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Interferon Shows Renewed Promise Researchers Find the Heralded Drug Works
 in a Surprising Variety of Illnesses.

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Nearly 20 years ago, a small Swedish study piqued the interest of key cancer researchers around the world. The Swedes found that a substance extracted from white blood cells showed promise in fighting bone cancer.

The drug was interferon-hailed as the "magic bullet" against cancer. Time magazine made interferon a cover story, and public broadcasting's "MacNeil-Lehrer NewsHour" devoted an entire program to the drug in 1980.

But nearly as fast, interferon's fame faded. Researchers became discouraged because the so-called "wonder" drug struck out in fighting most types of cancer. The British scientific journal Nature described it as the "Rise and Stall of Interferon."

Today, however, interferon is making a quiet, but dramatic, comeback. It is the standard treatment for conditions as varied as hepatitis, hairy cell leukemia and genital herpes. Interferon now battles certain AIDS-related complications, and most recently, a form of the drug, Betaseron, won Food and Drug Administration approval for the treatment of multiple sclerosis.

"There is a major resurgence in the interest of this drug," said Scott Lippman, associate professor of medicine at the M.D. Anderson Cancer Center in Houston, which has pioneered much of the research on interferon.

Regaining Momentum

Catch a cold or become stricken with the flu, and your body will begin to manufacture interferon. The substance is a naturally occurring protein produced largely by white blood cells in response to any type of viral infection.

Commercially produced interferon was one of the first of the so-called "biologicals," drugs manufactured in the laboratory that are identical to substances produced naturally by the body. Discovered in 1957 by Alick Isaacs and Jean Lindenmann at the National Institute for Medical Research in London, interferon drugs seem to work by boosting the immune system. They appear to keep viruses from overtaking the body as well as preventing abnormal growth of cells.

Initial research on interferon was limited because it was tedious and expensive to extract the substance from white blood cells. But in 1976, Swiss scientists announced that they could clone human interferon genes; large-scale production of genetically engineered interferon began a few years later.

By the mid-1980s, researchers found that interferon turned a fatal disease, hairy cell leukemia, "into one with almost 100 percent survival," said Jordan U. Gutterman, professor and chairman of clinical immunology and biological therapy at M.D. Anderson and a strong advocate of the drug.

The expectation was that interferon would prove to be a powerful weapon against a wide array of cancers. "We had all hoped that this would be the answer and that it would come in minutes, and if not in minutes, in days," said John Kirkwood, professor and chief of medical oncology at the University of Pittsburgh Medical Center and associate director of the Pittsburgh Cancer Institute.

That never materialized, and interferon was nearly abandoned, a victim "of high expectations that led to a lot of disappointment," said M.D. Anderson's Lippman.

Today, the story is different. Estimates are that at least 30,000 Americans will be treated in the coming year with one of three forms of interferon known as alpha, beta or gamma. Abroad, its use is even more widespread.

According to Kathryn C. Zoon, director of the FDA's Center for Biologics Evaluation and Research, interferon "has the ability to affect so many things that we really haven't yet learned all of its potential."

The years of research are starting to pay off. "We are seeing right now the beginning of the translation of knowledge from the laboratory bench to the clinic," she said.

Worldwide sales of alpha interferon alone reached \$565 million in 1992, according to industry analysts Decision Resources of Waltham, Mass. Nearly a quarter of those sales, roughly \$135 million, occurred in the United States. By 1997, Decision Resources predicts, sales will run \$1 billion worldwide and hit \$300 million in the United States, outstripping most other biotechnology drugs.

During the next decade, these drugs can be expected to expand their clinical usefulness, according to Ernest C. Borden of the University of Wisconsin in Madison. In an editorial on interferon published in 1992 in the New England Journal of Medicine, Borden noted that interferon drugs are now licensed in more than 40 countries for at least a dozen indications.

As a group of medications, interferon drugs "will definitely be among the top 20 drugs sold worldwide," said David A. Godolphin, vice president at Decision Resources.

Of the three main classes of human interferon, alpha is most in demand and the subject of the greatest amount of study. Two of the three interferon drugs now approved for use in the United States-Intron A made by Schering-Plough and Roferon-A by Hoffmann-La Roche-each contain alpha

interferon.

In the body, alpha interferon is produced mainly by leukocytes, white blood cells, but nearly every cell in the body has the capacity to secrete tiny amounts of alpha interferon. Beta interferon comes from fibroblasts, cells located throughout the body that secrete collagen, a protein that gives resiliency to skin. Gamma is produced largely by T cells, the foot soldiers of the immune system that are responsible for, among other things, identifying viruses as foreign invaders.

Each type of interferon seems to have a slightly different function in the body. "Alpha interferon's role seems to be in regulating abnormal growth," said M.D. Anderson's Gutterman. "Gamma, which is primarily effective in infectious diseases, is an immune stimulator. Beta interferon's role is still being identified."

Despite the recent successes of interferon and its future promise, there are some serious drawbacks to these new medications, including side effects and cost. Some conditions need only short courses of treatment, but others, such as leukemia and multiple sclerosis, can require a lifetime of therapy.

Daily injections can run \$10,000 a year, and not all insurance companies pick up the cost. Some forms of interferon, such as Betaseron, are in such short supply that a lottery is used to decide which patients will receive the drugs until production can catch up with demand.

Those who use interferon must also often cope with its flu-like side effects, which include fever, loss of appetite, fatigue, as well as joint aches and pains. Taking interferon requires another inconvenience: regular blood tests to make sure that the drug is not damaging the liver or the immune system.

But to those for whom the drug makes the difference between illness and health, the benefits can far outweigh the risks and side effects. At 6 months of age, Glynnis Eldridge labored to breathe while awake. Asleep, her narrowed airways collapsed, under the pressure of a large and rapidly growing tumor of blood vessels, known as a hemangioma. These rare, noncancerous growths strike about 10 percent of newborns, but they are usually inconsequential and go away without treatment. For a small number of children such as Glynnis, however, these tumors grow beneath the skin and become life-threatening as they encroach upon vital organs. Glynnis's airways and spinal cord were threatened. Standard treatment with steroid drugs didn't work. She woke throughout the night gasping for breath.

Until, that is, she began receiving daily injections of alpha interferon as part of a study at Children's Hospital in Boston in June 1991.

Ten weeks after the shots began, the tumor had shrunk enough for Glynnis to breathe normally. By 20 weeks, an MRI scan showed the growth continuing to regress. Glynnis is now 3, and she and 16 others in the study of 20 children remain healthy as their tumors continue to shrink, according to R. Alan B. Ezekowitz, who published results of his study last year in the New England Journal of Medicine.

"For us," said Glynnis's father, Dan Eldridge, "interferon is a miracle drug."