

BLSA

With the Passage of Time

The
Baltimore
Longitudinal
Study
of Aging



■ ◆ ★ ✨ National Institute on Aging National Institutes of Health

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TABLE OF CONTENTS

A TREASURY OF DATA	2
THE STUDY	6
Every Two Years	6
Themes	8
Exploding Stereotypes	12
Traditions	14
At the Cutting Edge	20
FINDINGS	28
The Aging Body	28
The Aging Mind	42
The Aging Spirit	46
SELECTED BIBLIOGRAPHY	49

The Baltimore Longitudinal Study of Aging (BLSA), as it passes its 35th birthday, is growing and changing. What began as a study with a few men in the late 1950s now has more than 1,100 active participants, both men and women, and continues to expand. Since the BLSA's inception, scientists using its data have published more than 600 reports and articles in the biomedical literature. Their findings have helped change aging research, clinical practice, and the way we view aging.

The first booklet about the BLSA was written by Les Higbie, a participant and science writer. In his foreword, Higbie talked about the value of aging research. His words bear repeating:

“Without such research, we can hardly expect to develop the base on which we can build and produce practical results, much less extend our life span. By expanding our understanding of the normal human aging process, we will ultimately acquire the knowledge needed to enhance the quality of life in our later years.”

The many hundreds of participants and scientists involved in the BLSA have already provided significant new insights into aging. This account of the Baltimore study tells what they have accomplished and where they are headed. It is dedicated to all whose long-term commitment makes the understanding of aging a realistic goal.

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A TREASURY OF DATA

In 1991, 54 men took part in a study that discovered something new, and potentially very important, about one kind of cancer. Eighteen of the 54 had had prostate cancer. All were participants in the Baltimore Longitudinal Study of Aging (BLSA).

The researchers began with frozen blood samples provided by the men over a period of years, during their regular visits to the BLSA. Using a test already common in medical practice, this team of scientists from the National Institute on Aging (NIA) and The Johns Hopkins University analyzed each of the samples for an enzyme called prostate-specific antigen or PSA.

The medical community already knew that most men with prostate cancer have high levels of PSA in their blood. What these investigators wanted to explore was the rate of change in PSA levels over time and how that rate differed among the 54 men in the study. Did the men who had developed cancer have a rate of change different from the others?

The answer, reported by H. Ballentine Carter, Jay D. Pearson, and their colleagues in the *Journal of the American Medical Association*, was yes. In the 18 men who had cancer, PSA levels began to rise rapidly about 5 years

before the disease had been diagnosed by traditional means. In the other men — including those with benign prostate growth or hyperplasia (BPH) and those without prostate disease — no such dramatic rise occurred.

This medical discovery had its origin in the rich treasury of data that has been carefully collected for more than three decades at the Baltimore Longitudinal Study of Aging. Launched in 1958, the BLSA is America's longest running scientific examination of human aging. Its aims are to measure the usual or universal changes that occur as people age and to learn how these changes relate to the fundamental causes of aging and to the diseases that sometimes accompany aging.

With the Passage of Time tells the story of the BLSA — a study conceived as a partnership between volunteer participants and researchers. It is a story that revolves around these two groups: the men and women who travel to the NIA's Gerontology Research Center (GRC) in Baltimore every 2 years to take part in the study and the scores of investigators, from the GRC and other academic centers around the world, who conduct studies with BLSA participants and analyze the data, putting together a picture of how we age.

The first part of this booklet describes the study itself, while the second highlights some key findings about aging that have emerged from the longitudinal data.

*...a study
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The BLSA at a Glance

Objectives:

- ◆ to measure changes in biological and behavioral processes as people age;
- ◆ to relate these measures to one another; and
- ◆ to distinguish universal aging processes from those associated with disease and particular environmental effects.

Founded: 1958. Women entered the study in 1978.

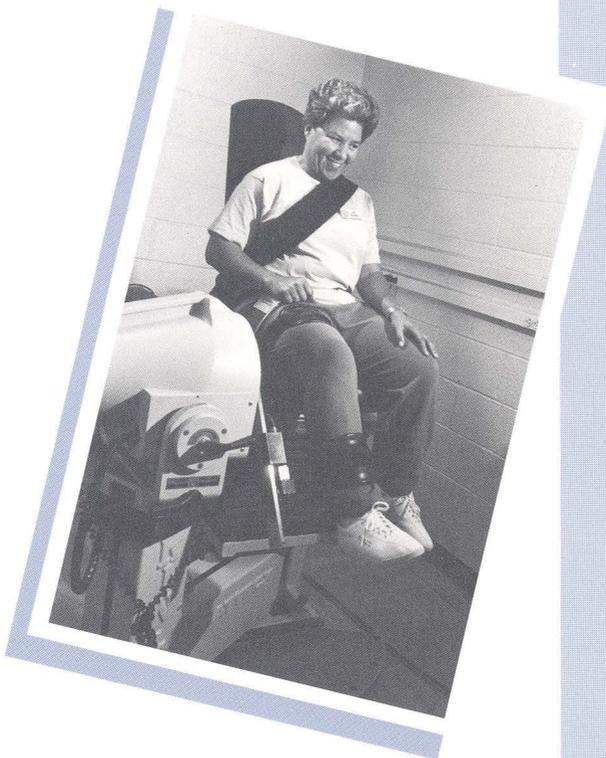
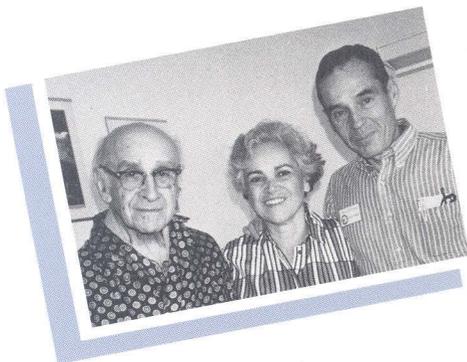
Location: Gerontology Research Center (National Institute on Aging), Frances Scott Key Medical Center, Baltimore, Maryland

Participants: Over the life of the study, the BLSA has had 2,227 participants. In 1993, active participants included 675 men and 503 women from their 20s to their 90s.

But the story told here is not complete. The prostate study, for example, has given hope and direction to other investigations. In Baltimore and elsewhere, researchers are testing a new hypothesis — that tracking PSA levels over time, or “serial testing,” may be a better way of detecting prostate cancer than single, isolated tests. This is because the BLSA data showed that rate of change in PSA level may be a more reliable and earlier marker of prostate cancer than the actual PSA level.

In addition, BLSA and Johns Hopkins investigators are following up with a 10-year investigation involving all BLSA men over age 30. This study is looking at a multitude of factors related to prostate cancer and BPH. It will examine PSA levels, hormone levels, and urination patterns. It will use magnetic resonance imaging to detect changes associated with prostate cancer and BPH. It will look for the reasons that the incidence of prostate cancer rises so steeply with age. A particular focus will be African Americans who have the highest rate of prostate cancer in the world.

The prostate study is just one example of how BLSA volunteers and researchers are contributing to scientific knowledge of health and aging. Each year the study adds to its treasury of data, generating new findings and new questions. It is an unfolding story with many chapters still to come.

**Researchers:**

- ◆ NIA/GRC scientists in six laboratories
- ◆ Guest investigators and collaborators

Training:

- ◆ Pre- and post-doctoral students

To Volunteer: Baltimore Longitudinal Study of Aging, NIA Gerontology Research Center, 4940 Eastern Avenue, Baltimore, MD 21224; 1-800-225-2572 or 410-558-8139.

To Inquire About Collaboration and Training: Associate Scientific Director, BLSA, NIA Gerontology Research Center, 4940 Eastern Avenue, Baltimore, MD 21224; 1-800-225-2572 or 410-558-8139.

THE STUDY

EVERY TWO YEARS

Eyes intent on the computer screen in front of her, Louise Capone pulls up on the armrest of the Kin-Com chair. The armrest rises and a line ascends the screen. She pulls again, harder, and the line climbs a little higher.

“Pull, pull, pull, KEEP PULLING, KEEP PULLING,” cheers Rosemary Lindle, the exercise physiologist who presides over strength tests at the Baltimore Longitudinal Study of Aging (BLSA), in which Ms. Capone is a participant. The Kin-Com, more officially known as a kinetic communications device, works in much the same way that weight resistance machines in gyms do. When someone applies force — pulling with the biceps muscle of the right arm, for instance — the apparatus resists. Inside the Kin-Com, intricate, state-of-the-art measuring devices register the degree of force and transmit this information to the computer.

“Pull, pull, pull, KEEP PULLING.” The third time the line peaks at 29 newton meters, its highest point so far. The computer, at a touch to the screen, commits the measurement to memory.

Louise Capone is one of more than a thousand BLSA participants who travel to Baltimore every 2 years to take part in this long-term study of human aging. Ranging in

age from their twenties to their nineties, BLSA participants come from every part of the United States. Some have been with the study since it began. But every year new volunteers of all ages join the BLSA and make their first visit, drawn in, they say, by twin lures: the opportunity to learn more about themselves and the satisfaction of being part of a major scientific investigation.

