SUN, SURF AND MELANOMA
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Melanoma—what is it?
- Most aggressive and life-threatening of cutaneous malignancies
- Develops from melanocytes.
- Adults and elderly patients.
- 2400 year old Peruvian mummies showed signs of melanoma.
- 1795 John Hunter was the first reported surgeon to operate on metastatic melanoma.

Melanoma—history
- René Laennec - 1804.
- William Norris - 1820.
- Samuel Cooper – 1840.

MELANOCYTES
- Synthesis and release of melanin.
- Derived from neural crest cells.
- Basal layer and hair follicles.
- Round cells with pale staining cytoplasm amongst basal cells.
Incidence

- Australia has the highest incidence of melanoma in the world, 4 times higher than in Canada, the US and the UK.
- Fourth most common cancer in Australia, nearly 10,000 new cases diagnosed each year.
- 2100 people diagnosed annually in Victoria.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Percentage of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>8.7</td>
</tr>
<tr>
<td>35-54</td>
<td>29.5</td>
</tr>
<tr>
<td>55-74</td>
<td>39.7</td>
</tr>
<tr>
<td>&gt;75</td>
<td>22</td>
</tr>
</tbody>
</table>

Incidence

- 1:19 lifetime risk by age 85.
- 15-44 year age group, melanoma and breast are most common cancers.
- Highest risk in Queensland and Western Australia.
- Australian adolescents have the highest rate of melanoma in the world, compared with adolescents in other countries.

Melanoma incidence in men

- Third most common cancer after bowel and prostate cancer, 5335 new cases P/A
- 1:15 lifetime risk by age 85
- Incidence increased by 19% between 1993 and 2003.

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<tbody>
<tr>
<td>&lt;35</td>
<td>6.7</td>
</tr>
<tr>
<td>35-54</td>
<td>26.6</td>
</tr>
<tr>
<td>55-74</td>
<td>43.1</td>
</tr>
<tr>
<td>&gt;75</td>
<td>23.6</td>
</tr>
</tbody>
</table>

Melanoma incidence in women

- Third most common cancer after breast and bowel cancer, 3989 new cases P/A.
- 1:25 lifetime risk by age 85
- Incidence increased by 6.8% between 1993 and 2003.

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<th>Age (years)</th>
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</tr>
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<tbody>
<tr>
<td>&lt;35</td>
<td>11.6</td>
</tr>
<tr>
<td>35-54</td>
<td>33.6</td>
</tr>
<tr>
<td>55-74</td>
<td>35</td>
</tr>
<tr>
<td>&gt;75</td>
<td>19.8</td>
</tr>
</tbody>
</table>
Death and Survival Rates

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths from melanoma per year</td>
<td>&gt;1270</td>
<td>862</td>
<td>411</td>
</tr>
<tr>
<td>5 year survival rate</td>
<td>-</td>
<td>90%</td>
<td>99%</td>
</tr>
</tbody>
</table>

• Survival rates have risen significantly since the 1980’s due to early detection.

• The estimated cost of treating melanoma during 2001-2002 was $AUS30 million.

Risk factors

• AGE
  - 70 year old man is 8 times more likely to develop melanoma than a 30 year old man (5.5%).
  - 70 year old woman 3 times more likely than one 30 years old (1%)

Genetic components

• Skin type
• Number of naevi (moles)
• Clinically atypical naevi
• Family history of melanoma

Genetic components

<table>
<thead>
<tr>
<th>Skin Type</th>
<th>Typical Features</th>
<th>Tanning ability</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Pale, white skin, blue/hazel eyes, blonde/red hair</td>
<td>Always burns, does not tan.</td>
</tr>
<tr>
<td>II</td>
<td>Fair skin, blue eyes</td>
<td>Burns easily, tans poorly.</td>
</tr>
<tr>
<td>III</td>
<td>Darker white skin</td>
<td>Tans after initial burn.</td>
</tr>
<tr>
<td>IV</td>
<td>Light brown skin</td>
<td>Burns minimally, tans easily.</td>
</tr>
<tr>
<td>V</td>
<td>Brown skin</td>
<td>Rarely burns, tans darkly easily.</td>
</tr>
<tr>
<td>VI</td>
<td>Dark brown or black skin</td>
<td>Never burns, always tans darkly.</td>
</tr>
</tbody>
</table>
Melanoma

Out of ~52,000 cases (~26,000 skins) 237 melanomas diagnosed from January to June 2011.

2006 – 6051 males; 4275 females diagnosed (10,326).
2008 – 965 males; 472 females died (1437).

