What’s New in Sunscreen

What your patients are asking and need to know

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What Causes Melanoma?
The overwhelming majority caused by UV exposure

UV and Melanoma Risk

- Sunlight is the major environmental risk factor for melanoma
- Examine if S-shaped curves describe the relationship between solar UV doses and MM incidence and the % of MM that can be directly related to UV exposure
- Analysis indicates that S-shaped associations describe the data well (P < 0.0001).
- Conclusion:
  - Between 89 and 95% of the annual CM cases are caused by solar UV exposure.
  - Avoidance of UV radiation will reduce the incidence of MM.


Melanoma vs. Latitude USA

SEER 2013
Social media that patients read...

2 things happen during the 3rd week of May

Consumer Reports
EWG

Get the Best Sun Protection

Consumer Reports

PERCENTAGE OF SUNSCREENS THAT TESTED SPF 30 OR HIGHER

PERCENTAGE OF SUNSCREENS THAT TESTED SPF 30 OR HIGHER
Hazard scores given to properties of particular concern for sunscreens including products that contain:

- Oxybenzone
- Vitamin A
- Products listing SPF values exceeding “SPF 50+
- Products in a spray or powder form that may pose a risk when inhaled
11 Worst Spray Sunscreens

These sunscreens are aerosol sprays with benzene and the harmful additives oxybenzone and retinyl palmitate.

Banana Boat Clear UltraMist Ultra Defense MAX Skin Protect Continuous Spray Sunscreen, SPF 110
Coppertone Sport High Performance AccuSpray Sunscreen, SPF 15
Coppertone Sport High Performance Continuous Spray Sunscreen, SPF 100+
CVS Clear Spray Sunscreen, SPF 100
CVS Sheer Mist Spray Sunscreen, SPF 20
CVS Sport Clear Spray Sunscreen, SPF 100+
CYS Wet & Dry Sunscreen Spray, SPF 30
Neutrogena Ultra Sheer Body Mist Sunscreens Spray, SPF 100+
Neutrogena Ultra Sheer Body Michael Jackson Sunscreen Spray, SPF 70
Neutrogena Wet Skin Sunscreen Spray, SPF 85+
Lawsuit accuses Jessica Alba’s $1.7 billion startup Honest Co. of selling ‘deceptively’ labeled products

Don’t buy @honest sunscreen unless you want to look like this. Second time I’ve tried this stuff and got tanned.

The new lawsuit seems to refer to this outcry, as it claims that contrary to Honest’s representations, Honest Sunscreen “was ineffective in preventing unhealthy exposure to harmful UV rays.”
Reduced melanoma risk after regular sunscreen use

- 1,621 randomly selected residents of Nambour (Queensland) Australia, age 25 to 75 years, were randomly assigned to daily or discretionary sunscreen application to head and arms
- Treated for 5 years then followed for 10 years

Conclusions:
- Melanoma may be preventable by regular sunscreen use in adults

Skin cancers in Australia prevented by regular sunscreen use

- Estimated the proportion of skin cancers that would have occurred but were likely prevented by regular sunscreen use
- Regular sunscreen use prevented around 14,190 persons from developing SCCs (PF 9.3%) and 1,730 from Melanoma (PF 14%)
- Conclusions:
  - Prevailing levels of sunscreen use probably reduced skin cancer incidence by 10-15%
  - Sunscreen should be a component of a comprehensive sun protection strategy

MM risk using SPF<15 vs SPF >15


Reduced melanoma risk after regular sunscreen use

- 1,621 randomly selected residents of Nambour (Queensland) Australia, age 25 to 75 years, were randomly assigned to daily or discretionary sunscreen application to head and arms
- Treated for 5 years then followed for 10 years
- Only 11 new MMs in daily group vs. 22 (p=0.051)
- 2 Invasive MMs in daily group vs.11

Conclusions:
- Melanoma may be preventable by regular sunscreen use in adults

Does SPF>50 provide additional benefit?

