



The Three S's

Sunshine
Skin Cancer
Sunscreen

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Disclosures

- ▶ Speaker for Abbvie
- ▶ Speaker for Regeneron Sanofi- Genzyme
- ▶ Speaker for Dermavant
- ▶ Ad Board Consultant for Arcutis
- ▶ Ad Board Consultant for Amgen
- ▶ Ad Board Consultant for Bristol Myers
- ▶ Ad Board Consultant for Lilly
- ▶ Ad Board Consultant for Johnson and Johnson
- ▶ Ad Board Consultant for Incyte
- ▶ Ad Board Consultant for Leo

Overview

- ▶ Sunshine
- ▶ Skin Cancer
- ▶ Sun screen and skin protection

Sunshine = UV Radiation

- ▶ UVC – doesn't reach the earth's surface
- ▶ UVA – comprises 96.5% of UV radiation
- ▶ UVB – comprises 3.5 % of UV radiation

UV Effects on Skin

- ▶ DNA damage
- ▶ Immunosuppression
- ▶ Sunburn
- ▶ Photoaging/Pigmentary Disorders
- ▶ Skin Cancers



UVA Damage

- ▶ Suppression of immune system – interferes with the immune system's ability to protect against the development of skin cancer
- ▶ Systemic immunosuppression has a clear association with increased risk of skin cancer, example renal transplant patients

UVA vs UVB

UVA

- ▶ 320-400 nm
- ▶ NOT absorbed by Ozone
- ▶ Penetrates GLASS
- ▶ Penetrates to DERMIS
- ▶ Aging Rays

UVB

- ▶ 290-320 nm
- ▶ Partially absorbed by Ozone
- ▶ NO penetration through glass
- ▶ Penetrates to EPIDERMIS
- ▶ Sunburn Rays

Sunburn

- ▶ Inflammatory process that initiates apoptosis
- ▶ Apoptosis – a process that removes the irreversibly damaged keratinocytes after excessive UV radiation
- ▶ Mechanism of programmed cell death in severely damaged keratinocytes

Skin Cancers/Sun Damage

- ▶ Actinic Keratosis - AK
- ▶ Basal Cell Carcinoma- BCC
- ▶ Squamous Cell Carcinoma- SCC
- ▶ MELANOMA

Actinic Keratosis

Occur on sun damage skin: Face, Scalp, Ears, & Arms

White/yellow Scaly Rough Patches

Potential to evolve into SCC: 0.1-20%



Actinic Keratosis Treatments

- ▶ Daily Sunscreen
- ▶ Topicals: 5% fluorouracil, Imiquimod, Diclofenac, tirbanibulin
- ▶ Cryosurgery: Liquid Nitrogen
- ▶ Photodynamic therapy: 5-Aminolaevulinic

Cryosurgery: Liquid Nitrogen

- ▶ Cure rate 57%-98.8%
- ▶ 5 seconds=39% 20 seconds=69% >20seconds=83%
- ▶ Blistering effect and potential dyschromia

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5% fluorouracil

- ▶ 0.5- 5% formulations
- ▶ Antimetabolic cytotoxic agent: Interferes with DNA synthesis
- ▶ Apply qd-bid for 2-4 weeks
 - ▶ 5% Bid for 4 weeks- 38% AK clearance
- ▶ SE: photosensitivity, redness, erythema, blistering
 - ▶ Resolves within 1-2 weeks after discontinuation of medication

J Am Acad Dermatol. 2021 Oct;85(4):945-

5% Fluorouracil Reaction



5% Fluouracil Reaction

4 weeks post therapy



Imiquimod

- ▶ FDA approved: AK, Bcc-superficial
- ▶ Immune Response Modifier
 - ▶ Toll like cell receptor
 - ▶ Stimulates production of cytokines in epidermis
 - ▶ Cellular immunity and direct apoptotic effect on tumor cells
- ▶ 2.5% , 3.75%, and 5% formulations
- ▶ Apply for 2 weeks to 4 weeks
- ▶ SE: flu like symptoms, redness, scaling , blisters, hypopigmentation

Imiquimod Reaction

11 days of Imiquimod



Post Topical Steroid



Imiquimod 5%: Superficial BCC TX

- ▶ Daily for 6 weeks
- ▶ Apply Monday through Friday : take weekends off
- ▶ SE: irritation and Flu like symptoms

5-Aminolaevulinic Acid (ALA) Photodynamic Therapy

- ▶ Blue light or Red light
 - ▶ Activation by photosensitizer by visible light
 - ▶ Rapidly dividing atypical keratinocytes
- ▶ Apply/incubate for 30- 2 hours- apply in office
 - ▶ Expose to light for 16 minutes
- ▶ No light exposure for 48 hours post procedure
- ▶ SE: burning, stinging, scaling, sun burn appearance for 1-2 weeks

PDT Reaction



Tirbanibulin 1%

- ▶ Microtubular Inhibitor: Antiproliferative against keratinocytes
- ▶ Apply to face or scalp : 25cm
- ▶ Apply once daily for 5 days
- ▶ Cure rates 44-54%
- ▶ SE: local skin irritation, flaking, Crusting, erosions, ulcerations: resolve by 30-40 days

Diclofenac 3%

- ▶ NSAID: inhibits cyclooxygenase 2
 - ▶ Decrease in PGE2 synthesis
- ▶ Apply twice a day for 60-90 days
- ▶ Cure rate 42%
- ▶ SE; eczema, cutaneous dryness, pruritus, scaly rash
 - ▶ Boxed warning : Increased risk of cardiovascular events

