



Agnes Buckley, one of the extraordinarily healthy elders whose genes and lifestyles are investigated in the Long Life Family Study, started working with watercolors a year ago, when she was ninety-five.

**Why is it that  
some people live  
so much  
longer than the  
rest of us? The  
quest to find out  
is alive and well.**

# Life Goes On

BY CHRIS  
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# One early summer Saturday,

Ted Clapp, a retired minister and psychologist, invited about twenty of his children, grandchildren, and great-grandchildren to lunch at his place north of Portland, Maine. He had set out some family treasures — including arrowheads found on his grandfather's farm, watercolor paintings by some "ancient ancestor," an antique trumpet, and his great-grandfather's sword — that he'd collected over his ninety years.

"I said, come and take whatever you think is right for you to have," Clapp recalls. His relatives obliged, relieving him of almost everything. "I was so grateful, because what do I want with those things? I don't worship them. They ought to be with the next generation."

The Clapp legacy, it turns out, has a lot more going for it than keepsakes. Some lucky combination of genetics and good living has blessed the family with an extraordinary record of long life. Many relatives have lived into their nineties, including Clapp's father, a couple of great-aunts, a sister, and his ninety-two-year-old brother Richard. The brothers remember meeting their great-grandfather, a twice-wounded Civil War veteran, before he died in 1922 at age ninety-two.

This rare clustering of longevity has brought the Clapps into the intellectual sights of Thomas Perls, a School of Medicine associate professor of medicine and geriatrics and director of the New England Centenarian Study. The Clapps, along with several hundred other families, are part of the Long Life Family Study (LLFS), a multi-site investigation funded by the National Institute on Aging (NIA) of the National Institutes of Health. Perls is a principal investigator of the study.

The LLFS findings could have implications well beyond helping people survive to extremely old age. That's because, in nearly two decades of studying longevity, Perls has discovered that people who live well beyond the average life expectancy also maintain their functional independence and are healthier than normal right up to the end. They're somehow shielded from cancers, strokes, Alzheimer's, and several other

debilitating diseases. Researchers such as Perls are hoping that whatever nature-nurture mix is protecting the Clapps and similar families could one day be harnessed for drug development, gene therapy, and behavioral interventions to keep the rest of us healthier longer, even if we don't live to 100.

"The reason these families are rare is that you need the right combination of a bunch of factors to stay healthy into your nineties and beyond," says Perls. "And what's right for one person may not be what's right for another. It's kind of like winning the lottery. Studying these families, who have so much in common in terms of both genetics and life circumstances, will go a long way toward solving these puzzles."

## CENTENARIANS AND SUPERCENTENARIANS

In the mid 1990s, Perls and his collaborators made a radical shift in the study of elderly people. Traditionally, says Winnie Rossi, NIA deputy director of geriatrics and clinical gerontology, much of the work on aging focused on the diseases associated with the elderly, searching for their causes and tracking their progression to find clues to potential therapies. "What we hadn't really done, and what seems so obvious now," Rossi says, "was to look at old people who aren't so sick. We can learn just as much from them about how to live longer and better."

Supported by the NIA, Perls began researching the lucky few (perhaps one in 10,000 people in the United States) who had reached 100 years of age. In 1994, he launched the New England Centenarian Study and started enrolling long-lived individuals from greater Boston. To date, about 1,500 people, consisting of centenarians, some immediate family members, and younger control subjects, have taken part in the study, which includes a detailed review of overall health, memory and cognition tests, and a blood sample. In 1997, the researchers began an offshoot study of those very rare individuals, known as "supercentenarians," who survive to 110.

"We demonstrated that these folks are a wonderful model of aging well," says Perls, who notes that 90 percent of the centenarians were functionally independent until an average age of ninety-two and 75 percent of them were the same at age ninety-five. So far, he and his fellow researchers have found at least one genetic variation (on chromosome four) associated with advanced age. They also found that while the extremely long-lived represent a wide variety of socioeconomic, religious, and educational backgrounds, they appear to have much in common. They are more often women (85 percent), rarely obese, typically nonsmokers, and seem better than average at handling stress.

Perls says most Americans *should* be living well into their eighties (eighty-six for men and eighty-nine for women), but don't because of our "rotten health behaviors." Americans, he says, "eat way too much red meat, are obese, smoke, and don't deal well with stress."

