

Secrets to a Longer, Healthier Life Studying Exceptionally Long-Lived Families

People who live in good health for 100 years and longer aren't just lucky. Researchers have found that those who live an exceptionally long and healthy life often have company... in their very own families. Scientists are now aiming to better understand the **genes**, lifestyle or other factors that make these people so unique. Hopefully, we can all benefit from their findings.

Recent studies have revealed that, as a group, people who lived to be 100 years or more (centenarians) were healthier at younger ages than their peers. The findings suggest that unique "protective" factors against disease and disability may have been at work throughout their lives, not just at very old ages. If the factors that lead to exceptional survival begin working much earlier in life, and if they could be found, they might point the way toward interventions to lengthen healthy lives. So what exactly is it that protects these people and contributes to their extraordinary survival?

Genetics may play a role. Studies of very old people and their families in specific populations—such as those in Iceland and Okinawa, and in

Ashkenazi Jewish, Mormon and Amish communities—have shown that exceptionally long life runs in families. Other studies

show that centenarians' siblings have a mortality risk at any age throughout their adult life of about half that of the general population. Centenarians' children tend to be healthier than their peers, too. They have lower mortality rates from cancer and heart disease, and fewer age-related diseases such as heart disease, hypertension, diabetes and stroke.

More specific findings support the idea that genes contribute to exceptional survival. For example, one form of a gene called apolipoprotein E seems to be associated with longer life, while another form has been linked to an increased risk of heart disease, stroke and Alzheimer's disease.

While genes likely play a role in exceptional survival, non-genetic factors that tend to run in families, such as lifestyles, can also contribute. For example, a family's eating and exercise habits, smoking habits and other factors have an effect on how long



family members live.

NIH's National Institute on Aging (NIA) is funding a variety of studies to better understand the factors

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Definitions

Genes

Stretches of DNA, a substance you inherit from your parents, that define characteristics like height, eye color and how likely you are to get certain diseases.

Genetics

Having to do with your genes.

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that lead to exceptional **longevity**. A major research effort called the Longevity Consortium was begun by NIA in late 2000. It brings together leading scientists from more than 30 institutions to exchange ideas about longevity research and develop new collaborations. Some members are trying to identify longevity-related genes and pathways in animal models. Others continue to study special populations of people in the search for genes associated with longevity.

Another ongoing study, the Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE), aims to understand the effects of eating fewer **calories** over time. Several animal studies have shown that restricting calories can extend the average life span of some laboratory animals and delay age-related problems. Whether a similar effect holds true in people remains to be seen. This study is still in an early phase.

Given family patterns of long life and good health, NIA has begun a



Definitions

Calories

A measure of the amount of energy stored in food.

Longevity

Long life.



The Long Life Family Study:

www.longlifefamilystudy.org

Bound For Your Good Health:

www.niapublications.org/pubs/bfygh.asp

major study to collect information on long-lived families. Winifred K. Rossi, deputy director of NIA's Geriatrics and Clinical Gerontology Program, said, "We want to learn why these exceptional families age so well."

Rossi is the program official for NIA's new five-year, \$18 million effort to learn more about the factors that contribute to a long, healthy life. It's called the Long Life Family Study (LLFS), and it's now recruiting families to participate. Usually, studies look at health problems. The LLFS is unique, Rossi said, because by following exceptional families over time, the researchers are focusing on what protects against disease and disability.

"We want to understand more about their health, lifestyle and their genes," Rossi explained. "Right now we don't understand all of the things that contribute to healthy longevity in these unique families. We hope that the LLFS will identify factors that can help other people live as healthy as possible as long as possible."

You may be able to help researchers discover the secrets to a longer, healthier life. The LLFS investigators are looking for people age 80 years or older who have at least one living brother or sister age 80 years or older.

If this describes you and your family, please go to the study web site <http://www.longlifefamilystudy.org/> or make a toll-free call to one of the recruitment offices listed below to get involved:

Boston University:
1-888-333-6327

University of Pittsburgh:
1-800-872-3653

Columbia University, New York:
1-800-304-4317

After you sign up, someone from the study will call you and ask for more information about your family. Calls may be followed by home visits, where researchers take physical measurements and blood for analysis.

