



SKIN CANCER: THE RISK IS REAL

Cancer Risk and Prevention Symposium
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Disclosure



- I have no conflict of interest in relation to this program/presentation.

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OVERVIEW

- I. Skin cancer epidemic
- II. Skin Cancer
 - I. Basal Cell Carcinoma
 - II. Squamous Cell Carcinoma
 - III. Melanoma
- III. Skin Cancer Prevention
- IV. Skin Cancer Screening

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SKIN CANCER

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WHAT IS SKIN CANCER?

Unregulated and uncontrolled
growth of abnormal skin cells

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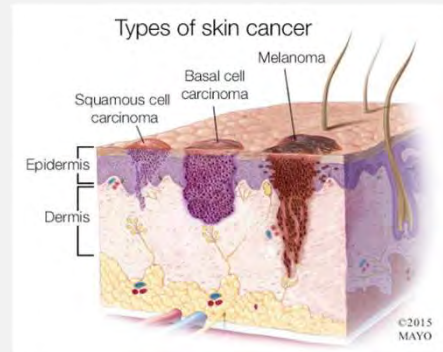
LIFETIME RISK OF SKIN CANCER:
1 IN 5

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SKIN CANCER OVERVIEW

- **Epidermal Carcinomas:**
 - Basal cell carcinoma
 - Squamous cell carcinoma
 - Merkel cell carcinoma
- **Melanoma:**
- **Adnexal Tumors:** Sebaceous carcinomas, Microcystic Adnexal Carcinomas
- **Sarcomas:** Dermatofibrosarcoma Protuberans, Atypical Fibroxanthoma, Undifferentiated Pleomorphic Sarcoma, Pleomorphic Dermal Sarcomas, Leiomyosarcoma

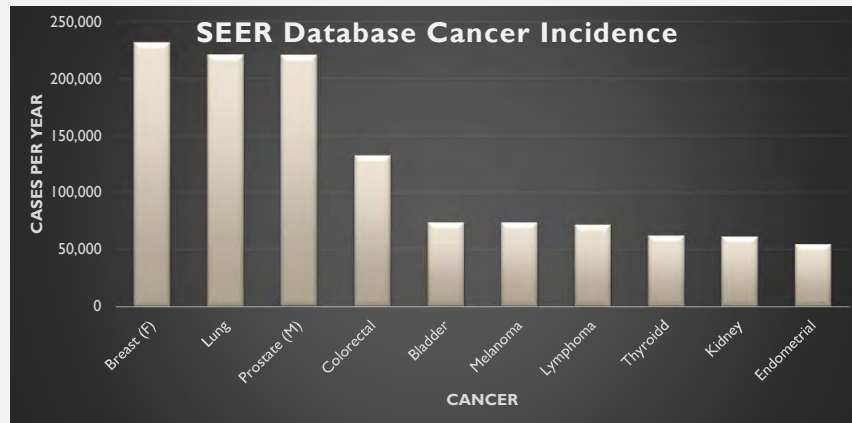
} Non-Melanoma Skin Cancer:
99% of skin cancers



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NMSC OVERVIEW

- Non-Melanoma Skin Cancer has become an **epidemic:**

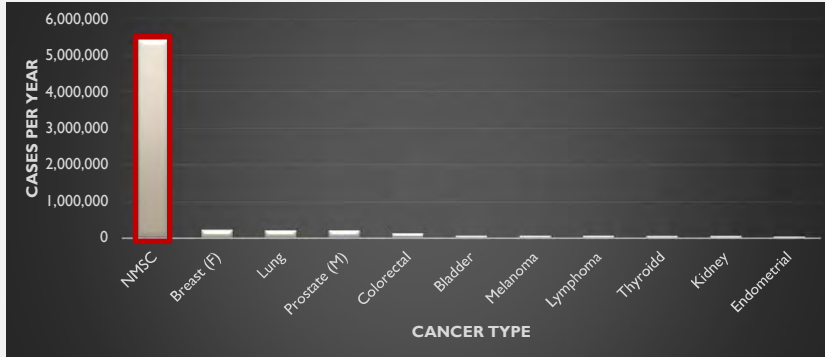


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NMSC OVERVIEW



- NMSC has become an **epidemic**:
 - Incidence – 1,200,000 (1994) → **5,434,193 (2012)**
 - Annual incidence **3-4 times greater** than all other types of cancer combined



JAMA Dermatol. 2015 Oct;151(10):1081-6. doi: 10.1001/jamadermatol.2015.1187.
 American Cancer Society. Cancer Facts & Figures 2013. Atlanta, GA: American Cancer Society; 2013.

