PATHOLOGY OF EYELIDS

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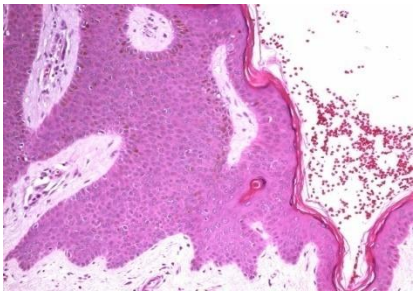
Objectives

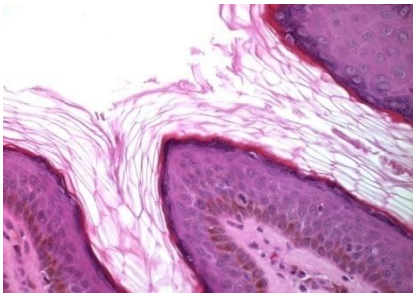
1- To become familiar with the Glossary of terms used in Dermatopathology which are applicable on eyelid pathology.
2- To apply the basic knowledge of the eyelid development for better understanding of the congenital disorders.
3- To be able to recognize the pathologic changes of aging process based on the normal anatomy and histology of the eyelid.
4- To be able to reach the diagnosis of inflammatory and structural skin lesions by proper clinicopathologic correlation.

Basic Terminology

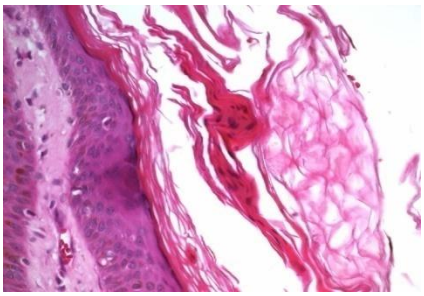
- **Acanthosis:** Increased thickness of squamous epithelium: regular or irregular



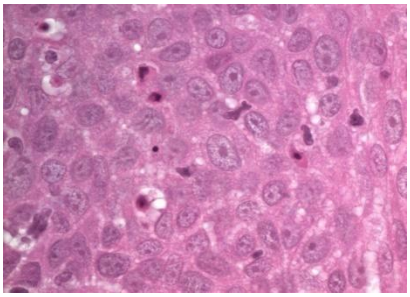
- **Acantholysis:** Rupture of intercellular bridges
- **Hyperkeratosis:** Excess production of the superficial keratin layer



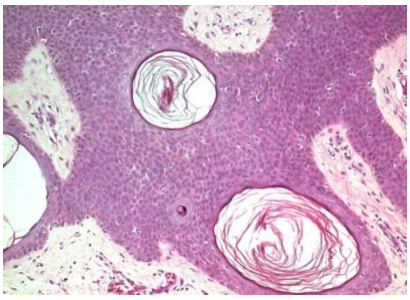
- **Parakeratosis:** Presence of retained pyknotic nuclei in the keratin layer.



- **Dyskeratosis:** Intraepithelial individual aberrant keratinization of single cells.



Squamous eddies: Circular whorls of squamous cells.



- **Dysplasia**: Disturbance of normal maturation sequence of epithelial cells.
- **Anaplasia:** Cytologic features of malignancy:
  Pleomorphism, abnormal nuclei and mitotic figures.

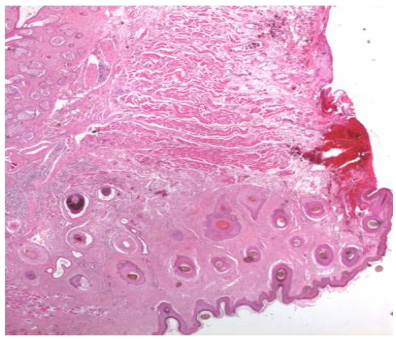
I-Anatomy & Histology

Each human eyelid is composed of six layers:

1) **Epidermis**

2 cell types: Keratinocytes and dendritic cells.

A-Keratinocytes;



-Basal single row

-Squamous cell layer

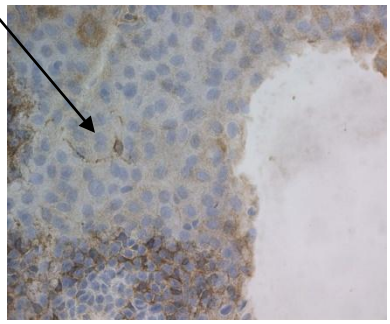
-Granular layer

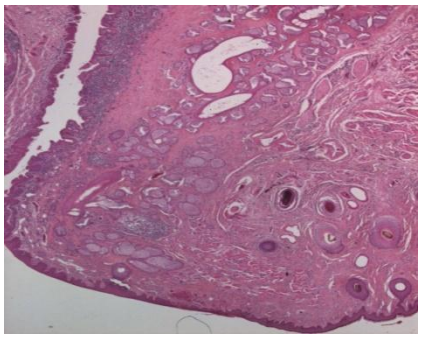
-Horny layer Histology

B-Dendritic Cells:

-Clear cell melanocytes

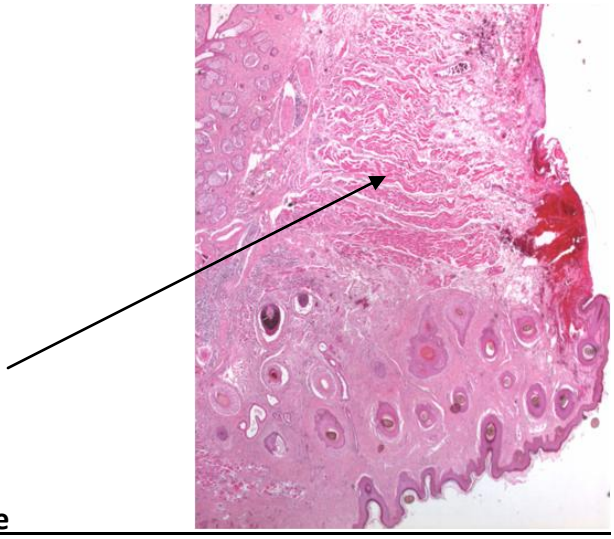
-Langerhans





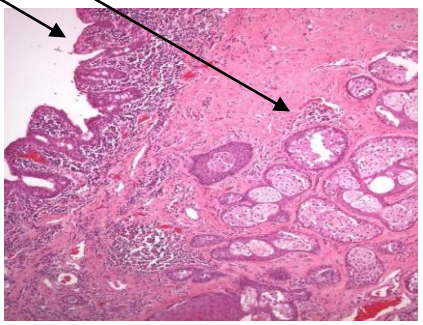
2)Dermis

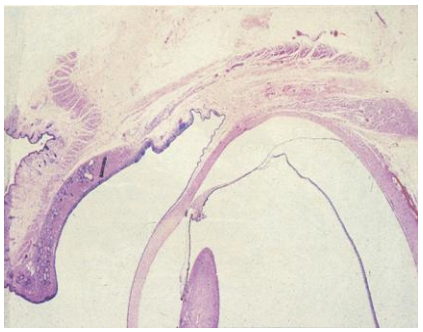
3)Subcutaneous Layer

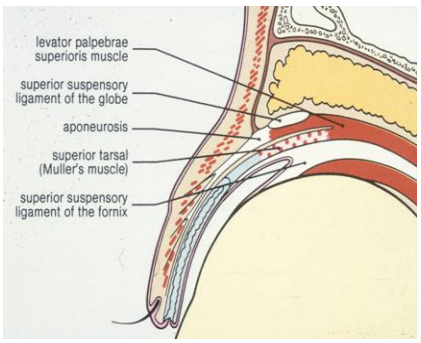


4)Orbicularis oculi muscle

5) Tarsal plate
6) Conjunctiva





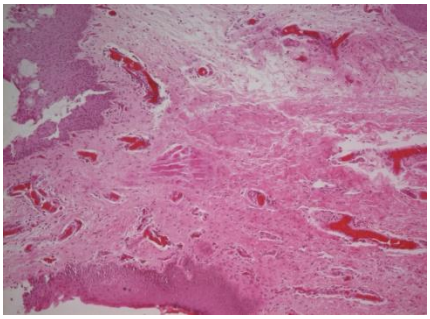


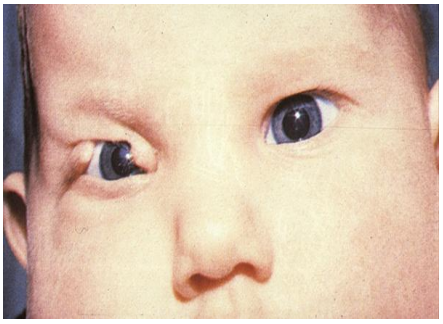
II-Congenital and Developmental abnormalities

1) Abnormal development of lid folds

- 6 - 8 weeks gestation
- results in gross abnormality eg. Cryptophthalmia

Coloboma (large)





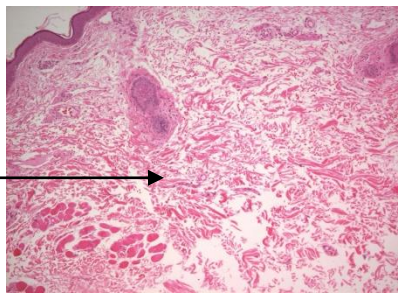
2) **Abnormal differentiation during lid fusion:**
   - 8th week - fifth month of gestation
   - premature separation: small coloboma
   - also: ankyloblepharon / rare ankyloblepharon filiforme adnatum
3) **Others:** Blepharophimosis, epicanthus, epiblepharon, distichiasis and ptosis

III - Aging Changes

<u>Causes:</u>

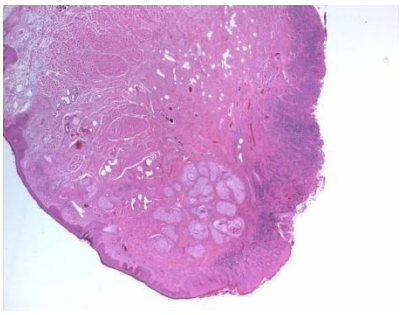
- Atrophy and laxity of the skin
- Loss of subcutaneous tissue.
- Relaxation of ligaments and attenuation of the orbital septum.
- Histologic degeneration of the collagen bundles of upper dermis, replaced by amorphous basophilic material + increase in the number of elastic fibers (curled and interwoven).

Curled Elastic Fibers



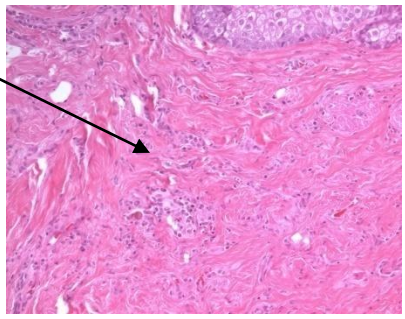
Changes:

- Dermatochalasis
- **Senile ectropion**

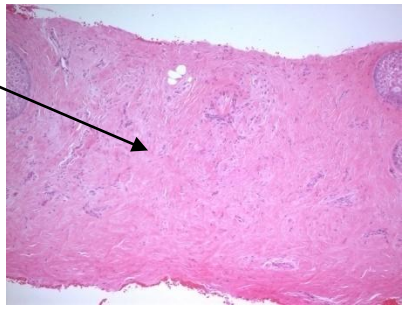


Entropion

Tarsal Scarring



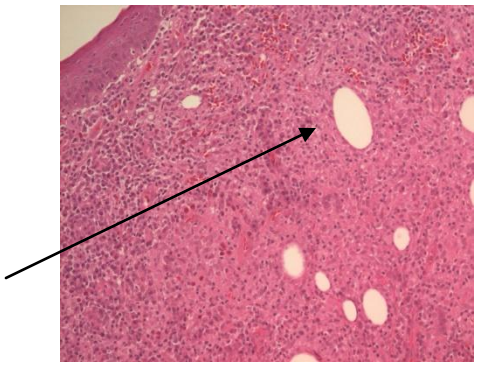
Tarsal Plate



Inflammatory lesions

- **Chalazion:** Most frequent granulomatous lesion of the eyelids.
  Histopathology: - epithelioid and giant cell response to liberated fat from sebaceous gland forming a ring around nonstainable lipid droplets.
  Old lesions: ± fibrosis and scarring.
  DDx: Sarcoidosis, TB, fungal disease.

