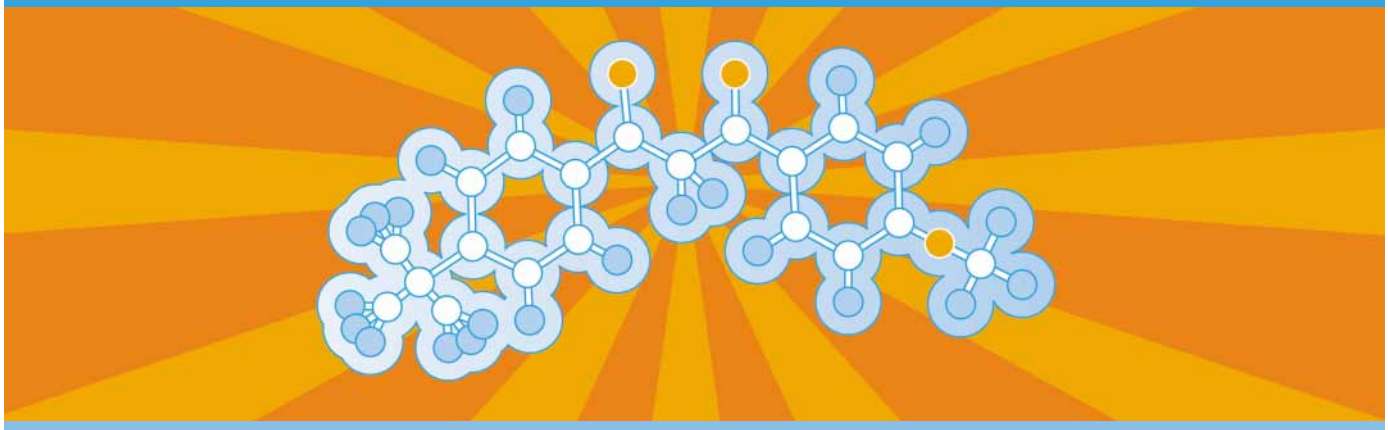
A SUPPLEMENT TO
Skin & Allergy News®

HIGHLIGHTS OF A ROUNDTABLE DISCUSSION

PHOTOPROTECTION: RECENT ADVANCES IN SUNSCREEN STABILITY



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HIGHLIGHTS OF A ROUNDTABLE DISCUSSION

Photoprotection: Recent Advances in Sunscreen Stability

TOPIC HIGHLIGHTS

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TARGET AUDIENCE

This supplement has been developed for dermatologists and other health care professionals who are concerned with issues involving photoprotection and who recommend sunscreen products to their patients.

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Dr Ceilley is a consultant to OrthoNeutrogena. He does not have any stock interests, equity interests, or patent-licensing arrangements that could be considered a conflict of interest for this supplement.

Dr Cole is an employee of, directs funding for clinical grants, and holds stock from Johnson & Johnson.

Dr Draelos is a consultant to Neutrogena Corporation. She does not have any stock interests, equity interests, or patent-licensing arrangements that could be considered a conflict of interest for this supplement.

Dr Rigel is a consultant to, and has received funding for clinical grants from, Neutrogena Corporation.

PHOTOPROTECTION AND OUR EVOLVING UNDERSTANDING OF THE EFFECTS OF ULTRAVIOLET LIGHT

INTRODUCTION

The deleterious effects of exposure to ultraviolet (UV) light have been well documented, and a national campaign to reduce sun exposure has been under way for some time. While it was once thought that ultraviolet B (UVB) light was responsible for the vast majority of damaging UV-related effects, over time evidence has also implicated ultraviolet A (UVA) light as playing a notable role in photoaging; UVA also appears to be involved in photocarcinogenesis.

The development of UVA-specific photoprotectants is paralleling our advancing understanding of UVA effects. Methods with which to establish the efficacy of these new products, as well as labeling guidelines to help communicate product efficacy to health care professionals and consumers, are also evolving.

Nearly 1,000 leading US dermasurgeons convened on October 27, 2005, at the combined meeting of the American Society for Dermatologic Surgery and the American College of Mohs Micrographic Surgery and Cutaneous Oncology to discuss the latest treatments and procedures in cosmetic surgery. In light of the aforementioned changes surrounding our advancing understanding of the impact of UVA on photoaging and photocarcinogenesis, we assembled a small group of meeting participants to provide their expert opinions on topics related to UV light exposure.

