

That Sometimes Leads to Cancer—

Scientists Discover Cause-Immune-Deficiency Disease

National Cancer Program scientists have discovered the cause of a rare immune-deficiency disease that sometimes leads to cancer, and in so doing have uncovered new information on the workings of the body's system of defenses against many diseases.

For several years, Thomas A. Waldmann, M.D., and his colleagues in HEW's National Cancer Institute, National Institutes of Health, have studied patients mostly children, with a life-threatening disease called common variable hypogammaglobulinemia (CVH), which is characterized by the patient's inability to make protective antibodies.

Fifty patients with the disease have been treated in the NIH Clinical Center. All such patients have recurrent severe infections, particularly pneumonia. Most also develop other destructive lung

diseases. Thirty per cent develop arthritis and ten per cent, cancer.

After a series of experiments, the investigators discovered that the patients' immune defect was due to an excess of a certain type of T-lymphocytes. These are white blood cells that originate in the bone marrow and migrate through the thymus (T) gland before becoming active immune agents. Dr. Waldmann and his colleagues found that the type of excessive T-lymphocytes in these patients were "Suppressor" T-cells.

Another subgroup, "helper" T-cells, assist mature B-cells (another class of white blood cells) in antibody production. An excess of "suppressor" T-cells, the NIH scientists found, blocks antibody production by the B-cells.

It is this defect that weakens children with CVH, making them vulnerable to infections and other diseases.

The scientists grew lymphocytes from 13 patients with CVH in laboratory cultures and found that, despite chemical stimulation, they produced from 16 to 37 times fewer antibodies of each of 3 important classes (IgG, IgA, and IgM) than lymphocytes from normal individuals under the same test conditions.

Moreover, during repeated cell culture tests, B-cells from normal persons produced 8 to 10 times fewer antibodies when lymphocytes from CVH patients were added to the cell cultures. Co-culturing of cells from unrelated normal individuals did not result in any significant reduction in antibody production.

The excessive numbers of suppressor T-cells in CVH patients prevent their B-cells from maturing into fully competent antibody-producing cells (plasma cells), Dr. Waldmann concluded.

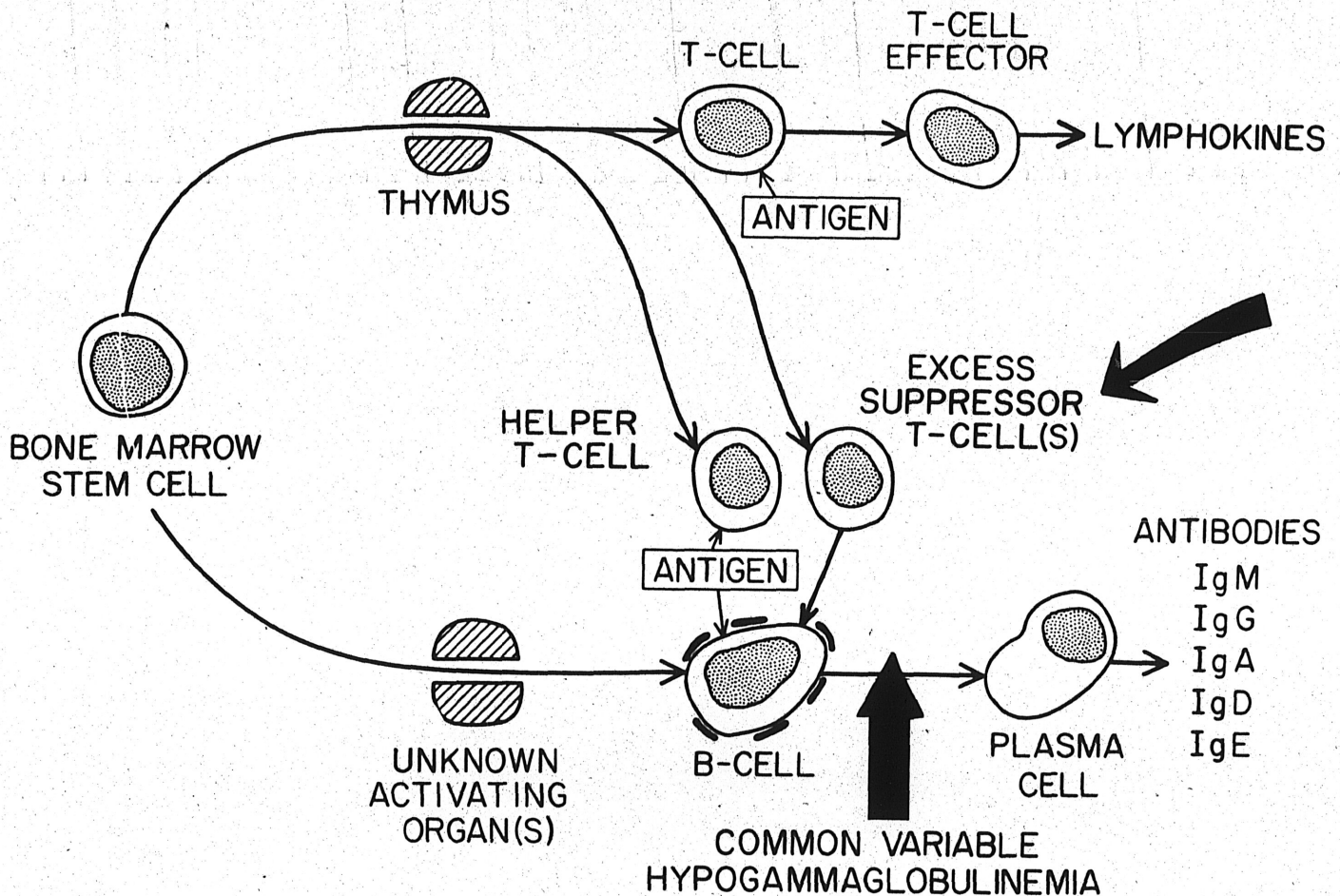
The findings may also have relevance in other diseases associated with abnormal antibody production, he said. In a disease called lupus, for instance, a lack of suppressor T-cells may be the runaway antibody production, creating antibodies against the patient's own normal tissues and organs. Chronic lymphocytic leukemia and cancers of the thymus and bone marrow may also be associated with T-cell imbalances.

