What’s New in Sunscreen

What your patients are asking and need to know

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Disclosures:
J and J – A, H, I
Beiersdorf – C, H
Ferndale – A, I

More Skin Cancers than all other cancers combined

Melanoma - USA

Rigal et al. NYU Melanoma Cooperative Group, 2017
US Lifetime Risk for Invasive Melanoma
Non-Hispanic Whites

- Male: 1 in 28
- Female: 1 in 44

Siegel et al., Ca J Clinicians, 2017

Melanoma – US 2017

- Invasive = 87,100
- In-situ = 63,410

Rigel et al., NYU Melanoma Cooperative Group, 2017

US Cancer Statistics, 2017

Siegel et al., Ca J Clinicians, 2017

US Annual Deaths from Melanoma

Skin Cancer Deaths US - 2017

Over 1 American dies of Melanoma every hour

Siegel et al., Ca J Clinicians, 2017
Importance of UV Protection

Protection

Melanoma is one of the few cancers that we know the cause – UV radiation exposure and where a simple behavioral change – UV minimization – lowers the risk of getting this cancer.

What Causes Skin Cancer?

Melanoma vs. Latitude USA
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.


Are ALL melanomas caused by UV exposure?

No, but the vast majority are!

Social media that patients read...

2 things happen during the 3rd week of May

Consumer Reports
EWG

Get the Best Sun Protection

All consumers should look up the SPF claim on their labels—the Food and Drug Administration requires it. But for four years straight, Consumer Reports found that many sunscreen in our tests fall short.

Can You Trust the SPF?

In four years of our sunscreen tests, almost half of the products failed to meet their SPF claim after water immersion—despite the fact that all featured claims of water resistance. And if you heat your skin by mineral products, you’re taking a greater chance of the chemical formulations.
Conflict!!!

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
Spray sales exceed lotions for the first time

Data Source: IRI, current 52 Weeks ending 09/22/2013

US Sunscreen Sales Last Year

Spray sales exceed lotions for the first time

11 Worst Spray Sunscreens

These sunscreens are aerosol sprays with SPF 15 or less and end the day with patches of coverage and breakdown.

- Banana Boat Clear UltraMist Ultra Defense MAX Skin Protect Continuous Spray Sunscreen, SPF 110
- Coppertone Sport High Performance Aqueous Spray Sunscreen, SPF 70
- Coppertone Sport High Performance Clear Continuous Spray Sunscreen, SPF 100
- CVS Clear Spray Sunscreen, SPF 100
- CVS Sheer Mist Spray Sunscreen, SPF 30
- CVS Sport Clear Spray Sunscreens, SPF 100+
- CVS Wet & Dry Touchless Spray, SPF 15
- Neutrogena Ultra Sheer Body Mist Sunscreen Broad Spectrum SPF 30
- Neutrogena Ultra Sheer Body Mist Sunscreen Spray, SPF 70
- Neutrogena Ultra Sheer Body Mist Sunscreen Spray, SPF 100
- Neutrogena Wet Skin Sunscreen Spray, SPF 85+

UVAX/VB Balance

EWG's estimate of the UV protection provided by this product. An ideal sunscreen filters UVA and UVB rays evenly, but some sunscreens let too many UVA rays through.

Best Beach & Sport Sunscreens

215 Beach & Sport Sunscreens Meet EWG’s Criteria
Does sunscreen usage lower skin cancer risk?

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

Green et al, J Clin Oncol, 2011
Sunscreen Usage and Melanoma Risk

- All Melanomas
  - Relative Risk
  - Discretionary: 1
  - Daily: 0.5

- Invasive MMs
  - Relative Risk
  - Discretionary: 1
  - Daily: 0.27

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)
- Only 2 Invasive MMs in daily group vs. 11
- Conclusions:
  - Melanoma risk may be reduced by regular sunscreen use

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

How high an SPF is high enough?
**SPF 50+ Status**

- Sunscreens with SPF of 50 or more are available in some other developed countries, including New Zealand, the US and many European countries.
- Australia and other countries have an SPF 50+ cap.