The resulting roundtable discussion, chaired by Darrell S. Rigel, MD, reviewed current issues and pertinent thoughts regarding UV protection of the skin. UVA and UVB protection issues were explored, and the development, efficacy, and labeling issues surrounding UVA photoprotectants were discussed. Presented within this special publication are highlights from the discussion among panel members, supplemented with additional background information from the literature. The information in this article is based on a roundtable panel discussion following the Stable Photoprotection Advisory Board Meeting, sponsored by Johnson & Johnson Neutrogena, held October 28, 2005, in Atlanta, Ga.

The Effects of UVA/UVB Radiation

Dr Rigel: Let's begin by discussing some of the issues related to UVA and UVB exposure of the skin. What are the key factors involved with UVA and UVB exposure in terms of skin damage?

Dr Berson: Exposure to UV light causes acute redness, sunburn, and inflammation.[1,2] UVA rays, which penetrate more deeply into the skin than UVB rays,[2] can cause deoxyribonucleic acid (DNA) damage, oxidative stress, and reduction of collagen and elastin fibers, the support structures of the skin.[3-6] We therefore see the classic signs of photoaging—wrinkles, blotchiness, discoloration, and tactile roughness. UVA light exposure also can contribute to photocarcinogenesis through suppression of the immune system.[3,6,7]

> "UVA rays, which penetrate more deeply into the skin than UVB rays, can cause DNA damage, oxidative stress, and reduction of collagen and elastin fibers, the support structures of the skin. We therefore see the classic signs of photoaging—wrinkles, blotchiness, discoloration, and tactile roughness."
>
> *– Dr Berson*

Background: Summary of Effects of Exposure to Ultraviolet Light[1-6,8-19]

UVA-Related Effects

- Skin sagging
- Reduction of collagen and elastin
- DNA damage
- Oxidative stress
- Immunosuppression
- Photocarcinogenesis (contributor)

UVB-Related Effects

- Sunburn
- Inflammation
- Skin wrinkling
- DNA damage
- Oxidative stress
- Immunosuppression
- Photocarcinogenesis (primary contributor)

Background: Pathophysiology

Photoaging

UVA appears to be of particular importance in the pathophysiology of photoaging.[4,5,7] This is the result, at least in part, of a remodeling of the extracellular matrix (ECM; the structural foundation of the dermis). With solar irradiation, matrix metalloproteinases (MMPs)—enzymes that degrade EMC components—are released.[5] Additionally, when human dermal fibroblasts in cultured collagen are exposed to suberythemal UVA radiation, a reduction of type 1 procollagen mRNA expression and an increase in mRNA expression of interstitial collagenase (MMP-1) and stromelysin (MMP-3) occur. These MMPs cleave the alpha chains of interstitial collagen; thus, collagen breakdown is accelerated as a result of increased MMP expression. Such changes are likely the cause of leathery skin associated with photodamage.

Photocarcinogenesis

The contribution of UVB to the development of skin cancer is well documented.[2-4,6,9,14] Pathophysiologically, absorption of UV radiation leads to C-to-T and CC-to-TT mutations in p53 that appear to result in DNA alterations; 90% of squamous cell carcinomas, 50% of basal cell carcinomas, and 60% of actinic keratoses are associated with mutated p53.[2] Suppression of cutaneous immunity is also an important component in the pathophysiology of photocarcinogenesis, as such immunosuppression inhibits the skin's ability to protect against carcinogenetic insults.[3,6] As a result of UV-induced cellular damage, inflammatory mediators are released into the dermis, initiating the well-known cytokine cascade. Research has implicated mast cells in systemic UVB immunosuppression, with histamine production inducing human keratinocytes to produce prostaglandins, further driving immunosuppression. UVB radiation can also damage nerve cells, causing them to release neuropeptides that induce mast cell degranulation. Membrane lipid peroxidation—which can induce the production of platelet-activating factor and immunosuppressive cytokines—also occurs secondary to free oxygen radical generation. In addition, after exposure to UVB and UVA radiation, Langerhans cells (the principle antigen-presenting cells of the epidermis) become depleted.[3,7]