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SKIN CANCER: MEDIA



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RISK FACTORS

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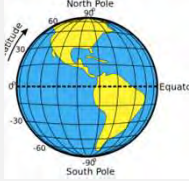
RISK FACTORS

Genetics

- Skin Type I, II
 - Light hair, light eyes, freckling
- Family Hx → 2x increased risk
 - Inherited mutations in CDKN2A, CDK4
 - BAP1
 - MCR1
- Number and Size of Nevi
- Atypical/Dysplastic Nevus Syndrome
- DNA repair defects (XP)
- Large Congenital Nevi
- Personal History of Melanoma

Environment

- **Ultraviolet Radiation**
 - Sunburns during Childhood
 - Intermittent intense UV exposure
 - Lifetime
 - Tanning Beds
- Latitudes
- High socioeconomic status (SES)
- Immunosuppression
- Environmental exposures (heavy metals, insecticides, hormones)

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SIGNS OF SKIN CANCER

- Non-healing sore
- Lesion that easily bleed
- Enlarging lesions
- Itching lesions



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BASAL CELL CARCINOMA

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BASAL CELL CARCINOMA

- **Most common** type of skin cancer
 - BCC:SCC 4:1
 - Male: Female 1.5:1
- Median Age of Diagnosis: 68 years
- Locally destructive, low risk of regional or distant metastasis
- **Association with other cancers:**
 - 20% of patients with frequent BCC (>6) had mutations in DNA repair genes
 - RR any cancer 3.5
 - RR increased for Melanoma (11.9), Colon (4.2), Ovarian (51.4)
- **Subtypes:**
 - Superficial
 - Nodular
 - Aggressive

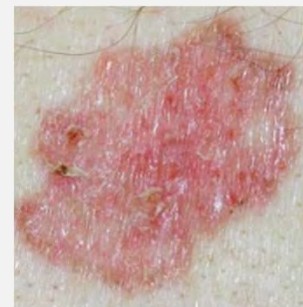
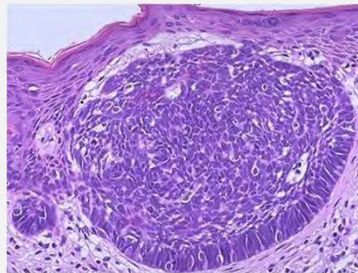


[JCI Insight](#). 2018 Aug 9;3(15). pii: 122744. doi: 10.1172/jci.insight.122744.

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SUPERFICIAL BCC

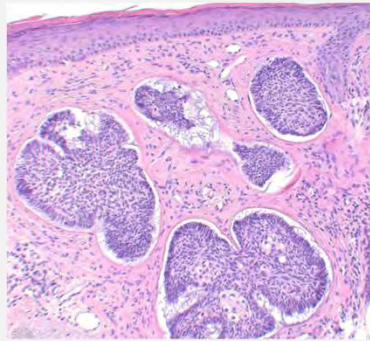
- **Clinical:**
 - Well demarcated erythematous macules or thin papules/plaques.
 - Most common trunk and extremities
- Mean age of diagnosis is 57
 - Most common subtype in younger patients
- Subclinical spread accounts for the **significant recurrence rate** in these tumors.



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NODULAR BCC

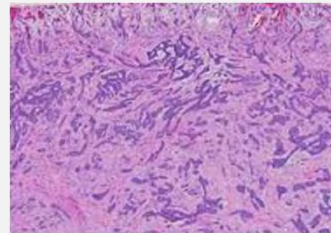
- **Clinical:**
 - Shiny, pearly papule or nodule.
 - Elevated border is clinical clue to diagnosis, can ulcerate
- Most common subtype, accounts for 50% of all BCC's



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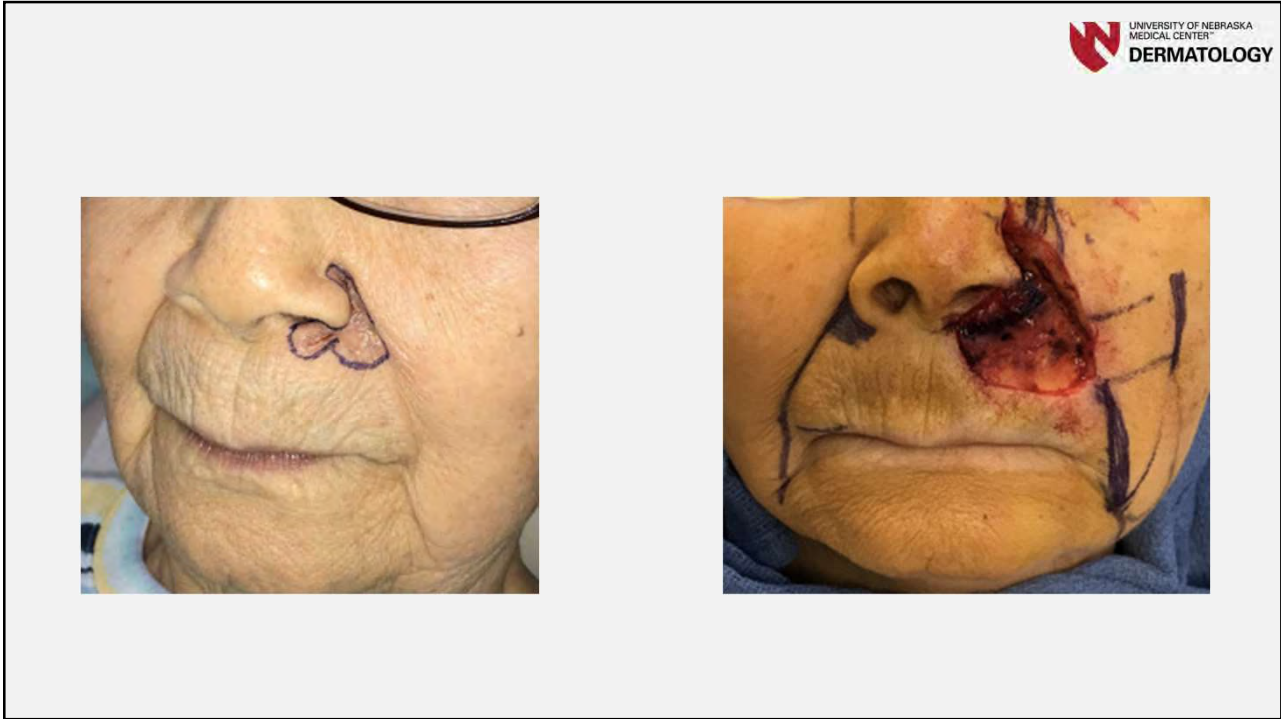
BCC: AGGRESSIVE SUBTYPES

