Recognition & Treatment of Pre-Malignant & Malignant skin lesions

Bruce Philp
St. Andrews Centre
Broomfield Hospital
Skin cancer

- 27% primary care consultations related to skin conditions
- 1.7% skin lesions

NICE Guidance on skin cancer
UK Incidence 2010

- Skin cancer most common form of cancer
- Incidence quadrupled in past 30 years
- Melanoma – 12,800/year
- NMSC – 99,549/year
- Majority BCC - 50-60,000 new diagnosis/year in UK
Structured Approach to Diagnosis

• Is it Cancer?
• Risk Group ? – high or low
• What referral pathway ?
Is it Cancer?

- Melanoma
- SCC
- BCC
- Low grade lesion (pre-malignant)
- Rare tumours
Relative Risk

• High
  - MM { - 2 week rule
  - SCC { - Urgent
  - Others }

• Low
  - BCC { - Soon 4 – 6 wks
  - AK /Bowens }

• Benign
  - Neavi etc { - Routine -13 wks
DIAGNOSIS ?
What do I do?

• If in doubt – cut it out

• …. or else get someone else to do it

• Dermoscopy allows more detailed examination, reduce delay in diagnosis of high risk lesions and reduce excision of benign lesions
Skin cancer & Pre-malignant lesions

• Pre-malignant lesions
  - Solar/Actinic keratoses → SCC
  - Bowens disease → SCC
  - Sebaceous naevus → BCC
    - Lentigo maligna → MM
  - Leucoplakia → SCC

• Very high risk
  - Xeroderma Pigmentosum
  - Immunosuppression (organ transplant)
Benign lesions

- Seborrhoeic keratoses
- Pigmented naevi
- Sebaceous hyperplasia
- Vascular lesions
Seborrhoeic Keratoses

senile wart, basal cell papilloma

- Most common benign skin tumour in older patients – epidermal proliferation, keratin cysts
- Multiple, Round/oval
- Various colours and sizes
- Brown macules become raised, verrucous papules
- Warty and “stuck-on”
- Removed bluntly → bleeds from multiple finger-like projections
Seborrheoeic Keratoses

- Fulfill “ABCD” criteria
- Sun exposed areas
- New lesions, itch, grow, may bleed, pigmented
- Brown macules, velvety surface, warty surface & plugged follicles
- Grow, crumble, dynamic, wax and wane
- Cosmetically unappealing
- Account for considerable diagnostic confusion in patients and professionals
Cerebriform patterns
Hairpin vessels

Share similar features to solar lentigous (basal keratinocyte hyperpigmenatation – possible precursor lesions to Seb K)
Seborrhoeic Keratoses
Dermatofibroma

- Benign fibrous tumour (superficial fibrous histiocytoma)
- Cutaneous nodule – dermal papule
- Lower legs
- Itchy and tender
Dermatofibroma

Peripheral pseudo pigment network, central scar like area
Sebaceous Hyperplasia
Vascular lesions
Key points

- Skin tumours grow and do not suddenly appear fully formed – improve outcomes by early diagnosis and treatment
- Skin cancers evolve – they are not static
- Magnification & bright light - Dermoscopy
- Multi-disciplinary team management
Clinical diagnosis

- Clinical history
- Clinical examination
- Dermoscopic examination

- Diagnosis is in the detail

Criteria for BCC

- Arborizing vessels
- Blue-grey dots and globules
- Blue-grey ovoid nests
- Spoke wheel pigmentation
- Erythema
- Erosions and ulceration
Skin cancer MDT

- Skin cancer clinical nurse specialist CNS
- Dermatologist
- Histopathologist
- Oncologist
- Radiologist
- Plastic surgeon
- MDT coordinator
- Clinic nurses
- Nurse practitioners
St Andrew’s Centre

- 22 Consultant Surgeons
- 32 Trainee Surgeons
- 7 dedicated operating theatres
- 24/7 cover for emergencies (Burns & Trauma)
- >400 microsurgical reconstructions per year
- Largest Burns, Breast Reconstruction/microsurgery, Cleft Lip & Palate, & Hand surgery service in UK
- Regional Head & Neck Service
- Regional laser service
- PDT service
- Sentinel Node & Lymph Node dissection Service
St Margaret’s Epping

- Weekly Consultant Clinic
- Bruce Philp & Bhagwat Mathur
- Weekly Fellow Clinic
- Oak Unit Day Surgery cases 1-2 lists per week
Skin Cancer at St. Andrew’s

- 4000 BCC per year
- 1000 SCC per year
- 400 new melanoma per year
Treatment Goals

• Early detection/diagnosis
• Prompt treatment and complete eradication
• Restore form & function
Treatment options overview

- Topical therapy
- Liquid nitrogen cryotherapy
- Photodynamic therapy (PDT)
- Curettage & cautery/electrodessication
- Surgical ablation (+/- reconstruction)
- Mohs micrographic surgery
- Radiotherapy
- Limb perfusion/infusion, electro-chemotherapy
- Laser ablation (CO2 or Erbium YAG)
- Chemical peels
- Monitoring – observation [Serial photography ]
Reconstruction principles

The “reconstructive ladder”

• Allow to heal by 2\textsuperscript{nd} intention
• Direct closure - Suture, staple, glue
• Local flap
• Skin graft – SSG or FTSG
• Distant flap
• Free flap with microvascular anastomosis
Reconstruction
Outcomes
Disease, Patient, Treatment factors

• Type of skin cancer NMSC / MSC, Histopathological type, Stage/Grade, Size & Location
• Patient factors – age, co-morbidities, fitness of surgery
• Treatment factors- local facilities, skill sets
Pre-malignant lesions
Actinic keratoses
Actinic/Solar keratosis

- Sun-damaged skin – atrophy, telangectasia, dyschromia
- 20% of patients over 60 have 1 AK
- Face, chest, back of hands
- Small rough spots- red & scaly-enlarge but wax & wane
- May produce an exaggerated hyperkeratosis – Cutaneous horn

