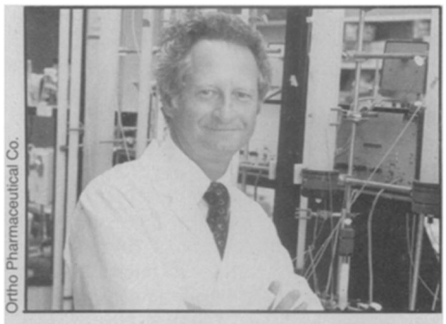
THE HUMAN SWEETBREAD

Thymic hormones are essential to the body's immune system and beneficial to patients with certain immune diseases, but they also may fight cancer, autoimmune diseases and aging

BY JOAN AREHART-TREICHEL

Chefs and gourmets have been enamored of the thymus for years. They take thymuses from young calves and serve them up as delicacies called sweetbreads. But now researchers are finding that the thymus, a pyramid-shaped organ located behind the mammalian breastbone, is much more than a palate pleaser. Their interest was aroused by two discoveries made in the 1960s: The thymus processes bone marrow stem cells into "T cells," the cells that provide the body with cellular immunity, and it makes protein hormones. These dual discoveries in turn have precipitated a rush of other findings about the thymus, particularly about its hormones. Many of the findings were reported at the recent Miles symposium on protein hormones, held at the Johns Hopkins Medical Institutions in Baltimore.

Various thymic hormones were described, and the link between thymic hormones and the thymus's processing of T cells was discussed, as was the use of thymic hormones in helping patients with immune diseases due to T-cell deficiencies. But what has turned out to be a surprise is that thymic hormones also look promising in countering cancer, autoimmune diseases and even that recalcitrant biological process, aging. Or as Nathan Trainin of the Weizmann Institute of Science in Rehovot, Israel, and one of the Miles symposium speakers predicts, "The thymic hormones are going to have an important role in therapy."



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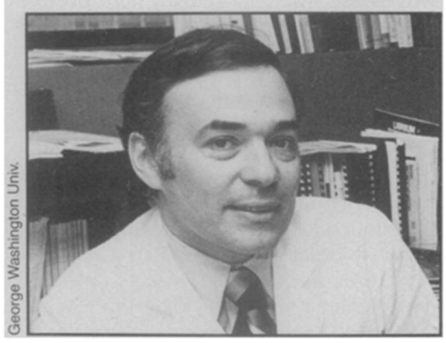


George Washington Univ.

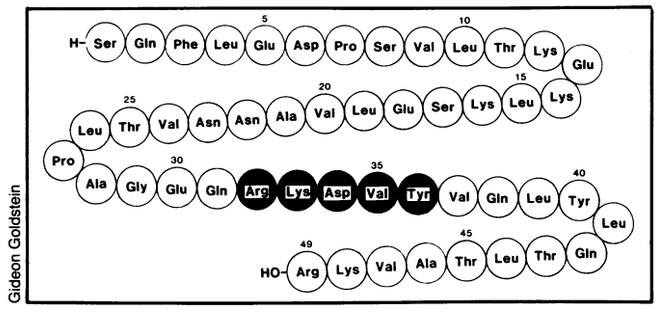
Nathan Trainin proposed thymus hormones. Gideon Goldstein (upper left) and Allan Goldstein (lower left) identified them. Thymopoietin (right) was identified by Gideon Goldstein.

In the early 1960s, Trainin and his colleagues proposed a hormonal mechanism for the thymus and established the existence of a hormone in thymic material taken from various animals. In the mid 1960s, two thymic hormones were identified — thymosin by Allan L. Goldstein of the Albert Einstein Medical College in New York City (and now with George Washington University in Washington) and his colleagues, and thymopoietin by Gideon Goldstein of New York University (now with Ortho Pharmaceutical Corp. in Raritan, N.J.). Since then, other thymic hormones have been isolated as well — another thymopoietin by Gideon Goldstein, thymic hormone factor (THF) by Trainin, *facteur thymique sérique* (FTS) by Jean-François Bach of Hopital Necker in Paris, and a four-amino acid hormone (or part of a hormone) by Alberto Astaldi of the Netherlands Red Cross Blood Transfusion Service in Amsterdam. And as these researchers reported, the main mission of all these hormones appears to be to influence T cells. Some of the thymosins, for instance, help bone marrow stem cells in the thymus to mature early into T cells, some help the stem cells to mature into T cells later; the thymosins also help alchemize stem cells into specific kinds of T cells, such as killer, helper or suppressor T's. FTS and the two thymopoietins likewise induce stem cells to differentiate in the thymus into specific kinds of T cells. THF, on the other hand, increases the effectiveness of helper and killer T cells after they are made, and the four-amino acid hormone increases the effectiveness of helper T cells, but not of suppressor T cells.