- **Subtypes:** Morpheaform, Infiltrative, Micronodular, Basosquamous
- Higher risk to be **locally destructive** with aggressive clinical behavior
- Higher **recurrence rates**
- Positive surgical margins are common after excision with standard margins
 - Range from 15-33% positive margins after excision



[An Bras Dermatol.](#) 2015 May-Jun; 90(3): 377-383.

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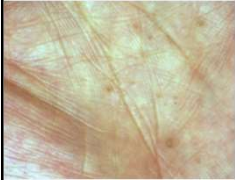


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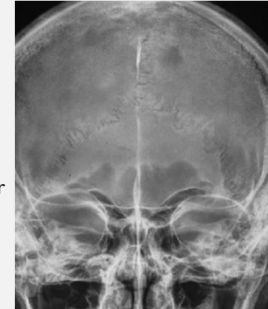


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BASAL CELL NEVUS SYNDROME



- Autosomal dominant inherited condition with majority of mutations in the PTCH Gene
- 1:40,000 – 30% of patients without a family history
- Associated with multiple BCCs, jaw cysts, pits on the palms/soles, calcium deposition in the brain, developmental disability and skeletal bony changes
- Screening:
 - Neurologic evaluation in infancy up to age 7 to eval for developmental disability or medulloblastoma
 - Measurement of head sizes
 - Yearly dental xrays
 - Annual skin exams



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CONCLUSIONS

- Basal cell carcinomas account for the majority of skin cancer
- ~40% of BCC's have more than one subtype
- Aggressive BCC's can have significant subclinical extension

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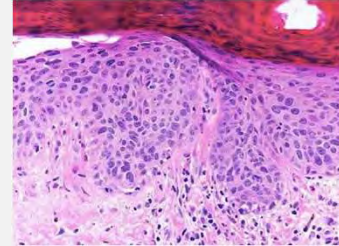
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DERMATOLOGY

SQUAMOUS CELL CARCINOMA

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ACTINIC KERATOSIS

- Dysplastic keratinocytes that are UV induced and act as precursor lesions to SCCis and SCC
- Temples and cheeks are most common location
- Risk of malignant transformation: range from 0.025-20%
- **Risk of progression in Veterans Affairs Population:**
 - SCC (invasive or in-situ):
 - 1 year: 0.6%
 - 4 years: 2.57%
 - BCC:
 - 1 year: .48%
 - 4 years: 1.56%



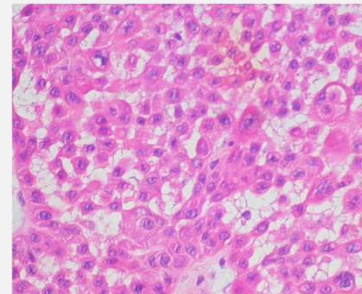
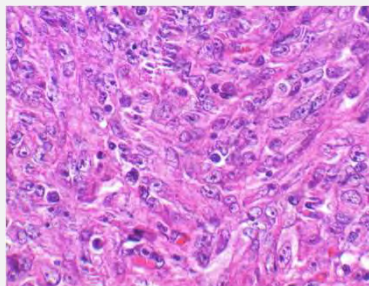
[Cancer](#). 2009 Jun 1;115(11):2523-30. doi: 10.1002/ncr.24284.

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SCC OVERVIEW

Subtypes:

- SCCis
- Well differentiated – KA Type
- Moderately Differentiated
- High Risk/Aggressive
 - Poorly Differentiated
 - Acantholytic



[Cancer](#). 2009 Jun 1;115(11):2523-30. doi: 10.1002/ncr.24284.

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NOT ALL SCC'S ARE CREATED EQUAL

- **More overall deaths** associated with SCC than Melanoma
 - Melanoma deaths: 9,320
 - **SCC: 15,000**
- **Risk of metastasis depends on risk factors:**
 - Patient characteristics
 - Tumor characteristics

<https://www.skincancer.org/skin-cancer-information/skin-cancer-facts#melanoma>

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PATIENT CHARACTERISTICS: HIGH RISK

- **HIV:** Immune dysfunction, impaired T-Cell immune surveillance
 - 2x Risk
- **Immune Modulating Medications:**
 - Use is on the rise
- **Solid Organ Transplant Patients:**
 - Over 34,000 transplants performed per year
 - Kidney > Liver > Heart > Lung > Pancreas > Intestine

[J Natl Cancer Inst. 2013 Mar 6;105\(5\):350-60. doi: 10.1093/jnci/djs529. Epub 2013 Jan 4.](#)

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MUIR TORRE

- Subtype of hereditary non-polyposis colorectal cancer (HNPCC) syndrome (Lynch syndrome)
- Affected individuals present with cutaneous manifestations at a mean age of 55
- Pathogenesis: Heterozygous germline mutation in DNA mismatch repair genes.
 - MSH2 (90%), MSH6 and MLH1
 - Somatic loss of heterozygosity (inactivation of non-mutated allele) results in microsatellite instability and tumor formation.