"The more families we get, the better the chance we can find robust results," Rossi emphasized. "We want to enroll as many families with long-lived members as possible." ■



Wise Choices Tips for a Healthy, Long Life

The Long Life Family Study aims to reveal the factors that lead to exceptional survival and teach us ways to lengthen healthy lives. In the meantime, we already know about some things that can help your chances of living a healthy, long life. You're probably already familiar with them from when you were a kid:

- Eat your fruits and vegetables.
- Don't smoke.
- Rest enough.
- Exercise several times a week.
- Monitor your health.
- See your doctor regularly.

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Office of Communications
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Building 31, Room 5B38
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Editor Harrison Wein, Ph.D.

wein@od.nih.gov
Tel: 301-435-7489 Fax: 301-496-0019

Contributors

Carla Garnett, Margaret Georgiann
(illustrations) and Harrison Wein.

Aches in Your Legs

Understanding Peripheral Arterial Disease

If you're past age 50, you may have resigned yourself to feeling a few more aches these days. However, if you've had pain or cramping in your legs when you're walking that goes away when you stop, don't shrug it off. It might be an early warning signal of a serious and sometimes-silent disorder called peripheral **arterial** disease (PAD).

Just like arteries in the heart, those in the lower legs can become clogged with fatty deposits. Imagine your arteries are a complex highway system. Fatty deposits, also known as plaque, are the traffic jams that limit blood flow. Clogged arteries—blood-flow traffic jams—anywhere in the body increase the risk of heart attack and stroke.

Between 8 million and 12 million people over age 50 have PAD. Many never notice any symptoms. PAD symptoms include heaviness in your legs, awakening at night with pain in your lower legs, and pain or cramping in the legs when you're walking that seems to lessen with rest. A lot of people who have these symptoms don't tell their doctors. They simply accept the discomfort as part of growing older. Another sign of PAD

that people may notice but dismiss is a change in the color of their feet.

Whether painful or silent, undiagnosed PAD is too dangerous to ignore. That's why NIH's National Heart, Lung, and Blood Institute (NHLBI) recently started a campaign to tell more people about the disorder, joining with 40 other organizations across the U.S. to raise awareness about PAD.

Campaign organizers want people to recognize the signs and alert their doctor if they notice the symptoms in themselves.

Those most at risk for PAD are people over age 50, especially African Americans. Smokers and former smokers, and people who have diabetes, high cholesterol or high blood pressure are also at risk. Those who have had **vascular disease**, heart attack or stroke, or have a family history of those disorders should also be on the lookout for PAD.

If you're over 50 or otherwise at risk, ask your doctor about being tested for PAD. A simple test called the ankle brachial index (ABI) can identify the problem. The ABI compares the blood pressure in your arm with blood pressure in your legs. Reduced



Definitions

Arterial

Related to arteries, the series of tubes that carry blood from the heart throughout the body.

Vascular Disease

A disease of the vascular system, the system of vessels that circulate blood throughout the body.



www.aboutpad.org
www.nhlbi.nih.gov/health/dci/Diseases/pad/pad_what.html



Wise Choices

Questions to Ask Your Health Care Provider

- Am I at risk for PAD?
- How can I lower my risk?
- Which screening tests or exams are right for me?
- What is my blood sugar level? If it's too high or if I have diabetes, what should I do about it?
- What is my blood pressure? Do I need to do anything about it?
- What are my cholesterol numbers? Do I need to do anything about them?
- If I have PAD, what steps should I take to treat it?
- Will PAD increase my risk for other conditions?

blood flow in the legs could signal artery disease.

Once PAD is detected, your doctor will offer several treatments to help clear out the blockages before they lead to more serious problems. Your doctor may tell you to get more exercise, if you don't have an active lifestyle. Recent results from a study of people with PAD showed that daily physical activity improves survival rates. Your doctor may also recommend changes to your diet and other efforts to lower high cholesterol and high blood pressure. Medications and surgery are also treatment options that can improve blood flow in the vessels.

What's most important is to take those aches seriously and seek help from your doctor. ■

Health Capsules

Insight into Ear Infections

Chronic infection or inflammation of the middle ear, the area just behind the eardrum, is a common problem for children. Technically called otitis media, this problem affects 3 of every 4 children at least once by their third birthday. Almost half of those who get them will have 3 or more ear infections during their first 3 years. A new study shows why the problem can be so persistent: bacteria can form a "biofilm" on the middle ear that helps them resist both the body's defenses and antibacterial treatments.

