SKIN CANCER: THE EPIDEMIC

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Disclosure

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

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

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WHAT DO THESE INDIVIDUALS HAVE IN COMMON?
SKIN CANCER

WHAT IS SKIN CANCER?

Unregulated and uncontrolled growth of abnormal skin cells
LIFETIME RISK OF SKIN CANCER: 1 IN 5

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
NMSC OVERVIEW

- Non-Melanoma Skin Cancer has become an epidemic:

  - Incidence – 1,200,000 (1994) \(\rightarrow\) 5,434,193 (2012)
  - Annual incidence 3-4 times greater than all other types of cancer combined

ECONOMIC BURDEN

- Costs are increasing:
  - Annually 5 million individuals treated
  - Annual cost $8.1 billion

Cost of skin cancer treatment in the US


SKIN CANCER: MEDIA
After decades of tanning, freckle on woman’s nose turns out to be skin cancer
Lisa Ryan thought that because she rarely burned she was immune from developing skin cancer.

Woman, 24, thought spot under eye was a pimple – it turned out to be skin cancer
Dr. Jon Miller encourages others to use sunscreen, sunglasses and hats to protect every inch of their skin.

RISK FACTORS
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
- 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)

SIGNS OF SKIN CANCER

- Non-healing sore
- Lesion that easily bleed
- Enlarging lesions
- Itching lesions
Diagnosis: Biopsy Techniques

Biopsy for initial diagnosis is critical for determining appropriate treatment.

- Punch Biopsy
- Shave Biopsy
- Excisional Biopsy

BASAL CELL CARCINOMA
**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

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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.
**SUPERFICIAL BCC**

- **Imiquimod is an immune response modifier:**
  - Activates TLR-7 and stimulates the innate and acquired immune system, ultimately leading to inflammation within the field of the drug.
  
  - Can develop flu-like symptoms with treatment
  
  - **Applied once daily for five days a week for six weeks total**
    - Tumor free survival at 5 years was ~80%
  
  

- **43% of BCCs have mixed histology on definitive excision**
  - 10% of these were initially diagnosed on original biopsy
  - Initial biopsy may not detect an aggressive growth pattern
  - >90% of mixed histology BCC's occur on the head and neck, with the nose the most common location
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

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

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

SQUAMOUS CELL CARCINOMA
ACTINIC KERATOSIS

- Dysplastic keratinocytes that are UV induced and act as precursor lesions to SCCs and SCC
- Temples and cheeks are most common location
- Risk of malignant transformation: range from 0.025-20%

- Risk of progression in Veterans Affair Population:
  - SCC (invasive or in-situ):
    - 1 year: 0.6%
    - 4 years: 2.57%
  - BCC:
    - 1 year: .48%
    - 4 years: 1.56%

*Pathogenesis*

- UVB (290-320) is principally responsible for mutations.
- UV exposure generates thymidine dimers in p53 tumor suppressor.
  - UVB signature mutations such as CC→TT and C→T transitions
SCC OVERVIEW

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


SQUAMOUS CELL CARCINOMA IN SITU

- Commonly referred to as Bowen’s Disease
- Erythroplasia of Querat when the male genital area is affected
- HPV is implicated in pathogenesis of anogenital SCC's:
  - High Risk Subtypes (16, 18, 31, 33, 45)
  - E6 and E7 more active in high risk, degrade p53 and interact with RB
5-FLUOROURACIL

- **Mechanism:** Thymidylate synthase inhibitor, blocking synthesis of the pyrimidine thymidine.

- **Treatment recommendations:** Twice daily for up to 8 weeks

- All studies involve **50 patients or fewer**:
  - 69% complete clearance after 4 weeks of treatment
  - 17 and 21% recurrence at 1 and 2 years respectively

*Takeaway:* Can be considered in appropriate immunocompetent patients in low risk locations.

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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](https://www.skincancer.org/skin-cancer-information/skin-cancer-facts/melanoma)
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

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SOTR: SPECIAL CONSIDERATIONS

- **Skin cancers represent 95% of cancers in organ transplant recipients**

- Risk of BCC is **10x greater**
- Risk of SCC is **65-100x greater**
- Melanoma risk is **3x greater**, Kaposi Sarcoma is **84x greater**
- Skin cancers are associated with higher morbidity and mortality

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CONCLUSION

• Genetic predisposition and cumulative UV exposure are greatest risk factors
• Actinic keratosis are precursors for squamous cell carcinoma
• Topical therapy can be considered for SCCs on low risk areas in immunocompetent patients
MANAGEMENT SKIN CANCER

- Electrodessication 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*

MOHS SURGERY

- Mohs surgery was developed by Dr. Fred Mohs at the University of Wisconsin in the 1930's
- Initially developed to treat melanomas
- In-vivo tissue fixation with zinc chloride was used until the 1970's
- The fresh frozen tissue technique is currently the standard
- Currently there are ~50 1-2 year fellowships in the US
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.