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**MEET THE HURLBURT CLAN, WHICH HAS EIGHT SIBLINGS RANGING IN AGE** from seventy-nine to ninety-six and is part of the Long Life Family Study at BU's School of Medicine and four other universities. At a recent gathering, there was much good-natured ribbing, some fond reminiscence, and a few thoughts about the secrets of long, long life.



**THE HURLBURT SIBLINGS** (below, clockwise from top left): Agnes Buckley (b. 1913); a gathering in Hingham, Massachusetts; Peter Hurlburt (b. 1928), with his wife, Joan; Mildred MacIsaac (b. 1916); Helen Caldwell (b. 1922); Peggy Condon (b. 1930); Muriel Gillooly (b. 1920); and, in an undated



photo (from left) Helen, Milly, Peggy, Evelyn, and their mother. **PETER HURLBURT:** I think what keeps everybody going is their hobbies. I write music, and I wrote a musical called *Ms. Biddy*. I've got a lot of songs that I wrote, and I taught figure skating for many years. But I still feel good, and I'm eighty.



**BUCKLEY:** I have been painting watercolors for the last year. I made a picture of my daughter Anne's house. I love drawing houses. **MACISAAC:** I do a lot of painting and reading. I belong to senior citizens clubs, and I exercise for an hour on Mondays and Thursdays. I don't like to sit around doing nothing.



So I keep going. **CALDWELL:** I do volunteer work. It keeps me busy. I sew, mainly quilts and aprons. **BUCKLEY:** I think if you eat good meals every day, that's a good thing. I like soup and vegetables. I eat all home-cooked vegetables. And it doesn't matter if you have a glass of wine once in a while.



PHOTOGRAPHS BY ROBIN BERGHAUS

**"None of us smoked or drank or really even swore in our house. We were never envious of each other as far as I know, and we all cared about each other."**



**THOMAS PERLS** suspects that genes of the longest-lived people are exceptionally influential.

#### INHERITED HEALTH

In addition to commonalities among individual centenarians and supercentenarians, Perls and his collaborators found that the children and siblings of the long-lived are in better-than-average shape. For example, by age seventy the children of centenarians had less than half the average rates of heart disease, stroke, diabetes, and high blood pressure of people their age. Brothers of supercentenarians in the United States survived, on average, nearly fourteen years longer than the average of those born in the same year. Sisters lived an extra ten years longer than average. These family effects were the catalyst for the Long Life Family Study.

"You can't truly dissect what is environmental and what is genetic by studying individuals," says Perls. Studies of twins suggest that for the general population, about 20 percent of one's life expectancy is determined by genes and the remainder is accounted for by environmental differences. But Perls hypothesizes that genetics plays a bigger role among those who live into their nineties and beyond. And because twin centenarians are too rare for a proper study, focusing on families is the next best alternative. "Families have a lot in common besides genes, from education to diet to health-care access," he says. "There are some very powerful statistical approaches we can apply to that data."

Besides unraveling the factors that contribute to disease avoidance and longevity, focusing on families with clusters of longevity has another research advantage: it allows the scientists to investigate the complex ingredients of a long life by following relatively young individuals over time.

Indeed, one of the unfortunate challenges in studying the oldest living people is that they die off rapidly

and often lack thorough medical records or the memory to recall the details of their history. The researchers needed to create a longevity score for families that would take into account relatives who died at a very old age as well as living family members who had reached advanced age but were still young enough for a thorough and ongoing study. The task fell to Paola Sebastiani, a School



VERNON DOUCETTE

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of Public Health professor of biostatistics. The big question, says Sebastiani, who spent a year developing and validating the statistical criteria, was "how do you rank these families and find a valid measure of their importance for study?"

Her answer was FLOSS (family longevity selection score). It requires at least two living siblings to be a minimum of eighty years old and takes into account the birth year of the oldest living relative, the ages of deceased siblings when they died, the gender of each long-lived relative, and the life expectancy (based on insurance actuary tables) of those still alive. To qualify for the LLFS, a family needs a FLOSS score of seven. While only about a quarter of those who volunteer to participate meet the mark, families with relatives who lived past 100 often score as high as forty.

"Centenarians are so rare that the FLOSS score values increase exponentially for families with people who die at such old age," says Sebastiani.

