Healthy Skin

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Healthy Skin

WARNING!

This presentation contains graphic images.
Viewer discretion advised.

No conflicts of interest to disclose
Tanning

- **Ancient Egypt:** Fair complexion reflected high rank
- **Middle Ages:** In Europe fair skin a sign of privilege. In Japan and China, pale skin was and still is aesthetic ideal
Tanning

- **1800s-1900s:** Excessive sun exposure viewed as unhealthy and cosmetically unacceptable in Northern Europe, especially among aristocracy
Tanning

- **1920s:** French fashion designer Coco Chanel often credited with developing concept of tanned skin as beautiful that still persists today.
Healthy Skin

- Sunscreen
  - Sunscreen and youthful appearance
  - Different types of sunscreen
    - Antioxidants
    - DNA enzyme repair
  - Prevention of actinic keratosis (red, scaly precancerous spots)
  - Prevention of non-melanoma skin cancer
  - Prevention of melanoma
Healthy Skin

- Polypodium Leucotomos
- Nicotinamide
- Clothing
- Actinic keratosis treatments
  - Field therapies
- Skin Cancer
Sunscreen and Aging

- 903 adults <55 years old
- Daily sunscreen use vs. discretionary sunscreen use
- After 4.5 years, people who used sunscreen daily showed no detectable increase in skin age.
- Aging from baseline was 24% less in those who used sunscreen daily.

Sunscreen and Aging
Sunscreen and Aging
The Terms

- **SPF: Sun Protection Factor.** A measure of protection against redness or burning.
- **Broad Spectrum.** Good protection against UVA and UVB

**What to look for in sunscreen?**
- SPF of at least 30
- Broad Spectrum
The Terms

- Water resistant (40 minutes)
- Water resistant (80 minutes)
- Terms “water proof” and “sweat proof” no longer valid.
Types of sunscreens

- **Chemical Sunscreens**
  - Chemicals absorb UV rays → get excited and dissipate energy as heat or infrared radiation

- **Physical blockers**
  - Reflect or scatter UV radiation
    - Newer microsized forms may absorb also
Common Sunscreen Components

- **UVB Blockers**
  - Aminobenzoates (PABA derivatives)
    - PABA - UVB
    - Padimate O - UVB
  - Cinnamates
    - Cinoxate - UVB
    - Octinoxate - UVB
  - Salicylates
    - Octisalate - UVB
    - Homosalate - UVB
    - Trolamine salicylate - UVB
  - Others
    - Octocrylene - UVB, UVA II
    - Ensulizole - UVB
Common Sunscreen Components

- **UVA Blockers**
  - Benzophenones
    - Oxybenzone - UVB, UVA II
    - Sulizobenzone - UVB, UVA II
    - Dioxybenzone - UVB, UVA II
  - Dibenzoylmethanes
    - Avobenzone - UVA I
  - Anthralates
    - Meradimate - UVA II
  - Camphors
    - Ecamsule - UVB, UVA
Common Sunscreen Components

- Physical Blockers
  - Titanium dioxide
  - Zinc oxide
Oxybenzone

- Protects against UVB, UVAII
  - Controversy regarding estrogenic effects
    - When given orally in rats, increased uterine size 23%
  - However, to achieve an equivalent dose in an average woman would have to apply 15 ml (1 tbs) per day to her entire body for 69.3 years

*Archives of Dermatology July, 2011. p.865*
Physical Blockers

- **Titanium Dioxide**
  - Chemically inert, safe, covers full UV spectrum
  - Previously limited by aesthetics, leaves white residue

- **Zinc Oxide**
  - Micronized form not visible in short wavelength visible range

- Both have *microsized* particles to improve cosmetics
**Actual Use**

- **SPF 15**... what does that mean??
  - If without sunscreen, you burn in 10 minutes, then with **SPF 15** you can stay in the sun **15X** longer.
  - $10 \text{ min} \times 15 = 150 \text{ min} = 2.5 \text{ hours}$
  - 1 application of **SPF 15** is good for 2.5 hours!
  - This assumes you apply $2 \text{mg/cm}^2$, but most only apply $1 \text{mg/cm}^2$
American Academy of Dermatologists recommends SPF 30+
- SPF 15 blocks 93.3% of UVB
- SPF 30 – 96.7%
- SPF 45 - 97.8%
- SPF 50 – 98%

New guidelines: *apply every 2 hours*
Sunscreen vehicles

- **Emulsions (lotions: oil-in-water, creams: water-in-oil)**
  - Oils most effective UV absorbers
  - “Ultrasheer” uses silica as vehicle

