An Overview of Melanoma

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Melanoma Statistics

- Median age at presentation – 45-55 years
- Incidence: 2003 – 54,200 cases
- 2008 (projected) - 62,480
  - 6th among men
  - 7th among women
- Increasing in incidence in men and women
- 1 in 17 white Australian males
Melanoma tumor formation

- Normal Melanocytes
- Dysplastic Nevi
- Early Primary Radial Growth Phase
- Advanced Primary Vertical Growth Phase
- Metastatic Melanoma

**Normal**
- **Benign/premalignant**
- **Malignant / Locally Invasive**
- **Metastasis**

**Gene Regulation in Melanoma Progression by the AP-2 Transcription Factor**

- p16
- Integrins
- p53
- c-kit↓
- E-cadherin↓
- N-cadherin↑
- MUC18/MCAM↑
- CREB/ATF-1↑

Angiogenesis, Invasion & Apoptosis:
- e.g., bFGF, IL-8, MMP-2, EGF-R, PAR-1, FAS/APO-1
Risk Factors for Melanoma

- Genetics & Environment
  - Race (Caucasians 5-20 fold increased risk over Africans, East Asians, Hispanics)
  - Geographic location (proximity to equator)

- Genetic Factors & Risk
  - Skin pigmentation and propensity for sunburn
  - Family history of melanoma
  - Density and type of nevi (common, ‘atypical’)
  - Genetic mutations: p16, CDK4

- Environmental Factors
  - Recreational and occupational sun exposure
  - Ozone depletion
ABCDE of diagnosis

- A: Assymetry
- B: Border irregularity
- C: Color - unusual or changing
- D: Diameter > 6mm
- E: Evolution or Elevation
- F: Funny looking
Changing or new moles
Variation in color
Irregular borders
The Pigmented Cell/Melanocyte

- Neural crest origin in embryonal life
- Function: synthesis, storage, and transfer of melanin (pigment) to surrounding cells
- Melanoma occurs anywhere melanocytes are found
Melanoma subtypes

- **Superficial spreading**: most common form, often arise in preexisting moles, mostly on the extremities, bleed, more common in women
Nodular melanoma

- 15% of melanomas
- dome shaped
- uniform color, like blood blisters
- Younger patients
- usually no prior mole in that area
Acral lentiginous melanoma

- palms, soles, nailbeds
- Often thick and wide
- Males > females
- Most common type in blacks and hispanics
Lentigo Maligna Melanoma

- 5-10% of melanomas
- Often on face and neck
- More common in the “elderly” (Median age 62)
- Females > Males
- flat, grow very fast, rarely metastasize to internal organs
Desmoplastic melanomas

- rare
- Often in “elderly” (6$^{th}$ or 7$^{th}$ decade)
- Often amelanotic (without pigment)
- Tend to grow on nerves
Non-cutaneous Melanoma (rare)

- Ocular melanoma, mostly choroid and ciliary body
- Mucosal melanoma: Head and neck
  - Vulva and vagina
  - Anal
  - Female urethra
  - Esophagus
Multi-disciplinary therapeutic approach to melanoma

Dermatologist or Primary Care Physician → Dermatopathology

Dermatopathology → Plastic or dermatologic surgery

Radiology → Pathology

Pathology → Medical Oncology

Medical Oncology → Radiation oncologist (for palliation)
Therapeutic approach to melanoma

- Initial diagnosis by dermatologist or primary care doctor
- Vast majority present with resectable primary skin melanoma and majority are cured by resection alone
- Relatively few have lymph node disease at the time of diagnosis
- Metastases detected months to many years later
- Patients can develop metastatic disease in almost any site, treated with surgery when resectable or “systemic therapy” (by mouth or IV)
- High propensity for brain metastases, which require radiation therapy
Clinical Staging of Melanoma to Assess the Prognosis

- Depth of primary lesion
- Microscopic ulceration of primary lesion
- Regional lymph node involvement
- Presence or absence of in-transit metastases
- Presence or absence of distant metastases (in other organs)
Relationship between Stage of Melanoma and Survival

Other important predictors of survival

- Location of the melanoma (Trunk vs. extremity)
- Age
- Sex
- Most important prognostic markers – depth of skin lesion, lymph node involvement and presence of ulceration
Topics to be covered – patient care

- Risk factors, sun exposure and prevention (Dr. Leffell, Dermatology)
- Skin cancer screening and diagnosis of melanoma (Dr. Bolognia, Dermatology)
Surgical resection (Dr. Ariyan)
Drug treatments for prevention of treatment of metastatic disease (Dr. Sznol)
Our other mission - research to improve outcome

- Target populations:
  a) patients at high risk for metastatic disease (understand what makes some melanomas metastasize)
  b) Patients with metastatic disease - develop novel drugs that attack the melanoma cells or enhance the immune system to attack those cells

- Dr. Halaban
- Dr. Sznol