The research was conducted by Dr. Waldmann, Samuel Broder, M.D., Mary Durm, Marcia Blackman, R. Michael Blaese, M.D., and Warren Strober, M.D.

of the Metabolism Branch of the National Cancer Institute at NIH, one of the six agencies of the Public Health Service. It was reported in a recent issue of the British journal *Lancet*.

The existence of suppressor T-cells was reported in 1970 by Phillip J. Baker, Ph. D. of the NIH National Institute of Allergy and Infectious Diseases.

Dr. Waldmann observed that research at Yale and Harvard Universities and the NIH National Institute of Arthritis, Metabolism and Digestive Diseases also provided background information contributing to this new understanding of the nature of common variable hypogammaglobulinemia. The current findings, in turn, help to delineate some of the mysteries of the entire immune system.



SCHEMATIC DRAWING OF THE COMPLEX MECHANISM OF ANTIBODY FAILURE IN COMMON VARIABLE HYPOGAMMAGLOBULINEMIA (CVH). Large arrow at bottom indicates blockage in normal B-cell* maturation into antibody-producing plasma cells. NIH scientists postulate that normal persons are capable of producing adequate amounts of "helper" and "suppressor" T-cells in response to disease agents, or antigens. Abnor-

mal "suppressor" T-cells production adversely affects B-cell maturation; excessive numbers of "suppressor" T-cells are conclusively linked to CVH. *B-cells and T-cells are believed to originate as primitive stem cells of the bone marrow. Other immunologic factors in the body's defense are lymphokines, eg. interferon, lymphotoxin, and macrophage-inhibiting factor, which assist in the rejection of grafts and in normal delayed hypersensitivity reactions.

'Wager with the Wind' Tells the Story—

Extraordinary Flyer -- Don Sheldon

FAIRBANKS — For years Alaskans have read in their newspapers of the aerial exploits of Talkeetna bush pilot Don Sheldon, but such items taken together form no more than a fragmentary account of the life of the extraordinary flier. And of necessity they dealt primarily with events rather than the human side of a rugged, compassionate individual with an enormous zest for living.

Now the Sheldon story has been told at length in a new book, "Wager with the Wind,"

by James Greiner, curator of exhibits at the University of Alaska Museum at Fairbanks and a close friend of Sheldon.

A limited number of copies of the 235-page book have been air-freighted to Fairbanks and Anchorage by the publisher, Rand McNally. The main shipment is due in the state at the end of October, and about that time several autograph parties will be scheduled with both Greiner and Sheldon present.

The foreword to the book and a number of photos contained in

it were provided by Dr. Bradford Washburn, director of the Boston Museum of Science. A long-time friend of Sheldon, Washburn has led numerous Alaskan mountaineering and scientific expeditions and three times has climbed to the summit of Mt. McKinley.

Greiner's book essentially is an account of Sheldon's career in high-risk flying — of his transporting mountaineering expeditions to lofty glaciers, resupplying them, and coming to their rescue when in trouble. Mt. Mc-

Kinley drew many of these expeditions and Sheldon's special relationship with this highest of North American peaks is central to the story.

During his 34 years of flying in Alaska, Sheldon has made almost a science of mountainside glacier landings. He is married to the daughter of famed "Glacier Pilot" Bob Reeve who as an early-day Alaska flier pioneered such landings.

There is a more mundane side to Sheldon's life: he regularly flies supplies and mail to

homesteaders, prospectors and other bush residents and puts hunters and fishermen down in prime locations.

Author Greiner's friendship with Sheldon began when he chartered him for a fishing trip some 10 years ago. Since then they've hunted and fished together. As a private pilot working toward a commercial license, Greiner has learned much from Sheldon.

Once he began work on the book, Greiner saw the flier of-

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