- Epidermal dysplasia and architectural disorder
- Abnormal basal keratinocytes, nuclear atypia, hyper- and para-keratosis, acanthosis
Actinic/Solar keratosis

- May progress to SCC (minority- 1 per 1000 per year), many regress
- Resultant SCC slow growing and unlikely to metastasize
Clinical characteristics

• Multiple erythematous scaly papules
  – Rough texture
  – Various sizes

• Sun-exposed areas
ACTINIC KERATOSIS
Actinic keratoses

Seborrheic keratoses
Bowen's disease
Actinic keratosis
Treatment of AK’s

- Liquid nitrogen cryotherapy

- Topical therapies
  - 5-FU (Efudix) (Actikerall)
  - Imiquimod (Aldara)

- Curettage for hypertrophic lesions
- Surgery
Cryotherapy
Liquid nitrogen cryotherapy

- Spray or cotton tip applicator
- 2 cycles
  - 3-10 seconds freezing time
- Painful
- 2 weeks healing time
Residual hypopigmentation
Blister formation
Curettage for hypertrophic AK’s

- Topical therapies and cryotherapy do not work well
- Fast and effective
- Local anesthesia
Photo Dynamic Therapy PDT

• **Methyl aminolevulinate (MAL)**
• Metvix cream is applied topically
• 2 hours later the skin is illuminated with a proprietary red light (630 nm) source (medical lamp 'Aktilite') to activate the photosensitiser.
• NICE approved for AK, Bowens disease and superficial BCC
Sebaceous/linear epidermal naevus

Organoid nevus”/ "Naevus sebaceous of Jadassohn” – small risk of BCC
NONMELANOMA SKIN CANCERS
• **Non-melanoma skin cancers (NMSC)**

  - Basal cell carcinoma
  - Squamous cell carcinoma
  - Keratoacanthoma
SKIN CELL LAYERS INVOLVED IN NMSC

- Squamous cell
- Epidermis
- Melanocyte
- Basal cell
- Hair follicle
- Lymph vessel
- Sweat gland
- Blood vessel
- Subcutis
- Dermis
- Epidermis
Risk factors for development of BCC and SCC

• Fair skin (Fitzpatrick’s types I-II)
  – Blue eyes
  – Red hair

• Family history
  – Genetic syndromes - XP, Gorlin’s syndrome

• Chronic sun exposure
  - sun beds, blistering sun burn

• Immunosuppression (organ transplant, HIV)

• Increasing age
  Chronic wounds and scars

• (Arsenic, tar)
RISK FACTORS FOR NMSC

- Fair skinned, freckled, red hair
- Blue or green eyes
- Elderly
- Burns easily, doesn't tan
- Scarring from burns
- Works outdoors
- HPV infection
- High lifetime sun exposure; early UV exposure
- Previous radiation exposure
- Immune-compromised
- Artificial tanning beds
Basal cell carcinoma

The most common of all cancers
BCC

- Slow growing
- Locally invasive
- Malignant tumour of basal keratinocytes
- Sun exposed areas in Caucasians
- 80% NMSC
- 4 x more common than SCC
BCC incidence & Aetiology

- Most common skin cancer in UK, Europe, Australia & USA
- Worldwide increase in incidence (predicted to continue to 2040)
- Genetic predisposition and UV radiation exposure (especially in childhood)
- Head & Neck, hands
Molecular changes

- Patched & Hedgehog signaling pathways
- Sonic Hedgehog (SHH), Patched and Smoothened (SMO) proteins involved resulting in abnormal epidermal proliferation
- Patched (PTCH) is a tumour suppressor gene – inactivation results in tumour formation
BCC- diverse clinical appearance

- Nodular
- Cystic
- Superficial
- Infiltrative
- Morphoeic

All types can be pigmented
BCC - Histological

- Nodular
- Superficial
  - Micronodular
  - Morphoeic
  - Infiltrative
- Basosquamous

Aggressive tissue destruction & invasion
Peri-vascular & peri-neural invasion
BBC morphology

- Nodular
- Morphoeic/Infiltrative Sub-clinical extension
Low & high risk BCC

Risk of incomplete 1st Rx and recurrence
Helps determine treatment plan and follow up

• Low risk – topical, cryotherapy, PDT, C&C, surgery (small margins)
• High risk – surgery, Mohs, radiotherapy
• **High risk**
  - Histological sub-type
    - Morphoeic
    - Infiltrating
    - Micronodular
    - Basosquamous
  - Histological features
    - Perineural invasion
    - Invasion below dermis
  - Sites
    - Nose
    - Periocular
    - Ears
    - Scalp/temples
    - Lips
  - Other factors
    - Size > 2cm
    - Immunosuppression
    - Genetic disorders e.g. Gorlin’s

• **Low risk**
  - Everything else
Increasing risk of recurrence

- Tumour size (increasing size)
- Tumour site (lesions on the central face, especially around the eyes, nose, lips and ears)
- Definition of clinical margins (poorly defined lesions)
- Histological subtype (Morphoeic/infiltritive subtypes)
- Histological features of aggression (perineural and/or perivascular invasion)
- Failure of previous treatment (recurrent lesions are at higher risk of further recurrence)
- Immunosuppression (possibly confers increased risk of recurrence)
# BCC subtype features

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Description</th>
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| Nodular         | - Commonly on the face  
|                 | - Cystic, pearly, telangiectasia  
|                 | - May be ulcerated  
|                 | - Micronodular and microcystic types may infiltrate deeply                                                                                   |
| Superficial     | - Often multiple  
|                 | - Usually on upper trunk and shoulders  
|                 | - Erythematous well-demarcated scaly plaques, often larger than 20 mm at presentation  
|                 | - Slow growth over months or years  
|                 | - May be confused with Bowen’s disease or inflammatory dermatoses  
|                 | - Particularly responsive to medical rather than surgical treatment                                                                           |
| Morphoeic       | - Also known as sclerosing or infiltrative BCC  
|                 | - Usually found in mid-facial sites  
|                 | - Skin-coloured, waxy, scar-like  
|                 | - Prone to recurrence after treatment  
|                 | - May infiltrate cutaneous nerves (perineural spread)                                                                                       |
| Pigmented       | - Brown, blue or greyish lesion  
|                 | - Nodular or superficial histology  
|                 | - May resemble malignant melanoma                                                                                                           |
| Basosquamous    | - Mixed basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)  
|                 | - Potentially more aggressive than other forms of BCC                                                                                         |
Improving Outcomes for People with Skin Tumours including Melanoma (update):
The Management of Low-risk Basal Cell Carcinomas in the Community

