NORMAL HUMAN AGING:

The Baltimore Longitudinal Study of Aging

NATHAN W. SHOCK

Richard C. Greulich
Reubin Andres
David Arenberg
Paul T. Costa, Jr.
Edward G. Lakatta
Jordan D. Tobin

U. S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health
National Institute on Aging
Gerontology Research Center
Baltimore City Hospitals

NIH Publication No. 84-2450
November, 1984

CHAPTER V

Cross-Sectional Studies of Aging in Men

The subjects from the Baltimore Longitudinal Study of Aging (BLSA) provide a rich resource for cross-sectional studies to extend knowledge about age differences in normal successful men living independent lives in the community. This chapter summarizes the results of many of the cross-sectional studies, which define average differences between groups or the average regression of the variable on age. To identify outcomes or the effects of specific events on later performance, the subjects must be re-examined or information about them must be gathered at a later time. Although longitudinal observations are helpful in identifying time sequences, they are not essential in determining outcomes.

Longitudinal studies in which serial changes are based on the analysis of repeated observations in the same subjects are described and summarized in Chapter VI, whose final section also summarizes studies of outcomes based on a single characteristic, such as survival.

Some of the studies reported in this chapter are based on tests that were systematically repeated, so that longitudinal analyses were ultimately possible. Others describe results of tests not repeated for a variety of reasons, among which were: The average trend with age was so small in comparison with the variance among subjects that the age regression lacked statistical significance; the test required more time with the subject than could be provided within the testing schedule; analytical procedures required more laboratory assistance than was available; the primary investigator had left the Gerontology Research Center (GRC); or from the outset there was no requirement that the test be repeated, as was the case with the study of ethanol metabolism (Vestal et al., 1977) described below.

In some instances it was possible to carry out well-designed interdisciplinary studies because of the close association among investigators from different scientific disciplines, who were brought together primarily because the BLSA provided a well-characterized population of normal males. Again, a good example is the detailed study of the effects of age on the physiological responses to ethanol, which required close collaboration among physicians, physiologists, pharmacologists, endocrinologists, and psychologists.

PHYSIOLOGY

1. Cell-Culture Senescence and *In-Vitro* Life Span

Although differences observed at the organelle and macromolecular levels in early and late passage cell cultures have been attributed to cellular "aging," there is concern that such changes may not accurately reflect human cellular aging *in vivo.* This problem was addressed in a study (Schneider and Mitsui, 1976) designed to determine: a) whether differences would be observed in the onset of cell-culture senescence and in the cumulative replication capacity of fibroblast cultures derived from 2-mm skin-punch

Table V.1. Characteristics of Skin Explants and Cell Cultures Derived from Young and Old Human Donors

	Young Donors (21–36 yr)	Old Donors (63–92 yr)
Successful cell outgrowth from explants	23/34	24/39
Cell cultures that senesced before 10 CPD[c]	0/23	3/24
Explant outgrowth at 1 week (units)	2.44 ± 0.30 (26)[a,b]	1.44 ± 0.15 (29)[b]
Onset of senescent phase (*A*) (CPD)	35.2 ± 2.1 (23)	20.0 ± 2.0 (24) 22.5 ± 1.7 (21)[d]
Onset of senescent phase (*B*) (CPD)	41.6 ± 2.4 (23)	26.3 ± 2.6 (24) 29.6 ± 2.1 (21)[d]
In-vitro lifespan (CPD)	44.6 ± 2.5 (23)	29.8 ± 2.9 (24) 33.6 ± 2.2 (21)[d]
In-vitro lifespan (days)	273 ± 11 (23)	218 ± 14 (24) 236 ± 12 (21)[d]

[a]Values are expressed as mean ± standard error of the mean. Numbers within parentheses indicate the number of individual cell cultures examined.
[b]Includes several measurements of outgrowth from two explants taken from the same donor.
[c]CPD = cell-population doublings.
[d]If only cultures with > 10 CPD included.
From Schneider and Mitsui (1976)

biopsies taken from young and old BLSA subjects; and b) whether parameters that change with increased *in-vitro* "aging" are altered as a function of donor age.

In comparison with fibroblast cultures derived from young donors, those derived from elderly donors showed statistically significant decreases in migration, *in-vitro* life span, cell-population doubling (CPD) rate, and cell number at confluency, although no significant differences were found in modal cell volumes or DNA or RNA content (Tab. 1). While these findings confirm the utility of fibroblast cultures for studying human cellular aging (Martin et al., 1970), the differences observed in cell cultures derived from young and old donors varied both quantitatively and qualitatively from the *in-vitro* "aging" seen in early and late passage WI-38 cells. Also, several changes that occurred *in vitro* were not a function of donor age. It was concluded that early and late passage human diploid cell cultures may provide a useful system for examining loss of replicative potential, but that fibroblast cultures derived from old and young donors may be more appropriate for the study of human cellular aging. The continuing participation of the fibroblast donors in the BLSA presents an opportunity for follow-up studies to determine how various *in-vitro* indices correlate with physiologic studies and whether *in-vitro* life span has any relation to *in-vivo* life span or to the development of age-related disorders.

This work was subsequently extended by Smith et al. (1978), who compared the growth patterns of BLSA skin fibroblasts with fetal lung fibroblasts to determine the relation between colony-size distribution and donor age. Fetal cell cultures and cultures established from skin biopsies of old (64+ yr) and young (20–34 yr) donors were examined after two weeks of incubation (5–15 population doublings). Both in human fetal lung and in adult skin fibroblast cultures the distribution of colony sizes (which ranged from one to several thousand cells) was an accurate indicator of the number of subsequent *in-vitro* population doublings that could be attained by the parent culture. In addition, the colony-size distributions were related to the chronological age of the cell-culture donor. The percentage of large colonies with significant proliferative ability was thus highest in cultures of fetal origin, intermediate in cultures from young adults, and lowest in cultures from the over-65 age group. It was concluded that colony-size distributions achieved in tissue culture are good indicators of both *in-vitro* and *in-vivo* human cellular aging.

These studies led to more extensive analyses of the relation between *in-vitro* measurements and *in-vivo* human cellular aging. The establishment of cell cultures derived from 400 participants in the BLSA by the technique of cell-banking (Schneider, 1979) will make possible such correlative analyses as the study of the relation between *in-vivo* glucose tolerance or immune responses and such *in-vitro* functions as cell replication. Perhaps the major question this study will address is whether *in-vitro* data will provide significant *in-vivo* predictive information about the original donor. It will also permit a longitudinal follow-up study of serially derived cultures from the same donors over extended periods.

Cellular aging has been described as a progressive conversion of proliferating cells from a cycling to a non-cycling state (Gelfant and Grove, 1974). A study (Tice et al., 1979) of the age-related decline in immunocompetence as it is manifest in a loss in cell-mediated immunity also found both a progressive inability of normally quiescent cell populations to respond to a proliferative stimulus and an increase in cell-cycle durations. Peripheral lymphocytes stimulated by phytohemagglutinin (PHA) were examined by the bromodeoxyuridine staining technique. Peripheral lymphocytes from aged subjects (> 75 yr) were stimulated at about one-half the rate of those from young subjects (< 21 yr). Cell-cycle durations were determined to be 10.0–25.0 hours in cultures from aged and 10.6–15.6 hours in cultures from young subjects.

Although the findings do not allow a determination whether the increase in cell-cycle durations is due to a slowing of all phases of the cell cycle or of one particular phase, the aging of cell populations capable of proliferation may perhaps be attributable to alterations in transition probability—a mathematical expression that defines the ability of a cell to initiate a proliferative response somewhere in the G_1 phase of the cell cycle.

2. Body Composition

Body composition and metabolism. Measurement of body composition is important in determining the degree to which the age-related changes in human functional capacities are due to simple loss of tissues (cells) or to reduced function in the tissue that remains. Age trends in selected indices of body composition were therefore measured in a study of 143 BLSA participants 20 to 99 years of age (Norris et al., 1963), to observe the relations among different methods of estimating body composition applied simultaneously in the same individual. Body fat was estimated by three mathematical procedures that use data on body density, body-water compartments, muscle mass, and bone-mineral mass. Measurements on each subject, made within a two-day period, included body-water spaces (total body water from antipyrine space and extracellular water from thiocyanate space), body density (helium displacement), x-ray bone density, height, weight, 24-hour creatinine excretion, and basal oxygen consumption. Significant annual decreases were found for height (–0.08%), creatinine excretion (–0.77%), bone density (–0.48%), and basal oxygen consumption (–0.41%). Subsequent longitudinal analyses of these observations are reported in Chapter VI.

Although measurement of the basal metabolic rate (BMR) has been replaced as a clinical tool by other tests of thyroid function, it is still of scientific interest as an estimate of the "active" cellular mass—the amount of functioning tissue—in studies of aging. Tzankoff and Norris (1977) examined the relation between basal oxygen consumption and 24-hour creatinine excretion in 959 healthy males aged 20 to 97 years in order to identify that component of the lean body mass responsible for the age-related decrease in the BMR. An age-independent linear relation was found between paired values of basal oxygen consumption, a measure of total metabolic activity, and 24-hour creatinine excretion, a measure of muscle mass. Although no age differences were found in mean basal oxygen consumption in subjects up to age 45, the average values were significantly lower for each decade thereafter; only the difference found in the oldest group failed to reach statistical significance (Fig. 1). Each succeeding age-group also had lower mean values for 24-hour creatinine excretion; the differences were statistically significant for all but the youngest group (Fig. 2). Since creatinine excretion was assumed to be proportional to muscle mass, the data indicated that

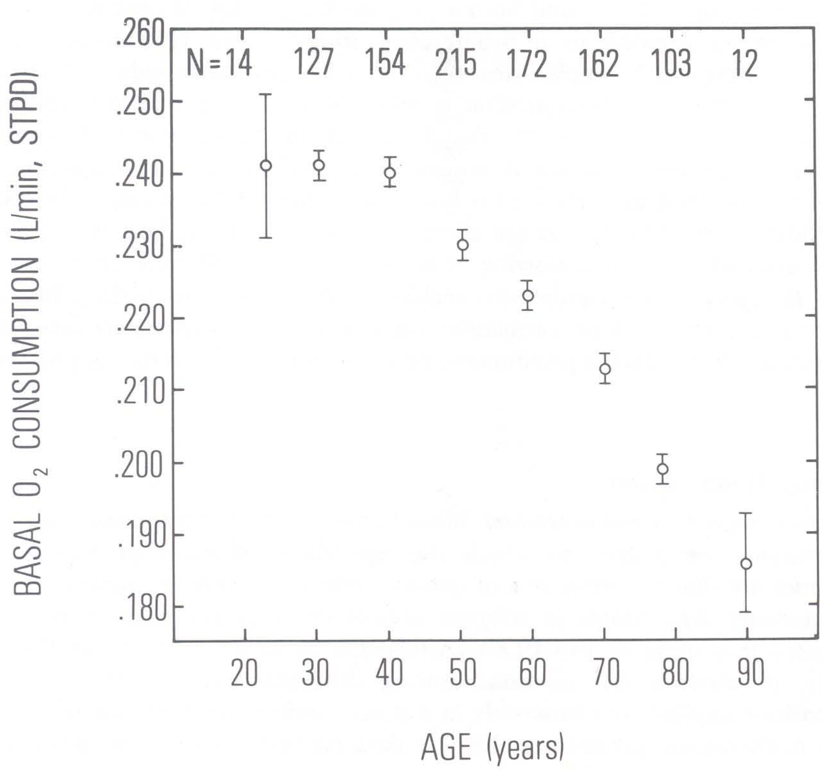

Figure V.1. Basal oxygen consumption (means ± SEM) for men grouped by age. From Tzankoff and Norris (1977).

muscle mass was lower for each older age-group. When basal oxygen consumption attributable to muscle was subtracted from whole-body basal oxygen consumption for each subject, the remainder showed no age-related decrease (Fig. 3). A linear relation was also found between anthropometrically derived lean body mass and 24-hour creatinine excretion for men up to age 65; one g of creatinine excreted in 24 hours was attributed to each 24.8 kg of muscle mass (Fig. 4). It was concluded that diminishing muscle mass may be wholly responsible for the age-related decrease in BMR. These results confirmed an earlier study which had indicated that the fall in basal oxygen consumption with advancing age was primarily a reflection of a loss of functioning tissue estimated from analysis of body water compartments (Shock et al., 1963).

Blood-lactate levels after exercise. Production of energy for muscular work occurs by two processes: aerobic oxidation and anaerobic glycolysis. Anaerobic glycolysis, which produces the smaller proportion of the body's energy, is accompanied by the production of lactate. During exercise, lactate diffuses rapidly from the muscles and is distributed throughout the body by the circulatory system. Most investigators agree that the maximal blood levels of lactate produced by vigorous exercise are generally higher in individuals who are physically fit, but there is disagreement about the best time after exercise to measure lactate and the optimal way to obtain blood samples for its measurement. Most important, there is no information on whether older individuals reach maximal lactate values within the same time as younger ones. To answer this

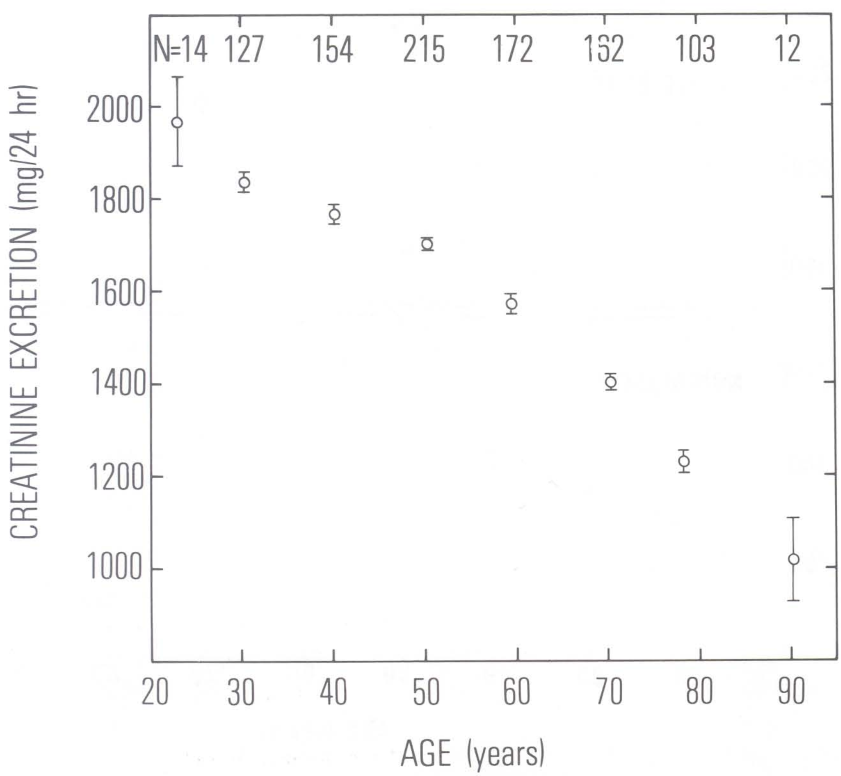

Figure V.2. Values of 24-hr creatinine excretion (means ± SEM) for men grouped by age. From Tzankoff and Norris (1977).

question, a study was conducted to determine whether lactate-distribution kinetics is influenced by age (Tzankoff and Norris, 1979).

The subjects of the study, consisting of 180 men selected from BLSA participants, were grouped in six age decades from the 20s to the 70s. None of the volunteers had clinically detectable cardiovascular disease. Each was given a multistage treadmill test designed to include measurements of maximal aerobic capacity. After an initial two-to-three-minute warmup, the treadmill grade was raised by 3% increments every two minutes until the subjects reported exhaustion. Blood for lactate analysis was drawn from an indwelling catheter at 3, 5, and 7 minutes after termination of the exercise only from subjects who, in the judgment of experienced observers, had exercised maximally.

Blood-lactate levels after maximal exercise were progressively lower with age. The fact that mean values for the youngest men showed no significant differences with sampling time suggests that the diffusion of lactate from muscle and its distribution through the body were complete by the third minute of recovery. In men 30+ years

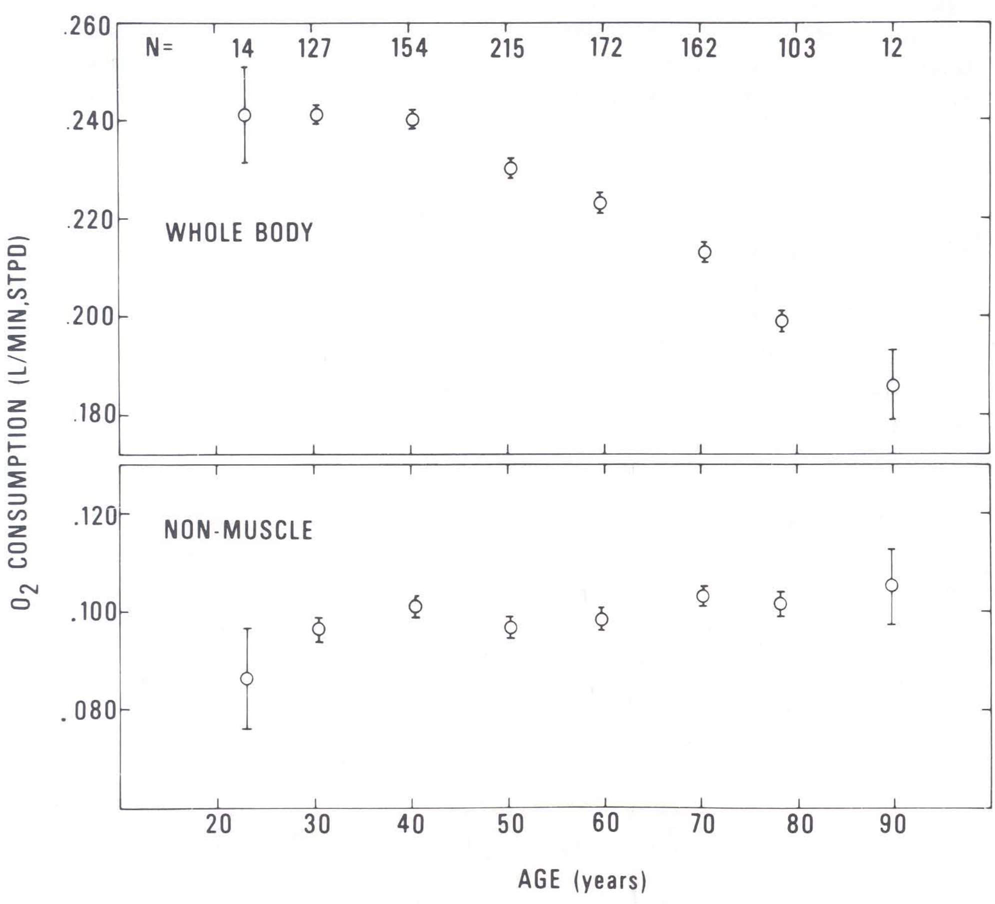

Figure V.3. Lower panel: means ± SEM of calculated nonmuscle oxygen consumption (see text) for subjects grouped by age. Upper panel: same data as in Fig. 1 shown here for reference. From Tzankoff and Norris (1977).

old, mean blood-lactate levels at three minutes of recovery were lower than at five minutes. Although lactate concentrations tended to plateau by the fifth minute in individuals in their 30s and 40s, they continued to rise through the seventh minute in men in their 50s and 60s.

The data suggest a progressive age-related decrease in the rate of diffusion of lactate from muscle and/or its distribution throughout the body, which may contribute to the prolonged recovery seen in old subjects. Although maximal lactate concentrations are best quantified by serial sampling during recovery, this approach is too expensive for most studies. The alternative, for men under 70, is to measure blood lactate in a single sample drawn at the time during recovery from exercise most appropriate for a given age group. Thus blood should be obtained after five minutes of recovery in men up to age 50, and at seven minutes in those between 50 and 70. Variability among men over 70 years of age precludes the use of single samples.

Body dimensions and fat. A radiographic study was undertaken to demonstrate the role of subcutaneous fat in altering external body dimensions in adult males *(Borkan and Norris, 1977).* The sample consisted of 699 men aged 20 to 92 years who were studied between 1958 and 1973. Each 7-x-17-inch soft-tissue radiograph contained views of seven body sites in the trunk and limbs. Measurements were made of skin and fat combined because radiographic differentiation of the two is difficult. Sites of fat measurements on the trunk were bony landmarks such as the top of the greater trochanter; for the calf and forearm, the widest part of the limb was used. When not precluded by factors such as improper body positioning or film handling, fat

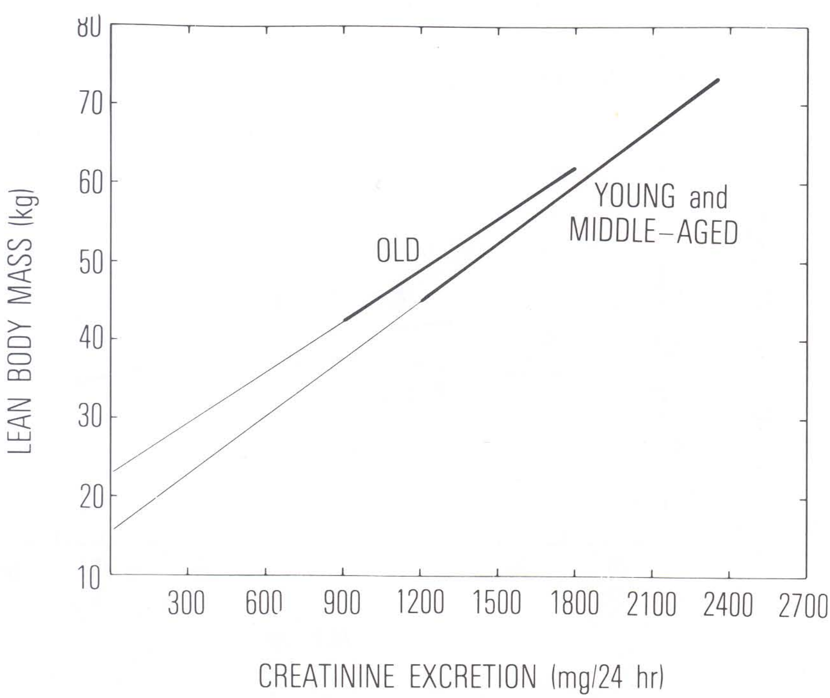

Figure V.4. Relation between lean body mass and creatinine excretion for 259 older (> 65 yr) and 670 younger (up to 64 yr) adult men.
From Tazankoff and Norris (1977).

measurements were made at the following locations: anterior calf, posterior calf, medial calf, lateral calf, lateral to greater trochanter, lateral to top of greater trochanter, lateral to anterior-superior spine of iliac crest, lateral to top of iliac crest, lower part of thorax (lowest rib), medial arm, and lateral arm. A number of new variables were also calculated from other data, including anthropometric body circumferences at sites corresponding to each radiographic fat measurement, height, weight, age, and biochemical assessments of extracellular water and total body water. The new variables included body diameters, muscle plus bone areas for the arm and leg, percentage of body water, percentage of fat, fat-free percentage of the body, and fat-free weight.

The weight of total body fat in this cross-sectional sample was relatively constant with age, but the average fat-free weight was lower in older subjects. In the trunk, data

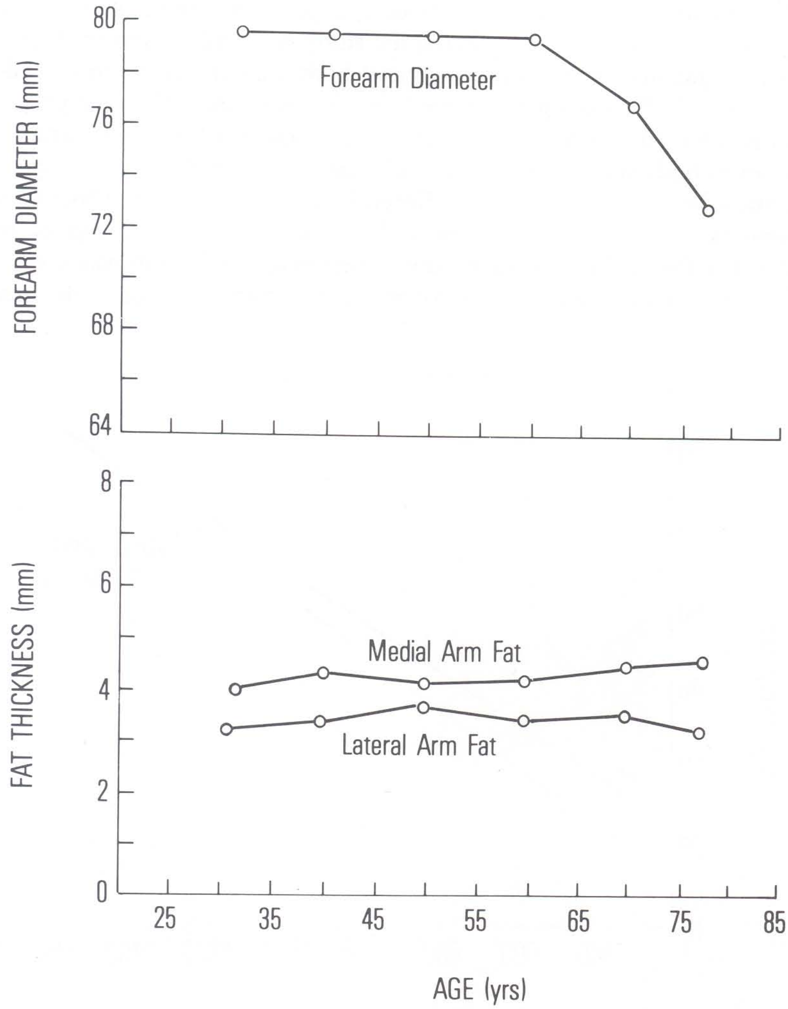

Figure V.5. Age trends in subcutaneous fat thickness and limb diameter at the widest part of the forearm. In the older ages there is a marked decline in diameter that is not attributable to change in fat thickness.
From Borkan and Norris (1977).

from the soft-tissue radiographs revealed that, on the average, subcutaneous fat increases in the region of the greater trochanter but decreases in the abdominal region through middle age. Abdominal diameter increases during this period, however, perhaps as a result of enlargement or sagging of the abdominal contents. The decline in the diameter of calf and arm while fat remains relatively stable suggests loss of lean tissue with age (Figs. 5,6). The findings in this study generally agreed with earlier findings that age changes in body dimensions that result in thin extremities and thicker trunk are only partly attributable to fat redistribution. A part of the age change is the result of tissue loss.

Alterations in bone. Bone loss with increasing age is a universal phenomenon in adults of both sexes, although the rate of loss and the total bone mass lost are greater in

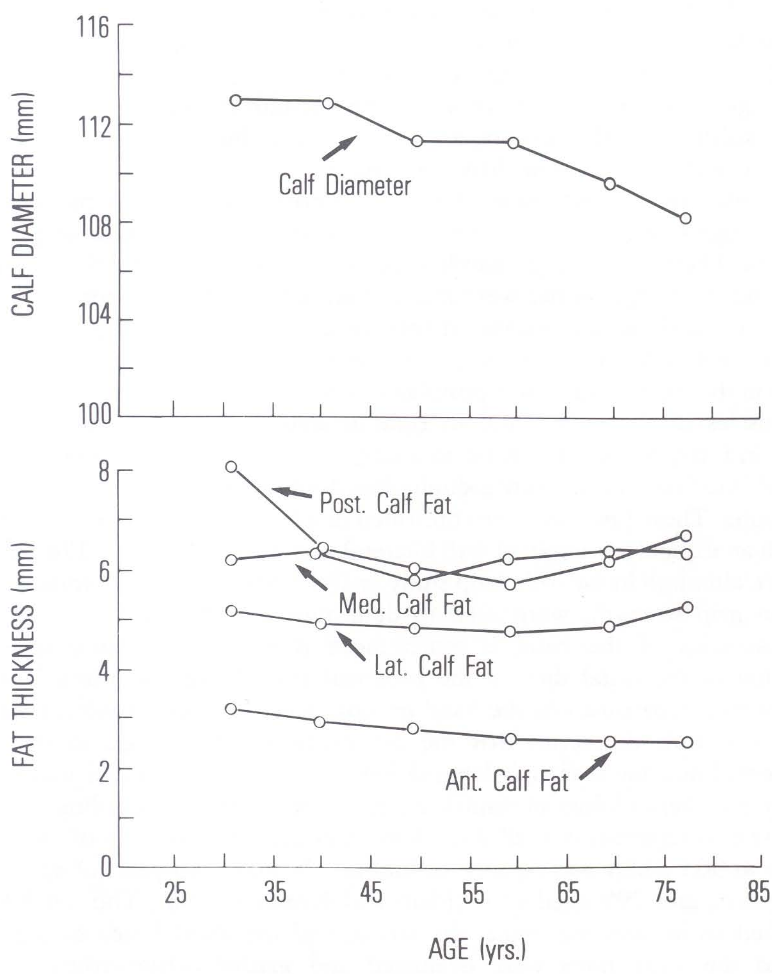

Figure V.6. Age trends in subcutaneous fat thickness and limb diameter at the widest part of the calf. Similarities with the forearm (Fig. 5) are indicated, with decline in limb diameter unaccompanied by loss of fat.
From Borkan and Norris (1977).

females than in males. A study (Plato and Norris, 1980) was undertaken to a) compare, cross-sectionally, the mean values of various bone measurements of the second metacarpal in subjects of different ages; b) investigate possible bilateral differences in bone measurements; and c) determine possible associations between bone measurements and grip strength. Radiographs of the right and left hands were obtained for 236 male BLSA participants whose age range was 25 to 95 years ($\bar{x}$ age = 58.6 yr). The total width, medullary width at the midshaft, and the length of the metacarpal bones were measured from the radiographs, and the data were distributed in seven decade groups between 20 and 89 years of age as well as a 90+ group. Grip strength was measured with a Smedley hand dynamometer.