On this Monday morning, five BLSA volunteers are here. Their schedules for the next two-and-a-half days are posted on a bulletin board outside the main office: a complete physical exam, tests of bone density, aerobic capacity, psychology, hearing, reaction time, glucose tolerance, lung function, and more. Each assessment will add detail and focus to the BLSA's slowly growing picture of how we age.

"This is really what keeps me coming back," says Ms. Capone, who is on her seventh visit. "We get the results of our own tests, which are nice to have, but also we learn what the study is learning, overall. There is a real sense of being a partner in the study, of working with the researchers toward a goal."

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Louise Capone



Longitudinal Study —

A “method of epidemiological study [which includes] observation of the population for a sufficient number of person-years to generate reliable [data]... This implies study of a large population, study for a prolonged period, or both.”

John M. Last, ed., *A Dictionary of Epidemiology*, Oxford University Press, 1983.

THEMES

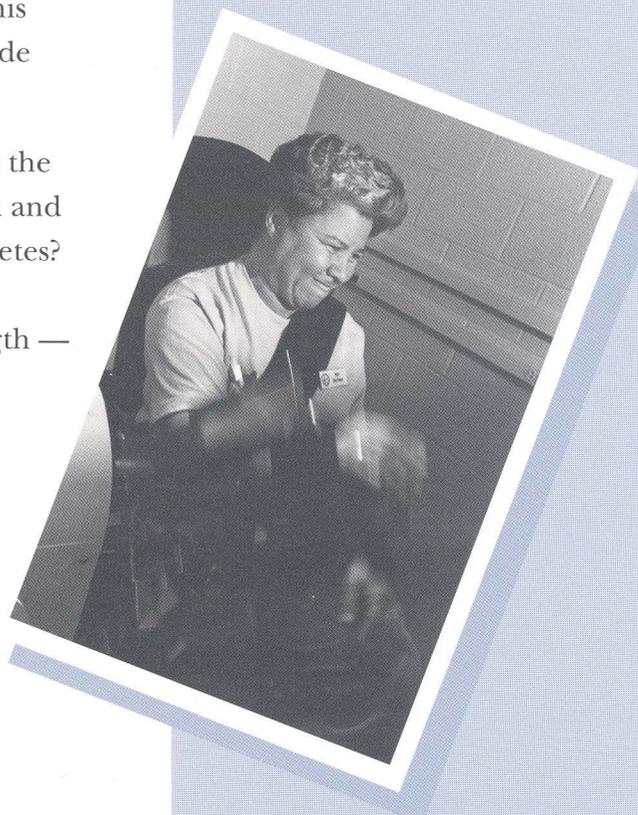
That goal, stated in its simplest form, is to describe systematically the process of aging. Often called a study of “normal aging,” the BLSA is examining the usual and universal changes that affect all people as they age, changes that can be attributed to aging per se, rather than to a disease or to specific environments.

“There are two ways to study aging,” explains James Fozard, the NIA’s Associate Scientific Director for the BLSA. “You can study it cross-sectionally, by comparing people of different ages. Or you can study it longitudinally, which means studying changes in the same individuals over time, as they grow older.” Much more can be learned from longitudinal studies. Cross-sectional studies cannot provide the same insight into the natural course of aging or the changes that lead to disease. But, longitudinal studies, by definition, are exhaustive, extended enterprises and therefore are relatively rare.

Because the BLSA is longitudinal, Louise Capone’s muscle strength at 47, her current age, can be compared to her strength at, for example, ages 53 and 67 and 81. This profile of one individual’s aging muscles goes into the BLSA’s data bank, along with strength test results from all the other volunteers in the study. The result is a record of how muscle strength changes over an adult’s life span.

One of the BLSA's objectives is to relate aging processes to one another. If Ms. Capone has a lower score on the Kin-Com when she reaches 53 or 67, that decline in strength may be associated with lower bone density and perhaps to declining glucose tolerance, the body's ability to use sugar. These possible interconnections intrigue Guest Scientists Ben Hurley and Rosemary Lindle, both from the University of Maryland and GRC/NIA researchers. They are using the Kin-Com data to explore such linkages. "We have smaller studies suggesting that when strength improves, bone density and glucose metabolism also improve," says Dr. Hurley. "The advantage of this study is the large number of participants and the wide range of ages. We're getting a big picture."

Theirs is one of many studies that is helping to map the territory that lies between health and disease. When and how do declines in glucose tolerance turn into diabetes? When does bone loss become osteoporosis? What difference do other factors — such as muscle strength — make?



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“The BLSA is a study of transitions,” points out Jeffrey Metter, the study’s Medical Officer. “Not only the transitions of normal aging, but the transitions from the usual aging process to the disease processes that sometimes accompany aging.”

If the strength study does find linkages between muscle strength and bone density or glucose tolerance, it could point the way to interventions, i.e., ways to keep bone loss from becoming osteoporosis.

Changes occur with aging not only in organs and tissues, but also in cells and molecules. “There are really three overall threads or themes to research with BLSA data,” points out Dr. Fozard. “The longitudinal changes are one, and the relationships between health and disease are another. A third is the fundamental biology of aging. A number of studies here are looking at the mechanisms of aging in cells and molecules, using data from BLSA participants.”

For example, while Louise Capone is recording her muscle strength on the Kin-Com, up one flight of stairs another BLSA participant could be having his muscle cell metabolism measured using nuclear magnetic resonance spectroscopy. “We’d like to find out whether the changes in metabolism — how the cell produces energy —

are intrinsic to the cell or whether they are due to extrinsic factors, like changes in muscle mass,” says Richard Spencer, who is conducting this study in the GRC’s Laboratory of Cellular and Molecular Biology. “Do young and old people with the same muscle mass have the same muscle metabolism? Or are there some cellular mechanisms that change with age, independent of muscle mass?” The answers to these questions, he says, should help show what kinds of interventions might keep muscles strong.

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EXPLODING STEREOTYPES

If Louise Capone fits the average, her glucose tolerance and bone density may decline as she ages. But this cannot be assumed. Many people do not conform to the average, according to BLSA data, which, in this and other areas, have overturned some once-common ideas about aging.

To date, two major conclusions have emerged from the Baltimore study: 1) aging cannot be linked to a general or universal decline in all physical and mental functions; and 2) there is no single, simple, pattern to human aging.

Consider heart function: It was once thought that resting cardiac output (the amount of blood pumped per minute) always declined with advancing age. However, studies with BLSA data have shown that when older persons' hearts are carefully screened and found free of disease, their cardiac output at rest is comparable to that of younger people.

Psychological stereotypes also are crumbling in the face of BLSA data. It was once believed that personality altered as people grew older. According to one popular image, age brought crankiness; according to another, people became mellower with age.

Neither view has held up under scientific scrutiny. The fact is that human personality remains remarkably stable. A person who is cheerful and optimistic when young usually stays that way throughout life. Someone who is irritable and impatient in early life keeps those traits with advancing age.

BLSA data also show that aging is a highly variable, individualized process. To take glucose tolerance as an example, studies have shown that in some people it begins to decline in the mid-thirties. The rate of decline, however, differs markedly among individuals. In the GRC's Laboratory of Clinical Physiology, researchers have found that three factors — fatness, distribution of fat on the body, and level of physical inactivity — account for many of these individual differences.

Even within a single individual, organ systems can change at different rates. This suggests that several processes are at work in aging, says George Martin, Scientific Director of the NIA. These include genetic, lifestyle, and environmental factors, and because they differ so widely among individuals, no two people age in the same way. In fact, individual differences increase as we age, according to studies which show that older people differ from each other to a greater degree than do younger people. Yet accumulated, longitudinal data can be analyzed to yield knowledge about the many processes of aging.

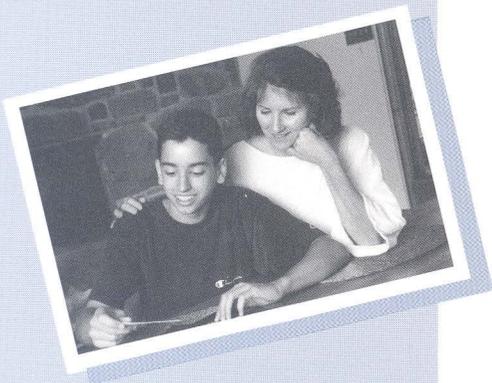
*There is
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TRADITIONS

After the strength test, Louise Capone returns to the corridor that serves the volunteers as living quarters, a wide, quiet hallway that has the air of an informal hospital ward. A bulletin board displays news about participants and researchers, announcements, lists of Baltimore restaurants, and old cartoons. Across the hall there's a small kitchen and next to it the dayroom, where breakfasts are served at a wooden table that fills one end of the room.

Over in this corridor, with its well-used bulletin boards and lived-in dayroom, the remarkable continuity of the BLSA is striking. Dozens of small signs reflect the constancy, the year-by-year steadiness that lies near the heart of a longitudinal investigation.

