Skin cancer's return: How big a threat?

People who have already suffered one bout with certain skin cancers are at risk of getting the disease again. A new study quantifies that menace and provides dermatologists with a more detailed picture of squamous and basal cell cancers, two very common and highly curable types of skin cancer.

Previous studies suggesting an increased risk of new tumors in patients treated for these nonmelanoma skin cancers were too small to provide definitive results. Now, Margaret R. Karagas and John A. Baron of Dartmouth Medical School in Hanover, N.H., and their colleagues report the results of the largest multicenter study of such skin cancers to date. Their research shows that people with a history of squamous and basal cell cancers run a 35 percent risk of developing another tumor within three years and a 50 percent risk within five years.

"It's the best study of its kind," comments dermatologist Howard Koh of Boston University School of Medicine. The findings indicate that the magnitude of the jeopardy for people with prior skin cancers is higher than previously suspected, Koh adds.

The researchers studied 1,805 people with a history of nonmelanoma skin cancer. Unlike melanoma, an aggressive cancer that often spreads lethally beyond the skin, nonmelanoma skin cancers behave more indolently. Basal and squamous cell cancers can appear as pale, waxy nodes or red, scaly patches on the skin. If promptly treated, nonmelanoma skin cancers rarely cause death.

The study involved patients visiting clinical centers in Los Angeles, San Francisco, Minneapolis and Hanover. All volunteers were free of cancer at the study's start and had completed a questionnaire about their exposure to sunlight and personal characteristics such as skin type and hair color. All participants agreed to visit their dermatologists annually. The research team kept track of any new skin cancers that surfaced during a five-year follow-up period.

The researchers discovered that new skin cancers reported during follow-up tended to be the same cell type as the patient's previous tumor. However, the additional tumors were not caused by spread of the original cancer, the researchers note.

The risk of a subsequent cancer was higher for men, for people age 60 and older, and for volunteers who had reported many previous skin cancers. People who burn easily when exposed to the sun had a heightened risk of developing another nonmelanoma skin cancer.

Baron suspects that men may face an increased risk because they are more likely than women to work outdoors and thus to receive more exposure to skin-damaging ultraviolet rays. Jeopardy may intensify with age simply because years of exposure to the sun take a cumulative toll, he adds.

In an intriguing finding, the study revealed a link between cigarette smoking and the risk of squamous cell cancer. "It is conceivable that cigarette smoke acts directly as a skin carcinogen," the authors write in the June 24 JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION. However, the association between smoking and skin cancer is preliminary, they note. At the same time, the researchers found no clear relationship between smoking and basal cell cancer.

Study participants who lived in Los Angeles and San Francisco ran a greater risk of developing another nonmelanoma skin cancer than did recruits who lived in Minneapolis and Hanover, the researchers discovered. They suggest that ongoing exposure to the sun may be to blame.

Koh and the researchers stress that limiting exposure to the sun is an important first step to prevention. "We think that a great deal of nonmelanoma skin cancer can be prevented with the proper sun precautions," he says. They advise everyone — especially people with a history of skin cancer — to wear strong sunscreen and protective clothing when outdoors. In addition, they recommend that people stay out of the sun at midday, when ultraviolet rays are strongest.

— K.A. Fackelmann

The malaria parasite: Change and conquer

A parasitic relationship resembles a biological arms race. Over evolutionary time, an infected host puts up a new defense to stave off a parasite, only to have that parasite evade the defense and sharpen its skills for circumventing the host's next defensive strategy. And so on, and so on, in a biochemical escalation process that usually ends with the parasite attaining the upper hand.

This change-and-conquer strategy has made it particularly difficult for scientists to develop vaccines against parasites, including the most dangerous malaria organism, *Plasmodium falciparum* (SN: 5/4/91, p.276). Now, researchers led by David J. Roberts of John Radcliffe Hospital in Headington, England, have figured out part of the protein shell game that keeps the malaria parasite in business. A better understanding of this process could lead to new approaches for treating and preventing the deadly disease.

Once the malaria parasite infects a host's red blood cells, it makes proteins that help the infected cells stick to the inner walls of blood vessels. In the June 25 NATURE, Roberts' group reports that *P. falciparum* can mutate these proteins at a rate of 2 percent each generation. This rapid mutation rate helps the organism evade the immune system and avoid traveling to the spleen, where a red blood cell carrying it could be destroyed, the researchers conclude.

P. falciparum has a complex life cycle. Infected mosquitoes inject the parasite's first stage, the sporozoite, into a host while drawing a blood meal. Sporozoites find their way to the host's liver, where each can divide into thousands of merozoites. After roughly a week, an army of merozoites leaves the liver to take up residence in the host's red blood cells. Later, the red cells explode, some releasing more merozoites and others releasing gametocytes, the parasite's sex cells. This causes the fever and chills characteristic of malaria. When another mosquito bites the host, ingesting gametocytes and merozoites, the sex cells combine to form new sporozoites — and the cycle begins anew.

Previous studies have shown that merozoites place proteins on the surfaces of the red cells they infect and that the proteins bind to so-called cell adhesion molecules on other cells (SN: 6/13/92, p.392). This makes the infected red cells stick to uninfected red cells and to the walls of tiny veins, preventing infected cells from being swept into the spleen. The spleen would normally filter out such bulging, parasite-packed cells.

In the new study, Roberts and his colleagues grew one type of *P. falciparum* merozoite in red blood cells maintained in culture dishes. They found that these merozoites divided to form a group of new merozoites that could stick to 10 different cell adhesion molecules.

The researchers conclude that this variation has two functions: It allows the parasite to stay one step ahead of a host's ability to make antibodies that could attack the merozoite proteins, and it ensures that the merozoite-infected red cells won't run out of cells to stick to in order to avoid the spleen.

The process "is really quite amazing," says Russell J. Howard, who studies malaria at the DNAX Research Institute of Molecular and Cellular Biology in Palo Alto, Calif. He adds that it might help explain cerebral malaria, which can cause coma and death.

In cerebral malaria, Howard speculates, *P. falciparum* merozoites might make proteins that stick only to cell adhesion molecules on the cells of blood vessels that serve the brain. This could gum up the specialized blood-brain barrier and block the movement of oxygen and nutrients into the brain — simultaneously strangling and starving that essential organ.

— C. Ezzell