Ingenol Mebutate

- ▶ Derived from surge sap
- ▶ Stimulate immune response to induce necrosis of dysplastic cells
- ▶ 0.05%: trunk & extremities 0.015% : face and scalp
- ▶ Apply daily for two or three days
- ▶ SE: erythema, flaking, scaling, crusting
- ▶ ****Removed from European Market 2019: 3x increase risk of skin Cancer
- ▶ **** Manufacturer pulled off market in 2020

Basal Cell Carcinoma

- ▶ Most Common Skin Cancer : 4 million per year
- ▶ Slow Growing/Rarely Metastasizes
- ▶ Can destroy tissue if not treated
- ▶ Types: Nodular, Pigmented, Superficial, Morpheaform
 - ▶ Can be infiltrative

Basal Cell

- ▶ Nodular
 - ▶ Pearly papule with telangiectasias and central umbilication
- ▶ Superficial BCC
 - ▶ Erythematous scaly patch
- ▶ Morpheaform
 - ▶ Scar like
- ▶ Pigmented
 - ▶ Purple/black pearly papule

Basal Cell/Nodular



Basal Cell/Nodular



Superficial Basal Cell



Basal Cell/Morphea Form



Squamous Cell Carcinoma

- ▶ 2nd Most Common Skin Cancer: 1 million per year
- ▶ Caused by Exposure from UV radiation
- ▶ Can Arise from Actinic Keratosis
- ▶ Types: Invasive, Superficial (In situ), Keratoacanthoma
- ▶ Transplant patients at Higher Risk

Squamous Cell

- ▶ Scc Insitu
 - ▶ Scaly well demarcated plaque
- ▶ Invasive
 - ▶ Erythematous keratotic plaque or nodule
- ▶ Keratoacanthomas
 - ▶ Rapidly growing erythematous nodule with central keratotic core

SCC/Invasive



SCC



SCC InSitu



SCC/Keratoacanthoma

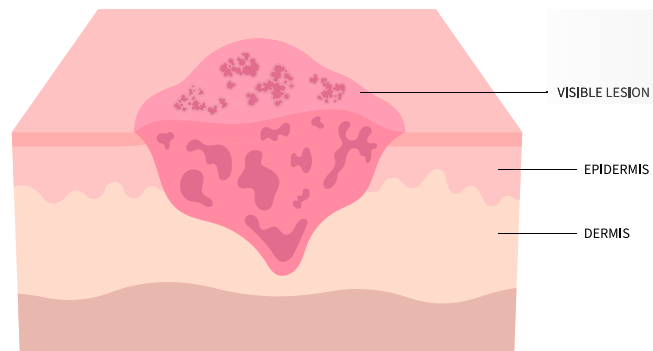


Treatments for BCC/SCC

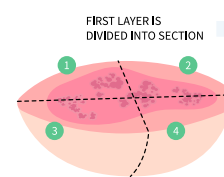
- ▶ Electrodesiccation and Curettage (ED& C)
 - ▶ SCC- insitu or superficial BCC
- ▶ Excision
- ▶ Topicals : Imiquimod, 5-FU
- ▶ Radiation
- ▶ Mohs Surgery: Face, Scalp, Ear , Body (>2cm)

MOHS surgery

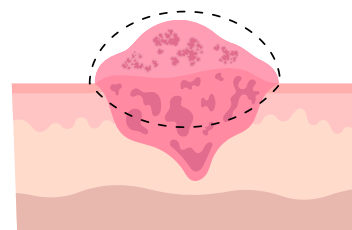
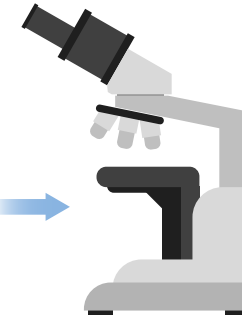
- ▶ Frederic Mohs 1930s
 - ▶ Modified by Tromovitch and Stegman in 1970s
- ▶ Tissue sparing technique, frozen section control of 100% surgical margin
 - ▶ Horizontal sections combined with precise mapping= cure rate 90-95%
- ▶ Indications
 - ▶ High risk location: H-zone
 - ▶ Tumors in previously radiated skin
 - ▶ Large tumors > 2 cm on body