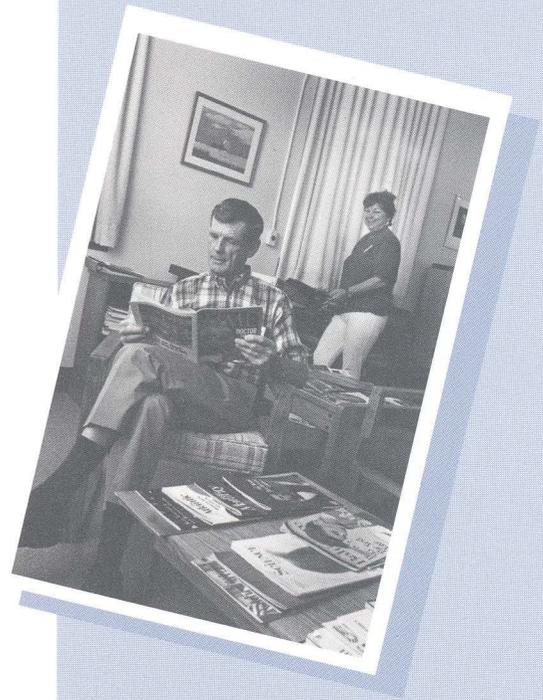
Photograph albums, ranged along a shelf in the dayroom beneath the window, hold pictures of every volunteer in the study, past and present. They include Louise Capone's father, John Frederick Kirby, one of the first to sign up when the BLSA was launched in 1958. Her grandfather, husband, brothers, sisters, several in-laws, and two nephews, — fourth-generation volunteers — also have places in the albums. "My sons will probably join too," she says. "It borders on being a family tradition."

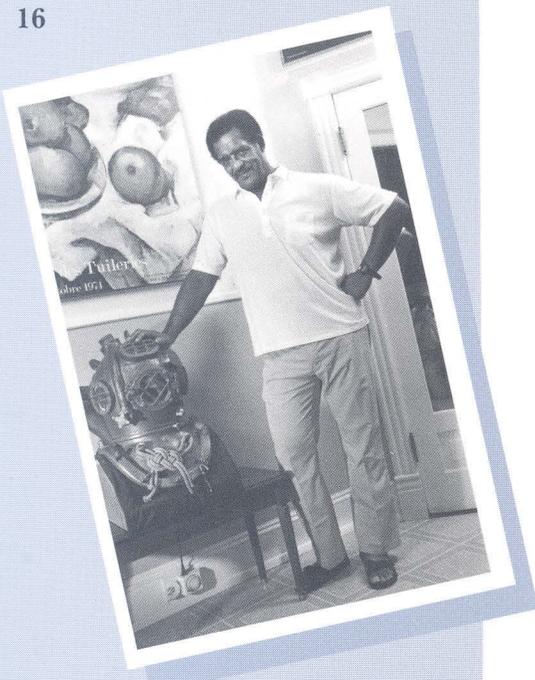


Because of the word-of-mouth recruitment that has characterized the BLSA since its beginning, dozens of volunteers, like Louise, have relatives in the study. But the great majority do not. Why then do people join the BLSA? “Curiosity,” says Lois Odell, who is here on her 9th visit. “I find it intriguing,” agrees Charles Wolfe, on his 19th visit. “And I’ve gotten some excellent medical advice over the years that has been of benefit.”

Many BLSA participants were recruited by friends and colleagues. Lenny Milner was persuaded to join in 1964 by two of his coworkers at the Federal government’s Naval Ordnance Laboratory, and he later recruited two others from that office. “I’ve never missed a visit,” says Mr. Milner. “It’s something to look forward to, and there’s a little challenge to some of it.” The co-founder of two outdoor groups in Washington, D.C. — Black Ski, Inc. and Underwater Adventure Seekers — Mr. Milner savors challenges, and tests like the Kin-Com and the treadmill let him track his own fitness levels.

Dee Milner who joined the study in 1979, has been impressed by what people can learn about their own health. “There are no medicines, no treatments,” she says. “It just allows you to monitor your own health. If there’s a problem, they’ll let you know. And if you don’t want a test, you can say no.”





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Lenny Milner

On the BLSA’s 30th anniversary in 1988, Barbara Hiscock, Senior Operations Manager, asked some of the volunteers why they had joined the study and kept coming.

“It’s a different experience — a break from work and the everyday routine.”

“I get some valuable medical tests.”

“I learn a lot about myself.”

“It’s probably the closest I’ll come to making a contribution to humanity.”

“I look forward to seeing the staff, like Mrs. Scott, Mrs. Carre. They are just wonderful people.”

“To see Cathy.”

Cathy Dent, one of several long-time staff members, schedules and guides the volunteers through their biennial round of tests.

One BLSA custom is celebrating anniversaries. Outside the dayroom, a small ceremony is being prepared for Alice Brands, who will receive a certificate on this, her 10th visit to the study. Mrs. Brands and Dr. Fozard are standing in front of the Founder’s Bulletin Board, where a photographer, Edward Billips, is trying out various distances and light settings.

The Founder's Bulletin Board is where many official BLSA photographs are taken, because the founders have come to stand as a symbol of the study itself. Nathan W. Shock, William W. Peter, and Arthur H. Norris were integral to the BLSA's beginnings, not only providing a strong original impetus but also, each in a different way, stamping the study with a character it still bears.

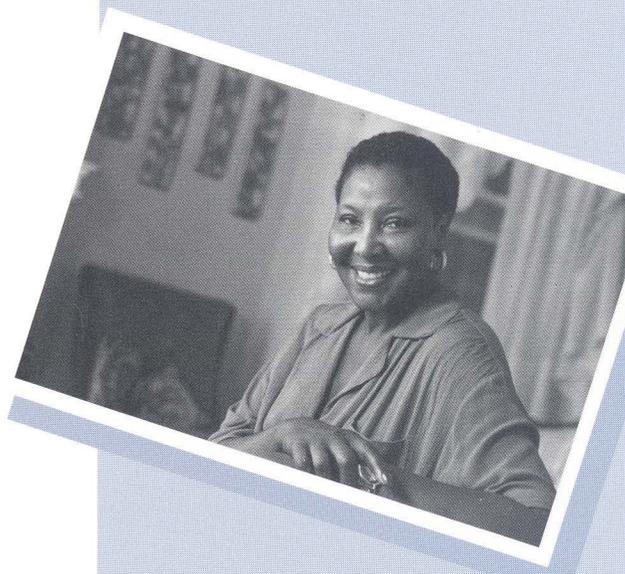
Their story goes like this: In 1958, Nathan Shock was the chief of the Gerontology Branch, now the GRC, of the National Institutes of Health. A pioneer in the relatively young science of gerontology, he had developed the Branch into the largest institution in the western hemisphere devoted entirely to studies of aging.

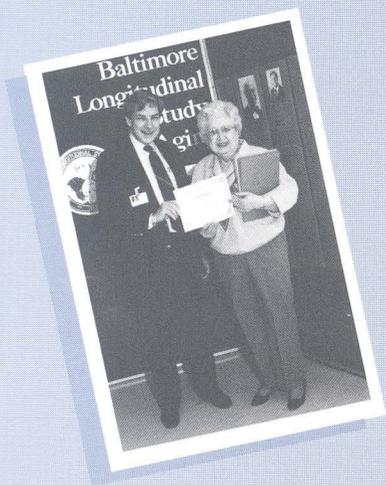
Dr. Shock was approached by William Peter, a retired medical missionary and officer of the U.S. Public Health Service. Then in his seventies, Dr. Peter wanted to make arrangements to bequeath his body to science when he died.

"We need live people," said Dr. Shock, who had for some time been convinced of the need to study healthy community-living volunteers. Up until then, most aging research had been carried out in hospitals or institutions where illness could mask normal age changes.

"There are no medicines, no treatments. It just allows you to monitor your own health."

Dee Milner





“Longitudinal studies demand commitment from everyone – researchers, staff, volunteers.”