Although UVB is the primary contributor to photocarcinogenesis, evidence supports a role for UVA involvement.[4] Psoralen and UVA radiation (PUVA; used for the treatment of psoriasis and other skin conditions) therapy has been shown to be associated with an increased risk of melanoma; in one long-term follow-up study, the incidence rate ratio was 8.4.[18] (However, in a more recent analysis of DNA sequencing in PUVA-induced skin cancer, UVB was found to be the major cause of the mutations.[20]) Experimental in vitro evidence indicates that UVA increases p38 mitogen-activated protein kinase activity and increases expression of Bcl-X_L.[10] Additionally, UVA has been shown to have immunosuppressive effects.[7,11,15,16]

Dr Rigel: What is the level of UVB versus UVA exposure in relation to time of year, time of day, and other parameters?

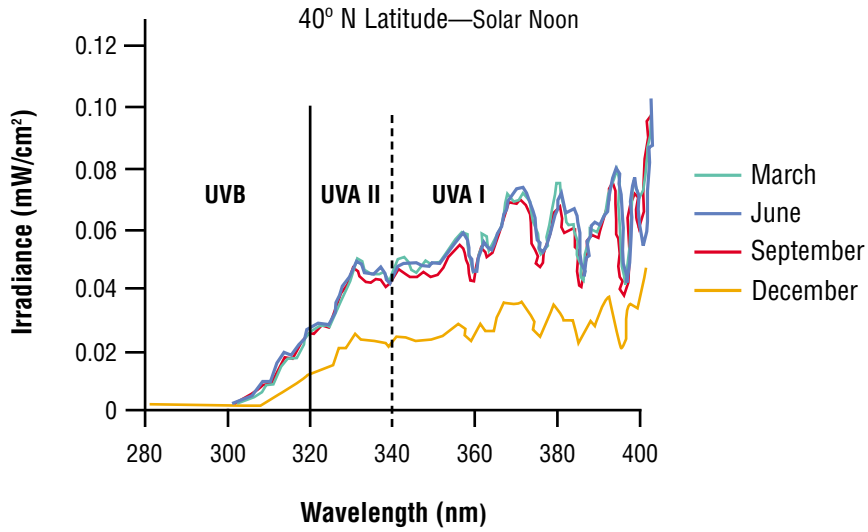
Dr Ceilley: Of the UV light from the sun that passes through the atmosphere, the vast majority of it is UVA, the long-wave UV light, while a smaller percentage is UVB.[13] About 90% to 95% of UV light is the long-wave light, while about 5% is the shorter-wave light.[2] The amount of UV light that reaches us varies throughout the day.[13,21] UVB is most intense during midday, roughly from 10:00 AM to 3:00 PM, while UVA tends to be fairly even throughout the day.[4] Also, UVB levels tend to be lower in the winter months, while UVA levels are relatively constant year-round—a little bit lower in the winter, but generally more constant than UVB levels (**Figure 1**).[4,13,21] Weather conditions, such as cloudy days, diminish UVB somewhat, but not UVA.[21] Most people only wear sunscreen when the sun is out, when they can get sunburned. However, to protect against UVA effects, one needs to apply an appropriate UVA protectant even on days when the sun is not shining brightly.

Sunscreens: A Historical Perspective

Dr Rigel: We know that traditionally most sunscreens have been focused on UVB protection, but it's really only been in the last decade that we've discovered that UVA protection is equally, if not more, important to protection against UV damage. What are your thoughts about that?

Dr Draelos: UVB protection has been the standard rating system for sunscreens, through the sun protection factor (SPF) rating system. However, there is the current recognition that UVA is just as important as UVB in damaging the skin, and this has led to the need for broad-spectrum sunscreens.[13] A variety of UVA protectants have been introduced into the marketplace, one of those being avobenzone. However, there are some photoinstability issues with avobenzone.[2] There are other physical sunblocks, such as zinc oxide and titanium dioxide, that also are able to block within the UVA range. However, these are white particulates, and as such they leave a white film on the skin that's unaesthetic, and they also cannot be used by individuals with darker skin colors. Thus, there is a need in the marketplace for good photostable UVA protectants.