**In-vivo comparison of SPF 100 vs 50 in Actual Use Conditions**

**METHODS**
- 199 healthy men and women ≥18 years of age participated in a one day split face, randomized, double blind study in Vail, Colorado.
- The difference in sunburn protection provided by two currently available sunscreens (SPF 50+ and SPF 100+) was evaluated.
- Products were supplied in a kit containing two overwrapped tubes of sunscreen marked “right” and “left.” Each subject wore both sunscreens simultaneously, with product application randomized to either the right or left side of the face.
- Subjects utilized the sunscreens as they would normally during ski activities. Diaries were used to record sun exposure time and the frequency and timing of sunscreen re-applications.
- Subjects reported the next morning for clinical evaluation.

**RESULTS**

**Primary Endpoint**
SPF 100+ sunscreen was significantly more effective at protecting against sunburn than was SPF 50+ sunscreen.

**Secondary Endpoint**
Erythema was significantly lower on the SPF 100+ protected side of the face, and erythema progression was observed to be more than twice as severe on the SPF 50+ protected side.

**Usage**
No differences were observed in usage, application density, or reapplication frequency of the study products.
RESULTS

Post Hoc Analysis

The number of sunscreen reapplications was not observed to diminish the enhanced protection benefit of the SPF 100+ product.

CONCLUSIONS

- The SPF 100+ sunscreen was significantly more effective in protecting against sunburn than the SPF 50+ sunscreen for all skin types evaluated.
- These findings demonstrate that there is a need for sunscreens labelled with SPFs greater than 50+ to provide consumers with better choices for sunburn protection.

Are vitamin A analogues in sunscreen risky?

Are Sunscreens with Retinyl palmitate Safe?

- Retinyl palmitate – cosmetic ingredient and antioxidant
  - 41% of sunscreens
  - photo degraded → induces ROS
  - photocarcinogenic
  - 10 year old FDA study of mice
- Concerns not supported by available literature

Safety of retinyl palmitate in sunscreens

- There is no published evidence to suggest that topical retinoids increase the risk of photocarcinogenesis.
- RP is regularly used in topical agents for >40 yrs
- Retinoids are used for chemoprevention of skin cancers in individuals at high risk, such as transplant populations and patients with xeroderma pigmentosum with no evidence for increased skin cancer risk.
- Conclusions:
  - Based on currently available data from studies, there is no convincing evidence to support the notion that RP in sunscreens is photocarcinogenic.
  - In fact, clinical observations spanning over decades suggest that retinoids are helpful in skin cancer chemoprevention.
  - Correcting this false impression is an important and necessary step to ensure that the public continues to use sunscreen as a component of photoprotective strategy.

Wang et al, JAAD, 2010
Are European sunscreens better?

UVA Sunscreening Agents available in the US

UVA Sunscreening Agents not yet available in the US

New Sunscreening Agents

- Currently 19 approved in the US
- Multiple sunscreening agents that are available in Europe and Asia are not available in the US
- FDA using TEA format considering approval

Conclusions:
- Newer agents will be incorporated into future sunscreen formulations

