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REPORT

Dr. Norman Orentreich
A True Pioneering
Researcher on Aging

Dr. Norman Orentreich enjoys a worldwide reputation for his body of research into the problems of aging. His career spans half a century, from performing the first hair transplants to participating in the treatment of erectile dysfunction in men.

By Vince Cappiello

The process of aging is complex, says Dr. Norman Orentreich, and thus, "There is no simple way to measure biologic age." That doesn't mean he's given up trying, however. At his Orentreich Foundation for the Advancement of Science, in Cold Spring, N.Y., he and a staff of scientists conduct independent research and collaborate with other researchers in such areas as aging and diet, cancer, hair loss, skin physiology, atherosclerosis, Alzheimer's disease, and hormone replacement therapy.



Research has identified numerous changes that accompany aging, but these are influenced by other factors than simply age itself. Complicating the issue further is the periodic change in the rate of aging that is cyclical and has been observed in men and women. The mechanism for this phenomenon is unknown, but Orentreich feels "it is crucial that researchers be aware of these seven-year rhythms when studying aging and integrating treatment modalities." Orentreich became interested in the problems of aging even before studying medicine. While still an undergraduate student, he worked as an instructor and research fellow in physiology, during which time he learned of the work of the Nobel laureate Alexis Carrell and co-worker Henry Dakin, who had developed a hypochlorite solution to disinfect war wounds during World War I. This treatment was an important advance because it did not impede the rate of wound healing. However, subsequent studies of Carrell and others showed that the rate of wound healing decreased with increasing age; further, the rate of cell proliferation in tissue culture could be increased or decreased by the addition of blood serum from, respectively, younger or older donors.

Orentreich developed enormous respect for the work of Carrell. In fact, one of his first research projects at the Orentreich Foundation, which he founded in 1961, was to repeat the wound-healing studies that confirmed the lessening rate of wound healing with age. "I have a bad habit of reading the old literature and rediscovering things," he says.

To enhance communication and the exchange of ideas with peers, researchers from around the world are invited to the Orentreich Foundation to discuss their work. Likewise, Foundation scientists travel to other research centers to participate in conferences and symposia. A staff of about 50 share the 30,000 square feet of research and administrative space located on 75 rural acres. The staff consists of personnel from various biomedical disciplines, and includes M.D.s, Ph.D.s, post-graduate fellows, and research assistants. Graduate students from New York City-area universities also work there. The Foundation is supported by private donations and research grants.

Upon receiving his M.D. degree in 1948 from New York University School of Medicine, Orentreich joined the Skin and Cancer Unit of the Post-Graduate Medical School where he was instrumental in establishing the first medical hair clinic in the United States. In 1952 he pioneered hair replacement and transplant surgery. His contributions to surgical dermatology led to his becoming the first president of the Society for Dermatologic Surgery in 1970.

In addition to serving as director of the Orentreich Foundation, he is also in private practice, and serves as clinical professor of dermatology at NYU's school of medicine.

Orentreich's interest in hair research did not end with his successful hair restoration and transplant surgery almost half a century ago. He has continued to study various types of hair loss, hirsutism (unwanted hair), and hair follicle physiology in animals and

humans. Using a mouse model for common baldness developed at his Foundation, he and his coworkers have shown that bald skin metabolizes androgens differently, and that this change precedes clinical changes in the hair itself. Research also is ongoing in developing topical medications to reverse the abnormal androgen metabolism that results in unwanted hair. Orentreich says, "In the future we will be able to fully control wanted and unwanted hair growth pharmacologically. We can do so partially now."

The Orentreich Foundation maintains a collection of some half-million samples of frozen sera obtained from patients during physical examinations. Originally, separate collections of sera were kept by the Foundation and by the Kaiser- Permanente Medical Care Program. In 1980 they were combined at the Foundation as the OFAS/KPMCP Serum Treasury, managed by a sophisticated tracking system for rapid serum sample location. These samples are used to search for disease markers in the same way that prostate specific antigen (PSA) is used to aid in the diagnosis of prostate cancer. Staff members at the Orentreich Foundation provide serum samples on a regular basis so that one could track age-related changes occurring in their blood should the need arise in the future.

The Serum Treasury is available to scientists studying the relationship between human diseases and serum markers. To access these sera, interested scientists must submit a proposal containing adequate justification for use of this unique and finite resource.

In 1984, Orentreich and coworkers published a landmark scientific paper on dehydroepiandrosterone-sulfate (DHEA-sulfate), a steroid secreted by the adrenal cortex and the major androgen precursor in females; it is also becoming increasingly studied and used by both men and women as an anti-aging hormonal supplement. In the body, DHEA-sulfate and DHEA are converted from one to the other in order to maintain balanced concentrations in blood and tissues. This research report established normal values of DHEA-sulfate in blood for various age groups of men and women, and subsequent studies showed that blood levels of DHEA-sulfate decreased with increasing age after peaking in early adulthood. The therapeutic benefits of DHEA supplementation can be many, but Orentreich believes that "it is sort of a nonspecific approach and certainly not the final answer for preventive gerontology."

"Hormone replacement therapy probably holds the best hope for [impacting] the process of aging," he notes, because it is easy to administer, and we know about the declines in many hormones that accompany aging. Current worldwide research studies of trophic factors, such as growth hormone and insulinlike growth factor-I, are looking into this. Orentreich predicts that testosterone-replacement therapy in men to combat the effects of andropause will be as common as estrogen-replacement therapy is for menopause.

An early interest was to determine whether the process of aging could be delayed if naturally accumulating "toxins" were removed from the blood. Orentreich is keenly interested in an ongoing collaborative study with the Tennessee Oncology Center in which cancer patients are being treated by "ultrapheresis," a blood-cleansing process. The rationale of the Tennessee study is to remove tumor necrosis inhibitor factor (TNIF) produced by a tumor. TNIF prevents the body's protective mechanism, called tumor necrosis factor (TNF), from destroying the cancer cells; removing TNIF from the blood allows the body's TNF to act against a tumor.

Foundation researchers also are studying hyperinsulinemia-excessively high blood insulin levels-as it relates to insulin resistance syndrome. This is the loss of sensitivity of the body's cells to insulin, which leads to a pre-diabetic condition. Left untreated, the long-term effects include coronary artery disease, obesity, and progression to non- insulin dependent diabetes. The role of glucose metabolism in the development of Alzheimer's disease also is being studied.

Other current studies are investigating how methionine-restricted diets increase longevity, the effects of growth factors on human hair follicles, autoimmune diseases of the skin, and the continuing search for disease markers by the use of the Serum Treasury.

Now a septuagenarian, Orentreich adheres to a busy work schedule of 10- to 12-hour days. He spends one day at the Foundation in Cold Spring and the remainder of the workweek at his private practice in New York City.

The logo of the Orentreich Foundation is an apt one for a lifetime's worth of work combating the diseases of aging. It depicts an hourglass with a stopcock between the two halves, and a caption that reads, "Life's blood flows through the hourglass; the stopcock represents the alteration of aging and disease as biomedical research progresses."

[Back to the Magazine Forum](#)

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