Lipid with surrounding granulomatus reaction

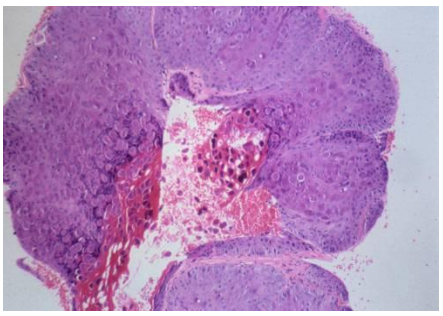


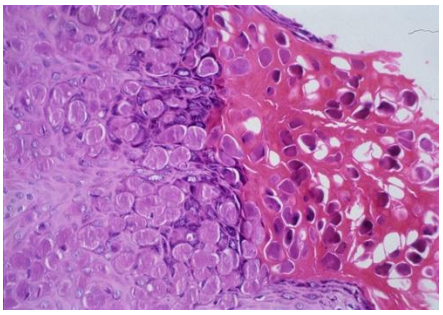
Molluscum contagiosum:

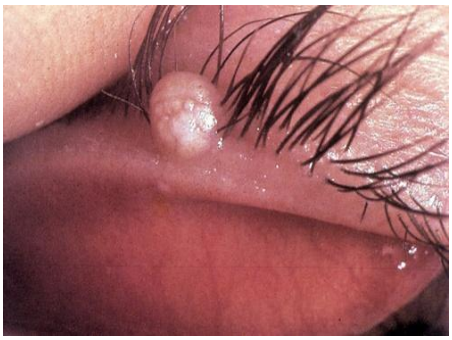
Clinically: - raised skin nodule with umbilicated center.
Cause: - Pox virus
Histopathology: - Acanthotic epithelium
- Molluscum (inclusion) bodies: infected epithelial cells with clusters of virus

become basophilic, replace the cytoplasm and increase in sIze.

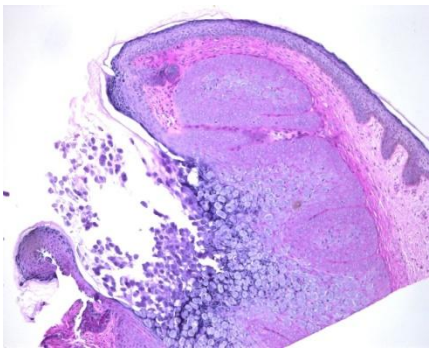
= Henderson - Patterson corpuscles.







Secondary Follicular conjunctivitis

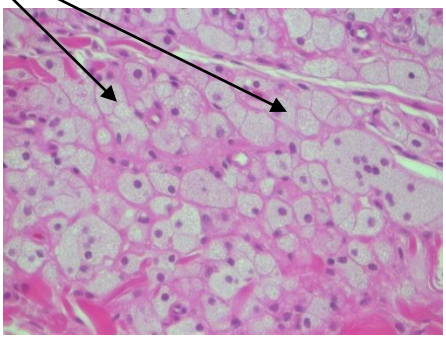


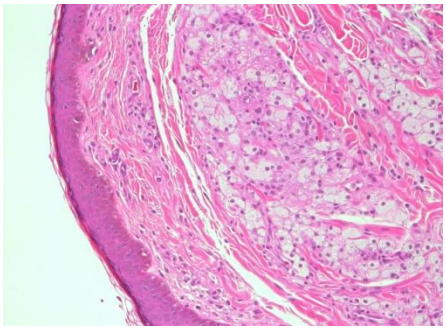
Xanthelasma:

- Usually in normal patients (2/3)
- Lipid analysis is necessary to R/O hypercholesterolemia
- Recurrence is more likely if:
  Multiple lesions or hyperlipidemia syndrome.

Eyelid xanthelasma = xanthelasma palpebrarum
soft flat or slightly elevated yellowish plaques.

- Histopathology:
- Nests of xanthoma or foam cells in superficial dermis
- cells: lipid - laden histiocytes





- **Fungal:**

  Blastomycosis: In North America
  Pseudoepitheliomatous hyperplasia
  Granulomatous reaction
  Microabcesses containing budding yeast of Blastomyces Dermatitidis.

- **Parasitic:**

  1-Phthiriasis Palpebrarum: Pubic louse. can cause follicular conjunctivitis.

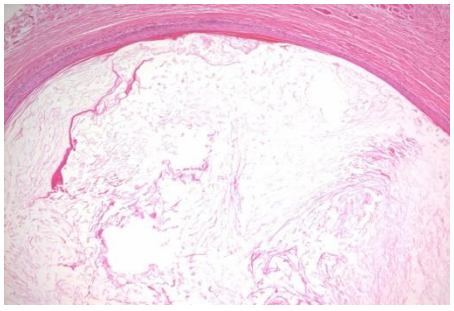
  2-Demodicosis: Demodex folliculorum/ brevis
  chronic blepharitis

Cysts

Skin cysts are named according to the derivation and type of epithelium that lines the lumen.

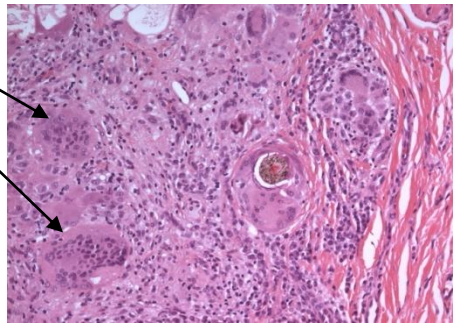
1) Epidermoid cyst:

- lined by keratinized stratified squamous epithelium
- contents: cheesy keratin material
- Epidermal inclusion cyst: (deposited epithelial cells within the dermis) Post Trauma or Surgery

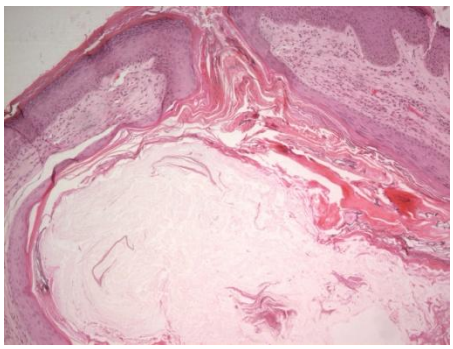


In case of rupture: foreign body granulomatous inflammatory reaction.

Giant Cells



- Others: Pilar/ Trichilemmal cysts



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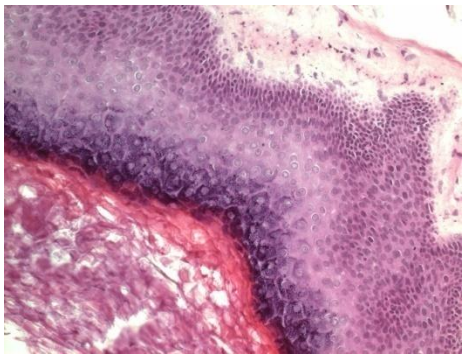
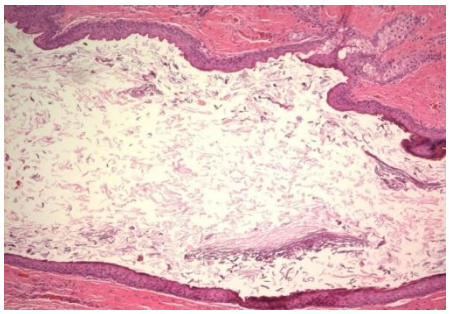
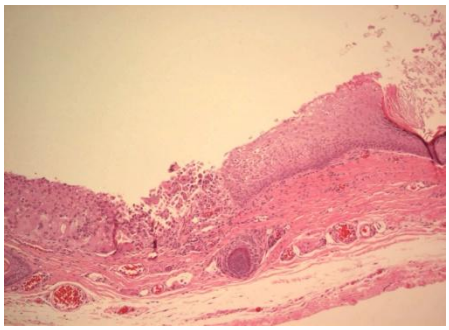


2) Dermoid cyst:

- lined by keratinized squamous epithelium
- Skin appendages: hair, sweat & sebaceous glands.
- Contents: Keratin



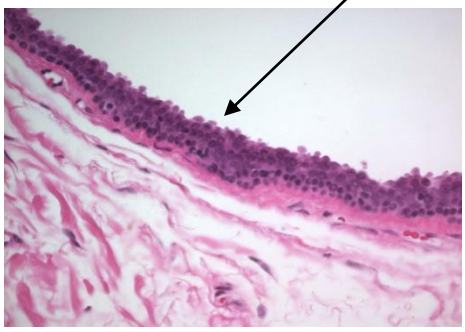


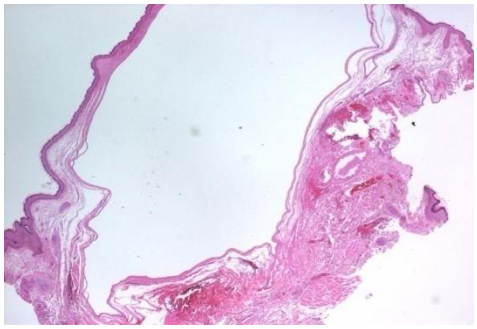
3) Sweat gland cyst:

= hidrocystoma or sudoriferous cyst.

- Eccrine lined by 1-2 layers of cuboidal epithelium resembling sweat duct, contains serous fluid.

- Apocrine: Similar but cells may show decapitation,
  clinically: often pigmented.

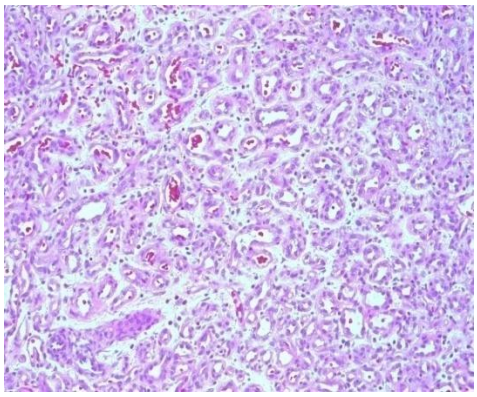
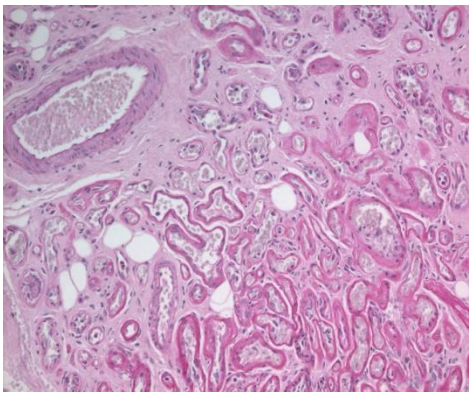




4) Ductal cyst: Dacryops

Vascular

- Capillary hemangioma is the most common, congenital
- Histology: endothelial - lined vascular channels similar to normal capillaries in contrast to large spaces in the cavernous type.