**SPF Cap 50+?**

**Pro**

- Increased cost for higher SPF formulations.
- Little marginal improvement in UVB protection for higher SPFs.

**Con**

- Higher SPFs have better protection at "real world" application concentrations.

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**Pro - SPF levels vs. UVB absorption**

Marginal increase in UVB protection from SPF 50 to SPF 100 is only 1%.

**Con - SPF levels vs. UVB absorption with real world application**

But this assumes sunscreen applied at tested concentration (2mg/cm²).

Typically, 25-50% of rated amount applied.

**Underusage of Sunscreen**

Large variation in sunscreen application (many use less than recommended 2mg/cm²).

Users received a mean SPF of 20-50% of expected due to inadequate application.

Underprotection due to inadequate application might explain why sunscreen use has been reported in some studies as a risk factor for melanoma.

Impact of under application of sunscreen

• SPF of sunscreens are tested using a thickness of 2 mg/cm²
• Investigations show that sunscreen under natural conditions is applied insufficiently with amounts about 0.39 to 1.0 mg/cm²
• Missing areas and UV radiation exposure before sunscreen application are other pitfalls that reduce the protective effect of sunscreens considerably

Patients Under Apply Sunscreen

• Numerous studies have shown that consumers typically under apply product by 1/4 to 1/2 of what should be applied
• Data shows that consumers seldom re-apply after the initial application
• Not all body areas get comprehensive application and coverage

Patients Often Don’t Apply Recommended Amounts of Sunscreen

• Numerous studies have shown that consumers typically under apply product by 1/4 to 1/2 of what should be applied
• Data shows that consumers seldom re-apply after the initial application
• Not all body areas get comprehensive application and coverage

High-SPF Compensates for Under-Application of Sunscreen

• OBJECTIVE: To measure the actual SPF values of various sunscreens (SPF 30 to 100) applied in the reduced amounts typically used by consumers

Actual SPF at different application doses

<table>
<thead>
<tr>
<th>A-Label SPF</th>
<th>Actual SPF at 2 mg/cm²</th>
<th>D-Label SPF</th>
<th>Actual SPF at 2 mg/cm²</th>
<th>F-Label SPF</th>
<th>Actual SPF at 2 mg/cm²</th>
<th>B-Label SPF</th>
<th>Actual SPF at 2 mg/cm²</th>
<th>E-Label SPF</th>
<th>Actual SPF at 2 mg/cm²</th>
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<tr>
<td>30</td>
<td>31.0</td>
<td>52.8</td>
<td>70.6</td>
<td>104.6</td>
<td>58.7</td>
<td>105.3</td>
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<tr>
<td>50</td>
<td>21.8</td>
<td>41.3</td>
<td>56.4</td>
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<td>70</td>
<td>16.0</td>
<td>26.0</td>
<td>37.1</td>
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<td>25.7</td>
<td>58.1</td>
<td></td>
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<tr>
<td>100</td>
<td>8.8</td>
<td>13.9</td>
<td>16.3</td>
<td>27.1</td>
<td>12.3</td>
<td>22.4</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Results

• There was a linear relationship between application density and the actual SPF
• Sunscreens labeled SPF > 50 provided significant protection even when applied at “real world” typical application densities
**SPF Cap 50+?**

**Con**
- Higher SPFs have better protection at "real world" application concentrations
- 50+... Is it 51 or 100?

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**Does SPF>50 provide additional benefit?**

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**High SPF Sunscreen Provides Significant Clinical Benefit in Actual Use Conditions:**

SPF 100+ Is More Effective than SPF 50+

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2 Icahn School of Medicine at Mount Sinai, New York, NY, USA
3 New York University Medical Center, New York, NY, USA