Potential Sunscreen Agents

<table>
<thead>
<tr>
<th>Sunscreen Agent</th>
<th>Spectrum of Action</th>
<th>FDA Status</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinosorb S</td>
<td>UVB, UVA1, UVA2</td>
<td>Not approved</td>
<td>Very photostable, minimal skin absorption</td>
</tr>
<tr>
<td>Tinosorb M</td>
<td>UVB, UVA1, UVA2</td>
<td>Not approved</td>
<td>Fairly photostable</td>
</tr>
<tr>
<td>Mexoryl SL</td>
<td>UVA2</td>
<td>Not approved</td>
<td>Not absorbed into skin</td>
</tr>
<tr>
<td>Uread T 500</td>
<td>UVB</td>
<td>Not approved</td>
<td>Not water soluble; Water resistant and long lasting</td>
</tr>
<tr>
<td>Eumelanin</td>
<td>UVB</td>
<td>Not approved</td>
<td>May have estrogenic effect when used. Does not absorb UVB</td>
</tr>
<tr>
<td>Bisabolol</td>
<td>UVA1</td>
<td>Not approved</td>
<td>Photostable, water soluble</td>
</tr>
<tr>
<td>Uvasorane Plus</td>
<td>UVA2</td>
<td>Not approved</td>
<td>Photostable, may provide active protection against free radicals</td>
</tr>
<tr>
<td>Pansorin R50</td>
<td>UVB</td>
<td>Not approved</td>
<td>Available in EU and Asia</td>
</tr>
<tr>
<td>Amiloxate</td>
<td>UVA1</td>
<td>Not approved</td>
<td>Available in EU and Asia</td>
</tr>
<tr>
<td>Uvasorane HEB</td>
<td>UVR, UVA1</td>
<td>Not approved</td>
<td>Available in EU and Asia</td>
</tr>
</tbody>
</table>
Sunscreen Innovation Act

Amends the Federal Food, Drug, and Cosmetic Act to establish a process for the review and approval of over-the-counter (OTC) sunscreen active ingredients.

The bill was approved by the House in July and different version of the bill was approved by the Senate in September.

Signed into law by the President in December 2014.

Of the original 5 filters up for review, the FDA concluded there was not enough data to approve 2 filters.

There is no final decision on whether there will be any regulations on high SPF or spray sunscreens.

Sunscreen Innovation Act - 2014

- Requires the Secretary to review any request regarding a sunscreen active ingredient or combination of ingredients that has been in use and that is not currently in the monograph.
- Requires the Director of the Center for Drug Evaluation and Research to complete a review of a filed request and determine the safety and efficacy of the sunscreen active ingredient within 200 days for new requests or a shorter timeframe for requests pending before enactment of this Act.
- Directs the Commissioner of Food and Drugs to make the determination if the Director does not make a determination in the allowed timeframe.
- Allows sponsors of eligible non-sunscreen OTC drug applications to request that the Secretary provide a framework for review of their application.
- Requires the Secretary to respond with framework options, including options that follow the review process set forth in this Act for sunscreen active ingredients.

Perspective

A Spotlight on Sunscreen Regulation

In my view, Congress should try again and pass legislation establishing an alternative approval pathway that combines the flexibility of the new drug pathway with the ability to simultaneously approve multiple formulations and concentrations. The FDA should be able to negotiate with sponsors to get the right data without years of rulemaking, establish postmarketing data requirements, consult with other countries’ regulators to establish consistent standards where possible, and move quickly in the event that safety concerns emerge. Congress should provide additional resources to facilitate timely analysis and review. That this path is viable is evidenced by the fact that the one approval of a product with a new sunscreen ingredient in the past decade came through the new drug pathway.

Do sunscreens protect from other photodamage?
Effect of Sunscreen Application on UV-Induced Thymine Dimers

- Unexposed buttocks skin irradiated with UV with and without SPF 15 sunscreen
- When sunscreen application was omitted even once prior to irradiation, a statistically significant increase in TD formation was found
- Conclusion:
  - Unprotected UV exposure leads to increased TD formation

Mahroos et al, Arch Dermatol, 2002

Sunscreen and Prevention of Skin Aging Randomized Trial

- 903 adults younger than 55 years randomly selected from a community register. Random assignment into 4 groups:
  - daily use of broad-spectrum sunscreen and 30 mg of β-carotene
  - daily use of sunscreen and placebo
  - discretionary use of sunscreen and 30 mg of β-carotene
  - discretionary use of sunscreen and placebo
- Change in microtopography in the sunscreen and β-carotene groups compared with controls, graded by blinded assessors
- Skin aging from baseline to conclusion was significantly less in the daily sunscreen group than the discretionary group (OR=0.76)
- Conclusions:
  - Regular sunscreen use retards skin aging in healthy, middle-aged men and women.
  - No overall effect of β-carotene on skin aging was identified

