Actinic Keratosis

**Precancerous**, risk of malignancy ~8-20% per year (progresses to SCC); Due to chronic sun exposure
Rough scaly plaque; typically due to sun exposure
Tx: liquid nitrogen, 5-FU, shave, curettage

- **Atypical keratinocytes in lower third** of epidermis
- Alternating orthokeratosis and parakeratosis
- **Sparing of cutaneous adnexa**
- Solar elastosis in dermis

Squamous cell carcinoma in situ (aka Bowen’s disease)

- No epidermal maturation
- **Atypical cells at all levels** of the epidermis → Loss of granular layer
- Epidermis appears disorganized

Squamous Cell Carcinoma

Second most common form of skin cancer (20% of cutaneous malignancies)
Locally destructive; metastatic potential
Tx: Depends on size, location and depth of invasion: Excision, Mohs micrographic surgery, Radiation

- Nests of atypical squamous cells arise from the epidermis and **invasive the dermis**
- Evidence of **squamous differentiation** (keratinization and intercellular bridges)
  - Dyskeratotic cells = squamous differentiation
- Often associated with AK or SCCIS
- Findings that suggest invasion
  - **Jagged** interface with dermis
  - Aberrant **deep keratinization**
  - Single cells invasion

**Variants:**

*Keratoacanthoma* - well-differentiated variant of SCC that spontaneously regresses in most cases.
Typically composed of large, crateriform (cup-like) lesion filled with abundant keratin debris

*Acantholytic SCC* – acantholysis with large epithelioid cells with dense eosinophilic cytoplasm and scattered dyskeratotic (apoptotic) cells

*Verrucous SCC* – Extremely well-differentiated, low-risk with pushing border and acanthotic papilla.
NO infiltrative growth. Associated inflammation at base.

*Desmoplastic SCC* – tumor cells become spindled/sarcomatoid
HMWCKs, p63, and p40 are most sensitive markers for poorly differentiated and spindle cell/sarcomatoid SCC (Pankeratin can be lost in poorly differentiated and spindle cell tumors)
Basal Cell Carcinoma

Most common malignancy in humans
Locally aggressive and destructive behavior
Very low metastatic potential (< 0.1%)
Pediatric BCC? → consider Gorlin’s Syndrome

- **Basaloid cells** with increased N/C ratio
- Nests with **peripheral palisading**
- **Cleft formation** between the tumor and surrounding stroma

Note: Some focal keratinization may be present!

May mimic adnexal structures, making margins challenging. However, basal cell carcinoma tumor cells should have darker chromatin, more apoptosis and mitoses, and paler cytoplasm than the hair follicles.

**Subtypes:**
- Nodular – Large, rounded nests
- Micronodular* – smaller nests
- Superficial – superficial nests separated by uninvolved areas
- Infiltrative*- small infiltrative cords
- Sclerosing/morpheic* - infiltrative nests with desmoplastic stroma
- Basosquamous* - Prominent areas of squamous differentiation
- Infundibulocystic – resemble hair follicle
- Fibroepithelioma of Pincus – anastomosing cords

* → more aggressive variants

**Stains:** BerEP4 will stain BCC but not SCC

Seborrheic Keratosis

- **Horn cysts**
- Interlacing pigmented epidermal strands
- Acanthosis
- Hyperkeratosis

**Solar lentigo** aka lentigo senilis, age spot

“Dirty feet”
Finger-like proliferation of **hyperpigmented** rete growing down from the epidermis. Keratinocytes, not melanocytes, are the pigmented cells

Verruca vulgaris

**aka Wart**
HPV-induced, circumscribed lesion
Cup-like rete ridges
Papillomatosis (“church spires”)
Hyperkeratosis often with parakeratosis
Koilocytes may be variably present
Verruca plana = flat wart
Epithelial Cysts

Epidermal Inclusion Cyst (EIC)
Acquired unilocular cyst due to trauma, etc.
Lined by squamous epithelium with granular layer
Contains laminated (basket weave) keratin
May rupture and become inflamed

Dermoid Cyst
Present at birth
Like EIC, but with hair follicles and sebaceous glands