- **Gel (water-based)**
  - Easily removed by sweat and water
  - Many have alcohol
  - Good for acne prone skin
  - ex: BullFrog, PreSun

- **Sprays**
  - Difficult to spray evenly

- **Sticks**
  - Good for limited areas: lips, nose, and around eyes

- **Cosmetics**
Water Protection

- Face Sticks
  - Watermans
  - Headhunter
  - Vertra
  - Zinka
  - Shiseido
Contraindications

- Infants < 6 months old
  - Not unsafe/not hazardous
  - Contraindication is just to encourage sun avoidance in infants
Indications

- FDA approved
  - New indications in 2012:
    - Prevents actinic keratosis
    - Prevents non-melanoma skin cancers
    - Prevents Melanoma
    - Only if broad-spectrum and SPF≥15
  - Sunburn
  - Skin or lip damage, freckling, skin discoloration
  - Skin Aging

- Other
  - Phototoxic/photoallergic drug reactions
  - Photosensitivity disease
  - Photoaggravated disease (ex. lupus)
Sunless Tanners

Dihydroxyacetone (DHA)

- Active ingredient: melanoidin
- Melanoidins form as a result of "browning reaction" in the stratum corneum.
- Provides SPF of 2 or 3
Antioxidants

- Much UV light damage caused by generation of reactive oxygen species (ROS)
- Many manufacturers now including antioxidants in sunscreens
- Recent data shows majority of reduction of ROS due to UV blocking effects and not presence of antioxidants.

DNA Repair Enzymes

- **Endonuclease**: enzyme manufactured by a bacteria that repairs DNA damage.
- Shown to be effective in topical treatment of actinic keratosis, especially in people who lack repair enzymes.

*J Drugs Dermatol. 2010 Dec;9(12): 1519-21*
DNA repair enzymes

- Elizabeth Arden Triple Protection Factor
- Neova Total DNA repair
- DNA EGF Renewal
- Skin Care Heaven DNA Repair Serum
Effects of Different Ingredients

Does sunscreen really work?
Sunscreen and Actinic Keratosis

- 53 people; half given SPF 29, other half given placebo cream
- After 2 years those given sunscreen had fewer AKs

Sunscreen and Actinic Keratosis

- 588 people; half given SPF 17, other half given placebo cream
- After 6 months those given sunscreen had fewer AKs from baseline. Those using placebo cream had increase in # of AKs

Sunscreen and Squamous Cell Carcinoma

- 1383 people; half given SPF 15, other half given placebo cream
- After 4.5 years those given sunscreen had 39% fewer SCCs.

Sunscreen and Melanoma

- 1621 people; half given SPF 16 other placebo cream for 4 years
- 10 years later those given sunscreen had 50% fewer melanomas.

Other ways to prevent skin cancer and precancers besides sunscreen
Nicotinamide and Skin Cancer

- 386 people; half given nicotinamide 500mg 2x/day, other half given placebo for 1 year.
- Those taking nicotinamide had 23% fewer basal cell cancers (BCC) or common skin cancers (SCC).

Polypodium Leucotomos

- **Polypodium leucotomos**: natural fern leaf extract with antiinflammatory and antioxidant (AO) properties.
- Shown to reduce sunburn, DNA damage and generation of ROS among others actions.
- 240mg 2x/day
Clothing

Coolibar
UPF 50+ PROTECTION
BLOCKS 98% UVA/UVB

WOMEN MEN GIRLS BOYS BABY SUN HATS UV SWIMWEAR SUN ACCESSORIES SALE FEATURED

Coolibar

365
UPF 50+

MERINO
Naturally temperature regulating year-round UPF 50+ wool.

LEARN MORE
Skin Cancers

- Precancerous lesions
  - Actinic Keratosis

- Types of Skin Cancer
  - Basal Cell Carcinoma
  - Squamous Cell Carcinoma
  - Melanoma
Actinic Keratosis

- Red, rough patches
- Considered “precancerous” or “premalignant” because the abnormal cell within these lesions are confined to the epidermis, the top layer of skin.
- No risk of spreading until these lesions evolve into an invasive cancer.
Actinic Keratosis

- Risk of turning into a cancer
  - Small! 0.075–0.096% per lesion per year
  - However …
    - For a person with 7.7 AKs, the average number present on the skin of an affected individual, squamous cell carcinoma would develop at a rate of 10.2% over 10 years.
    - Other estimates are even higher, with rates of 13–20% over a 10-year period (if lesions left untreated).
Actinic Keratosis

