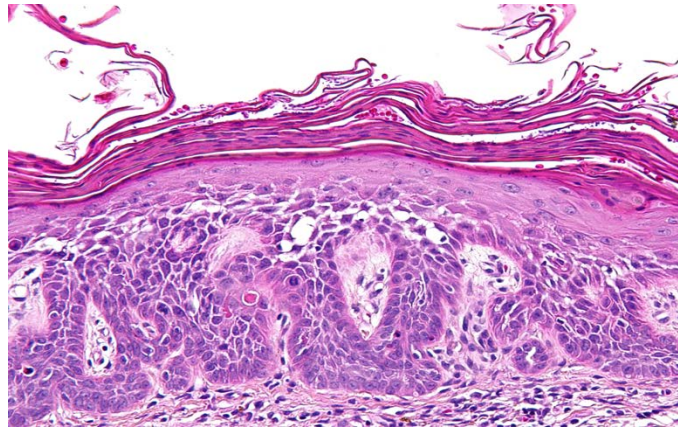


# Keratinocyte tumors

## 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 **invade 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)

### Risk factors for metastasis (high risk):

- location (ear, lip)
- size (>2 cm)
- depth
- evidence of perineural invasion
- evidence of desmoplastic features

## 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

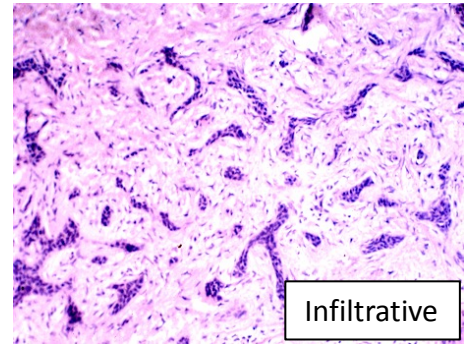
*Basosquamous\** - Prominent areas of squamous differentiation