James Fozard

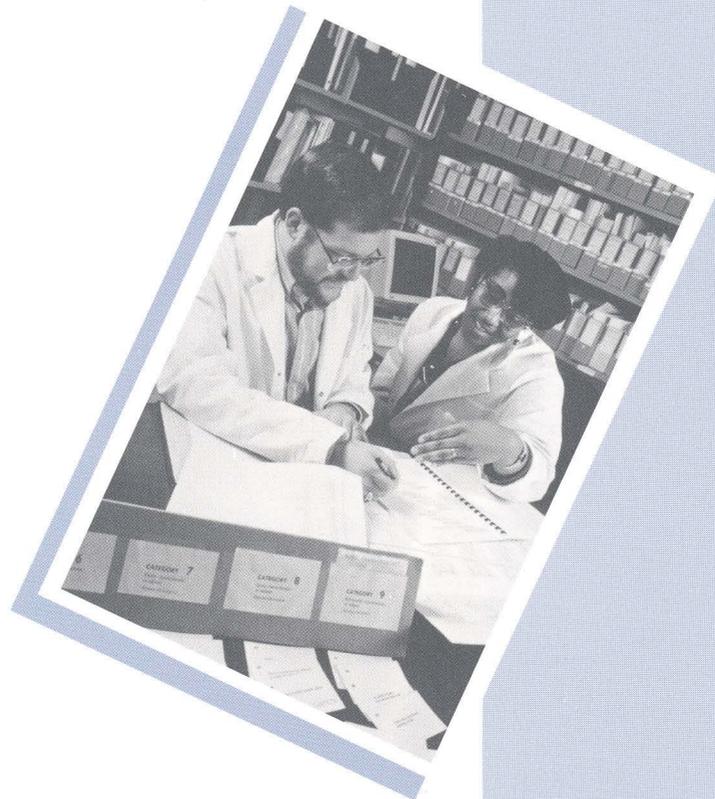
Convinced, Dr. Peter became the BLSA’s first volunteer. As Dr. Shock began building the scientific framework, Dr. Peter embarked on a personal quest to find others. He organized an intensive word-of-mouth campaign, starting with his own family, friends, and neighbors. Each of the early recruits was asked to find friends and acquaintances, and by 1967, more than 500 people had signed up.

The Founder’s Bulletin Board also tells the story of Arthur Norris, coordinator of the BLSA for 22 years, who implemented many of the original research designs. Renowned for his efforts to stay in close touch with volunteers, staff, and researchers, he knit together a cohesive and ongoing venture. One volunteer recalled that “he made me feel not like a guinea pig, but like a human being who is part of a great scientific enterprise.”

One of Dr. Peter’s early recruits was Andrew N. Thompson, the first husband of Mrs. Brands who has just received her certificate. When the study expanded to include women in 1978, Mrs. Brands recalls, the administrators called the long-timers, like her husband, and asked them to recruit their wives. Mrs. Brands herself was one of the first women to enter the study. But not, she recalls, before Eleanor Peter, who was William Peter’s widow.

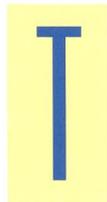
“She was wheeled in the door in a wheelchair at the age of 94, about a month before her 95th birthday,” says the Peter’s daughter, Jane Coffin, also a volunteer. “She had always wanted to be part of the study, and she was determined to live until they opened it to women.”

As the study passed its 35th anniversary in 1993, it included about 500 women and nearly 700 men. Its goal is to expand, with new recruitment efforts focusing on women and minorities.



*Data from
BLSA bone scans
help show when
and how fast bone
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various ages.*

AT THE CUTTING EDGE



he next test on Louise's schedule is labeled "bones." It is in fact a measurement of both bone density and body composition using a state-of-the-art scanning device called the Dual Energy Xray Absorptiometer or DEXA.

Bones lose some of their density with age, an example of an aging process that is linked, through a transition not yet completely understood, to a medical condition. Bone loss can lead to brittle bones or osteoporosis. Osteoporosis is especially common among older women, although it also occurs in men, according to Jordan Tobin, who studies osteoporosis and osteoarthritis in a section of the GRC's Laboratory of Clinical Physiology. Data from BLSA bone scans help show when and how fast bone loss occurs at various ages.

The DEXA has an unassuming look. There is a long, narrow cushioned surface, like a doctor's examining table, and a small scanning arm. The arm is attached so that it rests about a foot above the head of the person reclining on the table. Beneath the cushioned surface, however, is an array of computer hardware that constitutes some of the most sophisticated scanning equipment now available.

The scanning arm moves from head to foot, taking its multiple measurements very quickly and at very low doses of radiation – “less than natural background radiation,” points out researcher Tracey Roy. On a nearby computer screen, a slowly evolving image of Louise’s bone structure marks the progress of the scanning arm. Two more times the scanning arm makes a sweep, measuring bone density in the lower part of the spine and the hip.

The DEXA tests are playing an important role in the BLSA’s Perimenopausal Initiative, a special study-within-the-study, which is examining three major factors — hormones, bone density, and body composition — and how they are affected by menopause. This study will take an intensive look at what precisely happens before, during, and after menopause in 100 white and 100 African-American women.

“We think that even before menopause there are things happening in bone, maybe in body composition, certainly in hormones,” explains Dr. Tobin. “This study will let us find out more about the rates of change and, most important, the interrelationships among these factors.” It will show, for example, how obesity is related to estrogen levels and how hormone levels interact with bone turnover (the process of bone loss and replacement), which speeds up during menopause. Because the BLSA participants in this particular study come to Baltimore every 3 months (for one morning),



“That’s the strength of this building... this potential for studying interrelationships that you can’t do anywhere else...”

the Perimenopausal Initiative will be able to track closely the changes that occur during menopause and provide more insight than has been available up to now.

“I really feel like sort of a pioneer,” says Rosalie Carr, a BLSA volunteer who is on her first visit and has signed up for this initiative. “Menopause used to be something you couldn’t talk about. I’m determined to talk about it. At least the next generation of women will know more than we do.”

Data from the Perimenopausal Initiative will also be used to measure changes in cholesterol and other fats in the blood, since women, as they pass through menopause, develop a higher risk for heart and blood vessel diseases. Another GRC research group will carry out these tests. “That’s the strength of this building,” says Dr. Tobin, “this potential for studying interrelationships that you can’t do anywhere else and the different kinds of expertise and laboratories in one place.”

The last test on Louise Capone’s schedule is hearing. At a desk in the hearing room, she first fills out a questionnaire on which she reports any difficulties in hearing that she herself has noticed. Then, in a small booth that blocks outside noises, she listens to a series of sounds of varying intensity, signaling with a push-button device whenever she hears one.

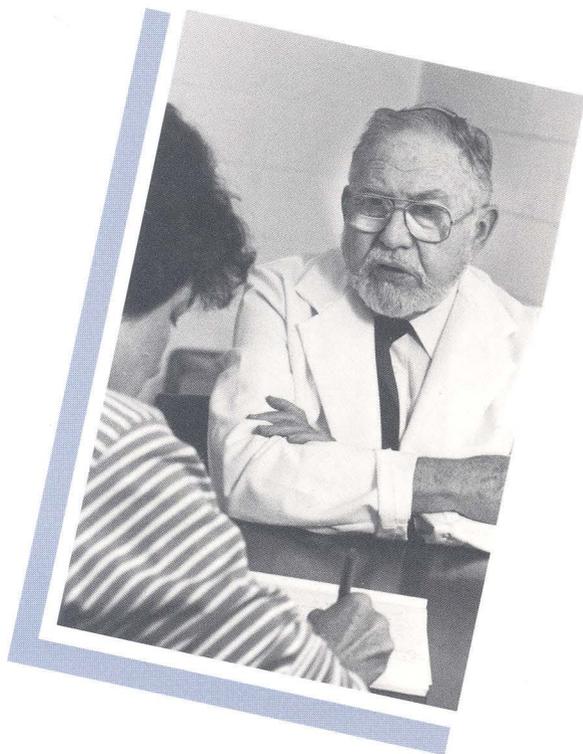
As part of this test, researcher James Wood plays a tape that sounds like people talking at a party. This is the babble threshold test, he explains. One sentence is made to stand out above the background babble, and the participant must repeat the last word of the sentence. Sometimes it's a word that makes sense in the context of the sentence, sometimes it is not. The percentage of word recognitions is used to determine babble threshold.

Sandra Gordon-Salant, a BLSA Guest Investigator from the University of Maryland, is working with the data from these tests to learn whether self-reported difficulties in hearing are predictable from the results of the babble threshold test. Because this study is just getting underway, no longitudinal findings will be available for several years — not until participants have gone through at least two cycles of testing. Eventually, though, the results will provide a clearer picture than is now available of the kinds of hearing loss that occur over time.

BLSA data on hearing have already surprised researchers on one front. In another study, Dr. Gordon-Salant and her BLSA colleagues have looked for links between hearing loss and three other factors — smoking, alcohol use, or high blood pressure. So far there is a suggestion — only a suggestion, she emphasizes — that high blood pressure in women may be linked in some way to a loss of hearing. More research will follow up on this possibility.



This sequence of events — data collection, analysis, findings, surprises, new questions — is a familiar one at the BLSA. “Many more surprises concerning the aging process are likely to be forthcoming,” notes Reubin Andres, Clinical Director of the NIA and chief of the GRC’s Laboratory of Clinical Physiology. “We did not think up all the important questions in the beginning....The questions never end, they just get more complex.”

