undergo fission unless injury occurs, but show evidence of aging which culminates in death. The aging process is being investigated in terms of longevity, cocoon production, viability of offspring, effects of fission, and changes in respiratory enzyme activity as a function of age. Effects of temperature, pressure, and other parameters are also considered.

Results to date indicate that fission is ineffective as a means of reproduction in the sexual race but may, nevertheless, be an important factor in promoting vigor in individuals which have undergone fission prior to sexual maturity.

Jones, Malcolm
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RADIOGRAPHY AND PATHOLOGY OF SPINE AGING

The specific aims of this study are to determine the age at which degenerative change appears in the primate spine through the use of radiographic methods; to consider the effects of weight bearing torque, sex, trauma and function; and to compare the areas of maximum degeneration observed in the primate spine and in the human spine. The radiographs are assessed for maturation of the spine, with particular emphasis on the detection of degenerative changes.

The induction of scoliosis by specific methods is being attempted in order to evaluate the causes of the development of scoliosis. A group of gibbons is used as subjects. Laminectomy in six of the colony has given rise to gibbus formation with irregularity of development of the vertebral bodies. This has coincided in form with the appearance of Scheuermann's disease in the human.

Specification of epidural and paraspinal veins has shown distortion of these structures. This appears to be a contributing cause in the abnormal vertebral development. Accelerated degenerative changes are occurring at the operative sites.

Distortion of motion potential of the spine by laminectomy with subsequent degeneration has been shown indicating an increasing rigidity. Such rigidity is comparable to that shown in the human spine as a result of degenerative changes.

Kabara, Jon
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DRUGS AND BRAIN CHOLESTEROL DURING DEVELOPMENT AND AGING

Little is known about the relationship between lipid metabolism and brain function. Studies thus far indicate that brain cholesterol metabolism continues throughout the lifespan of an animal, but not much is known about factors affecting this process. The rate and importance of metabolism occurring during developmental and aging phases remains controversial.

This project is an evaluation of the effects of drugs on brain cholesterol in mice. Hypocholesterolemic agents and drugs known to affect the CNS are being tested. The content of cholesterol in brain is measured as well as the uptake of labeled acetate and glucose into cholesterol. Long range effect of drugs is studied by injecting pregnant mice and following the growth and lifespans of their progeny.

Klein, LeRoy
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Case Western Reserve University
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COLLAGEN BIOCHEMISTRY IN WOUND HEALING AND AGING

A determination of the kinds of metabolic pathways that exist in vivo for collagen, the relationship between these pathways and the changes

that occur in this relationship with age are the concerns of this research.

A clear-cut separation of old and new collagen and their respective metabolic pathways was accomplished by establishing a sound basis for the quantitative interpretation of isotopic data in prelabeled animals and a means for detecting and minimizing the reutilization of radioactive amino acids. With sufficient passage of time an isotopic steady state has been achieved in prelabeled animals. The level of radio-activity in salt-soluble collagen has been found to estimate the degree of reutilization of radioactive amino acids (proline) by synthetic pathways. The use of diets with a high content of nonradioactive proline has been shown to reduce the reutilization of radioactive proline to an insignificant level.

The proliferation of collagen in the connective tissue induced by sponge implantation or carrageenin inoculation separates newly formed collagen from old collagen. This separation has permitted a study of the biological interactions of a "metabolic inert" macromolecule like collagen and how these interactions change with age. It has been found that pre-existing fibrous collagen may be reused in a nondestructive manner by being solubilized in vivo, translocated locally as citrate-soluble collagen and repolymerized to fibrous collagen. This cyclic change of collagen would not be visualized by morphological or pulse-labeling techniques.

Kreilick, Robert
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Rochester, New York

HINDERED PHENOLS AS RADICAL SCAVENGERS AND SPIN LABELS

Radiation damage of cells is known to produce radicals. This study is examining the production of free radicals by the ultraviolet irradiation of mixtures of hydrogen peroxide with an amino acid or polypeptide. By electron spin resonance spectroscopy the investigator is following the reactions of the radicals with various antioxidants, mainly hindered phenols and nitrones which function as radio-protective agents. The general type of antioxidants investigated have been shown to have an important effect on the aging process and may serve as radio-protective agents. Kinetic experiments are carried out by flash photolysis combined with electronic time averaging of data. New phenoxy radicals are being attached to purine or pyrimidine groups to serve as spin labels in studies of base pairing, including the determination of the equilibrium constant and of thermodynamic data.

Krizek, Thomas
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Yale University
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AGING RATES OF HETEROCHRONIC ISOGENIC TRANSPLANTS

The aging processes are gradual, and their effects on the organism are cumulative. A basic unanswered question concerning the aging processes is whether each organ system contains a specific, built-in program for aging or whether these processes are related to and under the overall control of the host-environment. Surgical techniques are advancing to the point where many human organs can be replaced if diseased or "worn out" and widespread clinical transplantation depends only on the solution to the allograft-rejection phenomenon. Although organs and tissues are being transferred to and from patients of different ages, the ultimate fate of these transplants related to aging is unknown. A direct approach to this question is the transplantation of tissue from a donor of one age to a recipient host of a different age. Allograft-rejection mechanisms prevent lasting transplants in other than immunologically uniform (isogenic) animals, of which rats and mice are the only laboratory animals sufficiently inbred as to provide readily available isogenic strains.

The present study is undertaken and aims to continue the development of an experimental model in an isogenic strain of rats. Heterochronic transplants of skin and kidney are measured against known quantitative, age-associated changes for each organ system. The model will provide the foundation for answering some important questions about aging: Is the rate of aging of an organ arrested or reversed when placed in a young environment and, conversely, does a young organ age more rapidly in an old animal; can an organ system or tissue be preserved indefinitely by successive transfers to young animals as each successive host ages.

Lang, Calvin
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University of Louisville
Louisville, Kentucky

METALS AND NUCLEIC ACIDS IN MOSQUITO GROWTH AND AGING

In an earlier study it was discovered that there could be obtained from the supernatant fraction of homogenates of mosquito larvae an unusual DNA. This soluble DNA was present in high concentration only during larval growth and not in subsequent developmental stages.

This appears to be a unique form of DNA which does not seem to be an artifact arising from breakdown of higher molecular weight DNA. The physical, chemical and metabolic properties of this new DNA are being studied following fractionation and its properties compared with those of nuclear DNA of the same species. The origin and fate of the new DNA within the larvae is being determined. By the use of C^{14} labelled thymidine and uridine in the diet of the larval medium, the metabolism of the DNA is studied.

Recently it has been discovered that soluble DNA is labelled 10 times faster than nuclear DNA. Moreover, other evidence suggests that it is probably involved as an intermediate in DNA replication.

Lindsay, Hugh
RO1 HD 02919
West Virginia University
Morgantown, West Virginia

AGE AND ATROPHY OF DISUSE

The purpose of this study is to survey various hormonal influences upon disuse atrophy in bone in relation to age. Comparisons of chemical and mechanical properties are made for bones from immobilized and weight-bearing legs in male rats throughout the lifespan. The degree and nature of these changes is studied at subnormal, normal, and excess levels of various hormones; those studied intensively are testosterone and parathyroid hormone. Pilot studies have been conducted on pituitary and adrenal hormones.

Interactions between disuse atrophy, hormone treatment, and age have been demonstrated for testosterone and parathyroid hormone.

Ling, Bing-Chung
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San Francisco, California

THE ATTITUDE OF THE AGED TOWARD AGING - A CROSS-CULTURAL STUDY

An attempt is being made to discover significant similarities and differences between the American and Chinese cultures in attitudes of the aged towards life in general and toward aging. The hypothesis that it is one's attitude toward old age, rather than old age per se that underlies one's happiness during the declining years of one's life is investigated.

An interview in depth has been conducted individually with 100 Chinese residents of Taiwan, 60 years of age and above, and with 100 native-born U. S. citizens, each of whom matches his Taiwan counterpart in age, sex, educational level and relative socio-economic status. A comparison is being made between the two samples with respect to their attitudes toward aging and life in general and an intensive analysis is being conducted of the background of each of the 200 subjects which may have contributed to a particular attitude.

Lowenthal, Marjorie Fiske
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ADULT DEVELOPMENT: CONTINUITIES AND DISCONTINUITIES

The global hypothesis of this study is that a significant component of the adaptive process in adulthood consists of the individual's efforts to achieve, restore, or maintain equilibrium between his aims in life (intentiality, goals) and his behavioral pattern or style. It is assumed that this process becomes particularly conscious and therefore accessible to study at transitional stages.

Major objectives of the study are (1) to determine lifecycle trends in the nature and direction of these intentions (e.g. toward growth or retrogression); (2) whether transitions which are normatively viewed as incremental (such as going to college, acquiring a first job, marriage, parenthood) reinforce growth-promoting processes; and (3) whether transitions normatively viewed as decremental (the empty nest, widowhood, retirement, serious illness of self or close other) result in equilibrium at a lower level of complexity than prevailed before the transition. Finally, (4) to explore the extent to which changes between the two domains take place in the absence of transitional stages, thus distinguishing between developmental and socializing processes. Variables being controlled for include incremental and decremental transitions, sex and socio-economic status (middle and lower middle class). Change in goals and the fit with behavioral pattern is measured after an 18 month interval which for some of the sample will include a transition. Stress perceptions, social perceptions and time perspective are examined as intervening variables. Several dimensions of the goals/behavior paradigm will be compared with conventional indicators of adaptation at Times One and Two.