*Infundibulocystic* – resemble hair follicle

*Fibroepithelioma of Pincus* – anastomosing cords

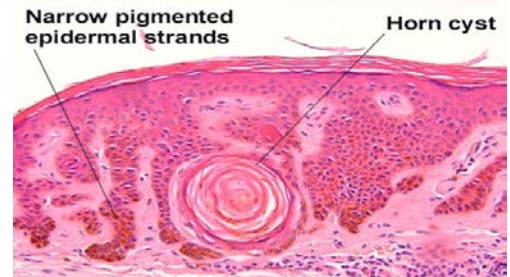
\* → more aggressive variants

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



## Seborrheic Keratosis

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

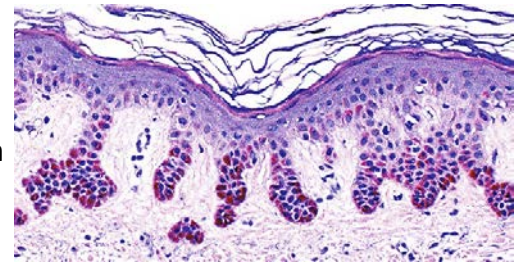


## Solar lentigo

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

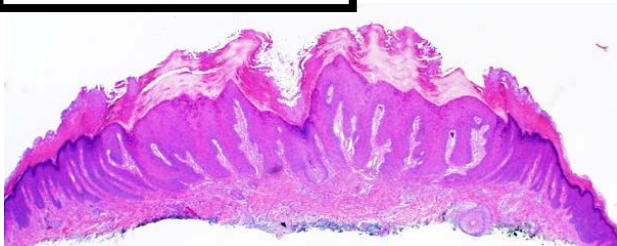
**Cup-like rete ridges**

**Papillomatosis** (“church spires”)

**Hyperkeratosis** often with parakeratosis

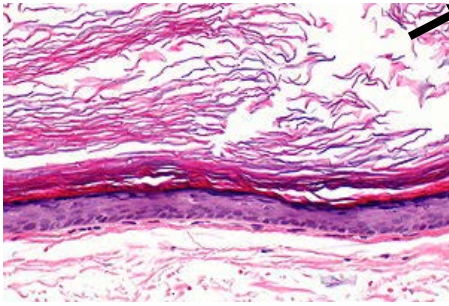
Koilocytes may be variably present

**Verruca plana** = flat wart



# More Skin Tumors

## Epithelial Cysts



### Epidermal Inclusion Cyst (EIC)

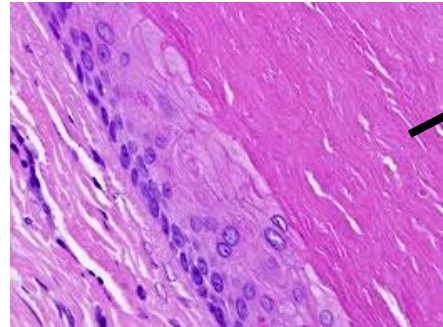
Acquired unilocular cyst due to trauma, etc..  
Lined by **squamous epithelium with granular layer**  
Contains laminated (basket weave) **keratin**  
May rupture and become inflamed

### 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**



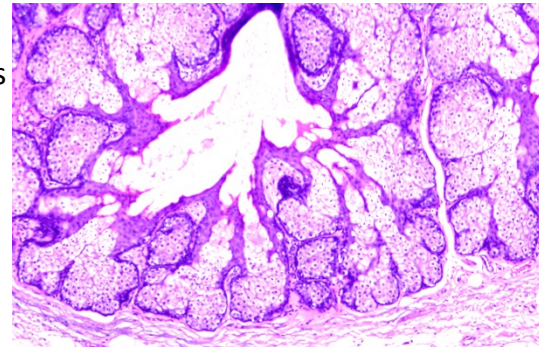
## Sebaceous Tumors

### Ectopic sebaceous glands

Not associated with hair follicles

### 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

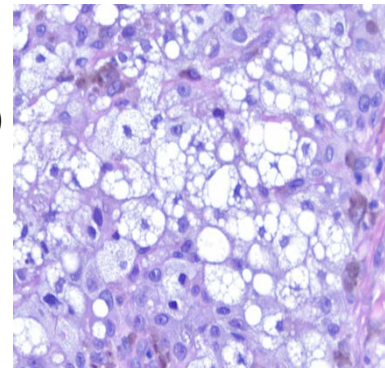
May have similar low-power architecture to sebaceous hyperplasia, but typically larger nodular aggregates. Lobular downgrowth from epidermis. Predominance (> 50%) of sebocytes. Cytologic atypia not prominent  
Composed of > 50% germinative/basaloid cells → **Sebaceoma**

### 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)

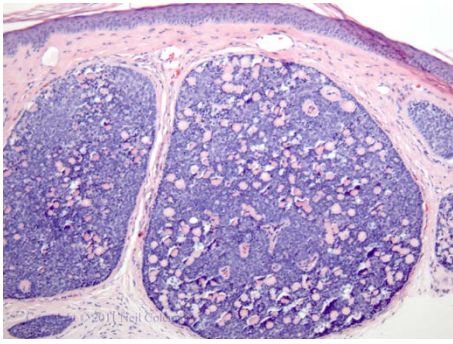
Clear cells often present but vary greatly in number  
Show prominent cytologic atypia and pleomorphism  
Mitotic figures, including atypical forms, are usually abundant

**Stains:** May stain with AR, EMA, and Factor XIIIa



## (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

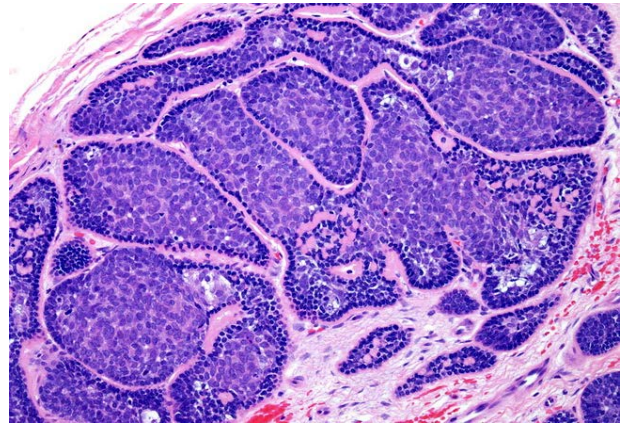
## Cylindroma

“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

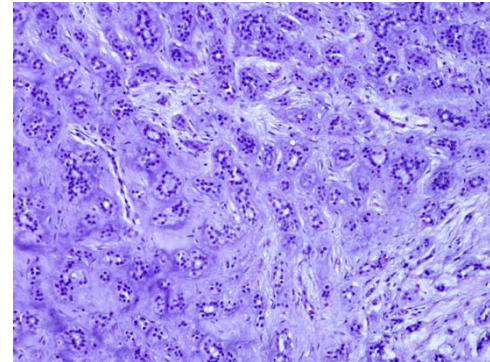
**Essentially a pleomorphic adenoma, but primary to the skin**

