# Pathology - Topic 33 - Skin

## Approach to Skin Tumours

- Skin tumours can arise from keratinocytes, melanocytes, skin appendages and other cells.

### Epidermal and Melanocytic Lesions

- Clinical appearance helps select a differential diagnosis, while histology establishes the nature of a sampled lesion.
- A change in size, colour, surface or symptoms is important, but no single visual feature identifies every malignancy.
- Some cancers are small, non-pigmented or deceptively well circumscribed.
    - The depth and orientation of a biopsy affect assessment of invasion. A superficial fragment may not show the deepest part of a tumour.

### Ultraviolet Injury and Susceptibility

- Ultraviolet radiation damages DNA and contributes to many keratinocyte cancers and cutaneous melanomas.
- Failure of repair or immune surveillance allows damaged clones to persist.
- Fair skin, cumulative sun exposure, previous skin cancer and immunosuppression increase risk in relevant tumour groups.
- Inherited DNA-repair defects can cause striking susceptibility at an early age.
    - Not every skin tumour is caused by ultraviolet exposure.
    - Acral and mucosal melanomas have different exposure patterns and molecular associations.

## Squamous Cell Carcinoma

- Cutaneous squamous cell carcinoma is a malignant tumour of keratinocytes with squamous differentiation.

### Nature and Risk Exposures

- Chronic ultraviolet damage is a major cause on exposed skin.
- Other settings include chronic scars or ulcers, certain carcinogenic exposures and immunosuppression.
- Selected HPV types contribute at some anatomical sites.

### Scar-related Cancer and Precursor Lesions

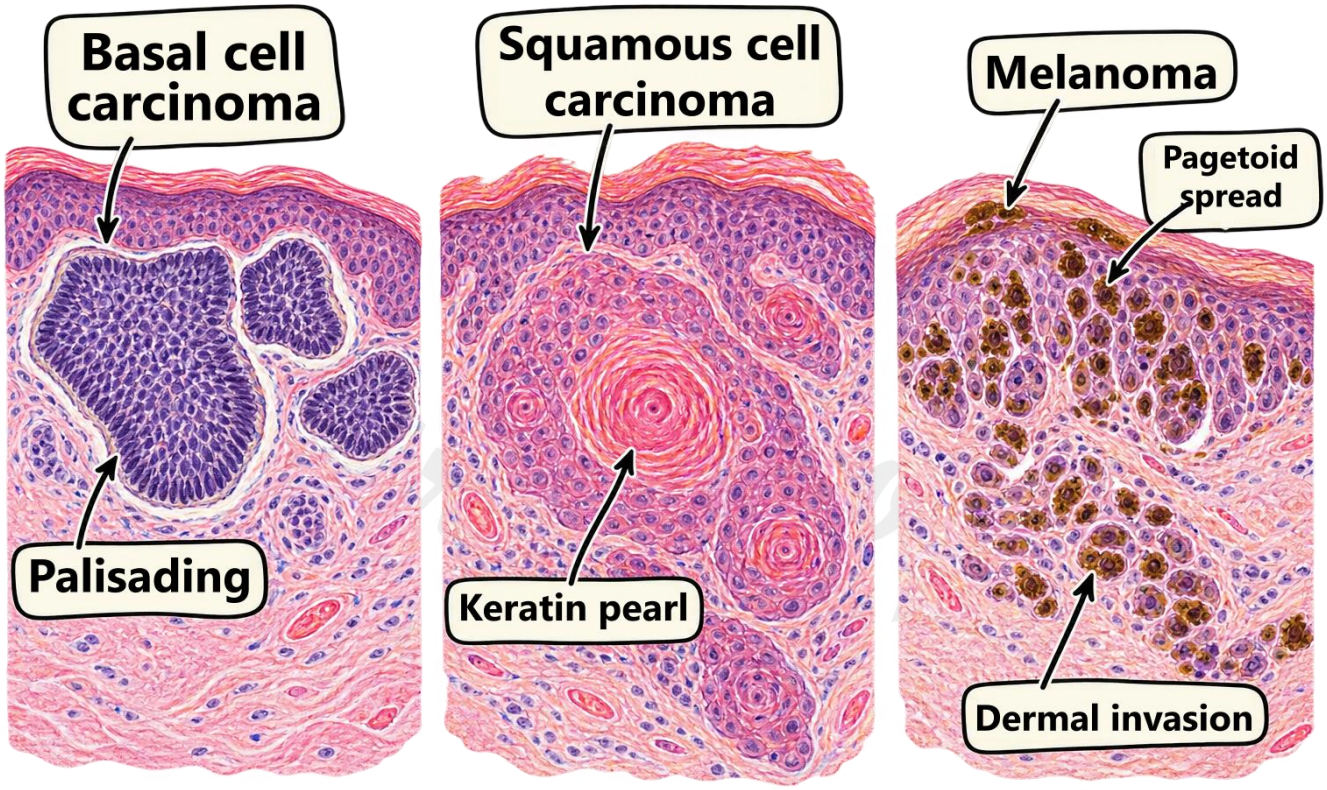
- A carcinoma developing in a long-standing scar or chronic ulcer is sometimes called a Marjolin ulcer.

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- Actinic keratosis is a sun-related keratinocytic precursor lesion.
- Squamous carcinoma in situ shows full-thickness epidermal atypia without dermal invasion.
    - Many actinic keratoses do not progress, while invasive carcinoma can also appear without an obvious previously recognised precursor.

## Epidermal Atypia and Proof of Invasion

- Actinic keratosis commonly shows atypia concentrated in the lower epidermis with abnormal keratinisation and solar elastosis in the underlying dermis.
- The extent of epidermal atypia and the presence or absence of dermal invasion distinguish a precursor, carcinoma in situ and invasive carcinoma.