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MUIR TORRE



- Cutaneous findings:
 - Sebaceous tumors – sebaceous adenomas are most common type (>20 fold risk sebaceous carcinoma)
 - Immunohistochemical staining for MSH2, MSH6, MLH1 and PMS2 can be a valuable screening tool for MTS-associated tumors, which typically show a lack of expression of one or more of these proteins
 - Squamous cell carcinoma – present in 25%
- Associated Malignancy:
 - Colorectal (61%) – often involve the proximal colon and occurs at an average age of 50
 - Genitourinary (22%)
 - Breast (6%), hematologic (11%), head and neck (5%), small intestine (3%)

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MUIR TORRE

- Medical Monitoring:
 - Colonoscopies every 1-2 years starting at 20-25
 - Transvaginal US
 - Upper endoscopies every 3-5 years
 - UA annually starting at 30-35
 - Skin exams every 1-2 years

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CONCLUSION

- Genetic predisposition and cumulative UV exposure is greatest risk factor
- Actinic keratosis are precursors for squamous cell carcinoma
- Topical therapy can be considered for SCCis on low risk areas in immunocompetent patients

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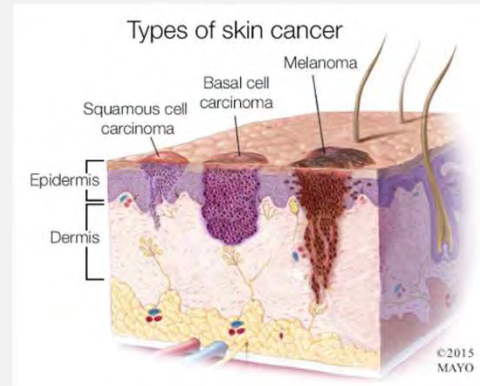
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MEDICAL CENTER
DERMATOLOGY

MELANOMA

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MELANOMA 2022

- 100,350 cases were diagnosed
- **7,650 people are expected to die**
- **Lifetime Risk:**
 - Caucasians: 2.6%
 - Hispanics: 0.6%
 - African Americans: 0.1%

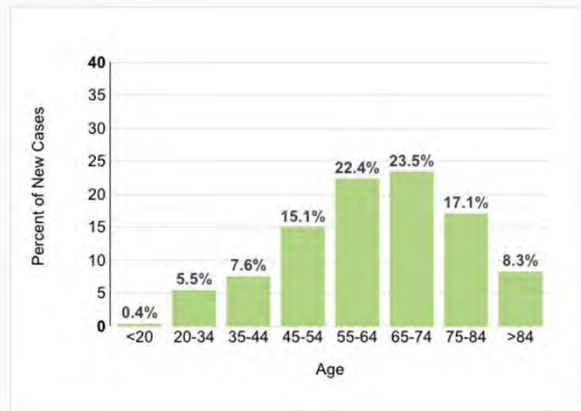


<https://www.cancer.org/cancer/melanoma-skin-cancer/about/key-statistics.html>

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WHO GETS MELANOMA

- **Melanoma accounts for:**
 - ~1% of all skin cancers
 - 1.5% of all cancer related deaths



Melanoma of the skin is most frequently diagnosed among people aged 65-74.

Median Age At Diagnosis
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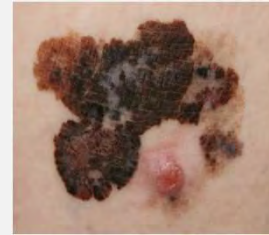
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MELANOMA



- **Superficial Spreading: 60-70%**

- Ages 40-60
- Locations:
 - Men – trunk
 - Women – legs
- Long radial growth phase



- **Nodular Melanoma: 15-30%**

- 6th decade of life
- Locations: trunk, head and neck
- Men > Women
- Associated with poorer prognosis



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MELANOMA



- **Lentigo Maligna: ~10%**

- Diagnosed later in life – 7th decade
- Chronically sun damaged areas
- Location: face, nose and cheek
- 5% progress to invasive melanoma



- **Acral Lentiginous Melanoma: ~5%**

- 7th decade
- Incidence is similar across all racial and ethnic groups
 - Disproportionate percentage of melanomas in blacks (70%) and Asians (45%)
- Often diagnosed at an advanced stage



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MELANOMA



- **Amelanotic Melanoma**

- All four subtypes can occur as “amelanotic” variants
- May be mistaken for BCC, warts or SCC