May 2010
LOW-RISK BCCs FOR DES/LES (SEE BOX 1)

Patient with skin lesion presents to GP: thought to be a low-risk BCC

Does the GP meet the requirements to perform skin surgery within the framework of the Direct Enhanced Services and Local Enhanced Services under General Medical Services or Personal Medical Services? Has the GP demonstrated surgical competency?

NO

REFER to a member of the LSMDT

YES

Is GP confident of the diagnosis of a low-risk BCC?

NO

REFER to a member of the LSMDT

YES

There is no diagnostic uncertainty that the lesion is a primary nodular low-risk BCC and it meets the following criteria:

- The patient is not
  - aged 24 years or younger (that is, a child or young adult)
  - immunosuppressed or has Gorlin’s syndrome

- The lesion:
  - is located below the clavicle (that is not on the head or neck)
  - is less than 1 cm in diameter with clearly defined margins
  - is not a recurrent BCC following incomplete excision
  - is not a persistent BCC that has been incompletely excised according to histology
  - is not morphoeic, infiltrative or basosquamous in appearance
  - is not located:
    - over important underlying anatomical structures (for example, major vessels or nerves)
    - in an area where primary surgical closure may be difficult (for example, digits or front of shin)
    - in an area where difficult excision may lead to a poor cosmetic result
    - at another highly visible anatomical site (for example, anterior chest or shoulders) where a good cosmetic result is important to the patient.

Criteria met? NO

REFER to a member of the LSMDT

Criteria met? YES

Manage low-risk BCC appropriately

Primary Care Trust governance (England)
Local Health Board governance (Wales)
Diagnosis

- Usually clinical
  - bright light, loupe magnification, Dermoscopy
- Biopsy – if in doubt or specialist treatment likely (high risk subtype, recurrence)
- Exfoliative cytology
- Imaging occasionally (bony or orbital invasion)
Absent pigment network
Arborizing vessels
Leaf like area
Large blue-grey ovoid nests
Multiple blue-grey globules
Spoke wheel pigmentation
Ulceration and erosions
The dermoscopic features typically found in BCC's include the pigmented structures relating to melanin inclusions and vascular features including erythema and ulceration.

- Multiple blue-grey dots and globules
- Spoke-wheel pigmentation
- Leaf-like areas
- Blue-grey ovoid nests
- Arborising vessels and erythema
- Erosions and ulceration
Nodular BCC

- Chronic lesion, slowly growing
- Easy bleeding, scabs & crusts but never heals
- Pearly border
- Surface telangetasias
- Head and neck, trunk, and extremities
Stretch sign
BCC stretch sign
“RODENT ULCER”
BASAL CELL CARCINOMA

DDx Chondrodermatitis nodularis helicis, scc, AK
BASAL CELL CARCINOMA
NODULAR BCC
Pigmented BCC

- Similar to nodular but with black discoloration
  - Melanin deposits
- Pigmented skin types
- Face, trunk, and scalp
Superficial BCC

- Erythematous scaly plaque
- Slow growth
- Asymptomatic
- Trunk, extremities, face
SUPERFICIAL BCC
Morpheaform BCC

- Resembles scar (sclerosing)
- Asymptomatic and slow growing
- Ill-defined margins
- Marked subclinical extension
MORPHEAFORM BCC
Morpheaform BCC
PIGMENTED BCC
PIGMENTED BCC
BASOSQUAMOUS CARCINOMA
– Local destruction of tissue
Treatment goals

- Complete ablation of tumour cells
- Acceptable functional & cosmetic outcome
Treatment of BCC

• Curettage & electrodessication (ED/C)

• Surgical excision
  • Traditional
  • Moh’s micrographic surgery (London or N&N)

95% Cure Rate

• Radiation therapy

50-75% Cure Rate

• Photodynamic therapy

• Topical therapy
  – Imiquimod
Surgical excision

- < 20 mm lesion
  - 3 mm margin – 85% complete excision
  - 4-5 mm margin – 95% complete excision

- Larger lesions and Morphoeic need greater margins or Mohs or 2 stage procedures
## Good Choices

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<tr>
<td><strong>Good Choices</strong></td>
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<tr>
<td><strong>Superficial</strong></td>
<td>Low Risk</td>
<td>High Risk</td>
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<td>C+C/Topical</td>
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## What **NOT** to do

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<td>C+C</td>
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Don’t let this happen to your patients…
First treatment is the most important!

Select option according to size, location, likely histology and patient’s preference
Keratoacanthoma (KA)

- Rapidly growing lesion
- Volcano shape with keratin plug
- May involute to leave a crater like scar
- Controversial if truly benign or malignant
Keratoacanthoma

- Low grade SCC
- Rapid growth over weeks
- Trauma, sun exposure, HPV 11 and 16
- May progress to invasive SCC
KERATOACANTHOMA
KERATOACANTHOMA
Squamous Cell Carcinoma
SCC
SCC – Squamous Cell Carcinoma

• **Incidence**
  - Skin phototype 1 & 2
  - late middle age onwards
  - M:F 2:1

• **Aetiology**
  - UV irradiation
  - burn scar, chronic wounds, immunosuppression
  - AK & Bowen’s disease, XP, Leukoplakia
SCC Epidemiology & Aetiology

