

The year in medicine: breakthroughs in science, but breakdown in policy

by John Grauerholz, M.D.

The end of 1984 presents the spectacle of a world on the edge of a totally unnecessary biological holocaust. At a time when millions are dying of starvation and pestilence in the developing sector and the health infrastructure of the advanced sector is collapsing at an accelerating rate, a revolution in the technology of diagnosis, treatment, and prevention of disease is occurring.

AIDS (Acquired Immune Deficiency Syndrome) is exemplary of this situation. A product of the cultural degradation of civilization, affecting primarily promiscuous male homosexuals and intravenous drug abusers, it has triggered fundamental advances in our understanding of the immune system. AIDS research, combined with other breakthroughs and breakdowns, has made 1984 the year of the immune system.

In April, scientists from the United States and France announced the isolation of a virus which selectively destroys T-cells, one of the two primary types of immune cells, as the causative organism of AIDS. Since then, a technique for growing the virus in quantity has been developed, and a blood test for exposure to the virus is now being used for screening tests on patients and donated blood. Ultimately this should lead to production of an effective vaccine.

In the meantime, over 7,000 cases of AIDS have been diagnosed in the United States, and nearly half of these have died from the disease. Present estimates are that as many as 300,000 people have been exposed to the virus in the United States and that 10% of them will come down with the disease. As striking as these figures are, the incidence of AIDS may be 10 to 20 times higher in Zaire and other areas of sub-Saharan Africa. Here the disease is apparently being spread by heterosexual contact and poor sanitation in a population whose immune systems are depressed by malnutrition and chronic infectious disease.

The search for a cure for AIDS has given additional impetus to the study of substances known as biological response modifiers, especially those produced by the white blood cells and called lymphokines. One of the most promising of these is a substance known as interleukin-2, or human T-cell growth factor.

Interleukin-2 is a critical factor for growth of T-cells and augmentation of T-cell function. It is especially effective in stimulating production of specific cytotoxic (cell-destroying) T-lymphocytes and other cells, known as natural killer (NK) cells. A number of studies in animals has shown protection against tumor growth and regression or control of established tumors. Interleukin-2 has the potential to reverse deficits in T-cell function caused both by cancer itself and as a side effect of chemotherapy.

Because of this, there has been intense interest in producing large quantities of this substance for use in clinical trials. Since IL-2 (Interleukin-2) is a polypeptide (a chain of amino acids), one approach has been to produce it by genetic engineering. While this has produced pharmacologic amounts of the amino acid chain, it does not add certain sugars which are also present in the naturally occurring molecule.

A more promising approach has recently been developed by a company with the appropriate name of Interleukin-2, Inc. It has developed and patented a process for producing human interleukin, with the appropriate sugars, from normal human blood cells. This product, actually a "cocktail" of a number of human lymphokines, was recently tested in Phase I trials on cancer patients at St. Thomas hospital in London and has proven non-toxic and clinically effective in reducing the size of tumors. Phase II trials are under way to evaluate therapeutic response in patients with cancer and AIDS.

One of the earliest, and still one of the most effective, methods of immune therapy is vaccination, a term derived from the virus Vaccinia. This virus, which causes cowpox, was used by William Jenner to inoculate against smallpox and has been responsible for the total eradication of this once dreaded disease. Scientists at the New York State Health Department have developed a technique for genetically altering this virus to express up to eight different antigens, thus enabling vaccination against eight different diseases with a single injection.

Other breakthroughs in vaccine development include:

- Development of a vaccine for chicken pox, which infects 2-3 million children a year, resulting in 60 to 100 deaths in those affected.

- A vaccine against hemophilus influenzae, the greatest cause of childhood infections, including pneumonia and meningitis, has been proven effective in infants as young as 18 months of age. Innoculation of all eligible children could prevent 60% of these infections, which are potentially life threatening.

- A synthetic protein has been developed which can provide an inexpensive vaccine against hepatitis B. This disease affects about a million people in the United States and 250-300 million people worldwide, primarily in the developing sector, where it is believed to be the cause of hundreds of thousands of cases of primary liver cancer. In a related development, French and American scientists have developed a quick, inexpensive test for primary liver cancer, utilizing monoclonal antibodies-chemicals which attach to specific target chemicals in the body.