Meyer, Karl
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Yeshiva University
New York, New York

MUCOPOLYSACCHARIDES OF CONNECTIVE TISSUE

These studies are designed to gain information on the role of mucopolysaccharides of connective tissues in development, skeletal degeneration, and aging. At present the approach deals mainly with studies on the chemical structure of mucopolysaccharides and their protein complexes from various embryonic, adult, and senile connective tissues and from tissues and body fluids in some inherited diseases. Special attention is being paid to the differences between the structure of keratosulfate of young and old persons.

Differentiated embryonic cartilage cells grown in tissue culture on longer incubation produce a sulfated glucosamine and galactose containing polysaccharide which appears to be keratan sulfate, and thus leads to a model of aging of cells in vitro.

Nandy, Kalidas
R01 HD 04188
Emory University
Atlanta, Georgia

GENESIS AND SIGNIFICANCE OF LIPOFUSCIN PIGMENT

There are many questions raised concerning lipofuscin age pigment. They relate to the formation of this pigment, whether the formation represents an intrinsic irreversible change associated with the aging of cells, does it have physiopathological or metabolic significance, and whether the pigment can be influenced by extrinsic factors so as to be increased or reduced.

This study is carried out in neurons, myocardium, adrenals, liver, kidney and skeletal muscle in control mice at different ages (newborn to 30 months) and mice subjected to Vitamin E deficient diet, hypoxic environment and Centrophenoxine treatment. It has been observed that mice kept on a Vitamin E deficient diet and in hypoxic condition show an increase in rate of formation of lipofuscin while a reverse effect has been noted in the mice treated with Centrophenoxine. The investigation includes the study of lipofuscin using histochemical, biochemical and fluorescence methods and also enzymes (acid phosphatase, succinate, lactate and glucose-6-phosphate dehydrogenase and cytochrome oxidase) which appear to be related to the

pigment. The genesis of lipofuscin may have important relation to the underlying mechanism of intracellular changes resulting from the aging process.

Quay, Wilbur B.
RO1 HD 04103
University of California
Berkeley, California

BIOGENIC AMINES IN MECHANISMS OF AGING

The objective of this research is to define the extent and ways in which functional mammalian cellular age changes may be related to changes in the metabolism and actions of biogenic amines especially indol- and catecholamines. These amines and their metabolic alterations are likely to be unusually informative both in terms of etiology of deleterious senescence changes and in terms of the possibility of common and basic or molecular changes in the aging process.

Quantitative and qualitative changes in enzyme that methylate these biogenic amines in selected mouse tissues are under study. Different strains of mice are compared in regard to age changes in this particular system of enzymatic activities. The hypothesis being tested is that aging in selected tissues and strains of mice and other mammals is related to, or accompanied by modifications in molecular structure of particular enzymes leading to changes in substrate specificities as well as activities revealed in vitro.

Rhudick, Paul
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Age Center of New England
Boston, Massachusetts

INTELLECTUAL FUNCTIONING IN LATER LIFE

The relationship between I.Q. patterns, age, sex, and socio-economic factors is being determined in this project through the use of a combined longitudinal and cross-sectional approach in which male and female aged subjects are given the Wechsler Adult Intelligence Scale along with personality, health, and other indices. The study focuses on deficits and gains in I.Q. over time, the differential contribution of life experience on various subtests and the relationship of I.Q. to survival status.

Specifically being examined are the direction and amount of change in WAIS performances in adults over 65 years of age during intervals of one, two, and three years in a longitudinal followup; the relationship of absolute levels of WAIS scores and survival rates after 65 years of age; the impact of health changes upon changes in WAIS performances over these intervals; and the comparability of factor structure at different age levels on the ability and personality measures.

Robinson, Sid
R01 HD 04056
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Bloomington, Indiana

PHYSIOLOGICAL AGING IN MAN

This is a research program in human stress physiology. Cross-sectional studies of the effects of age on man's physiological adjustments to work and thermal stresses are carried out. The overall aim is to study the effects of age on work capacity, particularly when combined with heat or cold stress. The chronic effects of vigorous physical training by older men on aerobic and anerobic capacities for work and the associated circulatory and respiratory changes are compared with similar data on young men. The immediate responses and tolerances of subjects 8 to 65 years of age to standard work-heat stresses are also studied. Acclimatization of young men and older men to work in the heat is compared. This includes temperature regulation, circulatory stability and heat transport to the skin, capacity of the sweat glands to secrete and to reduce their output of sodium in response to salt deficiency, and the ability of the kidneys to conserve water in dehydration and to retain sodium in salt depletion. The effects of age on resting men's responses to cooling are also studied.

Rockstein, Morris
R01 HD 00571
University of Miami
Miami, Florida

AGING IN MUSCA DOMESTICA L

The primary objective of this study is to investigate the structural, functional, and biochemical changes at the cellular level in the flight muscle of aging houseflies, which characteristically show a decline in flight ability as well as the ultimate failure of flight

altogether in very old male flies. Studies include cytological, histochemical, gross anatomical changes, and evaluation of a number of biochemical parameters in the flight muscle with advancing age, prior to and concomitant with the actual failure of this motor function.

Current studies include basic chemical studies on the enzyme arginine phosphokinase and, ultimately, the changes in this important, high-energy phosphorylating enzyme in relation to aging of flight ability. Also carried out is a study of the possible role of diet in determining ovary development and, concomitantly, senescence in female house flies.

Ross, Morris
RO1 HD 00086
The Institute for Cancer Research
Philadelphia, Pennsylvania

EFFECT OF CHANGES IN ENZYME LEVELS OF LIFESPAN

This is an investigation of the effects of diet on lifespan and age-related diseases in rats. When experimental, dietary regimens are begun immediately after weaning, the life expectancy patterns of male rats are found to be influenced by the proportion of protein and carbohydrate in the diet and by the amount of food consumed. Both the levels of caloric and of protein intake have a modifying influence on the prevalence and degree of severity of a variety of age-associated diseases. For example, the risk of spontaneous tumors relates directly to caloric intake but the malignancy and proportional incidence of certain tumor types correlates with the level of protein intake. Tumor incidence is also found to relate to the growth rate in earlier life as well as to the mature body weight. Within each dietary group, rats of heavier weight suffer a greater risk of spontaneous neoplasms than lighter rats. The lowest incidence of degenerative disease, the greatest delay in time of occurrence, and the greatest life expectancy is observed when intakes of protein, carbohydrate and total calories throughout post-weaning life, has been low.

A correlation between life expectancy of these rats and the levels of activity for a number of hepatic enzymes on a cellular basis has been established. When the age-related enzyme activity patterns are modified by dietary means, there are corresponding modifications in lifespan. Rapid growth rates, structural or biochemical, are not commensurate with prolonged lifespan and reduced risk of age-associated diseases.

When, however, the same experimental regimens are imposed on older rats, the response with regard to life expectancy differs from that obtained when the dietary regimen is initiated early in life. Regimens which are satisfactory when begun early in life may not be suitable when begun later in life; significant extensions in lifespan have been observed only for those rats maintained under restricted conditions of feeding after reaching maturity on a diet having a protein-caloric ratio of 1 to 5.

Ross, Morris
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The Institute for Cancer Research
Philadelphia, Pennsylvania

AGING OF CELLS AND TISSUES: ENZYMATIC CORRELATIONS

This is the study of the effects of age and of several life-long dietary regimens upon the progressive biochemical and cytological changes in the rat. The incidence of age-specific degenerative disease, life expectancy and the progressive histological and cytological changes are being correlated with changing levels of activity of a number of hepatic enzymes and with the effects of limitation of intake of certain dietary components during the lifespan of the rat. The studies are also designed to determine whether changes in enzyme activity levels during aging and during the course of disease processes are the result of a reduction or increase in number of cells, in cell volume and in cell type, or the result of a reduction or increase in actual enzymatic activity level of the individual cells.

For each of the enzymes studied the activity levels were found to vary with the age of the rat and with the diet fed. Concomitantly, the average volume of the hepatocyte and the total number of hepatocytes also varied throughout the life of the rat and both were significantly influenced by the dietary regimen imposed. The progressive changes, with age, in the enzyme activity level of the cell appears to represent an adaptation to the change in requirements of a larger cell.

The data accumulated in the course of these studies indicate that among populations of varying life expectancy there is a remarkable uniformity in the sequence and in the proportion of time required for biochemical, structural and pathological events to occur.