Figure 1. Spectral irradiance of sunlight as measured at solar noon in central New Jersey (40° N latitude) as the season changes. Adapted with permission from Cole C.[13]



> "There is the current recognition that UVA is just as important as UVB in damaging the skin, and this has led to the need for broad-spectrum sunscreens."
> *– Dr Draelos*

Testing Standards and Labeling Issues

Dr Rigel: We've all heard so much about the US Food and Drug Administration (FDA) sunscreen monograph.[22] This was originally issued over two decades ago, and I think we're all a little confused about where it stands with respect to being finalized. I'd like to learn more about what the monograph provides in terms of testing standards and labeling issues.

Dr Cole: The monograph has been under development since 1978. It is currently in a stay of enforcement while a comprehensive UVA/UVB rule is being completed. As it is currently proposed, it is very inadequate in providing guidance to consumers and physicians regarding exactly what protection is provided by products. For example, according to the monograph, a product with an SPF

Background: FDA-Approved Active Ingredients for Sunscreens*[2,22]

Ingredient	UV Absorbance
Aminobenzoic acid	UVB
Avobenzone	UVA
Cinoxate	UVB
Dioxybenzone	UVA, UVB
Homosalate	UVB
Methyl anthranilate	UVA
Octocrylene	UVB
Octyl methoxycinnamate	UVB
Octyl salicylate	UVB
Oxybenzone	UVA, UVB
Padimate O	UVB
Phenylbenzimidazole sulfonic acid	UVB
Sulisobenzone	UVA, UVB
Titanium dioxide (inorganic)	UVA, UVB
Trolamine salicylate	UVB
Zinc oxide (inorganic)	UVA, UVB

*Products must provide an SPF value of at least 2. Certain agents can be combined in established concentrations that provide an SPF of at least 2 for each ingredient.

Adapted from Edlich RF, et al,[2] and Sunscreen drug products for over-the-counter human use; final monograph.[22]

over 30 should simply be labeled "30+."[22] The other issue with the FDA monograph is that it does not adequately address the labeling of the degree of UVA protection afforded by sunscreens. The only way manufacturers are allowed to label products for UVA protection is by including a claim that states "broad spectrum." This is based on whether or not a UVA filter in the appropriate concentration is included in the product formulation. While UVB filters must be shown in vivo to be efficacious (ie, protect against sunburn) and are labeled accordingly with an SPF to indicate the degree of protection, testing of UVA protection currently is not required for UVA claims. Neither doctors nor consumers can readily determine exactly which filters protect against which part of the spectrum, or the degree of UVA protection afforded by a sunscreen.

We are hoping the next version of the FDA monograph will include a better system for classifying protection, so that we will be able to better communicate to consumers and doctors exactly what level of UVA and UVB protection is being provided by the product.

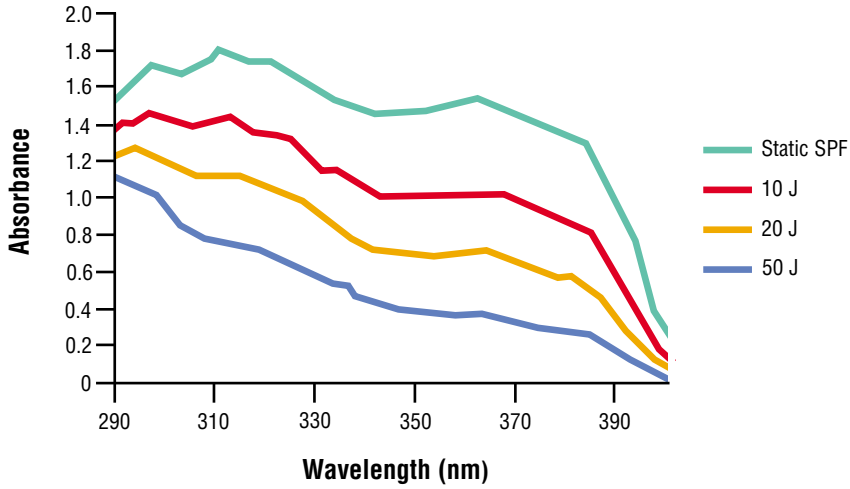
"We are hoping the next version of the FDA [sunscreen] monograph will include a better system for classifying protection, so that we will be able to better communicate to consumers and doctors exactly what level of UVA and UVB protection is being provided by the product."
– Dr Cole

Public Health Concerns

Dr Rigel: We know that melanoma rates are dramatically increasing in the United States, despite everything we're doing.[2,4,23] And yet in Australia, the rates appear to be flattening and falling.[24] What do you think the difference might be?