Age-group comparisons showed that total width and length of the second metacarpal do not change significantly with age after skeletal maturity, while medullary width and area increase and combined cortical thickness decreases significantly. In all age groups the right second metacarpals were wider and longer, and had a thicker cortex, than the left. Medullary width is positively correlated with age, while bone size, total width, and length show no such correlation. After adjustment for age and weight, age and height, and age and surface area, grip strength showed a positive correlation with total width, cortical thickness, and cortical area, but not with medullary width (which is an indicator of bone loss) or length.

In a related study (Plato et al., 1980), 235 normal male BLSA participants were classified as right-handed, left-handed, or ambidextrous on the basis of grip-strength performance. Their left and right hands were also radiographed, and the measurements of the second metacarpal bones were interpreted in terms of hand dominance. Results indicated that the right-hand measurements are generally higher than those of the left hand, regardless of hand dominance, and suggested an inherent tendency to greater bone mass in the right hand. It was postulated that differential stress placed on the bone by the muscles of the right hand in right-handed persons enhances this inherent difference in favor of the right hand to a degree that is statistically significant. In the left-handed, the bilateral difference diminishes because of the increasing stress on the left-hand bone. These findings were confirmed in a follow-up study (Plato and Purifoy, 1982) with an expanded sample of 448 bilateral x-rays from male and 176 from female participants, although in the follow-up study lateral functional hand-dominance criteria, rather than grip strength, were used to determine handedness.

Osteoarthritis of the hand is much more prevalent and more severe in its manifestation in the distal than in the proximal interphalangeal joints. The present system reports osteoarthritis of the hand in most severely affected joints regardless of their position, with the result that the expression of the disease in the proximal interphalangeal and metacarpophalangeal joints is often ignored and underreported. To remedy this methodological insufficiency, a new system of recording the presence and severity of osteoarthritis in all three joints was applied to a study of its age-specific prevalence in 903 BLSA participants, including 228 under 40 years of age, 376 aged 40 to 59 years, and 299 aged 60+ (Plato and Norris, 1979a). The left hands were radiographed to include the digits, the wrists, and the distal heads of the ulna and radius, and the x-ray films were evaluated and graded. Osteoarthritis was more prevalent in older age groups regardless of the joint or digit examined, was more prevalent in the distal than in the proximal joints, and occurred most frequently in the little finger and least frequently in the thumb. It was more severe and its onset earlier in the distal than in the proximal interphalangeal or metacarpophalangeal joints. An unforeseen but statistically verified preponderance of digits with osteoarthritis in both their distal and proximal interphalangeal joints suggests either a common etiology or that the presence of osteoarthritis in the distal joint enhances the likelihood of its development in the proximal joint of the same digit.

3. Nutrition

Caloric intake—diet. In a study of the effect of age on nutrient intakes and energy expenditure (McGandy et al., 1966), intakes of calories and various nutrients were estimated from the daily diet records maintained for one-week periods by 252 healthy male BLSA subjects aged 20 to 99. Because of their high educational level and income, socioeconomic influences on nutrient availability were minimal. Estimates of physical activity were made from detailed interviews, and basal oxygen uptake was also measured. The oxygen required daily for the activities reported by each subject was calculated from estimates of oxygen required for the activity as reported in the literature (Tab. 2). The daily energy expenditure (calculated calories for activity + measured calories for BMR) and its relation to total caloric intake (Tab. 3) were

Table V.2. Calories Expended during Various Physical Activities

Activity	Energy Cost[a] (C/kg per min)
Sitting	
"Active" sitting (writing, talking, etc.)	.027
"Quiet" sitting (reading, watching TV, etc.)	.025
Unspecified active or quiet	.026
Driving car	.035
Eating	.027
Standing	
Unspecified	.03
At drawing board	.035-.04
Teaching, lecturing, etc.	.045-.05
Lying	
Awake	.022
Asleep	.02
Dressing	
Washing, shaving, etc.	.04 (.028-.05)
Walking	
Slow	.04
Moderate	.05 (.04-.06)
Fast	.06 (.06-.08)
Housework	
Making beds	.06
Preparing food, washing dishes	.04
Sweeping floors	.05
Mopping, scrubbing, etc.	.06-.067
Washing windows	.06
Unspecified or miscellaneous housework	.05
Shopping for groceries	.05
Waiting while wife shops for groceries	.025-.04
Caring for young children (feeding, dressing, etc.)	.06
Stairs	
Ascending	.056/flight
Descending	.032/flight
Both ascending and descending (1 flight = 12-16 stairs)	.088/flight

Table V.2. Calories Expended during Various Physical Activities—(*Cont'd.*)

Activity	Energy Cost[a] (C/kg per min)
Gardening	
Dig with hoe	.04-.07
Weeding	.05-.07
Transplanting	.07-.08
Miscellaneous gardening	.06-.08
Mow lawn with hand mower	.09
Mow lawn with power mower	.07
Mow lawn with self-propelled power mower	.06
Mow lawn with riding mower	.045
Driving tractor without attachments	.038
Driving tractor with attachments	.05
Tending greenhouse plants in home or laboratory	.035
Tending greenhouse—commercial	.06-.075
Miscellaneous farm chores	.06
Household Maintenance	
"Unspecified"	.06
"Heavy"	.07-.09
Hand saw	.09
Power saw, drill, etc.	.04
Lay flooring, measure wood, etc.	.07
Paint walls	.07
Paint objects	.04
Repair gadgets, radio mechanics, etc.	.04
Auto repairs	.05-.06
Chopping wood	.09
Sports and Leisure	
Conversing, entertaining	.027
Slow dancing (waltz, fox-trot, etc.)	.06-.065
Fast, vigorous dancing (twist, polka, etc.)	.07-.08
Playing cards	.026
Playing organ or piano	.045
Playing stringed instrument	.04
Playing brass or woodwind	.045
Marching and playing in band	.05
Golf, with caddy	.06
Golf, carrying bag	.075-.08
Golf, unspecified	.07
Swim, vigorous (race)	.07-.08
Swim, relaxed	.06
Ping pong	.06
Bowling	.035
Fishing	.027-.04
Attending sporting events	.03-.05
Singing	.03
Cycling	.05
Fast cycling (race)	.09
Pitching horseshoes	.045-.06
Play baseball	.07
Calisthenics (unspecified)	.07
Playing with young children	.06
Running	.09
Tennis	.09

[a]In each case, .02 cal represents basal energy expenditure. If S's own basal rate is used, subtract .02 from figures above (e.g., lying awake = .022 C/kg per min + basal, sitting = .006 + basal, etc.).

From McGandy et al. (1966)

Table V.3. Total Daily Intakes of Various Nutrients in Men of Different Ages

Age (Yr)	20–34	35–44	45–54	55–64	65–74	75–99
N	13	50	52	50	50	37
Height (cm)	180.0 ±4.97[a]	177.8 ±4.58	177.1 ±3.02	175.7 ±4.10	174.4 ±4.03	172.3 ±3.80
Weight (kg)	74.5 ±4.41	77.8 ±6.94	77.6 ±5.16	77.2 ±6.98	77.7 ±7.41	70.9 ±5.79
Total calories	2688 ±584	2639 ±548	2454 ±432	2332 ±345	2297 ±498	2093 ±441
Protein (g)	105 ±16.6	102 ±19.5	98 ±20.3	92 ±17.7	92 ±21.6	81 ±19.1
Fat (g)	123 ±30.6	123 ±29.7	116 ±24.2	105 ±21.8	99 ±30.3	86 ±24.5
Carbohydrate (g)	279 ±73.4	265 ±82.5	240 ±61.9	237 ±52.7	256 ±68.9	244 ±64.6
Alcohol (g)	12	15	14	17	8	9
Calories from protein (%)	15.9 ±1.7	15.6 ±2.1	16.1 ±2.7	15.8 ±2.4	16.1 ±2.7	15.5 ±2.5
Calories from fat (%)	41.0 ±3.2	42.0 ±4.7	42.5 ±4.6	40.3 ±5.2	38.5 ±6.4	36.9 ±6.5
Calcium (g)	1.29 ±0.83	1.00 ±0.38	0.79 ±0.32	0.74 ±0.26	0.91 ±0.44	0.89 ±0.42
Iron (mg)	16.2 ±4.3	14.5 ±2.6	15.0 ±2.7	14.3 ±3.3	14.0 ±2.5	12.3 ±2.8
Vit. A (I.U. x 10^{-2})	119 ±70.1	78 ±51.2	78 ±35.0	79 ±56.8	89 ±45.8	81 ±36.6
Thiamine (mg)	1.67 ±0.77	1.38 ±0.33	1.28 ±0.32	1.20 ±0.28	1.35 ±0.37	1.20 ±0.28
Riboflavin (mg)	2.70 ±1.26	2.21 ±0.72	1.91 ±0.56	1.83 ±0.64	1.98 ±0.74	1.87 ±0.59
Niacin (mg)	23.1 ±6.2	20.1 ±4.1	20.0 ±4.7	18.5 ±4.4	18.0 ±4.6	15.0 ±4.5
Ascorbic acid (mg)	106 ±55.4	107 ±44.6	106 ±44.2	115 ±55.7	142 ±62.0	119 ±51.3
Calories from saturated fat (%)	16.4 ±1.1	16.7 ±2.5	16.7 ±2.3	15.5 ±2.8	14.8 ±2.4	14.4 ±3.0
Calories from polyunsaturated fat (%)	5.4 ±1.3	5.2 ±1.1	5.4 ±1.0	5.3 ±1.2	5.2 ±2.5	4.8 ±1.3
Cholesterol (mg)	580 ±281	610 ±200	620 ±190	600 ±214	540 ±220	480 ±181

[a]Mean ± S.D.
From McGandy et al. (1966)

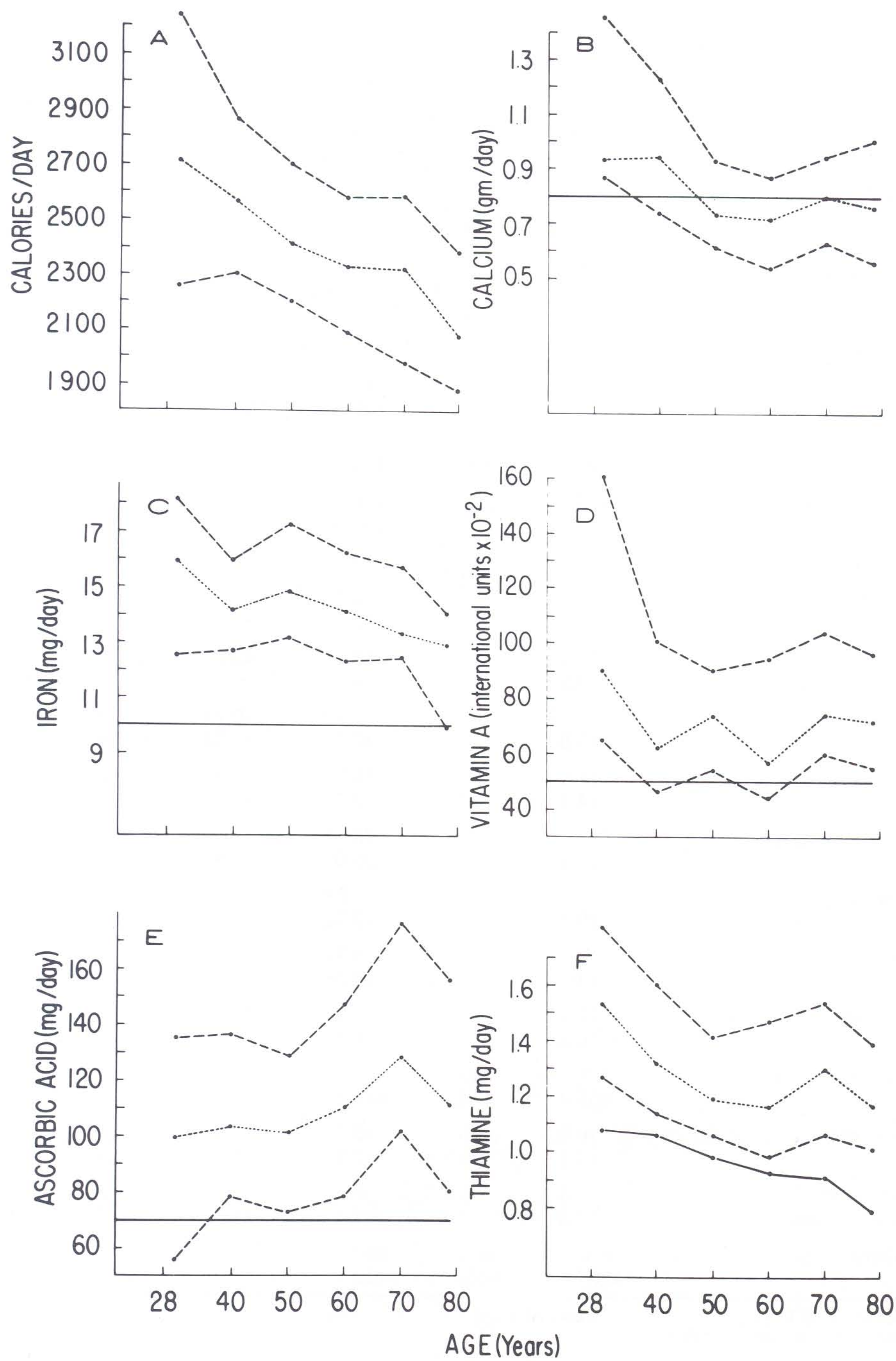

Figure V.7. Total daily intakes of calories (A), calcium (B), iron (C), vitamin A (D), ascorbic acid (E), and thiamine (F) in men of different ages. The medians are represented by the dotted lines and the first and third quartiles by the dashed lines. Solid lines represent National Research Council recommended allowances.
From McGandy et al. (1966).

measured in subjects of different ages. Older subjects were found to consume markedly fewer calories than younger subjects (Fig. 7A). Figure 7 shows that the pattern of average age differences varied considerably among nutrients. None followed the almost linear drop observed in the average decrement in total calories consumed (Fig. 7A). In the case of vitamin A the decrement in intake was confined to the age span of 20 to 40 (Fig. 7D); for calcium, the span was from 20 to 50 (Fig. 7B). In contrast, the average intake of ascorbic acid increased after age 50. Except perhaps for calcium, the daily allowances recommended by the National Research Council were met by most of the subjects.

Although the percentage of calories from protein was remarkably constant with age (Fig. 8A), calories derived from fats dropped from 42% in the 45-54-year age group to 36% in the 80-year-old group, while the contribution of calories from

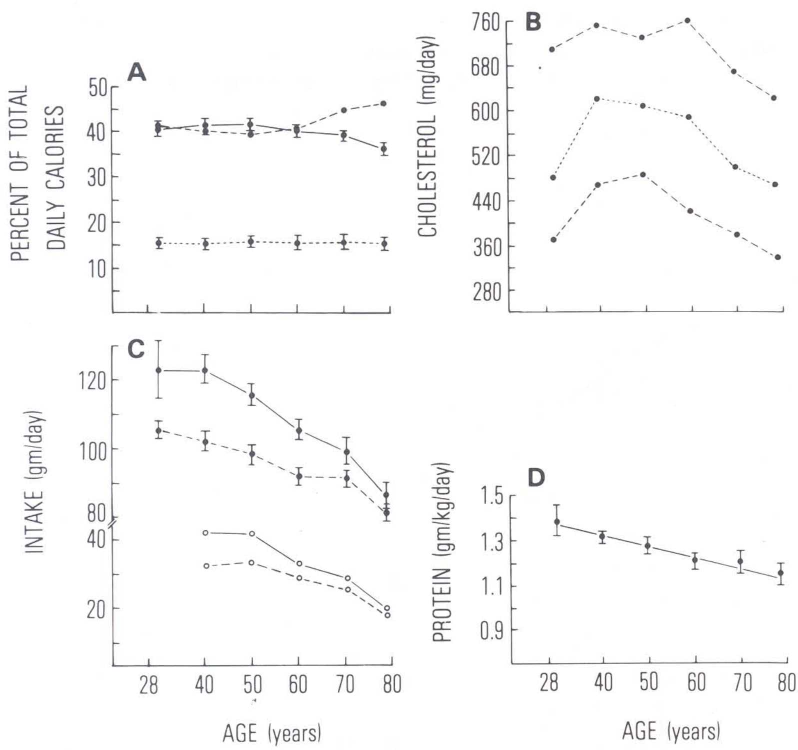

Figure V.8. A. The percentage of the total daily caloric intake derived from fat (——), carbohydrate (----), and protein (...) in men of different ages. Vertical bars represent SEM. Correlation coefficients for regressions on age of percentage of calories from fat and from protein were –.37 ($p < 0.01$) and –.004, respectively.

B. Total daily intakes of cholesterol in men of different ages. The medians are represented by the dotted line and the first and third quartiles by the dashed line.

C. Total daily intakes of fat (●——●) and protein (●----●) in men of different ages. Vertical bars represent SEM. The lower curves represent the intakes of fat (○——○) and protein (○----○) derived from meats exclusive of poultry and fish.

D. Total daily intakes of protein per unit of body weight in men of different ages. Vertical bars represent SEM. Correlation coefficient = –.242 ($p < 0.01$). From McGandy et al. (1966).

carbohydrates increased correspondingly. A decrement in cholesterol intake was related to and largely accounted for by the reduced use of meats (except poultry and fish) in the older subjects (Fig. 8B).

Basal metabolism decreased by 5.23 cal/day per year of age (Fig. 9B), while total caloric intake fell 12.4 cal/day per year (Fig. 9A). The difference, 7.17 cal/day per year, must be related to a reduction in calories required for other purposes, including physical activity. When expressed in relation to body weight, this decrease in non-basal energy expenditure showed a plateau from age 60 (Fig. 9D). There was close agreement between the total caloric requirement per day (activity cal + basal cal) and the total caloric intake calculated from dietary diaries.

Vitamin B_6. The vitamin-B_6 status of 617 men ranging in age from 18 to 90 years was investigated by use of plasma pyridoxal phosphate (PLP) and glutamic-oxaloacetic transaminase (GOT) concentrations to assess B_6 nutrition and to determine the effects of vitamin-B_6 supplements (Rose et al., 1976) (Fig. 10). The studies provide the most extensive normative data to date on the vitamin-B_6 status of normal men in the adult years. Almost half the men in the 60s and 70s, and one fourth of the younger men and

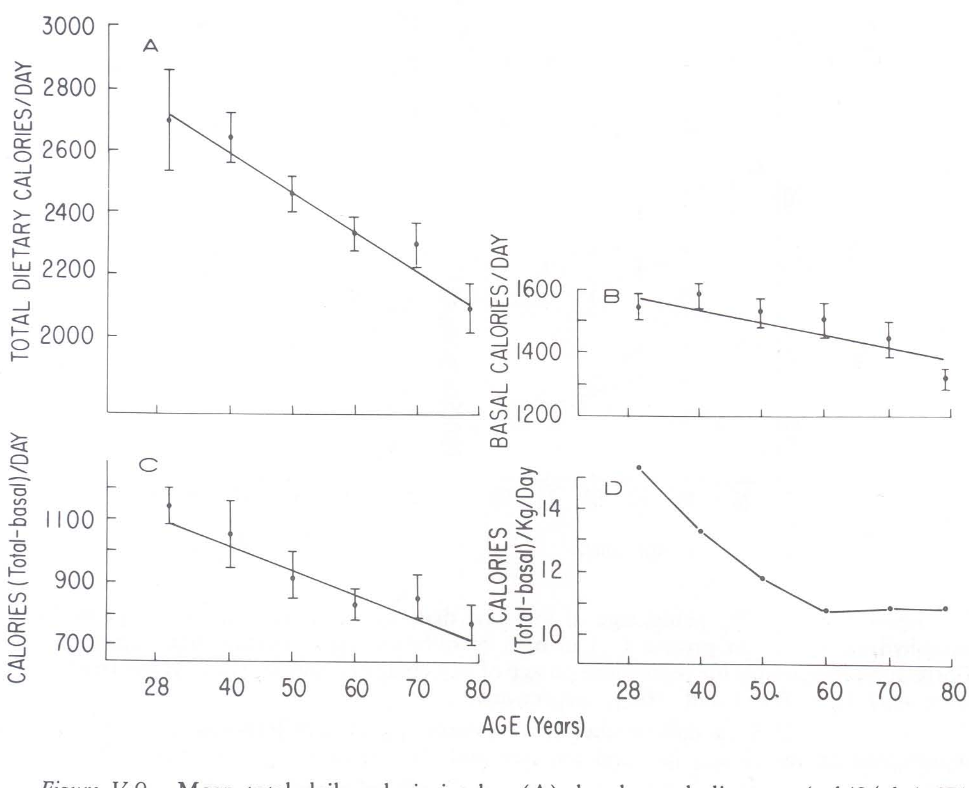

Figure V.9. Mean total daily caloric intakes (A), basal metabolic rates (cal/24 hr) (B), energy expenditures (C), and energy expenditures per unit of body weight (D) in men of different ages. Vertical bars represent standard errors of the means. Correlation coefficients for regressions on age of total calories, basal calories, and total-basal calories were –.374, –.374, and –.231, respectively; all were statistically significant ($p < 0.01$).
From McGandy et al. 1966).

of those over 80, were taking a vitamin supplement containing B_6. The average PLP level for the 203 men taking vitamin supplements was 20.5 ± 1.0 ng/ml, compared to 12.3 ± 0.3 ng/ml in the 414 not taking supplements. Subjects not taking B_6 supplements showed a statistically significant decrease in plasma PLP with age (0.9 ng/ml per decade of age). Although subjects taking supplements also showed a decline in PLP with age, the decline was not statistically significant. Plasma GOT levels varied little with increasing age, although they were significantly higher in the group taking vitamin supplements.

Serum albumin and aging. One cellular theory assumes that aging is a consequence of the reaction between metabolically produced free radicals and easily oxidized chemical groups, such as sulfhydryl groups (D. Harman, 1981). Consistent with this theory is the finding that the concentration of sulfhydryl groups in serum declines with age. Most serum-sulfhydryl groups, however, are associated with albumin, and since albumin levels also decline with age, lower serum-sulfhydryl levels in older people may be due either to free-radical oxidation or to lower levels of albumin production. A study was therefore undertaken to determine to what degree age-dependent decreases in serum-sulfhydryl concentration are due to decreased levels of serum albumin (Leto et al., 1970).

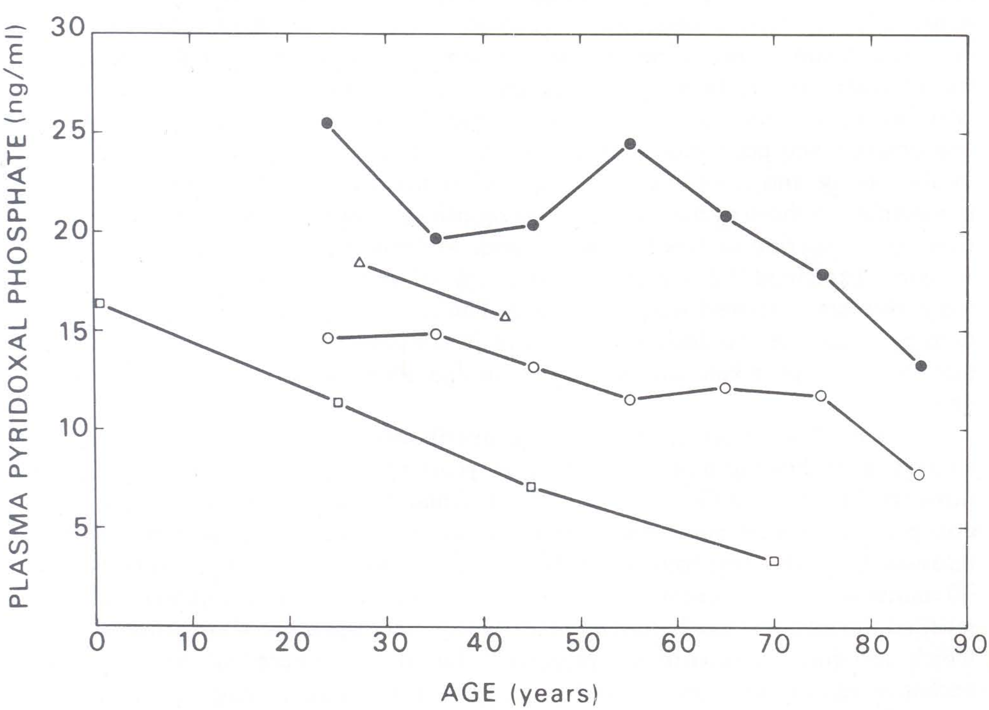

Figure V.10. Plasma pyridoxal phosphate levels reported by Rose et al. for the BLSA and by other investigators. (●) Rose et al., vitamin-B_6 supplemented; (△) Chabner et al.; (○) Rose et al., unsupplemented; (□) Hamfelt.
From Rose et al. (1976).

Fasting blood samples were obtained from 194 apparently healthy male volunteers participating in the GRC's longitudinal program. After assay for total albumin concentration, sera from the samples were fractionated to isolate albumin, which was then assayed for sulfhydryl content.

In men, the concentration of albumin, albumin sulfhydryl, and serum sulfhydryl was significantly lower in the ninth than in the third decade. Measurement of the readily reducible sulfhydryl/albumin ratio in a subsample of the men failed to demonstrate age differences. The data suggest that decrements in the sulfhydryl/albumin ratio result from changes in the redox potential of sera rather than from qualitative age changes in the structure of newly synthesized albumin. The observations failed to provide support either for the free-radical theory of cellular aging (D. Harman, 1981) or, incidentally, for the "error" theory (Medvedev, 1964; Rockstein, 1974) of aging.

4. Drug Metabolism

The effect of aging on drug metabolism was examined in two studies.

Antipyrine. The influence of age, alcohol consumption, caffeine consumption, and smoking on antipyrine metabolism was studied in 307 healthy male subjects aged 18 to 92 years (Vestal et al., 1975). The plasma half-life of intravenously administered antipyrine was 16.5% longer and metabolic clearance rate 18.5% lower in the older group (60–92 yr) than in the younger group (18–39 yr). There was a small, but statistically significant, negative correlation (–0.25, $p < .001$) between age and metabolic clearance rate of antipyrine. Consumption of caffeine and alcohol, as well as use of cigarettes, declined across the age span. Caffeine consumption was positively correlated with the rate of antipyrine metabolism in all age groups. Cigarette consumption was positively correlated with metabolic clearance rate of antipyrine only in the young and middle-aged groups; clearance rates in the older smokers were comparable to those of nonsmokers. No significant relation between alcohol consumption and antipyrine metabolism was found. Multiple regression analysis showed that smoking explained 12% and age only 3% of the variance in the rate at which antipyrine was removed from the blood. The results suggested that habits that differ with age—such as the decline found here in consumption of caffeine, cigarettes, and alcohol—must be taken into account in studies attempting to quantify the effects of aging.

Ethanol. The effect of aging on the distribution and elimination of ethanol was studied in 50 healthy men aged 21 to 81 years who had abstained from alcohol for three weeks (Fig. 11) (Vestal et al., 1977). Ethanol doses of 375 mg/m^2 body-surface area per minute were administered to the subjects by continuous one-hour intravenous infusion. Over the next four hours, blood samples were obtained at intervals of 15 to 30 minutes for measurement of ethanol concentration. The minimal model that satisfied the ethanol distribution and metabolism data was a two-compartment model in which an initial compartment represents blood and interstitial fluid spaces that exchange rapidly with blood, while a secondary and larger compartment represents more slowly equilibrating interstitial fluid and intracellular fluid spaces. Rates of ethanol elimination were not affected by age, but a significant correlation was found between age and the peak blood-ethanol concentration at the end of the infusion period (Fig. 12). Since all subjects received equivalent ethanol doses on the basis of

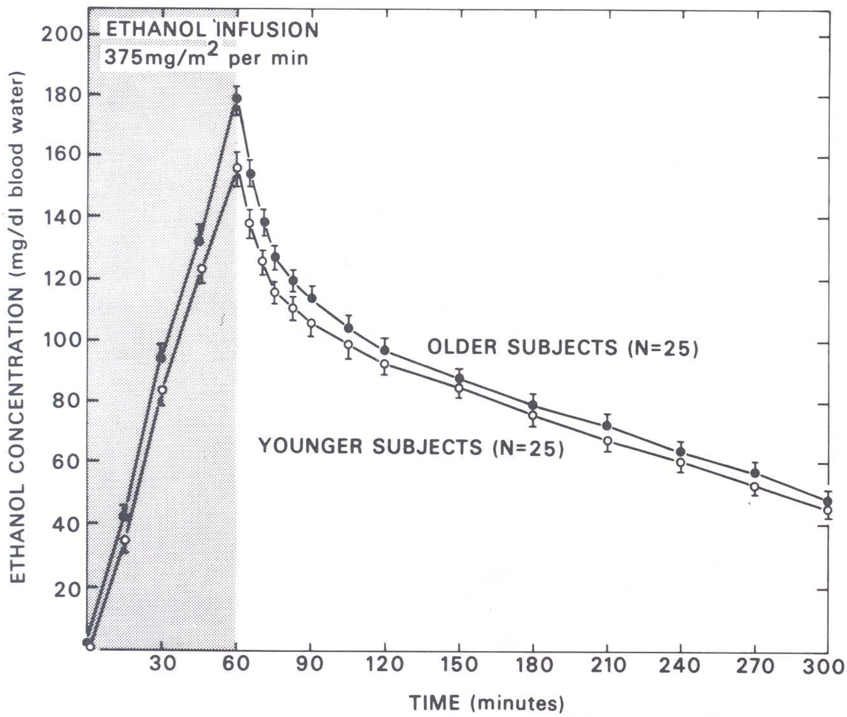

Figure V.11. Mean ethanol concentration in blood water (± SEM) for younger (aged 21–56) and older subjects (aged 57–81).
From Vestal et al. (1977).