- **Childhood Melanoma**

- 2% of melanomas occur in patients younger than 20

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GENETIC TESTING



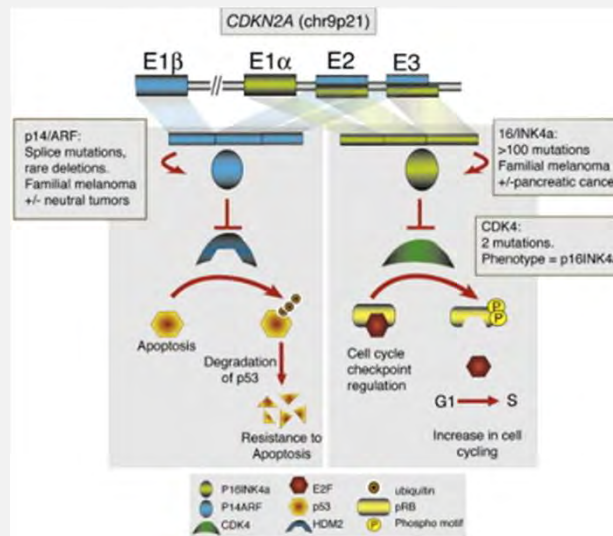
- **Complex decision** based on pedigree structure, cancer patterns, patient wishes, and perceived risks versus benefits.
- ~10% of melanomas are caused by an inherited gene mutation
- **Features of cancer predisposition include:**
 - Onset of disease < 40 years of age
 - Multiple cancers or cancer types
 - Multigenerational familial involvement
 - Aggregation of other rare malignancies



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TUMOR SYNDROMES

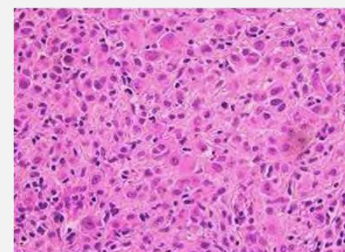
- **CDKN2a/PI6:**
 - Tumor suppressor gene located on 9p21 that codes for **p16** and **p14arf**
 - ~ 28% of carriers develop CM
 - Associated cancers: head and neck SCC, gastric lymphoma, pancreatic cancer and non-small cell lung cancer.



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TUMOR SYNDROMES

- **BAP1 (BRCA associated Protein 1):**
 - Tumor suppressor gene located on chromosome 3p21
 - 13% of carriers develop CM
 - Associated cancers: uveal melanoma, atypical spitz (BAP-oma), CM, renal cell carcinoma, mesothelioma



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GENETIC TESTING

30% chance of CDKN2a/P16 mutation

Table XX. Recommendations for genetic counseling of patients with CM

- Cancer risk counseling by a qualified genetic counselor is recommended for patients with CM who have
- A family history of invasive CM or pancreatic cancer (≥ 3 affected members on 1 side of the family)
 - Multiple primary invasive CM (≥ 3), including 1 early-onset tumor (at age < 45 y)
 - ≥ 1 MBAIT and a family history of mesothelioma, meningioma, and/or uveal melanoma
 - ≥ 2 MBAITs

[JAmAcad Dermatol.](#) 2018 Oct 29, pii: S0190-9622(18)32588-X. doi: 10.1016/j.jaad.2018.08.055. [Epub ahead of print]

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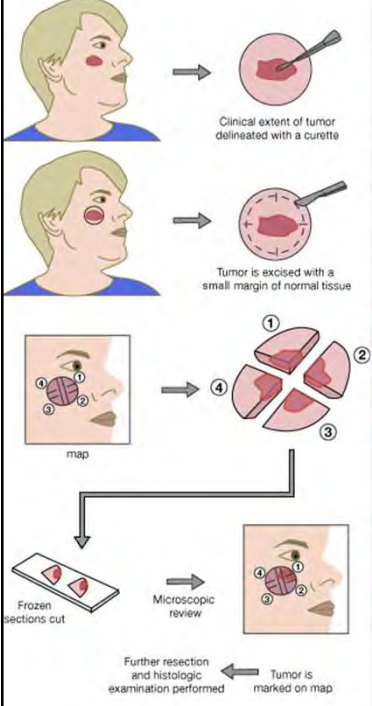
MANAGEMENT SKIN CANCER

- Electrodesiccation and curettage
 - Small and superficial lesions on trunk
 - Higher recurrence rates with no margin assessment
- Wide Local Excision (Standard Excision)
- Mohs Micrographic Surgery
- Radiation Therapy




Early Diagnosis and Effective Surgical Therapy Represents the Best Treatment for Skin Cancer

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MOHS MICROGRAPHIC SURGERY



- Specialized technique for excision of skin cancer with complete margin assessment (100% of tissue margin).
- Complete margin assessment allows for the tumor to be precisely mapped, which leads to **high cure rates and tissue conservation**