- 2\textsuperscript{nd} most common skin cancer
- Incidence rising
- Aetiology similar to BCC: chronic sun damage
  - develop de-novo
  - from Bowens disease (intra epidermal scc)
  - chronic wounds or scars (Marjolin ulcer)
  - immunosuppressed or leukemia/lymphoma
  - HPV infection
SCC – Squamous Cell Carcinoma

- Malignant tumour arising from keratinising epidermal cells or skin appendages
- Locally invasive with potential to metastasise
- Pathology
  - epidermal atypia and differentiation
SCC Clinical

- Indurated nodular keratinising or crusted tumour
- May ulcerate
- May ulcerate without keratinisation
SCC types

• Bowen’s disease
  – Erythroplasia of Queyrat

• Invasive SCC

• Verrucous carcinoma
Bowen’s disease

- In-situ SCC
- Arsenic, HPV 16, radiation
- No association with internal malignancies
BOWEN’S DISEASE

DDX AK, Superficial BCC
BOWEN’S DISEASE
Invasive SCC

- Erythematous nodule
- Induration
- Sun-exposed skin
  - Men > women
- Slow growth
Squamous cell carcinoma (SCC) and keratoacanthoma share clinical and dermoscopic features; diagnosis should always be confirmed on histology. Well-differentiated SCCs and keratoacanthomas will show more keratinising structures, whereas less-differentiated SCCs will tend to show fewer keratinising structures and more vascular features, including ulceration.

An erythematous papule on the nasal side wall: dermoscopy shows linear irregular vessels and few features of keratinisation; histology confirmed a moderately differentiated SCC.

A well-circumscribed nodule on the arm, with a central crust: dermoscopy shows hairpin vessels at the margin of the tumour typical for a keratinising tumour, with arborising vessels centrally; histology confirmed a keratoacanthoma.

A well-circumscribed nodule on the arm, with a central keratotic plug: dermoscopy shows a combination of vascular features, with hairpin vessels at the periphery and larger arborising vessels centrally in this proliferating tumour; histology confirmed a well-differentiated SCC.
Invasive SCC
SQUAMOUS CELL CARCINOMA (SCC)
Early SCC-In Situ

AK
Not so early SCC’s
SQUAMOUS CELL CARCINOMA

DDX BCC
SQUAMOUS CELL CARCINOMA
SQUAMOUS CELL CARCINOMA
Differential diagnosis - SCC

- Bowen disease
- Superficial BCC
- Eczema
- Psoriasis
- Tinea
Differential diagnosis - SCC

Squamous cell carcinoma

Basal cell carcinoma
Treatment of SCC

- Bowen’s disease
- (Erythroplasia of Queyrat)

- Efudix or aldara
- PDT
- Liquid nitrogen cryotherapy
- Radiation therapy
- Curettage electrodessication (ED/C)
- Surgical excision very prone to complication
• Invasive squamous cell carcinoma

• Surgical excision
  – Traditional
  – Mohs surgery

• Radiation therapy
SCC management

- Fast track/rapid access skin cancer clinic
- Clinical diagnosis +/- biopsy
- Assessment of draining lymph nodes
  - clinical, FNA, imaging
- **Surgical excision treatment of choice**
  - <2cm minimum 4 mm margin
  - >2cm wider margins >6mm
  - Mohs micrographic surgery
- LSMDT/SSMDT discussion
- Post operative radiotherapy high risk/incomplete
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<th>Indications</th>
<th>Contraindications</th>
<th>Notes</th>
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<tr>
<td>Surgical Excision</td>
<td>All resectable tumours</td>
<td>Where surgical morbidity is likely to be unreasonably high</td>
<td>General treatment of choice for SCC</td>
</tr>
<tr>
<td>Mohs Micrographic Surgery / Excision with histological control</td>
<td>High risk tumours</td>
<td>Where surgical morbidity is likely to be unreasonably high</td>
<td>High risk tumours need wide margins or histological margin control</td>
</tr>
<tr>
<td>Radiotherapy</td>
<td>Non-resectable tumours</td>
<td>Where tumour margins are ill-defined</td>
<td></td>
</tr>
<tr>
<td>Curettage and Cautery</td>
<td>Small, well-defined, low-risk tumours</td>
<td>High risk tumours</td>
<td>Only suitable for experienced practitioners</td>
</tr>
<tr>
<td>Cryotherapy</td>
<td>Small, well-defined, low-risk tumours</td>
<td>High risk tumours, recurrent tumours</td>
<td>Only suitable for experienced practitioners</td>
</tr>
</tbody>
</table>
SCC histology

- Histo-pathological subtype
- Degree of differentiation (good, moderate, poorly, un-)
- Histological grade (Broder’s)
- Macroscopic size
- Microscopic depth in mm
- Level of dermal invasion
- Peri-neural, lymphatic or vascular invasion
- Margins and completeness of excision
• SCC is locally invasive and destructive

• Metastases in 1-3% of cases
  – To lymph nodes
    – 50-73% survival
  – Distant sites (lungs)
    – Incurable
High Risk SCC

Tumour characteristics associated with increased risk of metastasis includes:

**Site**
High risk sites include lip & ear, non sun-exposed sites (e.g. perineum, sacrum, sole of foot), SCC in areas of radiation or thermal injury, chronic draining sinuses, chronic ulcers, chronic inflammation or Bowen’s disease.

**Diameter**
Tumours greater than 2cm in diameter are twice as likely to recur locally (15.2% vs. 7.4%), and three times as likely to metastasise (30.3% vs. 9.1%) as smaller tumours.

**Depth**
Tumours > 4mm in depth or extending to the subcutaneous tissue are more likely to recur and metastasise compared with thinner tumours.

**Histological differentiation**
Poorly differentiated tumours have double the local recurrence rate and triple the metastatic rate of better differentiated SCC. Tumours with perineural involvement are more likely to recur and to metastasise.

