San Francisco Examiner
SPECTRA
SCIENCE, HEALTH & TECHNOLOGY

HEALTH

NEW AGE, OLD AGE

As the baby-boom generation continues to grow, so does its quest for a fountain of youth and its desire to understand the aging process- a complex set of reactions, processes, and thermostats that scientific researchers are just beginning to sort out

By Margie Patlak
SPECIAL TO THE EXAMINER

ALTHOUGH RECENT research on aging hasn't yet hit upon the "fountain of youth," it is providing some fascinating glimpses of what might prompt wrinkles, cataracts, hardening of the arteries, arthritis and other signs of aging.

Findings over the last five to 10 years indicate that hormones, a buildup of certain compounds in the body, genetic controls and general wear and tear play key parts in aging, a process that has puzzled people for millennia.

The Pacific salmon offers a significant piece in the aging puzzle. After the fish mates and generates enough fertilized eggs to ensure survival of the species, it secretes large quantities of adrenal or "stress" hormones. These hormones prompt it to age rapidly and die.

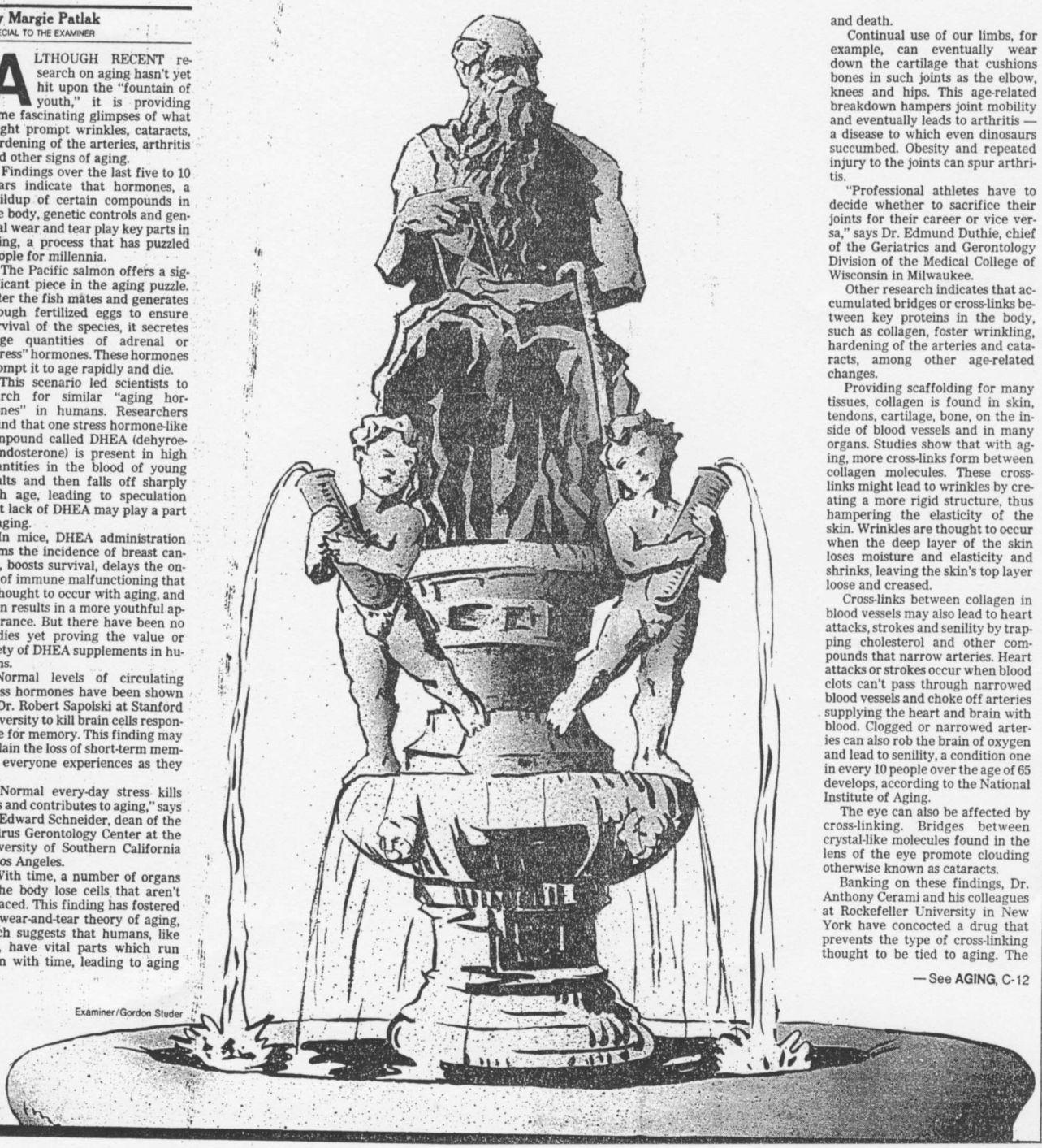
This scenario led scientists to search for similar "aging hormones" in humans. Researchers found that one stress hormone-like compound called DHEA (dehyroepiandosterone) is present in high quantities in the blood of young adults and then falls off sharply with age, leading to speculation that lack of DHEA may play a part in aging.