MOHS SURGERY



TUMOR TISSUE ARE EXAMINED
BY THE MICROSCOPIC



1
STEP 1



FIRST TUMOR LAYER REMOVED

2
STEP 2



THE REMAINING TUMORS ARE REMOVED

3
STEP 3



FINAL LAYER REMOVED UNTIL NO MORE
TUMOR CELLS REMAINING

MOHS Surgery



MOHS Surgery



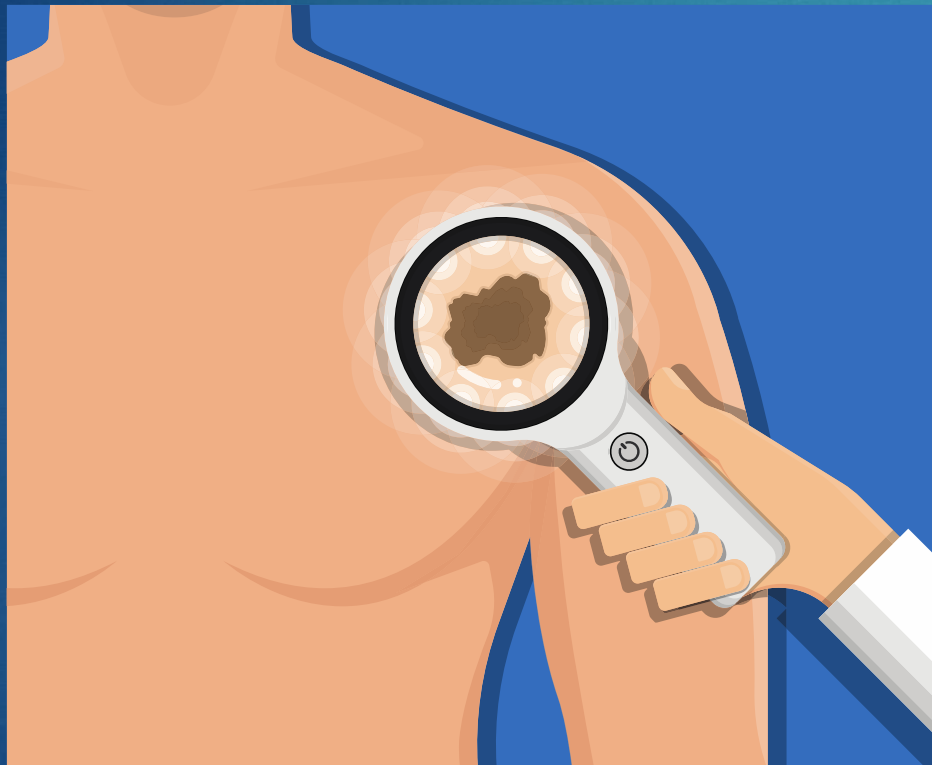
Mohs



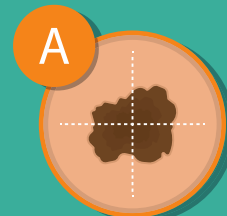
Melanoma

- ▶ Most Fatal Skin Cancer: doubled in the last 30 years
 - ▶ Approx 76,000 per year
- ▶ Risk Doubles if a Patient has had 5 or More Sunburns in a Lifetime
- ▶ More common in **Men: 45,845** 31,845 in Women (2011-2016)
 - ▶ Most common skin cancer in Caucasian Women aged 15-29
- ▶ Back : Men Leg: Women
- ▶ Types: In situ, Invasive, amelanotic

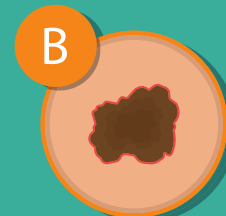
<https://www.cdc.gov/cancer/uscs/about/data-briefs/no9-melanoma-incidence-mortality-UnitedStates-2012-2016.htm>



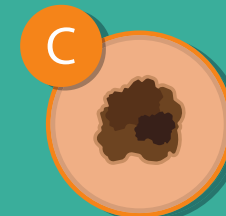
ABCDEs Of Skin Cancer



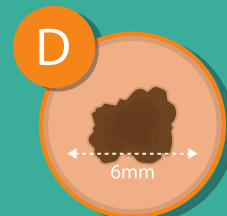
Asymmetry



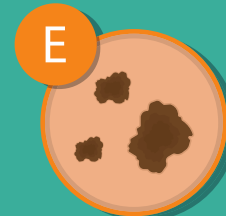
Border



Colour



Diameter



Evolving

Melanoma Detection

- ▶ A: Asymmetry
- ▶ B: Border - irregular
- ▶ C: Color - variation
- ▶ D: Diameter – larger than pencil eraser
- ▶ E: Evolving - changing

Melanoma Stages

- ▶ Stage 0: Insitu , only involves top layer of the skin
- ▶ Stage 1: Only in the skin, but tumor has grown thicker
- ▶ Stage 2: has grown thick with Breslow Thickness 1.01 – 4.0 mm
 - ▶ Send for lymph node if Breslow 0.8mm thickness
- ▶ Stage 3: Has grown beyond skin, one or more lymph node +
- ▶ Stage 4: has spread to organs, example lung or brain