**Host immunosuppression**
Tumours arising in patients who are immunosuppressed have a poorer prognosis.

**Previous treatment and local recurrence**
Metastatic Disease SCC

- Lymph node dissection
- Adjuvant radiotherapy
- Adjuvant chemotherapy
Melanoma
The progressive development of an atypical mole, into a superficial spreading melanoma over time.
What is melanoma

- Melanoma = an invasive malignancy of melanocytes
  - i.e. not just skin! (unknown primary)
  - 91.2% cutaneous
  - 6.2% ocular
  - 1.2% internal organ

Melanocytes

- Melanocytes are located in the stratum basale of the epidermis
Incidence/Statistics

• 5th most common Ca in UK in 2010
  • 4% of all new diagnoses
• 12,818 new dx in 2010
  • 48% males
  • 52% females
• 20 per 100,000 pop

• Office of national statistics (CRUK website)
Aetiology

- Premalignant condition
- Previous melanoma
- Age
- Race
- Economic Status
- Naevus
- Type 1 Fitzpatrick
- Sunburn
Sunburn/Ultraviolet Radiation

- MM 4X more frequent with severe sunburn before age 10
- Higher economic status = more likely to have sunburn as a child, due to holidays abroad.
- UVA
  - 314-400nm
  - Sunbeds
  - No proof of increase in MM
• UVB
  – 280-315nm
  – Produces sunburn
  – Known risk factor for MM

• UVC
  – 200-280nm
  – Mostly filtered out by ozone layer
Premalignant Condition

• Approx 7% of gen pop.n have = or >1 atypical naevi
  – Atyp naevus synd. = >100 melanocytic naevi
    – Autosomal dominant
    – Absent at birth
    – At puberty increase in size and multiply throughout life
    – Av size 6-15mm
    – Macular, pebbly plaque appearance
    – ANS 12X more likely to develop melanoma

• Most MMs in ANS arise de novo not in atyp. Naevus

• Giant Hairy Naevus ?increased risk - maybe as high as 40%

  Key Notes in Plastic Surgery Adrian Richards
Melanoma Precursors

• Premalignant conditions have atypical melanocytes
  • Potential for malignant transformation
• 3 lesions thought to be melanoma precursors:
  • Dysplastic Naevus
  • Lentigo Maligna
  • Melanoma In Situ
Dysplastic Naevi DN
Clinical characteristics DN

- Diameter >6mm
- Tan color with darker brown or black
- Elevated center
- Irregular border
Dysplastic Naevus

• Sup. spr. MM arises by malignant transformation of melanocytes (60%) or malignant transformation of dysplastic naevus (40%) McGovern VJ, Shaw HM, Milton GW: Histogenesis of malignant melanoma with an adjacent component of the superficial spreading type. Pathology 17:251, 1985.

• If from Dysp. Naevus, progresses to melanoma in situ, then onto melanoma

• Very small % go on to melanoma

• Histologically:
  • Proliferation of intraepidermal melanocytes singly or in nests in basal epidermis
  • Variable and discontinuous melanocytic cellular atypia

• AKA: atypical junctional naevus, active junctional naevus, intraepidermal melanoma
• **Dysplastic naevi are**
  
  – Precursors for melanoma
  
  – Markers for melanoma
Dysplastic naevi
Differential diagnosis - DN

Dysplastic Naevus

Pigmented BCC
Differential diagnosis - DN
Differential diagnosis- DN

Seborrheic keratosis
Treatment of dysplastic naevi

• Excision Biopsy
• Local anesthesia
• 1-2mm margins
• Excision down to fat
• Clinically indistinguishable from melanoma in situ
• Wide variations in shape and colour
• Junctional naevi seldom bigger than 3mm
• Dysplastic naevi often 5-10mm
• Most common on back
• Average age at first occurrence is 38 years
Lentigo Maligna

• Non-nested proliferation of atypical melanocytes in an atrophic epidermis
• May progress to melanoma in situ or invasive melanoma
• AKA Hutchinson’s freckle/senile freckle/malignant freckle/premalignant lentigo
Lentigo Maligna
Melanoma in Situ

- Melanoma most commonly arises de novo in melanoma in situ
- Intraepidermal melanocytic proliferation with fully evolved cellular atypia
MM Diagnosis

• MacKie seven point checklist (for referral)
  – **Major** – change in ..
    • Shape
    • Size
    • Colour
– **Minor** - DISC
  • Diameter >6mm
  • Inflammation
  • Sensory changes/itch
  • Crusting/bleeding

– 95% of patients presenting with MM will have at least 1 major feature
– 50% of patients have 1 or more minor feature

MacKie R at al. *Seven-point checklist for melanoma*. Clinical and Experimental Dermatology, 16: 151–152
ABCDE

• The ABCDE rule adapted from the American Cancer Society's check list is also simple and easy to remember
  • Asymmetry
  • Border irregularity
  • Colour irregularity
  • Diameter greater than 6 mm
  • Elevation/evolution

A descriptive not diagnostic classification
<table>
<thead>
<tr>
<th>Normal Mole</th>
<th>Melanoma</th>
<th>Sign</th>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1.png" alt="Normal Mole" /></td>
<td><img src="image2.png" alt="Melanoma" /></td>
<td>Asymmetry</td>
<td>When half of the mole does not match the other half</td>
</tr>
<tr>
<td><img src="image3.png" alt="Normal Mole" /></td>
<td><img src="image4.png" alt="Melanoma" /></td>
<td>Border</td>
<td>When the border (edges) of the mole are ragged or irregular</td>
</tr>
<tr>
<td><img src="image5.png" alt="Normal Mole" /></td>
<td><img src="image6.png" alt="Melanoma" /></td>
<td>Color</td>
<td>When the color of the mole varies throughout</td>
</tr>
<tr>
<td><img src="image7.png" alt="Normal Mole" /></td>
<td><img src="image8.png" alt="Melanoma" /></td>
<td>Diameter</td>
<td>If the mole’s diameter is larger than a pencil’s eraser</td>
</tr>
</tbody>
</table>