Rubenstein, Irwin
R01 HD 04012
Yale University
New Haven, Connecticut

A STUDY OF THE SENESCENCE FACTOR OF P. ANSERINA

Senescence is used to refer to the well-known situation in fungi whereby cultures lose viability and characteristics with continued sub-transfer. This senescent phenomenon as described initially was attributed to the presence of an infective particle which causes cessation of elongation of hyphae and occasionally dissolution of the hyphal tip. The factor was shown to be maternally inherited. Hyphal fusion of a normal strain with a carrier causes the former to enter the state of senescence. The state of senescence can be reversed by various storage techniques or by growth on certain media not favoring abundant growth.

The objective of this research is the isolation and physical and chemical characterization of the factors responsible for senescence and growth stoppages in P. anserina. A secondary objective is the elucidation of the mechanism of induction of senescence and the localization of the genetic information determining the nature of the "senescence factor."

Sallman, Bennett
R01 HD 01971
University of Miami
Coral Gables, Florida

STUDIES IN THE AGING OF CELLULAR COMPONENTS

This is a study of the effects of aging on the metabolic activities of rabbit cardiac tissue. The heart was selected because its cells do not divide, thus constituting a uniformly aging population and because of the high metabolic level of the cells of the organ. Heart homogenates are being purified by fractionation, yielding intact cells, nuclei, mitochondria and microsomes. Enzymatic analysis, physiochemical characterization and chemical analysis are employed.

Comparisons of the energy metabolism of cardiac tissue mitochondria in young (4-6 months) and old (4-7 years) rabbits indicate changes with aging in the left ventricle. P:O and coupling ratios with tricarboxylic acid intermediates, lipids and glutamic acid as substrates show decreases with age. The most marked aging changes are in the

uncoupling of oxygen uptake linked to adenosine triphosphate formation from adenosine diphosphate. Measurements of specific mitochondrial enzymes correspondingly demonstrate significantly lower activity levels.

The effects on cardiac mitochondria of administering various corticosteroid hormones (corticosterone, cortisal and cortisone) in physiological dosages to young and old rabbits are currently being studied. Reports of other investigations indicate that such steroid administration appears to decrease the age-associated deficit in left ventricular work output and that cardiac tissue is a body depository for exogenous steroid introduction.

Scott, Earl
RO1 HD 01186
University of South Dakota
Vermillion, South Dakota

ELECTRON MICROSCOPE STUDIES OF AGING AND DEFICIENCY

The project consists of studies of the ultrastructure of cells and tissues of young and aged rats and the alterations and pathology resulting from specific dietary deficiencies. Groups of normal, deficient and pair-fed animals are included. These animals are sacrificed and prepared for study by electron microscopy. Among the tissues and organs examined are all endocrine glands, liver, heart, muscle, pancreas, accessory sex glands, and kidney.

Results show that modification, in the form of basal protrusions, occurs in renal tubule cells of aged rats in areas where the peritubular basement membrane has become thickened. These changes are present in all aged rats regardless of the type, quality or quantity of their diet. It is suggested that this alteration is an attempt by the cell to compensate for an increase in resistance to transport presented by thickening of the basement membranes.

In a group of 50 aged rats fed a complete valine-deficient, or hypocaloric (pair-fed) diet for 8 days, 60% had one or more tumors in one or both lobes of the thyroid. On the basis of their histology and organization it was evident that they were derived from thyroid parafollicular cells. Formation of the tumors was not influenced by either the quality or quantity of the diets employed.

Selye, Hans
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University of Montreal
Montreal, Canada

STUDIES ON TISSUE DEVELOPMENT AND AGING

This project is a systematic study of tissue development and aging using the techniques of "tissue-scaffolding" and the "progeria-like syndrome." Tissue-scaffolding refers to the regenerative growth of tissue in specially constructed, chemically inert tubes. Work with tissue-scaffoldings have shown that by varying the duration of the experiment or the configuration and dimensions of the scaffoldings it is possible to induce the development of different tissues (bone, bone marrow, cartilage) and of malignant neoplasms. The present research is aimed at providing more information about the laws governing the induction of normal and neoplastic growth by physical means in other tissues (epithelial, nervous) and the influence of humoral agents upon this type of metaplasia.

A "progeria-like syndrome" has been produced in the rat by chronic treatment with small amounts of Vitamin D derivatives. This syndrome is inhibited by "calciphylactic challengers" or catatoxic steroids. Plans are to explore the chemical or pharmacologic properties of calciphylactic challengers and hormones and their roles in this prophylactic effect.

Snook, Jean
R01 HD 022077
Cornell University
Ithaca, New York

DIET AND PANCREATIC ENZYMES IN DEVELOPMENT AND AGING

These investigations are carried out to determine the extent to which dietary protein, fat and carbohydrate control enzyme synthesis in the exocrine pancreas during development and aging and to study physiological mechanisms mediating the adaptation of the exocrine pancreas to changes in diet.

Albino rats ranging in age from 0 days to 28 months are used. Findings indicate that concentrations of amylase and chymotrypsinogen, but not lipase and trypsinogen are high at birth but fall rapidly. Enzyme as well as RNA levels do not begin to increase rapidly until rat pups are about 14 days of age. When access to the mother's food is prevented at this time, amylase concentration remains low while the concentration of the other three enzymes is elevated. This effect is due to the high fat, low carbohydrate

content of rat's milk which does not stimulate amylase production.

Pancreatic levels of all four enzymes are reduced in 28-month-old rats as compared to rats 1-12 months of age. Amylase levels are reduced to zero. Impairment in the ability of the pancreas to synthesize digestive enzymes may be a natural result of aging. The amylase deficiency may be related to impairment in the ability of the aged rat to synthesize and/or utilize insulin. Results demonstrate that pancreatic amylase is drastically reduced in rats made diabetic with insulin. However, starch diets are digested adequately by the diabetic rats.

Currently, amino acids labelled with C^{14} are being used to measure the rate of pancreatic enzyme synthesis in developing and aging rats fed diets in which the amount and type of fat, carbohydrate and protein are varied.

Swenseid, Marian
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Los Angeles, California

SINGLE AMINO ACID DEFICIENCIES IN AGING

It is often assumed that a dietary lack of any of the essential amino acids produces the same metabolic end results, a protein deficiency state. It is possible that the early metabolic response to dietary restrictions of various single essential amino acids might be quite different and characteristic for the specific amino acid that is limiting.

In this project the metabolic responses to different essential amino acid deficiencies in the rat are to be compared by measuring alterations in amino acid pool composition, in RNA metabolism and liver content and in the activity of enzymes catabolizing the amino acids. In particular, the amino acid acceptor activity of transfer RNA will be measured in the different amino acid deficiency states. Both young and old rats are used in the investigation to ascertain whether the stress of an amino acid deficiency serves to demonstrate age-related changes in either the processes of protein synthesis or of amino acid catabolism.

This study of single amino acid deficiencies may be useful in defining more precisely the role of nutrition in regulating protein synthesis and in providing a metabolic basis for considering problems of protein nutrition in old age.

Tappen, Neil
R01 HD 02033
University of Wisconsin
Milwaukee, Wisconsin

STRUCTURE AND FUNCTION OF BONE IN GROWTH AND AGING

The normal processes of growth, aging and structural organization of bone in man and other species, particularly primates are being investigated at gross and microscopic levels. Split-line techniques (the appearance of splits rather than holes when decalcified compact bone is punctured with a needle) are used in determining structural orientation of bone in different areas and in different species. The remodeling of compact bone is being examined microscopically after the special differential staining by methods developed within the laboratory. The study aims at determining the relationship of microscopic structure to gross split-line findings, and the reasons for the absence of patterns in some skeletal regions. Obtaining information on remodeling of compact bone is basic to an understanding of metabolic bone disease and the correlation of age changes in bone with those in arteries.

Primates are proving to be most similar to man in skeletal development aging criteria, enhancing their value as laboratory animals. There is also evidence that primates will be more valuable for microscopic analysis of remodeling of human compact bone than are common laboratory animals, on the basis of this investigation.

Tobis, Jerome
R01 HD 00599
Montefiore Hospital
Bronx, New York

STUDY OF THE PHYSICAL PERFORMANCE OF THE ELDERLY PATIENT

This project is concerned with the physiological effects of activities of daily living or rehabilitation exercises on the cardiopulmonary system of elderly disabled individuals. The rehabilitation programs are aimed at improving cardiopulmonary or motor performance of small groups of individuals studied intensively.

Methods of measurement include complete pulmonary function testing, cardiac catheterization, cardiac output by dye dilution methods and measurements of energy cost lactate pyruvate ratios and cardiac electrical activity. Measurements are made during activity, as well as at rest, and during recovery periods, on patients rather than normals, and during actual treatment rather than in a laboratory. By this means more realistic measurements of performance are being obtained which may serve as guidelines for the prescription of activity.

A portion of the project involves developing new instrumentation and methodology for this type of research.

