Melanoma

The scientific flap over

By KATHLEEN FACKELMANN

Today's beaches are jammed with people who rely on sunscreen for a safe tan. Yet epidemiologists note that the rise in sunscreen use has proceeded in tandem with an increase in skin cancers.

Epidemiologist Marianne Berwick of Memorial Sloan-Kettering Cancer Center in New York carefully laid out the data on sunscreen use and skin cancer at the annual meeting of the American Association for the Advancement of Science (AAAS) in Philadelphia last February.

Sunscreens may not protect against skin cancer, including melanoma, the deadliest form, she concluded. "We don't really know whether sunscreens prevent skin cancer," Berwick says. People ought to be cautious about relying on these products, she told those attending the meeting.

The American Academy of Dermatology promptly denounced Berwick's conclusions. In a March press release, it called her message "misleading and confusing." Berwick, the release said, was telling the public that sunscreens "do not protect against melanoma."

Roger Ceilley, immediate past president of the academy calls Berwick "a numbers cruncher," not a doctor. He believes that when people hear a conflicting scientific message, they'll simply eschew sunscreen. "We're going to have millions more cases of skin cancer in the next decade" if people forgo it, warns Ceilley, a dermatologist in Des Moines, Iowa.

Frank Gasparro of Thomas Jefferson University in Philadelphia says the academy had a knee-jerk reaction to Berwick's talk. Gasparro, who organized the AAAS session, says Berwick accurately portrayed the data on sunscreen and skin cancer. Put her conclusions together with basic research on sunscreen chemistry, he contends, and there is good reason for concern about these products.

No one interviewed for this article took a position against using sunscreens. However, Gasparro, Berwick, and others suggest that science doesn't offer any firm answer to the question of whether sunscreens prevent skin cancer. "Let's get the facts," Gasparro says.

In her review of scientific studies on skin cancer, Berwick looked first at four studies of squamous cell cancer, a skin cancer that appears on the head, neck, and arms and is generally not lethal. Two of the studies concluded that sunscreen protected against a skin condition thought to lead to squamous cell cancer. The other two reported that sunscreen did not shield people from this type of skin cancer.

Continued on p. 363

n Madness

r sunscreens and skin cancer

By CORINNA WU

The parallel rise in skin cancer and sunscreen use has prompted chemists to reexamine the behavior of the products' active ingredients.

Because sunscreens absorb light energy and must then release it in some form, they may deliver damaging ultraviolet (UV) radiation to sensitive cells. That raises the troubling, but unproved, possibility that sunscreens may have a hand in promoting skin damage. To learn more, chemists are testing sunscreens' responses to UV light.

"Since [sunscreens] are so widely used, it is important to know as much as possible about them," says John Knowland of the University of Oxford in England.

Surprisingly few reports on the chemistry of sunscreens have been published, says John M. Allen of Indiana State University in Terre Haute. So far, cosmetics companies have done most of the work, and they generally don't make their results available.

"Sunscreens have—at least in theory—the potential to inflict damage. That is, of course, a far cry from saying that they actually do inflict this damage in humans," says Knowland. Are they beneficial or harmful? Indeed, that's the burning question researchers want to answer.

The sun bathes Earth in UV rays—short, energetic wavelengths of light that can damage cells. Most of the UV light that reaches Earth falls in the ultraviolet A (UVA) range, having wavelengths of 320 to 400 nanometers (nm). Such rays penetrate deep into the base layer of the skin, or dermis.

Less of the light that reaches Earth's surface is in the ultraviolet B (UVB) range, with wavelengths of 290 to 320 nm. This light doesn't penetrate skin as deeply as UVA light, but it is more damaging.

Scientists have only recently started paying attention to UVA radiation, once known as "tanning rays" in contrast to UVB's "burning rays." Tanning booths, for example, emit mostly UVA light.