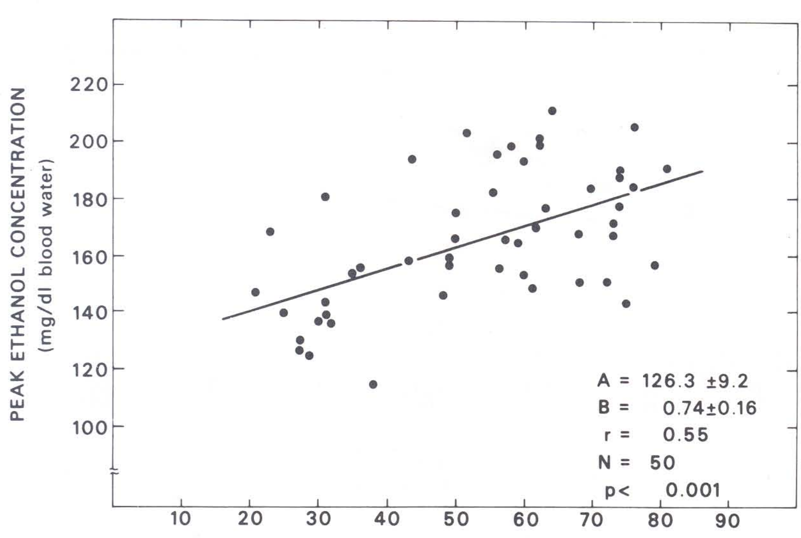

Figure V.12. Correlation with age of peak ethanol concentration in blood water at the end of ethanol infusion. A indicates the intercept and B the slope.
From Vestal et al. (1977).

body-surface area, it was concluded that the higher peak ethanol levels in the body water of old subjects were probably due to smaller volume of body water and lower lean body mass. Age-related changes in body composition are thus important factors in the metabolic and pharmacologic effects of drugs.

5. Pulmonary System

Age differences in pulmonary function. Earlier studies of age differences in lung volumes and maximal breathing capacity were usually carried out in hospital environments, often in subjects whose pulmonary status may not have represented that of active, successful people living at home. In addition, older hospital patients selected for pulmonary studies were seldom drawn from higher socioeconomic groups. A study

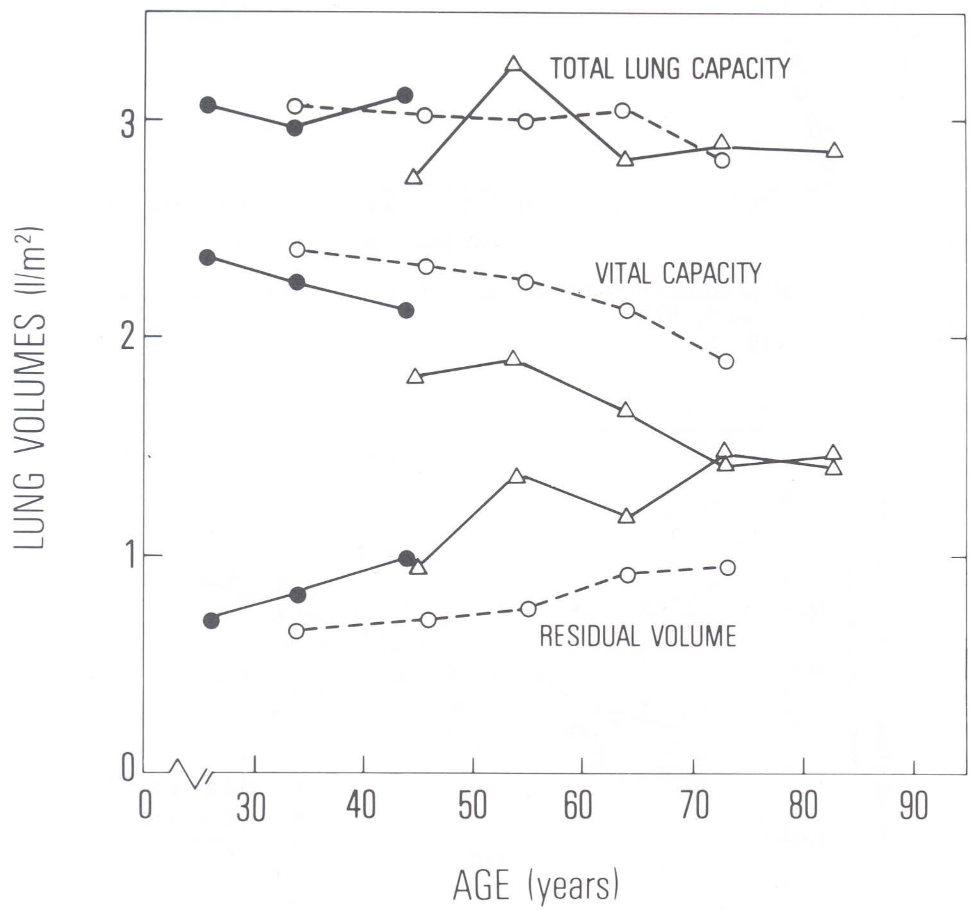

Figure V.13. Lung volumes divided by body-surface area (l/m^2) are plotted against age (yr). A hospital indigent group (△), a hospital staff group (●), and a community-residing group of BLSA participants (○). Average values by age decades (20–29 yr, etc.) are shown.
From Norris et al. (1962).

was undertaken to compare lung volumes and maximal breathing capacity in residents of the Infirmary Division (old people's home), employees, and short-term patients of Baltimore City Hospitals (BCH) (group A) and a sample of the BLSA study population (group B) (Norris et al., 1962).

Group A comprised 135 subjects whose age range was 20 to 89 years. Group B consisted of 166 BLSA participants whose age range was 30 to 79 years. Individuals from group B were generally taller, heavier, and better educated than individuals selected from the BCH population.

In group B, a statistically significant regression on age was found for maximal breathing capacity, vital capacity (both are lower with age), and residual volume (which is higher with age), but not for total lung capacity (Fig. 13). Age thus had a greater effect on a dynamic measurement of lung function that required a coordinated neuro-muscular response—breathing at a maximum rate and volume—than on a measurement of a single response, such as the single maximum expiration required for the measurement of vital capacity. Vital capacity was higher in group B than in group A, whereas residual volume was lower in group B than in group A for the sixth and eighth age decades. Total lung capacity did not differ in the two groups. Residual volume was significantly higher in 40-49-year old hospital-staff members of group A than in members of the same age group in group B. The group differences suggested a relation between pulmonary functional capacity and socioeconomic status (Fig. 14).

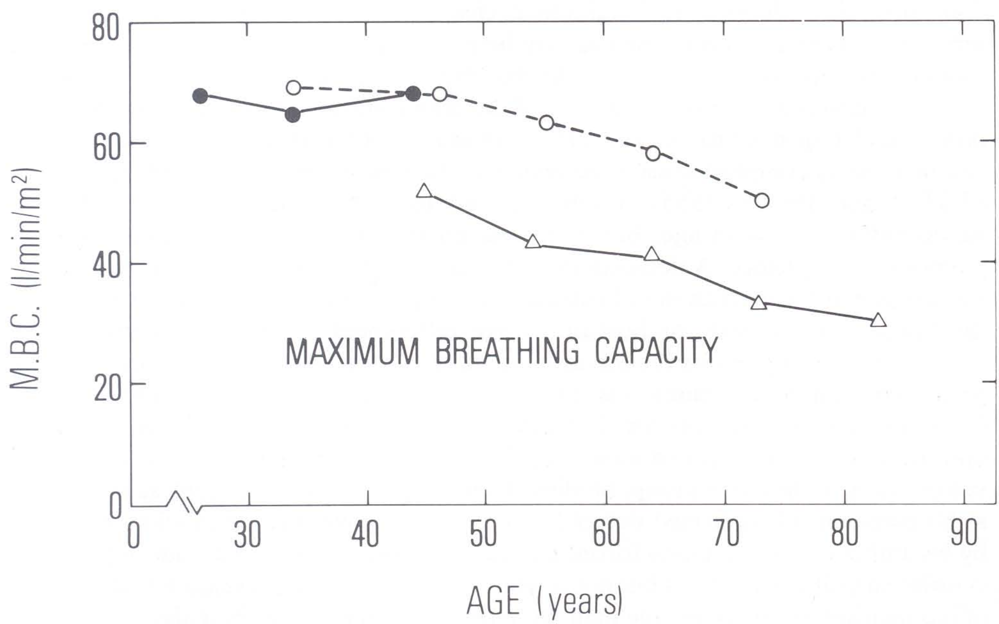

Figure V.14. Maximal breathing capacity in a hospital indigent group (△), a hospital staff group (●), and a community-residing group (○). Average values by age decade (20–29 yr, etc.) are shown.
From Norris et al. (1962).

Table V.4. Mean Values, Range of Values, and Standard Deviations of the Distributions of Lung-Clearance Index by Age Groups

Age in Yr	Mean Value	Range of Values	Standard Deviation	Number of Subjects
29–39	9.17	7.91–11.04	1.02	7
40–49	13.66	10.82–19.80	3.20	7
50–59	12.06	9.62–14.80	2.02	11
60–69	12.87	9.96–18.00	2.20	12
70–90	14.86	11.28–17.36	2.08	10

From *Norris et al. (1964)*

A comparison was made between BLSA participants and residents of the BCH old people's home to re-examine a previous finding that the ratio of ventilation to consumption of oxygen increases with age *(Norris et al., 1964).* Minute volume and breathing rate were similar for young and old persons in both groups, although vital capacity and maximum breathing capacity declined with age. Minute volume and alveolar ventilation in resting subjects were significantly higher in residents of the old people's home than in BLSA subjects. Nitrogen-washout curves analyzed in 47 BLSA subjects revealed significant age difference in the lung-clearance index (Tab. 4). This measurement indicates that older subjects are unable to maintain uniform ventilation of their lungs. A sample of 108 BLSA subjects who were tested at 18 and 36 months after their first visits showed no longitudinal changes in pulmonary function except an increase in maximum breathing capacity between the first and second visits in all age groups; the increase was attributed to the effects of practice in performing the test.

Age-related differences in the size of the lung compartments were examined in 42 normal males aged 24 to 78 years (Mittman et al., 1965). Measurements of chest-wall and pulmonary compliance used the static and the positive-pressure breathing methods of Heaf and Prime (1955). Chest-wall and total compliance were found to be significantly lower with age, but there was no significant relation between age and pulmonary compliance. A decrease in pulmonary compliance with higher lung volume was greater in young than in old subjects, possibly because of a loss of elastic recoil in the lungs of the elderly or because of age differences in chest-wall compliance.

The uniformity of distribution of pulmonary ventilation was assessed in 117 BLSA participants whose age range was 20 to 103 years (Edelman et al., 1968). The data from nitrogen-washout studies demonstrated that ventilation was significantly less uniform in old than in young men. Ventilation uniformity improved with higher tidal volume only in the older group. Studies of smaller groups in which each subject served as his own control confirmed that old men could improve their ventilation uniformity by breathing deeply. A single forced expiration before nitrogen washout impaired the ventilation uniformity of old but not of young men. The findings suggest that the lungs of old men are more susceptible than those of young men to localized alveolar collapse.

Effects of cigarette smoking on pulmonary function. Significant differences were found in the performances of cigarette smokers and nonsmokers on several spirometric tests (Edelman et al., 1966). The subjects, including 360 men participating in the BLSA and 50 medical and laboratory personnel, ranged in age from 20 to 103 years ($\bar{x}$ age = 52). Subjects were accepted if they had no history or signs of bronchopulmonary disease, cardiovascular insufficiency, or muscular weakness. Smoking habits were assessed by a

Table V.5. The Prevalence of Coronary Artery Disease in the Elderly as Assessed by Resting[a] and Stress Criteria[b]

	Age			
	51–60	61–70	71–80	81–90
N	70	73	36	10
% CAD by resting	13	15	22	20
% CAD by resting *and* stress	24	37	56	50

[a]History of angina or myocardial infarction; abnormal resting ECG, i.e., Minnesota codes 1:1, 1:2, 1:3, or 4:1.
[b]ECG positive for ischemia during maximum exercise treadmill test, i.e., Minnesota code 11:1 or an abnormal thallium scan during maximum exercise but not at rest.
From Gerstenblith et al. (1980)

questionnaire; spirometric data were analyzed by dividing the subjects into four groups based on their smoking histories: nonsmokers, current cigarette smokers, former cigarette smokers, and current and former pipe and cigar smokers. Current cigarette smokers had significantly lower values for vital capacity, maximal ventilation, and maximal expiratory flow rates than a comparable group of nonsmokers. Former cigarette smokers had significantly lower vital capacity than nonsmokers. Pipe and cigar smokers performed as well as nonsmokers in all tests.

Although comparison of former cigarette smokers with nonsmokers and current cigarette smokers did not provide clear evidence for or against reversibility of ventilatory impairment, analysis of the former smokers showed that those with the longest smoking-free interval performed significantly better on several tests of pulmonary function. Within the limitations of a retrospective cross-sectional survey, the findings are consistent with reversibility of pulmonary impairment upon cessation of smoking.

6. Cardiovascular System

Cardiac Performance and Aging: Occult Disease

Previous cross-sectional studies have characterized the effects of aging on a number of cardiovascular functions. Findings included a progressive fall in resting cardiac function with advancing age, a rise in peripheral resistance, and a wide range of individual differences in all measurements (Brandfonbrener et al., 1955). None of these earlier studies was able to control for the presence of occult coronary-artery disease (CAD), nor did the studies consider the average daily level of physical activity. The BLSA population provides a unique opportunity to reassess the effect of aging on the cardiovascular system for at least three separate reasons: Stress testing is used to screen for occult CAD; the elderly participants in whom cardiovascular function is tested maintain a level of physical activity required for independent community living; and recent technological advances that have made possible more accurate non-invasive measurements of cardiac function are currently available for application to BLSA participants.

The value of stress testing to detect occult CAD is illustrated in Table 5 (Gerstenblith et al., 1980). A subset of the population in the sixth to ninth decades was evaluated for CAD by both resting and stress criteria, which included exercise ECG and thallium testing described in Chapter IV. When stress criteria are employed in subjects in the sixth through the ninth decades, CAD is found in roughly twice as many cases, so that its rate in the aged approximates that found in unselected necropsy reports (Gerstenblith et al., 1980). It is likely that the high prevalence of occult disease in the older age range has had a major impact on studies attempting to assess the effect of age *per se* on cardiovascular performance. In the BLSA approach, data from subjects with either clinically overt or latent disease are excluded from studies whose purpose is to specify age effects; the result has in many instances been a perspective on the aging heart that is somewhat different from those of earlier studies: Some decreases in cardiovascular performance with age are due to disease, and the impact of age *per se* may not be as great as has been thought.

Cardiac Function at Rest

Systolic time intervals. Systolic time intervals provide a non-invasive assessment of general cardiovascular performance. In a series of 315 BLSA participants aged 20 to 89 years, a slightly longer ejection period was observed with age (Shaw et al., 1973).

One-dimensional echocardiography. The advent of ultrasound as a tool to test cardiac dimension and motion has permitted a more direct non-invasive assessment of cardiac function. A major determinant of cardiac stroke volume is the end-diastolic filling

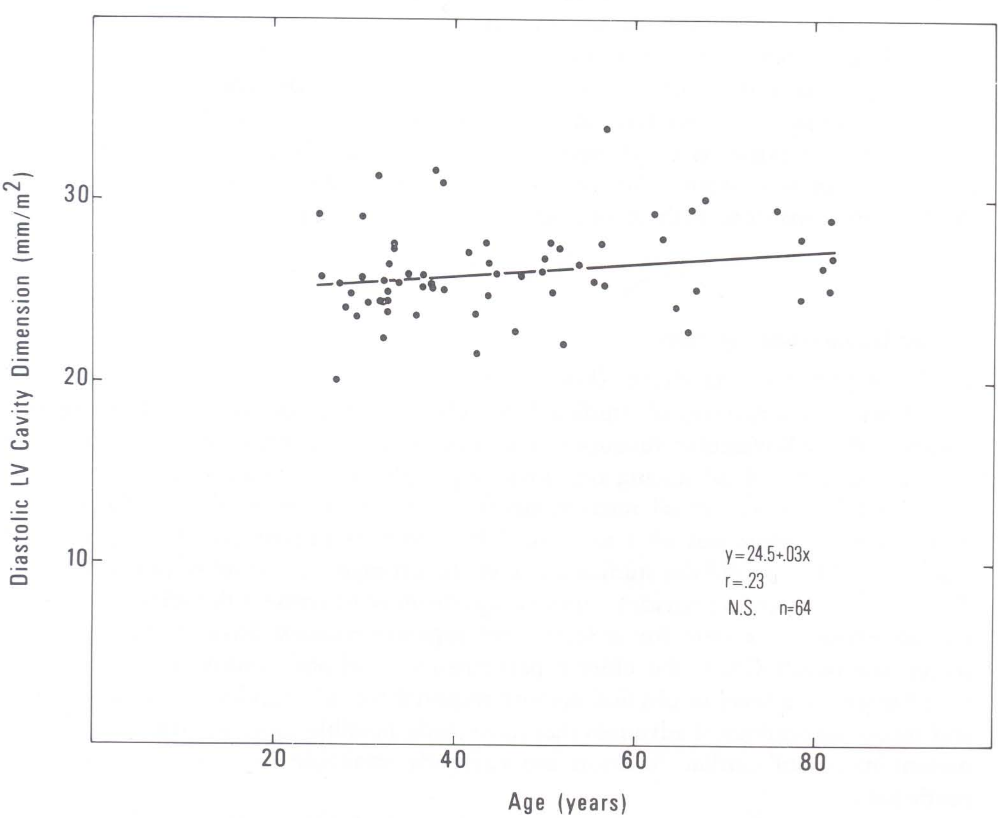

Figure V.15. Linear regression plot depicting the relationship between age and diastolic cavity dimension in healthy participants from the BLSA.
From Gerstenblith et al. (1977).

volume. Studies utilizing M-mode (one-dimensional) echocardiography in BLSA participants have indicated that, at rest, the left-ventricular end-diastolic diameter is not significantly altered with advancing age (Fig. 15) (Gerstenblith et al., 1977), and that ejection fraction index is also not age-related (Fig. 16). In view of the fact that the resting heart rate did not vary with age in these subjects, and if it can be assumed that the heart does not change its shape with age, the results suggest that cardiac output at rest is also not age-related. But since the assumption about shape may not be warranted, one-dimensional echograms permit no firm conclusion about the effect of age on cardiac output.

Two-dimensional echocardiography. Technological advances have resulted in the evolution of an echogram that measures cardiac chambers in two dimensions. Two-dimensional studies in an additional subset (n = 25) of BLSA participants indicated that end-diastolic and end-systolic cardiac areas were not changed with age (VanTosh et al., 1980); since the study found no age-related change in heart rate, it also suggested that resting cardiac output did not vary with age.

Multiple-gated cardiac blood-pool (MUGA) scans. More recently, it has been possible to measure cardiac volumes directly by multiple-gated cardiac blood-pool scans

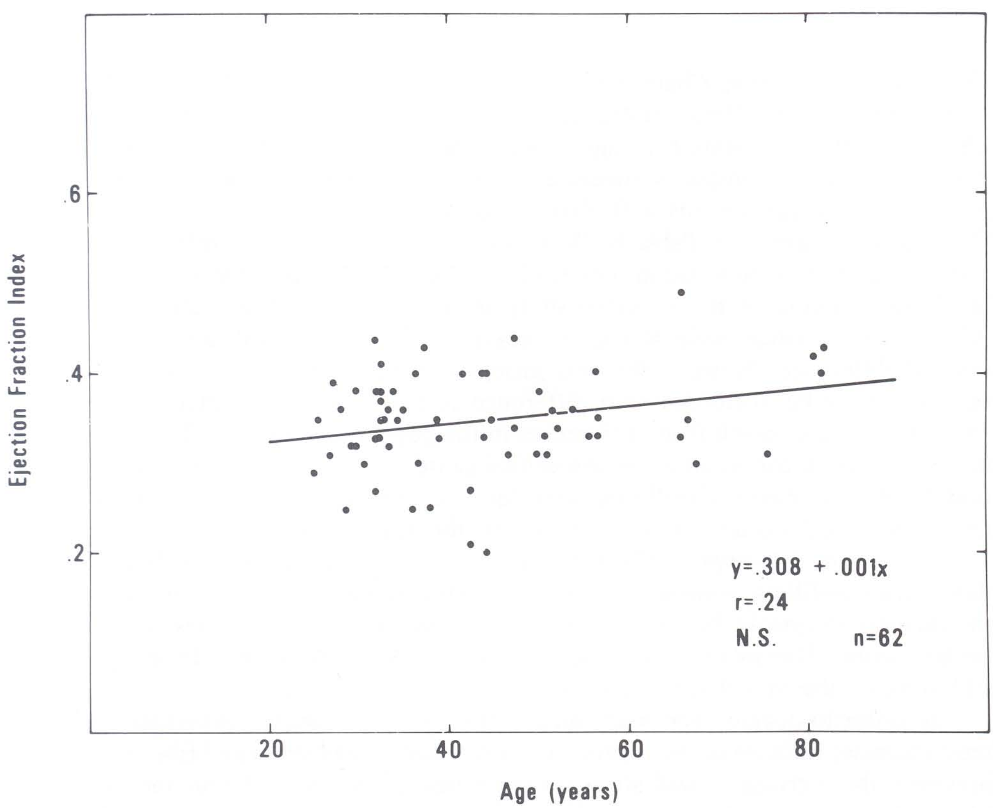

Figure V.16. Linear regression plot depicting the relationship between age and ejection fraction index in healthy BLSA participants.
From Gerstenblith et al. (1977).

Table V.6. Effect of Adult Age on Resting Cardiac Function

	Population A Institutionalized Unscreened for Occult CAD[a] Age range, 19–86 yr	Population B Active in Community Life Screened for Occult CAD[b] Age range, 24–79 yr
Heart rate	Slight decrease	No effect
Stroke volume	Decrease	No effect
Stroke-volume index	Decrease	No effect
Cardiac output	Decrease	No effect
Cardiac index	Decrease	No effect
Peripheral vascular resistance	Increase	No effect
Peak systolic blood pressure	Increase	Increase
Diastolic pressure	No effect	No effect

[a]From Brandfonbrener et al. (1955)
[b]From Rodeheffer et al. (1981)

(MUGA) described in Chapter IV. Analysis of studies in the first 37 participants (Rodeheffer et al., 1981) confirms the interpretation of the earlier studies with ultrasound, that no relation to age is found when end-diastolic, end-systolic, stroke volume, or cardiac output is measured at rest. A comparison of the hemodynamic profile of these participants with that of institutionalized subjects of an earlier non-BLSA study is given in Table 6. With the exception of the age-related increase in systolic blood pressure noted in both studies, the age-related differences in cardiovascular function found in the previous study were not observed in BLSA participants. Although the earlier study was more heavily weighted on both age extremes, the marked differences between the two groups between the ages of 30 and 80 years cannot readily be attributed to a difference in age range or in methodology. The contrast must thus result from differences in the populations studied. While this might in part be a birth-cohort effect of unspecified cause, a more attractive hypothesis would point to the likelihood of cardiovascular "deconditioning" secondary to convalescence or bed-rest, and occult coronary disease in the earlier sample.

Ventricular hypertrophy. Although at rest cardiac output and its hemodynamic determinants—filling volume, ejection fraction, and heart rate—are not age-related, the increase in systolic blood pressure with advancing age necessitates an increase in cardiac work. The increase in systolic pressure apparently results from age-related stiffening of the vasculature (Lakatta, 1979).

In order to develop and maintain greater systolic pressure, ventricular wall stress must increase. Because of the inverse relation between wall stress and fiber shortening, however, the increase in wall stress compromises shortening and thus the ejection of blood. To maintain normal shortening in the face of an increased pressure load, the heart can hypertrophy, i.e., thicken its wall, since wall stress is force per unit thickness. The presence of cardiac hypertrophy with advancing age has been sought in 67 healthy BLSA participants. Gerstenblith et al. (1977) have demonstrated a mild age-related increase in left-ventricular wall thickness in men over the age range of 25 to 80 years (Fig. 17) that may be considered an adaptation to maintain normal systolic function. Although the increase in diastolic wall thickness may be a major factor in producing the progressive age-related limitation of cardiac filling during the early diastolic period (Fig. 18), the fact that end-diastolic volume is not compromised renders it unlikely that the reduced filling rate at rest has physiologic significance.

Cardiovascular Response to Stress.

The fact that overall cardiac performance at rest is not altered by age in normal man by no means indicates that performance during stress is unaffected. Classic studies of exercise physiology have indicated that maximum exercise performance diminishes with age in apparently healthy persons. Age-related declines have been identified in maximum aerobic capacity, heart rate, stroke volume, cardiac output, and arterio-venous O_2 differences (see review by Gerstenblith et al., 1976). These comparisons, however, are made not at standard exercise levels across all ages but at the voluntary maximal exercise level in each subject, which is substantially reduced with age. Since no plateau is evident in the workload curves, it cannot be ascertained whether maximum cardiac performance was achieved in the elderly, or whether the limitation in workload with advanced age might have been due to other factors.

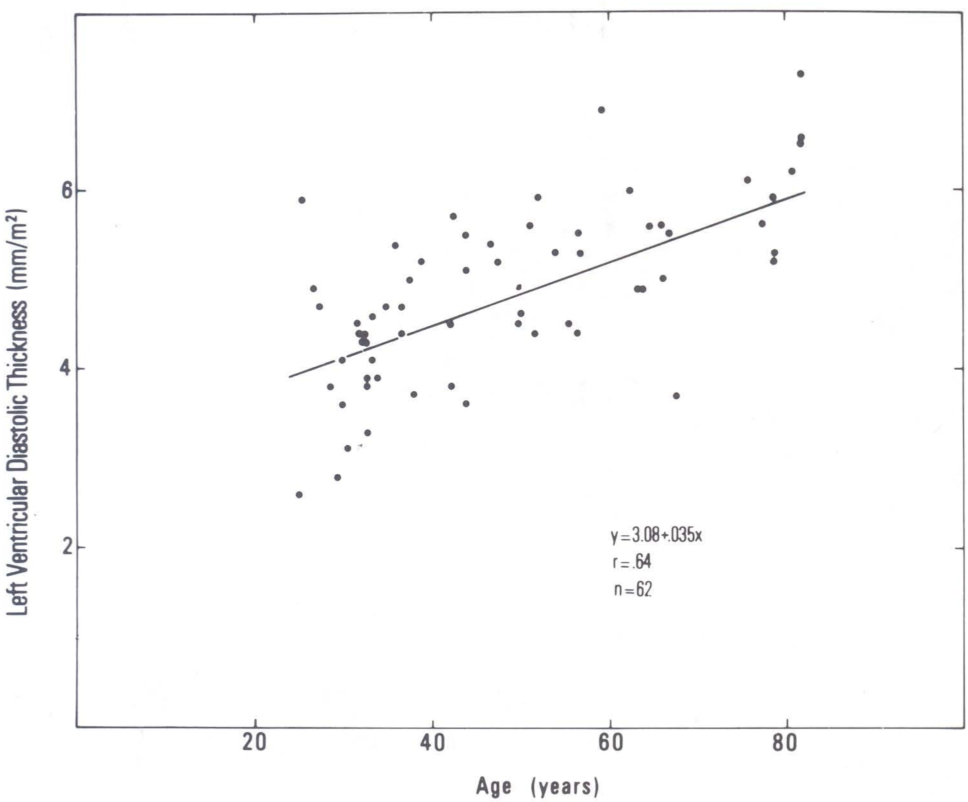

Figure V.17. Linear regression plot depicting the relationship between age and left-ventricular diastolic wall thickness.
From Gerstenblith et al. (1977).