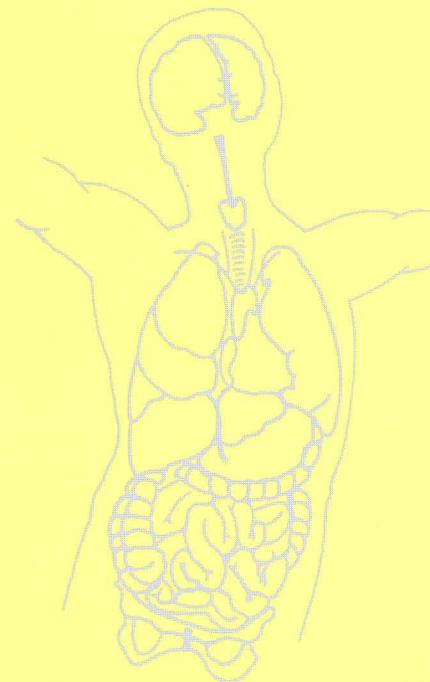


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Reubin Andres, M.D.

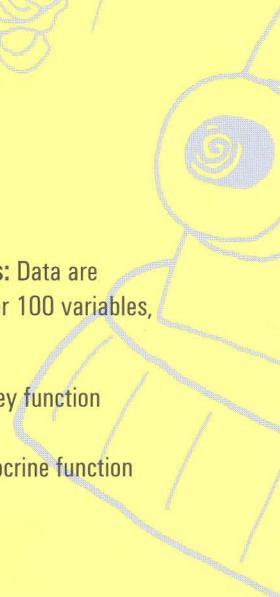
The BLSA: Gathering, Studying, Storing, and Disseminating Data

1 Volunteers: BLSA data come from studies with more than 1,100 volunteers from their twenties to their nineties who return every 2 years for two-and-a-half days of testing. In 1993, there were 675 active male participants and 503 active female participants. Recruitment goals call for more women in the perimenopausal period and African-American men and women.



2 Assessments: Data are collected on over 100 variables, including:

- ◆ heart, lung, and kidney function
- ◆ immune function
- ◆ metabolism and endocrine function
- ◆ body composition
- ◆ sensation
- ◆ cognition
- ◆ personality factors
- ◆ dietary history



3

Researchers and Students:

The BLSA data are used by numerous researchers and students. They include scientists who are:

◆ *Affiliated with the GRC:*

Investigators from laboratories at NIA's Gerontology Research Center conduct research involving BLSA participants.

◆ *From collaborating institutions:*

Pre- and post-doctoral students, faculty, and scientists from other academic centers collaborate, either at the GRC or from their own institutions. More than 250 scientists and physicians received research training or collaborated with GRC staff scientists in the study's first 35 years.

5

Dissemination: The results of studies get to the medical and scientific community and the public via:

◆ *Journal articles:* More than 600 reports of BLSA findings had been published in the scientific and medical literature as of the study's 35th anniversary.

◆ *Publications:* Occasional technical reports have summarized BLSA findings on men and women in the study.

◆ *Media reports:* A multitude of newspaper and television feature stories have told the story of the BLSA and reported many of its findings.

4

Data Storage:

BLSA data are stored in:

◆ *Information Archives:*

Data sets associated with specific procedures are stored for ongoing and future longitudinal studies by GRC scientists and collaborators.

◆ *Tissue Bank:* Frozen skin and fibroblast samples are stored at NIA's Aging Cell Repository where they are available to qualified researchers.

◆ *Serum Bank:* Frozen blood serum is stored at the GRC for research by NIA scientists and collaborators.

FINDINGS

THE AGING BODY

F eet moving rhythmically, Lawrence Nielsen, a BLSA volunteer since 1963, strides at the measured pace set by the treadmill's moving belt, body bent forward, eyes ahead, intent, focused on the steady muscular rhythms of this test which measures physical fitness levels and detects latent heart and blood vessel problems.

Cardiologist Jerome Fleg and technician Jeanette Wright stand at Dr. Nielsen's side, taking his blood pressure at intervals and monitoring the electrocardiogram (ECG) and other readouts on the nearby computer. After a few minutes the treadmill's pace increases, the moving belt slants upward; ECG lines race across the computer screen.

Later Dr. Nielsen will remark that this is "a fatiguing test, but fun; you push yourself to the limit." Now, more than 10 minutes into the test, he signals that he is reaching that limit, and a few seconds later the pace relaxes and the moving belt comes to a stop. He walks in place for several seconds and then sits down as the instruments record the gradual return of his blood pressure and pulse to normal levels.

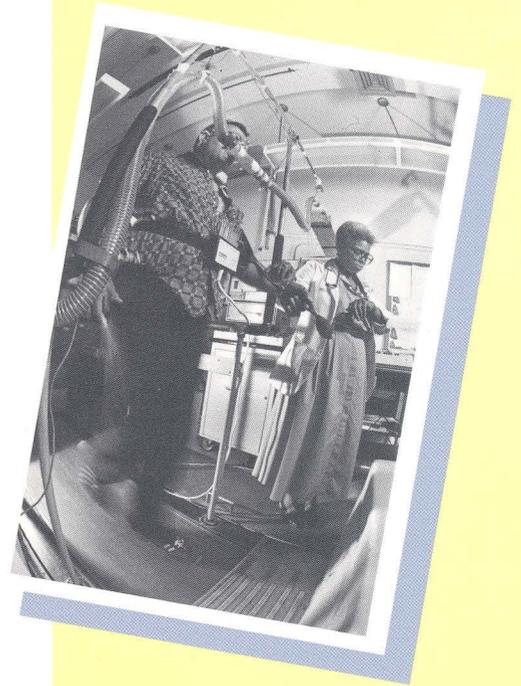
Most of the BLSA tests, like the treadmill, are designed to assess the physical changes that come with age. Following are a few of the key findings that have emerged to date on the aging body.

The heart adapts with advancing age.

The treadmill tests have shown, over the years, that the older heart adapts to the effects of age. While it is unable to increase its pumping rate during exercise as much as a younger heart, it makes up for this by expanding to a greater extent, delivering more blood per beat. In other words, the healthy, exercising older heart increases its output in a somewhat different but just as efficient manner as the younger heart.

On the other hand, coronary artery disease (CAD) does increase as people age. Studies using BLSA treadmill data show that CAD is more prevalent than previously thought, even in people without symptoms, according to Edward Lakatta and Jerome Fleg, of the Laboratory of Cardiovascular Science.

In one well-known study, they gave 233 men small doses of the radioactive element thallium during maximal treadmill exercise and then used a thallium scan to assess the adequacy of blood flow to the heart. This technique, says Dr. Fleg, revealed that more than half of the men in



*“It’s a fatiguing
test, but fun.*

*You push yourself
to the limit.”*

Lawrence Nielsen, M.D.

The Vascular Initiative

The BLSA is one part of a wide-ranging Vascular Initiative at the GRC. This group of interrelated studies is examining blood vessels and blood flow and how they are related to heart disease and stroke in African-American and white BLSA participants.

For example, could the stiffening of blood vessels that often occurs with advancing age have something to do with the fact that the heart muscle thickens with age and the heart's compartments, its ventricles, fill more slowly? To learn how these developments are related, Drs. Lakatta and Fleg in the Laboratory of Cardiovascular Science are collecting and analyzing data on participants' blood vessels and heart function.

Or could differences in blood vessel stiffening and circulation help explain the differing rates of stroke between African Americans and whites? Another study, conducted by the BLSA's Medical Director, Jeffrey Metter, is looking at blood flow in the brain in these two groups.

their 70s had evidence of CAD, although many had had no overt signs or symptoms of heart disease. In contrast, conventional clinical history and resting electrocardiograms had a much lower detection rate, finding CAD in only 22 percent of the men in the same group. The findings suggest that this kind of exercise screening could be more useful than standard clinical criteria in detecting CAD in people who have a family history or other risk factors for the disease.

High blood cholesterol at older ages remains a risk factor for cardiovascular disease.

Other studies with BLSA data have yielded new information on cholesterol and cardiovascular disease (CVD). High blood cholesterol, according to these findings, remains a significant risk factor for cardiovascular disease, even into very old age. Earlier studies of cholesterol and CVD, including those used to establish cutoff points for treatment of high cholesterol, had focused primarily on middle-aged men. BLSA data show that people ages 65 to 96 with high cholesterol levels continue to be at increased risk. "Even at the very end of life," says Dr. Andres, whose Laboratory of Clinical Physiology made this discovery, "in men without evidence of CAD, cholesterol levels were a risk factor." The finding suggests that preventive measures, such as a prudent diet, continue to be important into old age.

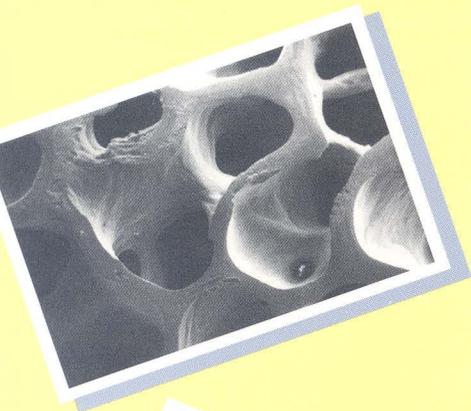
Scientists examine factors that affect bone loss and arthritis.