Dr Ceilley: Australia is way ahead of the United States. They have had a very active program of education about sun protection, and the risks of skin cancer.[2,24] This has been at the national level. These education programs start in the early grades—policies such as "Slip, Slop, Slap," instructing children to slip on a shirt, slop on some sunscreen, and slap on a hat. Children at school need to either play in the shade or they have to have sunscreen and hats on when they're outdoors. There also are other programs encouraging sun protection. For example, you see free sunscreens available at the beaches and other public places frequently. The Australians recognize the effect skin cancer has had on their health system. They see that it is a huge burden, much in the way smoking is recognized as a drain on our health care dollars. So the Australians have undertaken a much more proactive sun protection educa-

Figure 2. Breadth of protection for a nonphotostable sunscreen containing avobenzone.[25] With increasing levels of UV energy, the ability of the product to absorb the energy is greatly decreased. This photoinstability can be negated with the use of a stabilizing compound(s).



tion program, instructing people to stay out of the sun, avoid the midday sun, wear protective clothing, and use good sunscreens.

> "The Australians have undertaken a much more proactive sun protection education program, instructing people to stay out of the sun, avoid the midday sun, wear protective clothing, and use good sunscreens."
> *– Dr Ceilley*

Dr Berson: I don't think we are doing as good a job as we could in getting the message across; we need to be more proactive in educating the public about the importance of sun protection. For instance, more and more people are going to tanning salons, without understanding that they are still being exposed to UV light.[2] Nonmelanoma skin cancer rates have actually increased in women under the age of 40, and I think part of that trend is due to increased exposure to natural sunlight, as well as tanning salon use.

Developing the Optimal Sunscreen

Dr Rigel: The key message I'm hearing is that protection is important. And one of the important components of protection is sunscreen. What are some of the challenges that face us in terms of developing the optimal sunscreen product?

Dr Cole: You need to look at sunscreens in several dimensions. You have to develop products that will provide broad-spectrum protection across the entire UVA spectrum, with as high a level of protection as possible. Sunscreen products also must be durable over time and with sun exposure. Keeping sunscreen on the skin is a critical requirement, so the substantivity of sunscreens is a very important measure.

We typically measure the *breadth* of protection by graphically looking at a spectrophotometric measure of the protection (absorbance over the spectrum of wavelengths), looking across the spectrum to see how much of it is actually blocked by the filters under conditions of increasing UV energy (an example of this can be seen in **Figure 2**).[4,13] The *height* of protection reflects the in vivo protection, which is confirmed by testing sunscreens on people against UV sources such as sunlight or solar simulators in the laboratory. And lastly, we test sunscreen *durability* by exposing sunscreens to water exposure and in-use tests. In these tests, people use the sunscreens in harsh conditions in order to test whether the products are staying on adequately when they are used.

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> *– Dr Cole*

Dr Rigel: What are the actual criteria used to measure efficacy in terms of sunscreens—UV in general, and UVA specifically?

Dr Cole: To establish overall efficacy, we use the SPF test, and that tells you how well protected you are against sunburn.[2,22] The UVA tests are not yet fully established.[4,13] There are several models and protocols that have been published and are widely used by industry, but they have not been codified in a way to establish efficacy for labeling purposes. There are tests, such as the protection factor for UVA (PFA) test and the persistent

pigment darkening (PPD) test, that test product on peoples' backs against a light source that is only UVA.[4,13] With these tests, you can obtain a number very similar to an SPF number that indicates the protection specifically provided for the UVA part of the spectrum.

UVA-Specific Photoprotectants

Dr Rigel: How do current products measure up in terms of efficacy?

Dr Cole: It's really a mixed bag. There are products that have very high UVB protection, but very little UVA protection. Some products are very broad spectrum but have a very low level of protection. This is typical of many products containing inorganic filters, such as titanium dioxide, in which a high concentration of the inorganic is needed to have higher protection, but this causes the skin to look very white.[2] There is a wide range of UVA protection values for sunscreen products. Some products may have high UVA protection values, but due to the labeling issues related to the monograph there's no way to communicate this to consumers.