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

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**High SPF formulation more effective during intense UV exposures**

- SPF 85 formulation tested vs. SPF 50
- 56 subjects applied sunscreen to face while skiing at Vail, Colorado 1/13/08
- 1 application only at start of day
- Average hours exposed 5.0 hours
- Noon Sun 22 minutes = 1 MED
- 7/28 sunburned SPF 50 vs. 1/28 SPF 85 (p=0.02)

Conclusion:
- SPF 85 formulation more effective than SPF 50 in protecting from sunburn with a single application in a high UV test environment

Russak et al., JAAD 2010
For each subject:
1. How much sunscreen was used?
2. How much time did each individual subject spend in the sun?
3. Were there reapplications (not allowed in study)?
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.

STUDY DESIGN
• Participants and evaluator were blinded to test product identity. Participants (Fitzpatrick skin type I to III, Erythema Score of 0.5 or less) were randomized to one of two treatment regimens for the face and neck:
  (SPF 50+ on left & SPF 100+ on right) or (SPF 100+ on left & SPF 50+ on right)
• Products Evaluated
  • Neutrogena® Ultra Sheer® Dry-Touch Sunscreen Lotion Broad Spectrum SPF 100+ (UPC 086800873105)
  • Banana Boat® Sport Performance® with Powerstay Technology Sunscreen Lotion Broad Spectrum SPF 50+ (UPC 079656045130)

STUDY DESIGN
• Participants self-applied the pre-weighed study products upon receipt, prior to outdoor sun exposure as they normally would. To address any questions by subjects about product application or usage, subjects were referred to the product study labels which contained the complete sunscreen Drug Facts information without ingredients list.
• Time spent outdoors was captured by the subjects in the provided exposure diary and solar conditions were tracked utilizing a stationary radiometer. An application diary was used to record the frequency and time of any product reapplications.
• Primary and Secondary efficacy endpoints were evaluated by clinical grading the morning after the recreational sun exposure period. At which time study products were also collected and weighed to determine usage.
RESULTS

Primary Endpoint

SPF 100+ sunscreen was significantly more effective at protecting against sunburn than was SPF 50+ sunscreen

Usage

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

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

Post Hoc Analysis

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

CONCLUSIONS

• Product usage data confirms that consumers apply sunscreen at densities far less than that utilized to determine the SPF value listed on the product label

• In this real-world, actual usage study, the SPF 100+ sunscreen was significantly more effective in protecting against sunburn than the SPF 50+ sunscreen

• Reapplication data confirms that consumers typically reapply the product less frequently than recommended on product label and that reapplication is observed to preserve but not enhance sunscreen efficacy
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.

Which is better?
Shade?
Sunscreen?

Objective:

- To directly measure sunburn protection offered by shade from a beach umbrella in comparison to a high SPF sunscreen.

Methods

- Randomized, Evaluator-blinded, Controlled Study
- Lakeside Beach near Dallas Texas, August 12
  - 75-90 degrees F
  - Horizontal UV Intensity 3-5 MEDs/hour
- 81 Participants
  - Sunscreen ONLY Group (SPF 100)
  - Shade ONLY Group (beach umbrella)

SUNSCREEN Group

- Neutrogena Ultra Sheer SPF 100
- Instructed to apply following label directions
- Sit at beach (no water activity) for 3.5 hours
- Reminded to reapply after 2 hours

SHADE Group

- Standard beach umbrella
- Round, 80” diameter, 75” height
- UPF rating 1000+
- Sit under umbrella shade at beach for 3.5 hours
  - Not allowed to use sunscreen
- Reminded to reposition as solar angle changed
Results

Sunscreen group had significant increase (p<0.05) in sunburn for face only

Shade group had significant increase (p<0.001) in sunburn for all body sites

Global Sunburn Scores:
- Shade Group ONLY: 79% subjects had increased sunburn score
- Sunscreen Group ONLY: 25% subjects had increased sunburn score