Consideration of the influence of occult disease is even more important during exercise than in studies of the cardiovascular system at rest. In fact, an age-dependent increase in ECG abnormalities during exercise, which may in some instances be indicative of coronary disease, has been observed in some of the classic studies (Montoye, 1975; Granath et al., 1964). Furthermore, the status of physical conditioning is also a major determinant of the exercise response. A true assessment of the effect of aging *per se* on the cardiovascular response to exercise, then, requires strict control of both parameters. The cardiovascular response to exercise has been measured by the MUGA scan in BLSA participants who had both normal ECG and normal thallium tests during treadmill exercise. The results obtained in the first 37 consecutive volunteers for this exercise protocol, like the findings at rest, differ in many ways from previous studies (Gerstenblith et al., 1976) that have examined the effect of age on the cardiovascular response to stress:

Maximum heart rate after exercise. The maximum heart rate decreased significantly with age (Tab. 7). It is important to note that the maximum heart rates achieved in this exercise protocol were comparable to those in other studies, including those in which the maximum work load was significantly reduced with advanced age. That this result

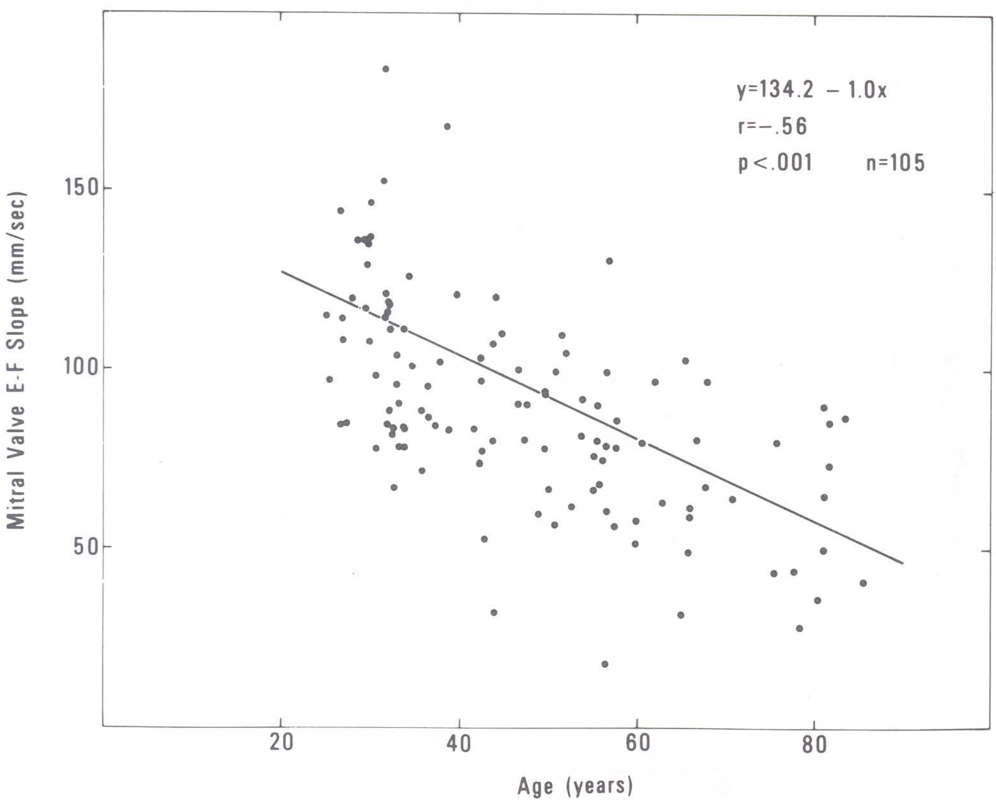

Figure V.18 Linear regression plot depicting the relationship between age and the rate of left-ventricular early diastolic filling as manifest in the closure rate of the anterior leaflet of the mitral valve (E–F) slope.
From Gerstenblith et al. (1977).

Table V.7. The Effect of Age on Hemodynamic Performance at Maximum Exercise in BLSA Subjects (N = 37)

Parameter	Linear Regression	r	p
Heart rate (BPM)	200.7 – .82 (age)	–.57	< .001
End-diastolic volume (cc)	126.2 + 1.28 (age)	.39	< .02
Stroke volume (cc)	107.6 + .69 (age)	.29	< .08
Cardiac output (4 min)	22.5 – .07 (age)	–.19	< .24
End-systolic volume (cc)	–.45 + .60 (age)	.50	< .002
Ejection fraction	92.9 – .20 (age)	–.35	< .03
Total peripheral vascular resistance	20.32 – .06 (age)	–.18	< .28
Systolic blood pressure (mm Hg)	177.9 + .34 (age)	.176	< .3

From Rodeheffer et al. (1981)

has been observed in virtually every population studied suggests that a diminished maximum heart rate is a true age-related phenomenon.

End-diastolic filling volume (pre-load). Blood filling the heart during diastole serves to stretch the fibers, in the process not only altering their geometry but also enhancing activation of the myofilaments. Through these mechanisms the heart can alter its stroke volume with changes in filling volume, an effect sometimes referred to as the Frank-Starling mechanism. It has previously been hypothesized (Gerstenblith et al., 1977) that because of changes in myocardial compliance—that is, the heart becomes stiffer with age—and because early diastolic filling rate is compromised with advancing age, diastolic filling volume may be lower in elderly than in younger adult subjects during exercise, when the filling time is reduced.

Not only is this not the case, but quite the opposite occurs: End-diastolic filling volume is increased rather than decreased as a function of age during the maximum exercise response (Tab. 7). In a previous study of another subset of the BLSA population at submaximal work loads—semi-supine exercise at a common heart rate of 120 bpm—the measured end-diastolic area determined by two-dimensional echocardiography was also greater in subjects 65+ years old than in those whose age averaged 30 years (VanTosh et al., 1980). The observed increase in filling volume was a major factor through which stroke volume not only was maintained, but actually tended to become larger, in the older group during exercise (Tab. 7). This in part balanced the effect of a decrease in maximal heart rate on maximal cardiac output, which in this population demonstrated only a slightly negative trend with age (Tab. 7). Enhancement of filling volume by the Frank-Starling mechanism may thus be construed as an age-related adaptive mechanism through which cardiac output is maintained during stress. A price is paid for this adaptation since, in accordance with LaPlace's law, generation of a given ventricular pressure requires greater wall stress (force per unit area) if the ventricular radius is increased; this in turn requires a greater level of cardiac work and energy production. Futhermore, enhanced filling volume, even in the absence of changes in compliance, results in an enhanced filling pressure, and may at least in part explain the age-related increase in filling pressure observed during exercise (Granath et al., 1964). An increase in left-heart diastolic filling pressure also produces an increase in pulmonary venous pressure, which increases the likelihood of pulmonary congestion.

Ejection fraction. An increase in diastolic filling volume should not only enhance stroke volume but also result in the ejection with each beat of a greater fraction of blood in the elderly than in young adults. The expected result, however, does not occur in the aged heart; end-systolic volume is not reduced during exercise in the elderly to the same extent as in younger adults; in fact, it increases with age (Tab. 7). Thus, although filling volume increases, the fraction of blood ejected is not increased but actually decreases with advancing age (Tab. 7). This indicates that the ejection of blood by the heart is compromised in the elderly subjects.

Autonomic modulation. During maximum exercise, when the sympathetic component is the exclusive autonomic modulator, a marked increase in catecholamine secretion occurs (Tzankoff et al., 1980). An age-related alteration in sympathetic modulation of the cardiovascular response to exercise could account for: a) the decline in maximum heart rate; and b) the apparent decline in maximum contractility, i.e., an increased end-systolic volume, and a decreased ejection fraction from a greater filling volume in the absence of an increase in systolic blood pressure in the elderly during exercise.

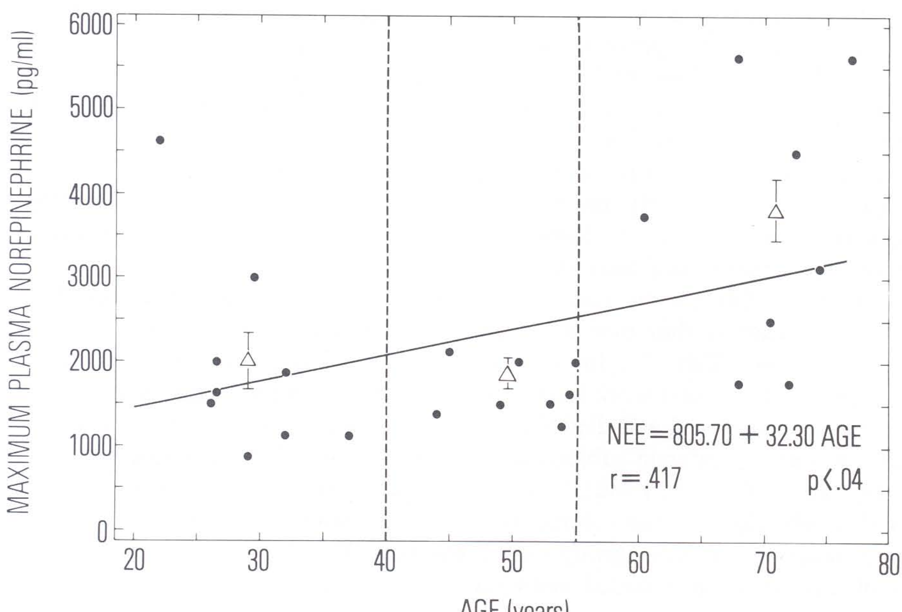

Figure V.19. The effect of age on plasma-norepinephrine concentration during maximum treadmill exercise in BLSA participants. Plasma norepinephrine concentration at rest did not differ in these subjects. In addition to the regression analysis across age, the subjects were divided into 3 age groups. The dotted vertical lines separate the 3 age groups in which the mean and SEM are denoted by △.
From Tzankoff et al. (1980).

A diminished sympathetic response during exercise could result from a deficiency in the elaboration of catecholamines in aged subjects. In a subset of the BLSA population (n = 27) both plasma epinephrine and norepinephrine, although not age-related at rest, demonstrated a substantial age-dependent increase during treadmill exercise (Fig. 19) (Tzankoff et al., 1980). A diminished maximum heart rate in these healthy subjects was thus accompanied by an increase rather than a decrease in plasma catecholamines. This result is consistent with the hypothesis that target-organ responsiveness to catecholamines declines with age. This was tested on a subset of the BLSA population by the infusion of incremental concentrations of isoproterenol in bolus form and monitoring of the resultant increase in heart rate (Lakatta, 1979). The same concentration of isoproterenol resulted in a greater increase in heart rate in younger than in older participants (Fig. 20). The result supports the notion that adrenergic responsiveness diminishes with age.

Summary: Hemodynamic Function at Rest and in Response to Stress

Age-related differences in the cardiovascular response to stress have often been observed in man. Their nature and magnitude have varied with the population studied. In apparently healthy populations that have not been screened for occult coronary disease, substantial decrements in maximum cardiopulmonary function and work capacity have been observed. In more selected populations, although maximum cardiovascular function does not markedly deteriorate with advanced age, definite age-related adaptations in hemodynamics serve to prevent substantial declines in cardiac

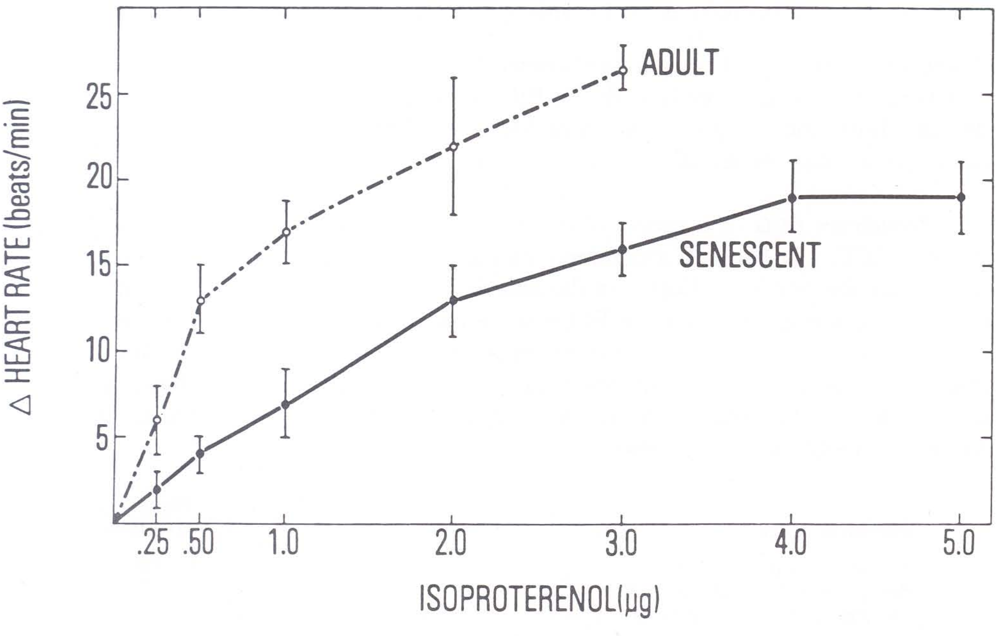

Figure V.20. The increase in heart rate induced by incremental intravenous boluses of isoproterenol in healthy adult (aged 18–34 yr) and 20 senescent (aged 62–80 yr) men. A significantly greater increment in heart rate is observed in the younger men at all isoproterenol dosages greater than 0.25 μg.
From Lakatta (1979).

output. A feature common to studies in a wide variety of populations is that the age-related differences observed may be attributed, at least in part, to altered responsiveness to adrenergic stimulation.

Electrophysiology

In addition to hemodynamic function, recent studies of BLSA participants have focused on the electrophysiological properties of the heart, in particular on the conduction system:

Non-invasive assessment of His-bundle ECG. It is not known whether the age-related increase in PR interval is due to slowed conduction proximal (PH) or distal (HV) to the His bundle, or to both. A microprocessor-assisted high-resolution ECG, which signal-averaged 512 cardiac cycles, recorded high-frequency, low-amplitude ECG signals from the body surface of 63 BLSA participants aged 21 to 70 ($\bar{x}$ age = 46.1 ± 17.0 yr) (Das et al., 1982). All subjects were clinically free of heart disease and displayed both normal resting ECG and normal maximal treadmill exercise tests. His-bundle potentials were identified in 53 individuals; the 10 persons in whom a His spike could not be identified did not differ in age or resting heart rate from those with His potentials, but had shorter PR intervals (131.5 ± 15.3 vs. 155.8 ± 18.5 msec, $p < .001$). In those subjects with demonstrable His activity, the following regressions were obtained:

$$PR = 139.6 \text{ msec} + 0.35 \text{ age}; (r = .32, p < .02)$$
$$PH = 101.1 \text{ msec} + 0.31 \text{ age}; (r = .33, p < .02)$$
$$HV = 38.3 \text{ msec} + 0.04 \text{ age}; (r = .09, p = NS)$$
$$HR = 72.6 \text{ beats/min} -0.11 \text{ age}; (r = -.19, p = NS).$$

These observations led to the conclusions that: The success rate of recording surface His potentials varies directly with the PR interval; HV interval does not change with age in adults; and the prolongation of PR interval seen with advancing age is due to conduction delay proximal to the His bundle.

Ambulatory ECG in a healthy elderly population. Although recording of ambulatory 24-hour ECG has become a common diagnostic tool on which anti-arrhythmic and pacemaker therapy is predicated in the elderly, no suitable standards of normality exist for this age group. Ambulatory ECGs were analyzed in 98 BLSA subjects who had demonstrated a normal response to maximum treadmill ECG. Of this carefully screened population, 88% demonstrated supraventricular ectopic beats and 80% showed ventricular ectopic beats. A further breakdown of arrhythmias (Fleg and Kennedy, 1982) is shown below:

Supraventricular	*Percentage of Subjects*
≥ 100 beats in 24 hours	26
Benign slow atrial tachycardia	28
Paroxysmal atrial tachycardia	13
Ventricular	
≥ 100 beats in 24 hours	17
Multiform	35
Couples	11
Ventricular tachycardia	4

Sinus bradycardia less than 40/min and sinus pauses exceeding 1.5 seconds were rare. No instance of high-degree AV block or sinus arrest was observed. These results provide a framework for the interpretation of ambulatory ECG results in symptomatic elderly subjects.

7. Renal System

Creatinine clearance. Creatinine clearance is frequently used as a clinical estimate of kidney function (glomerular filtration rate, GFR). Although the published criteria for severity of renal disease included classification of patients according to their creatinine

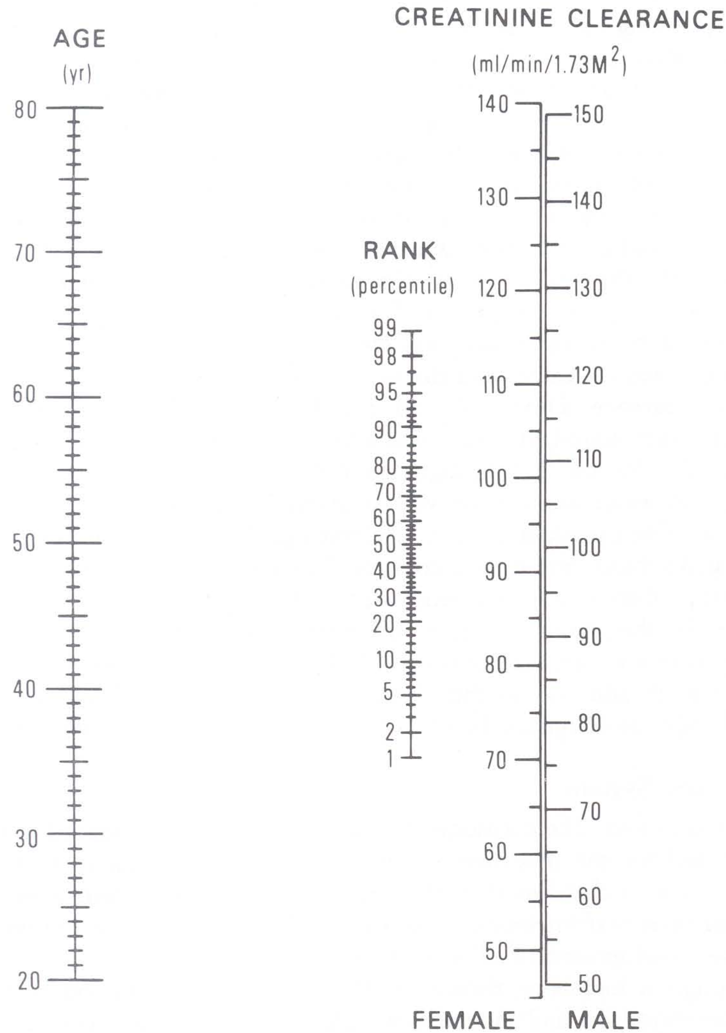

Figure V.21. Nomogram for ascertaining age-adjusted percentile rank in creatinine clearance. For use with creatinine determinations by automated "total chromogen" method. See text for derivation of data for females. A line through the subject's age and creatinine clearance intersects the percentile rank line at a point indicating the subject's age-adjusted percentile rank. From Rowe et al. (1976a).

clearance in comparison with the "predicted normal," no age-adjusted normal standards for creatinine clearance were available until 1976, when the GRC provided them (Rowe et al., 1976a). Standard 24-hour creatinine clearance measurements were made on 884 adult male participants (age range = 17–96 yr) in the BLSA. True creatinine was measured in both serum and urine. There was a highly significant reduction in creatinine clearance with age in 548 carefully screened subjects, and the relation between creatinine clearance and age was found to be best described by the linear equation: Creatinine clearance (ml/min · $1.73m^2$) = 133 − 0.64 · age (yr). Nomograms for ascertaining age-adjusted percentile rank in creatinine clearance were constructed for men and, by derivation, for women (Fig. 21). The conversion factor of 0.93 to derive values for females was taken from the literature review by Wesson (1969). The longitudinal analysis of renal function is summarized in Chapter VI, and the study *(Rowe et al., 1976b)* is reprinted in the Appendix.

Concentrating ability. Several cross-sectional studies have shown that the ability to concentrate urine declines with age after maturity. A BLSA study was performed to determine cross-sectional age differences in solute and water conservation, independent of the effects of disease or medication (Rowe et al., 1976c). The 97 participants included in the analysis ranged in age from 20 to 79 years. At 6:00 P.M. each subject was asked to void and the urine was discarded. Subjects were then instructed not to eat or drink until 6:00 A.M. Urine specimens representing three time periods were then collected between 9:00 P.M. and 6:00 A.M. At 6:00 A.M. a blood sample was collected for determination of osmolality and creatinine concentration. At 10:00 A.M., a final urine sample was collected, and the total 16-hour pool was used for determination of creatinine clearance. During Period 1 (6:00-9:00 P.M.), no significant age-related differences were found in urine osmolality, urine flow, solute secretion, or osmolar clearance. By Period 3 (midnight to 6:00 A.M.), however, young subjects had responded to water deprivation with a marked decrease in urine flow, a moderate increase in urine osmolality, and a resultant significant decrease in osmolar clearance. Middle-aged subjects also decreased urine flow and increased urine osmolality, but to a lesser extent than young subjects; the result was a small net decline in osmolar clearance. In the elderly subjects urine-flow rate, urine osmolality, and osmolar clearance were not significantly altered during the period of dehydration. These effects indicate that in addition to the reduction in glomerular filtration rate there is an impaired response of renal tubules to changes in plasma osmolality in the old subjects.

8. Endocrine System

Age and diabetes. The cortisone glucose tolerance test, introduced in the mid-1950s, was proposed for the detection of the prediabetic state, that is, to provide a more sensitive index of diabetes than the oral glucose tolerance test. Several studies had shown that poor performance on the cortisone glucose tolerance test was predictive of the future development of clinical diabetes.

Although it had been shown by 1965 that performance on both the standard glucose tolerance test and the cortisone glucose tolerance test declines with age, the studies failed to quantify the age effect or define the age at which it begins (Andres, 1971). To test the assumption that the age-related loss of glucose tolerance might be clinically significant, a BLSA study was undertaken to quantify the effect of aging on cortisone glucose tolerance test performance over the entire adult age span (Pozefsky et al., 1965).

Of the 89 male subjects, aged 21 to 95 years, initially selected for study, data from 15 were eliminated because they had diabetes, reported a positive family history of diabetes that was less than first-degree, or were taking drugs known to alter carbohydrate metabolism. An additional 13 subjects with a primary family history of diabetes were analyzed separately. The final group consisted of 61 individuals.

Cortisone acetate based on body weight was given orally in two equal doses 8.5 and 2 hours before glucose administration. After withdrawal of a fasting blood sample, 1.75 g of glucose/kg of body weight was administered orally as a 30% solution. Blood samples were then obtained at 20-minute intervals for two hours. Blood glucose was measured by ferricyanide reduction. An obesity index was computed for each subject from the ratio of actual weight to the mid-weight for the medium frame in the 1959 Metropolitan Desirable Weight Table (Metropolitan Life Insurance Co., 1959).

Fasting blood-glucose levels were elevated by cortisone in subjects of all ages, but sensitivity to this effect increased significantly with advancing age: The average increment was 2.1 mg/dl for each age decade. Blood-glucose concentration also increased with age after glucose administration. By 120 minutes the average increase in glucose level was 17.6 mg/dl per decade of life. The subjects were divided into three age groups (20–44, 45–64, and 65–95 yr) for comparison of mean cortisone glucose

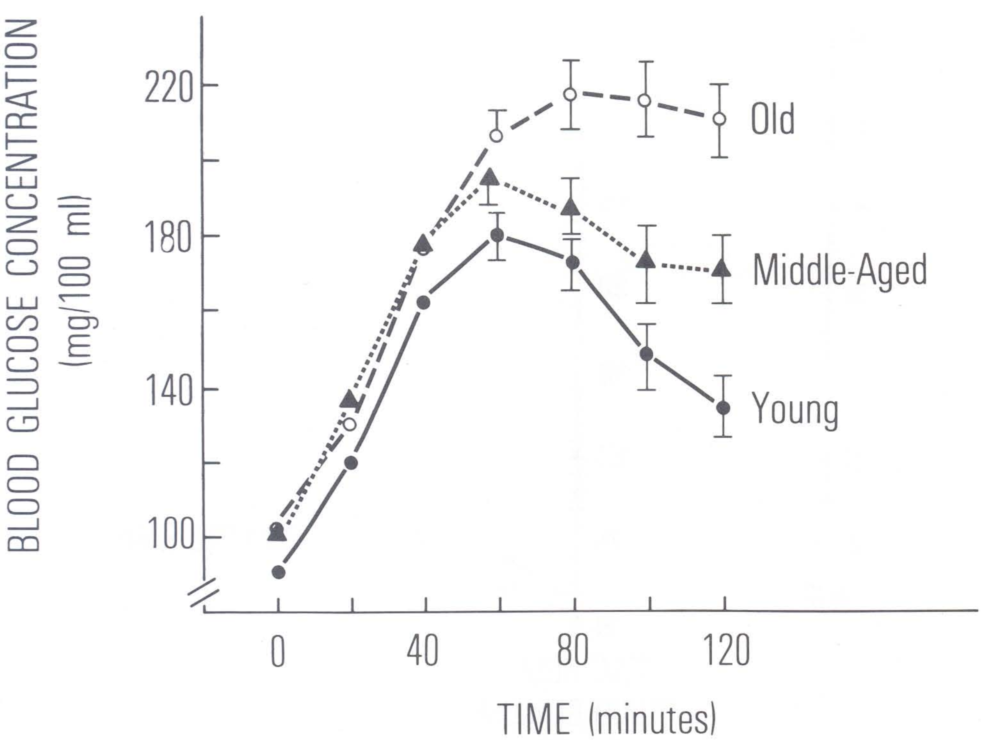

Figure V.22. Mean cortisone-glucose tolerance test curves for negative-family-history subjects in 3 age groups. The SEM for each time period after 40 min is also shown. Differences between these groups were not significant before 60 min. The 15 young subjects were aged 21-44, the 26 middle-aged 45-64, and the 20 old 65-95 yr.
From Pozefsky et al. (1965).

tolerance test curves. The oldest group reached peak blood glucose levels at 80 minutes and showed only a slight decline thereafter. Young subjects peaked at 60 minutes, and fell more rapidly in the second hour of the test. The response of the middle-aged group was intermediate (Fig. 22). The effect of age on glucose levels was thus not simply a difference between young and old but manifest throughout the adult age range.

A comparison of tolerance curves revealed higher glucose intolerance in subjects whose families had histories of diabetes. The differences between this group and the control group, which although small were statistically significant, confirmed the observation that performance on this test is poorer in subjects at higher risk of developing diabetes.

The profound age influence on performance made it clear that reliance on a single standard for the upper limit of normality was unrealistic. A nomogram was therefore proposed to permit percentile ranking of an individual within his age group, although prospective studies are required to determine the prognostic implications of specific percentile ranks (Fig. 23).

The application of separate standards to different age groups assumes that deterioration in glucose tolerance with increasing age does not necessarily indicate diabetes mellitus. The question whether the decrement is the result of pathology or a

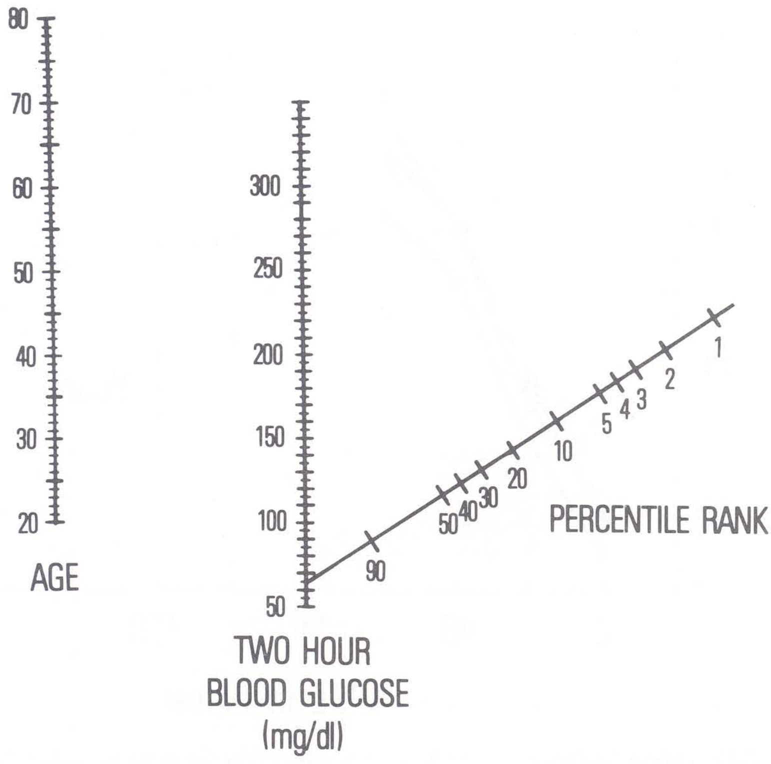

Figure V.23. Cortisone-glucose tolerance test. Nomogram for establishing an individual's percentile rank in his birth cohort, based on 2-hr blood-glucose concentration. From Pozefsky et al. (1965, adapted).

part of normal aging might be solved by a test for diabetes that does not involve measuring glucose tolerance. A BLSA study (Swerdloff et al., 1967) was undertaken to test the possibility that the intravenous tolbutamide test might be an age-independent method of detecting diabetes without reference to glucose tolerance. The decline of blood-glucose concentration that occurs after tolbutamide administration is markedly influenced by diabetes, occurring more slowly and to a lesser degree than in normal individuals.