Glandular / Adnexal Tumors:

I – Eccrine/Apocrine Gland Origin:

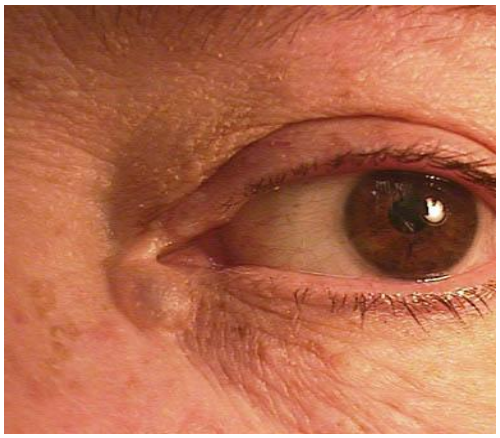
A) Benign Tumors:

1. Syringoma:

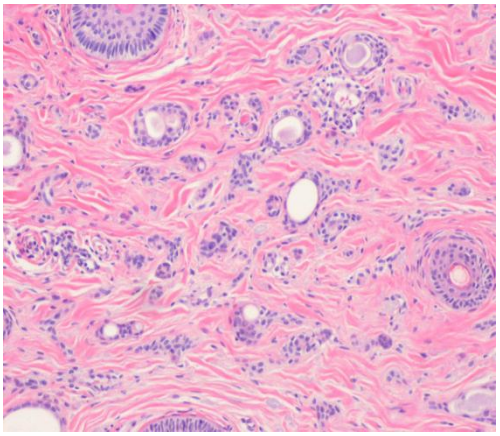
Clinically:

- Young women, common, benign
- Multiple yellowish, waxy nodules (1-2 mm)

Syringoma

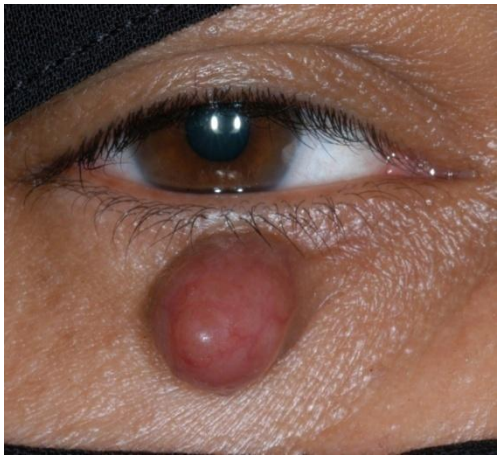


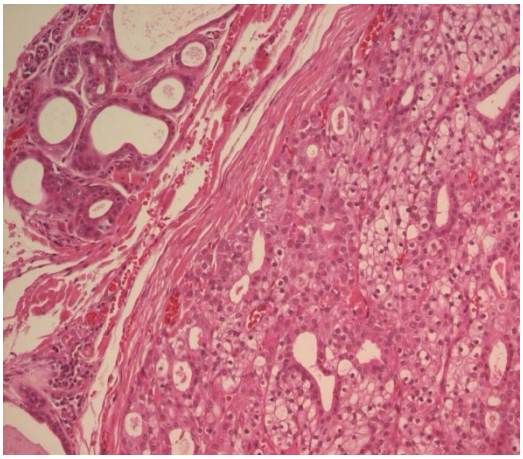
Paisley-tie pattern of tadpole-shaped ducts with horn cysts
Dense sclerotic strom



I - Eccrine/Apocrine Gland Origin:

2. Eccrine Acrospiroma = clear cell Hidradenoma

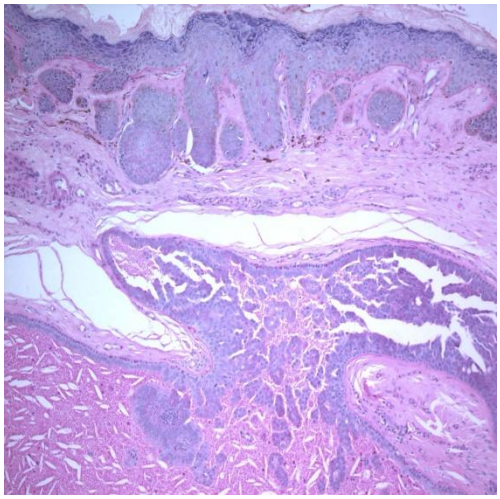




Histopathology:

- Cuboidal cells with pink cytoplasm
- Clear cell
- Cuticle-lined ducts & cystic degeneration

I - Eccrine/Apocrine Gland Origin:



3. Syringocystadenoma Papilliferum

Raised warty plaque.
One third occur within nevus sebaceus

Opens to surface.
Papillary fronds
Decapitation secretion

I - Eccrine/Apocrine Gland Origin:

B) Malignant tumors:

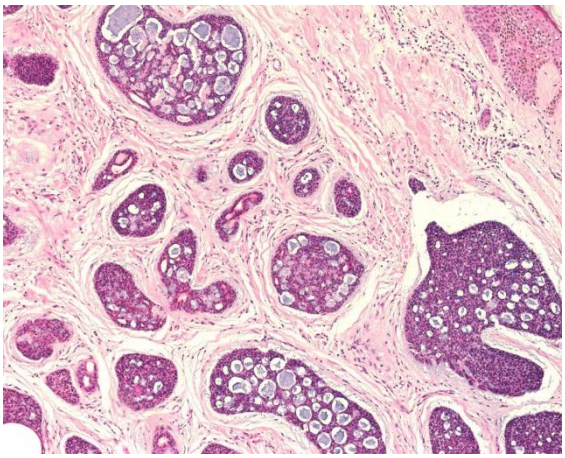
Adenoid cystic carcinoma:

- May resemble adenoid basal cell ca.

- Rare.

- Metastasis: uncommon.

- Histopathology: cribriform and tubular patterns



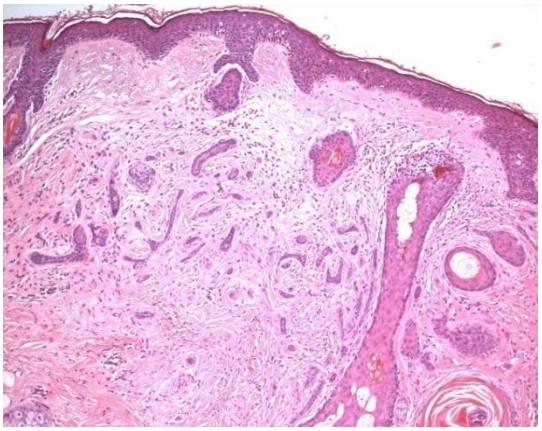
II - Hair Follicle Origin:

1. **Trichoepithelioma** = Brooke's tumor

   a. Solitary

   b. Multiple - autosomal dominant

Microscopy: Multiple horny cysts showing fully Keratinized center surrounded by islands of basaloid cells.



III - Hair Follicle Origin cont'd.:

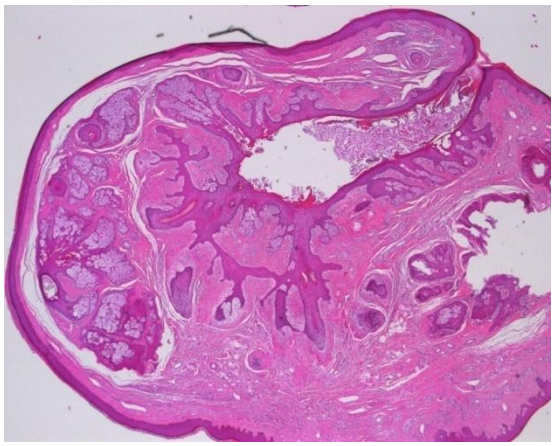
2. Trichofolliculoma:

a. Hamartomatous: most differentiated form of a pilar tumor.

b. Clinically: elevated nodule with central umbilicated area.

Central pore with small white hairs growing is strongly suggestive.

Small hair follicles emptying into a central infundibulum



3. Trichilemmoma:

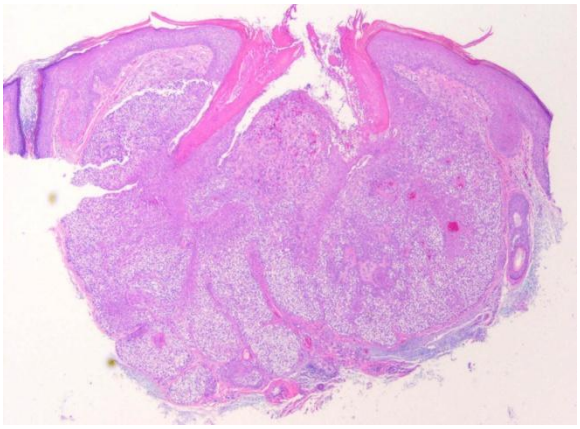
a. Benign tumor of outer hair sheath.

b. Clinically: - Predilection for the face

- Eyelid: most common after the nose.

- Cowden disease: AD, associated with breast and thyroid lesions, multiple skin lesions.

c. Histologically: Lobular acanthosis, composed of clear glycogen rich cells outlined by thick basement membrane



4. **Pilomatrixoma:**

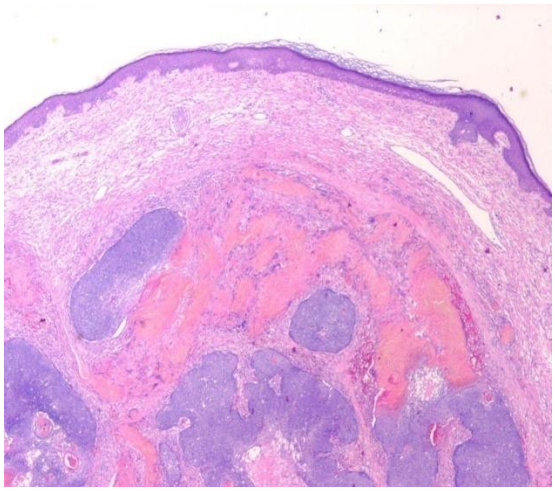
= Calcifying epithelioma of Malherbe.

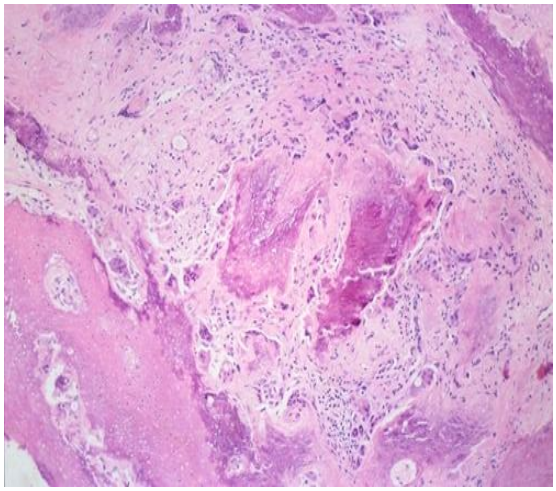
- Clinically: Subcutaneous nodule covered by normal skin.