Sunscreen only group vs. Shade only group:
- Shade only Group: 16 participants
- Sunscreen only Group: 2 participants

Conclusions
- Seeking shade alone may not provide sufficient protection for extended sun UV exposure
- Shade Protection Factor: challenging to quantify given multiple factors
Conclusions

- Seeking shade alone may not provide sufficient protection for extended sun UV exposure
- Shade Protection Factor: challenging to quantify given multiple factors
- Neither shade nor high SPF sunscreen alone prevented sunburn completely
  - National Societies/Groups should consider changing messaging to combining multiple sun protective measures, rather than rely on a single approach

Are vitamin A analogues in sunscreen risky?

- 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

Are European sunscreens better?
### Geographic Region Number of Approved Sunscreening Agents

<table>
<thead>
<tr>
<th>Geographic Region</th>
<th>Number of Approved Sunscreening Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>United States</td>
<td>18</td>
</tr>
<tr>
<td>Europe</td>
<td>23</td>
</tr>
<tr>
<td>Japan</td>
<td>19</td>
</tr>
<tr>
<td>Australia</td>
<td>26</td>
</tr>
</tbody>
</table>

### Sunscreen Agent Spectrum of Action FDA Status Considerations

<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 XL</td>
<td>UVA2</td>
<td>Not approved</td>
<td>Not absorbed into skin</td>
</tr>
<tr>
<td>Emaxcavene</td>
<td>UVB</td>
<td>Not approved</td>
<td>Not water soluble; Water resistant and long lasting; May have estrogenic effect when used; Helps to stabilize avobenzone</td>
</tr>
<tr>
<td>Bisdisulizole</td>
<td>UVB</td>
<td>Not approved</td>
<td>Photostable; Water soluble</td>
</tr>
<tr>
<td>Uvinul A Plus</td>
<td>UVA2</td>
<td>Not approved</td>
<td>Photostable; May provide some protection against free radicals</td>
</tr>
<tr>
<td>Parsol SLX</td>
<td>UVB</td>
<td>Not approved</td>
<td>Available in EU and Asia</td>
</tr>
<tr>
<td>Amiloxate</td>
<td>UVB</td>
<td>Not approved</td>
<td>Available in EU and Asia</td>
</tr>
<tr>
<td>Uvasorb HEB</td>
<td>UVB, UVA1</td>
<td>Not approved</td>
<td>Available in EU and Asia</td>
</tr>
</tbody>
</table>

### 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 300 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.
Of the original 8 filters up for review, the FDA concluded there was not enough data to approve 5 filters.

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.

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

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.

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.

DNA Dosimetry Assessment for Sunscreen Genotoxic Photoprotection

- Sun Protection Factor for DNA (DNA-SPF) is calculated by using specific DNA repair enzymes, and it is defined as the capacity for inhibiting the generation of cyclobutane pyrimidine dimers (CPD) and oxidized DNA bases compared with unprotected control samples.
- 5 commercial sunscreens and 17 sun protection formulations were tested.
- All of the commercial brands of SPF 30 sunscreens provided sufficient protection against simulated sunlight genotoxicity.

Conclusions:
- DNA dosimeter is an alternative, complementary, and reliable method for the quantification of sunscreen photoprotection at the level of DNA damage


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 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.


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 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.


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:
  - unprotected exposed to 0, 1 and 3 MED
  - 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 Photimmunol Photomed. 2014


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

- Microsized TiO\(_2\) and ZnO have been increasingly replaced by TiO\(_2\) and ZnO nanoparticles
- Use of TiO\(_2\) and ZnO NPs makes the undesired opaqueness disappear
- Leads to incorporation of TiO\(_2\) 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

Smijs et al, Nanotechnol Sci Appl. 2011

New Formulations...

UV induced Free Radical formation

Sunscreen + Antioxidants = More Effectiveness??

