Taking a Shot at Melanoma

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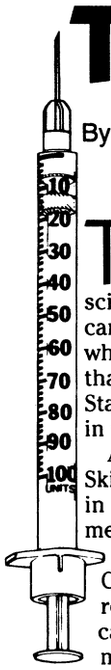

These are the memories of summer: fun in the sun . . . brilliant days at the beach . . . and, according to scientists, a "bright future" for a skin cancer called malignant melanoma — whose incidence is growing faster than that of any other cancer in the United States, with the exception of lung cancer in women.

According to the New York City-based Skin Cancer Foundation, for those born in 1930, the lifetime risk of developing melanoma was 1 in 1,500; the risk today is 1 in 150 and rising. The American Cancer Society, also in New York City, reports that 5,800 of the 7,800 skin-cancer deaths each year are caused by malignant melanoma, and that an estimated 26,000 new melanoma cases are diagnosed annually.

While the data linking most types of skin cancer with repeated sun exposure are considered conclusive, scientists have been less certain about sunlight as a cause of the more serious malignant melanoma. Melanoma, which occurs when the pigment-containing skin cells called melanocytes become malignant, differs from most other skin cancers in that it can spread from the surface into the body. Although 85 percent of non-melanoma skin cancers are on the face and hands, only about 20 percent of melanomas first appear on these traditionally sun-drenched areas.

There is increasing evidence, however, that intense doses of ultraviolet radiation from the sun might be the triggering factor. "It is the sunburn you get in your teens or early 20s, rather than chronic sun exposure, that does you in," says Darrell S. Rigel of New York University's Medical Center. He told SCIENCE NEWS that other risk factors for melanoma include the presence of abnormal moles, fair skin color and residence nearer the equator — all supporting the sun-exposure theory.

Fortunately for everyone under the sun, malignant melanoma detected early is considered "a curable cancer" amenable to surgical removal. Although incidence has jumped 83 percent in the last seven years, says Rigel, the death rate has risen more slowly because of early treatment. Far too often, however, the suspicious mole or dark patch on the skin is ignored until the melanoma has grown deep into the skin or spread to organs.

Advanced melanomas mean a poor prognosis, and surviving them can require more complicated treatment strategies. Among experimental approaches being studied are those that alter a patient's immune response. Like other cancers, a melanoma is the patient's own cells spreading out-of-bounds, and scientists reason that different types of immunotherapy may help stop their trespassing in otherwise normal tissues.

Among the potential therapies studied are classes of proteins, such as interferon and interleukin-2, that provoke the immune system into attacking foreign objects like cancer cells. But a lack of specificity and problems with toxicity may limit their use. Some scientists, like Rigel and Malcolm S. Mitchell of the University of Southern California at Los Angeles, are assessing antimelanoma vaccines as more specific alternatives for human treatment. Animal studies already have shown that the vaccines are nontoxic and protect mice against injected melanoma cells. Unlike other vaccines, however, these are not designed primarily to *prevent* a tumor from starting, but to stop its continued growth.

Mitchell and his co-workers are in the middle of a clinical trial of their particular vaccine, which is made from human melanoma cells grown in culture dishes. They break the cells apart and use components from cell-membrane surfaces as antigens to immunize patients, whose killer T cells apparently are stimulated by the vaccine. How this stimulation leads to tumor shrinkage is unclear, Mitchell said in an interview. The current phase II study — designed to test the efficacy of the vaccine in a dozen patients — is measuring whether the vaccine halts proliferation of melanoma cells *in vivo*.

Patients receive weekly injections of the vaccine for a month, followed by a booster shot two weeks later. In an earlier study, the researchers also treated half the vaccinated subjects with an anticancer drug called cyclophosphamide, which selectively inhibits suppressor T lymphocytes. Promising results from that clinical trial have been submitted for publication in a scientific journal, Mitchell says. He suggests that "the vaccine may be setting up the patients immunologically [so they're more receptive to other agents like interleukin-2 or chemotherapy]."

Results from the current study are incomplete, says Mitchell. But, he says, in about one-third of the patients, the tumors have shrunk by more than 50 percent. And a patient receiving monthly booster shots following an earlier trial is still in remission a year later. "I'm convinced the vaccine has extended her survival," says Mitchell, adding that booster shots probably would be needed throughout a patient's life.

A problem in making antimelanoma vaccines, says Rigel, is that the surface antigens on melanoma cells are constantly changing, so "essentially you're injecting yesterday's news" if using only a small number of surface antigens in vaccine production. To circumvent this, New York University's Jean-Claude Bystryn has concocted what Rigel calls "a smorgasbord of the 100 most common [melanoma] antigens."

Bystryn's clinical study of 100 patients thus far shows that about half the patients have increased antibody production against melanoma cells, or enhanced cellular immunity so more immune cells attack the cancer cells. "We are trying to find ways to maximize the vaccine's augmentation of the immune system," Bystryn told SCIENCE NEWS. "Melanoma is an erratic tumor, so it is difficult to tell whether the vaccines will work in patients [as standard therapy]." Despite good results from his research and that of others, Bystryn cautions that currently "there is no conclusive evidence that any immunotherapy affects the final outcome of melanoma."

As by-products of melanoma research, monoclonal antibodies specific for melanoma cells have exciting potential, says Rigel. Whether or not they play a role in future vaccines, he says, they could be used during diagnosis to separate malignant melanoma from so-called dysplastic nevi, moles that resemble melanomas but are benign.

As to whether antimelanoma vaccines may someday actually prevent the onset of melanoma, Bystryn says that "it is a hope, but at this stage, it is purely speculative. Vaccine development for cancer is not a hot area — but there are a number of people [doing the research], and it will attract more." Other groups are working on vaccines against cancers of the colon and kidney.

Mitchell also has hopes for preventive melanoma vaccines. "It could be a vaccine in the true sense of the word, but [vaccine development] is a tough business," he says. He points out that most vaccines are designed to attack the basic cause of a disease, but the fact that no one knows what causes malignant melanoma makes this approach impossible. □