Solitary, peculiar pink to purple color, tend to occur in children

Most common sites: face & upper extremities

- Histopathology: Basophilic cells & shadow cells which often calcify



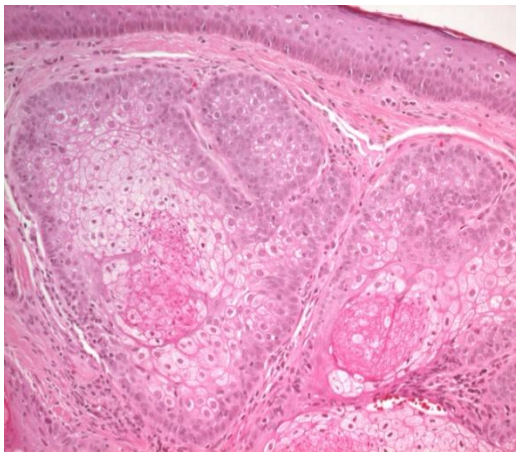


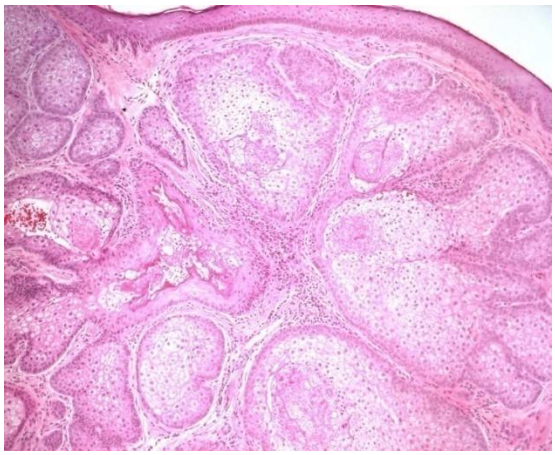
IV – Sebaceous Gland Origin:

1. **Adenomatoid sebaceous hyperplasia**

   Cluster of sebaceous glands, around follicular opening.

   Normal germative basaloid layer at lobule periphery.



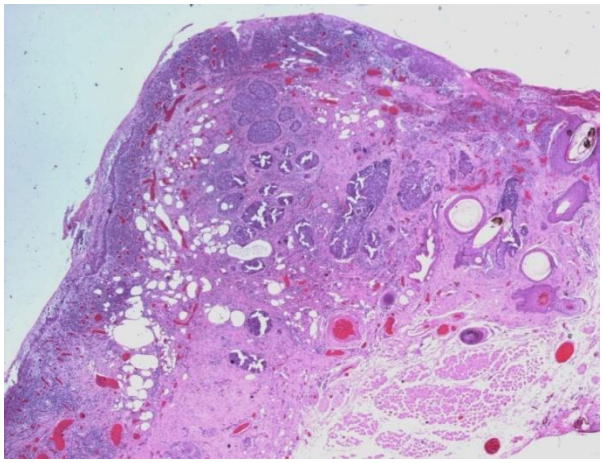


Muir-Torre Syndrome

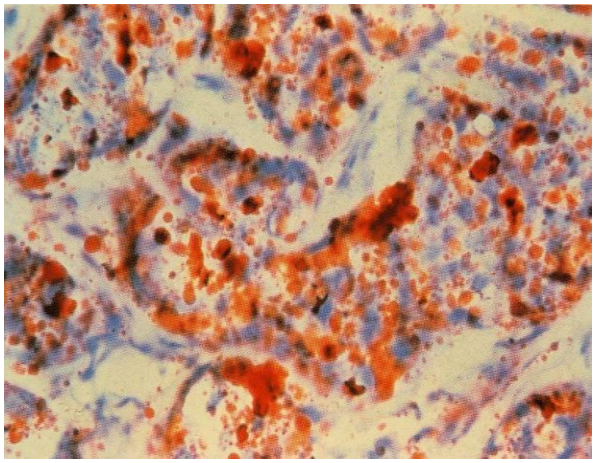
= Association of sebaceous gland tumors of skin (mostly adenomas) and visceral malignancy (most common colorectal ca., genitourinary & breast.)

Sebaceous gland carcinoma:

- Arise from sebaceous glands (meibomian, glands of Zeis, hair associated or of the caruncle)
- Site: eyelid is the most common site in the body
  mostly on the upper lids (2/3) because meibomian glands are more numerous (x2)
- 1 - 3% of all malignant lid tumors.



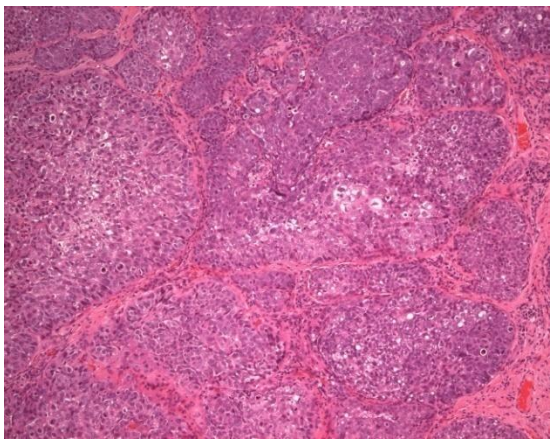
- Histologically:
- Differentiation: - well, moderate and poor = anaplastic carcinoma, with atypical and bizarre
  - mistoses => frozen section with oil red 0 stain.



Histologically:

b) Patterns:

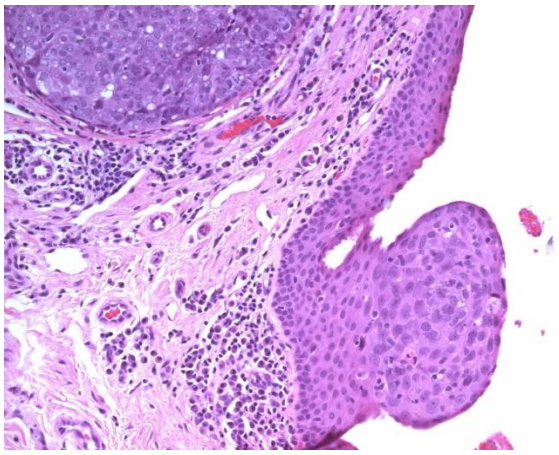
Lobular:	Basaloid features
Comedoca:	Central foci of necrosis
Papillary:	Fronds of neoplastic cells => resemble squamous cell +foci of cells with sebaceous differentiation (foamy, vaculated) mixed

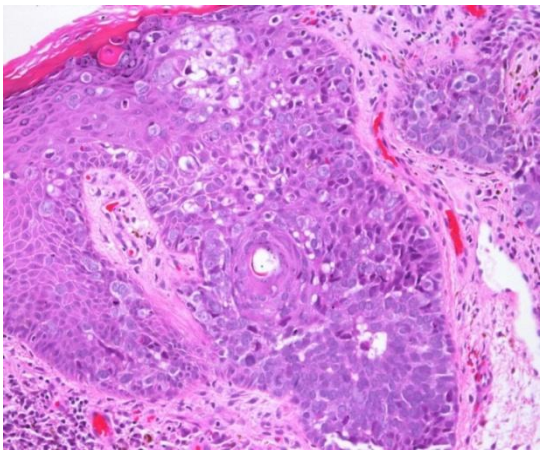


c) Spread:

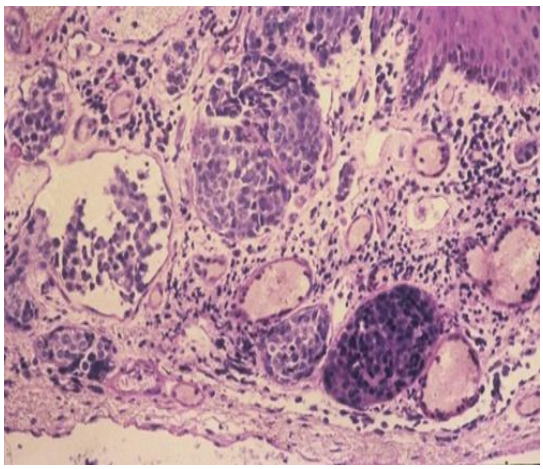
Pagetoid: Invade overlying epithelium
Direct extension: ± perineural, into lymphatics
Vascular invasion -> distant metastasis after regional L.N.

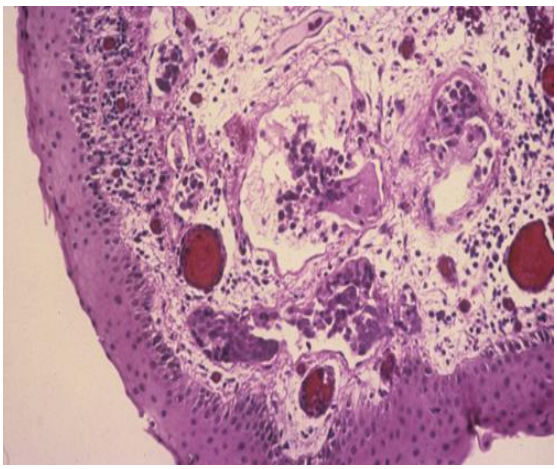
Pagetoid spread to conjunctiva/skin





Intralymphatic spread





Sebaceous gland carcinoma:

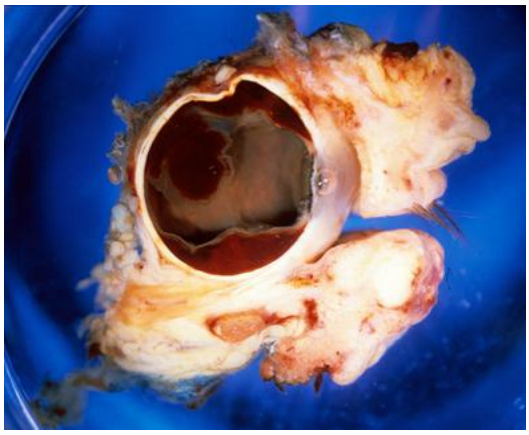
- Prognosis: Bad prognostic factors

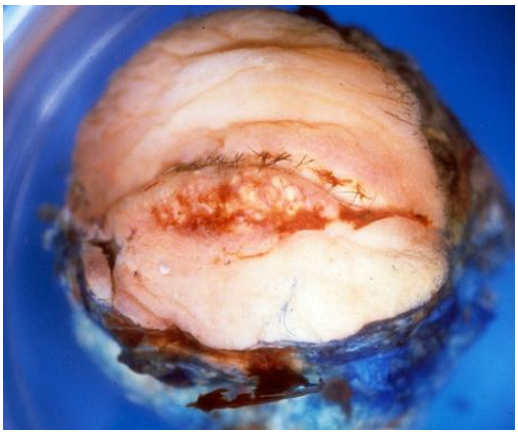
a) location: in upper lid
b) size: 10 mm or more in max diameter
c) origin: meibomian gland
d) duration: symptoms > 6/12
e) growth pattern: infiltrative
f) differentiation: moderate to poor
g) others: multicentric, intraepithelial carcinomatous changes (pagetoid), lymphatic or vascular invasion.

- Tm: Wide surgical excision + frozen section control

Palliative radiotherapy: in none surgical cases

- Mortality: 15% old AFIP series.