MOHS SURGERY MAP

Referring Provider: ________________________________

Type of Tumor: ________________________________

Location: ________________________________

LN: ________________________________

Recurrence? Yes No

Prior treatment:

- WLE
- Mohs
- LN2
- Radiation
- ED&C
- Other

Immunosuppression? Yes No

Pathology Accession #:

Pre-op Size: ________________________________

Final Defect Size: ________________________________

Repair Type: linear / flap / graft / delayed

Repair Length/Area: ________________________________

Sutures:

- Vicryl
- Monocryl
- 3-0
- 4-0
- 5-0
- 6-0
- Nylon
- Prolene
- Gut
- Silk
- 3-0
- 4-0
- 5-0
- 6-0

Mohs Layers

Specimen received: ________________________________

Time: ________________________________

Stage I II III IV V

- Invasion beyond subcutaneous fat

# Sections

- Perineural invasion

# Slides

- Lymphovascular invasion

Stains

- H&E
- T Blue
- Other: ________________________________

SCC:

- well
- mod
- poor
- acantholytic
STANDARD EXCISION VS. MOHS

<1% of margin examined

100% of margin examined

OUTPATIENT SETTING
MOHS CURE RATES

• Basal Cell Carcinoma: ~99%
• Squamous Cell Carcinoma: 97%
• Recurrent BCC/SCC: ~95%
MELANOMA

• 91,270 cases will be diagnosed this year

• 9,320 people are expected to die

• Lifetime Risk:
  • Caucasians: 2.6%
  • Hispanics: 0.58%
  • African Americans: 0.1%

https://www.cancer.org/cancer/melanoma-skin-cancer/about/key-statistics.html
WHO GETS MELANOMA

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

MELANOMA

- Incidence of melanoma is **increasing**: 1 in 54 in 2016
  - 1 in 58 in 2009
EN-BLOC EXCISION
26 transected melanomas (500 cases reviewed)
- 15 of 26 (58%) melanomas had residual tumor in the excision specimen
- 8 of 26 (31%) had greater breslow depth at excision, but tumor staging change in only 3 (12%)

**Conclusion:** Punch and excision biopsy techniques were more likely to transect tumors than excisional biopsies. The transection of melanoma did not affect overall disease-free survival or mortality in the population studied. (J Am Acad Dermatol 2013;68:452-8.)
UV SPECTRUM

[Diagram showing the electromagnetic spectrum with an expanded UV region, indicating UVC, UVB, and UVA wavelengths.]
ULTRAVIOLET AT THE EARTH’S SURFACE

- **UVB (290-320nm)**
  - 5% of total UV at surface
  - Blocked by glass
  - Effects on skin
    - Burning
    - Tanning
    - SCC
    - Aging

- **UVA (320-400)**
  - 95% of total UV at surface
  - Penetrates glass
  - Effects on skin
    - Tanning
    - Photoaging

- **UVC (200-290nm)**
  - <1% of total UV at surface
  - Blocked by ozone

SUN/UV FACTS

- % UV Exposure By Age
- 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
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

SUNBLOCK

Physical sunscreens prevent UV rays from hitting the skin at all.

Chemical sunscreens allow UV rays to hit the skin but transform it into non-damaging wavelengths of light or heat.

- Zinc Oxide
- Titanium Oxide
- Octylcrylone
- Avobenzone
- Octinoxate
- Octisalate
- Oxybenzone
- Homosalate
- Homosalate
- HEIOPLEX
- PAROX 1789
- 4-MBC
- MEOMYL S AND XL
- UVINUL T 150
- UVINUL A PLUS
SUN PROTECTION FACTOR

- Sun Protection Factor (SPF)
  - Measured with sunscreen applied at 2 mg/cm²

- SPF = MED Protected/MED Unprotected
  - Minimal Erythema Dose
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—avobenzone, oxybenzone, ecamsule and octocrylene—and found that three exceeded the threshold set by the FDA for absorption into the bloodstream

- 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.**
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.

CONCLUSION

- The incidence of melanoma and 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.
KEEP CALM AND STAY SAFE IN THE SUN

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