Melanoma In Situ



Melanoma In Situ



Melanoma



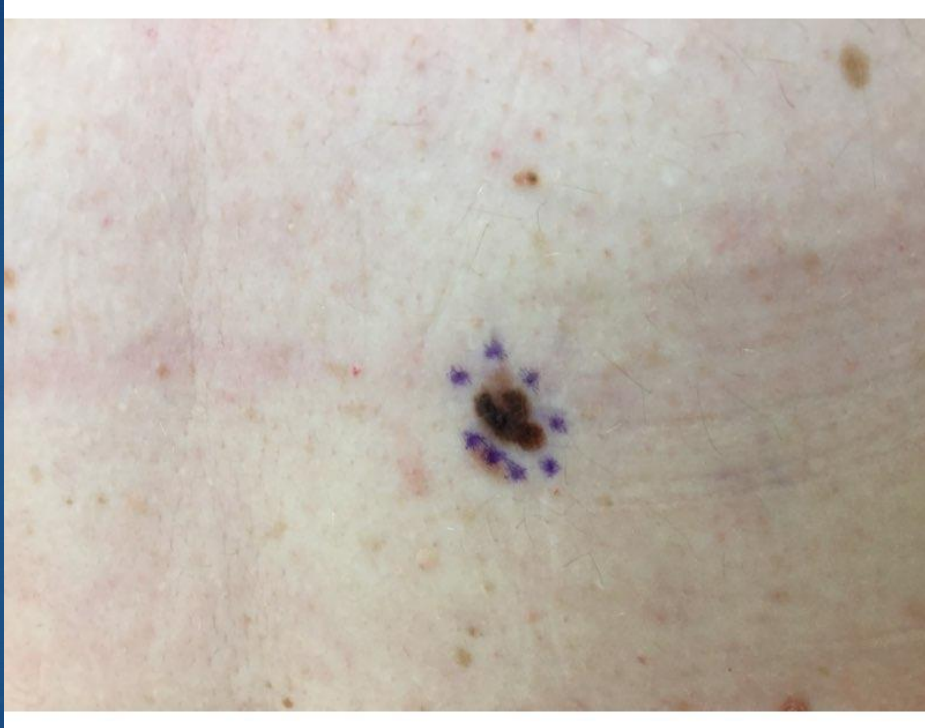
Melanoma



Melanoma



Melanoma



Melanoma



Melanoma



Melanoma Insitu treatments

- ▶ Excision with 0.5mm margins
- ▶ Slow Mohs
- ▶ Skin cancer screening every 6 months for one year than once a year

Melanoma Tx

- ▶ Breslow Thickness $<0.8\text{mm}$
 - ▶ Wide Excision down to muscle with 1.0cm margins
 - ▶ Skin Cancer screening every 3 months for one year, then every 6 months for one year, then once a year
- ▶ Breslow Thickness $>0.8\text{mm}$
 - ▶ Wide excision down to muscle with 1.0cm margins
 - ▶ Sentinel lymph node biopsy
 - ▶ Skin cancer screening every 3 months for one year, then every 6 months for one year, then once a year

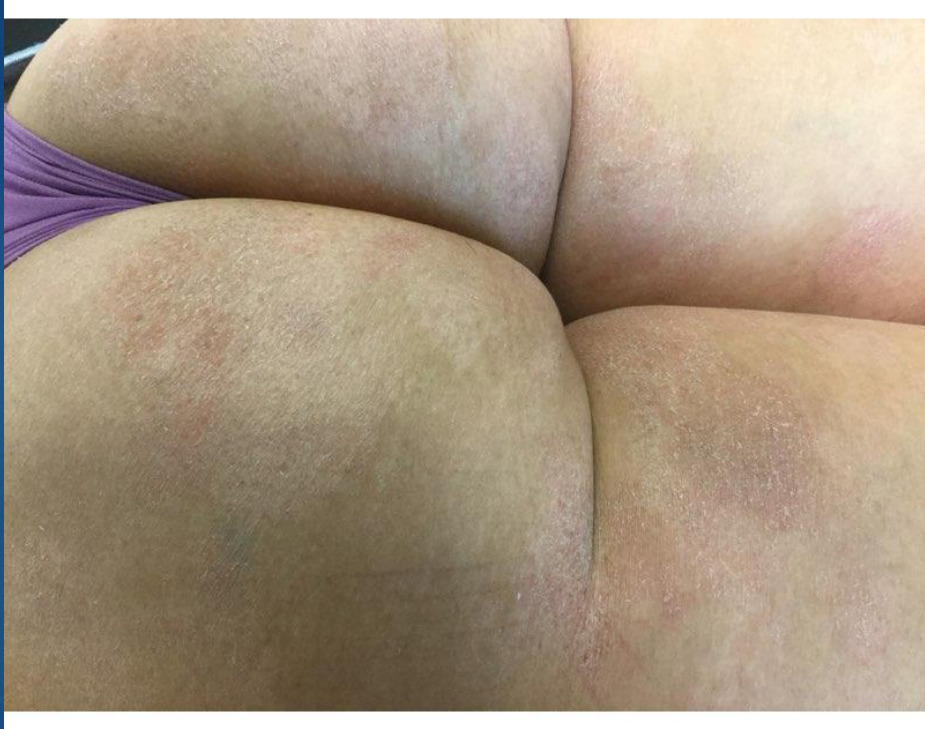
Cutaneous T cell Lymphoma

- ▶ Primary cutaneous lymphoma in the skin
- ▶ Most common Variant Mycosis Fungoides
- ▶ Chronic/slow progressive patches/plaques/parapsoriasis
 - ▶ Many times misdiagnosed as Atopic Dermatitis or Psoriasis
 - ▶ On average 5-6 biopsies to make DX
- ▶ Trunk, abdomen, upper thighs, buttocks
 - ▶ Double clothed area