Hughes et al, Ann Int Med, 2013

Enhanced sun protection of metal oxide nanoparticles over conventional particles: an in vitro comparative study

- In vitro method to determine sun protection factor of the investigational sunscreen cream samples containing zinc and titanium dioxide with a varied range of particle size
- Comparative study conducted between metal oxide particles, conventional as well as nanoparticles
- Nanoparticle formulations had better spreadability and better SPF values by a 2X margin
- Conclusions:
  - Good texture, better spreadability and enhanced in vitro SPF proved the advantageous role of nanoparticles in sunscreens

Singh et al, Int J Cosmet Sci, 2014

Are nanoparticles in sunscreen a concern?

Broad spectrum high-SPF photostable sunscreen with high UVA-PF can protect against cellular damage at high UV levels

- To evaluate if high-SPF sunscreen can protect skin at the cellular level under UV exposure doses [>50 MEDs] similarly to the SPF value
- Sunburn cells, Langerhans cells, thymine dimers, protein 53 (p53), and matrix metalloproteinase (MMP)-1 and MMP-9 endpoints were evaluated in biopsies from 12 subjects:
  - SPF 55 protected exposed to 55 MED of UV radiation
- After 55 MEDs, sunscreen-protected sites showed either significantly less damage or no difference than the 1 MED-exposed unprotected sites
- Conclusions:
  - High-SPF sunscreen with high UVA-PF can provide proportionately high protection against multiple cellular damage markers

Cole et al, Photodermatol Photomed Photomed, 2014

Enhanced sun protection...in...proven the advantageous role of nanoparticles in sunscreens

Singh et al, Int J Cosmet Sci, 2014
Gold nanoparticles as novel agent to enhance SPF of commercial sunscreens

- Latex fabricated gold nanoparticles were analyzed by different analytical techniques such as UV-Vis spectroscopy, Fourier transforms infrared spectroscopy, zeta potential, transmission electron microscopy and X-ray diffraction.
- Transmission electron microscopy and UV-Vis spectroscopy techniques were used to get insight into mechanism by which AuNPs enhance sunscreen SPF.
- Adding gold nanoparticles to commercial sunscreens increased the SPF from 2 to 24.
- Gold nanoparticles enhance the SPF of commercial sunscreens due to reflection and scattering of UV.
- Conclusions:
  - Gold nanoparticles are a potent alternative to traditionally used TiO2 and ZnO nanoparticles.

Titanium dioxide and zinc oxide nanoparticles in sunscreens: Focus on safety and effectiveness

- Microsized TiO2 and ZnO have been increasingly replaced by TiO2 and ZnO nanoparticles.
- Use of TiO2 and ZnO NPs makes the undesired opaqueness disappear.
- Leads to incorporation of TiO2 and ZnO NPs in the stratum corneum.
- Sunscreen NPs induce (photo)cyto- and genotoxicity which have been sporadically observed in viable skin layers.
- Conclusions:
  - Caution should still be exercised when new sunscreens are developed.
  - Research that includes sunscreen NP stabilization, chronic exposures, and reduction of NPs’ free-radical production should receive full attention.

New Formulations...

Sunscreen + Antioxidants = More Effectiveness??

UV induced Free Radical formation

Non-sunscreen photoprotection: antioxidants add value to a sunscreen

- Polyphenols such as (-)-epigallocatechin-3-gallate (EGCG) has been shown to protect against UV-induced DNA damage even when added to low SPF formulations.
- The addition of botanical antioxidants and vitamins C and E to a broad-spectrum sunscreen may further decrease UV-induced damage compared with sunscreen alone.
- Conclusion:
  - Non-sunscreen materials such as botanical extracts, antioxidants, and DNA repair enzymes can contribute value when applied topically to human skin in vivo.