Epithelial Tumors cont'd.:

I. Benign:

1) Squamous papilloma:

- most common benign lesions of the eyelid.
- Sessile or pedunculated.
- Often multiple ± small Keratin crust.
- Histology: benign hyperplasia of squamous epithelium overlying fibrovascular core: derived from dermis, epidermis = acanthotic ± hyper & parakeratosis.

NOTE: Verruca vulgaris is similar but with viral inclusions (HPV_2)

2) Pseudocarcinomatous Hyperplasia:

a. associated with chronic inflammation.
b. Histologically:
- interconnected islands of well-dif. Squamous epithelium + invasive acanthosis.
- moderate inflammatory rx.

3) Keratoacanthoma:

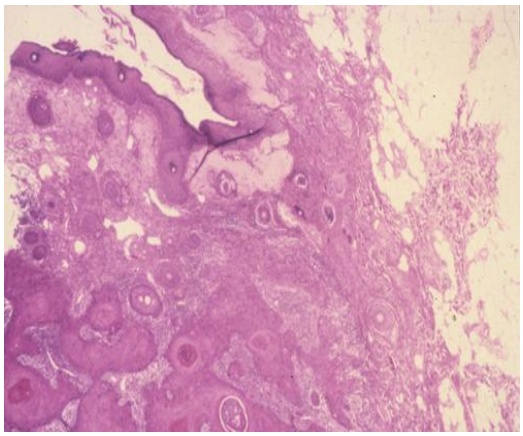
a. Special variant of pseudocarcinomatous hyperplasia that occurs in exposed areas of skin vs. variant of squamous cell ca.
b. Clinically: rapid onset dome - shaped nodule with central keratin filled crater and elevated margins.

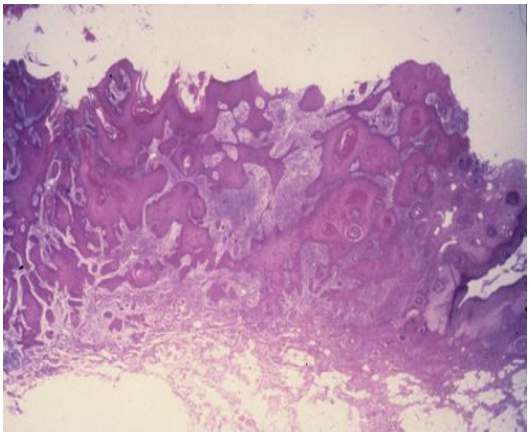
Spontaneous regression.

Can occur in immunosuppressed individuals.

c. Histology:

Islands of well-diff. squamous epithelium surrounding central mass of keratin.
Base is well demarcated by moderate inflammatory rx.
± epithelial infiltration of striated ms (orbicularis fibers) and around nerves.





4. Seborrheic keratosis:

a. Common benign lesions of the eyelid in elderly.
b. Clinically: Raised mass usually hyperpigmented +
c. Histology:

Three types:

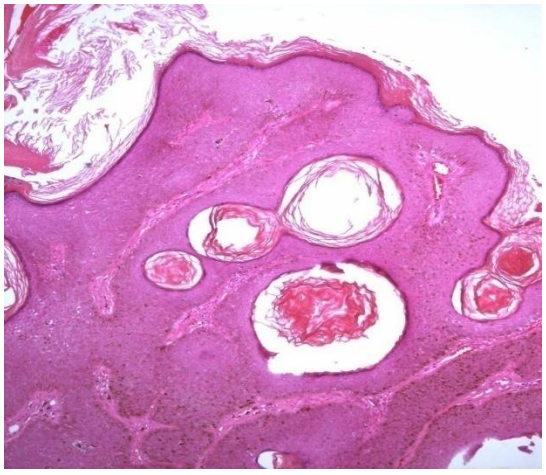
- hyperkeratotic: tendency for papillomatosis

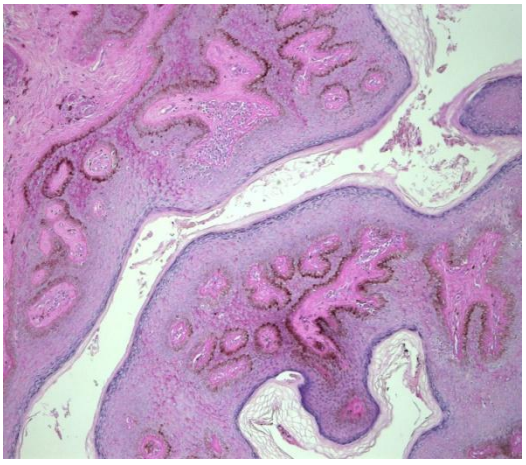
- acanthotic: horn cysts

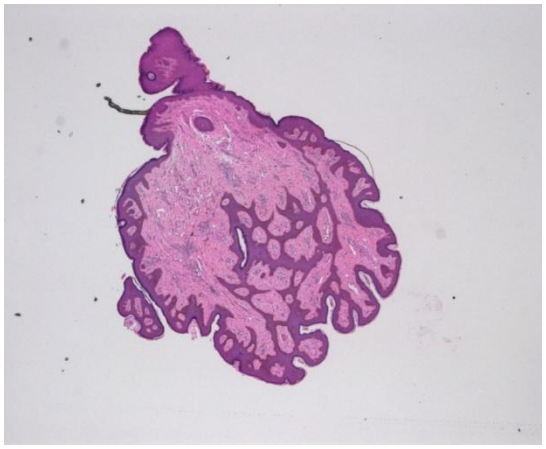
- adenoid: less keratinization, branching strands: double row of basaloid cells.

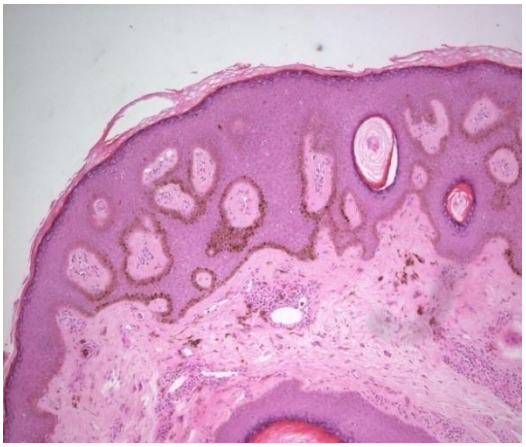
± increased melanin in keratinocytes.

± chronic inflamm. In dermis = irritated Seborrheic Keratosis



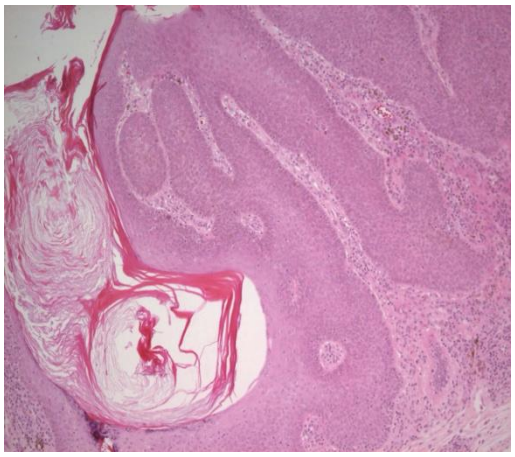


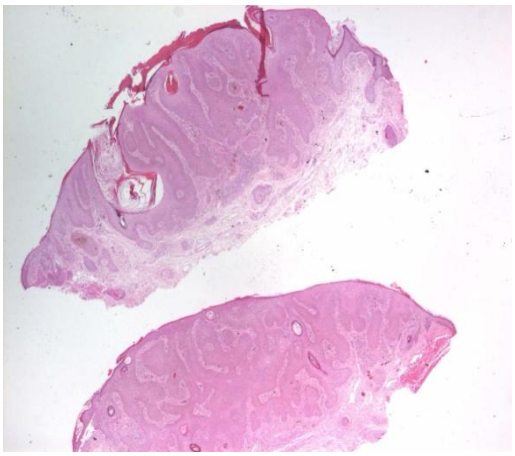




5. Inverted follicular keratosis:

- nodular keratotic mass + pigmented
- tendency to recur if incompletely excised
- histology: proliferation of both basaloid and squamoid elements with area of acantholysis + squamoid eddies.
  ? Form of irritated seborrheic keratosis.





II. Precancerous:

1) Actinic Keratosis:

= solar or senile keratosis.
- most common precancerous cutaneous lesion.

a. Clinically:

Most common sites: face (<u>+</u> eyelids), dorsum of hand, scalp.
Sun exposed areas
Fair - skinned middle-aged to elderly
Single or multiple scaly keratotic flat - topped lesions

Size: few millimeters
Early lesions: erythematous scales.
± other cutaneous lesions.

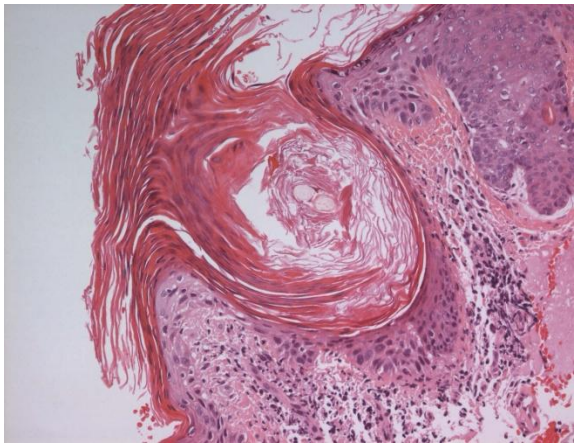
b. Histology:

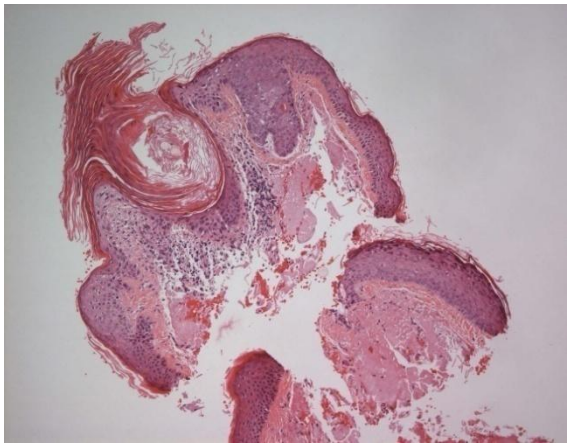
- Epithelium:

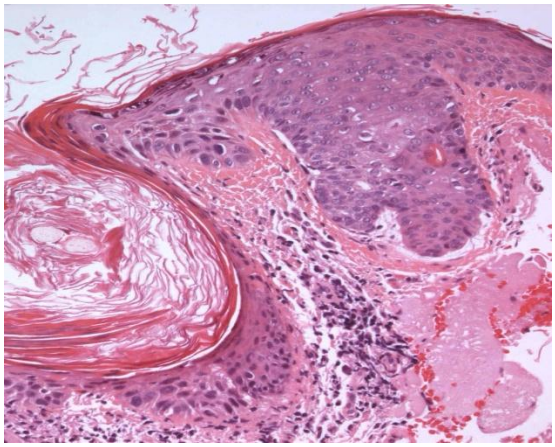
  - acanthosis, hyper & parakeratosis and individual cell dyskeratosis as an indicator of propensity toward malignancy.
  - Atypical Keratinocytes (epithelial dysplasia), loss of intercellular bridges => clefts with sparing of the ostia of pilosebaceous structures.