Researchers now know that UVA radiation both tans and burns the skin. Moreover, both UVA and UVB play a role in initiating skin cancers—UVB by damaging DNA and UVA by suppressing the immune system. With the skin's defense and repair mechanisms held in check, damage goes unrepaired, thus leaving the door open for cancers to develop.

Sunscreens prevent UV light from reaching the skin in one of two ways—by absorbing it or by scattering it. Active ingredients such as Padimate O, octyl methoxycinnamate, and octyl salicylate absorb

Continued on p. 365

Continued from p. 360

Berwick also reviewed two studies of basal cell carcinoma, another nonlethal skin cancer, at the AAAS meeting. Basal cell cancer, the most common form of skin cancer, also appears most frequently on the head, neck, and arms. Those studies showed that people who used sunscreen were more likely to develop basal cell cancer than people who did not, she told SCIENCE NEWS.

She included 10 studies of melanoma, the skin cancer that gets the most attention because of its virulent nature. Melanoma often develops in or near moles on the skin. In later stages, such cancer can be lethal because of its tendency to spread throughout the body.

In five of the studies, people who used sunscreen were more likely than nonusers to develop melanoma. In three studies, including one done by Berwick, no association appeared between sunscreen use and melanoma. In two studies, people who used sunscreen seemed to be protected.

The epidemiological data are all over the map. The question is, how does one interpret these back-and-forth findings?

One view is that such studies simply do not tell researchers much about sunscreen and skin cancer. Richard P. Gallagher, chief of the cancer control research department at the British Columbia Cancer Agency in Vancouver, says that most of the studies on skin cancer were conducted during the 1970s and 1980s on people in their fifties. Companies marketed the first effective sunscreens during the 1960s, Gallagher notes, so participants couldn't have worn effective sunscreens during childhood, when exposure is thought to kick off the events leading to a skin cancer.

Cancer, including skin cancer, develops in a multistep process. In theory, a skin cell first sustains some injury to its DNA. This initial event, when coupled with subsequent injury, results in a cancer many years, even decades, later. Studies of people who have worn sunscreens for decades have yet to be completed.

Researchers who have become concerned about the safety of sunscreens because of the epidemiological studies have suggested several possible ways in which the products may increase cancer risk.

Berwick, for example, thinks that people who use sunscreen stay out in the sun longer. Sunscreens effectively block the ultraviolet B radiation that causes sunburn, Gasparro says, but they don't all shield the skin from potentially harmful ultraviolet A rays. People who use sunscreen for all-day exposure may get enough ultraviolet radiation to damage the DNA in their skin, he says.

"Sunscreen is a help, but it's not an excuse to stay out in the sun," agrees Rosemary D. Cress of the Cancer Surveillance Program in Sacramento. Cress' 1995 study in the May 15 AMERICAN JOURNAL OF EPIDEMIOLOGY showed that women who used sunscreen appeared to be protected from melanoma. Nonetheless, she recommends caution until that finding is confirmed.

If sunscreens don't effectively block harmful radiation, people at high risk of melanoma may be especially vulnerable. Berwick contends that people who burn easily are the ones who rely most on sunscreens to extend their time outdoors.

In a 1996 study, Berwick and her colleagues showed that people with fair hair and complexions were six times as likely to develop melanoma as people with darker skin and hair. In addition, having numerous skin moles increases the risk of this lethal cancer six fold.

While exposure to the sun plays a role in melanoma, Berwick says, underlying genetic factors may also exert an influence on an individual's risk of this cancer.

The pattern of exposure may be important too. After reviewing several epidemiological studies, Berwick suggests that recreational exposure, in which people get too much sun on their occasional day off, may contribute to the epidemic of melanoma cases seen in the United States and other countries.

The scientific debate doesn't appear on the back of sunscreen bottles, so what's the average sun worshipper to do?

"We do know that both [ultraviolet A and ultraviolet B radiation] cause damage" to the skin, Berwick says. "But life causes damage." She recommends a cautious, yet not unreasonable, approach to summer fun.