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

Polypodium leucotomos

- Polypodium leucotomos is a natural fern leaf extract with antiinflammatory and antioxidant (AO) properties.
- The administration of oral P leucotomos to a group of high-risk patients with MM or DNS led to a significant reduction in sensitivity to UVR in all patients.
- Other studies have found that oral administration of 480 to 1200 mg daily of this extract can prevent polymorphous light eruption lesions in patients with PMLE.
- Has been shown to reduce the known effects of UVR, including minimal erythema dose, minimal phototoxic dose, UV-induced epidermal proliferation, development of DNA damage, and the generation of ROS.

Polypodium leucotomos
Decreases UV induced skin damage
- Investigated photoprotective effects of oral administration in 9 patients
- Measured erythema (MED) and biopsied skin and measured sunburn cells, pyrimidine dimers, dermal mast cell infiltration and Langerhans cells
- All of these measures were improved with the administration of polypodium
- Conclusion:
  - Effective systemic chemoprotective agent against UV radiation exposure skin damage
  
Middelkamp-Hup et al, J Am Acad Dermatol. 2004

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

Aguilera 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

New measures of measuring sunscreen effectiveness

New non-invasive approach assessing in vivo SPF using Diffuse Reflectance Spectroscopy and in vitro transmission
- Seventeen test materials with known in vivo SPF values were tested
- Combines the evaluation of UVA absorption spectrum as measured by diffuse reflectance spectroscopy (DRS) with the spectral absorbance "shape" of the UVB absorbance of test material as determined with in-vitro thin film spectroscopy
- Strong correlation of this new method with in vivo clinical SPF values $r^2 = 0.98$
- Conclusion:
  - This methodology provides a new approach to determine SPF values without the extensive UV irradiation procedures (and biological responses) currently used to establish sunscreen efficacy

Rusko et al, Photodermatol Photoimmunol Photomed, 2014
**Immune Protection Factor of Sunscreens**

- UV exposure leads to decreased immune response in skin
- UV induced suppression of Nickel allergy measure in subjects wearing sunscreen
- IPFs derived from the ratio of the minimal immune suppression dose (MISD) of UV in sunscreen applied sites vs. MISD of unprotected sites

**Conclusions:**

- IPF can be used as a measure of UV protection

**Accumulated p53 protein and UVA Protection Levels in Sunscreen**

- 2 sunscreens (SPF 7 – PFA 3 or 7) tested
- p53 levels measured in biopsies from UVA exposed skin
- Increased p53 with same exposure levels with lower UVA protection

**Conclusions:**

- p53 levels could be a biologic measure of UVA protection

**Chemiluminescence Evidence of Free Radical Generation**

![Chemiluminescence Evidence of Free Radical Generation](image)

**Radical Sun Protection Factor - RSF**

- Free radical formation from UV exposure in the skin measured in pig skin biopsies with electron spin resonance spectrometry
- Correlated with in-vivo measurements in human skin
- The effectiveness of UV filters inversely correlate with level of radical generation

**Conclusions:**

- Biophysical endpoint of free radical and reactive oxygen species in skin (RSF) can measure UV protection in sunscreens

**Integrated Sun Protection Factor - IPF**

- Free radical formation occurs from UV, IR-A and visible light exposure in the skin
- Measured in skin biopsies with electron spin resonance X-band spectrometry
- Integrates radiation exposure effects in all skin layers

**Conclusions:**

- Method effective for testing overall UV protection

**DNA Dosimetry Assessment for Sunscreen Genotoxic Photoprotection**

- Sun Protection Factor for DNA (DNA-SPF) is calculated by using specific DNA repair enzymes, and it is defined as the capacity for inhibiting the generation of cyclobutane pyrimidine dimers (CPD) and oxidised DNA bases compared with unprotected control samples
- 5 commercial sunscreens and 17 sun protection formulations were tested
- All of the commercial brands of SPF 30 sunscreens provided sufficient protection against simulated sunlight genotoxicity

**Conclusions:**

- DNA dosimeter is an alternative, complementary, and reliable method for the quantification of sunscreen photoprotection at the level of DNA damage
Enhancing Sunscreen Usage...