*Photographs Used By Permission: National Cancer Institute*
<table>
<thead>
<tr>
<th>NORMAL</th>
<th>CANCEROUS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>“A” IS FOR ASYMMETRY</strong>&lt;br&gt;• If you draw a line through the middle of the mole, the halves of a melanoma won’t match in size.</td>
<td></td>
</tr>
<tr>
<td><img src="image1" alt="Normal Mole" /> <img src="image2" alt="Cancerous Mole" /></td>
<td></td>
</tr>
<tr>
<td><strong>“B” IS FOR BORDER</strong>&lt;br&gt;• The edges of an early melanoma tend to be uneven, crusty or notched.</td>
<td></td>
</tr>
<tr>
<td><img src="image3" alt="Normal Mole" /> <img src="image4" alt="Cancerous Mole" /></td>
<td></td>
</tr>
<tr>
<td><strong>“C” IS FOR COLOR</strong>&lt;br&gt;• Healthy moles are uniform in color. A variety of colors, especially white and/or blue, is bad.</td>
<td></td>
</tr>
<tr>
<td><img src="image5" alt="Normal Mole" /> <img src="image6" alt="Cancerous Mole" /></td>
<td></td>
</tr>
<tr>
<td><strong>“D” IS FOR DIAMETER</strong>&lt;br&gt;• Melanomas are usually larger in diameter than a pencil eraser, although they can be smaller.</td>
<td></td>
</tr>
<tr>
<td><img src="image7" alt="Normal Mole" /> <img src="image8" alt="Cancerous Mole" /></td>
<td></td>
</tr>
<tr>
<td><strong>“E” IS FOR EVOLVING</strong>&lt;br&gt;• When a mole changes in size, shape or color, or begins to bleed or scab, this points to danger.</td>
<td></td>
</tr>
<tr>
<td><img src="image9" alt="Normal Mole" /> <img src="image10" alt="Cancerous Mole" /></td>
<td></td>
</tr>
</tbody>
</table>
7 features of melanoma

- Eccentric atypical network
- Blue–white veil
- Regression structures
- Irregular streaks
- Atypical vessels
- Eccentric homogeneous pigmentation
- Asymmetrical pigmented globules
# 7 Dermascopic Features of MM

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition</th>
<th>Histopathological correlates</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Atypical pigment network</td>
<td>Brown, black or grey (BBG) network with irregular meshes and thick lines</td>
<td>Irregular and broadened rete ridges</td>
</tr>
<tr>
<td>2. Blue-white veil</td>
<td>Irregular, confluent, grey-blue to whitish-blue diffuse pigmentation</td>
<td>Acanthotic epidermis with focal hypergranulosis above sheets of heavily pigmented dermal melanocytes – &quot;mist&quot; obscures the detail</td>
</tr>
<tr>
<td>3. Atypical vascular pattern</td>
<td>Linear-irregular or dotted vessels, mixture of vessel types</td>
<td>Neovascularisation</td>
</tr>
<tr>
<td>4. Irregular streaks</td>
<td>Irregular linear structures not clearly combined with pigment network lines</td>
<td>Confluent nests of melanocytes</td>
</tr>
<tr>
<td>5. Irregular pigmentation</td>
<td>BBG Pigmented areas with irregular shape of distribution</td>
<td>Hyperpigmentation throughout the epidermis/upper dermis</td>
</tr>
<tr>
<td>6. Irregular dots/globules</td>
<td>BBG round to oval variously sized structures irregularly distributed in lesion</td>
<td>Pigment aggregates in stratum corneum, epidermis, DEJ or papillary dermis</td>
</tr>
<tr>
<td>7. Regression structures</td>
<td>White scarlike areas and blue areas</td>
<td>Thickened papillary dermis with fibrosis and/or variable melanophages – immunological storm has wiped out the detail</td>
</tr>
</tbody>
</table>
Seven features of melanoma

- Eccentric atypical network
- Blue-white veil
- Regression structures
- Irregular streaks
- Asymmetrical pigmented globules
- Atypical vessels
- Eccentric homogeneous pigmentation

The following structures form the basis for a variety of scoring systems, or algorithms, that have been reported for melanoma diagnosis.
Seven features of melanoma

Irregular pigmentation

Irregular dots and globules

Irregular streaks

Regression structures

Atypical vessels

Atypical vessels
MM Classification

• Histology
  – Superficial spreading 60%
  – Nodular 30%
  – Lentigo maligna 7%
  – Acral 2%
    – Amelanotic <1%
    – Desmoplastic <1%
Clinical types- MM

Superficial spreading melanoma

Lentigo maligna melanoma

Acral lentiginous melanoma

Nodular melanoma
Superficial Spreading Melanoma

- Usually arises in pre-existing naevus
  - History of slow changes
  - Rapid growths in months before diagnosis
- Can occur anywhere any age after puberty
  - Legs of women
  - Backs of men
- Mean size 2cm
- Darkly pigmented area in brown junctional naevus
- Initially flat
- Dark areas expand with areas of pale regression (amelanosis)
- Surface becomes crusty
• Development of shiny nodule = start of vertical growth phase
• Perimeter is notched +/- thin pink rim or halo
Nodular Melanoma

- 15-30% of melanomas
- Shorter clinical onset than SSM
- Typically arises in uninvolved skin NOT pre-existing naevus
- More common in men
- Trunk and head and neck commonly
- 1-2cm
- Dome shaped or polypoidal
- Lacks a radial growth phase and is therefore more sharply demarcated from surrounding normal skin
- About 5% are amelanotic
Nodular MM
Lentigo Maligna Melanoma

- 4-10% of cases
- Appear as skin stain in multiple shades of brown
- Flat and large
- Older people
- Vertical growth = uncommon
  - Vertical growth results in plaques/nodules
- Convoluted edges
- Higher correlation with continued intense sunlight exposure
- More common in women
- Face and hands
- Not aggressive: indolent course of 5-15 years
- Little propensity to metastasize
Acral Lentiginous Melanoma

