



BENCHSIDE DISPATCHES By William Ju, MD

PHOTOPROTECTION

AN INTERVIEW WITH STEVEN Q. WANG, MD

Welcome to the fourth installment of *Benchside Dispatch*, a series of interviews with top researchers in the field of dermatology intended to highlight important advances in the care of medical skin disorders. In this installment, Steven Q. Wang, MD, discusses photoprotection. Dr. Wang is a board certified dermatologist and Director of Dermatologic Surgery and Dermatology at the Memorial Sloan-Kettering Cancer Center in Basking Ridge, New Jersey. Dr. Wang serves on the board of the Photomedicine Society and on the Photobiology Committee of the Skin Cancer Foundation. He has published extensively in peer reviewed scientific journals on photoprotection and is co-editor of the academic textbook "Principles and Practice of Photoprotection."

Photoprotection seems like such a simple thing. Patients should wear sunscreen and they should know that taking precautions against harmful ultraviolet (UV) radiation is in their own best interest. However, as we learn in an interview with Steven Q. Wang, MD, there are a lot of misconceptions about photoprotection and our current view of the topic may be over simplified. From a public health perspective, there are limitations in being able to influence good behavior on the part of patients, even with a seemingly simple task such as applying and re-applying sunscreen. Moreover, although we are readily counseling patients against UV light, newer evidence suggests that exposure to energy from the visible and infrared regions of the solar spectrum can also induce biologic changes in the skin that can have unhealthy consequences.

Thankfully, as Dr. Wang points out, emerging research is unveiling novel strategies to provide more robust protection, and new technologies in the pipeline may even facilitate greater compliance.

William Ju, MD: What is the current state of the science in photoprotection and what is the focus of your research in this area?

Steven Q. Wang, MD: There are a number of aspects to improving the state of the science. The first is that we know that when it is used properly, sunscreen can help prevent skin cancer and prevent cutaneous signs of aging; however, unfortunately, most people do not remember to use it, and, when they do, they may use it incorrectly. We have been trying for decades to educate the public about the risk of skin cancers and the harmful effects of UV radiation, and although prog-

ress has been made, behavior can be even further improved. So one challenging question we are looking at is, how do we change behaviors?

A second focus can be aimed at understanding the effects of visible light and infrared on the skin and looking for ways to protect through that part of the spectrum. For example, visible light can cause hyperpigmentation in darker skin types, which may be a factor in conditions such as melasma, but current sunscreen offerings only protect against UV.

Third, I think additional strategies can come out of preventing damage to skin structures from free radicals generated by interactions with light. This can be blocking the formation of free radicals after chromophores absorb light and release energy, or this can come from intercepting free radicals that are produced.

Dr. Ju: Does that imply that the products currently on the market may be suboptimal for complete photoprotection?

Dr. Wang: Overall, currently available sunscreens actually do a very good job in preventing harmful effects from UV radiation, assuming people use them correctly. Yet, they do not block all the long range UVA, visible light, or infrared. We have learned in the past 3 to 4 years that all of those unblocked wavelengths of light can interact with chromophores and trigger the production of free radicals, which may be a mechanism for hyperpigmentation, breakdown of collagen, and formation of wrinkles.

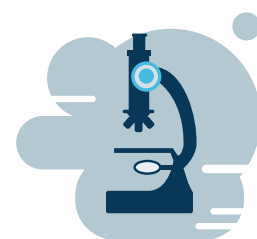
Dr. Ju: Are there potentially novel strategies for more robust skin protection?

Dr. Wang: One of the interesting strategies being explored is the use of molecules to prevent the production of or neutralize free radicals after they have formed. When light reacts with skin chromophores in the ground state, the energy moves them into an excited state. When the excited chromophore reverts back to its resting phase, energy is released that has potential to interact with oxygen and yield free radicals as a byproduct. And so an idea is to intervene with a molecule that could quench that energy to prevent free radical formation. Another plausible approach is the use of antioxidants that would neutralize free radicals once they have formed.

Along these lines, there is interesting research being performed by Salvador Gonzalez with *Polypodium* fern, botanical extracts of which have a rich content of polyphenols and other antioxidant components.

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That group has shown that ingesting *Polypodium* extract before sun exposure has a sun protective factor effect. For reversing skin cell injury after free radicals have been produced by light, an example is bench research from Diona Damin's lab indicating that nicotinamide can enhance energy-dependent DNA excision repair after UV damage. Clinically, in results published in the *New England Journal of Medicine*, oral nicotinamide reduced the rates of new nonmelanoma skin cancers and actinic keratosis in high-risk patients. Other innovative approaches for photoprotection include alfamelanotide, delivered by subcutaneous implant, which is approved in Europe for photoprotective use in erythropoietic protoporhyria. This drug is an analog of alpha-melanocyte stimulating hormone, and in binding to the melanocortin-1 receptor, increases the production of melanin, which in turn has both antioxidant activity and filters UV and visible light. This approach of systemic distribution for protecting the integumentary system from solar radiation currently has more use in Europe than in the U.S.

Dr. Ju: How do you foresee this changing paradigm affecting how photoprotection will be accomplished in the next 5 to 10 years?

Dr. Wang: In addition to new active molecules that broad-

en the spectrum of photoprotection and that prevent the production of and mitigate the damage from free radicals, there can be advances in vehicle innovation. Easily and evenly distributing and then maintaining topical protection in a more efficient and aesthetically pleasing manner can increase effectiveness and compliance. Novel polymers for example may be able to keep higher concentrations of light filters for longer periods of time on the skin surface while minimizing systemic absorption. Conversely penetrating the stratum corneum and appropriately delivering molecules to deeper skin compartments will be important in strategies aimed at reducing light-induced free radical production and reversing the damage they cause.

I think that digital technology can also play an increasingly important role. For example, recently we have seen the introduction of thin sensors that can be applied like an adhesive tape and provide feedback to a smartphone app on the level of UV light exposure. This may help change behaviors, reminding people to use sunscreen. Going forward, we can expect to see further development of these types of wearables for photoprotection and the expanding application and utility of medical informatics in dermatology. ■

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