- Dermis:

  - basophilic degeneration of collagen = solar elastosis
  - chronic inflammation
  - Types: hypertrophic
    atrophic
    bowenoid
    Solitary lichen planus - like keratosis







c. Prognosis:

- Progression to squamous cell carcinoma: variable, old series 12-13%.
  As high as 25% and recently much lower incidence 0.1%
- Excellent prognosis of squamous cell ca. arising in actinic keratosis, rarely metastasize (0.5%)

2) Bowen's Disease

= carcinoma in situ.

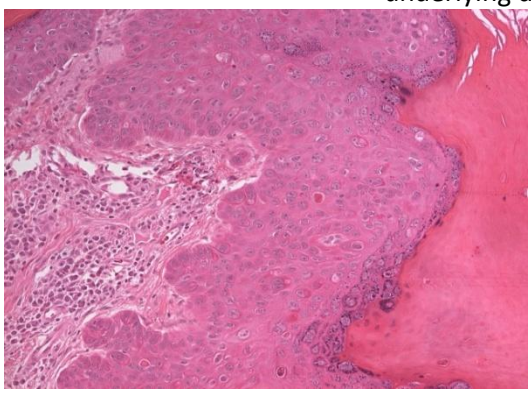
Occurs only in both non-exposed and sun-exposed areas of skin association with internal or visceral malignancies (≥ 25%)

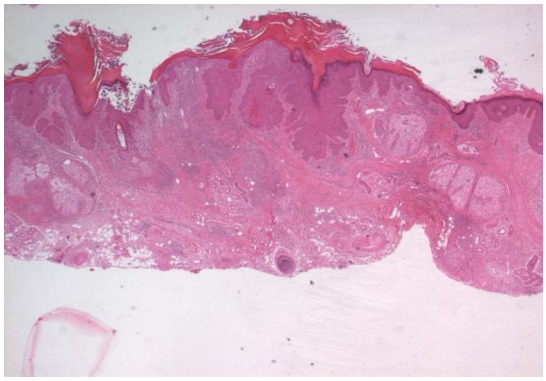
a. Clinically:

erythematous, pigmented, nodular or ulcerated
average age 55 yrs.
? Arsenic exposure.

b. histologically:

- Epidermis:
  striking loss of polarity
  atypical epithelial proliferation at all levels
  Involvements of the ducts of hair follicles and sebaceous glands.
  Intact basement membrane. (PAS)
- Dermis:
  lack of penetration of cancerous cells into the underlying dermis is the histologic hallmark.





3) Radiation Dermatosis:

a. associated with high radiation doses 8000 - 12,000 rads
b. basal keratinocytes are more susceptible
c. Principal lid changes:
- loss of lashes
- chronic dermatitis
- pigment. Changes
- atrophy
- telangiectasis
- postradiation tumors.

4) Xeroderma pigmentosum:

- Progressive, sun-exposed skin starting in early childhood.
- Autosomal recessive
- Defect in DNA repair secondary to deficiency of ultraviolet light - specific endonuclease.

- Stages of skin manifestation:
a) Erythema, scaling and freckles
b) pigmentation and telangiectasis
c) various malignant neoplasms: sq. cell ca., BCC, sarcoma and 3% incidence of malignant melanoma.
- Also: conjunctival malignancy, reported malignant melanoma of the iris.
- Prognosis: metastasis, death can occur.

EPITHELIAL TUMORS, cont'd.:

III. Malignant:

1) Basal cell Carcinoma:

c. Histology

- Histogenesis is disputed

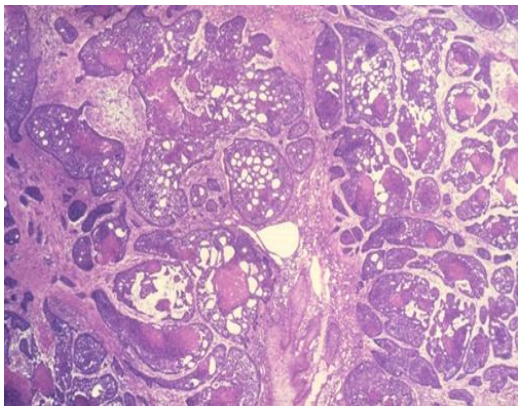
- Theory: ? From primary basal epithelial germ cells (primordial cell derived from surface ectoderm).

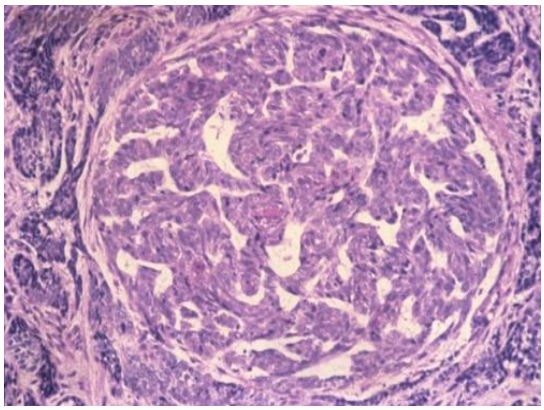
Pluripotential embryonal cells remain within epidermis throughout life -> propensity of BCC to differentiate toward a wide variety of skin and skin appendage - like structures.

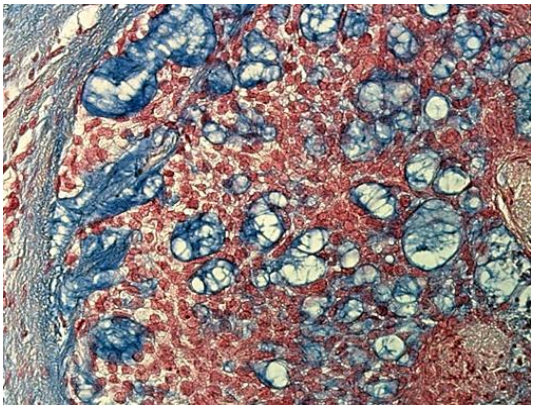
- Differentiation:

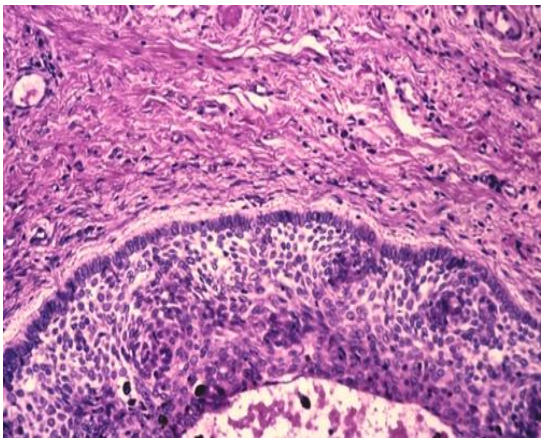
- Differentiated:

  features of several cutaneous appendages & named accordingly (keratotic - hair structures, cystic - sebaceous gland, adenoid - apocrine & eccrine glands) more in nodulo-ulcerative type of BCC.







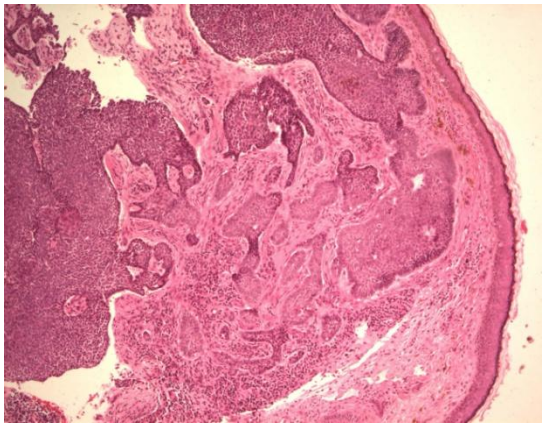


- Undifferentiated:
  solid epithelial lobules with prominent peripheral palisading.
- Metatypical = basosquamous
  intermediate morphology between BCC & SCC.

III. Malignant:

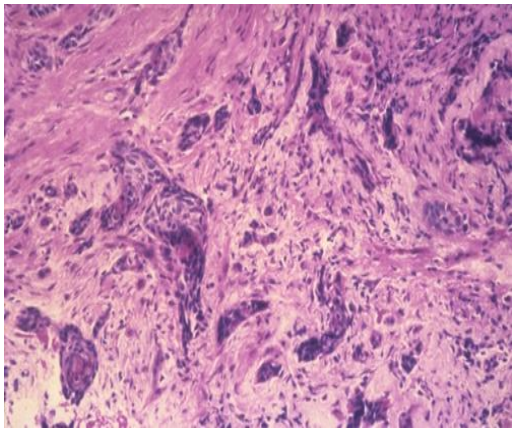
1) Basal cell Carcinoma:

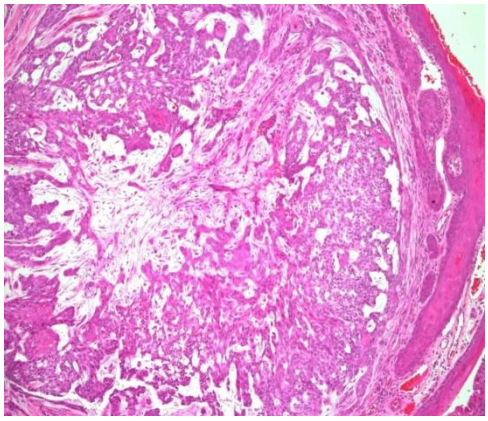
- Growth pattern:
- Nodular - localized lobules of tumor with pseudocapsule can be solid or cystic - retraction artifact.
- Ulcerative - chronic dermal inflammatory infiltrate.

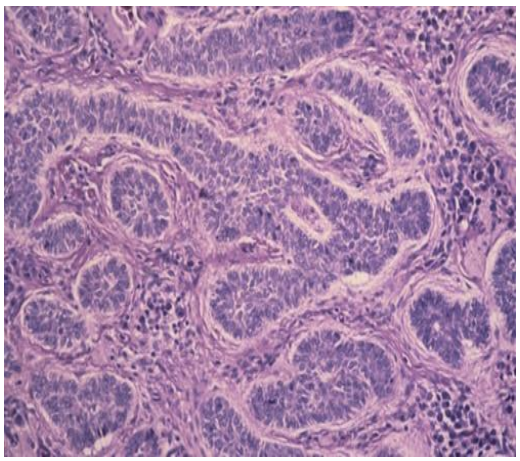


- Growth pattern:
  - Sclerosing - strands of basaloid cells embeded in dense fibrous stroma (stromal desmoplasia). These strands are often called Indian file => aggressive and deeply infiltrating into dermis and subcutis.
  - Multicentric - diffuse involvement of epidermis & superficial dermis.

The last three types often extend beyond the margins of apparent clinical involvement
-> Frozen section control is essential at time of surgical excision.