Tolbutamide tests were performed in 141 male subjects, 117 of whom (age range = 25–81 yr) were randomly selected from participants in the BLSA. The other 24 were college students and hospital employees 21 to 36 years of age. Forty-one subjects were

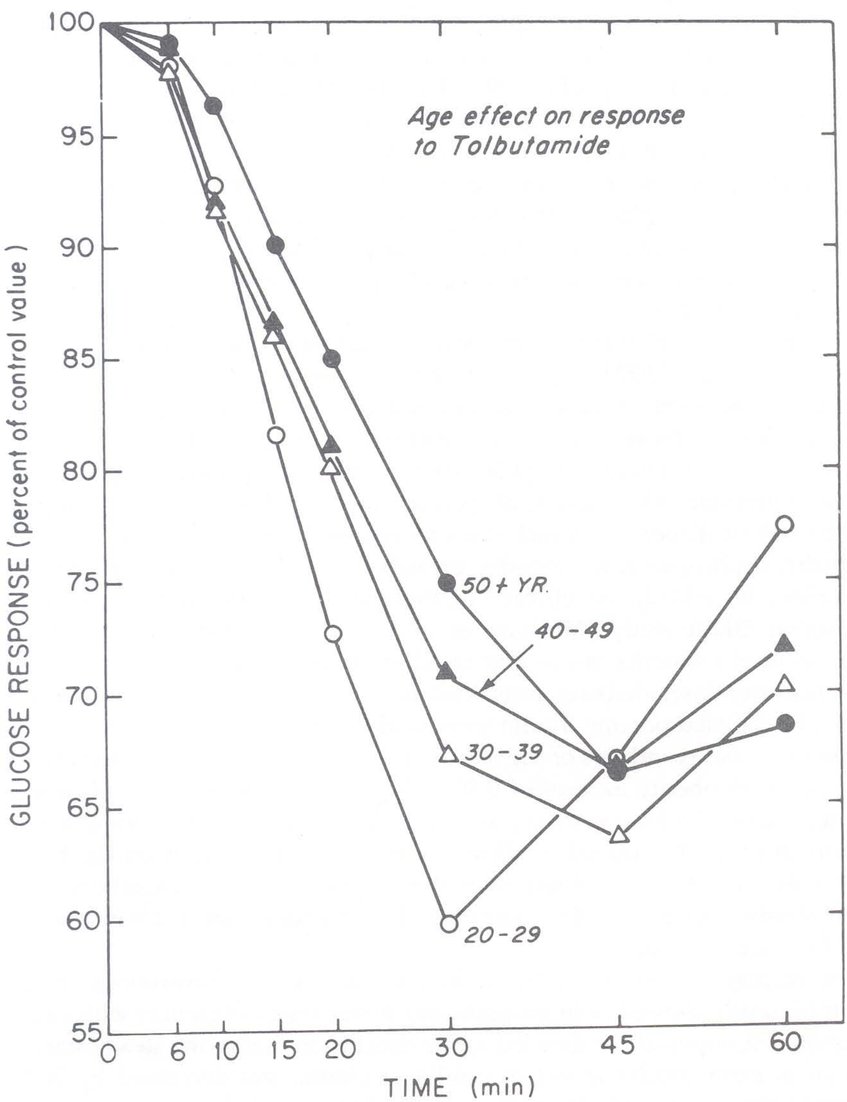

Figure V.24. Age effect on response to tolbutamide. From Swerdloff et al. (1967).

subsequently excluded for characteristics that were likely to confound the results, such as those noted above for the cortisone-glucose tolerance test. After overnight fasting, a baseline blood sample was taken. Then sodium tolbutamide in distilled water at a dose of 1 g/70 kg body weight was injected, and blood samples for glucose analysis were obtained at 6, 10, 15, 20, 30, 45, and 60 minutes.

A significant increase in fasting blood-glucose concentration with advancing age was found in the group, in contrast with other groups in which there was no difference with age, but the increment was only 0.9 mg/dl per decade of life. The fall in glucose concentration after tolbutamide administration was markedly affected by the age of the subject. Blood-glucose levels fell rapidly in the youngest subjects, usually reached a minimum in 30 minutes, and generally rebounded by 60 minutes. In the older subjects, glucose fell more slowly, reaching a minimum at an average of 45 minutes, and the decrease was smaller. The greatest age effects were seen at 20 and 30 minutes after tolbutamide administration (Fig. 24). The decline in response to tolbutamide was progressive in the four decades from age 20 to age 59. There was, however, no further decline in response in subjects over age 59.

Since age effects were pronounced in the tolbutamide test, it was concluded that this method, like the glucose tolerance method, requires age adjustment for proper interpretation. Accordingly, a nomogram was provided to permit the rapid computation of age-adjusted percentile ranking of an individual's response to intravenous tolbutamide (Fig. 25).

The limitations of various methods of diagnosing diabetes in the elderly were discussed by Andres (1971) in a symposium on diabetes mellitus. He concluded that statistical manipulations of survey data cannot resolve the question whether standards of normality should be adjusted for age, and recommended that long-term longitudinal follow-up studies be made in populations that have participated in glucose tolerance tests, to determine what levels of performance in different age groups indicate increased risk of diabetes and such diabetes-related events as atherosclerosis, diabetic neuropathy, nephropathy, retinopathy, or, indeed, death itself. Once a high-risk group is identified, he added, the efficacy of therapeutic regimes can be assessed.

Another BLSA study (McGuire et al., 1979) provided some insight into the changes in insulin kinetics *in vivo* that are characteristic of aging, of moderate obesity, and of maturity-onset diabetes insufficiently severe to require insulin therapy. The kinetics of unlabeled porcine insulin were studied in 69 nondiabetic males aged 18 to 83 years with obesity indexes of 0.93–1.51, and in 12 maturity-onset diabetics aged 46 to 78 years with obesity indexes of 0.95–1.56, by use of the insulin-infusion glucose-clamp technique (DeFronzo et al., 1979) to maintain constant blood-glucose levels. The individuals were grouped to allow comparison of the results on the basis of age, obesity index, or diabetes. Analysis of the kinetic data with a mathematical model allowed steady-state distribution masses and degradation-rate constants to be determined for each subject.

The responses over a period of 120 minutes to an intravenous infusion and washout of insulin showed both transient and steady-state differences with age, obesity, and diabetes. Analysis of the data led to the conclusion that in the steady state the ratio of insulin in extravascular spaces to insulin in plasma was decreased by 26% in the moderately obese group and by 17% in the diabetic group, but was increased by 13% in the older group, when each was compared with the appropriate control. It was concluded that these changes probably reflect changes in the binding of insulin to receptors, although the magnitude of the changes would be somewhat modified by alterations in the size of the interstitial space in relation to plasma volume.

In addition, the rate of entry of new insulin into plasma was increased by 45% in the diabetics and by 27% in the moderately obese group, but was decreased by 11% in the older group.

These findings led to the following general conclusions. The pattern of changes seen with obesity is similar to that in maturity-onset diabetes. In obesity and maturity-onset diabetes, the decrease in the ratio of insulin in extravascular spaces to insulin in plasma cannot be accounted for solely by changes in fasting plasma-insulin levels. The fact that the pattern of changes seen in the older subjects is the opposite of that in maturity-onset diabetics suggests that diabetes is distinct from the changes in normal aging. Finally, since the changes in the metabolism of insulin are small, it is unlikely that they are the sole cause of the major alterations in glucose tolerance that occur with age, obesity, or diabetes.

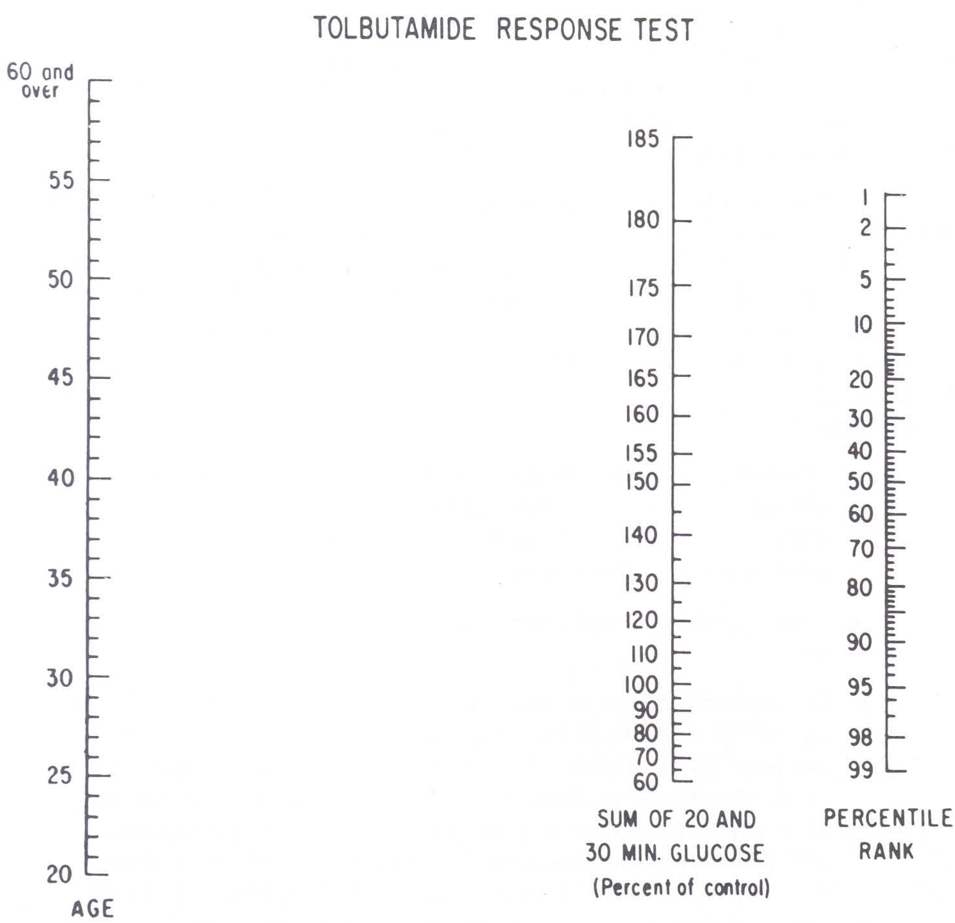

Figure V.25. Nomogram for judging percentile rank on tolbutamide response test using sum of 20- and 30-min values.
From Swerdloff et al. (1967, adapted).

Hypothalamic-pituitary-testicular axis. A number of investigators looking at the effects of age on sex hormones in men have come to the conclusion that the major male hormone, testosterone, decreases with age (Stearns et al., 1974; Vermeulen et al., 1972) and that, because of an increase in the specific sex hormone binding globulin (SHBG), the unbound (bioavailable) hormone decreases even more prominently than the total. Along with these changes, increases in plasma estrogens have also been reported (Rubens et al., 1974; Pirke and Doerr, 1975). Most investigators have found an increase with age in the plasma levels of the pituitary gonadotropins, luteinizing hormone (LH), and follicle-stimulating hormone (FSH); the increase presumably reflects the decline in testicular function with subsequent reduction in inhibition of gonadotropin secretion by negative feedback (Stearns et al., 1974; Vermeulen et al., 1972; Baker et al., 1976).

In a study of 76 BLSA men (Harman and Tsitouras, 1980), we measured basal circulating levels of gonadotropins, four sex steroids (testosterone [T], dihydrotestosterone [DHT], estradiol [E_2], and estrone [E_1]), an index of sex steroid binding to plasma globulin, testicular volumes, and, when possible, sperm production. An index of sexual activity was obtained by Dr. Clyde Martin of the Human Performance Section. In addition, provocative studies of pituitary and gonadal secretory function used luteinizing hormone-releasing hormone (LRH) (Harman et al., 1982) and human chorionic gonadotropin (hCG) to test secretory reserve capacity. Results of these studies can be summarized as follows:

Unlike the subjects in previous investigations, who showed decreased T and free T index and increased E_1 and E_2, our healthy volunteers revealed no significant changes in prevailing blood levels of sex steroids over the age range from 25 to 90 years.

Leydig-cell reserve capacity was somewhat diminished after hCG stimulation, although the differential narrowed with time after hCG stimulation.

Basal levels of both LH and FSH were increased with age despite the absence of a change in sex steroids.

Pituitary response to LRH:

- LH response, after correction for effect of basal LH level, was moderately decreased in the oldest men (age range = 70–89 yrs), but significantly so only in comparison with the middle-aged men (age range = 50–69 yr). LH peak response time was significantly delayed with age.

- FSH response showed a significant decrease with age, but no delay in peak time.

- Glycoprotein hormone sub-unit secretion. Measurements of α and LHβ and FSHβ sub-units in the sera obtained in this study showed increases in the basal levels of each sub-unit with age, but these increases were low in proportion to the increase in intact gonadotropins. Thus, the ratios of α/(LH + FSH) decrease as gonadotropins rise. This phenomenon presumably results from more efficient synthesis and combination of sub-units into the heterodimer form. Responses of α, LHβ, and FSHβ to LRH injection were reduced in aged men (after correction for basal level), but to a lesser extent than the LH and FSH responses. The secretory ratios of sub-unit to intact hormone after LRH stimulation were thus relatively higher in aged men than in their younger counterparts.

In unpublished data sexual-activity levels decreased with age, despite the maintenance of normal sex-steroid levels. Nonetheless, high free T index was weakly but significantly correlated with higher sexual-activity level, and low free T index with reduced activity in the oldest (and only in the oldest) men. No significant differences were found in testicular volumes with age, nor in mean sperm counts per ml or per ejaculate.

From the above data, we conclude that elderly but healthy middle-class men, living at home, may not manifest decreased androgens or increased estrogens. These findings contrast with those in previous study populations, which often included older subjects from clinics, nursing homes, and similar institutions and may thus have reflected the effects of variables other than aging *per se.* The reduced hCG response and elevated gonadotropin levels suggest that although some age-related defect in testicular function may occur in these men it is compensated by increased pituitary activity. The pituitary-response data suggest reduced sensitivity of pituitary gonadotrophs to LRH with age. The decreased sexual activity in men with normal androgens must be produced by something other than hypogonadism, perhaps by alterations in central or peripheral nervous-system function. The better-maintained sexual function in old men with higher free T indices suggests that high levels of androgen activity may partially overcome the age-related deterioration of sexual function.

In order further to investigate the relationships of aging, sexual activity, and sex hormone levels, we used lyophilized sera and other data obtained from 180 BLSA men aged 60 to 80 years (Tsitouras et al., 1982) in a retrospective survey of the relation of sexual activity to serum T, body composition, alcohol and tobacco habits, and cardiac status. The study confirmed the correlation of serum T and sexual-activity level in older men and suggested that the relation is not mediated by obesity, muscle mass, alcohol consumption, smoking, or coronary artery disease. A tendency toward decreased sexual activity, but no decrease in T, was found in men consuming the largest amounts of alcohol, and a tendency toward decreased T, but no decrease in sexual activity, in men having the greatest percentages of body fat.

Arginine vasopression. Secretion of arginine vasopressin (AVP), a natural peptide antidiuretic hormone, by the hypothalamic-neurohypophyseal-renal axis is inhibited by ethanol and stimulated by hypertonic saline. The impact of age on these responses was determined by direct assay of AVP (Helderman et al., 1978). Subjects in two age groups (9 men 21-49 and 13 men 54-92 yr) were administered ethanol intravenously at the rate of 375 mg/m^2 surface area per minute for one hour. Sixteen other subjects in two age groups (age ranges = 22-48 and 52-66 yr) were given an intravenous infusion of 3% NaCl for two hours at the rate of 0.1 ml/kg body weight per minute. Young and old control subjects received normal saline intravenously. Blood and urine samples were collected from all subjects and analyzed. AVP levels fell progressively during ethanol infusion in the younger group, but in the older group they fell for only 30 minutes, then paradoxically rose to nearly basal levels as ethanol levels continued to increase; after infusion ceased, the AVP values continued to rise to nearly twice basal values. In the hypertonic saline group, serum AVP rose to 2.5 times the basal level in young men and 4.5 times the basal level in old men despite identical free-water clearances. The paradoxical AVP response of the older subjects to greater osmolality induced by ethanol administration was partly due to their significantly greater osmoreceptor sensitivity (Fig. 26), which may compensate for the decreased ability of their aging kidneys to conserve salt and water.

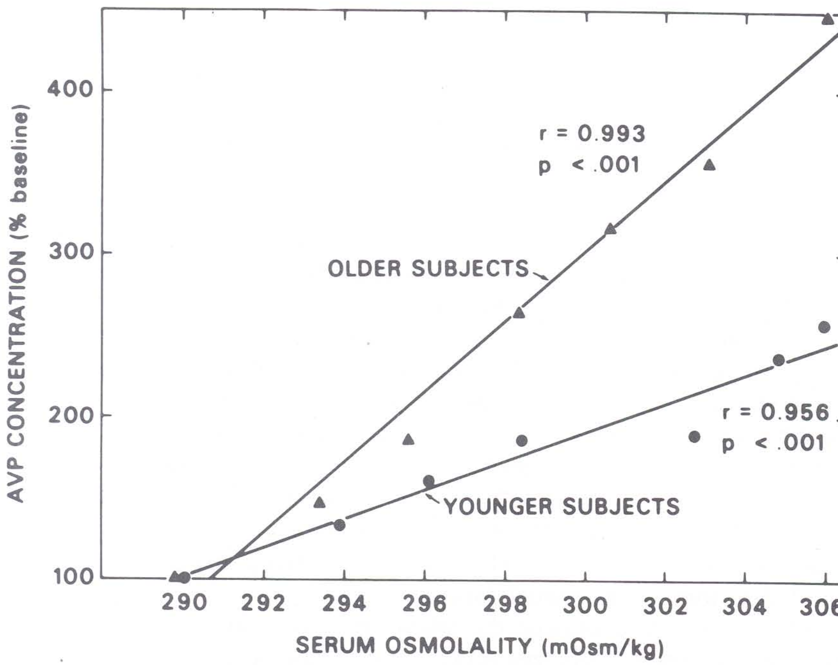

Figure V.26. Correlation between serum osmolality and AVP concentration in young and old subjects during 2-hr intravenous infusion of 3% NaC1 at the rate of 0.1 ml/kg per min. The points represent mean values of osmolality and AVP at successive 20-min intervals in each group. From Helderman et al. (1978).

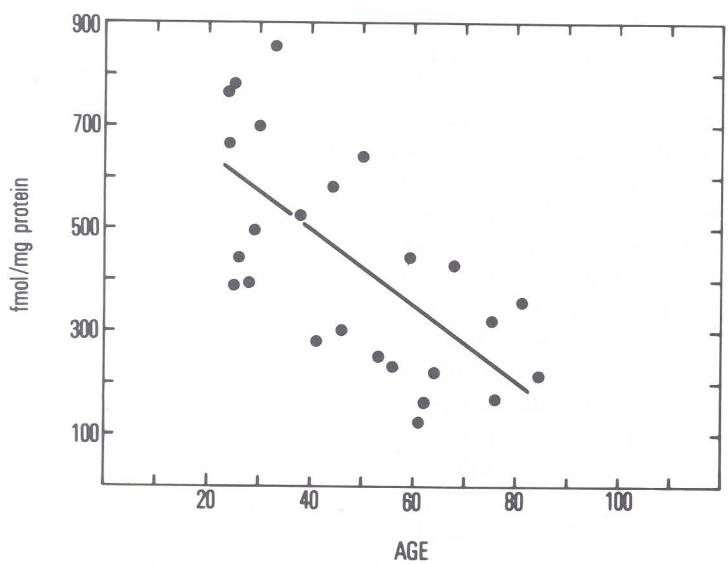

Figure V.27. Maximal specific binding of (——) ^{3}H-dihydroalprenolol to crude mononuclear cell membranes of subjects aged 24–81 yr.
From Schocken and Roth (1977).

Hormone receptors. Although previous studies have shown that the concentrations of hormone receptors are reduced during aging in several animal species, most of the work has been limited to intracellular receptors for steroid hormones. A BLSA study (Schocken and Roth, 1977) found that cell-surface binding sites for β-adrenergic hormones in humans also decrease in number with advancing age. Mononuclear cell fractions obtained from BLSA subjects aged 24 to 81 years were assayed for β-adrenergic receptors using ^{3}H-dihydroalprenolol. Although the binding sites retained a high affinity for dihydroalprenolol irrespective of the age of the donor, the concentration of receptors dropped significantly with age (Fig. 27). The mean saturation level was 572 $\pm$ 58 pmol/mg protein in subjects 24 to 41 years old and 332 $\pm$ 48 pmol/mg protein, or slightly more than half, in subjects over 46 years. Likewise, the number of sites per cell correlated inversely with age (14,000 in the young and 8000 in the old group). While previous hormone-receptor studies in man have dealt with either intracellular receptors or cells in tissue culture, this investigation was the first to demonstrate age-associated alterations of surface hormone binding sites in cells taken directly from humans. The results support the idea that loss of certain hormone receptors is a common manifestation of aging and also offer a possible explanation of age-associated loss of responsiveness to adrenergic hormones.

More recently, a β-adrenergic binding site with an affinity approximately ten times higher has been detected by two other laboratories (Abrass and Scarpace, 1981; Landmann et al., 1981). Its concentration is apparently not affected by aging, although β-adrenergic stimulation of adenylate cyclase is markedly reduced in lymphocytes of aged subjects. Thus β-adrenergic mechanisms in these cells may be altered at the level of adenylate cyclase itself, and the role of age changes in the lower-affinity binding site remains to be elucidated.

It has been suggested that the insulin binding system undergoes a genetically programmed aging. Previously reported differences in insulin binding in fibroblast samples are most striking when data from children are compared with data from adults. Since the differences may be interpreted as representing developmental changes rather than adult aging, a study (Hollenberg and Schneider, 1979) compared ligand binding and biological responsiveness to porcine insulin and murine epidermal growth factor-urogastrone (EGF-URO) in skin fibroblast cultures derived from men 22 to 31 years old with those of cultures from men 65 to 80 years old. The receptor characteristics of the cells from the two age groups did not differ.

9. Immune System

Immune function has so many facets that it requires a variety of assay procedures, including *in-vitro* cell culture and the determination of serum immunoprotein and antibody levels. Although serum samples can be obtained from all BLSA subjects during their visits to the GRC, the culture of the peripheral blood white cells and some of the cell-culture assays are so time-consuming that cells from only one individual can be examined during a day. As a result of the difference in time and effort required by various assays, the number of individuals who constitute the data base varies with the assay, and not every assay has been performed on every BLSA participant. The first set of assay results to be discussed is concerned with cellular function in the host immune response.

Number of white cells in peripheral blood. From longitudinal data collected during five visit cycles, the number of the various types of white cells present in the peripheral

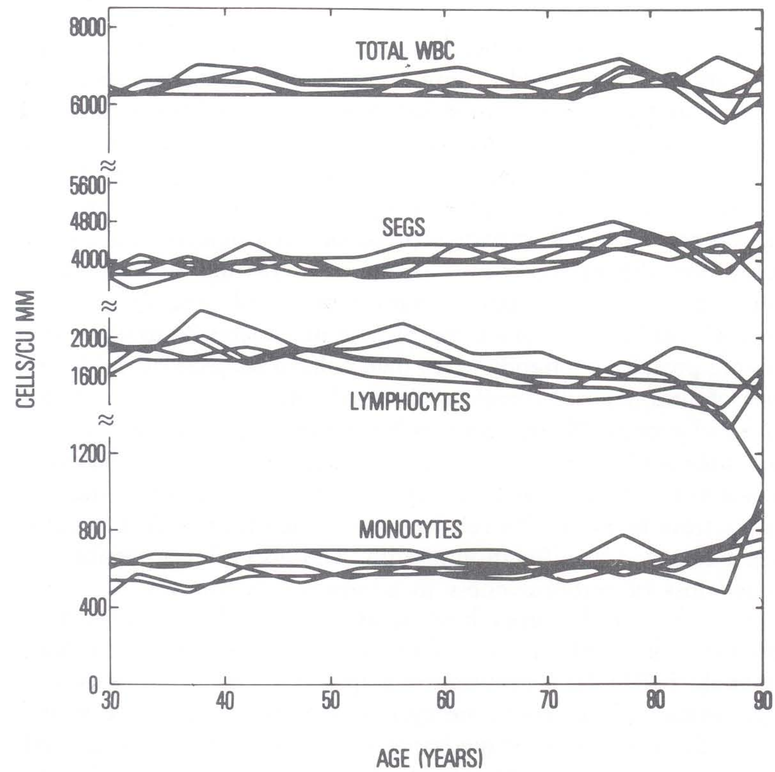

Figure V.28. Counts of total white blood cells (WBC), segmented neutrophiles (SEGS), lymphocytes, and monocytes were determined at each visit of the BLSA participant. Visits occurred at 1- or 2-yr intervals. Each line in each grouping represents one cycle of visits. Five cycles are presented for each white-cell group.
From Adler and Nagel (1981).

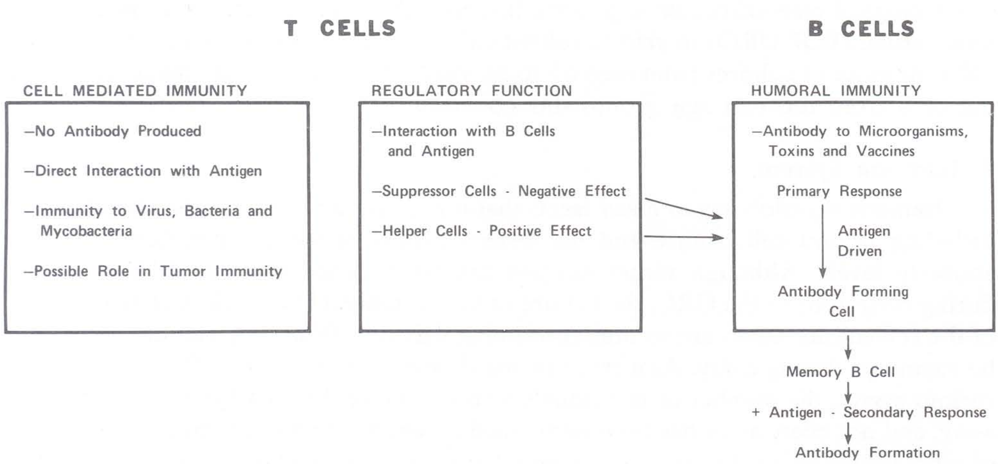

Figure V.29. Functional characteristics of T lymphocytes and B lymphocytes.

blood was determined over the age range from 20 to 90 years (Fig. 28). There were no differences in the total white-cell count or in the number of the various white cells in the peripheral blood (Adler and Nagel, 1981; Nagel et al., 1982b). Granulocytes, lymphocytes, and monocytes maintain the same relative representation and absolute numbers throughout this age range. Use of antisera with specificity against membrane components makes it possible to examine subtypes of lymphocytes such as the B lymphocyte, which has antibody-synthesizing ability, and the T lymphocyte, which is thymic-derived and important in host defense in cell-mediated immune activity and serves in the regulation of B-cell activity (Fig. 29). Antisera with binding specificity against B cells, T cells, and the subsets of T cells are available to quantify these populations (Nagel et al., 1981b; Nagel et al., 1983). Figure 30 shows that the representation of B cells in the peripheral blood of individuals of different ages remains constant. The determination of T cells and T-cell subsets has been studied not across the age span but in young (age range = 20–40 yr) and old (60+ yr) subjects. It was found that the total number of T lymphocytes is lower in the older population because

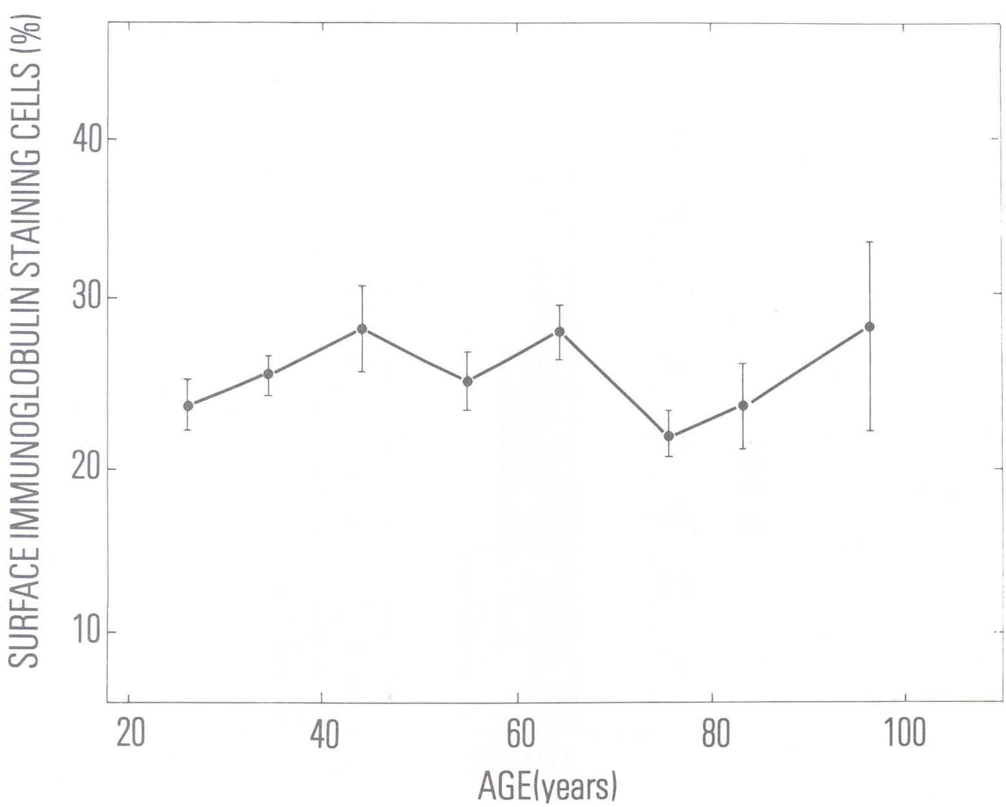

Figure V.30. The percentage of blood lymphocytes with membrane immunoglobulin was determined on 350 individuals of varying age. Each point represents the mean value for a 5-year interval and is plotted in the mean position for that age group. The bar at each point represents plus or minus one SEM.
From Adler and Nagel (1981).

of the decrease in the T-cell subset known as the "cytotoxic-suppressor" population (Fig. 31). These studies led to the *in-vitro* cell-culture experiments detailed below.