Most products have UVA absorbers in them. Avobenzone is one of the best, but unless it is a *stabilized* avobenzone product, it is not going to give a very high UVA protection value. Typically, if avobenzone is not well stabilized, the protection factor is only 4 or less. When avobenzone is properly stabilized, it can provide a PFA of 10 and greater.

Dr Rigel: So people may not be getting the types of protection they think they are getting, even though the SPF levels are high.

Dr Cole: Exactly.

Dr Rigel: What are Mexoryl® and Helioplex™, and where do they fit in, in terms of available sunscreens?

Dr Draelos: Mexoryl SX and Mexoryl XL are UVA filters that are added to sunscreen products in combination with avobenzone. These filters are neither FDA approved nor available in the United States. The combination of Mexoryl and avobenzone is photostable.

Avobenzone is a very important UVA photoprotectant, but it is not photostable.[26,27] The longer avobenzone stays on the skin and is exposed to UV radiation, the more it degrades. What this means is that people are not getting the full photoprotection they need over the duration of time that the sunscreen is on their skin. Technologies could be developed that possibly would utilize substances approved for use in the United States and, thus, could be made available in the United States immediately.

Dr Cole: Helioplex is a patented complex that stabilizes avobenzone, both in breadth and height of protection.[25] Helioplex combines two components: diethylhexyl 2,6-naphthalate and a benzophenone derivative, such as oxybenzone, which together are very effective in the complete stabilization of the avobenzone molecule. The oxybenzone also provides additional UVA protection on top of the avobenzone. The combination of the three substances provides a very stable

Background: Measuring Sunscreen Effectiveness

The SPF rating system was designed to provide a ranking system for sunscreen potency using solar simulators most like tropical noon. However, SPF measures primarily UVB protection.

There is no consensus as to how to measure UVA protection, and because of this lack of agreed-upon methods, the current FDA monograph does not address UVA protection by sunscreens.[4,22] However, a number of UVA-specific methods are available. In vitro spectroscopy has the advantages of being inexpensive and fast; however, as there are some disadvantages associated with it, and the method is not yet validated, it is currently most often used for screening purposes.[13] In vivo human testing includes the determination of UVA protection by irradiating skin with UVA light and measuring the protection against acute pigmentation or erythema. While these methods are most relevant to the efficacy of a filter to protect from UVA, the processes are expensive and slow, and risks are incurred with human exposure. Efforts are under way to achieve a consensus on the most appropriate UVA photoprotectant quantification technique(s), and it is hoped that the next version of the FDA monograph will contain relevant guidance.[4]

Background: Selected Helioplex Studies[25]

Study	Findings
In Vitro Studies	
Efficacy studies	Excellent breadth and height of protection in the UVA range
Photostability studies	Helioplex is not degraded by sunlight
In Vivo Studies	
Suppression of UVA-induced free radical generation	Three times fewer free radicals were generated with Helioplex vs control
Protective effect on UV-induced cellular damage	In vivo photostability demonstrated
Protective effects at high altitude and under extreme sun conditions	In vivo efficacy (sunburn prevention) demonstrated
Use in patients with polymorphous light eruption (multicenter study)	Safe for use

product with very high UVA protection. We have tested Helioplex in vivo, in vitro, and in extreme conditions, and we have found it superior to products available in the United States, and comparable to the best-in-class Mexoryl technology.[25]

> "We have tested Helioplex in vivo, in vitro, and in extreme conditions, and we have found it superior to products available in the United States."
> *– Dr Cole*

Dr Rigel: Based on what we've discussed at this session, how do you think Helioplex will fit into our photoprotectant armamentarium?

Dr Ceilley: The development of Helioplex is a major advance for us, because we have long needed better UVA protection for the prevention of skin cancer and photoaging,[2,4,13] but also an adjunctive component to treat pigmentation disorders and UVA-induced phototoxic-type reactions to certain medicines.

Dr Draelos: I think having a broad-spectrum photoprotectant that is protective for 4 to 8 hours after you apply it—that isn't degraded by light—is very important. It is a big enough challenge to get people to reapply sunscreen; consumers should be able to assume that it is stable over the period it is being worn. The improved photostability seen with the new formulations is an important step forward.