- Soles (and palms, nailbeds - subungual)
- 2-8% of melanomas in whites
- 35-60% in blacks/asians/hispanics
- No increase incidence in blacks c.f. whites, but fewer other types of melanoma in blacks
- Average patient age is 60
- Flat and large (av. Diameter 3cm)
- Irregular border + multiple colour shades
Desmoplastic Melanoma

- 1% all MM
- High perineural invasion (especially in H&N)
- Appears innocuous + amelanotic plaque or nodule
- Immuno +ve for S100
- No higher risk of regional spread than others
Amelanotic Melanoma

- Notoriously difficult to diagnose
- Immuno-staining useful for diagnosis
- Lesion usually in vertical growth phase
<table>
<thead>
<tr>
<th>Type of melanoma</th>
<th>Frequency (%)</th>
<th>Duration before diagnosis (yr)</th>
<th>Mean age at diagnosis (yr)</th>
<th>Site</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Types with radial growth phases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial spreading melanoma</td>
<td>70%</td>
<td>1-7</td>
<td>Mid-40s</td>
<td>Any site; lower legs in females, back in both sexes</td>
<td>Raised border on palpation or inspection; pinks, whites, grays, and blues in brown lesion</td>
</tr>
<tr>
<td>Acral lentiginous melanoma (including subungual melanoma)</td>
<td>10%</td>
<td>1-10</td>
<td>60s</td>
<td>Sole, palms, mucous membranes, subungual</td>
<td>Flat, irregular border; predominantly dark brown to black</td>
</tr>
<tr>
<td>Lentigo maligna melanoma</td>
<td>5%</td>
<td>5-50</td>
<td>70s</td>
<td>Nose, cheeks, temples</td>
<td>Highly irregular border with areas of regression; brown-tan macular lesion with variation in pigment pattern; may be amelanotic</td>
</tr>
<tr>
<td>Type with no radial growth phase</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nodular melanoma</td>
<td>15%</td>
<td>Months</td>
<td>Mid- to late-40s</td>
<td>Any site</td>
<td>Nodule arises in apparently normal skin or in a nevus; brown to brown-black; may have bluish hues; may be amelanotic</td>
</tr>
</tbody>
</table>

Revised UK Guidelines for cutaneous melanoma 2010

J.R Marsden et al., JPRAS 2010 (63), 1401 - 1419
In General

- AIM: Good standard of care across the country
- Evidence based treatment
- Multidisciplinary working party group
- Consensus in areas of conflicting evidence
- Individualized care where appropriate
Treatment Melanoma

• Surgical Excision
• ?Sentinel Node Biopsy
• ?Adjuvant Therapy
• Follow up
Malignant Melanoma Excision

• Initially 1-2 mm margin – excision biopsy
• Then guided by Breslow Thickness
  – <1 mm 1 cm margin
  – 1-2 mm 1–2 cm margin
  – > 2 mm 2-3 cm margin

• Lymph Node Dissection
  – For enlarged nodes or after positive sentinel node biopsy
Table 7  Recommended surgical excision margins.

<table>
<thead>
<tr>
<th>Breslow thickness</th>
<th>Excision margins</th>
<th>Level of evidence</th>
<th>Grading of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>In situ</td>
<td>5 mm margins to achieve complete histological excision</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>&lt;1 mm</td>
<td>1 cm</td>
<td>Ib</td>
<td>A</td>
</tr>
<tr>
<td>1.01–2 mm</td>
<td>1–2 cm</td>
<td>Ib</td>
<td>A</td>
</tr>
<tr>
<td>2.1–4 mm</td>
<td>2–3 cm</td>
<td>Ib</td>
<td>A</td>
</tr>
<tr>
<td>&gt;4 mm</td>
<td>3 cm</td>
<td>Ib</td>
<td>B</td>
</tr>
</tbody>
</table>
Multidisciplinary care

- **LSMDT**
  Local skin cancer multidisciplinary team
  Core services - generally by dermatologists

- **SSMDT**
  Specialist skin cancer services multidisciplinary team
  Specialist services
Urgent Referral to LSMDT

- 2 week rule
- Mole changing in size shape or colour
- Mole which has 3 or more colours
- Loss of asymmetry
- Mole itching or bleeding
- Pigmented or vascular lesion if growing
- Pigmented line in nail
- Lesion growing under nail.
Table 2  Recommendations for Local Skin Cancer Multi-disciplinary Team record-keeping of clinical features.

As a minimum the following should be included:
History (the presence or absence of these changes should be recorded)
- Duration of the lesion
- Change in size
- Change in colour
- Change in shape
- Symptoms (itching, bleeding, etc.)

Examination
- Site
- Size (maximum diameter)
- Elevation (flat, palpable, nodular)
- Description (irregular margins, irregular pigmentation and if ulceration is present)

(Level III, Grade B)
Prognostic features - MM

- **Good prognosis**
  - Breslow < 1mm
  - Clark level I-III

- **Intermediate prognosis**
  - Breslow 1-4mm

- **Bad prognosis**
  - Breslow >4mm
  - Clark level IV-V
  - Angiolympathic invasion
  - Ulceration
Table 5  Requirements for microscopy of melanoma.

<table>
<thead>
<tr>
<th>Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Ulceration</td>
</tr>
<tr>
<td>• Thickness</td>
</tr>
<tr>
<td>• Mitotic count&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>• Histologic subtype</td>
</tr>
<tr>
<td>• Margins of excision</td>
</tr>
<tr>
<td>• Pathological staging</td>
</tr>
<tr>
<td>• Growth phase</td>
</tr>
<tr>
<td>• Regression</td>
</tr>
<tr>
<td>• Tumour-infiltrating lymphocytes</td>
</tr>
<tr>
<td>• Lymphatic or vascular invasion</td>
</tr>
<tr>
<td>• Perineural invasion</td>
</tr>
<tr>
<td>• Microsatellites&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Mitotic count is included in the 2009 AJCC staging system.