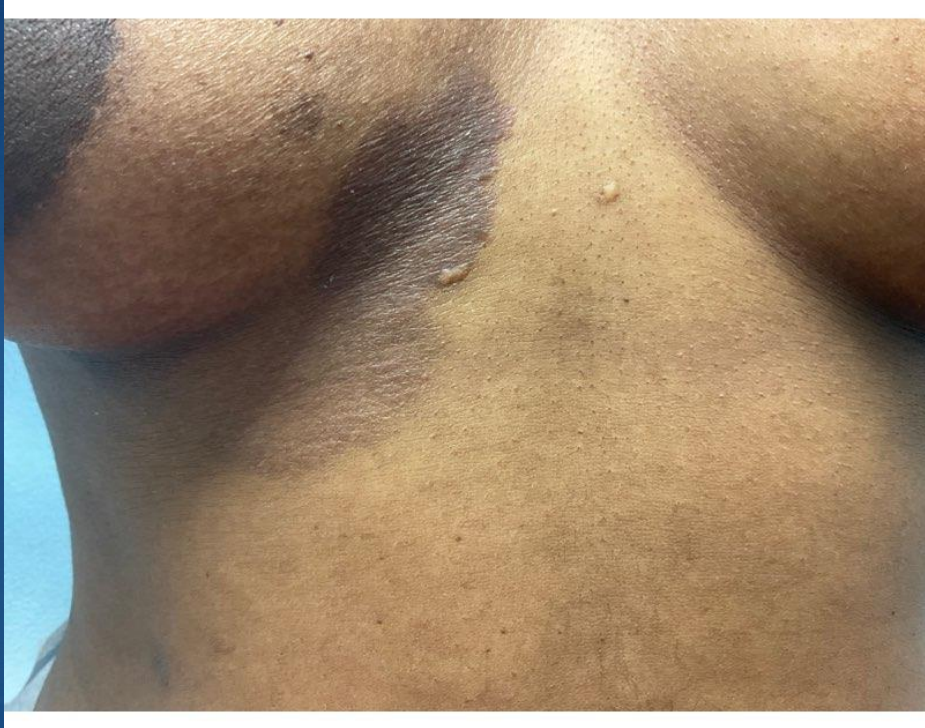
Cutaneous T Cell Lymphoma



Mycosis Fungoides



Mycosis Fungoides



CTCL TX/early

- ▶ Topical corticosteroids
- ▶ Topical Nitrogen Mustard
- ▶ NBUVB
 - ▶ Patch stage

Merkel Cell Carcinoma

- ▶ Solitary, rapidly growing pink to red nodule
- ▶ Older pts: mean age 76/74
- ▶ Head and Neck most common location
- ▶ Aggressive: Metastasis in 40%
- ▶ Tx: Wide excision with SNL

Merkel Cell



Merkel Cell





Causes of Skin Cancers

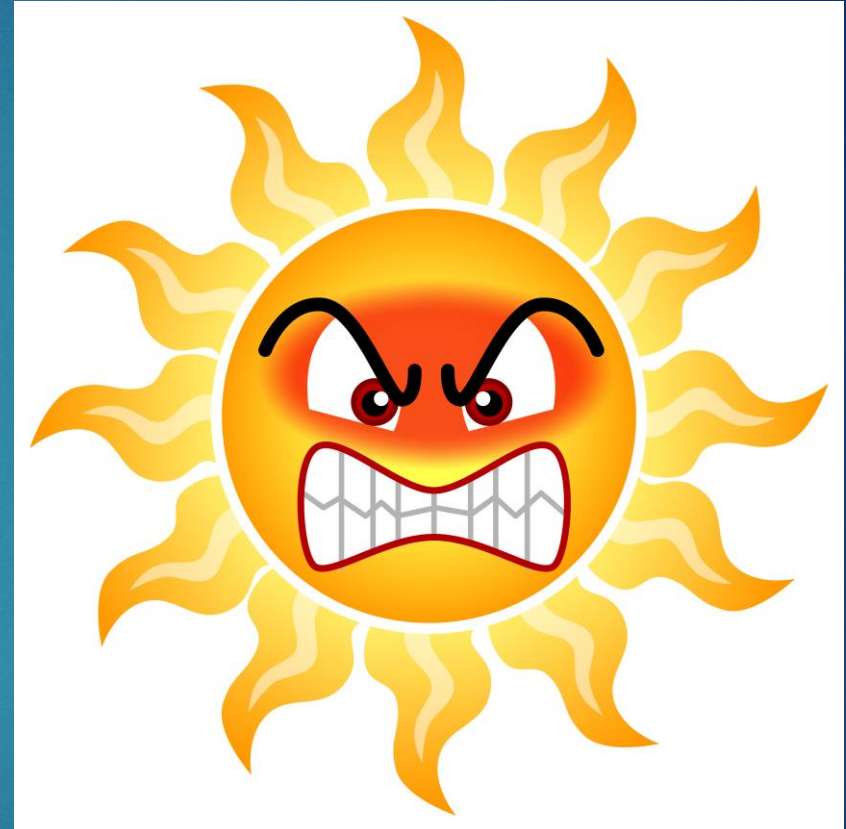
Sun = UV RADIATION

UV Radiation

- ▶ UVC – doesn't reach the earth's surface
- ▶ UVA – comprises 96.5% of UV radiation
- ▶ UVB – comprises 5 % of UV radiation

UV Effects on Skin

- ▶ DNA damage
- ▶ Immunosuppression
- ▶ Sunburn
- ▶ Photo aging/Pigmentary Disorders
- ▶ Skin Cancers



UVA

- ▶ Longest wave length 320nm-400nm
- ▶ 95% of UVR that reaches Earth
- ▶ Not absorbed by ozone
- ▶ Penetrates GLASS
- ▶ Penetrates to DERMIS
- ▶ AGING RAYS – wrinkles, spots
- ▶ CARCINOGENIC RAYS
- ▶ TANNING BEDS

UVB

- ▶ 220-390nm
- ▶ 5% of UVR that reaches earth
- ▶ Partially absorbed by Ozone
- ▶ Does not penetrate Glass
- ▶ Tanning, BURNING

UVA Damage

- ▶ Suppression of immune system – interferes with the immune system's ability to protect against the development of skin cancer
- ▶ Systemic immunosuppression has a clear association with increased risk of skin cancer, example renal transplant patients

DNA Damage

- ▶ Absorbed by fibroblasts, induces reactive oxygen species which leads to the induction of matrix metalloproteases and mitochondrial DNA mutation

UVA vs. UVB

UVA

- ▶ 320-400 nm
- ▶ NOT absorbed by Ozone
- ▶ Penetrates GLASS
- ▶ Penetrates to DERMIS
- ▶ Aging Rays, CARCINOGENIC