Tonna, Edgar A.
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New York University
New York, New York

SKELETAL CELL AND MATRICAL CHANGES DURING AGING

How age changes affect the cellular kinetic behavior during growth, development, maintenance and repair potentials of skeletal tissues is a basic question of paramount importance. To this end these studies are designed to determine age changes in the cellular and matrical complement of skeletal tissues in both normal and injured mouse femora. A variety of techniques encompassing morphological, autoradiographic and histo-cytochemical methods at light-microscopic, as well as, electron-microscopic levels are employed. In order to develop a better understanding of changes in the cellular proliferative kinetic, cellular behavior and repair potentials of aging skeletal cell systems, tritiated compounds, such as tritiated thymidine, tritiated uridine, tritiated amino acids and tritiated carbohydrates are used.

The data collected and knowledge gained from these studies will serve as a base line for a wide variety of future undertakings devoted to assessing the response and behavior of bone to perturbations such as radiation injury, nutrition and hormonal variations, and physical, chemical and bacterial trauma, concomitant with aging.

Tsaltas, Theodore
R01 HD 01502
Jefferson Medical College
Philadelphia, Pennsylvania

EFFECTS OF AGING AND HORMONES ON THE CARTILAGE MATRIX

Cartilage is the main substance of investigation in this examination of the chemical composition of various tissues of the body as they are altered by the aging process.

It has been shown that the chemical composition of the cartilage matrix is profoundly affected by the aging process, and that hormones naturally present in the body (estrogens, cortico-steroids, thyroid hormone) retard the chemical composition changes of these tissues, thus indicating a possible retardation of the aging process.

Of significance is the finding that the permeability of the cartilage matrix decreases with aging and such decrease in permeability affects the total function of the cartilage. This may result in degenerative changes so frequently seen in aging individuals. An experimental model is being devised to simulate the aging process by injecting papaine intravenously in rabbits. Such injections change the chemical composition of the cartilage matrix and its permeability. Tissue cultures of chondrocytes from higher mammalian tissues have been developed and well established. Such cultures have been derived both from embryonic and adult rabbit cartilage. These tissue cultures of chondrocytes produce matrix and their appearance is consistent with that of mature chondrocytes. The production of matrix will be used for the study of polysaccharide production under the influence of various hormones as shown in our previous studies with intact animals.

Wachsman, Joseph
RO1 HD 02566
University of Illinois
Urbana, Illinois

UNBALANCED GROWTH: A MOLECULAR BASIS OF DEATH

This project is concerned with the molecular basis of bacterial death triggered by exposure to analogues such as 5-fluorouracil and 8-azaguanine, or by depriving cells of the DNA precursor thymine. These conditions lead to unbalanced growth and are highly lethal to bacterial cells. The bactericidal effect is most pronounced when RNA and/or protein synthesis is allowed to occur. The aim of this project is to determine the possible involvement of each of the following factors in bacterial death:

The synthesis of new classes of protein molecules not ordinarily formed during normal exponential growth.

Changes in the specificity of cellular regulatory mechanisms (repression and feedback inhibition).

The synthesis of RNA and DNA with altered biological properties.

The induction of normal and defective phage.

Walford, Roy
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Los Angeles, California

THE ROLE OF IMMUNE PHENOMENA IN AGING

Immunologic aspects of aging are studied in order to provide evidence for or against the immunologic theory of aging. This theory postulates that aging may be an immune reaction to one's own cells as they lose self markers through a process of somatic mutations. Several types of "model" experiments are carried out. In one, newborn co-isogenic mice are injected with adult spleen cells which are immunologically competent and the mice are observed for changes in lifespan and in disease patterns. In another "model" parabiosis between animals differing at weak histocompatibility loci is being investigated using mice and hamsters. Determination is being made as to whether changes noted in lifespan are correlated with corresponding variations in biochemical and other parameters of the aging process. The validity of these parameters is tested through the use of annual fish whose lifespan can be altered by different environmental temperatures. This should lead to an indication of the tissue enzymes to measure as indications of the aging process.

Weil, William
RO1 HD 03970
Michigan State University
East Lansing, Michigan

EARLY NUTRITION, BODY COMPOSITION AND AGING

There is believed to be a relationship between nutrition and maturation. This project is examining the relationship between nutrition during the perinatal and postnatal periods of animal growth and the maturation and senescent phases of later life. Alterations in maternal nutrition during pregnancy and lactation in rats, which have a brief intrauterine existence, are being contrasted with those of guinea pigs, which are born in a more mature state. The effects of the dietary alterations, produced by diets with varying protein content, are also compared within each species. Effects on the offspring are assessed by determination of dietary patterns during growth, growth rates, results of deprivation at various ages, occurrence of pathologic processes and the duration of life of animals, as well as the analysis of body composition of the animals by direct analytical techniques at various ages.

Weinberg, Eugene
RO1 HD 03038
Indiana University
Bloomington, Indiana

SENESCENCE OF MICROBIAL CELL POPULATIONS

Certain environmental and nutritional factors determine the rate of death of microbial cells in non-multiplying cultures. The approach of the study is designed to determine whether culture senescence is retarded or enhanced when cultures are prevented from initiating secondary metabolism and whether the selection of mutants that cannot produce the designated compounds is responsible for senescence.

To test the theory that successful secondary metabolism is required for culture longevity, conditions are required that support excellent growth but which preclude completion of secondary metabolism. Specific trace metals whose concentrations are critical are for fungi, zinc; for Bacillus species, manganese; and for other bacteria, iron. Quantities of the critical metals that prevent secondary metabolism likewise cause very rapid death of stationary phase cultures; the metals apparently are needed for transcription of secondary metabolic synthetases. Other trace, as well as bulk, metals whose concentrations need not be adjusted for secondary metabolism have no effect on the rate of death. The interaction of environmental factors with the metal-induced lethal effect is now being examined.

TRAINING GRANTS

Birren, James
T01 HD 00157
University of Southern California
Los Angeles, California

MULTIDISCIPLINARY APPROACH TO GERONTOLOGY

This program provides training for doctoral and post-doctoral candidates in the following areas: biology, psychology, physiology of exercise, sociology, social work, public administration. The curriculum is organized within the academic department of the university, with coordination and facilities provided by the Gerontology Center of the University. The program is designed to equip an individual with the methodology and content of a specialty area, such that he would be prepared to teach in a university and conduct research on the problems of adult development and aging within his scientific discipline or profession.

Graduate students apply for admission to a particular department or school and following their acceptance are considered for traineeships in this program. The academic program of the student is prescribed by the departments and schools with the guidance and approval of the Gerontology Center's faculty preceptors in the various disciplines. The program is flexible so that students may participate in special symposia as well as in ongoing research of the Gerontology Center. Trainees take some courses and at least two research seminars in gerontology, within and outside of their major discipline. Students from other programs also participate in such seminars. Trainees from a parallel training program relating aging to environmental studies, and urban and regional planning, are among those who attend.

In addition to coordinating training and research, the Gerontology Center staff also arranges special courses including Summer Institutes for Advanced Study staffed by distinguished visiting faculty. Other institutes are organized throughout the year serving continuing education in the relationship between gerontology and such areas as: nursing, religion, ethnicity, research in mental health and environmental studies.

As of February 1970 there are 40 students in the total gerontology program, 24 are trainees funded by NICHD, 4 have received their doctoral degrees, and 10 persons trained in this program have accepted responsible academic, research or administrative positions.

Blake, William
TO1 HD 00167
University of Maryland
Baltimore, Maryland

TRAINING IN PHYSIOLOGICAL GERONTOLOGY

The Department of Physiology at the University of Maryland offers an individualized program leading to a PhD degree in physiology with specialization in the area of gerontology. This is accomplished through the association of students with scientists active in physiological research, formal coursework, and direct participation in active research programs. The program is run in close collaboration with the Gerontology Research Center, Baltimore City Hospitals. Collaboration of the staff of the two institutions makes possible a program of study of basic physiological function and the impact of the aging process on that function. Active research on many physiological aspects of aging is being conducted. Course work on many aspects of the aging process is offered.

There are currently three students enrolled in the program. None of the students have received degrees to date.

Bunch, Marion
TO1 HD 00047
Washington University
St. Louis, Missouri

PSYCHOLOGY OF AGING

The primary purpose of this program is to develop trained research and teaching personnel in the psychology of aging. Students study psychology as both a social and a biological science and are given special training in psychology rele- to the aging process. The program includes courses and

seminars on psychological, social and clinical aspects of aging, the biology of aging, and special seminars on the medical aspects of aging. Research, supervised experience in practicum work in an appropriate facility, additional studies in related areas, and seminars are emphasized during the last years of graduate study.

The Psychology Department at Washington University has been offering a doctorate in the Psychology of Aging since 1958. During the past few years there has been an expansion of the psychological, clinical and biomedical segments of the program. The number of graduates to date is seventeen. Twelve predoctoral students are currently enrolled and one postdoctoral student. Tentative titles of dissertation research of trainees currently in progress are: Retroactive interference or facilitation in memory from a period of free association; Perceptual maturity of the elderly as measured by projective methods; The effects of ventromedial hypothalamic lesions on hunger and thirst motivation in rats; The frequency of brain autoantibodies in a normal population at various ages and in several psychopathic states; and The role of transitional objects in the development of the self concept in young children.