- **Risk factors:**
  - Lighter skin
  - Chronic sun exposure

- **Clinical**
  - On sun-damaged skin of the head, neck, upper chest and back, and arms and legs
  - May be tender
Actinic Keratosis
Actinic Keratosis
Actinic Keratosis
Actinic Keratosis
Actinic Keratosis
Actinic Keratosis

- **Treatment**
  - Cryotherapy (liquid nitrogen)
  - 5-FU
  - Diclofenac 3% gel
  - Imiquimod
  - Ingenol mebutate
  - Photodynamic Therapy (PDT)
  - Medium depth chemical peel
Liquid Nitrogen

- 82.5–88% effective
- Ensures treatment
- Some pain
- Can leave skin a lighter color
Field (Regional) Therapies

- 5-FU (Efudex, Fluoroplex, Carac)
- Imiquinod (Aldara, Zyclara)
- Ingenol Mebutate (Picato)
- Diclofenac (Solaraze)
- PDT (Photodynamic therapy)
- Thulium 1927nm Laser
- and more
Imiquimod/Aldara/Zyclara

- Immunomodulating agent
- Activates TLR 7
- Anti-viral and anti-tumor effects
- FDA approval:
  - AKs on face and scalp
  - Superficial BCC
  - External genital and perianal warts
Imiquimod/Aldara/Zyclara
Imiquimod/Aldara/Zyclara

How to use
- Put on at night, leave on 6-10 hours then wash off
- Aldara – 5% imiquimod
  - AKs – 2x/week for max of 16wks
  - Only 2” x 2” area on face or scalp
- Zyclara – 3.75% imiquimod
  - AKs – every night for two 2-week cycles
  - Entire face or balding scalp
Diclofenac

- COX-2 inhibitor
- Topical 3% gel used 2x/day for 30 – 90 days
  - Efficacy similar to 5-FU
  - Well-tolerated, redness most common side effect
Ingenol Mebutate (Picato)

- Derived from sap of the plant Euphorbia peplus
Ingenol Mebutate (Picato)

- For AKs
- 98% compliance in studies
- Face + scalp for 3 days
- Trunk + extremities for 2 days
- 2” x 2” area at a time
Photodynamic Therapy (PDT)

- **PDT**: Activation of a photosensitizer by light to induce a therapeutic effect

- **Photosensitizers**
  - ALA (aminoevulinic acid) aka 5-ALA
  - MAL (methylaminolevulinate)
Photodynamic Therapy (PDT)

- Pretreatment can reduce incubation times
  - acetone scrubs
  - microdermabrasion
  - light chemical peels
PDT - Photosensitizers

Peak fluorescence reached 11-12 hours after topical application
PDT - Photosensitizers

Half life in lesional and perilesional skin is 30 and 28 hours respectively – so stay out of sun for 2 days after...
PDT – Mechanism of Action

- Neoplastic (cancerous) cells are hypermetabolic and take up more medication
PDT – Clinical Use

- Currently only FDA approved for AKs
- ALA – blue light
  - Apply to AKs only ➔ 14-18 hours later, blue light
  - 91% Complete response of individual lesions at week 12
  - 75% showed complete response at week 12 following single treatment
- Treats photoaging and subclinical lesions as well; no more than 1 hour incubation time though
## PDT – Comparison

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Cost</th>
<th>Downtime</th>
<th>Treatment of Large Areas</th>
<th>Cosmetic Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDT</td>
<td>Expensive</td>
<td>~1 week</td>
<td>Off-label</td>
<td>Excellent</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>Variable</td>
<td>Few weeks</td>
<td>No</td>
<td>Scar/PIH</td>
</tr>
<tr>
<td>5-FU</td>
<td>Cheap</td>
<td>&gt;1 month</td>
<td>Yes</td>
<td>Excellent</td>
</tr>
<tr>
<td>Imiquimod</td>
<td>Expensive</td>
<td>&gt;1 month</td>
<td>Yes</td>
<td>Excellent</td>
</tr>
<tr>
<td>Curettage</td>
<td>Variable</td>
<td>&lt;1 month</td>
<td>No</td>
<td>Scar</td>
</tr>
</tbody>
</table>
Non-Melanoma Skin Cancer (NMSC)