UVB

- ▶ 290-320 nm
- ▶ Partially absorbed by Ozone
- ▶ NO penetration through glass
- ▶ Penetrates to EPIDERMIS
- ▶ Sunburn Rays

Skin Protection against UV

- ▶ Photolyase
- ▶ Nucleotide excision repair enzymes
- ▶ Antioxidant network
- ▶ Melanin synthesis

Mechanism of skin pigmentation



UV

1 By exposure of UV rays, reactive oxygen is generated.

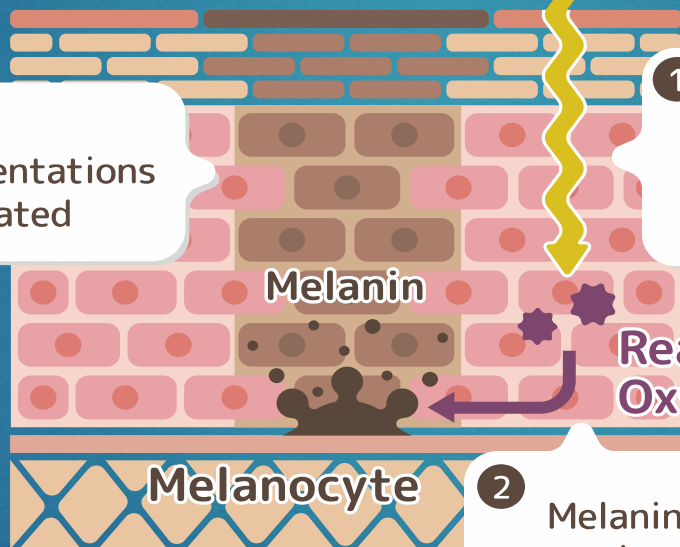
Reactive Oxygen

2 Melanin is excessively produced by melanocytes.

Melanocyte

Melanin

3 Skin pigmentations are generated



Melanin

- ▶ Acts as a neutral density filter to equally reduce penetration of all wavelengths of light
- ▶ Ultimately prevents damage to DNA contents of the cells
- ▶ Caucasians have **5x more UV light reaching the upper dermis as compared to African Americans**
- ▶ Offers **SPF 13.4 for AA vs. 3.4 for Caucasians**



Methods to Block UV radiation

- ▶ Limiting sun exposure : avoid sun from 10am -3pm
- ▶ Wearing appropriate clothes, hats, sunglasses
- ▶ Sunscreens/photo protective agents
- ▶ Non sunscreen photo protective agent: antioxidants



Protective Clothing

- ▶ Ultraviolet Protection Factor (UPF): indicates what fraction of the sun's UV rays penetrate fabric
 - ▶ Shirt with UPF 50 blocks $1/50^{\text{th}}$ of sun's UV rays
 - ▶ Columbia, Mott 50, Roxy, Quicksilver
- ▶ Tighter Weave Fabric: Lycra/polyester
 - ▶ Darker Colors
- ▶ Laundry Products: Rit Guard, contains Tinosorb which is a UVA/UVB filter

Eye Protection



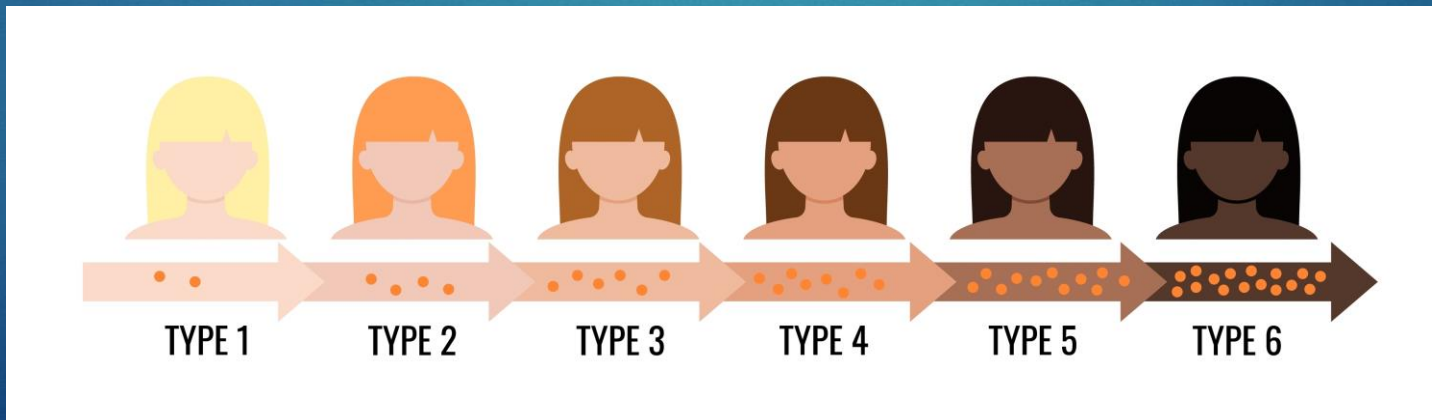
- ▶ Chronic sun damage causes cataracts and macular degeneration,
- ▶ Sunglass: FDA approved parameters
 - ▶ Wrap around
 - ▶ UV absorption up to 400nm
- ▶ 5-10% of all skin cancers arise on the eyelids
- ▶ Minorities and Men less likely to wear sunglasses