#### DATA ABOUT EVERYTHING

In addition to Boston University, there are four other LLFS sites: the University of Pittsburgh, Columbia University, Duke University, and the

University of Southern Denmark, each working with approximately 130 families. Researchers visit study subjects for about three hours, asking basic medical and demographic questions about disease history, medications, education, and household income. The subjects fill out surveys about how often they get together with family and how often they spend an entire day alone, whether they ever smoked, how much they drink, and their level of physical activity at various life stages. There's a memory test and tests of physical function,

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such as repeatedly getting in and out of a chair. The researchers also measure subjects' height, weight, arm span, waist circumference, heart rate, and blood pressure and take a blood sample for DNA analysis as well as for glucose, cholesterol, and

triglyceride tests. They follow up every year with more condensed questionnaires.

In short, they collect data on just about everything. The researchers recently started scouring that data for clues about the biology and the family dynamics that underlie these longevity clusters, and they expect to see some meaningful results within a year. Meanwhile, they're applying for more NIH funding to complete a genome-wide scan of the blood samples and to target specific genes that researchers suspect may play a role in longevity. Next, says genetics researcher Clinton Baldwin (GRS'86), a MED professor of pediatric medicine and a Perls collaborator, "the scientists will try to identify what exactly about those genes is different and beneficial."

The DNA data from both the centenarians and the LLFS will be archived in a searchable NIH database, allowing other researchers to try to replicate the results in different populations.

"We may need to go back to animal studies on specific genes to understand them more clearly," says Rossi of the NIA. "The next phase is to find out what can be done in terms of interventions. Could we develop an intervention that takes multiple diseases into account?"

Indeed, because the very long-lived seem immune to so many diseases, Perls and his collaborators are sharing data with researchers at BU who study Alzheimer's, Parkinson's, and sickle cell diseases and are doing their own genome-wide surveys.

Of course, even before the scientific and

statistical verdicts of the LLFS are rendered, one can't help but notice something special about LLFS families, such as that of eighty-seven-year-old Helen Hurlburt Caldwell. In that family, eight siblings (out of eleven), ranging in age from seventy-nine to ninety-six, are still living. They grew up in a working-class section of Boston in the 1920s and 1930s, lining up for weekly baths in a single tub of hot water in the kitchen. They ate soup all the time, Caldwell recalls, to stretch as far as they could the food they could afford.

Remarkably, while a couple of aunts lived past 100 and several uncles made it into their eighties and nineties, Caldwell's parents died relatively young. Her father, a truck driver, died of tuberculosis at age forty-five, forcing the older children to work to support the family and the younger ones to help their mother, who died at sixty-three, keep house.

Recently, some of Caldwell's siblings gathered at her apartment in Hingham, Massachusetts. Amid the laughter, they told family stories — how one sister used to sneak out the bathroom window as a teenager to go on forbidden dates with a motorcycle-driving cad; how a brother wrote vivid letters from distant lands while in the Navy during World War II; how another brother left home at seventeen to work on a New Hampshire farm because "there wasn't enough room in our house to sleep." All the kids grew up, got married, and raised families. Every one of them seems to have an artistic drive, writing poetry and plays, composing songs, painting, playing piano, or quilting. And while they think the Long Life Family Study is an excellent idea, they have their own ideas about how to live a long life.

"Good living," is Caldwell's succinct answer. Her sister Agnes Buckley, who is ninety-six, thinks "good eating" is more like it. "I eat all home-cooked vegetables," she says. "And, of course, a good breakfast, too. I never could wait for my breakfast. Also, it doesn't matter if you have a glass of wine once in a while."

"Doing things, keeping busy," adds their brother Peter Hurlburt.

"None of us smoked or drank or really even swore in our house," says Peggy Condon, a third sister. "We were never envious of each other as far as I know, and we all cared about each other."

Back in Maine, Ted Clapp is planning another family-treasure giveaway. "The longer you live, you discover that life is a pretty difficult assignment," he says. "But there's nothing more interesting on this Earth than a human being, and if you can develop a sense of appreciation of others, and not be judgmental, then that's an enormous achievement, and it leads to an emotional health that often can extend your own physical life." ■



SADIE DAYTON

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Study participants talk about their lifestyle at [www.bu.edu/bostonia](http://www.bu.edu/bostonia).