Melanoma: neoplasm of melanocytes

→ Site: – skin

– oral & anogenital mucosal surface

– leptomeninges, substantia nigra

Predisposing factors: Sun exposure, inherited genes

① **Sun Exposure:** melanomas most commonly develop in sun-exposed areas like back & legs

→ lightly pigmented individuals are at greater risk than darkly pigmented individuals

② **Inherited Genes:**

i) Mutations in tumor suppressor gene: – CDKN2A gene

– RB gene

– silencing of PTEN gene ⇒ activation of PI3K/AKT signalling

ii) Oncogene activation: – mutations in NRAS

– mutation in BRAF

iii) Mutations that Activate telomerase.

Growth Phases:

Ⅰ **Radial Growth Phase:** melanoma spreads horizontally within epidermis & superficial dermis

→ tumor cells lack the capacity to metastasize

i) Lentigo maligna: presents as indolent lesion on the face of older men

ii) Superficial spreading: involves sun-exposed skin surfaces

iii) Acral/mucosal lentiginous melanoma: usually seen in palm, sole or mucosa

Ⅱ **Vertical Growth Phase:** tumor cells invade downward into deeper dermis

→ appears as a nodule → tumor cells have metaplastic potential

→ Risk of invasion ∝ depth of invasion

[Depth of invasion = distance from superficial epidermal granular cell layer to deepest intradermal tumor cells = Breslow thickness]

Microscopy:

- **Tumor Cells:** → larger than normal melanocytes or nevus cells
  → nuclei are large with irregular contours, clumping of chromatin at periphery, prominent eosinophilic nucleoli, mitotic figures
  - **Melanin pigment:** seen in melanoma
    → melanomas which do not show melanin ⇒ amelanotic melanoma
    → melanin is seen in cytoplasm as uniform brown fine granules.

Clinical Features: usually asymptomatic

→ Itching or pain at site of lesion
→ melanomas show variation in colours – black, brown, gray, etc. (unlike benign nevi)
→ > 10 mm diameter
→ irregular, notched borders

- A symmetry
- B ⇒ irregular borders
- C ⇒ variegated colour
- D ⇒ increased diameter

Squamous Cell Carcinoma: arises on sun-exposed sites

→ more common in men

→ appears as sharply defined, red, scaling plaques

Risk factors:

① Exposure to UV light: UV light produces DNA damage

② Chronic immunosuppression: due to chemotherapy / organ transplant

③ Industrial carcinogens:

④ Chronic non-healing ulcers

⑤ Old burn scars

⑥ Ionizing radiations

Genetics:

→ Mutations in tumor suppressor gene TP53

→ Mutations in DNA repair genes (eg: Xeroderma pigmentosum)

→ Mutations in RAS

→ loss-of-function mutation in Notch receptors

Gross: appear as nodular growth & may ulcerate

→ surrounded by a wide, elevated, indurated border

Microscopy: irregular masses of epidermal cells that proliferate downward into dermis

- Well-differentiated: polygonal squamous tumor cells arranged in orderly lobules
  → produce large amounts of keratin which forms epithelial/squamous keratin pearls
- Moderately differentiated: anaplastic squamous cells with single-cell keratinization (dyskeratosis)
- Poorly differentiated: highly anaplastic cells

Basal Cell Carcinoma: slow-growing invasive cancer that rarely metastasizes

→ occurs at sun-exposed sites ; more common in lightly pigmented individuals

→ Usual site ⇒ above a line drawn from angle of mouth to pinna of ear

→ Origin: endubitable hair follicle derivation

Risk factors: • Immunosuppression • inherited DNA repair defects (xeroderma pigmentosum)

Genetics: — Loss of function mutation in PTCH tumor suppressor gene

- mutations in TP53
- Defect in DNA repair gene

Clinical Presentation: pearly papules containing prominent, dilated subepidermal blood vessels

→ advanced tumors may ulcerate & locally invade & erode underlying bone or facial sinuses ⇒ rodent ulcers

Gross: nodular / ulcerative / superficial / erythematous

→ slowly-enlarging ulcer surrounded by a pearly rolled border

Microscopy: tumor cells resemble normal basal cell layer of epidermis

→ deeply basophilic epithelial cells with large, oval nucleus & narrow rim of cytoplasm

→ tumor cells are arranged in nests

→ at periphery of each nest, columnar cells are arranged radially with their long axes parallelly aligned ⇒ peripheral palisading

→ clefting artifact between tumor islands & adjacent stroma

→ 2 growth patterns — multifocal growth

- nodular lesion