Curtis, Howard
T01 HD 00199
Associated Universities
Upton, Long Island, New York

POSTDOCTORAL TRAINING IN GERONTOLOGY

One of the primary objectives of the Departments of Biology and Medicine at this laboratory is a broad attack on the problem of aging. Part of this program involves the training of postdoctoral fellows. The chief emphasis of the research involves an attack on the problem of aging from point of view of modern cell biology and molecular biology. Some of the specific projects now in progress include an analysis of the role of somatic mutation in aging; changes in DNA function with age; a study of the aging changes in an irradiated human population; studies of aging cells by tissue culture methods, age changes in the capillary circulation of mammals; and changes in molecular structure with age as measured by electron spin resonance

methods. Each postdoctoral fellow works closely with a staff member in developing a specific aspect of the aging problem, which usually takes about two years.

Eisdorfer, Carl
TO1 HD 00164
Duke University
Durham, North Carolina

BEHAVIORAL PHYSIOLOGY IN AGING AND HUMAN DEVELOPMENT

This training program enables interested predoctoral and postdoctoral students to undertake research training in selected aspects of aging and human development with a specific focus on individual and group behavior and behavioral physiology. Course work supplements laboratory and training seminars.

The program stresses methodology and acquisition of specialized skills, which are required by working in a laboratory or in field research under the personal supervision of an experienced investigator. The predoctoral trainees are involved in studies of personality and motivational factors in responsivity in aged persons, conditioning of autonomic responses in the aged and aspects of the sociology of retirement.

Forbes, William
TO1 HD 00133
University of Rochester
Rochester, New York

BIOLOGICAL ASPECTS OF AGING

This program offers basic research training in biophysics and biochemistry and includes a series of lectures and seminars on the molecular biology of aging, provided by members of the Biochemistry and Biophysics Departments. Trainees in the program carry out their research on biophysical and biochemical aspects of aging. Compounds investigated are mainly collagen fractions, age pigments and appropriate model compounds. The aim of the investigations is to study the changes which are observed

in these substances when they are obtained from young and old animals, and also how these changes can be simulated in model compounds. The methods used are electron spin resonance spectroscopy, electronic absorption spectroscopy, amino acid analysis and related techniques. Mathematical models of disease processes are also investigated using statistical techniques and computer facilities. Four trainees are presently enrolled in the program and four trainees have completed their studies in the program.

Hamilton, James
T01 HD 00245
State University of New York
Brooklyn, New York

AGING IN RELATION TO THE REPRODUCTIVE AND ENDOCRINE SYSTEMS

This program in the Department of Anatomy at the Downstate Medical Center trains graduate students in the biological aspects of the aging process with particular emphasis on the effects of genetic and endocrine factors on aging of reproductive processes. The laboratory offers an opportunity to distinguish between genetic sex (sex chromosomes) and endocrine sex (gonadal secretions). This is possible because of the presence of a colony of killifish having the sex chromosome genotypes: fertile XX males and females, XY males and females, and YY males and females. Other studies are in progress on the effect of maternal age on reproductive capacity in mammals.

This is a joint PhD-MD training program aimed at preparing individuals for careers in research and teaching. The basic requirements for the PhD whether granted alone or as part of the MD-PhD program are the same. All trainees take medical school anatomy, physiology, and biochemistry courses as well as seminar courses which are particularly related to aging. This type of training prepares students to relate their specific interests to anatomical, physiological, biochemical and pathogical changes and to the behavior of the whole organism.

Harmon, Denham
T01 HD 00162
University of Nebraska
Omaha, Nebraska

BIOCHEMISTRY OF AGING

This training activity is located in the Department of Biochemistry and is aimed at producing PhD's in this discipline with an emphasis on aging. Throughout the training period the student is exposed to various aspects of aging through coursework, research seminars, and contacts with established visiting investigators in the field of aging. The first portion of the training period is devoted to coursework while during the latter portion most of the time is devoted to research.

Work on aging in the Department of Biochemistry has been mainly concerned with the role of endogenous free radical reactions to aging. Studies in this area are currently being conducted and provide opportunities for research experience for the trainees. At present efforts are being made to determine the extent to which free radical reactions contribute to changes in chromosomal material with time and how such changes may be inhibited by diet and dietary free radical reaction inhibitors.

Horvath, Steven
T01 HD 00235
University of California
Santa Barbara, California

PHYSIOLOGY OF EXERCISE AND STRESS

There is interest developing in physical activity programs for the aging. These programs require scientific scrutiny not only as to their content but to their potential value for the aging population. A latent source of scientific manpower which can be utilized under the direction of medical scientists, as well as for carrying out independent research in this area, are physical educators. This training program is aimed at developing the competency of such persons to improve the level of their scientific education, to provide them with a more adequate background for teaching courses in physiology of exercise, and to improve the quality of research they conduct.

A postdoctoral training program for the purpose of developing competency in a group of scientists interested in the basic physiology and biochemistry of aging was initiated in 1967. Each year the program takes on two new postdoctoral trainees, four have completed their training and two are currently aboard.

Lansing, Albert
T01 HD 00040
University of Pittsburgh
Pittsburgh, Pennsylvania

CELL BIOLOGY AND AGING

This training program was initiated in 1956 and is designed to prepare qualified personnel for teaching and research careers in cell biology with emphasis on problems related to the aging process. The objective is to train beginning graduate students, retrain postdoctorals in cell biology and aging, and reorient trained postdoctoral cell biologists into research on aging mechanisms. The graduate student is required to complete courses in gross and microscopic anatomy, neuroanatomy, biochemistry, and cell biology, as well as other courses in chemistry and biology. All students participate in a journal club and seminar, both dealing with current topics in cell biology during each year of training. Material relating to aging is transmitted to students through lectures in courses, research presentations and seminars. Reference is made to aging as a biological parameter in the various research activities in the Department of Anatomy and Cell Biology.

Loeb, Martin
T01 00160
University of Wisconsin
Madison, Wisconsin

MULTIDISCIPLINARY RESEARCH TRAINING IN AGING

The University of Wisconsin research training program in aging is designed for predoctoral students pursuing graduate study in any of six cooperating schools and departments in the University. Participants work

toward the PhD degree in Business, Economics, Industrial Relations, Rural Sociology, Social Work, or Sociology. The program is administered through the School of Social Work with an executive committee composed of faculty representatives from each of the cooperating schools and departments.

Each trainee receives basic research training in his own discipline and is expected to complete a dissertation pertaining to aging under the direction of a preceptor in his school or department. All trainees participate in an advanced seminar on gerontological research that extends over each academic year. Faculty for the seminar is drawn from the pool of preceptors for the trainees who represent several disciplines, as well as from other departments. The faculty is supplemented by visiting lecturers to the seminar noted for their research in particular areas of social gerontology.

Most trainees get experience as Teaching Assistants in an undergraduate course, Social Problems of the Aging, which includes supervision of a class research project on some aspect of aging. Some of the dissertation topics are: An analysis of factors related to decions concerning retirement options; Grandparenthood; A study of role conceptions; Marital commitments through the family cycle; and Savings and investment decisions in the retirement plans of working women.

There are six trainees currently in the program and there have been four graduates of the program.

Lowenthal, Marjorie Fiske
T01 HD 00238
Adult Development Research and Training Program
Langley Porter Neuropsychiatric Institute
University of California
San Francisco, California

TRAINING PROGRAM IN ADULT DEVELOPMENT AND AGING

This program offers formal research training in adult development and gerontology for predoctoral and postdoctoral students in the behavioral and health sciences. Seminars and courses are offered on the multidisciplinary theories, concepts and research data in adult development and gerontology, taking into account subcultural and

crosscultural variations. Seminars and research practicums provide training in field, laboratory and clinical research methods, and in qualitative and quantitative analytic methods appropriate to these techniques. Degrees are obtained in the various cooperating departments (Berkeley and San Francisco campuses), and disserations are supervised jointly by faculty in these departments and ADRP staff. Each trainee takes a 9-unit core interdisciplinary seminar in development and aging, a methods seminar, and such other courses and seminars as are deemed appropriate. They also conduct their dissertation research in this field. The ultimate objective is to train students for independent research and teaching. Upon completion of the program individuals should also be equipped to interpret and apply research findings to policy and planning for the aged.

Makinodan, Takashi
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University of Tennessee
ORNL Biology Division
P. O. Box Y
Oak Ridge, Tennessee

TRAINING FOR RESEARCH IN AGING

This program prepares trainees, mainly at the postdoctoral level and to some extent at the terminal predoctoral level, for independent multidisciplinary research in aging. Each trainee has the opportunity to obtain research experience in established laboratories where problems related to senescence are being actively studied by reputable scientists in a national laboratory. Trainees are drawn from a variety of disciplines and the research training program may be tailored to the needs of each trainee. For example, those trainees who have had limited research training in biology may obtain intensive research training in basic biological sciences such as biophysics, biochemistry, genetics, cell biology and developmental biology; and be able to associate with several different groups during the first year, before committing himself to a special interest. More advanced trainees may enter the program by choosing to associate with the established group or groups most closely related to their recognized

research interests. All trainees are expected to participate in journal clubs and seminars.