Granulocyte function tests. One arm of the host defense against infectious disease is the function of the polymorphoneutrophile (PMN). Since previous quantitative morphologic work had shown no change with age in PMN numbers in peripheral blood, it was important to determine PMN function. A variety of assays were used. Metabolic activity was measured by Nitro-Blue-Tetrazolium (NBT) dye reduction. The reduction of NBT to formazan requires the generation of H^+ through the metabolism of glucose. Another system measured the generation by the PMN, in response to a

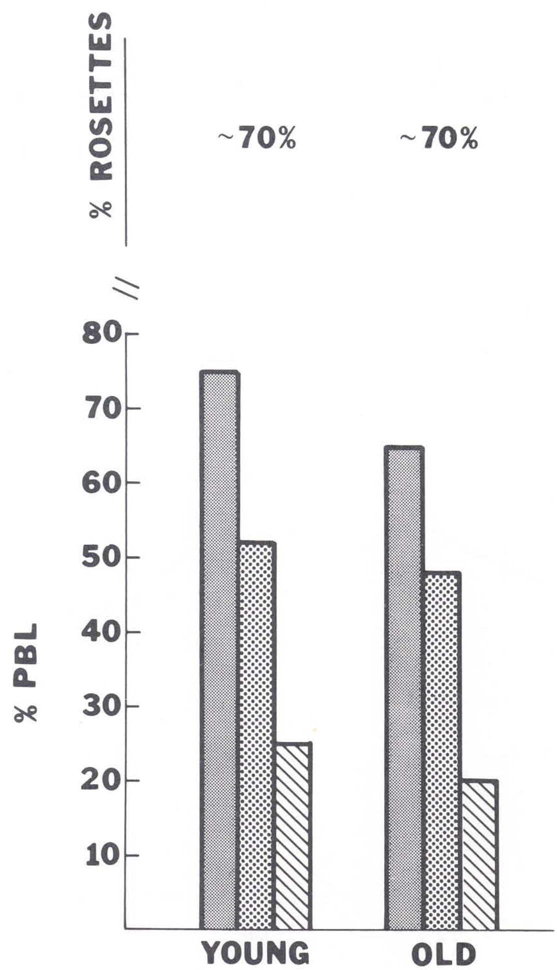

Figure V.31. The percentage of blood lymphocytes that react with the monoclonal antibodies OKT3 (an anti pan T cell antibody), OKT4 (an anti T helper cell), or OKT8 (an anti T suppressor, cytotoxic cell) was determined on samples from young (<age 40) and old (>age 60) BLSA participants. Rosette determination for T-cell identification showed no age-related changes. The monoclonal antibodies showed a drop in the number of T cells in the old group that was due mostly to a decrease in the suppressor population.

stimulus, of lysosomal enzyme, which is necessary for the PMN to kill ingested bacteria. The last assay measured phagocytic and bacteria-killing ability of the PMN challenged *in vitro* by staphylococci. None of the assays demonstrated age-related change in granulocyte PMN function *in vitro* (Nagel et al., 1982b) (Figs. 32, 33). The study has not, however, addressed the question of PMN function and reserves in the whole person, especially during a period of physiologic stress.

Antibody-forming ability of peripheral blood lymphocytes (PBL). Since morphologic studies of the PBL subpopulation had shown relatively minor age-related changes, a study was undertaken to measure the functional ability of these cells *in vitro*. PBL from

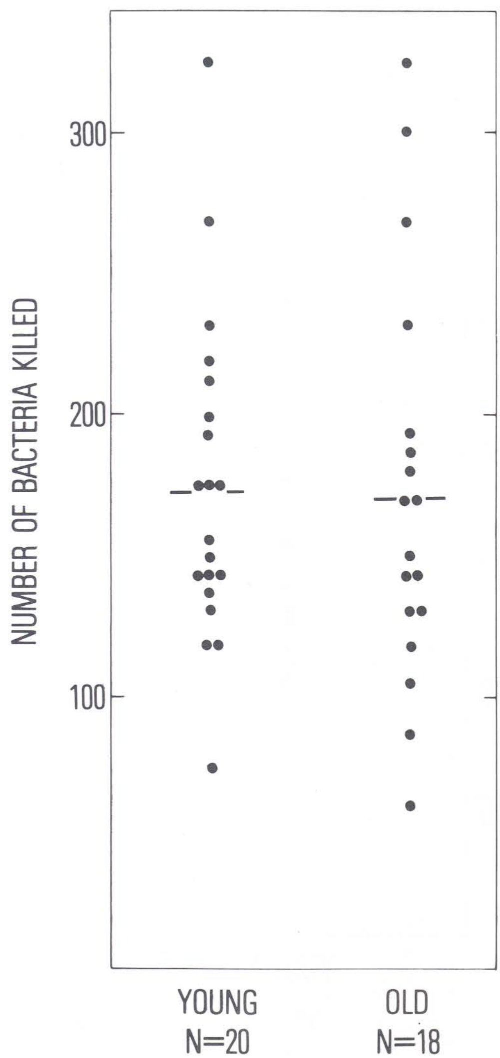

Figure V.32. The bactericidal capacity of granulocytes was determined *in vitro* using the *Staphylococcus aureus* organism. Young participants were less than than 40 years of age, old over 60. The mean number of bacteria killed by PMNs in 60 min was the same in both groups. From Nagel et al. (1982b).

individuals were placed in culture with a polyclonal B-cell activator, Pokeweed Mitogen (PWM). PWM will induce antibody synthesis in B cells if the appropriate functionally active helper T-cell population is present. In a large series of determinations of antibody synthesis *in vitro*, it was found that PBL in about 13% of the BLSA individuals, most of whom were over age 50 (Fig. 34), could not be induced to synthesize immunoprotein (Nagel et al., 1981a). More detailed analysis of cells from the nonresponder group demonstrated that B-cell function was normal and that the lack of response resulted from a decreased ability of the helper T-cell population to interact with the B cell (Chrest et al., 1983) (Fig. 35). Without a functional helper T cell, the B cell cannot be induced to synthesize antibody protein.

Natural killer (NK) cell activity. A population of lymphoid cells found in human peripheral blood lacks the membrane markers associated with T or B cells. These, designated "null" cells, have an interesting *in-vitro* function that is indicated by their

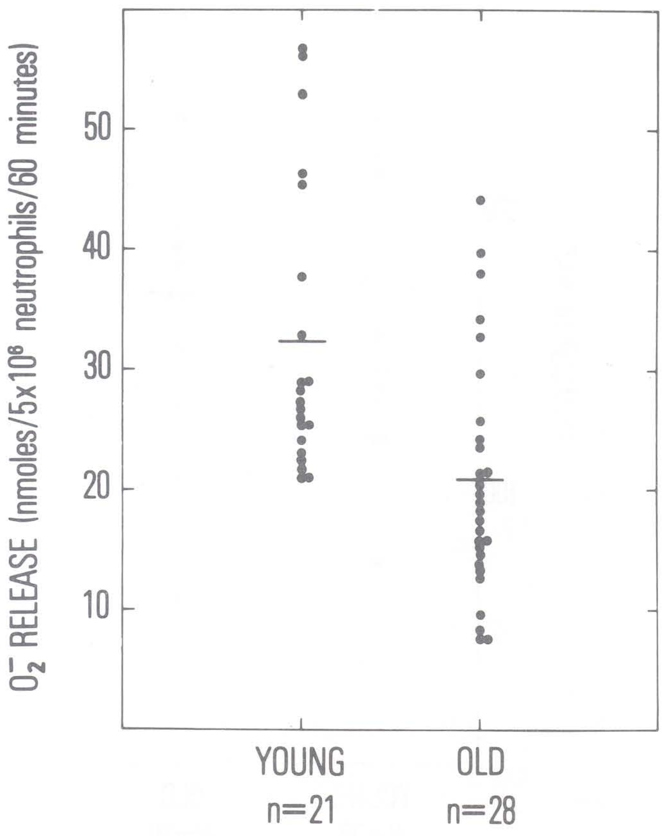

Figure V.33. Superoxide generation by granulocytes from young (<age 40) and old (>age 60) was determined in stimulated PMN cultures. Although the mean superoxide level generated by PMNs from elderly participants was lower, there was no significant difference between the groups.
From Nagel et al. (1982b).

further designation as "natural killer" cells: They can kill a variety of tumor cells *in vitro* without previous sensitization with the tumor-cell antigen either *in vivo* or *in vitro*. A survey of the BLSA volunteers for levels of NK activity in their PBL populations revealed no age-related change (Nagel et al., 1981c). Nor was there any difference between the male and female groups (Fig. 36). Another finding was that NK-activity levels of PBL from the same individual remained relatively the same over a three-year period. A dietary factor, the ingestion of ethanol (Saxena et al., 1980), was nevertheless found to elevate NK activity. The NK activity of PBL in individuals who regularly consumed ethanol was consistently higher than that in age-sex-matched controls. A dietary factor can thus change a result in an assay system. But since the significance of NK-cell activity *in vivo* is not now known, it is difficult to determine whether a dietary item can affect a clinical problem such as the development of cancer.

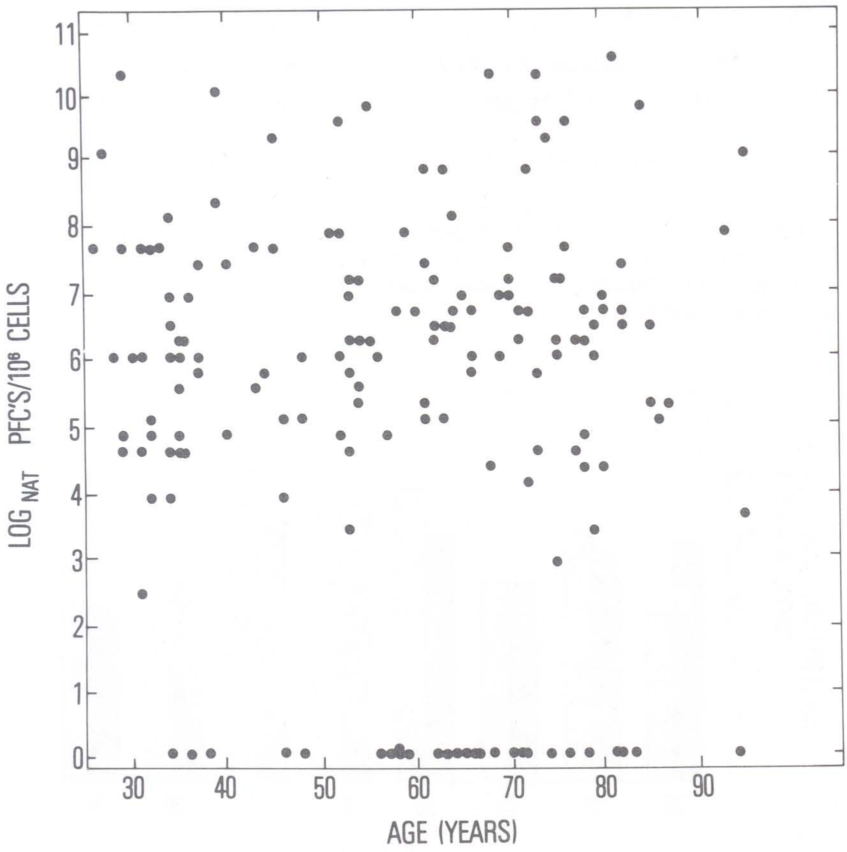

Figure V.34. In these experiments the number of immunoglobulin-producing cells (PFCs) induced by Pokeweed Mitogen stimulation of lymphocytes from BLSA participants of varying age was determined. Each point represents the mean PFC number for replicate PWM-stimulated cultures from each individual.
From Adler and Nagel (1981).

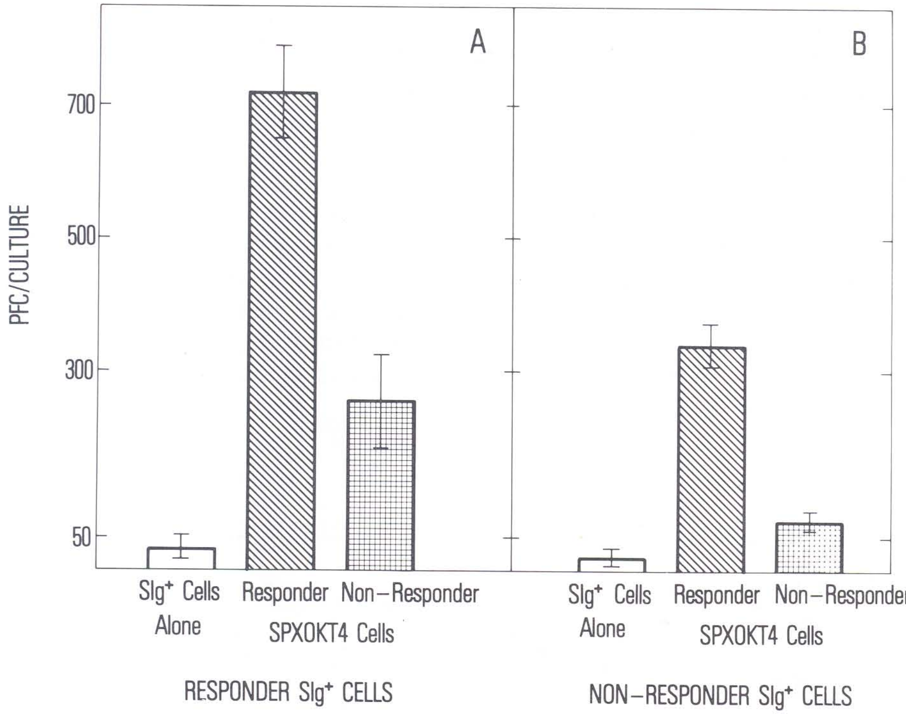

Figure V.35. B cells from a responder (panel A) or a nonresponder (panel B) were cultured alone, or with active helper T cells from a responder or a nonresponder individual. The bars represent the mean PFC number in replicate cultures ± 1 S.D.
From Chrest et al. (1983).

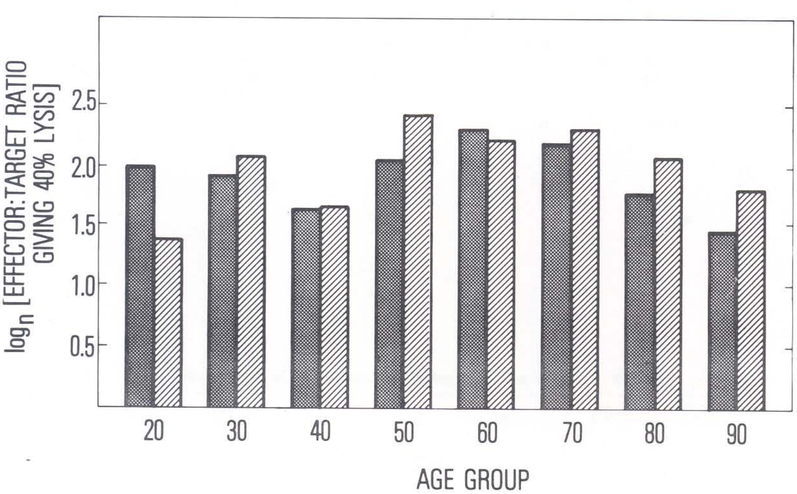

Figure V.36. The geometric mean percentage of the ^{51}Cr release at a 5:1 effector:target ratio was determined as a function of age and sex. There were no statistical differences between sexes or among ages.
From Nagel et al. (1981c).

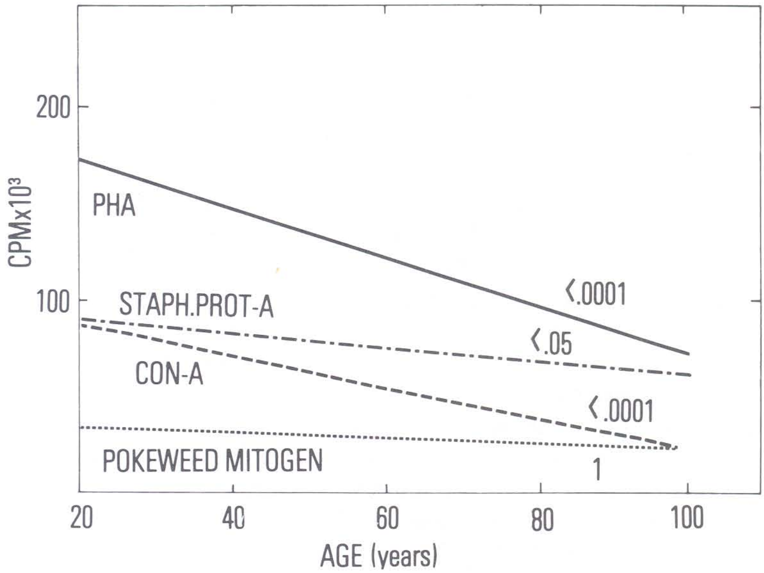

Figure V.37. PBL were stimulated *in vitro* with phytohemagglutinin (PHA), Concanavalin A (Con A), Pokeweed Mitogen (PWM), or Staphylococcal Protein A (SPA). After 5 days of culture the cells were pulsed with tritiated thymidine and one day later the level of radioactivity in the cellular DNA was determined. The P values for each regression line were: PHA = $< .001$, Con A = $< .001$, SPA = $< .05$, and PWM = 1. The regression lines were drawn using the mean values of replicate cell cultures obtained from blood samples from 230 individuals.
From Adler and Nagel (1981).

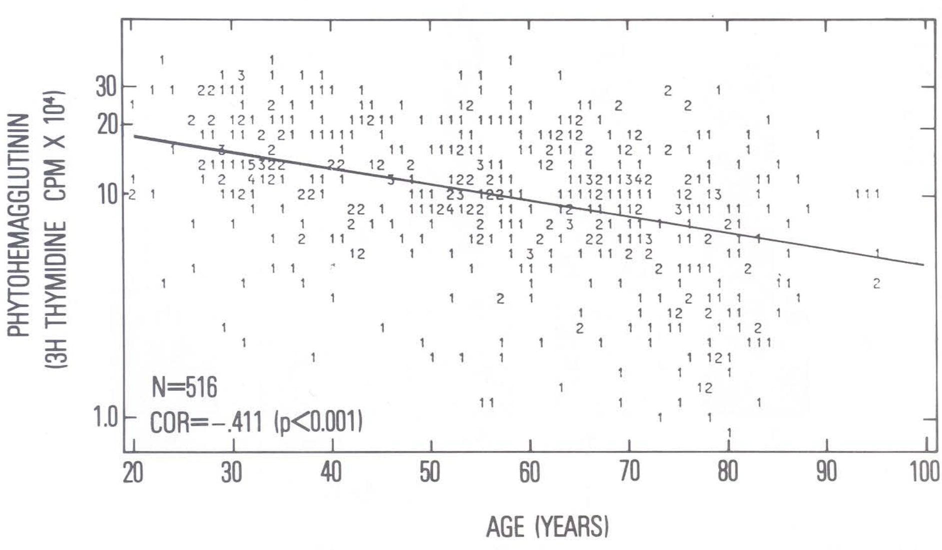

Figure V.38. These experiments are exactly as described in Fig. 37, with PHA used as the mitogen. The data are presented as the mean cpm for the peak response of cell cultures from individuals of varying age. The numbers at each data point show how many individuals of that age had the same amount of thymidine incorporation in their cell cultures.

Mitogen responses of peripheral blood cells. The ability of some PBL to divide *in vitro* in reponse to a mitogenic stimulus makes it possible to determine the presence and functional activity of these cells. Different types of PBL respond in varying degrees to different mitogens. In general, the mitogens phytohemagglutinin (PHA) and concanavalin A (Con A) stimulate T lymphocytes, while Staphylococcal Protein A and PWM stimulate both T and some B lymphocytes. A study of the age of the cell donor and the responsiveness of their cells *in vitro* to a mitogenic stimulus showed that the ability of the T lymphocyte to divide was significantly reduced as the age of the cell donor increased (Adler and Nagel, 1981; Nagel et al., 1982a) (Fig. 37). Some cell cultures from the youngest BLSA age group respond poorly to a PHA stimulus, while some from the oldest age group respond well (Fig. 38). A difference has, however, been found among age groups. The number of poorly responding cultures increases and the number of good reponses decreases with age. The age at which the number of high- and low-responder cultures seems to change markedly is the seventh decade. The populations below age 60 are similar to one another, as are those over age 70 (Fig. 39). Although the reason why the T cells appear to lose the ability to divide *in vitro* is still obscure, it is not a decline in the numbers of T cells. An inherent defect in the T cell must limit its proliferative ability.

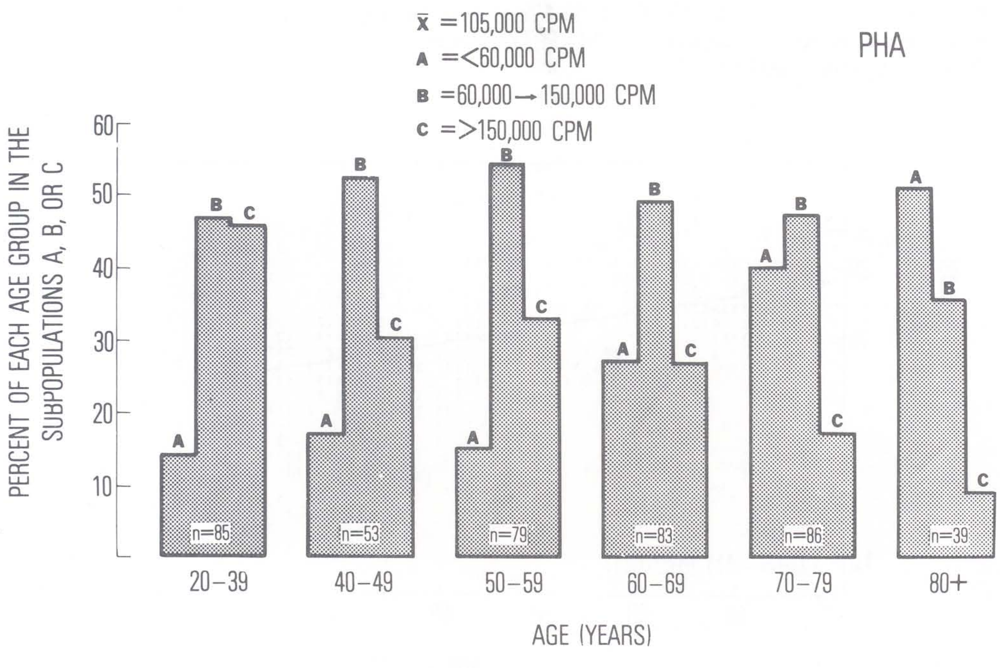

Figure V.39. The experiments are as described in Fig. 37 and in the separation of the data presented in Fig. 38. For each decade of age the individual culture results were divided into 3 groups. One group was composed of results with less than 60,000 cpms (Group A); Group B had results from 60,000 to 150,000 cpms; and Group C had results over 150,000 cpms. The mean cpm for all the data was 105,000.

Serum immunoprotein levels. Immunoglobulins comprise several subclasses: IgG, which constitutes most of the serum immunoprotein; IgM, a macroglobulin immunoprotein; and IgA, a serum immunoprotein that can also be found in secretions. When these were quantified across the age range, no significant differences with age were seen in their representation in serum, except possibly in the group 90+ years old (Adler and Nagel, 1981). The group has so few members, however, that the findings are heavily influenced by a few individuals with serum immunoprotein levels much different from the "normal" levels (Fig. 40).

Summary. The most consistent age-related immunologic findings are the defects seen in the T lymphocyte. The representation of T cells in peripheral blood decreases with age. Both the functional ability of T helper cells and the proliferative ability of T cells in response to a mitogenic stimulus decline with age. It is interesting to speculate that these changes are related to the age-associated involution of the thymus seen in humans and animals.

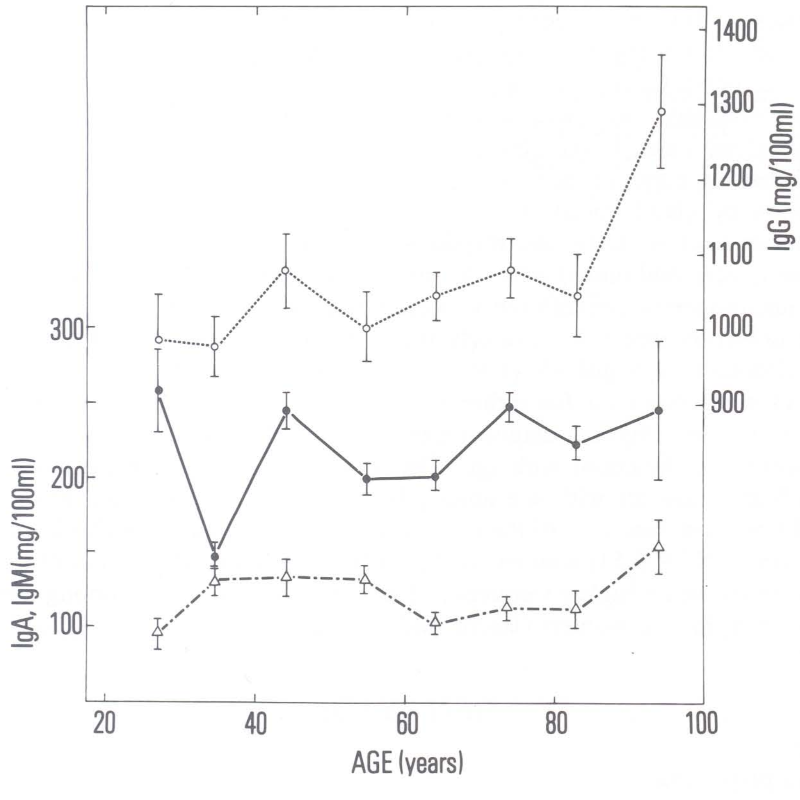

Figure V.40. Serum immunoglobulins G, A, and M were determined on samples from 250 individuals of varying age. The left ordinate refers to the IgA and IgM values, the right ordinate to the IgG values. The data points and standard error bars represent the mean value for a 5-yr interval and are plotted in the mean position for that age group. ○···○ = IgG; ○---○ = IgA; △-·-·-△ = IgM. From Adler and Nagel (1981).

10. Oral/Dental

General dental characteristics. The participants in the oral physiology component are a substantially dentate group, even in the upper age category. The total number of natural teeth in persons aged 60+ is about 23 of 28 maximum (Baum, 1981a). These persons have regular dental care; about 80% visit a dentist at least once a year for preventive as well as problem-oriented care. The prevalence of cervical caries is markedly elevated in older persons; those 40 and younger average one affected tooth in 28, those 60+ four in 28. The average gingival-disease index was quite similar over age groups, while indices of periodontal disease showed a significant increase with age.

Salivary-gland function. Detailed evaluation of stimulated parotid-gland secretion found no difference in the ability of non-medicated men and women of various ages to secrete parotid fluid after stimulation by 2% citric acid (Baum, 1981b). Among subjects taking prescription medication, post-menopausal women showed significantly lower stimulated parotid flow than their non-medicated counterparts.

The secretion of acinar-cell exocrine proteins was studied by following the concentration, output, and percentage in saliva of the anionic-proline-rich proteins. These molecules have been localized to human parotid acinar cell secretory granules. No differences in any of these parameters were observed among non-medicated males and females of any age category (Baum et al., 1982).