- More skin cancers in the US population than all other cancers combined
- Estimated that one in 5 Americans will develop skin cancer during their lifetime (over 95% will be NMSC)
- More than 3.5 million NMSCs occurred in approximately 2.5 million individuals in the US in 2006
- In Australia, the cumulative risk by age 70 years of having at least one NMSC is 70% for men and 58% for women
Non-Melanoma Skin Cancer (NMSC)

- Risk factors:
  - Skin type
  - UV radiation
INCIDENCE OF BASAL CELL CARCINOMA (BCC) AND SQUAMOUS CELL CARCINOMA (SCC)

- BCC men
- BCC women
- SCC men
- SCC women

Incidence/100,000

Age at diagnosis (years)

<20 20-29 30-39 40-49 50-59 60-69 70-79 ≥80
BCC

- 75–80% of NMSCs are basal cell carcinoma
- Arises on sun-damaged skin
BCC
BCC
BCC
BCC
BCC
BCC
BCC
BCC
BCC

Superficial
BCC

Superficial
BCC

Superficial
BCC

Morpheaform
BCC

Fibroepithleioma of Pinkus
BCC

Pigmented
BCC

Pigmented
BCC

Pigmented
BCC

Pigmented
BCC

Pigmented
BCC

Nodular
BCC

Rodent Ulcer
BCC

Cystic
BCC
BCC
SCC in situ

- Squamous cell carcinoma that has yet to invade deeper
- May arise from a pre-existing AK or normal skin
SCC in situ
SCC in situ
SCC in situ
SCC in situ
SCC in situ
SCC in situ
SCC, invasive

- Often nodules or ulcers
SCC
SCC
SCC
SCC
SCC
SCC
SCC
SCC
SCC
SCC

![Image of SCC on a hand](image-url)
SCC
SCC
SCC
SCC
Treatment

- Cryotherapy (Liquid Nitrogen)
- Electrodesiccation and curetage (scrape and burn)
- Excision (cut out)
- Mohs Surgery
Mohs Surgery

Conventional excision

Superior view

Tumor

Elliptical excision margin
Mohs Surgery

Extension of tumor beyond surgical margin
Mohs Surgery

Breadloaf sectioning

Extension of tumor not represented in histology sections (A–F)
Mohs Surgery

Extension of tumor not represented in histology sections (A–F)

Breadloaf section on histologic slides

A
Surface

B

C

D

E

F

Deep
Mohs Surgery

Excision for Mohs micrographic surgery

Superior view

Tumor
Mohs Surgery

Mohs surgical margin
Layer I

Mohs surgical margin
Layer II

Surface

Deep

Extension of tumor represented in Mohs histology sections
Mohs Surgery

Extension of tumor represented in Mohs histology sections
Mohs Surgery

Extension of tumor represented in Mohs histology sections

Layer I

I₁

I₂

I₃

I₄

Layer II

II₁

Deep and peripheral margins
Mohs Surgery

- Improved method of evaluating the margin
- 5-year cure rate for primary cancers treated by Mohs surgery is 99%, compared with 93% for conventional excision
- For recurrent cancers, 5-year cure rate is 95%, compared with 80% for excision or any other treatment modality
Melanoma

Epidemiology

- Rising incidence of cutaneous melanoma worldwide over the past four decades in white populations
- One of the most common forms of cancer in young adults

Rate per 100,000 population

Year of diagnosis

White male
White female
Black male
Black female

Superficial Spreading Melanoma
Superficial Spreading Melanoma
Superficial Spreading Melanoma
Superficial Spreading Melanoma
Superficial Spreading Melanoma
Superficial Spreading Melanoma
Superficial Spreading Melanoma
Superficial Spreading Melanoma in situ
Superficial Spreading Melanoma in situ
Superficial Spreading Melanoma in situ

Ugly Duckling
Nodular Melanoma
Nodular Melanoma
Nodular Amelanotic Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Lentigo Maligna Melanoma
Acral Lentiginous Melanoma
Acral Lentiginous Melanoma
Acral Lentiginous Melanoma
Melanoma

- Treatment
  - Chemotherapy only for Stage IV
    - Dacarbazine
    - IL-2
    - BRAF inhibitors – vermurafenib, dabrafenib
    - MEK inhibitors – trametinib
  - Immunotherapy
    - Anti-CTLA-4 – ipilimumab
    - Anti-PD-1 receptor – Nivolumab, Pembrolizumab/Lambrolizumab
Melanoma

- Prevention
  - Wear sunscreen properly
  - Annual skin checks
  - Treat early
Questions?