Skin Types



Skin Types

- ▶ Type I: Always burns easily, never tans, extremely sun sensitive
- ▶ Type II: Usually burns, tans minimally, very sun sensitive
- ▶ Type III: Sometimes burns, tans gradually to light brown, sun sensitive
- ▶ Type IV: Burns minimally, always tans to moderate brown
- ▶ Type V: Rarely burns, tans well
- ▶ Type VI: Never Burns, deeply pigmented



Tanning Beds



Tanning Beds

- ▶ 30 million Americans use artificial tanning each yr
- ▶ Mostly used by females aged 16- 18y/o caucasian females
- ▶ Bulbs emit **MOSTLY UVA** radiation and **5% UVB**
- ▶ Multiple studies prove use increases risk of melanoma and nonmelanoma skin cancers
- ▶ 44 states have regulations in place for minors to use tanning beds
- ▶ 20 States restrict use of Minors

Tanning Beds

- ▶ Group 1 Carcinogen: asbestos, arsenic, Tobacco smoke
 - ▶ WHO classification
- ▶ Melanoma risk increased by 75% if use regularly before the age of 30
- ▶ Can cause Sunburns: 60% have experienced
- ▶ Ineffective source of Vitamin D
- ▶ FDA advised against use in <18 years of age (2014)

Sunburn

- ▶ Inflammatory process that initiates apoptosis
- ▶ Apoptosis – a process that removes the irreversibly damaged keratinocytes after excessive UV radiation
- ▶ Mechanism of programmed cell death in severely damaged keratinocytes

Goals of Sunscreen

- ▶ Protect against UVB radiation and long term UVA
 - ▶ **BROAD SPECTRUM**
- ▶ Scavenges Reactive Oxygen Species (ROS)
- ▶ Activate cellular repair systems- DNA repair

SPF

- ▶ Sun Protection Factor
- ▶ Developed in 1962 by Swiss researcher Franz Greiter
- ▶ A product's ability to deflect the sun's **BURNING RAYS (UVB)**



SPF calculation

- ▶ Compare amount of time needed to produce a sunburn with sunscreen & amount of time needed to cause a sunburn without sunscreen
- ▶ SPF 2 = sunburn at 10 minutes, SPF 15 = 150 minutes
- ▶ UVB protection doesn't increase proportionately with SPF SPF 2 = 50% SPF 15 = 93% SPF 30 = 97%
- ▶ NOTHING BLOCKS UVB 100%



SPF Recommendations

- ▶ Apply BROAD SPECTRUM 30 or higher SPF
 - ▶ UVA and UVB
- ▶ Apply 15 minutes before exposure to sun
- ▶ Reapply every 2 hours
- ▶ Reapply after swimming, sweating, ect
 - ▶ NO SUNSCREEN IS WATERPROOF



<https://www.aad.org/public/everyday-care/sun-protection/shade-clothing-sunscreen/how-to-select-sunscreen>

Sunscreen Tidbit

- ▶ Most people only apply 25-50% of the recommended amount of sunscreen
- ▶ 2mg/cm², 30ml to cover the body: 1 SHOT GLASS
 - ▶ 1-2 teaspoons for face and neck
 - ▶ 2-3 tablespoons for body
- ▶ May lose effectiveness 40 minutes after swimming
- ▶ Can rub off as well as wash off
- ▶ 65% do not reapply



Sunscreen Ingredients

- ▶ Chemical blockers
- ▶ Physical Blockers
- ▶ UVA & UVB Protection



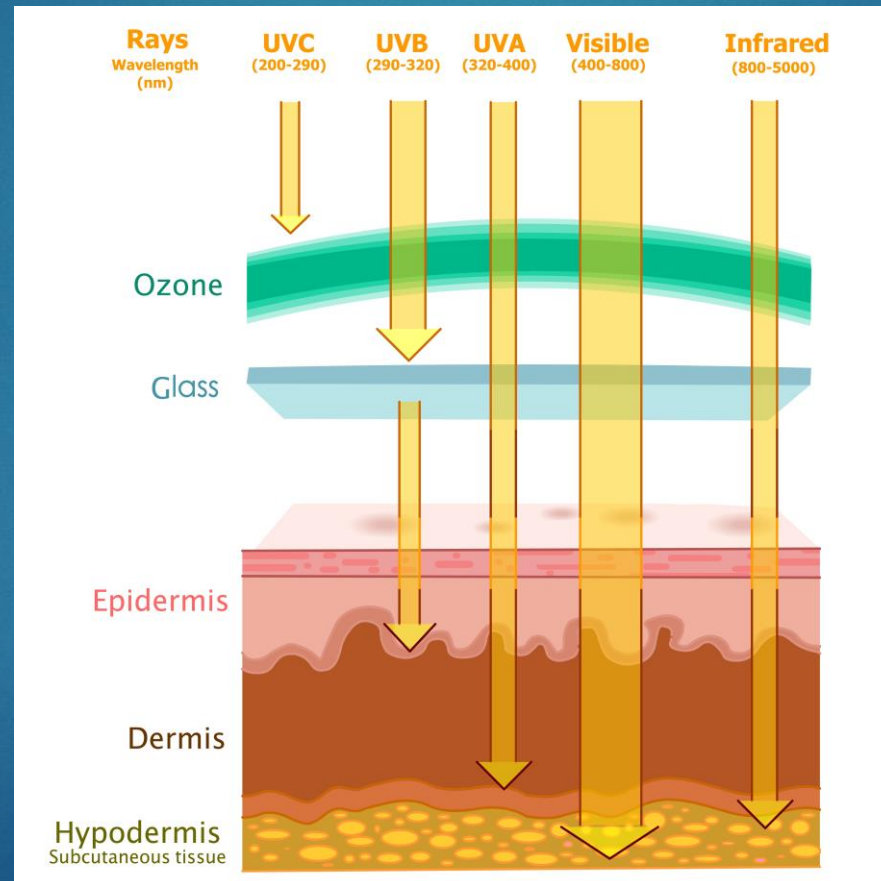
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UVB