Matsui et al, J Investig Dermatol Symp Proc, 2009
**Sun Protection and Anti-oxidants**

- Vitamin E
- Vitamin C
- Polyphenols (Green tea) epigallocatechin-3-gallate (EGCG)
- Genistein (soybeans)
- Resveratrol (grape skins, peanuts, and red wine)
- Lycopene (an isomer of beta carotene - red fruits and vegetables, such as tomatoes, watermelons)
- Combinations may be synergistic

Junkins-Hopkins et al, JAAD, 2010

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**Oral Polypodium Leucotomos extract**

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**Edible Sunscreens Are All the Rage, but No Proof They Work**

*The New York Times*

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**Recommended Usage:** One bottle per day 30 minutes before sun exposure for 3 to 5 hours of protection. Half a bottle for children 6 to 12 years old.

**Ingredients:** Water, Orange Juice (Orange Juice Concentrate, Water), Peach Juice (Peach Juice Concentrate, Water), Sugar, Natural Flavor, Ascorbic Acid, Polypodium Leucotomos, Carrageenan, Milk Thistle Extract, Coenzyme Q10, Zinc Gluconate, Citrus Bioflavonoid Complex, Soy Lecithin, Lycopene, Konjac, Alpha Lipic Acid, Beta Carotene, Xanthan Gum, Biotin,Steve Extract, Grape Seed Extract, Alpha- Tocopherol Acetate, Nicotinamide, Green Tea Extract, Copper Gluconate, Resveratrol, Cholecalciferol, Sodium Selenite, Bilberry Fruit, Folic Acid. Contains Soy.

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**Misquoted out of context!!**

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**Benefits of oral Polypodium Leucotomos extract in MM high-risk patients**

- 61 pts (25 familial and/or multiple MM, 20 sporadic MM and 16 with DNs without history of MM) were exposed to varying doses of artificial UVB radiation without and after oral administration of a total dose of 1080 mg of PL.
- Oral PL treatment significantly increased the MED mean in all groups
- Conclusions:
  - Oral PL leads to a significant reduction of sensitivity to UVR ($p<0.05$) in all patients in study

Aguerra et al, JEADV, 2013
**Polypodium leucotomos extract (PLE): a status report on clinical efficacy and safety**

**25 studies showing safety and efficacy**

Conclusion:
Current level of evidence suggests oral PLE can be prescribed confidently for long-term use.

Winkelmann et al, J Drugs Dermatol. 2015

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**What are Dermatologists views, beliefs and recommendations?**

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**Dermatologists’ Perceptions Recommendations and Usage of Sunscreen**

**Dermatologists’ Views**

- Lowers SkCA Risk: 97%
- Reduces photaging: 100%
- Rec to friends/family: 99%
- Pts use too little: 99%

**Dermatologists’ Beliefs**

- Sunscreens safe: 96%
- Oxybenzone safe: 91%
- Retinyl palmitate safe: 87%
- High SPF’s safety margin: 83%
- Recommend SPF50+: 97%

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**Dermatologists’ Perceptions Recommendations and Usage of Sunscreen**

**Dermatologists’ Recommendation Factors**

- SPF level: 99%
- Broad spectrum: 96%
- Photostability: 95%
- Feel/elegance: 71%
- SPF50+ vs Other: 42%

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**Answering Our Patient’s Questions**
Assessment of Levels of UVA Protection in Automobile Windshields and Side Windows

• UVA levels inside windshields and side windows in 29 automobiles (1990-2014) from 15 automobile manufacturers were measured.

Assessment of dermal absorption of DEET-containing insect repellent and oxybenzone-containing sunscreen

• Concerns about oxybenzones increasing the dermal absorption of DEET
• Sought to determine the best way for concurrent use of these two products without extra absorption of either
• 4 dermal application methods were used: DEET only, OBZ only, DEET on top of OBZ, and OBZ on top of DEET
• Applying OBZ over DEET on the skin lead to significantly higher absorption of DEET. Using both products in reverse order, did not result in extra DEET absorption significantly
• Conclusions:
  – Enhancement of DEET absorption is confirmed for OBZ being applied after DEET application on the skin
  – Applying sunscreen (OBZ) first and then insect repellent (DEET) with a 15-min interval is recommended

Do you need to wear sunscreen while in a car?