Pilar (Trichilemmal) Cyst
Filled with dense, “wet” eosinophilic keratin
Stratified squamous epithelium
Granular layer generally absent

Sebaceous Tumors

Sebaceous hyperplasia
Overgrowth of Sebaceous glands. Lobules of sebocytes arranged around infundibulum of central hair follicle. 1 layer of basaloid cells compressed at periphery of sebocytes. No cytologic atypia

Sebaceous Adenoma
May have similar low-power architecture to sebaceous hyperplasia, but typically larger nodular aggregates. Lobular downgrowth from epidermis. Predominance (> 50%) of sebocytes. Cytologic atypia not prominent
Composed of > 50% germinative/basaloid cells → Sebaceoma

Sebaceous Carcinoma
Aggressive tumors with high incidence of metastasis (> 30%)
Strong association with Muir-Torre syndrome if patients have multiple sebaceous tumors (Genes implicated include MLH1, MSH2, MSH6, PMS2)
Eyelids are most common site (~ 75% of cases)
Clear cells often present but vary greatly in number
Show prominent cytologic atypia and pleomorphism
Mitotic figures, including atypical forms, are usually abundant

Stains: May stain with AR, EMA, and Factor Xila
(Eccrine) Spiroadenoma

“blue cannonballs in the dermis”
Basophilic tumor nodules in dermis
Tumor lobules may be partially encapsulated
Biphasic appearance with 2 cell types:
1) Peripheral small cells with scant cytoplasm and small hyperchromatic nuclei
2) Central larger cells with eosinophilic cytoplasm and oval, vesicular nuclei
Tumor lobules sometimes surrounded by thickened basement membrane, similar to cylindroma

Cylindroma

“jigsaw puzzle”
Also has basaloid (blue) nests in the dermis, also with two cell populations and basement membrane matrix.
Multiple nodules/lobules of basaloid cells surrounded by dense eosinophilic basement membrane
Tumor lobules have complex pattern, where tumor lobules appear to fit together in irregular jigsaw puzzle-like pattern

Chondroid Syringoma

aka Cutaneous mixed tumor
Essentially a pleomorphic adenoma, but primary to the skin
Epithelial cells embedded in myxoid, chondroid, or fibrous stroma
Tumor shows eccrine and apocrine differentiation
Ductal structures of variable size and shape present
Ducts lined by 2 layers of cuboidal cells and peripheral layer of myoepithelial cells

Small ducts, nests, cords, and cysts in superficial dermis
Ducts and cysts lined by 1 or 2 layers of small, bland-appearing cuboidal cells
Some ducts have tadpole-like appearance with comma-like tails (like paisley)
Dilated ducts may have eosinophilic contents
Most common in head/neck, esp. eyelids

If deep/perineural invasion → consider Microcystic Adenexal Carcinoma (MAC)
Pilomatrixoma

Well-circumscribed with mixture of 1) basaloid and 2) shadow/ghost cells (abundant pink cytoplasm and open space at their center where nucleus was)
Dystrophic calcification is frequently seen
Foreign-body giant cell reaction surrounding tumor is common
Infiltrative, prominent nucleoli, necrosis, mitoses? → Pilomatrical Carcinoma

Trichofoliculoma

Cystic tumor that communicates to overlying epidermis
Cystic space filled with keratinous debris and hair shafts
Lined by squamous epithelium with thin granular layer
Numerous small, primitive follicles radiate around periphery of tumor and communicate with central cystic space

Trichilemmoma

Lobular proliferation of mature squamoid cells with pale-to clear-staining cytoplasm
Peripheral palisading of basaloid cells
Cells are surrounded by thickened, glassy-appearing basement membrane
Multiple broad connections to epidermis and follicles
Associated with Cowden’s Syndrome

COWden’s Syndrome

PTEN mutation (tumor suppressor)
Multiple hamartomas (mouth, GI tract)
Thyroid carcinoma (usually Follicular)
Breast Cancer (very high risk)
Endometrial Cancer
Macrocephaly
trichilemmomas

Macrocephaly
& Uterine Cancer

Thyroid Cancer

Breast CA