Focusing our efforts

**Association of UV Index and Sunscreen Use Among White High School Students in the US**

- White male students, as the mean UV index increased, the adjusted odds of never wearing sunscreen increased (OR = 1.15 p < .01) and the adjusted odds of most of the time or always wearing sunscreen decreased (OR = 0.85 p < .01).
- There was no association between sunscreen use and mean UV index among White female students.

**Conclusions:**
- Need for renewed public health efforts among school, clinical, and public health professionals to promote sunscreen use as part of a comprehensive approach to prevent skin cancer

**Everett et al, J Sch Health, 2013**

**Reasons for Using and Failing to Use Sunscreen**

**Comparison Among Whites, Hispanics, and Asian/Pacific Islanders in Southern California**

- "I often forget" was the most common reason for failing to use sunscreen
- The second most common was that "it is too greasy."
- Approximately one-third of whites and more than 43% of Asian/Pacific Islanders, but only 16% of Hispanics, indicated that sunscreen use is "too much trouble."
- 26% of Asians indicated that sunscreen is too messy, and 29% of Hispanics checked that they do not use sunscreen because they have dark skin.

**Mahler et al, JAMA Dermatol, 2014**

**Sun safety behaviors among farmers and farmworkers**

- Retrospective review of 22 studies
- Female farmers were more likely than male farmers to use sunscreen and engage in indoor tanning behavior.
- All sun safety educational interventions studies reviewed reported positive increases in behavioral change.
- Adequate sun protection is lacking and varies geographically among farmers.

**Conclusion:**
- Although targeted education is key to making improvements on sun protection behavior in farmers, aggressive attempts have to be made.

**Kearney et al, J Agromedicine, 2014**

**Sunscreen use in NCAA collegiate athletes: Identifying targets for intervention and barriers to use**

- Study conducted in 290 collegiate athletes from April 2010 to June 2011 at Duke and Stanford
- Average athlete spent 4h per day and 10 months per year training outdoors.
- While 96% agreed that sunscreen helps prevent skin cancer, over 50% never used sunscreen and 75% used sunscreen 3 or fewer days/week.
- Predictors of sunscreen use were female gender, sunburns in the last year, belief at risk for skin cancer, knowing someone with skin cancer, and being worried about wrinkles, sun burns, or skin cancer.

**Conclusion:**
- Continued identification of characteristics and barriers to sunscreen use can lead to targeted interventions and education in this high-risk group with early and elevated total lifetime UV exposure

**Wyson et al, Prev Med. 2012**

**UV Exposure in Athletes: Risks and Opportunities**

- Hours spent outside during peak UV hours
- Time spent outdoors from an early age
- Sweat related increase to photosensitivity
- Altitude related increase in UVR
- Reflection of UV off water and snow
- Lack of adequate UV protective clothing/equipment
- Lack of sunscreen usage
- Study of 274 collegiate athletes, only 11% reported consistent use of sunscreen (<75% of the time).

**Jinna et al, Sports Med, 2013**
Sun behavior after dx of cutaneous MM

- 24 pts recently dx'ed with MM, 29 pts diagnosed >1 yr ago vs. 51 controls matched for age, sex, occupation and skin type
- Sun exposure diaries daily maintained and subjects wore personal electronic UVR dosimeters
- UVR dose of recently dx'ed patients was 1/3 lower, and the number of days using sunscreen was 2x that of matched controls
- In pts dx'ed more than 1 year earlier, the UVR dose on days with body exposure was 1/3 higher and the number of days using sunscreen was 1/2 that of recently dx'ed pts
- Conclusions:
  - Patients with CMM limited their UVR dose on days with body exposure, and by using sunscreen further reduced UVR reaching the skin, although only immediately after diagnosis