• 96% UVA blocked
  – 2011 Lexus Rx350
  – 2011 Mercedes-Benz E550
  – 2014 VW Golf
  – 2013 BMW 320i

• 95% UVA blocked
  – 2011 Lexus Rx350
  – 2011 Mercedes-Benz E550

• 97% UVA blocked
  – 2014 VW Golf
  – 2013 BMW 320i

• UVA levels inside windshields and side windows in 29 automobiles (1990-2014) from 15 automobile manufacturers were measured.
• Average percentage of front-windshield UVA blockage was 96% (range 95%-98%) and the side-window blockage, which was 71% (range 44%-96%).
• Conclusions:
  – These results may in part explain the reported increased rates of cataract in left eyes and left-sided facial skin cancer.
  – Automakers may wish to consider increasing the degree of UV-A protection in the side windows of automobiles.

Does artificial UV use prior to vacation protect from vacation related sunburns?

• Examined associations in college students between potential risk factors and the development of one or more sunburns during spring break
• Risk of obtaining a sunburn increased with: time spent in the sun during spring break; light complexion, as assessed by various sun-sensitivity factors; and lack of sunscreen use.
• Tanning using an artificial UV source during the 10 weeks prior to spring break was not associated with reduced risk of sunburns during spring break, but rather with an increase in this risk
• Conclusion:
  – Maintaining a tan may not provide protection from sunburns.
  – Public health messages need to address this misconception, stating clearly that a tan does not protect against or reduce the chances of developing a sunburn

Yin et al., Environ Sci Polut Res Int. 2014


Dennis et al, Photodermatol Photoimmunol Photomed. 2013
Stability of sunscreens following exposure to extreme temperatures

• 9 commercially available sunscreens after an 8-hour exposure to a range of temperatures including −20°C, 4°C, 21°C, 30°C, and 60°C
• Phase separation and failure to rehomogenize on shaking
• Conclusions:
  – Extended exposures to high temperatures can degrade sunscreen

Evaluation of a sunscreen during a typical beach period

• UV protection is strongly dependent on the properties of these sunscreen agents, it is very important to ensure their stability at the typical higher temperatures of summer
• Sunscreens tested in vitro for a period of time intended to simulate a beach period of 15 days, with regard to the maintenance of its SPF.
• No significant alterations were observed during the considered period under the specific conditions of this study
• Conclusions:
  – Sunscreen protection does NOT degrade at outdoor summer temperatures during a typical vacation period

Evaluation of a sunscreen during a typical beach period

Do you really have to wait 15-20 minutes for sunscreen protection?

• Sunscreen testing protocols mandate drying times of 15-20 minutes before SPF testing can begin: mandatory labeling reflect this instruction
• UV Protection is actually instantaneous
• Water resistance MAY require more drying time

Re-application is Important

• Re-application after 2 hours is mandatory labeling by FDA
  – Based on JAAD paper, 2011, AAD comment to FDA
• Photostable sunscreens do not “wear out” and will continue to protect as long as they are on the skin
• Re-application is advisable to assure proper application level and to hit “missed spots,” and after toweling or wiping off

Rules of Sunscreen Application

• Patients tend to “rub in” sunscreens – so you can’t see it anymore. Does “rubbing in” assure best protection? NO!
• Best protection is achieved by having uniform film on the surface of the skin
  – Spread lightly on the skin and let it be…
  – For inorganic filters (ZnO, TiO2) it is even more important not to “rub” it till you can’t see it
  – For Spray products – spray the surface until it glistens “wet” and then gently spread to make sure all spots are covered
• Best to spray in sheltered area so the sunscreen is not blown away
What is the Best Sunscreen?
The best sunscreen is the one a patient will use regularly and as recommended.

When your patients ask about...
Photoprotection

- Photoprotection important and lowers melanoma risk
- SPF >50 is efficacious
- The best sunscreen is the one that a person will use
- Learn what your pts are hearing and have the answers ready