Dr Berson: I agree. I think we have all learned that it is the chronic, incidental exposure to the sun which contributes not only to photocarcinogenesis but to photodamage and premature aging of the skin. If we can have a photostable product that provides broad-spectrum photoprotection against both UVA and UVB for hours after it is applied, I think it will be helpful for our patients, both cosmetically and medically. Hopefully, with the use of photostable, broad-spectrum sunscreen products, we will eventually see a reduced incidence of skin cancer.

> "If we can have a photostable product that provides broad-spectrum photoprotection against both UVA and UVB for hours after it is applied, I think it will be helpful for our patients, both cosmetically and medically. Hopefully, with the use of photostable, broad-spectrum sunscreen products, we will eventually see a reduced incidence of skin cancer."
> *– Dr Berson*

Dr Rigel: I would agree with you. I think compliance is a key issue. If a sunscreen does not have to be applied frequently, patients may be more compliant and, therefore, better protected.

SUMMARY

The importance of protecting ourselves from UV radiation has been recognized for many years. Historically, the focus has been on the UVB portion of the spectrum, which has clearly been shown to be primarily responsible for the acute effects of sun exposure (eg, sunburn), and implicated in photocarcinogenesis. However, there is a growing body of evidence indicating that UVA is involved in the pathophysiology of long-term sun damage, specifically as a contributor to immunosuppression and photocarcinogenesis, and as a primary factor in photoaging.

Modern-day sunscreens were originally developed to provide protection against the effects of the sun that are readily seen, ie, erythema and inflammation, which arise from UVB exposure. However, as we begin to understand the damage that can be done by UVA, product development is changing. Testing and labeling for UVA-related products are evolving simultaneously with this development effort, and currently there is no standardized testing method(s) for establishing UVA protection, or clear guidelines governing how information about a product's UVA protection should be communicated to health care professionals and consumers. Efforts are currently under way to establish such parameters.

UVA absorbers are available and used in sunscreens, but photoinstability issues limit their usefulness. A number of UVA photoprotectant/stability systems are available or in development. Of note are Mexoryl and Helioplex, both of which stabilize the extremely effective—but photounstable—UVA photoprotectant, avobenzone. The photoprotectant Mexoryl was the first technology to photostabilize avobenzone and is effective in that regard; however, it is only available outside the United States. Helioplex recently became available in the United States. Data indicate that sunscreens with Helioplex protect against the damaging effects of UVA exposure while providing a high SPF. This breakthrough in UVA protection as well as the local availability of Helioplex may be of help to US health care professionals in their efforts to address their patients' concerns with photoaging. Long-term evidence is needed to determine the effects on skin cancer.