Beach related hazards

<table>
<thead>
<tr>
<th></th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crocodile</td>
<td>1 per year</td>
</tr>
<tr>
<td>Shark</td>
<td>24 in the past 20 years</td>
</tr>
<tr>
<td>Stone fish</td>
<td>0</td>
</tr>
<tr>
<td>Cone snails</td>
<td>1 in 1935</td>
</tr>
<tr>
<td>Sting-rays</td>
<td>3 deaths since 1945</td>
</tr>
<tr>
<td>Blue-ringed octopus</td>
<td>2 recorded</td>
</tr>
<tr>
<td>Box jelly fish</td>
<td>60 in the past 100 years (Irukandi 3 in past 20 years)</td>
</tr>
<tr>
<td>Drowning</td>
<td>82 coastal drownings in 2009-2010</td>
</tr>
<tr>
<td>Melanoma</td>
<td>2008 - 1437</td>
</tr>
<tr>
<td>(Road Toll)</td>
<td>2008 – 1463, lowest in 5 years</td>
</tr>
</tbody>
</table>

Environmental-sun exposure

- Intermittent exposure to ultraviolet radiation (UVR) during childhood.
- Types I and II skin.
- Genetic predisposition.
- Compromised immunity.
- Proximity to equator.
- Depletion of the ozone layer.

Sun exposure

- Dose.
- Intermittent vs chronic.
- Critical time periods.
- Site of primary and type of exposure.
- Head and neck - chronic
- Trunk-melanocytic naevi which proliferate due to sun exposure.
Sun exposure

- Agricultural chemicals and high cumulative UVR-acral melanoma.
- Occupational sun exposure- ocular melanoma

Geographical

- Nature of the population.
- Caucasian vs African or Asian.
- Migrant studies in Australia and New Zealand.
  - Mortality rates of native Australians and New Zealanders
  - Mortality rates of recent British immigrants.

Socio-economic factors

- Before the Industrial Revolution, pale skin was a sign of wealth.
- After 1850’s working class moved indoors.
- 1900’s - sun-exposure for health!
- 1950’s - holidays to sunny destinations.

Tanning

- Exposure to solar radiation (λ 290–320nm).
- Pre-existing melanin is darkened and released into keratinocytes.
- Rate of melanin synthesis increases.
- Amount of pigment increases.
- Protection from UVR.
Artificial UV
- Sun beds emit UVR.
- Australian Study 2010.
- Use between the ages of 18-39 yrs increases the risk of developing a melanoma by 41%.

Clare Oliver died from melanoma in 2007, aged 26.

Skin circulation
- Nutrition of skin and appendages.
- ↑ blood flow for heat loss.
- ↓ blood flow to conserve heat.

Presentation
- Most common site in males and females is the face.
- Males: ear, head and neck, back and shoulders.
- Females: lower limbs.
- Variable clinical features.
- Half of melanomas are detected by the patient.

Dermoscopy
- Examination of the entire skin surface.
- Skin surface microscopy.
- 6-100 fold enlargement of the view of a pigmented skin lesion.
- Sequential digital dermoscopy.
Melanoma sub-types

**Lentigo maligna melanoma (LM)**
- Hutchinson's melanotic freckle is a pigmented macular lesion.
- Sun-damaged skin.
- Face, head and neck.
- Elderly patients.
- Outdoor workers.
- 10-15% of melanomas.
- Prognosis: reasonably good.

**Superficial spreading melanoma**
- Most common.
- Lateral growth before invasion.
- Young patients.
- Intermittent sun exposure
- Prognosis: reasonably good.

**Nodular melanoma (NM)**
- Rapidly growing.
- Symmetrical.
- Raised, firm uniformly coloured.
- 15% of overall melanomas, majority of thick melanomas.
- Older patients, intermittent sun exposure.
- Head and neck.
- Most aggressive.

**Acral lentiginous melanoma (LM)**
- 1-3% of melanomas in Australia.
- Palm of the hand or sole of foot.
- Pigmented.
- Light-coloured or pink.
- May not be associated with UV exposure.
Subungual melanoma

- Variant of ALM.
- Nail matrix.
- Brown to black stripe.
- May not be related to sun exposure.

Desmoplastic melanoma

- De-novo
- Lentigo maligna.
- Firm, even-coloured enlarging nodule.
- 1 – 3% of melanomas
- Older age group, head and neck
- Dermal spindle cells in fibrous stroma
- Thicker primary tumours
- Amelanotic, S-100 positive
- Overall survival is the same for other melanomas of the same thickness.
- Complete excision with 1cm margin.

Clinical features

- Variable, depending on type, stage and location.
- Melanocytic naevi (moles).
- Spitz naevi.
- Pre-existing scars.
- Incomplete excision recurrence vs complete excision recurrence.
**ABCDE RULE**
- Asymmetry
- Borders
- Colour
- Diameter
- Elevation

**Growth and spread**
- Pigmented, flat, brown, slightly irregular borders.
- Horizontal spread - involve papillary dermis.
- Vertical growth - through dermis to involve subcutaneous tissue.
- Partial regression.

