



# Exploring the Effects of Aging on Chronic Illness

While research concerning the link between aging and chronic illness is still in the beginning stages, it is believed that discovering the underlying causes of aging will help to improve quality of life.

By Jim Trageser

**AGING AS A** health issue permeates the history of medicine. The Charaka Samhita Sanskrit text from India, dating from the time of the Roman Empire or earlier, prescribes light but nutritious meals for older patients. And, fifth century Greek physician Aëtius of Amida specialized in studying the health of the elderly. However, while doctors have always known aging affects all aspects of health, from general fitness to the body's reaction to various illnesses, the formal scientific study of the specific changes in the body as it ages is a fairly recent development. "Geriatrics" was first used as a term for the study of medicine among the elderly population in 1909 by Ignatz Leo Nascher, MD, of Mt. Sinai Hospital in New York City. This was after Ukrainian researcher Ilya Ilyich Mechnikov coined the term gerontology in 1903 to describe the larger, multidisciplinary study of aging across medicine, sociology, anthropology and other fields. However, gerontology was slow to gain academic acceptance, with the University of Southern California offering the first degrees only in 1975.

The link between aging and chronic illness is something that has long been recognized, or at least suspected. A fairly common example is prostate cancer: Doctors have known for decades that the older a man is when he develops prostate cancer, the more slowly it is likely to grow and the less likely it will spread.<sup>1</sup> Today, the National Institutes of Health's (NIH) National Institute on Aging is funding research to look at

how changes in the body as it ages affect the way a host of diseases progress, particularly chronic illnesses. And, NIH is funding the Geroscience Network to study not only aging, but the effects aging has on chronic illnesses and how those effects might be lessened.<sup>2</sup> With the number of Americans over age 65 expected to double to almost 100 million by 2060,<sup>3</sup> and with up to half of any person's entire medical expenses coming in the last five years of life, this is an issue that will only grow in importance in coming years.

### **What Is the Geroscience Network?**

The Geroscience Network is an affiliation of clinical institutions and researchers formed in 2013 by James L. Kirkland, MD, PhD, at the Mayo Clinic, professor Steve Austad, PhD, at the University of Alabama at Birmingham and Nir Barzilai, MD, at the Albert Einstein College of Medicine. Other member institutions include Harvard, Stanford, Johns Hopkins and Wake Forest universities. Funded by a grant from the NIH's National Institute on Aging, the network ties together existing programs that conduct research about aging to help scientists map out promising new leads. It also shares research data across institutions, helps organize retreats for scientists to come together to plan future research strategies, and facilitates faculty exchanges to help nurture new research into aging.<sup>4</sup> "Aging is the largest risk factor for most chronic diseases," explained Dr. Kirkland in a 2016 interview provided by the Mayo Clinic. "The goal of our network's collaborative efforts is to accelerate the pace of discovery in developing interventions to delay, prevent or treat these conditions as a group, instead of one at a time."

In the summer of 2016, the Geroscience Network published six papers that laid out a road map for developing new drugs that target specific biological processes associated with aging, getting those drugs into clinical trials, developing standards for measuring "health span" and using mice as a vehicle for testing new theories on aging.<sup>5</sup>

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### **What Is Aging?**

Asking "What is aging?" may seem a bit silly; it's one of those common-sense concepts people grow up with. Aging is what happens to the body over time, and the external signs are embedded in our cultural view of growing older: Grandpa's hair turns gray, Grandma's face wrinkles and our favorite athletes see their physical abilities decline over the course of just a decade or so.

At the clinical level, there is a solid road map of the changes that happen in a body. After hitting peak physical strength and condition at about age 30, the following happens:



- Metabolism slows (and, for many, this is accompanied by weight gain)
  - Hearing clarity is lost
  - The eyes become less able to refocus between different distances
  - Muscle mass begins to decrease, and the heart becomes less efficient
  - Blood vessels lose elasticity, and high blood pressure is more likely to develop
  - Memory isn't quite as sharp
- All of these developments can influence the way a chronic disease affects a patient, whether it's a malignancy, a neuropathy or an immunodeficiency disease.

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It is only in recent years, though, with the development of new technology that researchers have been able to dig deep into the body's biology to find out what is occurring at the cellular, chemical and molecular levels in the body as it ages and what specific processes underlie these externally observable changes. Researchers believe it is not until we more fully understand the biological and chemical changes that drive the aging process that we'll be able to more effectively treat age-related risk factors that can complicate chronic diseases in the elderly. And, right now, this process of discovering the underlying biological causes of the symptoms of aging is in a very early stage, with many answers yet to be discovered.