In mice, DHEA administration stems the incidence of breast cancer, boosts survival, delays the onset of immune malfunctioning that is thought to occur with aging, and even results in a more youthful appearance. But there have been no studies yet proving the value or safety of DHEA supplements in humans.

Normal levels of circulating stress hormones have been shown by Dr. Robert Sapolski at Stanford University to kill brain cells responsible for memory. This finding may explain the loss of short-term memory everyone experiences as they age.

"Normal every-day stress kills cells and contributes to aging," says Dr. Edward Schneider, dean of the Andrus Gerontology Center at the University of Southern California in Los Angeles.

With time, a number of organs in the body lose cells that aren't replaced. This finding has fostered the wear-and-tear theory of aging, which suggests that humans, like cars, have vital parts which run down with time, leading to aging and death.



Examiner/Gordon Studer

Continual use of our limbs, for example, can eventually wear down the cartilage that cushions bones in such joints as the elbow, knees and hips. This age-related breakdown hampers joint mobility and eventually leads to arthritis — a disease to which even dinosaurs succumbed. Obesity and repeated injury to the joints can spur arthritis.

"Professional athletes have to decide whether to sacrifice their joints for their career or vice versa," says Dr. Edmund Duthie, chief of the Geriatrics and Gerontology Division of the Medical College of Wisconsin in Milwaukee.

Other research indicates that accumulated bridges or cross-links between key proteins in the body, such as collagen, foster wrinkling, hardening of the arteries and cataracts, among other age-related changes.

Providing scaffolding for many tissues, collagen is found in skin, tendons, cartilage, bone, on the inside of blood vessels and in many organs. Studies show that with aging, more cross-links form between collagen molecules. These cross-links might lead to wrinkles by creating a more rigid structure, thus hampering the elasticity of the skin. Wrinkles are thought to occur when the deep layer of the skin loses moisture and elasticity and shrinks, leaving the skin's top layer loose and creased.

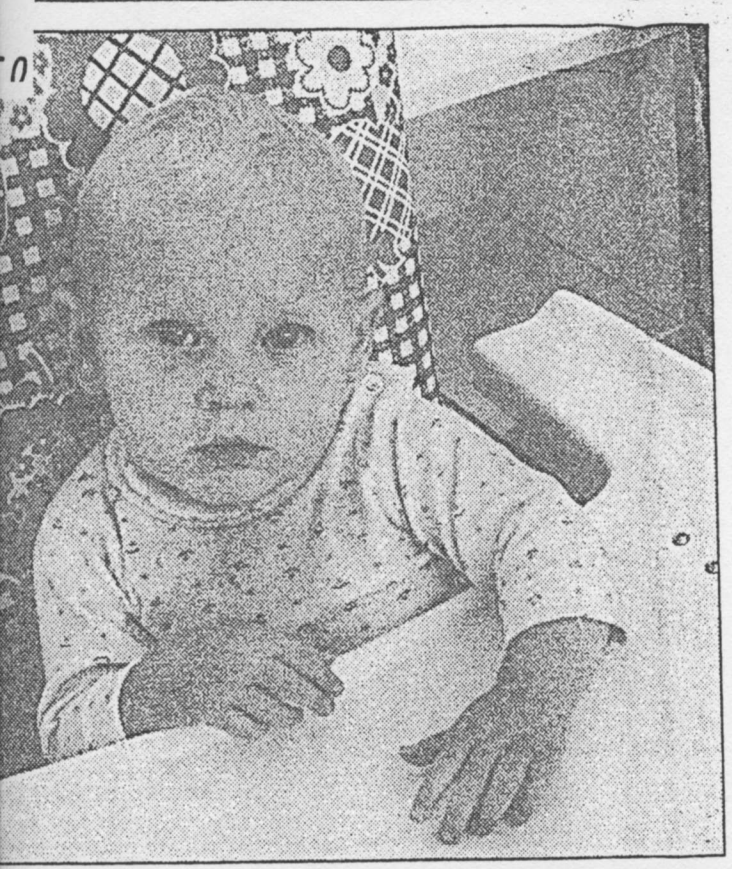
Cross-links between collagen in blood vessels may also lead to heart attacks, strokes and senility by trapping cholesterol and other compounds that narrow arteries. Heart attacks or strokes occur when blood clots can't pass through narrowed blood vessels and choke off arteries supplying the heart and brain with blood. Clogged or narrowed arteries can also rob the brain of oxygen and lead to senility, a condition one in every 10 people over the age of 65 develops, according to the National Institute of Aging.