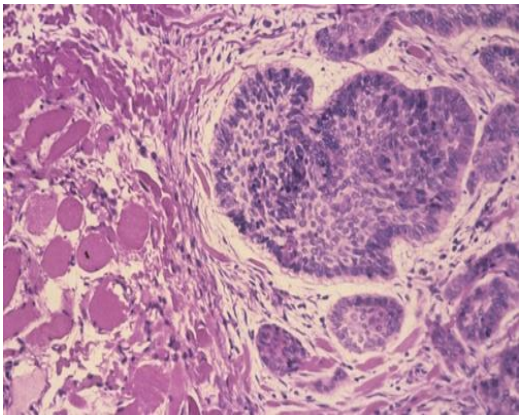






d. Prognosis:

- Recurrence rate: Variable - depends on surgical technique (some report no evidence of recurrence with frozen sections)
- Invasion: Rare intraocular invasion.
  May invade cranial cavity -> 2^0 meningitis
- Metastasis: Rare incidence range 0.028% to 0.55%



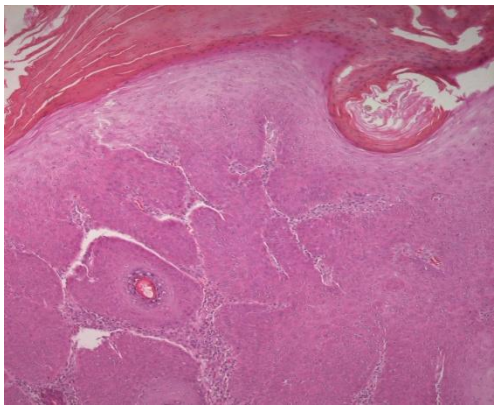
2) Squamous cell carcinoma:

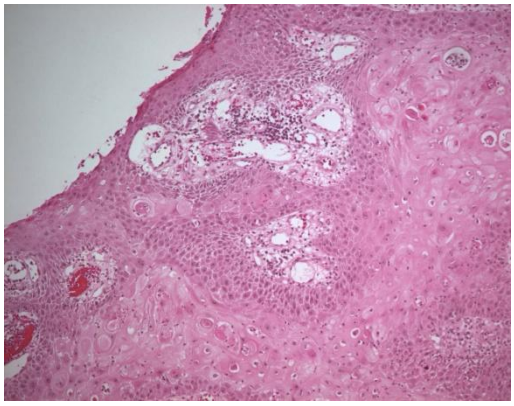
a. Incidence:
- elderly, fair - skinned
- most commonly lower lid margin
- accounts for less than 5% of epithelial neoplasm of eyelids.
- arise de novo or from preexisting lesions.

b. Clinical:
- elevated indurated plaque or nodule, may ulcerate.
- ± grayish - white in well differentiated tumors (keratin)
- early lesions: excellent prognosis (especially within actinic keratosis), wide local excision is curative.

c. Histology: Variable differentiation.

- Well diff.: polygonal cells with prominent nuclei, keratin pearls, intercellular bridges, dyskeratotic cells.
- Spindle cell variant:
confused with fibrous histiocytoma or fibrosarcoma





c. Histology:

- Adenoid variant:
uncommon eyelid involvement
atypical cuboidal epithelial cells forming pseudo-glandular structures.
Good prognosis, wide local excision is curative

Melanocytic Tumors:

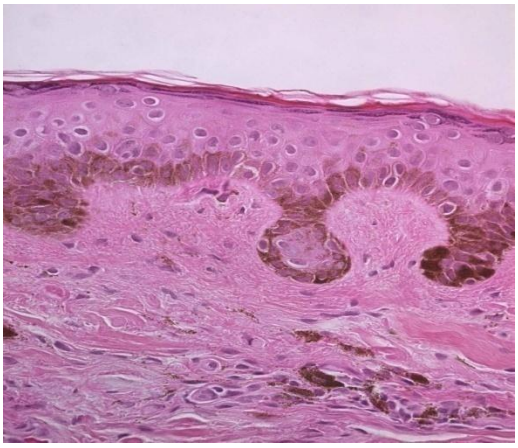
I - Benign:

1) Nevocellular Nevi:
   - Has variable clinical appearance.
   - Kissing nevus:
     simultaneous involvement of upper and lower lids (with lid margin involvement) - embryologic nests of nevus cells meet during lid fusion (18th week until 5th month)

   - Classification: Depends on the position of nevus cells in the skin layers.

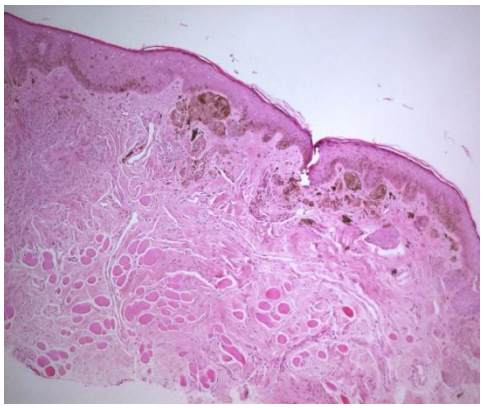
     a. Junctional:

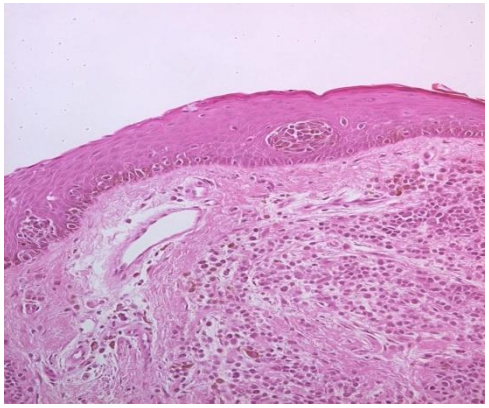
     - Proliferation at nevus cells in the deeper layers of epithelium and at the epidermal - dermal junction.
     - Have the capacity of "dropping off" into the dermis.
     - Clinically flat pigmented lesions.



     b. Compound:

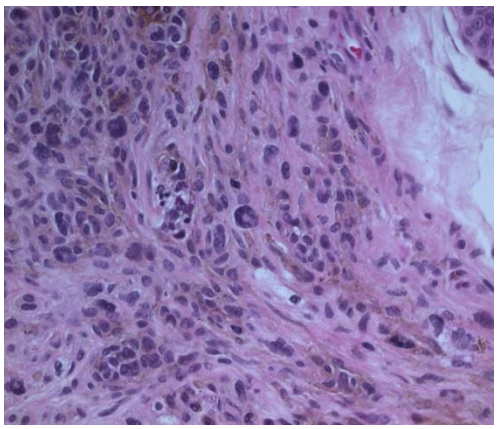
     - Junctional activity + intradermal nests of nevus cells.
     - More common than pure junctional nevus.
     - Both can undergo malignant change.

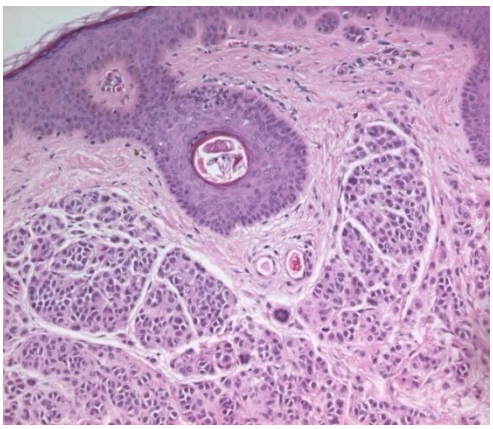




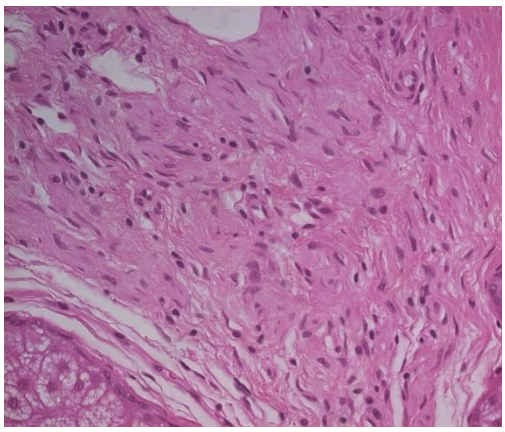
c. Intradermal:

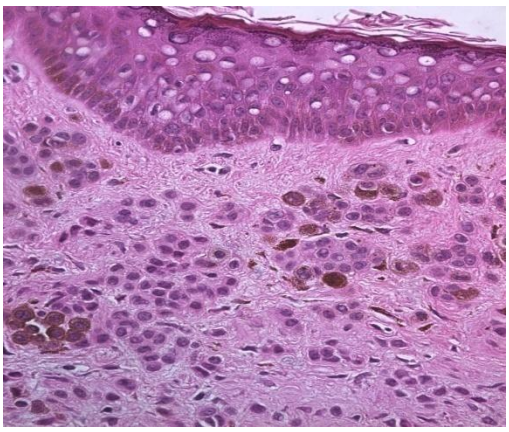
- Most common & most benign.
- Clinically: papillomatous or pedunculated ± hair, can be amelanotic
- Histology:
  - nests of nevus cells totally confined to the dermis, separated from the epidermis by a band of collagen = Grenz Zone.
  - in the eyelid nevus cells may extend into deeper dermis reaching orbicularis ms.
  - giant multinucleated nevus cells occur only in mature intradermal nevi -> indicate the benign nature of the lesion.





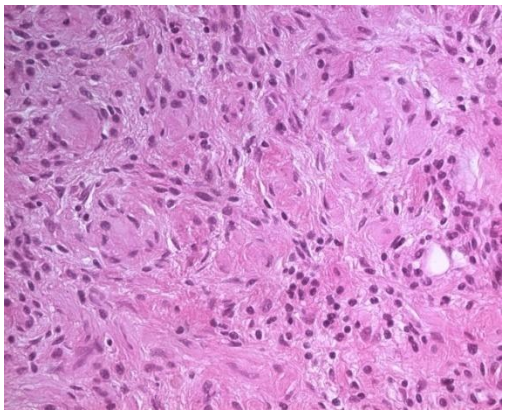
- Types of nevus cells: depending on their location in the dermis
  - Type A: upper dermis
    resemble epithelioid cells.
  - Type B: middle dermis
    smaller, resemble lymphoid cells
  - Type C: lower dermis
    elongated, resemble fibroblasts, little or no melanin.