**Clark staging**
- Level I - confined to the epidermis.
- Level II - invasion of the papillary dermis.
- Level III – filling the papillary dermis.
- Level IV – Invasion of the reticular dermis.
- Level V – Invasion of the deep subcutaneous tissue.

**Breslow thickness**
- \(<1\) mm: 5 year survival is 95-100%
- 1 - 2\(\) mm: 5 year survival is 80-96%
- 2.1 – 4 mm: 5 year survival is 60-75%.
- \(>4\) mm: 5 year survival is 37-50%.
Excision of suspected melanoma
- Complete excisional biopsies.
- Narrow margin of no less than 2mm, and no greater than 3mm of normal skin. (US NCCN).
- British Journal of Dermatology 2-5mm.

Complete excision

Excisional biopsy
- Measure three dimensions.
- Describe skin surface and any lesion present.
- Mark margins.
- Transverse slices, all processed.

Partial biopsies
- Less accurate.
- Inadequate sampling for histological assessment.
- Include most suspicious areas.
- Diagram and good clinical notes on the request form.
- Dermoscopy may be helpful.
Processing of skin biopsies
- Use biopsy pads when indicated.
- Small skins and punches: 3 hours.
- Larger skins: 6 hours.
- Very large skins: 10 hours
- Formalin, alcohol, xylene, wax.

summary
- Complete excision.
- Interpret partial biopsies in conjunction with clinical findings.
- Partial biopsies are appropriate in certain circumstances.
- Incisional, punch or shave biopsies.

The histopathology report
- Correct diagnosis.
- Completeness of excision.
- Tumour thickness.
- Macroscopic description includes:
  - Dimensions of specimen and lesion.
  - Description of lesion.

Format of the report
Descriptive
- Describe all histological features.
- Cytologic features
- Growth patterns

Synoptic
- Tabulated results.
- Essential components include:
  - Diagnosis
  - Histological features
  - Tumour thickness
  - Margins of excision
  - Mitotic rate
  - Ulceration
  - Level of invasion
Case study

- 76 year old male.
- Clinical notes: SCC/melanoma on forehead, suture at 12 o’clock. BCC on left forehead.
- Specimen 1: Right side forehead lesion, 59x43x6mm.
- 2 tan nodules 24mm and 8mm.
- 9 blocks are taken through the ellipse, including end pieces.

Case study

- Specimen 2 – Lesion on left side forehead, suture at 12 o’clock.
- Circular excision, 26x25x5mm.
- 11 mm tan plaque.
- Borders marked.
- 9 slices submitted in three blocks.
- Clusters of atypical melanocytes at the dermo/epidermal junction.

IMMUNOHISTOCHEMISTRY

S-100, HMB-45 strong positive, Melan-A, moderate, AE1/AE3 neg

SYNOPTIC CONCLUSION

- Site: Forehead.
- Specimen type: Wide local excision.
- Malignant melanoma of nodular type. There are two separate tumours.
- Clark Level: larger V Smaller V
- Breslow thickness: Larger 9mm. Smaller 2.3mm
- Growth phase: vertical.
- Predominant cell type: Epithelioid.
- Mitotic index: Larger 4-5 per sq.mm. Smaller 18 per sq.mm
Synoptic conclusion cont....

- Lymphovascular invasion: Both – absent
- Perineural invasion: Both – absent
- Satellitosis: Both – absent
- Regression: Both – absent
- Inflammatory host response: Both – weak
- Associated naevus: Both – not present
- Clearance: Both – well clear
- Margins: Larger transverse 10mm, longitudinal well clear, deep 15mm.
- Margins: Smaller transverse 6mm, longitudinal well clear, deep 4mm

Melanoma staging

TNM classification and staging system

- Practical, reproducible and applicable.
- Accurately reflects the biology of melanoma.
- Evidence based.
- Relevant to current clinical practice.
- Easily identifiable data

Yervoy

- Ipilimumab - cytotoxic T-lymphocyte antigen 4 immune therapy.
- Immune system recognises, targets and attacks cells in melanoma tumours.
- Side effects – diarrhoea, vomiting, septicaemia, renal failure.
- 676 patients: 45% - 1 year survival; >20% 2 - years; small number – 6 years.
Case study
- 56 year old male.
- Clinical notes: enlarging lymph gland right groin?
  Lymphoma.
- Dense black pigment.
- Perl's negative
- Schmori's positive

References
- WHO Classification of Tumours - Pathology and Genetics of Skin Tumours, Vol 6 Ed: Philip E. Le Boit, Gunter Burg, David Weedon, Alain Sarasin 2006
- NordiQC: www.nordiqc.org
- The Melanoma Foundation
  www.melanomafoundation.org.au
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The end