A biofilm is a rich community of bacteria attached to a surface by sugars that the bacteria produce. The structure created by the bacteria protects them from the body's defense system. Bacteria deep within the biofilm can also enter a metabolic state that makes antibiotics ineffective.

Previous studies showed that a biofilm grows on the middle-ear mucosa (MEM)—a mucus-secreting membrane in the middle ear—in chinchillas with otitis media. Researchers funded by NIH wanted to see whether children with chronic otitis media also have biofilms on their MEMs.

The researchers took MEM biopsy specimens from 26 children, from 2½ to 14 years old, who were undergoing a surgical treatment for chronic otitis media. For comparison, they took MEM specimens from three children and five adults undergoing another surgical procedure for the ear unrelated to otitis media. They then looked at the samples using a high-tech microscope that uses laser

light to produce a three-dimensional image of a specimen.

The researchers saw biofilms in 92% of the samples from children with otitis media. They confirmed the presence of disease-causing bacteria in the biofilms. In contrast, they didn't see biofilms in specimens from the people without otitis media.

This study supports the idea that chronic cases of otitis media, so common in children, are caused by the formation of biofilms. Recent research suggests that biofilms may also play a role in other types of chronic human infections. In order to develop better treatments for such infections, researchers are now investigating how bacteria form biofilms, and how these structures help them to resist both the body's defenses and antibiotic treatments. ■



www.nidcd.nih.gov/health/hearing/otitism.asp

Molecules in Blood Signal Preeclampsia

High levels of 2 proteins in the blood of pregnant women may be a warning sign of preeclampsia, a life-threatening complication of pregnancy.

Preeclampsia often occurs without warning. It may begin with mild symptoms, but can progress to severe preeclampsia and then to eclampsia—dangerously high blood pressure and convulsions. When preeclampsia is not severe, the high blood pressure it causes can usually be treated in the short term. Unfortunately, the only cure for preeclampsia is delivery of the baby.

The levels of two proteins circulating in the blood called sFlt1 and PlGF appear to be involved in the development of preeclampsia. Another protein called endoglin acts together with sFlt1 to induce a severe preeclampsia-like syndrome in pregnant

rats. Researchers thus set out to see whether endoglin might also be associated with preeclampsia in women.

They found that levels of endoglin were significantly higher in those women who, 2-3 months later, went on to develop preeclampsia. An increased level of endoglin was usually accompanied by increased levels of sFlt1. The risk of preeclampsia was greater for those women with the highest levels of both, but not for either alone.

High levels of both endoglin and sFlt1 early in pregnancy might be a useful early sign of preeclampsia. However, attempts to develop drug treatments targeting these proteins need to proceed carefully. Restoring normal blood pressure and blood flow to the mother could potentially harm the fetus. ■



www.nhlbi.nih.gov/hbp/issues/preg/preg.htm
www.nhlbi.nih.gov/health/public/heart/hbp/hbp_preg.htm



Featured Web Site Child Health and Human Development

www.nichd.nih.gov

This newly redesigned web site provides fast and easy access to a wide array of information about child health, developmental disorders, women's health and both basic and clinical research supported by NIH's National Institute of Child Health and Human Development.

The screenshot shows the NIH Child Health and Human Development website. At the top, there is a navigation bar with links for Health Information, Research, Funding, News & Media, and About NICHD. Below this, there are several sections: "Health and Human Development Information" with links to A to Z health & human development topics, Clinical trials, Health education, and Publications & materials; "Research" with links to Research Labs, Branches, Centers, & Divisions, Resources for researchers, Supported research networks & more, and Who can I talk to about my research?; "Funding for Research and Training" with links to Are you looking for funding information?, Career development and training/fellowships, Current Funding Opportunity Announcements (FOAs), Funding news flashes, Funding policies and peer review, and Research grants and contracts; "NICHD SPOTLIGHT: Zeroing in on preeclampsia" with a featured article about preeclampsia; "News Releases" with a link to New National Institutes of Health studies for Child Health and Human Development; "Molecular in Blood Level" with a link to Development of Preeclampsia Background—Pursuing the Causes of Preeclampsia; and "Funding News Flash" with a link to Transition to Electronic Submission of Grant Applications Using the 424 Forms. There is also a "More news releases" link.