Bones continually lose cells and replace them throughout life, but around age 35, the rate of bone loss speeds up, gradually gaining on and outstripping bone replacement. Among women, bone loss speeds up again around the time of menopause. On the average, as women age they lose more than half the density of the top of the femur or hip bone, and 42 percent of the density of vertebrae in the lower back. Men lose bone also but at a lower rate.

Ongoing studies with BLSA data are looking for factors involved in bone loss. One study found that the rate of bone loss is similar for young and old men. What was different was bone turnover (bone loss and replacement), according to Jordan Tobin from the Laboratory of Clinical Physiology. In the young men, the rate of bone turnover was high; in the older men it wasn't. Differences like these are intriguing because they provide new clues to the biological mechanisms that differ between young and old, mechanisms that may eventually explain why the prevalence of some diseases, like osteoporosis, increase with age.

Still another study is exploring the links between blood pressure and glaucoma, an eye disease that is much more common among African-American men and women than among whites. Drs. Fozard, Fleg, Metter and their colleagues at the Johns Hopkins Wilmer Eye Institute are studying long-term changes in the relationship between glaucoma and blood pressure.

Scientists at the GRC are also probing the basic cell biology of vessel stiffness, such as changes in the cells lining the walls of blood vessels. Taken together, the results of the Initiative will offer greater insight into changes in blood vessels on several levels and how these changes contribute to disease.



Arthritis is another focus of GRC scientists who are studying hand and knee x-rays to see if certain risk factors — body fat or bone density, for example — can be linked to arthritis. So far, excess fat (obesity) and body composition (percentages of fat and lean tissue) have been associated with arthritis of the knee in women; bone density does not appear to be a factor.

Physical fitness declines about 5 to 10 percent per decade on the average.

Oxygen use or consumption during exercise (the best measure of physical fitness) declines as people age. In each decade of adult life, otherwise healthy people experience a 5 to 10 percent decline in physical fitness by this measure. But like many age-associated changes, this decline in oxygen use is not inevitable. Older athletes maintain higher levels of oxygen consumption, for example, than people who are less active.

Scientists once thought that the decline in oxygen use was linked to decreases in thyroid function as people grew older. But a study of 184 BLSA participants showed that a major reason consumption of oxygen declined was that muscle mass was also declining. Muscle tissue consumes the vast majority of oxygen during exercise, and when it declines, oxygen use also declines.

Healthy bones (top) lose density with age, leading in some people to osteoporosis (bottom).

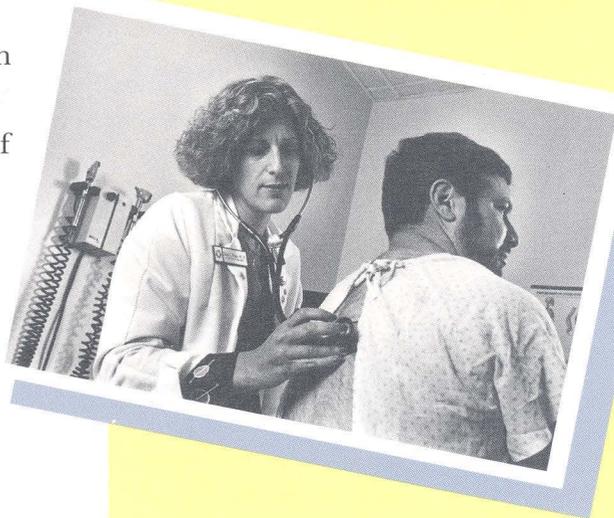
A related study has provided a clue to why, at any age, men have about a 20 percent higher measure of oxygen use than women. BLSA scientists hypothesized that the smaller amount of lean muscle mass in women could account for the supposed gender differences in physical fitness. To test this idea, they compared oxygen consumption to total muscle mass (rather than total body weight, the factor traditionally used in calculating oxygen consumption). Gender differences disappeared, suggesting that women's smaller muscle mass, not lower levels of physical fitness, may be the major factor in their lower oxygen consumption.

Fat around the abdomen is linked to heart disease risks.

While lean muscle tissue generally declines with age, the other side of the body composition coin is fat, which tends to increase with age. Analysis of BLSA data and other studies have shown that where fat builds up on the body may have something to do with health.

Fat around the waist, which is more common among men than women, goes with an increased risk for heart disease and diabetes. Fat around the hips, more common among women, does not. The BLSA's longitudinal data demonstrate that across the adult age span, increasing fatness around the abdomen is associated with lower

A team of nurses, nurse practitioners, and physician assistants carries out the clinical evaluation of each participant.



glucose tolerance, increased blood pressure, and shifts in levels of cholesterol and other fats.

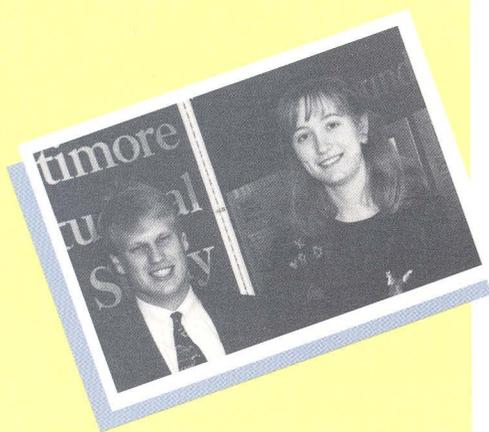
Moderate weight is linked to longer lives.

People who are very fat or very thin do not live as long as those with medium weights. Dr. Andres, whose laboratory has tracked the relationship between weight and mortality, also notes that BLSA participants who gained a moderate amount of weight over the years have lived longer, in general, than those who remained youthfully slim. These findings are now reflected in the ideal weight/height ratios recognized by the National Academy of Sciences and the Federal government.

Lung capacity falls by about 40 percent between ages 20 and 80.

In one BLSA test, volunteers fill their lungs with air and then force it out through tubes with various size openings. Known as spirometry, this measures lung capacity or pulmonary function (the total amount of air that can be expired in a single breath).

Over the years, spirometry has revealed that lung capacity falls with age and that the decline occurs regardless of other factors, such as how large the lungs were to begin with or how much an individual exercises. The bottom



line: About 40 percent of lung capacity is lost between ages 20 and 80, a decline that appears to be universal and due, therefore, purely to aging.

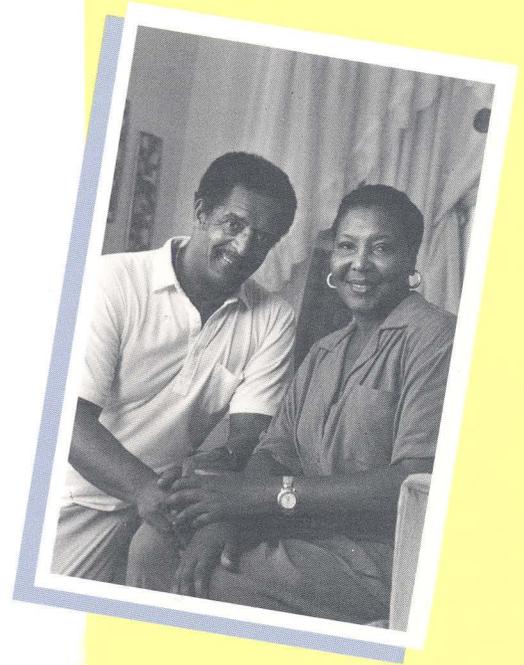
Lung capacity, however, can be lost more quickly because of smoking or a disease. Analyses of BLSA data have linked low lung capacity to subsequent illness and death, particularly to ischemic heart disease in BLSA men.

Standards for diagnosing diabetes in older people were too stringent, have been revised.

The ability of the body to metabolize sugar — glucose tolerance — declines with age and can lead to diabetes. But it does not always do so. In fact, BLSA data have shown that lower levels of glucose tolerance at older ages are often *not* associated with diabetes.

“BLSA data called attention to the fact that the standards in use in the 1960s for diagnosing diabetes were too stringent at older ages,” says Dr. Andres. “Use of these old standards resulted in the over-diagnosis of diabetes in middle-age and older people.” New standards were developed and the number of false positive tests for diabetes has dropped significantly since then.

Dr. Andres’ laboratory also explores the underlying processes that lead to lower glucose tolerance. “In aging,” he says, “the problem is not insulin secretion; it is that



Lifestyle and Time Use

The complex interplay between lifestyle and aging is an important focus of research at the BLSA. About 75 percent of BLSA men reported smoking in 1958, compared to 16 percent in the early 1990s. Participants also report drinking fewer alcoholic beverages in the later years of the study.

Researchers are also looking at how participants spend their time, through an activity questionnaire that has been filled out by each participant since 1966. The findings are complex, according to Linda Fried and her colleagues, Drs. Fleg and Fozard. In their study, older men were less active than younger men. Over several decades, however, all age groups have reported increased levels of physical activity.

Recently guest researchers Lois Verbrugge and Ann Gruber-Baldini of the University of Michigan found significant changes in time use among BLSA participants. Not surprisingly, men report less time spent in child-rearing activities than women, but that trend is changing.

cells are not as sensitive to the insulin as they were at younger ages.”