For anyone who has to be out in the sun, she suggests protective clothing, including hats, to shield the skin. Far from delivering a no-sunscreen message, Berwick recommends such protection when exposure is unavoidable, such as on a visit to the beach.

Ironically, the American Academy of Dermatology takes much the same approach.

Its literature recommends wearing tightly woven clothing, such as a long-sleeved shirt and pants, and using a sunscreen with a sun protection factor of at least 15. The group also advises people to avoid the midday sun.

Some epidemiologists say that message just won't sell to a sun-seeking public. Residents of Vancouver, for example, would have a hard time complying with the skin cancer guidelines put out by the experts. "If you get sunlight 3 months a year, there's no way you're going to be inside," Gallagher says.

Researchers don't know how much sun is required to cause the damage that leads to skin cancer, although they will someday develop a precise indicator of how much exposure is too much, Gallagher says. Until then, sunscreen, a hat, and a liberal dose of common sense appear to be the best protection. □

Continued from p. 361

primarily UVB rays. The first sunscreen developed, para-aminobenzoic acid (PABA), fell out of use because it stained clothing and was found to cause allergic reactions in some people. Last year, FDA approved avobenzone, also known as Parsol 1789, as a UVA absorber.

Other substances, such as titanium dioxide and zinc oxide, can scatter both types of UV light. So-called chemicalfree sunblocks often contain these compounds, as did the white paste that decorated the noses of lifeguards years ago. Sunscreens today use smaller titanium dioxide particles, which are invisible.

Most sunscreen formulations contain a mix of these compounds to provide broad-spectrum protection over UVA and UVB wavelengths.

If sunscreens absorb light, they must also re-emit it. "They cannot destroy that energy, they can only convert it to some other form," says Knowland. Moreover, scattering compounds that reflect light off the skin also redirect some of it onto the skin.

When exposed to UV light, a sunscreen's active compounds interact with inert ingredients and with each other, as well as with the skin. The first step in deciphering this complex interplay is to conduct test-tube studies of the chemicals involved.

The results may not reveal what sunscreens actually do on the skin, but they do indicate what sunscreens are capable of doing—"so that if you want to examine what these chemicals might do in a realistic situation, then at least you know what to look for," Knowland explains.

In the early 1980s, researchers demonstrated that PABA increases the formation of a particular DNA defect in human cells. This defect occurs when two adjacent molecules of thymine, one of the four bases of DNA, link together chemically to form a dimer. People who lack the mechanism to repair these defects are more susceptible to skin cancer, says Knowland. "Thymine dimers in your DNA are bad news."

Last year, Knowland and Oxford colleague P.J. McHugh found in test tubes and in laboratory-grown human cells that Padimate O, a derivative of PABA, does not generate such thymine defects. However, it does oxidize DNA, and it produces free radicals that break DNA strands.

Titanium dioxide and zinc oxide create similar strand breaks. Aware of the compounds' potency, manufacturers coat the sunscreen particles to make them less active. "These treatments do indeed reduce the activity," Knowland notes, "but they don't seem to eliminate DNA damage altogether."

Experiments have shown that sunscreen-protected skin seems to suffer less DNA damage than unscreened skin, notes Frank Gasparro of Thomas Jefferson University in Philadelphia. "However, DNA damage isn't the only thing that contributes to skin cancer." In recent years, dermatologists have also become concerned about sunlight's ability to suppress the immune system, but little is known about this effect.

Knowland says that hydroxyl radicals probably caused the DNA strand breaks he observed in his laboratory experiments. Allen adds that oxygen radicals, while not as reactive, can also harm DNA and other cell components. In collaboration with Sandra K. Allen, he used a filtered lamp that simulates sunlight to illuminate various sunscreens and gauge their ability to produce oxygen radicals.