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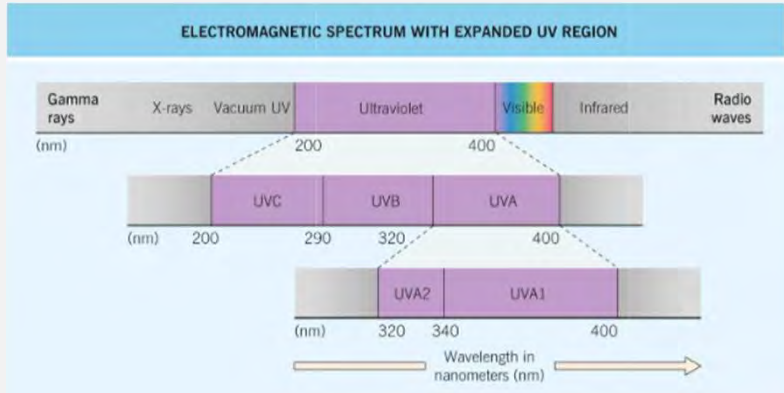
PROTECT YOUR

SEEK SHADE
Avoid Tanning Bed
UVA/UVB
HAT'S hats
PANTS CLOTHES
Sunglasses
check Spots ch
water-resist
HATS
SPF30 SP
Sunglasse
water-resist
sun protectio
SUNSCREEN
PANT!
water-resist
SPF 30
SUNSCREEN

Protecting yourself from skin cancer is easy. Make it a daily habit to seek shade, wear protective clothing and use sunscreen. Do not use tanning beds. To find a dermatologist, a free SPOTSM skin cancer screening, or to learn more about skin cancer detection and prevention, visit www.SpotSkinCancer.org.

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UV SPECTRUM



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SUN/UV FACTS

- **% UV Exposure By Age**

Ages	Average Accumulated Sun Exposure*
1-18	23 percent
19-40	47 percent
41-59	74 percent
60-78	100 percent

*Based on a 78-year life span

- **UVA is not blocked by glass**

- >50% penetrates glass

- UV Exposure:

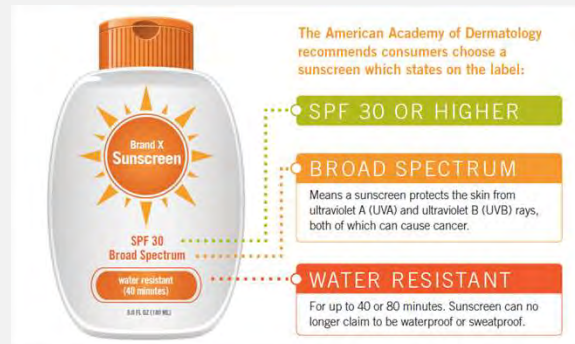
- **Clouds:** 80% of UV can pass through clouds
- **Umbrella:** UV beneath umbrella can be 84% that of the sun
- **Broad Brimmed Hats:** SPF ~5



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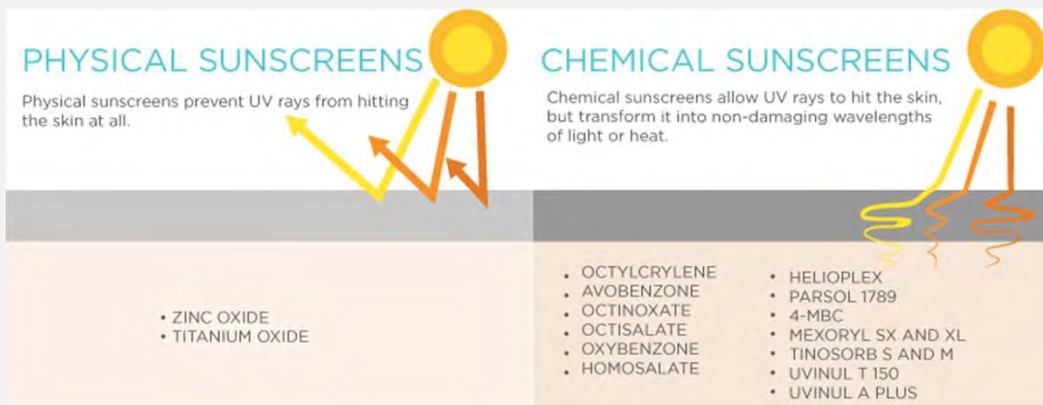
PRIMARY PREVENTION

- **Sun Avoidance:**
 - Avoid sun during peak hours of 10 am – 3 pm
 - Seek shade
- **Sun Protection:**
 - Broad spectrum sunscreen
 - SPF 30 or higher – 50+ is more effective
 - Sun protective clothing - UPF



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SUNBLOCK



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Sunscreen use and Melanoma Prevention

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SUNSCREEN AND PREVENTION



- Sunscreens have proven to lower risk for AKs, SCC and nevi
- Historic retrospective studies have not shown a clear direct benefit of using sunscreen to reduce risk of melanoma
 - Sunscreen used in historical studies lacked UVA protection
- Historically, data regarding the role of sunscreens in preventing melanoma has been controversial...

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SUNSCREEN AND MELANOMA THE VERDICT IS IN!

- A landmark study was published by Green et al. – the first **RCT** of 1621 adults in Australia followed > 10 years → 50% fewer melanomas in the daily sunscreen use group (and fewer invasive melanomas)
 - Intervention = broadspectrum SPF 16 applied to head, neck, arms, and hands daily + reapplication after heavy sweating, bathing, or long exposure
- Commentary in JAMA (Robinson & Bigby, July 2011) – **“this research has conclusively proven the value of sunscreen use in preventing melanoma and other skin cancers”**

[J Clin Oncol](#), 2011 Jan 20;29(3):257-63. doi: 10.1200/JCO.2010.28.7078. Epub 2010 Dec 6.