<sup>b</sup> Microsatellites are not included in thickness measurement.
AJCC 2009 Staging System

<table>
<thead>
<tr>
<th>Stage</th>
<th>Primary tumour (pT)</th>
<th>Lymph nodes (N)</th>
<th>Metastases (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>&lt; 1 mm, no ulceration, mitoses &lt; 1 mm⁻²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB</td>
<td>&lt; 1 mm, with ulceration or mitoses ≥ 1 mm⁻²</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1·01–2 mm, no ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIA</td>
<td>1·01–2 mm, with ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIB</td>
<td>2·01–4 mm, with ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt; 4 mm, no ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIC</td>
<td>&gt; 4 mm, with ulceration</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIA</td>
<td>Any Breslow thickness, no ulceration</td>
<td>Micrometastases</td>
<td>1–3 nodes</td>
</tr>
<tr>
<td>IIIB</td>
<td>Any Breslow thickness, with ulceration</td>
<td>Micrometastases</td>
<td>1–3 palpable</td>
</tr>
<tr>
<td></td>
<td>Any Breslow thickness, no ulceration</td>
<td></td>
<td>metastatic nodes</td>
</tr>
<tr>
<td></td>
<td>No nodes, but in-transit or satellite metastasis/es</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIIC</td>
<td>Any Breslow thickness, with ulceration</td>
<td>Up to three palpable lymph nodes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any Breslow thickness, with or without ulceration</td>
<td>Four or more nodes or matted</td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ lymph nodes</td>
<td>nodes or in-transit disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any Breslow thickness, with ulceration</td>
<td>No nodes, but in-transit or satellite</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>metastasis/es</td>
<td></td>
</tr>
<tr>
<td>IV, M1a</td>
<td></td>
<td>Skin, subcutaneous or distant nodal</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>disease</td>
<td></td>
</tr>
<tr>
<td>IV, M1b</td>
<td></td>
<td>Lung metastases</td>
<td></td>
</tr>
<tr>
<td>IV, M1c</td>
<td></td>
<td>All other sites or any other sites of</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>metastases with raised lactate</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>dehydrogenase</td>
<td></td>
</tr>
</tbody>
</table>

*In the rare circumstances where mitotic count cannot be accurately determined, a Clark level of invasion of either IV or V can be used to define T1b melanoma. Every patient with melanoma should be accurately staged using the AJCC system; this may include performing a sentinel lymph node biopsy when this is recommended by the Specialist Skin Cancer Multidisciplinary Team. Staging should be updated following relapse.*
Sentinel lymph node biopsy - MM

- Recommended for MM with Breslow thickness 1-4mm
  - Lymphadenectomy for positive nodes

- Powerful prognostic feature for disseminated disease

- It does not affect survival of patients
SLNBx

- Part of AJCC 2009 classification
- Gives information on prognosis
  - Pts with BT 1.2-3.5mm = 75% five year survival with +ve SNB vs 90% with -ve SNB
  

- Used in clinical trials
- Normally performed if BT >1mm
  - 20% +ve
  - If <1mm 5% +ve

- 5% morbidity
- MSLT1 showed no overall 5 year survival following SNB and completion lymphadenectomy
Other treatments- MM

- Radiation therapy
  - Palliative
- Biologic therapy (Interferon)
- Immunologic therapy (vaccines)
- Novel therapies - antibodies
Interferon therapy - MM

- Used in melanomas with “high risk” for dissemination or metastases
  - Breslow 1-4mm with ulceration
  - Breslow >4mm
  - Positive lymph nodes

- High dose for 1-2 years
- Considerable morbidity

- It does not increase overall survival
Adjuvant Therapies

• Clinical Trials
• Interferon
• Vaccines
• Numerous current trials
ST ANDREWS CENTRE SKIN CANCER FOLLOW UP GUIDELINES

**BCC**
- **HIGH RISK**
  - SITE: EARS/ NOSE /EYES/ PERI ALAR
  - SIZE: > 2cm
  - TYPE: MORPHOEOIC / INFILTRATIVE
    - RECURRENT / INCOMPLETE
  - FOLLOW UP:
    - 1 – 3 MTHS POST OP
    - THEN
    - 3 - 6 MTHS FOR 2 YRS
    - THEN 6 MTHS FOR 2 YRS
- **LOW RISK**

**SCC**
- **HIGH RISK**
  - SITE: LIPS/ EARS / EYES / HANDS
  - SIZE: 2cm WIDTH >4mm DEPTH
  - TYPE: POORLY DIFFERENTIATED
    - RECURRENT / INCOMPLETE
    - IMMUNOSUPPRESSED PATIENTS
  - FOLLOW UP:
    - X 1 1-3 MTHS POST OP
    - THEN
    - 3 MTHS FOR 2 YRS
- **LOW RISK**
  - OTHERS
    - COMPLETE EXCISION
    - >5mm MARGIN
    - FOLLOW UP:
      - X 1 1 - 3 MTHS THEN DISCHARGE

**INVASIVE MELANOMA**
- FOLLOW UP:
  - 3 MTHLY 2-3 YRS
  - 6MTHLY 2-3 YRS (.5YRS)
  - >1 mm YRLY (5-10YRS)
- **IN SITU MELANOMA**
  - FOLLOW UP:
    - X 1 1 – 3 MTHS POST OP
    - THEN DISCHARGE

**individual consultant variations may apply**

P.D. / L.C. Nov 2004
Resources

• BAD Guidelines
  http://www.bad.org.uk/site/622/default.aspx

• Primary Care Dermatology Society
  http://www.pcds.org.uk/a-z-clinical-guidance/clinical-a-z-list

• Medscape
  http://emedicine.medscape.com/dermatology#malignant
Thank you
Biopsy

• Excision biopsy
  2mm margin with cuff of subcutaneous fat

• Shave biopsy has no role

• Incision or punch biopsy
  Occasionally acceptable
  Differential diagnosis of LM
  Acral melanoma

• Subungual melanoma
  Nail removal + Adequate sampling of nail matrix

• Not recommended
  Prophylactic excision of naevi
  <5cm congenital nevi

• Clinical details including history and differential diagnosis to histopathologist