The secretion of several inorganic ions (Na^+, Ca^{++}, K^+, and inorganic phosphate) was also examined. Of these electrolytes, only Na^+ showed a consistent alteration with age. Non-medicated men and women both showed significantly lower levels of secreted Na^+ with age. In men 60 and older, the average secretion of Na^+ was about 50% of that of men 40 and younger. These differences suggest increased Na^+ reabsorption by gland ductal cells in older persons.

Gustatory function. Detection thresholds for each of the four basic taste qualities (sweet, sour, salty, and bitter) were obtained from 81 men and women of varying ages. Modest quality-specific age differences were observed. Sodium chloride (salty) showed a higher detection threshold with advancing age ($r = 0.38$), as did quinine sulfate (bitter), although its magnitude ($r = 0.25$) remained lower than that of salt. No age differences were observed for either citric acid (sour) or sucrose (sweet).

Motor function. Physical diagnostic evaluations observed specific decrements in certain oral motor functions with age. The frequency of altered masticatory function was significantly greater with age among both men ($X^2 = 16.3$) and women ($X^2 = 23.2$). The postural functions of the circumoral muscles appeared similarily diminished with age (men, $X^2 = 9.51$; women, $X^2 = 4.52$), while postural function of the tongue musculature showed a higher frequency of age-related dysfunction among men ($X^2 = 12.4$) but not among women (Baum and Bodner, 1983).

BEHAVIOR

1. Psychophysiology

Effect of Age on Reaction Time and Vigilance

Cross-sectional studies have shown that aging is associated with a reduction in the speed of responses and an increase in the probability that the response will be inaccurate. In short, with aging speed diminishes and errors increase.

A number of studies also showed that the effects of age became greater as the complexity of the responses increased. Tasks that required the subject to choose among a number of responses showed greater impairment (more time required with more errors) than tasks eliciting a single response.

In some instances physiological indices could be included as a measure of the response. Thus reaction time, latency of response, vigilance, EEG response, heart rate, blood pressure, galvanic skin response (GSR), and skin potential were examined in subjects of different ages in a search for relations between behavioral and physiological events.

A study was undertaken to test the effect of age on reaction time (Suci et al., 1960). Old (age range = 60–70 yr, median = 63) and young (age range = 17–38 yr, median = 18.5) subjects were individually tested for choice reaction time by an apparatus consisting of four small electric lights mounted on a panel. A varying number of lights was illuminated; when one was turned off, the subject was asked to name it, using a previously assigned code name, as quickly as he could. A plot of reaction time against bits per stimulus in the two age groups showed that reaction time in both old and young subjects increases linearly with the number of stimuli from which the subject must choose, and that age differences in reaction time increase as a function of increasing stimulus information; older subjects show longer reaction times at all levels of stimulus information (Fig. 41).

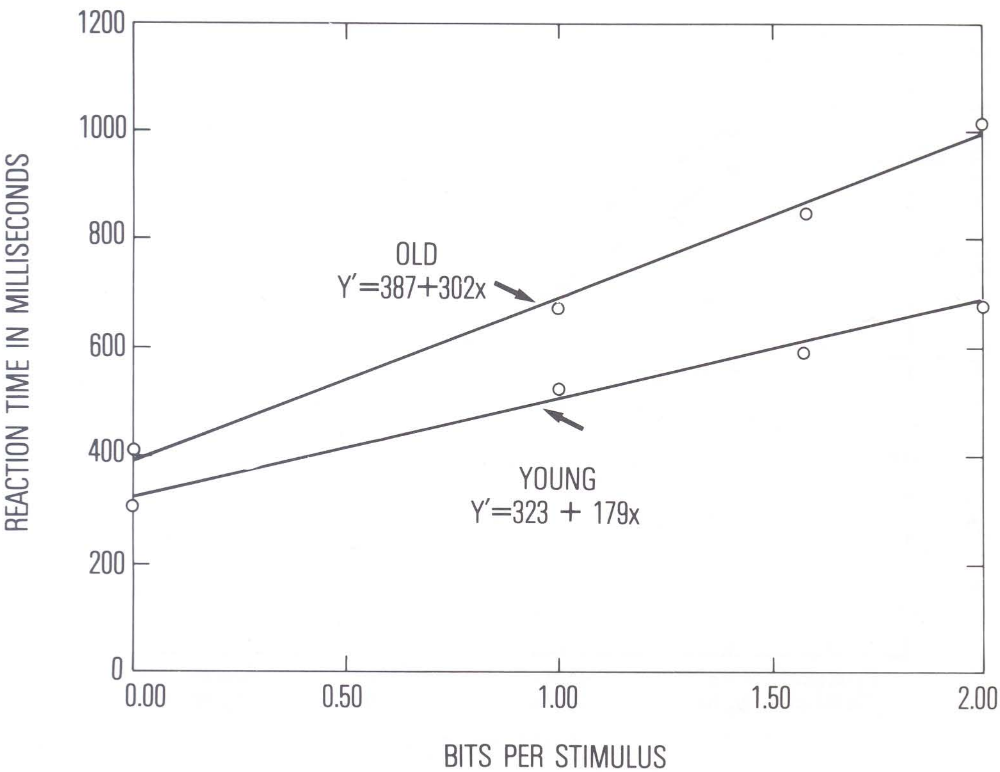

Figure V.41. Reaction time as a function of stimulus information and age. From Suci (1960).

A study was undertaken to determine the relation of vigilance to age and whether lowered vigilance is associated with age-related slowing in reaction time (Surwillo and Quilter, 1964). The subjects, 106 men aged 22 to 82 years, were given Mackworth's Clock-Test. The "clock" is a metal box with a plain circular white face 12 inches in diameter, and a single black pointer six inches long, mounted from the center of the clock. The pointer moves in discrete steps like the second hand of an escapement clock. The full circle is completed in 100 steps, one per second. At long and irregular intervals, the pointer jumps through twice the usual distance in one step. Twenty-three "double jumps" (0.64% of all pointer movements) occur per hour.

After instruction, demonstration, and practice sessions, the subjects were asked to watch the clock-pointer for one hour and to press the response key as fast as possible whenever a double jump occurred. The mean percentage of double jumps detected by the younger group (< 60 yr) was 72.9%, by the older group (> 60 yr) 64.4%. It was concluded that, under the conditions of the experiment, old people were less vigilant than young people. Fractionation of the data into quarter-hour periods showed that the old subjects were not significantly less vigilant than the young subjects during the first 15 minutes of the test, but the mean difference between the first and fourth quarter-

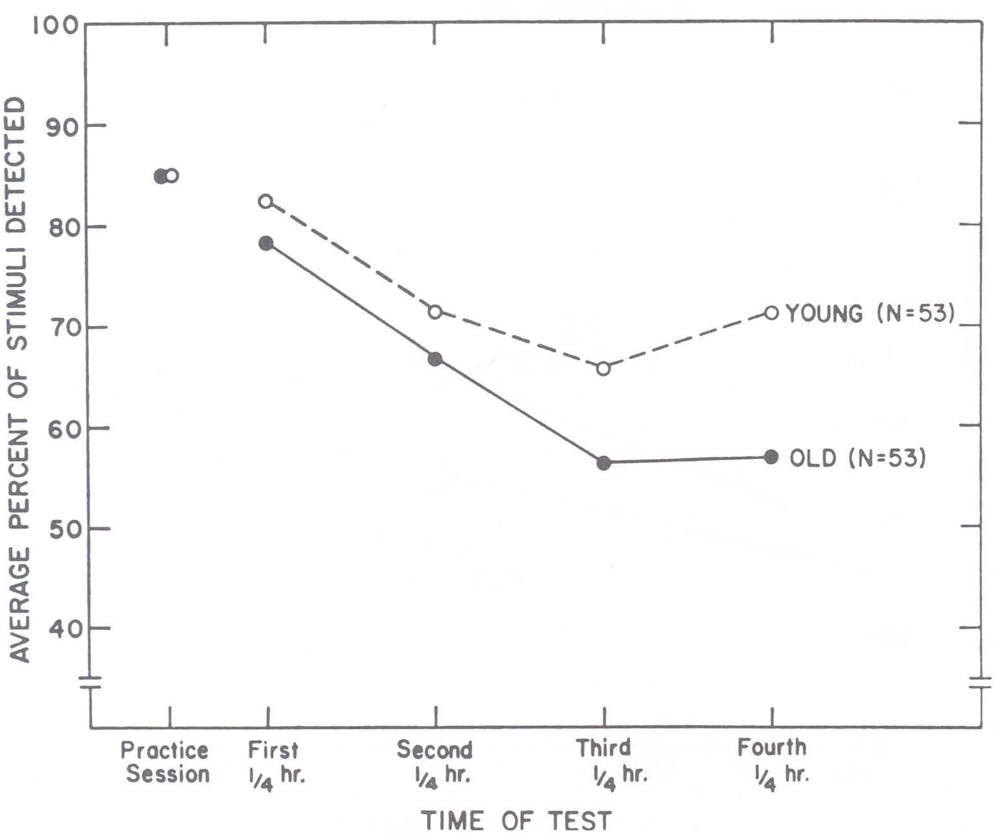

Figure V.42. Decline of vigilance during prolonged visual search. From Surwillo and Quilter (1964).

hour periods was significantly greater in the old group (21.3%) than in the young group (11.2%) (Fig. 42). The conclusion was drawn that vigilance declines more in old than in young persons. At the same time, the lack of an age difference in vigilance during the early periods of the task has important implications for the employment of older men. The effect of short rest periods on vigilance in older subjects deserves further investigation.

Electroencephalographic (EEG) Studies

Several studies have been made of the relation between reaction time and brain waves recorded by electroencephalography.

Since the early 1930s several investigators have advanced the hypothesis that the EEG frequency, which is not constant in an individual but varies from one instant to the next, represents the basic unit of time in the central nervous system. Further testing of the hypothesis was undertaken by Surwillo (1961, 1963a). In a sample of 100 males aged 28 to 99 years ($\bar{x}$ age = 55.3 yr), reaction time to a sound stimulus was related to the alpha frequency at the time the stimulus was given. Stimuli, responses, and EEG were recorded simultaneously. A correlation of 0.72 was obtained between average reaction time and the average period of the EEG (Fig. 43). This coefficient was scarcely altered by exclusion of age from the relation by means of partial correlation. Age was

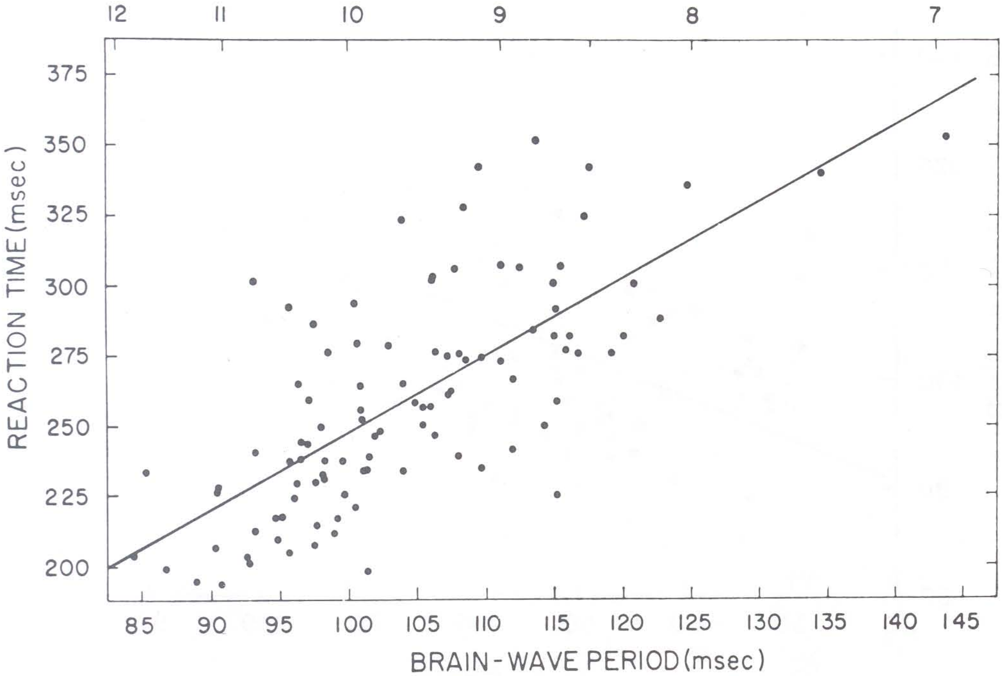

Figure V.43. Reaction time plotted against brain-wave period for data from the high-vigilance, high-motivation condition. Each point represents the average reaction time and average brain-wave period of a single subject, and is derived from a mean number of 14 observations. Numbers at the top of the graph refer to the corresponding frequencies in c/sec. The coefficient of correlation, r, = 0.72; N = 100.
From Surwillo (1963a).

thus not a factor in the observed correlation. A significant positive correlation (r = 0.57) was found between age and the average period of brain waves (Fig. 44). A low but statistically significant positive correlation between average reaction time and age vanished and became negative when brain-wave period was partialled out; the implication is that EEG frequency and not age is the central-nervous-system factor that determines the age-associated slowing in response time. A positive correlation was found in individual subjects between brain-wave period and reaction time. These data are consistent with the hypothesis that the brain-wave cycle is the basic unit of time by which a response is programmed by the central nervous system.

The evidence that variability in response time within subjects increases with age led to a study to determine whether this could be accounted for by differences in variability of brain-wave period (Surwillo, 1963b). A sample of 100 male subjects aged 28 to 99 years ($\bar{x}$ age = 55.3 yr) was tested essentially as in the preceding study. The

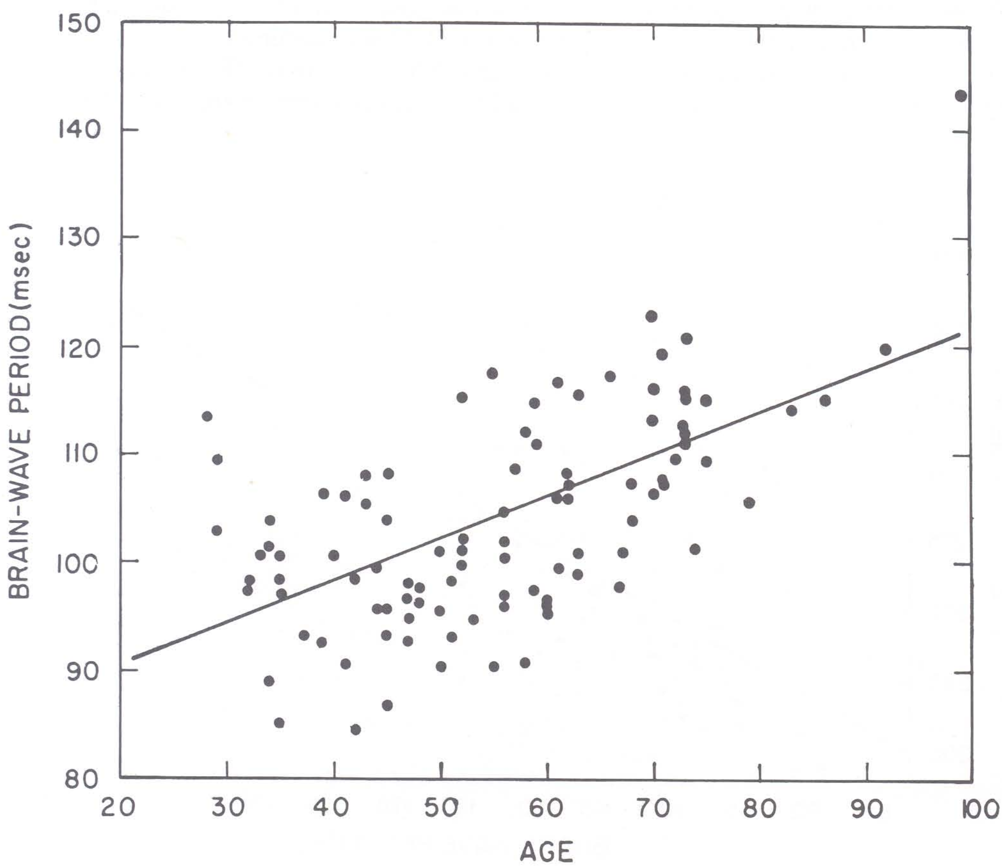

Figure V.44. Period of the electroencephalogram plotted against age. Each point represents the age and average brain-wave period, recorded in the interval between stimulus and response, of a single subject. The correlation coefficient, r, = 0.57; N = 100. Regression line is defined by the expression: P = 0.388 AGE + 82.79, where P = brain-wave period. Standard error of estimate, δ (est. P) = 8.37.
From Surwillo (1963a, adapted).

previous results were confirmed by the finding of a statistically significant positive correlation between age and individual variability in reaction time. Although the relation could not be accounted for by differences in variability of brain-wave period within individual subjects, when average brain-wave period was held constant through partial correlation the positive coefficient relating reaction-time variability and age vanished. The inference was thus drawn that differences in variability of response time are a consequence of differences in average brain-wave period.

The finding that EEG frequency and reaction time are correlated permits no conclusions as to cause and effect. An attempt was therefore made to determine causality by altering the EEG frequency experimentally and measuring the effect on response time (Surwillo, 1964a). It has been observed that repetitive flashing of a light (photic "driving") can produce frequency changes in the EEG; it was assumed for this study that the photic response and the normal brain rhythm are produced by similar mechanisms.

A sample of 48 healthy males aged 34 to 101 years was photically stimulated, and EEGs were recorded as has been described. Subjects whose tracing showed clear evidence of synchronization were given a reaction task to perform while the light was flashing: They were instructed that whenever an auditory signal, which occurred without warning, was presented, they were to press a response key as quickly as possible. Approximately 30 signals were given at random in about ten minutes, while flash frequency was varied. Synchronization of the EEG and the flashing light occurred in 18 subjects, but of these six failed to maintain synchronization while performing the reaction task, six others showed it only over a very narrow frequency range, and one revealed it in only one brain hemisphere; only five of the 18 subjects could synchronize their EEGs with a flashing light over a wide frequency range while performing the reaction task. The findings indicate that at least in some subjects reaction time can be influenced by EEG frequency.

All the EEG studies described above concerned voluntary responses. The generalization that the period of the alpha rhythm is an important factor in the temporal organization of behavior requires that the relation hold for involuntary responses as well. Since studies by earlier investigators had demonstrated latency of attenuation (delay in "blocking") of the alpha rhythm in children and had found a relation between response speed and latency of alpha attenuation, a study (Surwillo, 1966a) was undertaken to determine whether the latency of alpha attenuation increases with increase in alpha-rhythm period independently of differences associated with age. A second purpose of the study was to test the hypothesis that latency of alpha attenuation increases in old age. A final purpose was to test the hypothesis that EEG reactivity, or the incidence of alpha attenuation, declines in old age. Ninety healthy males aged 17 to 91 years ($\bar{x}$ age = 49.7 yr) were tested. The EEG was attenuated by high-intensity flashes of white light lasting approximately one second; 25 flashes in about eight minutes were distributed more or less randomly but occurred mainly during periods when well-defined EEGs were being recorded. Average latency of alpha attenuation and average period of the EEG, in the interval between flash and initiation of the involuntary response, were determined along with the number of times the stimulus failed to attenuate the EEG. A significant positive relation, independent of age, was found between attenuation latency and EEG period. A low but statistically significant positive correlation was found between age and latent time of alpha attenuation. A low correlation was also found between EEG reactivity and age.

Although it was concluded that age cannot account for the relation between attenuation latency and EEG period, the finding confirms earlier work suggesting that old persons are as a group less activated or aroused than young persons by sensory stimulation. It remains to be determined whether this represents an age difference at the level of the cerebral cortex.

Electrodermal Activity

Electrodermal activity (EDA) includes both skin conductance and skin-potential phenomena. BLSA studies have focused an age differences in skin-potential response (SPR) and level (SPL), and skin-conductance response (SCR) and level (SCL). Although age differences in EDA may reflect age differences in responsiveness of the autonomic nervous system, they also may reflect age differences in the peripheral sudomotor system.

Skin-potential response and vigilance. The frequency of spontaneous SPRs in relation to vigilance and age was examined in a BLSA study (Surwillo and Quilter, 1965b) of 132 healthy males, aged 22 to 85 years. The subjects were given Mackworth's Clock-Test described above ("Effect of Age on Reaction Time and Vigilance"). Their task was to press a response key as quickly as possible whenever a double jump occurred. If the subject did not press the response key within six seconds of the appearance of a double jump, it was assumed that he had not perceived the signal. Skin potential between the palm and the ventral surface of the left forearm was recorded from Ag-AgCl electrodes. The primary datum in the investigation was the number of SPRs (negative deflections only) that occurred within the 18 seconds immediately preceding the double jump. This frequency was considered a measure of vigilance, since detected double jumps were preceded by significantly more SPRs ($\bar{x} = 1.62$) in this period than were undetected double jumps ($\bar{x} = 1.22$).

The frequency of spontaneous SPRs was lower with age. Mean values for 42 subjects aged 22–47, 47 subjects aged 48–67, and 43 subjects aged 68–85 years were respectively 1.70, 1.52, and 1.30 SPRs.

Effect of age on the latency of involuntary and voluntary responses. Before 1965, numerous investigations of voluntary reaction time showed a general increase in response latency with increasing age. The latency of involuntary responses, on the other hand, had not received much attention, nor were the findings clearcut or consistent. A BLSA study was therefore undertaken to measure simultaneously the latency of voluntary and involuntary responses to the same stimulus (Surwillo and Quilter, 1965a). Involuntary response latency was measured by the latency of the galvanic skin response (GSR), while voluntary response latency was the reaction time. The aim was to see whether old persons show greater latencies than young persons on both measures.

One hundred thirty-two healthy males, aged 22 to 85 years, were classified in three age groups: Group I (42 men aged 22–47 yr); Group II (47 men aged 48–67 yr); and Group III (43 men aged 68–85 yr). As in the research described in the preceding section, the subjects performed an hour-long watchkeeping task in which they monitored the movements of a clock pointer and responded to double jumps by pressing a key. GSRs (negative deflections only) and the instant of a subject's voluntary response were recorded on the same chart. Lack of an involuntary or voluntary response within six seconds of a double jump was considered an indication of failure to perceive the stimulus.

The mean GSR latency for Group I was 1.81 seconds, that for Group II, 1.82 seconds; the latency for Group III, 1.95 seconds, was significantly higher. The latency of voluntary responses to the same stimuli, however, showed no increase with advancing age.

Effect of age on skin-potential level (SPL). A BLSA investigation was made to determine whether age differences also occurred in SPLs (Surwillo, 1965). One hundred twenty-two healthy males, aged 22 to 85 years, were selected for SPL measurements. SPLs between the palm and ventral surface of the forearm were recorded from Ag-AgCl electrodes during the first 15 minutes of the previously described hour-long vigilance task. (Although previous studies had found old persons less vigilant in performance of the entire task, age differences were not apparent during the first 15 minutes.) SPL was measured at 42 different points in the 15-minute recording, and the mean of these measures was calculated.

In all subjects, the palm was always electrically negative with respect to the forearm. Individual values of skin potential ranged from –12.3 to –56.8 mV (average for the group was –31.5 mV). A low but statistically significant negative correlation was found between age and SPL.

Relation of autonomic activity to age differences in vigilance. Because autonomic activity is related to the level of activation, a BLSA study was performed to determine whether differences in autonomic activity are associated with the age differences in vigilance (Surwillo, 1966b). The hypothesis tested was that, during the vigil (the Mackworth's Clock-Test), measures of autonomic activity (heart rate, palmar skin temperature, and palmar skin potential) change at different rates in old and in young persons.

Sixty-six healthy males were divided into two age groups of equal size, 22 to 45 years ($\bar{x}$ age = 36.4 yr) and 69 to 85 years ($\bar{x}$ age = 74.3 yr). The subjects' heart rates, palmar skin temperatures, and SPLs were recorded during the 18 seconds preceding each double jump. In the final 45 minutes of the task, heart rate declined and SPL became more negative. Skin temperature, however, declined progressively in the young but not in the old group, a finding that is consistent with the hypothesis that differences in autonomic activity are associated with the more rapid decline of vigilance in old subjects.

Effect of epidermal hydration on skin potential and conductance. Although age differences in EDA may reflect age differences in activation of the sympathetic nervous system, age differences in the peripheral sudomotor system also influence the results. Edelberg's (1968) model illustrates how peripheral characteristics can influence the expression of nervous activity. Of critical importance is the ratio of epidermal resistance to sweat-gland resistance. The larger the ratio the greater the sweat-gland contribution to the electrodermal recording. Hydrating the epidermis lowers the epidermal/sweat-gland resistance ratio and thus reduces the sweat-gland contribution to EDA (Edelberg, 1968).

The following studies demonstrate that age differences in SPL occur only when a nonhydrated recording site is used (i.e., when conditions maximize the sweat-gland component). The finding may reflect a less negative sweat-gland potential in old age and/or age differences in epidermal/sweat-gland resistance ratio.

Garwood et al. (1979) studied 12 young men (age range = 23–36 yr, $\bar{x}$ age = 30.75 yr) and 12 old men (age range = 63–82 yr, $\bar{x}$ age = 75.50 yr). Three skin-hydration conditions were produced on sites used for electrodermal measurements. In order of increasing hydration, they were: a) 0.5% KCl-glycol electrolyte, b) 0.5%

KCl-agar electrolyte, and c) presoaking with distilled water followed by 0.5% KCl-agar electrolyte.

Three tasks were given to the subjects. In task 1, the subjects received eight presentations of a 50-dB, 250-Hz tone. In task 2, a reaction-time task, the subjects received a 50-dB, 250-Hz warning signal, then a 50-dB, 1000-Hz signal, to which they had to respond by pressing a key. Task 3 was a choice-reaction-time task in which the warning signal was again 50-dB, 250-Hz, which was followed either by a response signal of the same loudness and frequency or by a 50-dB, 1000-Hz tone; the subjects were to respond only when the low-pitch warning signal was followed by another low-pitch tone. During both reaction-time tasks the subjects were repeatedly urged to respond more rapidly.

There were no significant age differences in the effect of electrolyte medium on SCL and SCR. The older subjects had lower SCL and SCR magnitudes than the younger subjects. There were age differences in the effect of electrolyte medium on SPL and SPR. The SPR in young adults was related to hydration, the largest response occurring with the least hydration, but electrolyte did not significantly affect the magnitude of SPR in the old subjects. Age differences in SPL and SPR occurred only with the glycol medium, the older subjects having smaller responses and less negative levels. The authors postulate that the reversal in hydration/SPL relation with age reflects a reversal in the relative magnitudes of the potentials of epidermis and sweat glands: In old persons the epidermal is greater than the sweat-gland potential.

Garwood et al. (1981), reporting that differences in SPL were dependent on epidermal hydration, also found that age differences occurred only when SPL was more negative than resting levels. Basal skin-potential-level (BSPL) procedures were used. Subjects were required to relax for 30 minutes until a minimum SPL (BSPL) was reached during an absence of electrodermal response. BSPL is considered to be a nonsudorific SPL component (Christie and Venables, 1971). Hydration conditions were as in Garwood et al. (1979). Again, age differences occurred only with the glycol medium. Furthermore, age differences occurred only at the start of the recording, when sweat-gland activity can be expected to contribute to SPL. There were no significant age differences at BSPL. Capriotti et al. (1981) also reported that with increasing age there is a decline in SPL negativity when the glycol medium is used.

An additional consideration in investigating age differences in EDA is recording site. Capriotti et al. (1981) reported that age differences in SPL were much larger when recordings were made from the medial phalanges than when they were made from the thenar eminence.

Time Perception and Psychomotor Function

Effect of age and institutionalization on perception of short intervals of time. While the common observation that time seems to pass more quickly as one ages has received some experimental support, the hypothesis has been challenged by some investigators. An investigation was undertaken to clarify the issue experimentally (Surwillo, 1964b). The study included a comparison of estimates of short intervals of time made by non-institutionalized subjects with those of an age-matched group of institutionalized subjects.

One hundred twenty healthy white BLSA males 27 to 90 years old were classified in three age groups of 40 subjects each with means of 37.5, 56.1, and 73.7 years. A group of 40 white males from the Infirmary Division at BCH with a mean age of 73.7 years (± 6.2) was compared with the old group of healthy subjects. The institutionalized subjects were low-income patients who were active, could feed, wash, and dress themselves, and had no apparent psychiatric disorder.

Each subject was asked to estimate intervals of 30, 60, and 180 seconds by holding a telegraph key closed for the stated period of time. Elapsed time was measured with a chronoscope that was activated by the telegraph key. Three estimates obtained for each interval were averaged to determine the subject's score.

Among the non-institutionalized subjects, there was no systematic increase with age in estimates of time intervals, and none of the mean estimates differed significantly from actual elapsed time. The hypothesis that a short interval of time is perceived by older persons to move at a faster rate was therefore rejected. The fact that the time estimates made by the group of institutionalized subjects were significantly shorter than those of age-matched non-institutionalized subjects may possibly reflect differences in the "content" of time for infirmary patients; it may equally well reflect differences between the two groups in education, intelligence, and socioeconomic status.