**Which Chronic Diseases Are Most Affected by Aging?**

As pointed out by Dr. Kirkland, aging is the leading risk factor for most chronic diseases. Nearly all primary immunodeficiency diseases (PIs) are exacerbated by the aging process: As people grow older, their immune systems gradually lose efficiency, even in healthy people. This not only makes older patients with a PI even more susceptible to an infection, but it can also make it difficult for a physician to differentiate between a PI's progression and the natural aging process — something doctors have recognized for several decades now.<sup>6</sup>

But, certain types of PIs are more predominant in older populations than others. One recent study found antibody (IgG) deficiencies comprise the overwhelming majority of PI cases among the elderly.<sup>7</sup> These classes of PI occur when the body doesn't make enough of a particular IgG protein. Therefore, after being exposed to a certain bacteria, they don't respond by producing new IgG proteins to fight that specific infection. This leads to longer infections and a higher risk of a more serious condition developing, and will normally require the use of antibiotics or other treatment to assist the body in fighting the infection.

Peripheral neuropathy is another chronic condition that is statistically more likely to manifest as individuals grow older. Researchers are still sorting out causation from correlation, but it seems since most cases of neuropathy are caused by immune reactions, trauma, diabetes or alcohol abuse, the longer people live the more likely they are to encounter any of these possible triggers.<sup>8</sup> When a peripheral neuropathy introduces numbness to the extremities, one result can be a higher risk of a fall. And, falls are the leading cause of death by injury among the elderly. Even without numbness as an associated symptom, the general loss of strength and impaired mobility caused by neuropathy can make falls more likely.<sup>9</sup>

Cancers may be the chronic disease most associated with longevity. And, like peripheral neuropathy, simply living a long time exposes a person to more instances of risk of developing the disease. With cancers, a long life also results in cumulative exposure to carcinogens.<sup>10</sup> Not only do seniors have a greater chance of developing a cancer, but physicians also know that the older people are, the more challenging it can be to treat their cancers. Older patients are more likely to experience side effects to radiation or chemotherapy, the side effects are likely to be more severe and they take longer to recover from these treatments than do younger patients.

Surgery in older patients also carries more risks of complication, and the recovery times are significantly longer.

Treating any chronic illness is made more difficult when also managing high blood pressure, arthritis, diabetes or any of the other conditions that often accompany living into one's 70s or beyond. And, there are drug interactions to consider since many seniors are on more than one maintenance drug.

## What Advances Are Being Made?

The overarching goal of geroscience is to uncover new findings that will give physicians tools to address the underlying causes associated with aging, allowing them to more effectively treat any chronic diseases affecting patients. But, that will be a long process — one that is just beginning.

In one advance already being made, however, geroscience researchers are tackling a phenomenon known as senescence, which occurs when cells in the body stop dividing and reproducing, but also don't die. These senescent cells, which were first discovered about 50 years ago, likely serve an as yet unknown biological purpose (perhaps slowing malignant cell growth) by churning out a variety of proteins (those not produced by normal cells) that affect neighboring cells. Senescence occurs throughout life, but in healthy young people, the immune system regularly kills off these cells so they can be replaced by normal cells of the same tissue type. New research suggests that as we grow older, senescent cells begin to build up, and the immune system can't keep up with eliminating them. It is thought senescent cells are associated with conditions ranging from osteoarthritis to atherosclerosis, but a deeper understanding of their role is needed.<sup>11</sup>

On a more practical level, there are some promising developments for drugs that can target senescent cells while leaving healthy cells alone. A 2018 Mayo Clinic study on aging in mice found giving them drugs that kill senescent cells reversed many of the symptoms of aging.<sup>12</sup> However, since senescent cells in different types of tissue (muscle vs. liver, for instance) produce far different proteins, it has been difficult to develop a test that can identify more than one type of senescent cell at a time, making measuring progress in killing off senescent cells throughout the body a challenge.

On another front, Grubeck-Loebenstein, MD, one of the researchers who first pointed out the challenge of differentiating a PI from normal aging, currently heads the Institute for Biomedical Aging Research at the University of Innsbruck in Austria. Its primary area of research now is to

prevent T cell function from declining in the elderly.<sup>13</sup>

Another study about PI and the elderly examined whether subcutaneous immune globulin (SCIG) treatment could be as effective in the elderly compared to those in their age group using intravenous immune globulin (IVIG) treatment. With fewer side effects than IVIG, the SCIG option offers promise for elderly patients. The study found home-based SCIG is safe and effective in elderly patients with PI, most of whom can self-infuse. Infection rates were low, and no adverse events or difficulties in administering SCIG occurred that resulted in treatment discontinuation.<sup>14</sup>

## The Future of Aging Research

Geroscience, geriatric and gerontology researchers all agree that prolonging “health span” is, if anything, more important to improved quality of life than simply prolonging “life span.” The goal is to lengthen middle age, not old age, so even if people don't live longer, they will enjoy a better quality of life and encounter fewer medical expenses.<sup>15</sup>

An essential part of an increased health span is improved treatment options for chronic diseases. As researchers develop their initial explorations of the cellular and molecular causes of aging, future decades should see a rapid expansion of the effectiveness of care for older adults suffering from a variety of chronic conditions, ranging from cancer to PIs. ■

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