Idorn et al, Br J Dermatol, 2013

Trends in Sunscreen Recommendation Among US Physicians

- Evaluated trends in sunscreen recommendation among physicians during visits 1989-2010
- MDs mentioned sunscreen at only 0.07% of visits
- Derms had 86% of the mentions but only mentioned sunscreens at 1.6% of visits

1 in 60 visits

Akamine et al, JAMA Dermatol, 2013

Trends in Sunscreen Recommendation
Among US Physicians

- Evaluated trends in sunscreen recommendation among physicians during visits 1989-2010
- MDs mentioned sunscreen at only 0.07% of visits
- Derms had 86% of the mentions but only mentioned sunscreens at 1.6% of visits
- Conclusions:
  - The high incidence and morbidity of skin cancer can be reduced with the implementation of sun-protective behaviors, which patients should be counseled about at visits
  - Despite encouragement to tell pts sun-protective behaviors, rate which physicians mention sunscreen at pt visits is quite low, even for patients with a history of skin cancer

Akamine et al, JAMA Dermatol, 2013
Sunscreen Discussion with Patients

- Email survey of US Dermatologists (n=530, 9% response rate) performed in July 2014.
- Asked how many pts seen in the prior 2 practice days and how many sunscreen were discussed with.
- Dermatologists reported discussing sunscreen with 58% of patients.

Conclusions:
- Demls discussed sunscreen with 18,090 of 31,253 (58%) pts over two practice days.
- Most Demls (72%) recommend SPF 30-49 to pts followed by SPF 50-69 (16%).

Patients Receiving Sunscreen Education by Latitude

What are Dermatologists views, beliefs and recommendations?
Dermatologists' Perceptions, Recommendations, and Usage of Sunscreen

**Dermatologists' Beliefs**

- Sunscreen safe: 99%
- Oxybenzone safe: 96%
- Retinyl palmitate safe: 99%
- High SPF safety margin: 71%
- Recommend SPF 50+: 42%

**Dermatologists' Recommendation Factors**

- SPF level: 100%
- Broad spectrum: 95%
- Feel/elegance: 82%
- Photostability: 55%

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**Answering Our Patient’s Questions**

- **Do you need to wear sunscreen while in a car?**
  - 2011 Lexus Rx350: 96% UVA blocked
  - 2011 Mercedes-Benz E550: 96% UVA blocked
  - 2014 VW Golf: 94% UVA blocked
  - 2013 BMW 320i: 93% UVA blocked

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**Do you need to wear sunscreen while in a car?**

- 2011 Lexus Rx350: 35% UVA blocked
- 2011 Mercedes-Benz E550: 37% UVA blocked
- 2014 VW Golf: 35% UVA blocked
- 2013 BMW 320i: 35% UVA blocked

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**Do you need to wear sunscreen while in a car?**

- 2011 Lexus Rx350: 25% UVA blocked
- 2011 Mercedes-Benz E550: 27% UVA blocked
- 2014 VW Golf: 25% UVA blocked
- 2013 BMW 320i: 25% UVA blocked

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**Do you need to wear sunscreen while in a car?**

- 2011 Lexus Rx350: 15% UVA blocked
- 2011 Mercedes-Benz E550: 17% UVA blocked
- 2014 VW Golf: 15% UVA blocked
- 2013 BMW 320i: 15% UVA blocked
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.
- Average percentage of front-windshield UV-A 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.

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

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

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

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Conclusions:
- Sunscreen protection does NOT degrade at outdoor summer temperatures during a typical vacation 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 til 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
- We don’t have answers to all of the questions and formulations can still be improved
- Formulations evolving in future with new agents and other ingredients
- The best sunscreen is the one that a person will use
- Learn what your pts are hearing and have the answers ready