Speed and accuracy of movement. The effect of age on speed and accuracy of movement was studied (Welford et al., 1969) in subjects who tapped a pencil back and forth as quickly as possible between two targets each consisting of two parallel lines drawn on paper. The target widths (the distances between the parallel lines) were 32 mm, 11 mm, and 4 mm. The distances between targets—from the center of one to the far edge of the other—were 50, 142, and 402 mm for each width. Observations of each subject were fitted to equations, based on information theory, that relate movement time to average distance from starting to finishing point and an estimate of the scatter of the points around each target (a measure of accuracy).

Data from 325 men ranging in age from 20 to 70 were analyzed in ten-year age groups. Performance, as measured by the time required to place 50 dots on each target, improved from age 20 to age 40 and then declined. At any age more time was required to place the dots in the narrow than in the wide targets. The greatest accuracy in positioning was achieved by the 20-year-olds. Analysis of the data led to the conclusion that two control processes could be distinguished—one controlling movement over distance (motor control) and a slower one that controlled "homing" onto the target (visual control). The authors concluded that position sense and motor control decline more with age than do the decisional processes responsible for homing on a target.

Muscle strength and coordination. Arm strength and manual cranking ability were measured in 218 BLSA participants 20 to 89 years of age (Shock and Norris, 1970). The maximum power output generated in the crank-turning task, which required coordination of several muscles, was compared with the strength of the same muscles when their movement was kept to a minimum (i.e., isometric strength measurement). In contrast with previous studies in large unselected populations, in which a decline in muscle strength was evaluated by strength of grip (Fisher and Birren, 1947; Welford, 1959, 1977), the study found that the strength of arm and back muscles in these selected subjects did not differ significantly over the age span from 20 to 65 years (Fig. 45). Significantly lower muscle strength was found only in subjects in their 70s and 80s. The 28% difference in muscle strength found in the 80-year-olds was reduced to 19% when allowance was made for the lower body weights of this age group. While muscle strength showed no significant differences until the last two decades, power

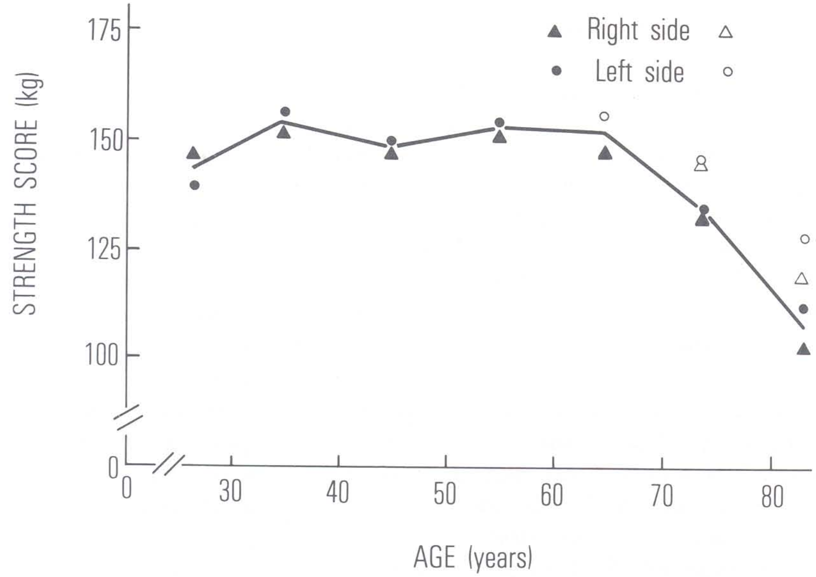

Figure V.45. A composite strength score (kg) for the arm and shoulder muscles is plotted against age (yr) for the right side (▲) and the left side (●). Values that would be expected if the oldest subjects had weighed as much as younger subjects are shown for right side (△) and left side (○).
From Shock and Norris (1970).

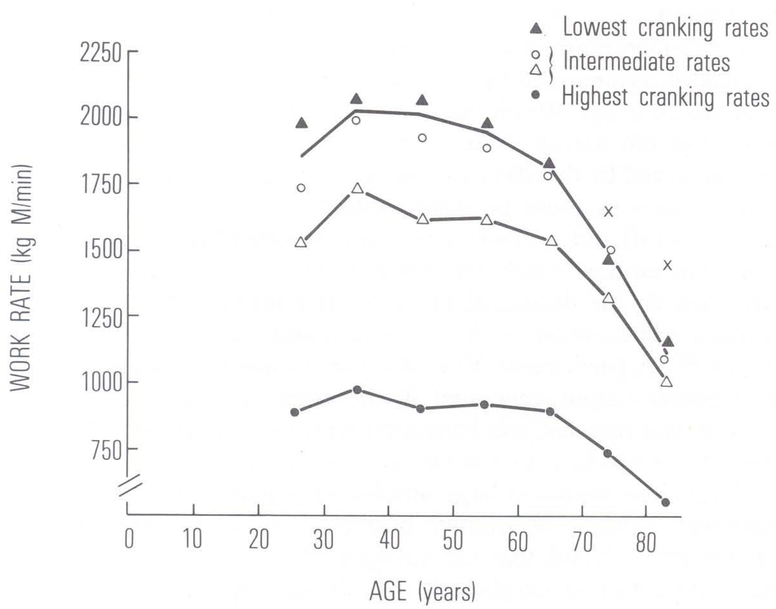

Figure V.46. Maximum work rate (power output) (kgM/min) is shown for 4 cranking rates for each of 7 age-decade groups. Values that would be expected if the oldest subjects had weighed as much as the younger subjects are shown for the 2 lowest cranking rates (X). From Shock and Norris (1970).

output showed significant differences as early as the fifth decade. The largest difference, 45% among 80-year-olds, was reduced to 30% when allowance was made for lower body weight (Fig. 46). Since the older subjects were highly motivated to achieve maximal results and the duration of the cranking exercise was too brief to manifest any cardiovascular or pulmonary limitations, the most likely cause of their power-output deficit was judged to be reduced coordination ability.

2. Cognitive Functions

Learning and Memory

Age differences in verbal learning. Although several studies have indicated that performance in verbal learning declines with age, it was not until the 1960s that the rate of presentation, or pace, of verbal information was evaluated as an independent variable. Since some errors in paced trials may be due to insufficient time to respond, rather than to failure to learn, direct resolution of the learning-performance problem requires measures of errors that are not attributable to pace. To provide such measures, a study of age differences in paired-associate learning (Arenberg, 1965) included self-paced trials (without feedback) alternated with paced trials. In addition, the anticipation interval (the time allowed for response) was independent of the inspection interval. In this way, differences between pace groups would not be attributable to variations in the time allowed to view the material to be learned. It was hypothesized that the old subjects would make more errors than the young, that age difference would be greater at the faster than at the slower pace, and that the pattern of self-paced errors would be similar to the pattern of paced errors despite the fact that each subject could take as much time as he needed to respond.

In Study I the subjects were 64 men participating in the BLSA. Participants were randomly assigned to the fast or slow pace; 32 men were 29–40 and 32 were 63–77 years old. On each trial the eight items were presented in one of five orders. The stimulus component of each item consisted of two consonants; the response component was a familiar two-syllable adjective. The material was presented by means of a card-changing instrument equipped with variable control of the shutters. The anticipation interval, during which the two consonants were exposed, was 1.9 seconds for the fast pace and 3.7 seconds for the slow pace. For both pace groups the inspection interval, during which consonants were exposed together with the word, was 1.9 seconds. The interval between the displays of items was 1.8 seconds for both groups. The procedure continued until one errorless trial or 52 trials occurred.

Although the mean number of errors during the fast-pace test was substantially greater in old than in young subjects (Fig. 47), it was impossible to judge whether the older subjects had difficulty in learning at that pace or had learned the material but could not respond in the short anticipation interval. Study II was designed to determine which explanation was correct.

Subjects in Study II were unemployed men, not members of the BLSA, with at least a sixth-grade education, who were seeking work at a state employment agency. Sixty-four men with raw scores of at least 20 on the WAIS Vocabulary test were recruited. The age ranges were 18 to 21 years for the young group and 60 to 77 years for the old. Subjects were randomly assigned to the fast or slow pace to provide 16 subjects in each of four age-pace groups. The eight-item list was reduced to six items.

To provide measures of errors not attributable to insufficient time to respond, self-paced test trials were alternated with paced acquisition trials for each subject. Timing of the paced trials was the same as in Study I. As with the better-educated subjects of Study I, the older group showed a significantly greater frequency of errors in the paced trials. Older subjects also committed more errors in self-paced trials, an indication that their poorer performance was due to a learning deficit rather than to an inability to respond quickly.

In another study (Arenberg, 1967b), men in the BLSA whose age range was 20 to 87 years were given a paired-associate learning task (335 men) and a serial learning task (322 men). The card-changing instrument and the eight-item list of the previous study were used for the paired-associate learning task; the anticipation, inspection, and between-item intervals were the same as before. The instrument was also used, with different time intervals, for the serial learning task, in which 12 familiar five-letter words were shown to each subject in a fixed order.

Polynomial regression analysis elicited linear components at both long and short anticipation intervals, but quadratic components only at the short interval. The

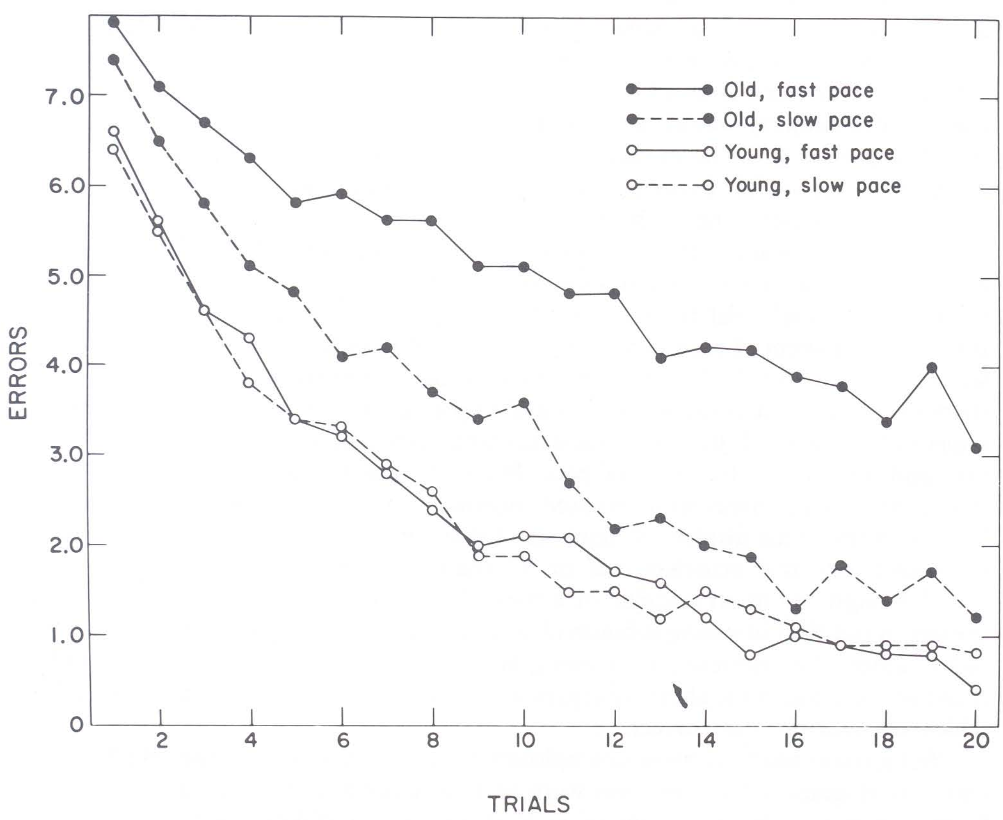

Figure V.47. Mean errors for all 4 age-pace groups plotted over the first 20 trials. From Arenberg (1965).

quadratic component indicated that the magnitude of age differences increased with age. It is possible that each passing year results in a larger decrement than the preceding one in an individual's performance; it is also possible that some threshold level of functioning of the underlying mechanisms must be reached, or some event must occur, in order to produce a performance impairment, and that the impairments are greater as age increases. The issue can be resolved only by longitudinal measurements.

Age differences in retroaction. "Retroaction" refers to the effect of an interpolated task on the recall or relearning of previously learned material. Two previous studies of age and retroaction had produced contradictory results. Gladis and Braun (1958), who used long anticipation intervals, found no age differences in retroaction, while Wimer and Wigdor (1958), who used short intervals, found that old subjects were affected more than young by the interpolated activity. A BLSA study (Arenberg, 1967a) used two anticipation intervals in a paired-associate learning task to test the possibility that the contradictions were due to the use of very different anticipation intervals. It was hypothesized that an age difference in retroaction would be found at the short anticipation interval but that no age difference, or a small one, would be found at the long interval.

The subjects were 24 young (age range = 30–39 yr) and 24 old (age range = 62–77 yr) BLSA participants. The men were randomly assigned to the short (1.9 sec) or long (3.7 sec) anticipation interval. Approximately two minutes elapsed between original learning and interpolated learning and between interpolated learning and relearning. An age difference in relearning was found at the short but not at the long anticipation interval. The results were thus in essential agreement with the earlier studies: Some part of the difference in those findings was apparently due to a difference in the anticipation interval.

Age differences in memory and decision performance. A study was conducted to assess the magnitude and pattern of age differences in experimental laboratory measures of cognitive and psychomotor performance (Robertson-Tchabo and Arenberg, 1976). Performance measures for a wide variety of cognitive laboratory tasks, mostly memory and decision tasks, were factor-analyzed. The sample consisted of 96 healthy BLSA men whose age range was 20 to 80 years. The factors were identified as speed of information processing, secondary memory, attention, and primary processing efficiency. All factor scores were correlated with age, better performance being associated with lower age. Attention was found to have the highest, primary processing the lowest correlation with age. The sample was divided into subsamples of 32 young (20–39 yr), 32 middle-aged (40–59 yr), and 32 old (60–80 yr) subjects, and each subsample was factor-analyzed separately to determine whether the factor structure was similar for all age groups. Evidence was found of factor-structure invariance with adult age; all four factors in the primary analysis were identifiable in each age subsample. The findings are consistent with a model of continual cognitive decline with age in healthy, educated adult males. The decline seems to be quantitative rather than structural in nature: Age appears to function as a scalar affecting the magnitude of a factor score.

Equivalence of Information in Concept Identification

A new method was designed at the GRC to provide equivalent amounts of information for logically equivalent selections in concept identification when subjects select instances (Arenberg, 1970). An "instance" is an item or stimulus configuration in a concept-identification task. A positive instance exemplifies the concept, that is, it includes the defining attributes of the concept; a negative instance does not exemplify the concept. Equivalence is maintained between comparable conjunctive and disjunctive problems as well as within a particular type of problem. The equivalence-of-information method permits the amount of information gained to be used to measure performance for each selection. The non-equivalence of available information, which usually results when subjects select instances, is avoided by this method. Data from an experiment in which the method was used suggest that the amount of initial information provided merits investigation as a variable. Moreover, pooling the results of concept problems with high and low initial information may obscure important group differences.

3. Daydreaming

Age differences in daydreaming. A BLSA study of daydreaming across the adult age span (Giambra, 1974) investigated the frequency, content, temporal setting, and precipitating instances of daydreaming. Daydreams were defined as spontaneous thoughts, unrelated to the task at hand, that intrude into the person's awareness.

Six age groups of BLSA participants were studied: 24–34 (n = 20), 35–44 (n = 13), 45–54 (n = 31), 55–64 (n = 46), 65–74 (n = 28), and 75–91 years (n = 26). In addition, a young group of college students 17 to 23 years old (n = 214) were recruited. The Imaginal Processes Inventory (IPI), a 28-scale questionnaire, was used to measure aspects of daydreaming and related activity. Linear declines with age were found in daydreaming frequency; absorption in daydreaming; imagery and vividness in daydreams; and daydreams about sex, bizarre and improbable events, achievement, hostility, heroism, fear of failure, and guilt. No decline was found in acceptance of daydreams, impersonal and interpersonal curiosity, mentation rate, past and present temporal setting in daydreams, or daydreams involving problem solving. Except in the youngest group, in which sexual daydreams predominated, problem-solving daydreams were predominant at every age. There was no concentration on daydreams about the past in any age group, including the oldest.

The study was later replicated (Giambra, 1977–78). The characteristics of daydreaming obtained in the original sample were also found in the replication, which thus supported the earlier findings. Combination of the original and replication samples allowed a closer analysis and provided tentative norms for the populations sampled. Two of the more salient findings were that daydreaming did not increase in the oldest ages, and that among BLSA men at any age daydreaming did not concentrate on the weird, outlandish, or improbable.

Daydreaming about the past. The common belief that old people spend much time daydreaming about the past is contradicted by a BLSA study of the past, present, and future settings of the daydreams of 1100 men and women aged 17 to 92 years (Giambra, 1977a). Using the three scales of the IPI that measure past, present, and future orientations, the study found no correlation between age and daydreaming about the past. Furthermore, temporal orientations were, with few exceptions, nearly the same in all age groups.

The relation between daydreaming and temperament. Reviews of studies in college students by other investigators have shown a connection between daydreaming characteristics and such measures of temperament as thoughtfulness, objectivity, masculinity, and emotional stability. Since Giambra (1974, 1977–78) had demonstrated that certain daydreaming characteristics in males are related to age, another BLSA investigation was conducted to determine how age may alter the relation (Giambra, 1977b).

The sample consisted of 170 males in six age groups: 24–34 (n = 17), 35–44 (n = 16), 45–54 (n = 28), 55–64 (n = 45), 65–74 (n = 36), and 75–91 years (n = 28). Aspects of daydreaming and related imaginal processes were determined by the IPI. Temperament traits were measured by scales from the Guilford-Zimmerman Temperament Survey (GZTS). A factor-analytic approach was used. Only one daydreaming-temperament factor—"neurotic-anxious absorption in daydreaming"—was age-related, and the relation was negative; older individuals had lower scores. Subsequent longitudinal analyses (see Chapter VI) demonstrate that this cross-sectional difference does not represent age change.

Sex differences in daydreaming. A study was subsequently undertaken to examine the daydreaming characteristics of a comparable sample of women of varying age (Giambra, 1979–80).

A total of 773 women (not drawn from the BLSA population) were divided into 12 age groups ranging from 17 to 92 years. The men were the sample from the BLSA used by Giambra (1977–78). The women were of the middle and upper-middle classes. Aspects of daydreaming and related mental activity were determined by the IPI. The frequencies of daydreaming about all subjects except problem solving decreased with age. Females reported higher frequencies than males of daydreaming and nightdreaming, as well as more problem-solving dreams. Females also reported lower frequencies of sexual, bizarre-improbable, heroic, and achievement-oriented daydreams. Most sex differences persisted over the life span, and the male-female difference in sexual daydreams increased with age. Except for sexual daydreams in males 17 to 29 years of age, daydreams in both sexes were primarily concerned with problem solving, which remained at a high level across the life span. After age 40, achievement-oriented daydreams were more frequent in females than in males. Females at all ages when contrasted with males reported more interpersonal curiosity. Males reported more curiosity than did females about things. An unexpected finding was that males were curious about things and people to the same degree. The results were interpreted as supporting the assumption that daydreaming is a way of dealing with current concerns or of solving problems.

Sexual daydreams and age. Retrospective reports of male sexual daydreaming and their relation to three behavioral aspects of sexual vigor were analyzed over the adult life span (Giambra and Martin, 1977). The three characteristics were frequency of coitus during the early years of marriage, number of partners before, during, and after marriage, and amount of sexual activity between 20 and 40 years of age. A total of 277 men from 24 to 91 years of age participated. The men were divided into six age groups: 24–34 (n = 23), 35–44 (n = 27), 45–54 (n = 56), 55–64 (n = 83), 65–74 (n = 48), and 75–91 years (n = 40).

Sexual daydreams declined in frequency and intensity with age and virtually disappeared after age 65. For men aged 24 to 64 years, scores on the sexual daydreaming scale of the IPI correlated with each of the three characteristics of sexual vigor. Men who had more frequent sexual daydreams tended to be more sexually active.

4. The Marital and Sexual History

In an introductory paper, in which the methods used in interviews to obtain marital and sexual information were described in detail, 603 BLSA men aged 20 to 79 were divided into age groups for a variety of comparisons with age (Martin, 1975). Across age groups numerous gradients were in evidence, some of which reflected the past experiences of different cohorts while others were accounted for by the effects of age.

The influence of birth cohort was apparent in the fact that, with increasing age at interview, proportionately more subjects reported early farm residence, late ages at onset of initial petting, coitus, and marriage, coital abstinence before marriage, and coital experience confined to a single partner. An aging effect was found in the gradients observed for a number of other variables: a history of marital dissolution and remarriage, the loss of erotic reactions to certain visual stimuli, an increase in the length of time during which abstention from sexual activity failed to produce discomfort, a reduction in kind and frequency of sexual expression, and recurrent erectile failure. The proportion of subjects who responded affirmatively when asked if they might want a restoration of sexual vigor, if this were possible, proved surprisingly small (33%) and showed no consistent trend with age. In view of the importance males are generally believed to place on sexual activity, it had been anticipated that with advancing age the prospect of renewed sexual vigor would have an increasing appeal.

Age, marital status, potency, and physical and emotional health are known to affect the frequency with which males engage in sexual activity. It is unclear, however, why males of similar age vary widely in frequency of sexual expression and why male sexual vigor declines with age. An analysis of the data obtained from 628 respondents was undertaken in an effort to identify correlates of sexual frequency while holding age constant (Martin, 1977). The hypothesis was that such correlates might identify factors or mechanisms that contribute to the loss of sexual vigor that sometimes accompanies aging.

Respondents were divided into five-year age groups, ranging from 25–29 years to 80–84 years at report. Mean and median weekly frequencies of coital and total sexual activity were computed from the frequencies reported for the five-year interval immediately preceding interview. Mean frequencies of total activity showed a slight increase from 20 to 34 years of age, but then declined steadily until age 65. The lack of a further decrement from age 65 to 79 was attributed to the above-average health of the older subjects. Coitus comprised an increasing proportion of total activity to age 34 and thereafter constituted 80% to 90% of total sexual activity.

A number of subjectively evaluated variables, most derived from the interview, proved unrelated to level of sexual activity irrespective of age. These included subject's religiosity, parental religiosity, economic status of the parental home, interpersonal relations within the parental home, number of times intoxicated, amount of physical activity, and health complaints on the Cornell Medical Index. Age at marriage was also independent of sexual frequency. However, total sexual frequencies at ages 20 to 39 were found to be significantly related to age at first coitus, number of coital partners, and maximum number of coital events reported for any single week of marriage, none of which appeared as correlates of total sexual frequency at older ages. On the other hand, the amount of sexual activity reported as having occurred between 20 and 39 years of age proved to be highly related to current rates of total sexual activity for all age groups past 40 years. Respondents had thus tended to maintain relatively high or low rates of total activity over most of their lives.

Physical and physiological variables that were found to be independent of current levels of activity at all ages included height, weight, lean body weight, percentage of body fat, size of prostate, hematocrit, hemoglobin, triglycerides, creatinine excretion, basal pulse rate, basal systolic and diastolic pressures, vital capacity, and forced expiratory volume at one second. Four variables appeared, however, as significant correlates of frequency of sexual activity at ages 65 to 79: chest circumference, maximum breathing capacity, and basal oxygen consumption as positive correlates, and serum cholesterol as a negative correlate. The small magnitude of the correlations, on the other hand, supported the conclusion that in persons of reasonably good health physical fitness is of minor importance to the maintenance of sexual vigor.

The problem addressed in a more recent paper (Martin, 1981) was to determine why some older men are more or less sexually active than others of comparable age. The study of 188 respondents 60 to 79 years of age provided a number of insights into the nature of male sexuality and served to generate several hypotheses concerning the factors that sustain sexual motivation in the later years of life.

Data analysis was limited to respondents who had been married throughout the year preceding the interview. Subjects were stratified into five-year age groups before being subdivided into categories of sexually least active (n = 63), moderately active (n = 63), and most active (n = 62), according to the quantity of sexual activity reported for the year prior to interview. Comparisons between least active and most active subjects revealed no important differences in occupational status, education, age at marriage, times married, number of years married before age 60, age of wife, or current marital adjustment. Nor were significant differences found between these groups in age at first coitus, number of coital partners, attitudes concerning coital and masturbatory activity, or perceived sexual attractiveness of wives.

Other variables, however, emerged as significant correlates. All four measures descriptive of past levels of sexual activity proved to be highly related to current levels of activity. This finding is consistent with the hypothesis that individual differences in level of sexual activity before middle age tend to be maintained past middle age, and that the persistence of these differences into old age accounts for a large portion of the variation observed in current frequencies.

An important conclusion from these findings is that men who were most sexually active in their 70s had also been highly active sexually in their 20s. The behavioral continuity is similar to the continuity of major personality dispositions.

The study also investigated sexual potency. Of the 88 men classified as less than fully potent at report, only 10% stated that they had sought medical advice for their condition, although none complained of fear of failure or of being unable to live up to some desirable standard of sexual performance. Moreover, questions about marriage and sexual experience, episodes of acute anxiety, and instances of resort to professional help for personal or sexual problems consistently failed to reveal evidence of the kinds of marital conflict, personal grievances, or expressions of dissatisfaction one would expect to find were emotional factors of critical importance for lack of potency. The vast majority of respondents appeared to be functioning at a level commensurate with their feelings of desire; because few were lacking in other resources for maintaining self-esteem, their condition failed to produce the emotional trauma that is often encountered in clinical practice.

5. Activities and Attitudes

A study was undertaken to measure the activities and attitudes of BLSA participants in order to compare the distributions of scores at different ages (Stone and Norris, 1966). The subjects were 463 men aged 20 to 99 years, 151 of whom were over 60. The Chicago Activity and Attitude Inventories of Burgess, Cavan, and Havighurst (Cavan et al., 1949) were administered to each participant. The scale is made up of three parts: background, including general information about the participant and his earlier life, an activity inventory, and an attitude inventory. The activity inventory, administered to all 463 men, contains five groups of statements dealing with leisure-time activities, religious activities, intimate contacts, security, and health. The attitude inventory, administered to 450 of the men, deals with the personal aspects of adjustment and contains eight groups of statements dealing with health, friends, family, work, happiness, economic security, religion, and feelings of usefulness.

No significant relations between activity or attitude scores and chronological age were found. In contrast with a previous study by other investigators (Mason, 1954) the older men in this group reported as much participation in and satisfaction with activities and relationships as the younger men. The contrasting findings were explained on the basis of differences in the study populations. The earlier study had compared a group of low-income institutionalized subjects, whose mean age was 74.2 years, with a group of high-income non-institutionalized subjects whose mean age was 70.2 years and a group of low-income non-institutionalized subjects whose mean age was 39.5; it found impressive differences in attitudes associated with age. In the BLSA study, the subjects were volunteers, were generally very well educated, and were working in or retired from high-level occupations. Most of the BLSA participants who have retired continue in activities that enhance their self esteem and allow them to feel that they are useful members of society. It is thus likely that the homogeneity of activity and attitude scores across age groups in the BLSA sample is a result of other similarities between the old and young participants.

6. Coping with Stressful Events

In a cross-sectional study of mechanisms used to cope with stressful life events (McCrae, 1982a), subjects from the Augmented BLSA Sample (participants plus their spouses) were administered questionnaires to measure coping behaviors and styles. A total of 255 men and women completed a Coping Questionnaire, and 150 completed a Coping Self-Interview. The Coping Questionnaire required subjects to indicate which of 118 ways of coping they had used in response to a recent life event selected by the investigator. The items were taken from the Lazarus "Ways of Coping" scale, together with fifty new items developed from a review of the literature. In addition, subjects indicated which ways of coping had been most helpful in their solutions of the problem and in making them feel better. The Coping Self-Interview required subjects to select three recent events—a challenge, a threat, and a loss—and to indicate which of 50 ways of coping they had used for each; whether the method had helped them solve the problem; and whether it had made them feel better.

Factor analysis of the 118 items in the Coping Questionnaire led to the identification of 28 coping mechanisms. Analysis of one step at a time found that restraint, rational action, expression of feelings, and positive thinking were the mechanisms most frequently used, whereas self-blame, intellectual denial, passivity, sedation, and hostile reaction were least frequently used. Although nearly half the mechanisms showed age differences in response to a recent life event, the kinds of events old people typically faced were systematically different from those young people faced; older men and women were more likely to have experienced a threatening event, younger individuals a challenge. The differences in type of stress were strongly related to the choice of coping strategy.

When statistical controls for type of event were used, eight mechanisms showed age differences. In order to replicate these findings, analyses of the Coping Self-Interview treated age and type of event as independent. Two of the eight age differences found on the Coping Questionnaire were replicated on the Coping Self-Interview: Older people (50–64 and 65–89 yr) were less likely than younger ones (21–49 yr) to use hostile reaction and escapist fantasy. These cross-sectional differences tend to support the work of Vaillant and to contradict the notion that older individuals are prone to the use of primitive and immature defenses. In addition, the many age differences related to the type of event testify to the fact that older individuals are able to adapt their coping behavior to the changing situational demands of their stage in the life span. Older men and women do not rigidly maintain habits of coping that, although appropriate in youth, have outlived their usefulness. Instead, as stresses change, so do coping responses. This finding was replicated in the second study, where non-significant age-by-type-of-event interactions indicated that older people showed the same differentiated and flexible responsiveness as younger ones to different types of stress.