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

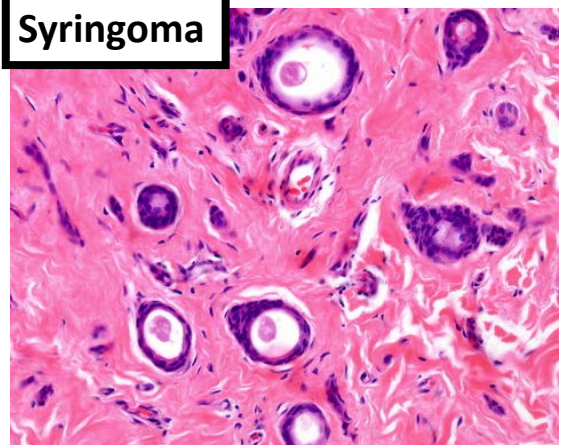
Some ducts have **tadpole-like appearance** with **comma-like tails** (like paisley)

Dilated ducts may have eosinophilic contents

Most common in head/neck, esp. eyelids

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

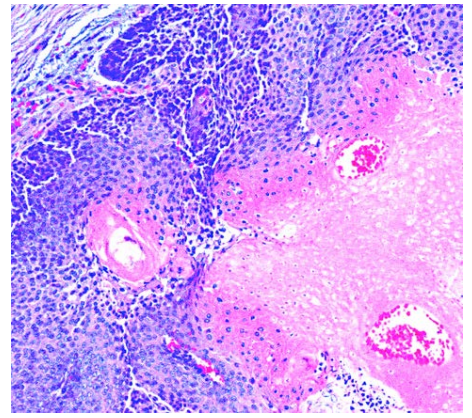
## Syringoma



## Pilomatrixoma

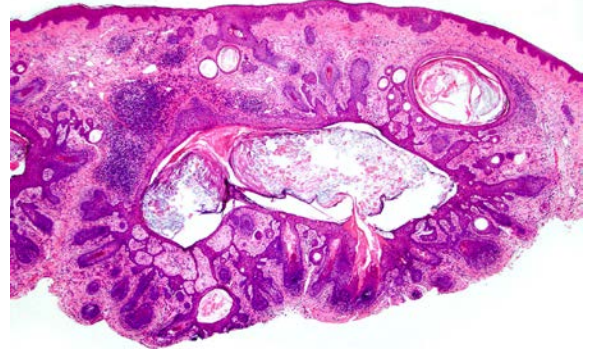
Well-circumscribed with mixture of **1) basaloid** and **2) shadow/ghost cells** (abundant pink cytoplasm and open space at their center where nucleus was)  
Dystrophic calcification is frequently seen  
Foreign-body giant cell reaction surrounding tumor is common

Infiltrative, prominent nucleoli, necrosis, mitoses? →  
**Pilomatrical Carcinoma**



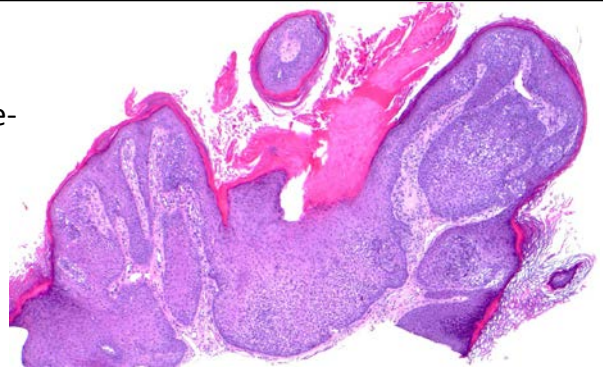
## Trichofolliculoma

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  
trichileMMOOOOmas