Because of their potent influence on T cells or their precursors, thymic hormones have been given to children with immunodeficiency diseases in which the deficiency concerns T cells. Allan Goldstein and his colleagues, for instance, have given shots of thymosin to 80 immunodeficient children over the past five years, and many of them have profited from treatment. One of the more dramatic cases concerns a frail five-year-old named Heather who had spent most of her life ill with one disease or another. Her thymus was underdeveloped, and her T cells were not working right, presumably because they were not mature T cells. Goldstein (then at the University of Texas Medical School in Galveston) and Arthur Ammann and Diane Wara of the University of California at San Francisco took some of Heather's T cells and placed them in a test-tube in the presence of thymosin. As they hoped, the hormone turned the T cells into immune fighters, apparently by maturing them. Then the investigators gave Heather thymosin injections, and her T cells also apparently matured and started to fight off infections in her body (SN: 1/8/75, p. 43). Today Heather is 10 and a half years old, relatively healthy, attending public school in Sacramento, Calif., and still receiving thymosin injections on a weekly basis. In fact, as Goldstein points out, "She has encountered chickenpox, which is normally fatal in a child with this disease."

Thymic hormones also are being given to children whose T cells are suppressed by drugs. During the past two years, for instance, Trainin and his colleagues have given THF to several dozen children suffering from viral infections because they are taking immunosuppressant drugs for cancer. The drugs presumably left them vulnerable to infections by suppressing their T cells. Thanks to THF, all of the children have overcome their infections.

Regarding thymic hormones' promise in countering cancer, the thymopoietins have been shown to reduce lung cancer growth in rats, Gideon Goldstein reports. Also, a recent study designed by Paul B. Chretien of the National Cancer Institute and headed up by Martin Cohen of the Washington Veterans Administration Hospital has shown that thymosin plus drug therapy can significantly prolong survival in patients with deadly oat cell (small cell) lung cancer. The patients getting thymosin



Gideon Goldstein

experienced a mean survival of 424 days, whereas patients not getting thymosin showed a mean survival of only 243 days. The hormones probably help counter cancer by maturing bone marrow stem cells into T cells that fight cancer. T cells are known to counter cancer and Chretien and his colleagues have found that thymosin can increase the number of T cells in the test-tube. Patients in their study had low levels of T cells before getting thymosin and higher levels after receiving it. Thymosin, however, does not appear to have any direct impact on tumors.

Because T cells seem to mistakenly attack the body in certain autoimmune diseases, such as allergic encephalomyelitis and myasthenia gravis, one might conclude that thymic hormones, which influence the effectiveness of T cells, would aggravate such diseases. But the opposite seems to be the case. Gideon Goldstein reports that the thymopoietins inhibit autoantibody formation by acting via T cells. Jerry Daniels of the University of Texas Medical School at Galveston has preliminary evidence that thymosin can help patients with lupus, an autoimmune disease that involves autoantibodies and decreased T-cell function, and with rheumatoid arthritis, in which antibodies adhere to each other. Bach and his colleagues have shown that FTS can help mice with autoimmune diseases, and Trainin and his co-workers are giving THF to 10 youngsters with encephalitis and juvenile arthritis (which possibly has an autoimmune basis). The results are not yet in on these studies.

Finally, because the immune system is known to lose its potency as a person or animal ages, it would make sense that a decrease in thymic hormones with aging might be the reason for this loss, and that exogenous shots of such hormones might help boost the aging immune system. There is some evidence, in fact, that this is the case. Allan Goldstein reports that levels of one of the thymosins decrease with age in the human body. Astaldi and his co-workers have found the same for their four-amino acid hormone, and Gideon Goldstein has discovered that thymopoietin enhances immune responses in old mice. No researcher has yet given older persons injections of thymic hormones to see whether it might bolster their faltering immune systems and, better yet, to see whether it might help protect them from diseases that tend to disable and kill the elderly. However, thymic hormone scientists are optimistic that the hormones will eventually be capable of achieving such dramatic therapeutic results. "Soon we expect to launch a major trial here at the George Washington University School of Medicine to determine the effect of thymosin on the immune systems of older people," Allan Goldstein says. Gideon Goldstein asserts, "We are just gleaning what these hormones can do." □