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- ▶ Sunburn Rays



Physical Blockers

- ▶ Prevent UV rays from reaching the skin by reflecting and dispersing the rays (mirror)
- ▶ Scatter and “physically block”
- ▶ Not systemically absorbed
- ▶ Zinc Oxide, Titanium Oxide, Iron Oxide
- ▶ Zinc: 290-379 nm Titanium 290-400nm

Chemical Blockers

- ▶ Absorb UV and dissipate it as heat
- ▶ The degree of absorption depends on the substance used
- ▶ Benzophenones: Avobenzone Oxybenzone,
- ▶ PABA Esters: Padimate-O
- ▶ Cinnamates: Cinoxate, Octocrylene
- ▶ Salicylates: Homosalate, Octyl Salicylate

Sunscreen Active Ingredients

UVA Protection

- ▶ Oxybenzone
- ▶ Meradimate
- ▶ Avobenzone
- ▶ *Ecamsule- photostable
- ▶ Octocrylene
- ▶ Zinc oxide
- ▶ Titanium dioxide

UVB protection

- ▶ Padimate
- ▶ Octinoxate
- ▶ Octisalate
- ▶ Ecamsule
- ▶ *Octocrylene
- ▶ Erisulizole
- ▶ Zinc Oxide
- ▶ Titanium Oxide

2011 FDA Sunscreen Regulations

- ▶ “Broad Spectrum”= UVA + UVB coverage
- ▶ SPF of 15 > can state it protects against skin cancer if used with other sun protection measures
- ▶ SPF 2-4 will have a warning: products not been shown to have skin cancer or skin aging protection
- ▶ “Sunblock” “Sweatproof” and “Water proof” no longer allowed

2011 FDA Sunscreen Regulations

- ▶ “Water Resistant”= must specify if it offers 40 or 80 minutes of protection while swimming or sweating
 - ▶ “not water resistant” must include a direction to apply water resistant sunscreen if swimming or sweating
- ▶ Cannot claim to provide sun protection for more than 2 hours without reapplication

2019 FDA Regulations Sunscreen

- ▶ Generally Recognized as Safe and Effective GRASE
 - ▶ Zinc and Titanium
- ▶ NOT SAFE: (aminobenzoic acid (PABA) and trolamine salicylate
- ▶ More Safety Information Needed:
 - ▶ cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, padimate O, sulisobenzene, oxybenzone, avobenzone

Sunscreen “Myths”

- ▶ Causes skin cancer- photocarcinogenic
- ▶ May cause free radicals
- ▶ Systemic Absorption- nano particles
- ▶ Reproductively toxic potential
- ▶ Hormone disruption



Retinyl Palmitate/Cancer Causing??

- ▶ When exposed to UV radiation it generates free radicals
- ▶ Study examined retinyl palmitate as an isolate exposed to UV radiation in MICE, 10 yr NON published study
- ▶ Repeat studies have failed to conclusively find a photocarcinogenic effect with combo of UV and retinoic acid

Nano particles/ ? Absorption

- ▶ Micronized Zinc and Titanium Oxide
- ▶ Concern is that nanoparticles interact with biomolecules penetrate cell walls and blood brain barrier
- ▶ Fact nanoparticle DO NOT penetrate living skin.....sunscreen applied to stratum corneum
 - ▶ <0.03% penetrated the stratum corneum
 - ▶ No particles detected in stratum corneum

Nanoparticles

- ▶ Must be 13nm to penetrate stratum corneum
- ▶ 2011 Study in Australia: ZnO nanoparticles rubbed on for 5 minutes and left on for 8 hours- no penetration was seen beneath the stratum corneum
- ▶ Zn absorbed as detected in blood and urine was smaller as compared to natural Zn normally present in the human body

Hormone Disruption?

- ▶ Oxybenzone/BP-3 -can penetrate the skin
- ▶ Reduced fecundity in Men
- ▶ Increase in male birth weight and decline in female birth weight and decrease male gestational age
- ▶ More studies needed
- ▶ BP3- found in cosmetic products, shampoos, lotions, hairsprays, nail polish, perfumes

Oxybenzone/Benzophenone 3

- ▶ Most common photoallergic contact dermatitis
- ▶ Environmental concerns of bleaching coral reefs
 - ▶ ? Role of warming ocean temps and pollutants
 - ▶ Banned: Hawaii, Key West, US Virgin Island, Aruba, Bonaire, and Palau

Advanced Technology

- ▶ Avobenzone not photostable-need to reapply 1.5-2hours
- ▶ Helioplex-photostable :avobenzone,oxybenzone,and diethylhexyl 2,6-naphthalate
- ▶ Ecamsule-photostable, water soluble effective against shorter UVA wavelengths (Mexoryl SX)

Skin Cancer Prevention

- ▶ SPF 30 or higher: reapply every 2 hours
- ▶ Avoid Sun Between 10am – 4pm
- ▶ Avoid Tanning Bed Use
- ▶ Sun Protective Clothing : UPF
 - ▶ Broad Rim Hats
 - ▶ Rash Guards
 - ▶ Sunglasses





Thank You!

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