To study glucose tolerance systematically, Dr. Andres and his colleagues developed a technique that is now the internationally accepted method for determining glucose levels. Called the glucose clamp, the technique enables scientists to establish or “clamp” the glucose concentration level in the blood at a specified, higher-than-normal level. By measuring the blood levels of glucose regularly and then adjusting the rate of infusion of glucose, this specified level of blood glucose can be maintained.

The glucose clamp has given researchers a standardized, reproducible method of studying the body’s response to glucose in people who are young and old, thin and fat, with and without diabetes. The paper describing this technique is one of the most highly cited reports in the biomedical literature.

Nutrition: Scientists study nutrient intake, anti-oxidants.

Many BLSA men and women do not eat the recommended dietary allowances (RDAs) of some vitamins and minerals. Even in this well-nourished and health-conscious population, vitamin B6, magnesium, and zinc intake is low among substantial numbers of men and

women; iron intake is inadequate among many younger women; and calcium intake is low in women of all ages.

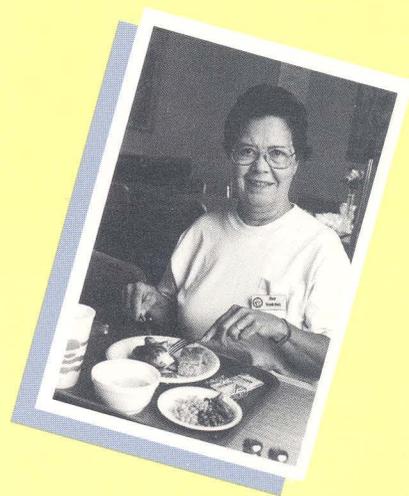
One former GRC researcher, Judith Hallfrisch, has found that BLSA participants with higher vitamin C levels also have high levels of HDL2-cholesterol, the “good” cholesterol that seems to protect against plaque build-up in the arteries. Vitamin C is one of the vitamins, along with beta carotene (related to vitamin A) and vitamin E, that are known as anti-oxidants.

Anti-oxidants help rid the body of harmful agents, called oxygen free radicals. Various studies around the country suggest that these vitamins may help protect against heart disease, cataracts, cancers, and other conditions that are more common with advancing age. Researchers at the BLSA are planning to see if the longitudinal data contain any sign of a link between the anti-oxidant vitamins and these or other diseases.

BLSA participants periodically keep diaries of what they eat and over time these have revealed significant changes in diet. Today, for example, participants on the average are consuming fewer cholesterol-rich foods and more dietary fiber than they were in the 1950s and ‘60s. These changes will be related to trends in disease incidence as the participants age.

After retirement, both men and women report more time spent socializing and in quiet activities; time spent in vigorous activity declines on the average.

The BLSA’s lifestyle and activity studies have taught researchers that it is impossible to describe aging within an individual without taking into account the era during which aging occurs; aging from 60 to 70 years old was different in the 1950s than it is in the 1990s.



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Different aspects of hearing decline at different rates.

Declines in hearing can begin in the twenties but often go unnoticed because it is only the high-frequency tones that become harder to hear at first. Most people are not aware of hearing problems until low-frequency tones, which are more common in speech, become difficult to hear. On the average, low-frequency hearing begins to fade between the ages of 60 and 70.

Men lose their hearing more than twice as fast as women, according to a study that tracked results of BLSA hearing tests on volunteers of all ages. Jay Pearson, Larry Brant, Jeffrey Metter, and their colleagues at the GRC found that both men and women had a gradual loss of hearing with age, but after age 30, men's average rate of loss speeded up until it was about twice that of women.

This finding confirmed previous cross-sectional studies showing that women on the average have more sensitive hearing at all ages and that men's hearing declines more quickly. But this study, the longest and largest longitudinal examination of hearing in the world, suggests that the earlier studies may have seriously underestimated the rate of hearing loss in younger men. The next step at the BLSA is to determine whether certain factors — noise exposure, high blood pressure, systemic illness, or drug use — could account for these differences between the sexes.

Studies of eyesight, cataracts, and contrast sensitivity explore changes with age.

Vision tends to decline with age, even without an eye disease such as cataracts or glaucoma. However, the ability to see fine detail changes little until one's seventies.

The eye's lens — three of them — become more cloudy and harden as we age, making it more difficult to see nearby objects, and leading in some cases to cataracts that block vision completely. One BLSA study tested the theory that this cloudiness was linked to heart attack or coronary artery disease but found no association. In another study using BLSA data, collaborating researchers from the Johns Hopkins' Wilmer Eye Institute found that volunteers who had higher levels of calcium and vitamin E in blood samples had a lower risk for cataracts.

Contrast sensitivity — the ability to see differences between light and dark — declines with age along with other measures of eyesight. Contrast sensitivity, however, may be a better gauge of how we see, according to Dr. Fozard and Frank Schieber, a collaborating researcher from the University of South Dakota. Their studies have shown that participants' reported difficulties with vision, particularly glare and seeing peripheral objects, correlates with their scores on the BLSA's

...the ability to see fine detail changes little until one's seventies.



contrast sensitivity test. Contrast sensitivity may be more useful in predicting difficulties with vision, while driving for instance, than the vision tests currently in use. Transportation agencies are beginning to follow up on these findings, reports Dr. Schieber.

The big picture: Relationships between health and aging are complex and variable.

The overall number of medical diagnoses of all kinds recorded in BLSA participants increases almost fivefold — from two to more than nine — between the twenties and the nineties. Yet the amount of increase varies tremendously from one class of diagnoses to the next. “Study after study reminds us that there is no simple relationship between health and aging,” says Dr. Fozard. “People have different genes, different lifestyles, different environments. All of this adds up over time to differences in aging. In fact, our older participants are much more heterogeneous in terms of their health than our younger participants.”

When asked to rate their own health, most BLSA participants of all ages choose “good” or “excellent” (rather than “fair” or “poor”). Fewer older participants, however, choose “good” or “excellent.” These self reports of health status have been linked to other factors. One is the number of medical diagnoses that a person has and

another is disposition; people who score higher on “neuroticism” in the personality testing (see page 46) tend to report poorer health.

BLSA studies show that measure of health can have different meaning in different age groups. For instance, in one study Dr. Metter identified a group of participants in their eighties who had no cancer, heart disease, or stroke. In a cross-sectional analysis, he compared their medical profiles to a group of men in their sixties who were also free of these diseases. However, the men in this second group did develop cancer, heart disease, stroke, and other medical problems by the time they were in their eighties. The lesson was that the two groups were not really comparable — more evidence that the proper study of aging and health requires a longitudinal study.

Mental Functions, the Brain, and Aging

Using BLSA data, researchers can approach the study of aging from different directions. Consider these three approaches to research on the aging mind.

◆ Changes in mental functioning

Longitudinal studies of mental functions have shown that some, like memory and problem solving, remain strong until at least age 70 and even then do not decline in a substantial proportion of people. These studies have overturned the popular notion that aging is linked inevitably to declining mental skills.

◆ Health and disease

BLSA data are throwing light on what changes take place as the brain passes from a healthy state to a diseased state. Research in this area can pinpoint early markers of disease. Studies have shown that a decline in immediate visual memory is linked to the later development of Alzheimer's disease and that this marker appears well before other signs appear.

THE AGING MIND



With courtesy and an occasional flash of amusement, Alice Brands names objects in the pictures that researcher Jim Segal is showing her. “Wrench...apple...house...cat...” she recites. Jim turns the page.

“Cup...book...horse...hammer...” Each page is divided into four squares with pictured objects, and she must name them beginning at the top left-hand corner. Flower...mouse...lemon...vase...”

“Now,” he warns, “it’s going to get harder.” The page turns to one that’s blank. There are no pictures — only the lines that divide it into four parts.

“Which corner of the page *was* the lemon in?”

“*That* one.” Mrs. Brands points to the top left quadrant, not without a touch of triumph.

Smiling, volunteer and researcher continue the game, making their way through all the variations of the cued selective reminding test, which measures short-term memory. After that, there’s the rest of the Neuro-psychological Battery, which is given to BLSA participants age 60 and over. Mrs. Brands draws geometric forms after seeing them on a card; says as many words as she can think of that fall into the category of fruits and

vegetables; writes a sentence (“Why am I doing this?”); and draws lines between numbers strewn at random on a page.

At 83, Mrs. Brands’ neuropsychological functioning is strong. In fact, the stereotype of dull-witted old age is rapidly being put to rest by results of tests like these with volunteers like her.

Mental skills may not decline as commonly or as early as once believed.

It’s true that some mental skills do begin to decline at about age 70, but this is highly variable. At the BLSA, more than a quarter of the volunteers over age 70 show no decline in memory. Some continue to perform well on the cognitive tasks as they move into their eighties.

The brain, like the heart, may do more adapting and less declining with age than previously thought. Take problem solving: When faced with a task, older volunteers may draw on different capacities to complete the task. For example, they may not use memory as well as a younger person but draw upon a greater reservoir of information and experience to solve the problem. At least up to age 70, there is little or no decline in problem solving.