That ability varied widely. PABA generated oxygen radicals most readily, whereas benzophenones, such as oxybenzone, and salicylates appeared to produce none. "They are not equal," Allen says. Based on these results, however, Allen hesitates to recommend any one sunscreen over another.

The picture gets even more complicated when one considers how the sunscreens interact with the radicals they have generated. "The sunscreen actually forms oxygen radicals that we would like to protect the skin against, but sunscreen also reacts with and traps them," mitigating harmful effects, Allen speculates. Some scientists argue that it is by trapping radicals that sunscreen blends offer their protection, he notes.

No one knows whether sunscreens form oxygen radicals under real-world conditions, nor, if such radicals do form, whether they would damage living cells, Allen cautions.

Much of the debate rests on whether a given sunscreen penetrates the skin. If it stays on the outermost layer, the epidermis, the effects of free radicals may not matter, since the epidermis is made of dead skin cells, says Allen. If a sunscreen penetrates the epidermis, enters the underlying cells, and is then excited by UV light, the picture becomes more disconcerting.

Studies have shown that skin does absorb certain sunscreens. The breakdown products of PABA, for example, can be detected in urine, Knowland says. The same is true of the UVA absorber oxybenzone, researchers from the University of Queensland in Australia reported in the Sept. 20, 1997 LANCET. Schering-Plough Health Care Products in Memphis, Tenn., manufacturer of several brands of sunscreen, countered in the Feb. 14 LANCET that the amount of absorbed compound the Australian team detected was too small to be harmful.

UV-scattering compounds don't sidestep the question of absorption either. Reducing the size of titanium dioxide particles to make them invisible could also enable them to enter cells more easily, Knowland suggests. "As far as published literature is concerned, my own personal view is that this question has not been adequately addressed yet."

"The bottom line is, are sunscreens a good thing or not?" Most experts would say yes, perhaps dismissing as irrelevant the effects observed in the laboratory, Knowland continues. "They may turn out to be right, but my own view is that you have to continue to explore that before making an absolutely definitive pronouncement."

"Wishing for a result isn't going to get that result," Gasparro remarks. "More research and understanding of basic science and biology in the skin—that's going to tell us what's going on." □

Letters continued from p. 355

Why platelets are stupid

"Genetic makeup can boost aspirin's benefit" (SN: 5/2/98, p. 278) states, "Platelets, the smallest blood cells, are indispensable." Technically, platelets are not cells—they lack nuclei and stem from cytoplasmic fragments of large bone-marrow cells.

This lack of genetic information explains why "'platelet cells are pretty stupid.'"

James G. Losser
Evanston, Ill.

Inserted genes and survival

For an inserted gene to spread to most mosquitoes in the wild ("Colorful gene marks mosquito manipulation," SN: 4/4/98, p. 213), wouldn't it have to provide some survival advantage to the insect? Doesn't the fact that mosquitoes are carriers of diseases such as malaria suggest that these pathogens themselves provide some survival advantage and that eliminating them from the mosquito would be a detriment to its survival?

Ted Toal
Nevada City, Calif.

Not necessarily. As for your second question, the malaria-causing parasites offer no known benefit to the mosquitoes that host them. Unlike genes, the parasites aren't inherited by a mosquito's offspring and therefore play no role in natural selection. —J. Travis

Early work on mutualism

"Mutualisms seen as partnerships for barter" (SN: 4/11/98, p. 230) is an excellent model, and I believe it applies to much more than fungi and plants.

In 1902, P.A. Kropotkin published an extended scientific study of animals and of human societies, looking for validation of the "standard" interpretation of Darwin's law of the survival of the fittest. What he and others found was that, as interpreted then, survival of the fittest operated primarily against nature.

The second great law of survival most prominent among animals, within or without the same species, was mutual aid. See *Mutual Aid: A Factor of Evolution* by Kropotkin, published originally in 1902 and still available.

John D. Shotzbarger
Minneapolis, Minn.