The eye can also be affected by cross-linking. Bridges between crystal-like molecules found in the lens of the eye promote clouding otherwise known as cataracts.

Banking on these findings, Dr. Anthony Cerami and his colleagues at Rockefeller University in New York have concocted a drug that prevents the type of cross-linking thought to be tied to aging. The

— See AGING, C-12

HEALTH/MEDICINE



AGING

—From C-11

artery walls of rats given the drug showed less cross-linking and cholesterol buildup than did those of control rats. The investigators are testing the drug on humans.

But cross-linking isn't the only factor in aging. "Cross-linking probably causes very few problems in most of our organs and tissues," Schneider says. "We don't necessarily age because we cross-link to death."

Similar to the cross-link theory is the free-radical theory. It suggests that there is an age-related buildup of damage from compounds called free radicals that ultimately interfere with the vital functioning of such key cell structures as membranes, proteins and genes. Free radicals are highly reactive compounds generated naturally by the body. These molecules are prevented from doing much harm by various enzymes manufactured by cells.

Some studies show that animals with longer life spans also have higher levels of one of the enzymes that combats free radicals. Some groups are touting a drug known as centrophenoxine as an "anti-aging" compound because it is thought to stimulate the enzymes that immobilize and break down free radicals. But there is no hard evidence that centrophenoxine is a fountain of youth.

None of these findings explains why people age at different rates. Because of this variability, many scientists believe aging and death are pre-programmed events controlled by the mix of genes inherited from parents. These genes may start or speed aging by affecting the production of hormones, the amount of cross-linking that occurs in the body, the amount of enzymes that breaks down free radicals or any of the other factors thought to influence aging.

"Something must set the clock in the body and control the rate of aging," Duffy says.

A number of findings support the notion that genes control the aging process, including those from studies of the geneticist's favorite creature — the fruit fly. Dr. Leo Luckinbill at Wayne State University in Detroit found that when long- and short-lived strains of fruit flies are crossed, they produce offspring with intermediate longevity, indicating that life span in this species is under genetic control.

Also, research on a disorder called Werner's syndrome discloses that the premature aging that is the disease's hallmark is caused by faulty chromosomes. Because chromosomes house an organism's genes, the findings further point to a genetic part in aging.

Genes are probably dictating the shrinking of the glands of the immune system that begins during the teen-age years. Infection-fighting glands called tonsils and adenoids that are found in the back of the mouth, for example, are large in children and barely noticeable in adults.

Linked to the shrinking immune system glands are white blood cells that become less efficient with age at fending off disease and ridding the body of abnormal cells. This finding explains why so many disorders such as cancer peak in old age.

A hampered immune system also explains why various auto-immune diseases, such as rheumatoid arthritis, in which the body attacks its own cells, become more common in older people. But still, most experts believe that aging is not explainable by a single mechanism, but represents many phenomena working in concert; an understanding of its complex workings probably won't evolve until the young science of aging gets older.

The changes wrought in the human body by the aging process can easily be seen by comparing a photo of an infant with that of a senior citizen