◆ **Biological changes in the brain**

Researchers are now following up on these earlier findings by examining changes in the structure and function of the brain. A 9-year study that began in 1993 uses brain scans to learn whether cognitive changes in BLSA participants, e.g., in visual memory and mental skills, can be related to biological changes in the brain.

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Moreover, when mental skills do decline, it may be later than commonly believed. The BLSA has studied “vigilance,” which describes the ability to respond to infrequent and unpredictable stimuli. In this test, volunteers watch a mock-up of a wall clock for an hour, reporting whenever the minute hand jumps two spaces instead of one. At age 65, men appear to be as vigilant, or more so, than those who are younger.

After age 70, vigilance declines sharply in many people, and more time is needed to respond to the stimuli. This suggests that a reduction in the ability to react is a true effect of aging, though it may occur at a later age than was once believed.

Some gender differences have emerged in BLSA studies of mental functioning. Women, for example, do better at remembering words and men have higher scores when it comes to immediate recall of numbers. However, men and women have similar rates of decline in memory for the most part. They forget sentences at identical rates, and older men and women recall fewer sentences after 24 hours than younger men and women.

Researchers at the BLSA, searching the longitudinal data for early markers of Alzheimer’s disease, have discovered that immediate visual memory may begin to fail long before this devastating disorder is detected by other methods.

Following up on this finding, Susan Resnick in the GRC's Laboratory of Personality and Cognition is studying changes in the structure and function of the brain. Using magnetic resonance imaging and positron emission tomography, this study will follow a group of BLSA volunteers for a period of years to learn how changes in visual memory and other mental functions are linked to changes in brain structure or function.



“We both felt strongly about making a contribution to our fellow man... And now I look forward to seeing the staff. It’s like going home.”

Alice Brands

The Five-Factor Model of Personality

Many psychologists use the five-factor model, which was refined at the GRC, to study personality. Each factor is defined on a scale of related traits, such as those listed below (e.g., someone who measures low on “neuroticism” is more likely to be calm; someone who measures high is more likely to be a worrier). BLSA data show that these basic dispositions endure through adulthood.

Neuroticism

Examples:

Calm - Worrying

Self-satisfied - Self pitying

Unemotional - Emotional

Extroversion

Examples:

Reserved - Affectionate

Loner - Joiner

Quiet - Talkative

THE AGING SPIRIT

Seated at the large wooden table in the BLSA dayroom, several volunteers attack a questionnaire that will probe their reactions to daily events, ways of coping with problems, customary attitudes and feelings and motivations — all the traits and dispositions that add up to personality.

Personality remains stable over the life span.

Personality is a constant in our lives. BLSA studies have produced conclusive evidence that age does not alter it, even in the face of serious physical problems. By following older men and women over many years, Paul Costa and his colleagues in the GRC’s Laboratory of Personality and Cognition have exploded one stereotype after another. As BLSA participants age, they are no more conservative or cranky or prone to complaining about their health than they were when young.

The five-factor model of personality, used and refined at the GRC and adopted by many researchers elsewhere, divides personality into five dimensions labeled neuroticism, extroversion, openness, agreeableness, and conscientiousness. Drs. Costa and Robert McCrae have found that the dimensions of neuroticism and extroversion are powerful predictors of psychological wellbeing, even

when the personality factors are measured years earlier. That is, people who scored high on measures of neuroticism when young tended to have low levels of wellbeing later in life; those with higher extroversion scores were more likely to report greater wellbeing later.

Nor does the ability to cope with stress decline with age, according to BLSA data. Personality traits help determine how one copes with a stressful situation. Extroversion, in one study, was linked to coping strategies labeled “rational action,” “positive thinking,” “substitution,” and “restraint.” “Open” individuals were more likely to use humor in dealing with stress, “closed” individuals more likely to use faith. The choice of coping strategies depended on both enduring personality traits and the specific situation to which people were responding.

BLSA findings on the stability of personality lay the groundwork for studies of personality change. When it does occur, is it the result of a particular disease process? There is some evidence that personality change is among the earliest markers of dementia. Studies are now exploring what specific aspects of personality change with the onset of Alzheimer’s disease.

Openness to experience

Examples:

Down-to-earth - Imaginative

Conventional - Unconventional

Prefer routine - Prefer variety

Agreeableness

Examples:

Ruthless - Soft-hearted

Suspicious - Trusting

Critical - Lenient

Conscientiousness

Examples:

Disorganized - Well-organized

Late - Punctual

Aimless - Ambitious

*“We need not
worry that we will
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with age or
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We need not dread
our future.”*

The BLSA personality studies stand as a good example of the BLSA as a whole. They encompass a solid body of accomplishment and a vision of future possibilities. They demonstrate what can be achieved through the patient, meticulous gathering of measurements over many years, the careful building of data banks, and finally the analysis of this unique longitudinal data. And like many BLSA findings, those on personality have opened a new perspective on aging. Dr. Costa has put it this way: “We need not worry that we will become crotchety with age or that only firm resignation can save us from despair and the fear of death. We need not anticipate increasing social isolation and emotional withdrawal from the world. There is no reason to think that our interests will atrophy or that our values and opinions will become increasingly rigid and conservative. We need not dread our future.”

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How the Body Ages

The Baltimore Longitudinal Study of Aging is yielding information on how people age *on the average*. It is important to remember that many people do not conform to these averages.

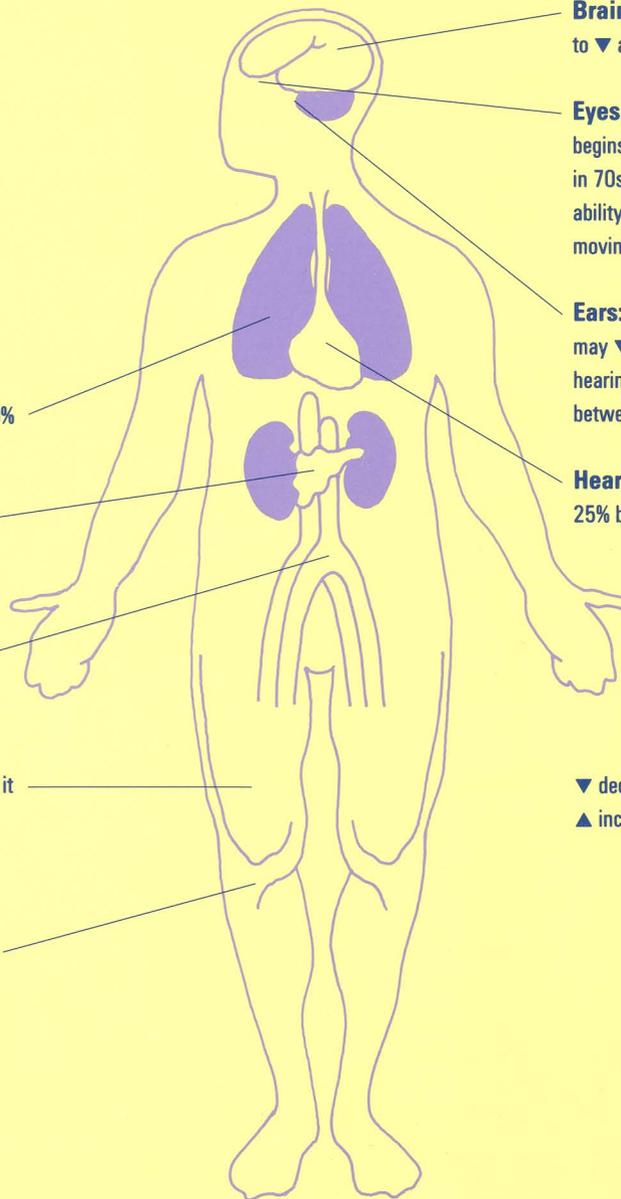
Lungs: Maximum breathing capacity ▼ 40% between ages 20 and 80.

Pancreas: Glucose metabolism declines progressively, as measured by glucose tolerance test.

Blood Vessels: Arterial walls thicken; systolic blood pressure ▲ 20-25% between ages 20 and 75.

Muscles: Muscle mass declines and with it oxygen consumption during exercise ▼ 5 to 10 percent per decade. Hand grip strength ▼ 45% by age 75.

Bones: Bone mineral is lost and replaced throughout life; loss begins to outstrip replacement around age 35; loss speeds up in women at menopause.



Brain: Memory and reaction time may begin to ▼ around age 70.

Eyes: Difficulty focusing on close objects begins in 40s; ability to see fine detail ▼ in 70s. From age 50, susceptibility to glare ▲, ability to see in dim light ▼, ability to detect moving targets ▼.

Ears: Ability to hear high-frequency tones may ▼ in 20s, low-frequency in 60s; men lose hearing more than twice as quickly as women between ages 30 and 80.

Heart: Heart rate during maximal exercise ▼ 25% between ages 20 and 75.

▼ decrease
▲ increase

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