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SUNSCREEN AND MELANOMA THE VERDICT IS IN!

- In the Norwegian Women and Cancer Study, a prospective population-based study of 143,844 women age 40 to 75 years -- **SPF ≥ 15 sunscreen use was associated with significantly decreased melanoma risk compared with SPF < 15 use** (hazard ratio, **0.67**; 95% CI, 0.53 to 0.83). (JCO, 2016)

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MELANOMA AND SUN SCREEN: YOUNG ADULTS


- Risk of melanoma was **less with higher use of sunscreen** in childhood (OR 0.6) and across lifetime (0.65).
- **Protective association of sunscreen** with melanoma was stronger for people reporting blistering sunburns, receiving a diagnosis at a younger age or having some or many nevi
- Regular users of sunscreen were more likely to be **female and younger**

JAMA Dermatol. 2018;154(9):1001-1009. doi:10.1001/jamadermatol.2018.1774

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SUN SCREEN: HOT TOPICS

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Preliminary Communication ONLINE FIRST


May 6, 2019

Effect of Sunscreen Application Under Maximal Use Conditions on Plasma Concentration of Sunscreen Active Ingredients

A Randomized Clinical Trial

- a. Study involved 24 volunteers who applied a spray, lotion or cream to 75% of their body four times a day for four days in a row
- b. The amount used was equivalent to two standard bottles of sunscreen
- c. Blood samples taken from study participants looked at four chemicals – avobenzene, oxybenzone, ecamsule and octocrylene – and found that three exceeded the threshold set by the FDA for absorption into the bloodstream

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J Am Acad Dermatol. 2018 May;78(5):902-910.e2. doi: 10.1016/j.jaad.2017.12.062. Epub 2017 Dec 29.


SPF 100+ sunscreen is more protective against sunburn than SPF 50+ in actual use: Results of a randomized, double-blind, split-face, natural sunlight exposure clinical trial.

- Split faced, randomized, double blinded trial. Outcome was erythema one day after exposure.
- After 6.1 hours of exposure 55% of participants were more sunburned on the SPF 50+ side and 40.7% reported increased erythema
- **SPF 100+ sunscreen** was significantly **more** effective protecting against sunburn than **SPF 50+ sunscreen** in actual conditions.

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SUNBLOCK SAFETY



- 70% of sunscreens in the US contain oxybenzone
- *There have been no demonstrable harmful effects in humans*

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Research

Original Investigation

Trends in Sunscreen Recommendation Among US Physicians

Kristie L. Akamine, MD; Cheryl J. Gustafson, MD; Scott A. Davis, MA; Michelle M. Levender, MD; Steven R. Feldman, MD, PhD

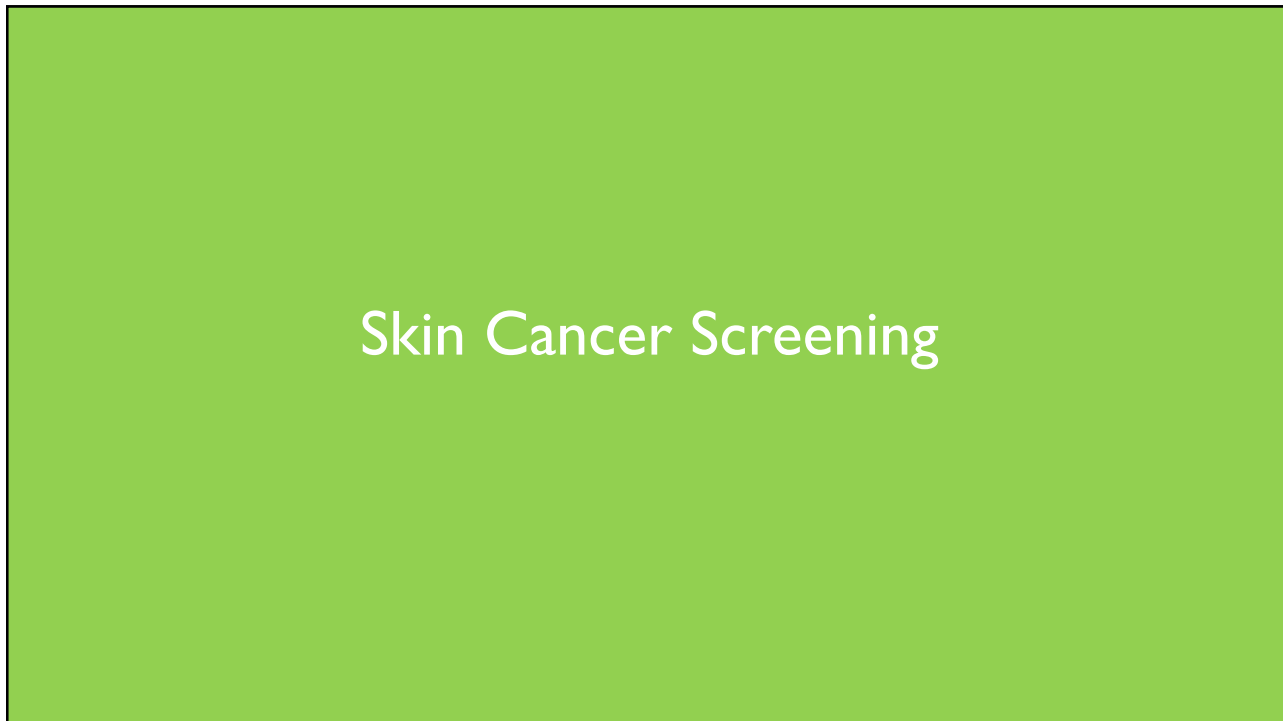
- National Ambulatory Medical Care Survey (NAMCS) found that **internists & pediatricians mentioned sunscreen at <0.1% of visits** (even those with a diagnosis of skin disease).
 - No differences despite active or remote history of skin cancer
- Despite the evidence and multiple health care organizations strongly recommending patient education on sunscreen and photoprotective behaviors – it is being mentioned at a very low % of patient visits.