Meyer, William
T01 HD 00144
Syracuse University
Syracuse, New York

DEVELOPMENTAL PSYCHOLOGY: DEVELOPMENT AND AGING

This training program emphasizes the lifespan approach and brings to bear the conceptualizations and methodologies of psychology on the understanding of human development. Emphasis on the lifespan approach lies in the conviction that antecedent condictions which determine the nature and course of behavior change may be widely separated in time from their consequence, and that the social environment of an individual typically includes persons of widely disparate ages, so that one cannot properly limit the study of development by arbitrary age boundaries.

The program aims to develop a strong background in general psychological theory and behavior assessment, in research design and statistics and in developmental psychology. All trainees are requred to take a core of three courses covering infancy and childhood, adolescence, and adult life and aging. This is followed by special seminars in the psychology of adult life and a research seminar in the psychology of maturity and old age. The doctoral dissertation is conducted on a topic related to the area of human development and aging. A substantial research program parallels the training program and is available for training purposes.

Neugarten, Bernice
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University of Chicago
Chicago, Illinois

TRAINING IN ADULT DEVELOPMENT AND AGING

This program is intended to increase the number of persons trained to carry out research on the interrelations

of social and psychological processes at various stages in the adult life cycle and on patterns of aging; on the American age-status system and the effects upon society of the presence of large numbers of aged people. It includes training at the predoctoral levels in Anthropology, Adult Education, Health Administration, Human Development, Psychology, Sociology, and Social Service Administration for students who combine training in their own field with specialized research training in the field of adult development and aging.

In addition to his regular PhD program each trainee participates in a seminar given by the Committee on Human Development which provides a common background on the adult and aging individual in his social environment, a course in research methods and research design, and he participates in ongoing research projects in the field of aging.

The training program provides stipends and tuition for 20 trainees. Some of the dissertation topics are: Age expectations and timing patterns in age-graded occupations; Effects of relocation upon aged institutionalized persons; Self conceptions of older women doctoral students; Sleep and dream patterns of older people; Ego functions in young adulthood and middle adulthood; and Impact of urban migration on adaptive patterns of Appalachian adults. Thus far 37 PhD's have been granted to persons participating in the Adult Development and Aging Program, of whom 20 have been supported through the NICHD supported training program.

Peterson, Warren
TO1 HD 00175
Institute for Community Studies
Kansas City, Missouri

MIDWEST INTER-UNIVERSITY TRAINING PROGRAM IN THE SOCIOLOGY OF ADULT DEVELOPMENT AND AGING

As part of the program of the Midwest Council for Social Research in Aging, this project is providing research training in adult development and aging for predoctoral and postdoctoral students from the sociology departments of several mid-western universities. The major emphases are to increase the research competencies of graduate

students interested in adult development and aging, to assist postdoctoral fellows in applying their research skills to the field, and to provide faculty from participating universities opportunities to increase their research and teaching skills.

In addition to regular course work on their home campuses, students participate in a series of advanced institutes and seminars held throughout the year at various locations in the midwest. The major institutes occur in the summer, a two-week session in June and another in August. Faculty for institutes and seminars is derived from members of the Midwest Council for Social Research in Aging and is augmented by visiting scholars from outside the region.

At present the program has 15 predoctoral trainees at various stages in their graduate education, and seven postdoctoral participants. These trainees represent participation in the program by 10 midwestern universities. To date, seven of the predoctoral trainees have graduated with PhD degrees. They are currently employed in a variety of settings--academic, research and government positions.

Pollak, Otto
T01 HD 00186
University of Pennsylvania
Philadelphia, Pennsylvania

TRAINING PROGRAM IN SOCIAL GERONTOLOGY

This training program emphasizes the study of aging as a normal social process. Students are trained to conduct research on problems which develop when employment has ended, and decreased income and increased demands for health care create major challenges for personal and social adjustment. The key problem is the use of time without the support of a social setting which is predefined and economically enforced.

Students carry out field work in agencies and organizations serving the aged, participate in survey research connected with problems of aging and gain firsthand experience in becoming aware of the impact of contact with the aged upon younger people. All trainees take courses in sociological theory and in quantitative

methodology as well as graded sequence of research seminars covering the sociology of intervention systems such as social work, urban renewal and public health.

Rosenberg, George
T01 HD 00119
Case Western Reserve University
Cleveland, Ohio

TRAINING IN SOCIOLOGY AND GERONTOLOGY

The aim of this program is to provide doctorate level training in sociology, with gerontology as the major substantive field. The program includes seminars, tutorial and collaborative experience, with strong emphasis on research training. Trainees are assigned to research projects during the training period, or are supervised in projects they initiate. Suitable projects include: urban kinship networks; emerging professions, and professions in the field of rehabilitation; technological unemployment and potential deviancy; patient social structure; social participation of the aged, and social isolation; class and ethnic comparisons of social factors influencing the aging process; and the utilization of health care by the aged. Some of the areas covered by courses are cultures and aging, personality and aging, and aging and the social structure. Students take courses outside the department which contribute to their competence in gerontology or to their specific research interests.

Departmental research and teaching in gerontology is expanding and communication with other departments in the university has led to interdisciplinary courses.

Schaie, Warner
T01 HD 00129
West Virginia University
Morgantown, West Virginia

LIFESPAN DEVELOPMENTAL PSYCHOLOGY

This is a training program for the PhD in psychology with specialization in lifespan developmental psychology for individuals interested in teaching and research related to developmental processes of the lifespan. Training

therefore has a behavioral approach, with a strong emphasis on human development. Students receive training in methods which can be brought to bear upon human development from the experimental, clinical, social, psychological and comparative approaches. Aging is viewed as a process rather than an episode. Some of the core courses are courses in infancy and childhood, adolescence and early adulthood, maturity and old age, comparative psychology, and seminars on research methodology in developmental psychology, developmental learning and social processes. Included in the training is some experience in research and field activities, making use of the facilities in the medical school, the university nursery school, the state institution for the retarded, and the VA domiciliary.

Sinex, Marott
T01 HD 00207
Boston University
Boston, Massachusetts

TRAINING FOR RESEARCH ON THE BIOCHEMISTRY OF AGING

This training program prepares PhD candidates and post-doctorals for the research and the application of techniques of modern biochemistry to the study of aging. Emphasis is placed on the role of DNA and RNA in the transcription and translation of genetically coded information to produce the phenotypes characteristic of aging tissue. Attention is also given to the changes which occur in elastin and acid mucopolysaccharides. A course in the biochemistry of aging is given to advanced students. In the course they are encouraged to suggest significant experiments to test hypotheses about the fundamental chemistry of the aging process. All trainees engage in laboratory research on some aspect of chromatin in aging mouse brain and the development and deterioration of aorta elastin.

Taylor, Charles
T01 00194
Pennsylvania State University
University Park, Pennsylvania

TRAINING PROGRAM IN ADULT DEVELOPMENT AND AGING

This program is designed to lead students from a number of disciplines through graduate study leading to a doctorate

with major emphasis upon gerontological research.

Each student has a major allegiance to his individual academic department, supported by an understanding of and respect for other disciplines which contribute to social gerontology. Courses of study must meet all general requirements of departments; in addition each student is required to take a specified group of courses designed to give him a background in the substantive and research aspect of the adult lifespan. Students participate regularly in a colloquium during the entire course of their doctoral training where they receive from resident and visiting faculty a sense of the current problems and strategies of social gerontology. Summer research experience at off-campus research institutions is arranged to meet desired skills and interests for each individual student.

Timiras, Paola S.
T01 HD 00101
University of California
Berkeley, California

DEVELOPMENTAL PHYSIOLOGY AND AGING

Established in 1965, this program is available to graduate and postdoctoral students who wish advanced training in specialized aspects of human or animal development throughout the lifespan. The program is enhanced by the participation of several departments on the Berkeley campus and the utilization of the facilities that are accessible to the University community. The core program is centered in the Department of Physiology-Anatomy and includes several advanced courses on developmental physiology and the physiology of the aging process at the molecular, cellular and organismic levels, as well as a number of related research programs. Supplementary course offerings, selected on the basis of the student's principal interest, are available in Anthropology, Medical Physics, Molecular Biology, Psychology and Zoology. In addition to formal and informal seminars in which the student has an opportunity to exchange ideas, frequent guest lecturers allow him to integrate the latest experimental research being conducted here and abroad with his own research endeavors.

Eleven trainees have been graduated from the program since 1965 and have assumed academic and administrative appointments in various institutions throughout the country. One postdoctoral and nine predoctoral students are presently enrolled.

Wilner, Daniel
TO1 HD 00120
University of California
Los Angeles, California

TRAINING IN GERONTOLOGY

The gerontology training program at the UCLA School of Public Health is part of the Division of Behavioral Sciences. This program is directed towards students who wish to pursue research and university-level teaching careers in social gerontology, and leads to the Doctor of Public Health (Dr.P.H.) degree. The program is built around formal courses and seminars, independent study, field work internship, and independent research. The formal course work includes, in addition to a gerontology sequence, offerings in behavioral science research methodology; behavioral science content-oriented courses, both in the School of Public Health and in the College of letters and Sciences; and general courses in public health including biostatistics, epidemiology, and public administration. The research training is aimed at laying the groundwork for participation in studies of health and social-psychological factors as related to the aging process.

