What is the most common cancer in people aged 25-29 years?

MELANOMA
3-5% of skin cancers, 65% of deaths
Melanocyte

- Originates from neural crest cells in the basal layer of epithelium
- All races have same density of melanocytes – difference is in production of melanin

Rigel, Cancer of the Skin, 1st edition.
• What are some risk factors for melanoma?

• Family history
• Prior melanoma
• Blistering sunburn/skin that sunburns easily
• Chronic sun exposure
• Multiple atypical moles/dysplastic nevi
• Inherited syndromes
  – Xeroderma pigmentosa
  – Wiskott-Aldrich syndrome
  – Familial BK mole syndrome
Asymmetry
irregular Border
variegated Color
>6mm Diameter
Superficial spreading – most common (70%)

Acral lentiginous – palms and soles, most common melanoma in blacks

Lentigo maligna – superficial, better prognosis

Nodular – no radial growth phase, poor prognosis 2/2 depth

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MCE – Friday afternoon

29F with suspicious lesion on right arm, biopsied by PCP, c/w malignant melanoma, depth 1.2mm.

On exam, skin lesion right upper arm w/ biopsy scar, no other lesions nearby, no palpable axillary lymph nodes.

1. Wide local excision
2. Sentinel lymph node evaluation
Wide local excision (WLE)

- Depth – muscle fascia
- Incorporate biopsy site
- Goal margin:

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<th>Thickness</th>
<th>Margin</th>
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<tbody>
<tr>
<td>In situ</td>
<td>0.5-1 cm</td>
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<tr>
<td>&lt;1 mm</td>
<td>1 cm</td>
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<td>1-2 mm</td>
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<td>2-4 mm</td>
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<td>&gt;4 mm</td>
<td>2 cm</td>
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Sentinel lymph node biopsy

- Preoperative lymphoscintigraphy
  - Technetium-labeled sulfur colloid, intradermal
- Intraoperative injection of vital blue dye
- Localize with gamma probe
- Remove all sentinel nodes
- If grossly metastatic nodes
  - Frozen section
  - Complete lymph node dissection if frozen is positive
Regional Lymphadenectomy

• One third of patients with macroscopic nodal disease are cured with regional lymphadenectomy
  + cervical nodes $\rightarrow$ modified radical neck dissection +/- superficial parotidectomy
  + axilla $\rightarrow$ remove all three levels
  + groin $\rightarrow$ inguinofemoral (superfical) node dissection
Staging

- **N Stage**
  - N1=one node
  - N2=two-three nodes
  - N3=four or more nodes or in-transit/satellite mets

- **M1** = any distant met

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<th>T Stage</th>
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<tr>
<td>1</td>
<td>≤ 1mm</td>
<td>a: no ulceration</td>
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<tr>
<td>2</td>
<td>1-2 mm</td>
<td>b: + ulceration</td>
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<tr>
<td>3</td>
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T Stage Thickness:
- 1 ≤ 1mm
- 2 1-2 mm
- 3 2-4 mm
- 4 >4 mm

a: no ulceration
b: + ulceration
Clark Level

Epidermis
Papillary dermis
Reticular dermis
Subcutaneous tissue

1. Epidermis
2. Papillary dermis
3. Reticular dermis
4. Subcutaneous tissue

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Poor Prognostic Factors

- Thickness
- Higher Clark level
- Ulceration
- High mitotic rate
- Age >60 years
- Truncal lesions
- Male gender
- Metastases
- Increased number of positive lymph nodes
- Elevated lactate dehydrogenase
Locoregional Recurrence

- 70-80% of regional recurrences occur within 3 years of initial resection
- Satellite lesions = within 2 cm of primary melanoma
- In transit metastases = >2 cm from primary lesion between primary site and regional nodes
- Treatment
  - Evaluate for distant foci of disease
  - Surgery to obtain negative margins
  - Regional therapy:
    - Hyperthermic limb perfusion
    - Isolated limb infusion
    - Intraliesional injection w/ BCG, dinitrochlorobenzene, interferon, or granulocyte-macrophage colony stimulating factor (GM-CSF)
    - Radiation
  - Systemic chemotherapy/immunotherapy
Metastatic Disease

• Median survival (Stage IV) 7-8 months
  – 5-year survival 5-6%
• Lung, skin, lymph nodes, brain, liver, bone, gastrointestinal tract
• 90% initially have only one site involved with metastatic disease
  → surgery recommended for isolated mets if patient is an operative candidate
Treatment of Metastatic Disease

- Surgery for single site involvement
- Chemotherapy – dacarbazine (15-30% response rate)
- Immunotherapy
- Molecularly targeted therapy
Immunotherapy

• IL-2 $\rightarrow$ 15% response
• Interferon $\alpha_2$b $\rightarrow$ 10-15% response
• Monoclonal antibodies against T-cell and melanoma cell surface antigens – Ipilimumab (Yervoy) $\rightarrow$ 30% response
• Adoptive cell transfer
• Melanoma vaccines

Bologna: Dermatology, 2nd edition
Sabiston Textbook of Surgery, 18th edition
Molecularly Targeted Therapy

• Vemurafenib – enzymatic inhibitor of BRAF (protein kinase involved in RAF/MEK/ERK cell signaling pathway)
  – 60% of pts have mutation in BRAF
  – BRIM3 trial (phase III) vs. dacarbazine
    • Death ↓63%
    • Disease progression ↓74%

• Antiangiogenesis agents (eg. bevacizumab)

Study Questions
When performing a sentinel lymph node biopsy in the axilla, you locate a node that is blue and hot. Your next step is:

- Close up and go home
- Examine the area for additional positive nodes
- Send the node for frozen section
- Proceed with three level axillary node dissection
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75% of recurrences will occur within what time interval after primary excision of a melanoma skin lesion?

• 3 months
• 1 year
• 3 years
• 5 years
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Patient presents 5 months after wide excision of a skin lesion on his right lower extremity (sentinel lymph nodes negative) with this finding. Which of the following would not be an appropriate next step?

- Shave biopsy of one of the lesions
- Consult medical oncology to initiate systemic therapy
- CT head, chest, abdomen, pelvis
- Wide excision with radical groin dissection
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50F otherwise healthy with h/o vulvar melanoma s/p radical vulvectomy and bilateral groin node dissections presents with crampy abdominal pain, nausea, vomiting, and dehydration. You obtain the following CT scan. What is your next step?

- Medical oncology consult for systemic therapy
- Resection of lesion, inspection for other intra-abdominal metastases
- Referral to hospice
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A New Era Approaches: Anti-CTLA-4 Monoclonal Antibodies for the Treatment of Malignant Melanoma

- Jeffrey S. Weber, MD, PhD