JAMA Dermatology, Jan 2014; 150(1): 51-55.


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The ABCDEs of Melanoma

Melanoma is the deadliest form of skin cancer. However, when detected early, melanoma can be effectively treated. You can identify the warning signs of melanoma by looking for the following:

- A** stands for **ASYMMETRY**. One half of the spot is unlike the other half.
- B** stands for **BORDER**. The spot has an irregular, scalloped, or poorly defined border.
- C** stands for **COLOR**. The spot has varying colors from one area to the next, such as shades of tan, brown or black, or areas of white, red, or blue.
- D** stands for **DIAMETER**. While melanomas are usually greater than 6 mm, or about the size of a pencil eraser, when diagnosed, they can be smaller.
- E** stands for **EVOLVING**. The spot looks different from the rest or is changing in size, shape, or color.

Example:




Skin Cancer Self-Examination
How to Check Your Spots:

Performing a skin self-exam means taking note of all the spots on your body, from moles to freckles to age spots. Skin cancer can develop anywhere on the skin and is one of the few cancers you can usually see on your body. Ask someone for help when checking your skin, especially in hard-to-see places like the scalp and back. Follow these steps:

- 1 Examine your body front and back in a mirror, then look at the right and left sides with your arms raised.
- 2 Examine the back of your neck and scalp with a hand mirror. Part your hair for a closer look at your scalp.
- 3 Bend your elbows and look carefully at your forearms, underarms, and palms.
- 4 Check your back and buttocks with a hand mirror.
- 5 Finally, look at the backs of your legs and feet, the spaces between your toes, and the soles of your feet.

If you wear nail polish, remember to check your nails when the polish is removed.

If you notice a new spot or an existing spot that changes, itches, or bleeds, make an appointment to see a board-certified dermatologist.




Self Skin Exams (SSE)

- There is evidence that the practice of SSE is beneficial for high-risk individuals. Empirical cross-sectional studies have found that **patients and family members detected up to 50-80% of all melanomas.**
- In a study with 1062 melanoma patients (stages I - II), among those who experienced a melanoma recurrence (19%), **most recurrences were self-detected (55%) and led directly to seeking early medical advice**
- **Only a small proportion of patients with a history of melanoma perform whole body SSE regularly**

Published online 2020 Feb 14. doi: [10.1186/s12885-019-6476-5](https://doi.org/10.1186/s12885-019-6476-5)

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WHO SHOULD GET A SKIN CANCER SCREEN?



- The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of visual skin examination by a clinician to screen for skin cancer in adolescents and adults.
- **Personal History:** Melanoma, Skin Cancer, Immunocompromised
- **Family History:** melanoma
- **Physician Features:** Light skin, blonde or red hair, > 40 nevi, two or more atypical nevi, freckles, severely sun-damaged skin
- **UVR Overexposure:** history of blistering sunburns, history of indoor tanning

Melanoma Manag. 2017 Mar; 4(1): 13-37.

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How do dermatologists become board-certified?


- ✓ Graduate medical school.
- ✓ Finish an internship and a dermatology residency program.
- ✓ Complete 12,000 – 16,000 patient care hours.
- ✓ Obtain a license to practice medicine.
- ✓ Pass the exams given by the American Board of Dermatology, the American Osteopathic Board of Dermatology, or the Royal College of Physicians and Surgeons of Canada.

Skin Exam with Board Certified Dermatologist

- A total 1563 biopsy-proven cutaneous malignancies were found on 1010 patients. Of these, 797 cancers (51%) were first identified by a dermatologist on TBSE and 764 (48.9%) by the patient or the referring provider.
- For melanomas, the mean Breslow depth was 0.53 mm (standard deviation: 0.31 mm) for melanomas found on TBSE versus 1.04 mm (standard deviation: 1.68 mm) if identified by patients or referring providers.

[Int J Womens Dermatol. 2021 Sep; 7\(4\): 411–414.](#)

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CONCLUSION

- The incidence of non-melanoma skin cancer **continues to grow**
- Metastasis is very rare with basal cell carcinoma, however, these tumors can become locally destructive
- Squamous cell carcinoma is a heterogeneous group of cancers and can behave aggressively
- Early Diagnosis and Effective Surgical Therapy Represents the Best Treatment for Skin Cancer

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