FELLOWSHIPS

Behan, Peter
F03 HD 40323
University of Oxford
Oxford, England

INVESTIGATIONS INTO THE PRE-SENILE DEMENTIAS

This investigator is examining senile intellectual deterioration and obtaining additional training in aspects of immunology and neuropathology. Amyloid deposition in the central nervous system is found in many of the pre-senile and senile dementias and very little is known about the causation of such. The incidence of Alzheimers' Disease is 6% of the general population over 60 years of age. This disease is characterized by cerebral amyloid deposition. Attempts are being made to experimentally produce cerebral amyloidosis by a method which consists of putting a transplanted reticuloendothelial system in the brain and then injecting with leishmaniasis. By injecting hamsters with leishmaniasis systemic amyloidosis can be produced in weeks and all but the brains of these animals are infected. The blood brain barrier may very well be instrumental in protecting the brain in the experimental animals and the short and long term effects of altering this in the presence of active experimental systemic amyloid induction is being studied.

Corso, John F.
F03 HD 44276
State University of New York
Cortland, New York

PSYCHOLOGICAL THEORIES OF ADULT AGING

The major concern of this project is the effect of adult aging on sensory and perceptual functions and the adequacy of current psychological theories which attempt to explain these effects. An evaluation is being made of the major theoretical approaches which appear applicable to the psychological aspects of aging in terms of sensory and perceputal functions. Experimental findings for the various human senses are being compiled and collated in order to establish the nature and the degree of the changes which occur with age.

A second phase of the project involves the theoretical interpretation of the experimental findings in relation to existing psychological theories. Primary attention is focused on information theory, signal detection theory, and adaptation level theory. This review and analysis is intended to provide a critical evaluation of the adequacy of these theories from an aging perspective and to suggest modifications which may be required in the development of a theory which can account for age effects across sensory modalities.

Finch, Caleb
FO2 HD 44147
The Rockefeller University
New York, New York

REVERSIBILITY OF AGING CHANGES

Humoral factors may have an important role in mediating age-related changes in mice, and investigations of this possibility are taking place. Skin is being exchanged between senescent and young male mice and the activities of hair follicles, which diminish with age, are quantitatively measured in the transplanted skin. If age changes in hair follicle activity can be reversed or accelerated at will by transplanting skin to a different aged mouse, the theoretically important concept that cellular aging changes are mediated by humoral factors will be substantiated.

Hettinger, William
FO3 HD 31,538
Gerontology Research Center
Baltimore, Maryland

ADVANCED TRAINING - GERONTOLOGY - PHYSICAL CHEMISTRY

This fellowship allows for the recipient to redirect his training in physical chemistry to gerontology at both the fundamental and clinical levels so that he might be better equipped to conduct research on the mechanisms of aging. An intensive course in cellular and molecular biology has been completed and a study of aging in the rotifer initiated. Courses were taken in anatomy and physiology while studies of the rotifer continue. The research objective is to develop an accelerated aging test which can be used to evaluate the effect of specific inhibitors of cellular mechanisms on the aging process in rotifers.

During the third year the recipient will also obtain experience at the clinical level by participating in the longitudinal study ongoing at the Gerontology Research Center meanwhile completing courses in pharmacology, microbiology and pathology.

Moore, Joan
FO3 HD 42,449
University of California
Riverside, California

AGE AND SOCIAL CHANGE - ETHNIC IDENTITY

The theoretical concentration of the research and training undertaken through this fellowship is on the relationship between social and personal change through the adult years of life. Focus is on social

change as manifested in changes in various forms of stratification. The principal activity is a secondary analysis of survey data to explore the relationships between ethnic perceptions and self concepts on the one hand and age, generational status and a number of background and milieu characteristics on the other hand. Data are drawn from several sources, most importantly from surveys of Mexican Americans in three cities. Under the fellowship, training in methods, mathematics and data processing is being received. Participation in workshops, seminars, and colloquia at the Gerontology Center of the University of Southern California is directed at broader familiarization with relevant research and theory.

Nadlehaft, Irving
FO3 HD 34950
University of Pittsburgh
Pittsburgh, Pennsylvania

FIBRINOGEN TURNOVER IN OLD AND YOUNG ANIMALS

This investigator measures the turnover of fibrinogen in Wistar male rats as a function of their age. Three age groups are examined -- young (3½ months); adult (13 months); and old (25 months). A two component model of fibrinogen balance has been applied to the data and used to determine the catabolic rate (equals the rate of synthesis), and the vascular to extravascular ration of fibrinogen. C^{14} labelled fibrinogen, made in a donor animal by intravenous injection of labelled amino acids, has been harvested, purified and injected intravenously into experimental animals. Samples of blood taken from the tail veins each day are processed and the plasma clotted with thrombin. The clots are solubilized and counted in a liquid scintillant. The turnover rate expressed as half-life in hours is: Young 30.8 ± 1.3; Adult: 39.8 ± 1.8. Old: 41.0 ± 1.8. The synthesis rate in units of %/day is: Young: 110 - 120; Adult: 67 - 72; Old: 53-55. The vascular to extravascular ratio of fibrinogen tends to become larger as the animal ages.

Peak, Daniel
FO3 HD 31794
Menninger Foundation
Topeka, Kansas

CHANGES IN MEMORY FUNCTION IN THE AGED OVER A FIVE YEAR PERIOD

A sample of subjects ranging in age from 40 through 90 years was retested with a bettery of short term memory tests after an approximate five-year interval. The battery of tests consisted of alternate forms of vocabulary

tests, immediate story recall, delayed story recall, and tests which measure attention, the capacity to keep newly formed paired associates in mind, and incidental memory for performed tasks. In addition to delineating changes which occurred during this five year period, attempts were made to isolate causative agents through the use of a detailed questionnaire concerning events and conditions which prevailed for each individual during this interim period. Attempts are being made to correlate twelve variables with the memory change. These variables are health, environment, occupation, activities, finances, retirement, religion, self concept, pessimism - optimism, social interaction and future planning.

Preliminary findings indicate that there is a decided decline in the memory function with age; that is, there is a greater decline in the older subjects whereas the younger subjects tend to remain the same. Findings thus far also indicate that no one of the particular variables correlates very highly with the decline in memory function. It is possible, however, that interaction of these variables may be of importance.

Rose, Charles L.
F03 HD 36600
Boston University
Boston, Massachusetts

OCIOLOGICAL PREDICTORS OF LONGEVITY

The recipient of this fellowship is interested in methodological problems of longitudinal studies on aging, the use of computer-based multivariate statistical analysis, and in social correlates of longevity. He is inclined towards interdisciplinary approaches to research since such teamwork is more meaningful for the study of aging processes, which by their nature require a multidisciplinary attack. Recipient is using data from a substudy of the Normative Aging Study, an interdisciplinary study in progress at the Veterans Administration out-patient clinic in Boston for his dissertation research. This is a long term longitudinal survey of "normal" aging processes. He is seeking a solution to the problem of removing secular trend from data on predictions of longevity.

RESEARCH CAREER DEVELOPMENT AWARDS

Binstock, Robert
K4 HD 41185
Brandeis University
Waltham, Massachusetts

AMERICAN POLITICAL SYSTEM AND HEALTH OF THE AGING

Few segments of the population are more affected by government decision in the routine of their daily lives than that of the elderly. However, little attention has been given to the politics of aging, and much of the attention given has focused upon the more obvious aspects such as voting behavior and neglected the more subtle aspects of political decision-making. The milieu in which the aged live and the ways that community members and organizations relate to the aged as an aggregate is such an area.

A great many governmental programs are directly concerned with health services and health care of the elderly. Therefore this research is examining the roles played by politicians in making demands upon and giving supports to governmental structures that make policies affecting the aging, especially in the area of health.

Gutman, David
K03 HD 06043
University of Michigan
Ann Arbor, Michigan

COMPARATIVE STUDIES OF EGO PROCESS IN LATER LIFE

This project consists of cross-cultural studies of the psychology of the aging process. Clinical personality theory and anthropological perspective are combined in the investigation of developmental and aging problems. Of particular emphasis are studies of ego development and how they relate to age and how they are seen in different cultural settings. Present work is being carried out in various subcultural groups in Israel while previous work has been carried out with the Navajo and Mayan groups.

Kohn, Robert R.
K3 34822
Case Western Reserve University
Cleveland, Ohio

AGING MECHANISMS OF CONNECTIVE TISSUE
AND MAMMALIAN CELLS

Three types of studies are in progress: Mice are employed in a study of the effects of antioxidants on lifespan. Butylated hydroxytoluene and 2-MEA are administered to C57BL/6J mice, and their weights and rates of dying are determined over the entire lifespan, and compared with those of control animals. An investigation of age-related cross linking of human collagen consists of purifying insoluble collagen from human tendon of various ages, studying the kinetics of degradation of the collagen by collagenase as a function of age, and of preparing soluble fractions so that colorimetric determinations can be made of groups believed to participate in cross links. The third undertaking deals with the role of age in neoplasia. AKR mice which develop leukemia at around 7-8 months of age are compared with a low leukemia strain. Tissue cultures of spleen and thymus are established to determine if there are any differences in growth potential or cell morphology as a function of age. Studies of immune potential as a function of age are being initiated to discover if there is any age-related alteration in possible feedback mechanisms in mice destined to get leukemia.