References

1. Bissonnette R, Allas S, Moyal D, Provost N. Comparison of UVA protection afforded by high sun protection factor sunscreens. *J Am Acad Dermatol*. 2000;43:1036-1038.
2. Edlich RF, Winters KL, Lim HW, et al. Photoprotection by sunscreens with topical antioxidants and systemic antioxidants to reduce sun exposure. *J Long-Term Eff Med Implants*. 2004;14:317-340.
3. Granstein RD, Matsui MS. UV radiation-induced immunosuppression and skin cancer. *Cutis*. 2004;74(suppl 5):4-9.
4. Lim HW, Naylor M, Hönigsmann H, et al. American Academy of Dermatology Consensus Conference on UVA protection of sunscreens: Summary and recommendations. Washington, DC, Feb 4, 2000. *J Am Acad Dermatol*. 2001;44:505-508.
5. Pascual-Le Tallec L, Korwin-Zmijowska C, Adolphe M. Effects of simulated solar radiation on type I and type III collagens, collagenase (MMP-1) and stromelysin (MMP-3) gene expression in human dermal fibroblasts cultured in collagen gels. *J Photochem Photobiol B*. 1998;42:226-232.
6. Phan TA, Halliday GM, Barnetson RS, Damian DL. Spectral and dose dependence of ultraviolet radiation-induced immunosuppression. *Front Biosci*. 2006;11:394-411.
7. Lavker RM, Gerberick GF, Veres D, Irwin CJ, Kaidbey KH. Cumulative effects from repeated exposures to suberythemal doses of UVB and UVA in human skin. *J Am Acad Dermatol*. 1995;32:53-62.
8. Anders A, Altheide HJ, Knälmann M, Tronnier H. Action spectrum for erythema in humans investigated with dye lasers. *Photochem Photobiol*. 1995;61:200-205.
9. Atillasoy ES, Seykora JT, Soballe PW, et al. UVB induces atypical melanocytic lesions and melanoma in human skin. *Am J Pathol*. 1998;152:1179-1186.
10. Bachelor MA, Bowden GT. Ultraviolet A-induced modulation of Bcl-X_L by p38 MAPK in human keratinocytes: Post-transcriptional regulation through the 3'-untranslated region. *J Biol Chem*. 2004;279:42658-42668.
11. Bestak R, Halliday GM. Chronic low-dose UVA irradiation induces local suppression of contact hypersensitivity, Langerhans cell depletion and suppressor cell activation in C3H/HeJ mice. *Photochem Photobiol*. 1996;64:969-974.
12. Bissett DL, Hannon DP, Orr TV. An animal model of solar-aged skin: Histological, physical, and visible changes in UV-irradiated hairless mouse skin. *Photochem Photobiol*. 1987;46:367-378.
13. Cole C. Sunscreen protection in the ultraviolet A region: How to measure the effectiveness. *Photodermatol Photoimmunol Photomed*. 2001;17:2-10.
14. De Fabo EC, Noonan FP, Fears T, Merlino G. Ultraviolet B but not ultraviolet A radiation initiates melanoma. *Cancer Res*. 2004;64:6372-6376.

15. Moyal DD, Fourtanier AM. Effects of UVA radiation on an established immune response in humans and sunscreen efficacy. *Exp Dermatol*. 2002;11(suppl 1):28-32.

16. Serre I, Cano JP, Picot MC, Meynadier J, Meunier L. Immunosuppression induced by acute solar-simulated ultraviolet exposure in humans: Prevention by a sunscreen with a sun protection factor of 15 and high UVA protection. *J Am Acad Dermatol*. 1997;37:187-194.

17. Staberg B, Wulf HC, Klemp P, Poulsen T, Brodthagen H. The carcinogenic effect of UVA irradiation. *J Invest Dermatol*. 1983;81:517-519.

18. Stern RS; PUVA Follow up Study. The risk of melanoma in association with long-term exposure to PUVA. *J Am Acad Dermatol*. 2001;44:755-761.

19. Trautinger F. Mechanisms of photodamage of the skin and its functional consequences for skin ageing. *Clin Exp Dermatol*. 2001;26:573-577.

20. Kreimer-Erlacher H, Seidl H, Bäck B, Cerroni L, Kerl H, Wolf P. High frequency of ultraviolet mutations at the *INK4a-ARF* locus in squamous cell carcinomas from psoralen-plus-ultraviolet-A-treated psoriasis patients. *J Invest Dermatol*. 2003;120:676-682.

21. Dummer R, Maier T. UV protection and skin cancer. *Recent Results Cancer Res*. 2002;160:7-12.

22. Sunscreen drug products for over-the-counter human use; final monograph. Food and Drug Administration, HHS. Final rule. *Fed Regist*. 1999, May 21;64:27666-27693.

23. Gilchrest BA, Eller MS, Geller AC, Yaar M. The pathogenesis of melanoma induced by ultraviolet radiation. *N Engl J Med*. 1999;340(17):1341-1348.

24. Edlich RF, Winters KL, Cox MJ, et al. National health strategies to reduce sun exposure in Australia and the United States. *J Long-Term Eff Med Implants*. 2004;14:215-224.

25. Data on file, Johnson & Johnson Neutrogena, Los Angeles, Calif.

26. Sayre RM, Dowdy JC, Gerwig AJ, Shields WJ, Lloyd RV. Unexpected photolysis of the sunscreen octinoxate in the presence of the sunscreen avobenzone. *Photochem Photobiol*. 2005;81:452-456.

27. Tarras-Wahlberg N, Stenhagen G, Larkö O, Rosén A, Wennberg AM, Wennerström O. Changes in ultraviolet absorption of sunscreens after ultraviolet radiation. *J Invest Dermatol*. 1999;113:547-553.