- A new polio vaccine, made from killed viruses, promises to eliminate the last traces of polio from the United States in the next two years. Scientists are also developing a polio vaccine which can be administered by inhalation and could be mass produced for about 10¢ a dose.

- One of the major breakthroughs has occurred in the long effort to develop a vaccine against the most serious form of malaria. Scientists have reproduced the genetic material which codes for a protein on the malaria parasite which stimulates the body to produce antibodies against the parasite. This genetic material can be inserted into bacteria, which will then produce the proteins in large quantities.

A needless health holocaust

Contrast the preceding to a recent World Health Organization report that every minute, 10 children under five years of age die and 10 more are handicapped for lack of vaccines against a few common childhood diseases. Almost all of these children live in the developing sector, where only 20% of children are fully immunized. Five million children die each year and five million are crippled for lack of vaccines that would cost about \$10.00 per child.

Similar situations are occurring in the United States itself, where the last few years have witnessed a sharply rising infant mortality rate in the inner city areas of such cities as Philadelphia, Boston, New York, and Detroit. This has been traced to lack of prenatal care, the result of closing clinics and dismantling health infrastructure in response to federal, state, and local budget cutbacks. Interestingly, the proposed alternatives of community health workers and low-technology primary care closely parallel World Health Organization proposals for low-technology "primary health care" in the developing sector.

The irony is compounded by the phenomenon of biotechnology as the "growth industry" of the 1980s. This has been the result of fundamental research on cell function and reproduction and the elucidation of the workings of the immune

system. This has led to the development of such techniques as the insertion of genes for the production of animal proteins into bacteria which then produce the proteins in large quantities, and the fusion of cancer cells and normal antibody-producing cells to make a "hybridoma" cell which then produces multiple copies of a single antibody, the so-called "monoclonal antibodies." These technologies, initially expensive to develop, hold the promise of ultimately producing relatively inexpensive treatments and cures for conditions ranging from cancer and infectious diseases to aging. The so-called "primary health care" approach is simply a shortsighted way to a biological catastrophe whose ultimate cost will make the Black Plague pale by comparison.

Significant breakthroughs are in sight in the prevention and treatment of diseases of aging. It has become evident that a great many of the diseases and disabilities that occur in aging individuals are correlated with a decrease in function of the immune system. This is especially true of the so-called T-cell, or thymus dependent immune system. Many changes of aging are directly traceable to a decrease in immune response to foreign organisms, including tumor cells, and an increase of autoantibodies against the body's own cells.

The key role of the thymus dependent system in these changes has spurred scientists such as Allan Goldstein of George Washington Medical School to examine the role of thymus hormones, such as thymosin, in preventing, or reversing, these aging changes. Studies in animals and in human cells in culture have repeatedly demonstrated reversal of age-associated changes in the immune system in response to administration of thymic hormones.

The first clinical trials of thymosin in the elderly will be conducted at the University of Vermont School of Medicine. This will test the ability of thymosin to boost the response to influenza vaccination. Influenza is still a major cause of death in the elderly, in spite of vaccination, because of the depression of immunity in these patients.

Thymosin, like interleukin-2, is a biological response modifier and shows promise in treatment of immune deficiency diseases, cancer, arthritis, multiple sclerosis, and allergies.

To close this article, I would like to quote from Dr. Allan Goldstein's testimony in the hearing on Longevity and the Lifestyle of Older Americans held before the Aging Subcommittee of the Labor and Human Resources Committee of the U.S. Senate on Sept. 27, 1984:

"Indeed, the decade of the '80s, I believe, is ushering in a new age which should properly be called the 'Age of Immunopharmacology.' Through the thymosins, monoclonal antibodies and other biological response modifiers, we are beginning to learn how to manipulate and harness the energy of the body's immune system in the same way that we have learned to harness the energy of the atom. Almost certainly, this information will translate itself into the conquest of many diseases which are thought today to be 'incurable.'"