*Contrasting microscopic patterns of basal cell carcinoma, squamous cell carcinoma and melanoma*

## Gross Appearance

- An invasive lesion may form a scaly plaque, a firm nodule or an ulcer with an indurated edge.
- Keratin may create a rough or crusted surface.

## Invasion and Squamous Differentiation

- Microscopy shows atypical squamous cells extending through the basement membrane into dermis.
    - They form nests or cords with variable keratinisation and intercellular bridges.
    - Well-differentiated lesions may contain concentric **keratin pearls**.
    - Poorly differentiated tumours can produce little obvious keratin.

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## Stromal Response and High-risk Invasion

- The surrounding stroma may show inflammation and a desmoplastic response.
- Perineural or lymphovascular invasion indicates a more concerning pattern.

## Natural History and Prognostic Factors

- Many localised cutaneous squamous carcinomas have a favourable outcome after adequate treatment. A subset invades deeply or spreads to regional lymph nodes and distant organs.
- Risk is influenced by tumour size, depth, differentiation, perineural invasion, location and the patient's immune status.
    - The lip, ear and certain other sites have clinically important risk considerations. A single low-power appearance should not determine prognosis.
- Recurrence, nodal involvement and deep invasion alter assessment.
- Histology reports therefore describe more than the presence of malignant squamous cells.

# Basal Cell Carcinoma

- Basal cell carcinoma is a malignant basaloid epithelial tumour that commonly develops on sun-exposed skin.

## Pathogenesis and Clinical Types

### Cellular Origin and Hedgehog Signalling

- Dysregulated Hedgehog signalling, often involving PTCH1 or SMO, is central to its biology.
    - Inherited PTCH1-related basal cell naevus syndrome predisposes to multiple lesions and other abnormalities.

### Nodular, Superficial and Infiltrative Clinical Patterns

- A nodular lesion often appears pearly, with surface telangiectasia and a rolled edge.
- Ulceration may produce the classical rodent-ulcer appearance.
- Superficial lesions form thin erythematous plaques.
- Morpheaform or infiltrative lesions may resemble a scar and have less obvious clinical borders.

## Microscopic Features and Behaviour

### Basaloid Nests and Stromal Features

- Microscopy shows nests or strands of basaloid cells in the dermis, often connected to epidermis or follicular epithelium.
- Peripheral nuclei may form a palisaded arrangement.
- Retraction clefts commonly appear between tumour nests and surrounding stroma.

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- Mucinous stromal change may also be present.

### Local Invasion, Metastasis and Recurrence Risk

- Basal cell carcinoma is locally invasive and can destroy underlying tissue if neglected.
- Distant metastasis is exceptionally uncommon, but rare occurrence means it is not biologically impossible.
- Recurrence risk depends on subtype, site, size, previous treatment and adequacy of removal. A tumour's low metastatic rate does not mean it cannot cause serious local damage.

### Morphological Variants

#### A. Nodular and Superficial Growth

- Nodular BCC forms rounded dermal aggregates, whereas superficial BCC has multiple small basaloid buds attached to the epidermis.

#### B. Infiltrative Growth

- Infiltrative and morpheaform patterns show thin irregular strands in fibrous stroma and may extend beyond the visible clinical edge.

## Benign Melanocytic Naevi

- A melanocytic naevus is a benign proliferation of melanocytes, often arranged in nests.

### Architecture and Maturation

- Acquired naevi are commonly symmetrical and well circumscribed.
  - In many benign dermal naevi, cells become smaller and less active with depth.
  - This **maturation** is a useful clue rather than an absolute rule in every special subtype.
- Congenital, blue, Spitz and dysplastic naevi have distinct patterns.
- Some require specialist assessment because their features overlap with melanoma.

#### 1. Junctional Naevus

- Melanocytic nests lie at the dermoepidermal junction and commonly produce a flat pigmented lesion.

#### 2. Compound Naevus

- Nests occur at both the junction and within the dermis, often producing a raised pigmented lesion.

#### 3. Intradermal Naevus

- Naevus cells are confined to the dermis and may become smaller and less pigmented with depth.

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## Dysplastic Naevi and Risk

- A dysplastic naevus can show architectural disorder, bridging of nests and variable cytological atypia.
- The clinical lesion may have an irregular outline or colour variation.
- Multiple dysplastic naevi may indicate increased melanoma risk, especially in a relevant family history.
- Most individual naevi never become melanoma, and many melanomas arise without a pre-existing naevus.

# Melanoma

- Melanoma is a malignant tumour of melanocytes.
- Susceptibility reflects interactions among inherited factors, environmental exposure and acquired molecular changes.
- Intermittent intense ultraviolet exposure and sunburn are important for many cutaneous melanomas.
- Chronic sun damage contributes to other forms, while acral melanoma can occur on palms, soles or nail units without the same ultraviolet association.
- Alterations in pathways such as BRAF, NRAS, NF1 and KIT occur in different biological groups. A specific molecular result must be interpreted within the tumour type and site.
    - Family history, numerous naevi and inherited variants such as CDKN2A can increase risk in selected families.

## Growth Patterns and Morphology

### Growth Phases and Clinical Recognition

#### Radial and Vertical Growth Phases

- Radial growth describes spread within the epidermis and superficial skin.
- Vertical growth produces a more substantial invasive dermal component with greater potential for dissemination.
- Nodular melanoma can develop a prominent vertical phase without a long recognisable radial phase.

#### Clinical Recognition

- Clinically, asymmetry, border irregularity, colour variation and evolution are useful clues.
- Diameter is one consideration, but melanomas can be smaller than traditional screening cut-offs.
- Amelanotic melanoma contains little visible pigment and may appear pink or red.

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