Lieberman, Morton
K3 HD 20342
University of Chicago
Chicago, Illinois

ADAPTATION AND SURVIVAL UNDER STRESS IN THE AGED

Two lines of inquiry are pursued in this research. The first deals with adaptation to stress in aged persons -- the effects of institutionalization, the effects of moving from one institutional setting to another, and the effects of moving from an institution to a community living arrangement. The second line of inquiry deals with psychological changes prior to death. The hypothesis is that distance-from-death is a more significant variable than chronological age. This idea relates to biological time-clocks and their manifestations in measurable psychological phenomena. Repeated observations are made on the same group of subjects.

The changes that preceded death are studied in the case of those subjects who die and compared to the changes of that in the survivors.

Data collected thus far is being analyzed in terms of psychological vulnerability, determining the personal characteristics or functions that are associated with adaptive and maladaptive reactions to the stresses associated with radical environmental shifts. Also being analyzed are the effects of institutionalizing the aged and the conditions and for whom institutionalization becomes productive or non-productive.

Schaiberger, George
K3 HD 34945
University of Miami
Coral Gables, Florida

BIOCHEMICAL CHANGES IN CELLS WITH AGING

The research conducted on this project is concerned with age-associated changes occurring in macromolecular chemical structure and function of the bacterial cell. The data indicate that DNA from aged cells have an altered template ability for new DNA synchesis which is probably due to a change in the DNA-protein association and that the DNA from aged cells is more resistant than that of younger cells to hydrolysis by certain nucleolytic enzymes. Under current investigation is the integrity of DNA derived from old cells and the ability of the enzymatic repair process to correct for age-associated defects.

Solomon, Neil
K4 HD 37275
University of Maryland
Baltimore, Maryland

PHYSIOLOGY OF AGING

This project consists of research on myocardial work performance as related to aging in the rat. The aim is to determine the underlying abnormality of the anatomically disease-free aged heart which is described clinically by the term presbycardia. To date light

microscopy has revealed no known anatomical defect in senescent hearts. Nor have levels of glucose free fatty acids and amino acid substrates been excessively low. High energy phosphate compounds and their intermediates have not been depleted. This project is designed to systematically investigate through the use of both the isolated rat heart and rat heart-lung preparation a function of left ventricular work and coronary flow, of both senescent and non-senescent hearts. Thus far it has been determined that 24-month-old rats cannot perform the left ventricular work of the 12-month-old rat.

Weiss, A. Kurt
K3 HD 21751
University of Oklahoma Medical Center
Oklahoma City, Oklahoma

TISSUE CHANGES WITH AGING IN HIGHLY INBRED RATS

A long-range examination of the physiological and biochemical characteristics of rat tissues from animals sacrificed at different periods during their normal lifespans is underway. The rats employed for this study belong to 2 highly inbred strains, the short-lived Fischer strain which has a 50% mortality rate at 12 months, and the longer-lived A x C strain which has a 50% mortality at 19 months.

The possibility is currently under investigation that autoimmune reactions occur with aging and may be the causative factor for some of the aging changes which are taking place. With the Ouchterlony double diffusion technique the occurrence of precipitin lines in the area between the serum and some of the tissue extract wells has been observed, even when the serum and tissue extracts came from the same animal. Among all the tissues surveyed, the spleen gives positive reactions most consistently and is followed, in the order of decreasing positive reactivity, by heart, kidney, lung, brain, skeletal muscle, liver and testis.

The occurrence of the autoprecipitation reactions appears to be age-related and the factor which seems to determine whether or not a positive reaction is obtained seems to reside in the serum rather than in the tissue extracts. A number of standard immunological tests support the contention that the precipitin lines represent autoantibody-antigen reactions.

CONTRACTS

Bierman, Edwin
University of Washington
Seattle, Washington

SYMPOSIUM ON INTERRELATIONS OF AGING AND DISEASE

The objective of this symposium is to accelerate the developing interest among academic physician-scientists in the contribution of aging processes to the development of diseases. There is a need for clinical investigators and basic scientists from a variety of disciplines to focus attention on aging processes in man.

The course emphasizes the interaction of intrinsic aging processes with diseases of multifactorial origin. Several processes and diseases that represent striking examples of a close interrelation between an aging process and an age-linked disease are emphasized. The major areas discussed are:

1. Changes in carbohydrate and lipid metabolism with age that result in a reduction of carbohydrate tolerance, and elevation of circulating lipids, and thus are closely related to the development of diabetes and atherosclerosis.

2. Changes in immunological reactivity with age that are closely related to altered resistance to infection, neoplasia, and the development of auto-immune disease.

3. Changes in mineral metabolism with age that are closely related to the development of osteoporosis.

4. Changes in connective tissue metabolism with age that are closely related to the development of degenerative diseases involving structural components.

Eisdorfer, Carl
Duke University
Durham, North Carolina

STIMULATION OF RESEARCH IN SOCIAL GERONTOLOGY

The objectives of the work conducted under this contract are to develop and implement a program for stimulating social gerontological research on university campuses nationally, to disseminate knowledge concerning the most recent issues in social gerontological research and to help improve the quality of such research. It is hoped that researchers in the social sciences who are not exposed to many of the issues in gerontological research will

be stimulated by such a program and will extend and elaborate their research foci or develop new lines of investigation into issues of social gerontology.

A visiting lecturers' series is being initiated and involves outstanding social gerontologists who spend a few days at a university or other research setting in an effort to stimulate interest in gerontological research. During this visit the scientist delivers an academic address or seminar to an audience which includes potential researchers and offers individual and group consultation on research methods and problems.

Hayflick, Leonard
Stanford University
Stanford, California

PRODUCE, STUDY, STORE AND DISTRIBUTE HUMAN DIPLOID CELL STRAINS FOR RESEARCH IN AGING

The specific objectives of the contract are:

1. To meet the present and anticipated demand for well characterized normal human diploid cell strains used for research in human aging.

2. To distribute the existing human diploid cell strain WI-38 derived from embryonic tissue.

3. To develop other human diploid cell strains from donors of different ages and to characterize these cell populations.

4. To preserve and store characterized human diploid cell strains in a liquid nitrogen facility for subsequent reconstruction and distribution.

5. To distribute the human diploid cell strains to cooperating laboratories working on the basic biology of aging.

6. To receive a limited number of investigators as trainees in the techniques by which normal human cells are isolated, grown, studied, stored, and reconstituted.

7. To conduct a small workshop or conference in which information will be exchanged relevant to the aforementioned technical aspects of normal human cell cultivation and as they pertain to experimental design, research results and theoretical implications in human aging.

The cell strains and the training and workshop provided by the contract will facilitate the progress of investigators supported by grants and working on problems of cellular aging involving the WI-38 and other human diploid cells.

Sallman, Bennett
University of Miami
Miami, Florida

WORKSHOP ON CELLULAR AGING AT THE MOLECULAR LEVEL

The objective of this contract is to assess the current state of research on the molecular biology of aging. It is hoped that discussions and critical evaluations made at the workshop will provide investigators with additional insight into the questions to be asked in research and the best methods of asking them.

Participants in the workshop include both persons who have been involved in studies of the molecular biology of aging and persons who have not been concerned with aging but who are experts in the conceptual and methodological basis of molecular biology. Each of the scientists engaged in research on aging gives a presentation of his work and when pertinent discusses the work of other investigators which is closely related. The other participants in the workshop then contribute to a critical evaluation of the presented work.

Shock, Nathan
Gerontological Society
St. Louis, Missouri

CURRENT PUBLICATIONS IN GERONTOLOGY AND GERIATRICS

This contract provides for the assemblage of a bibliography of research in the field of aging consisting of approximately 3,000 citations and covering biological clinical, psychological and social aspects. This bibliography is edited and prepared for publication quarterly in the Gerontological Society's publication, "Journal of Gerontology." This provides for publication in a single source of current information related to gerontology and geriatrics.

Stern, Herbert
University of California
San Diego, California

SUMMER COURSE IN THE BIOLOGY OF AGING

This course is designed to give an overview of biological aging and to then concentrate on aging at the cellular and molecular level. The primary aims of the course are to interest biologists chosen as faculty and young biologists chosen as students in the biology of aging, and to provide an opportunity for crystallization of concepts in aging and consideration of scientific strategy and tactics in the advance of knowledge in this area. It may also serve as a model for university graduate or advanced undergraduate courses in the biology of aging, and provide for the preparation and discussion of lectures on topics in the biology of aging.

If the biology of aging can be established as an explicit topic in the minds of biologists, research in aging should be greatly accelerated.

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