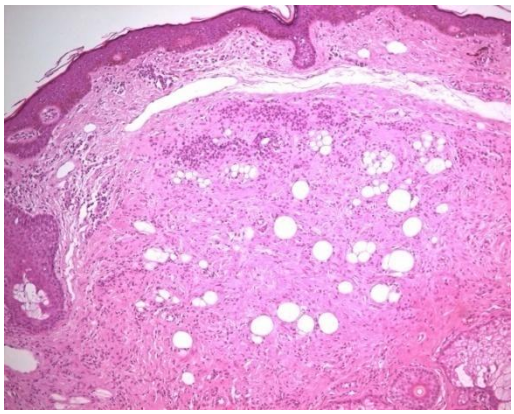


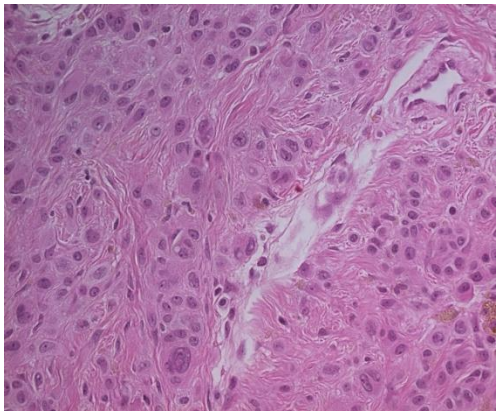


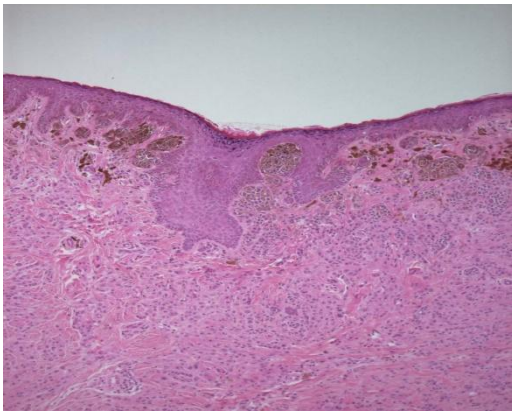
2) Other variants of nevi

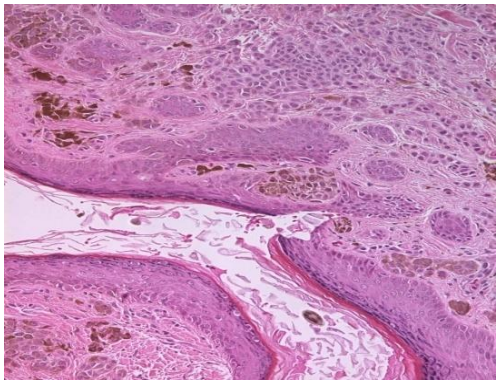
- Balloon cell nevi
- Spindle or epithelioid nevi = compound nevus mainly affecting children & young adults.
- Giant congenital melanocytic nevi
- Blue nevi - from dermal melanocytes
- Freckle - from epidermal melanocytes

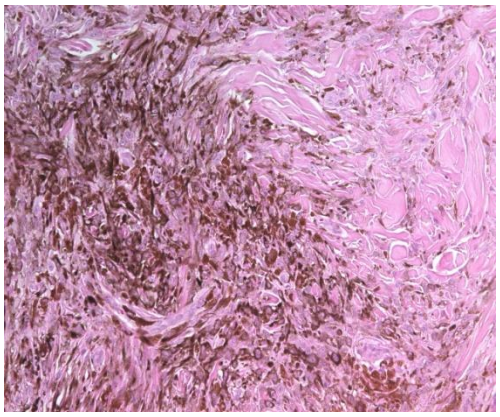


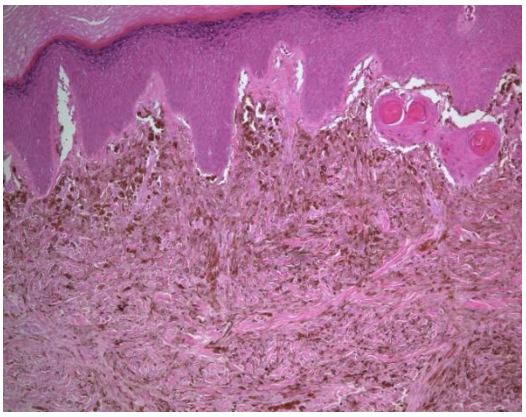












II – Malignant Melanoma:

a) Incidence:

- 1% of all malignant neoplasms of the eyelid in USA.
- Recent 3 - 5 fold increase in the incidence of cutaneous m.m.? Due to increased voluntary exposure to sun.
- almost 2/3 of all deaths from cutaneous cancer are by m.m.
- involves lower lid more often than upper.
- may arise from pre-existing nevus, may arise de novo.

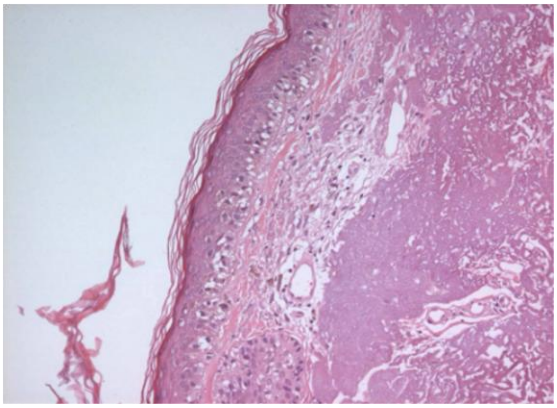
b) Types:

1. Lentigo maligna melanoma:

develops in a preinvasive lesion called:

- **Hutchinson's Melanotic Freckle or lentigo maligna =**

- Flat macule with variable degree of pigmentation in elderly individuals (sixth decade), sun-exposed skin.
- Histopathologically:
  - diffuse hyperplasia of atypical pleomorphic melanocytes along the basal cell layer of epidermis = (radial growth phase)
  - extends into outer sheaths of pilosebaceous structures.



2. Superficial spreading melanoma:

= pagetoid Melanoma

- Younger individuals (fifth decade), nonexposed skin.
- Most commonly: upper back, legs
- Clinically:
  - spreading pigmented macule (variable color) with irregular outline & palpable borders.
  - white areas of spontaneous regression
- Microscopically:
  Atypical melanocytes with pagetoid features invasive vertical growth: variable types of melanoma cells.
- 5 - year survival 69%

3. Nodular melanoma:

- Small blue-black or amelanotic pedunculated nodule rapidly growing.
- usually in 40-50 y., twice as common in men as in women.
- microscopically: adenoid structures - large anaplastic epithelioid cells, ? only vertical growth phase.
- 5 - year survival 44%

4. Acral Lentiginous Melanoma:

- Mainly on palms & soles.

Note:

a. 20% of nodular melanoma & 50% of superficial spreading m. arise from nevi.

Clinical signs of malignant transformation:

- Change in color, size or shape
- Crusting, bleeding or ulceration
- Pain, itching or tenderness
- Change in surrounding skin

b. In eyelid malignant melanoma, lid margin or conjunctival involvement has ? worse prognosis.

- Clark Classification:

c) Prognostic Factors:

Level of Invasion (5 - year survival)

Level 1 - confined to epidermis with intact B.M.	100%
Level 2 - early invasion of papillary dermis	100%
Level 3 - fills papillary dermis & reaches interface (papillary/reticular)	80%
Level 4 - penetrates reticular dermis	65%
Level 5 - invades subcutaneous tissue	15%

III – Dysplastic Nevus Syndrome:

- Atypical cutaneous nevi in children and adolescence.
- Autosomal dominant.
- Family members are at high risk for cutaneous melanoma.
- Histologically:

identical to areas of regression frequently observed in superficial spreading m.

Miscellaneous lesions:

I - Lipoid Proteinosis:

a) Autosomal recessive

b) Clinically:

1. Small nodules along lid margins
2. Waxy appearance
3. Distortion of cilia

c) Microscopic:

1. Early lesions: thickening of capillary wall + deposition of hyaline material around basement m.
2. Fully developed lesions: homogenous eosinophilic hyaline material in dermis => strongly PAS positive.

II - Merkel Cell Tumor:

a) Uncommon generally in the skin.

b) Origin: - Merkel tough spots in the deeper layers of epidermis adjacent to hair follicles (cilia in eyelid)

c) Merkel cell CA of the eyelid: 1st case reported in 1980.

d) Clinically: painless nodule with reddish - blue hue resembling an angiomatous lesion.
e) Microscopic: poorly differentiated with immunohistochemical studies similar to apudomas.
f) Tm: wide surgical excision with frozen section control, to overcome the high incidence of local recurrence.

III - Carney's Complex:

a) Clinical:
   1. Cutaneous and cardiac myxomas
   2. Multiple pigmented skin lesions (also conjunctival)
   3. Endocrine overactivity.

b) Eyelid myxomas:
   1. Found in up to 70% of patients.
   2. Histologically:
      Nonencapsulated dermal hyaluronic acid substance with stellate mesenchymal cells -> myxoid stroma.

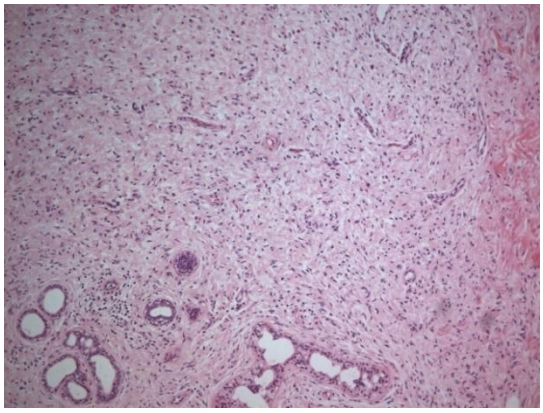
IV - Calcinosis Cutis:

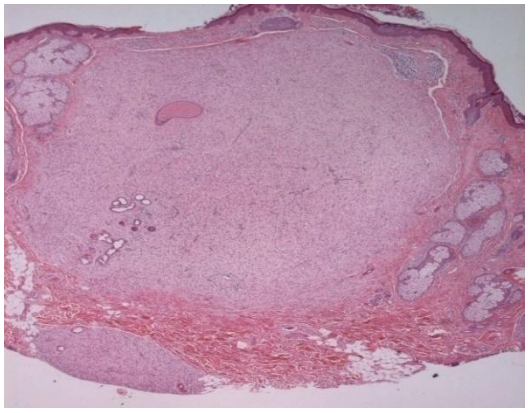
a) Types of calcinosis cutis:
   1. Metastatic
   2. Dystrophic
   3. Idiopathic

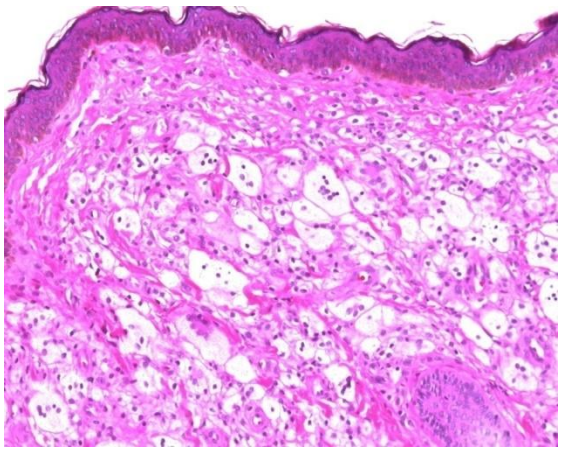
4. Subepidermal calcified nodule:

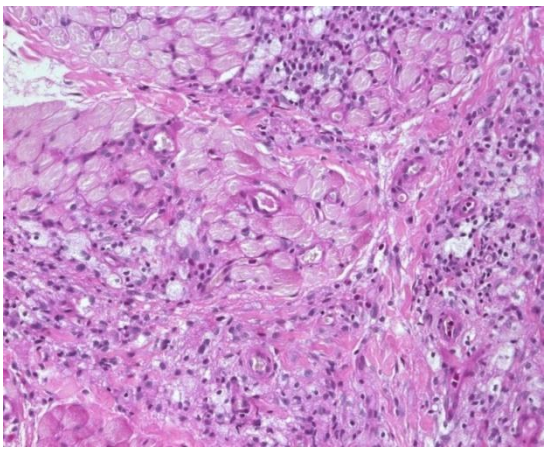
- small raised yellowish - white nodule
- firm or hard on palpation.
- histopathology: epidermis: acanthosis
  dermis: homogenous masses of calcified material.
  ± macrophages & FB-type giant cells.
- pathogenesis: unknown
  ? From pre-existing structure (e.g. sweat ducts or nevus cells)

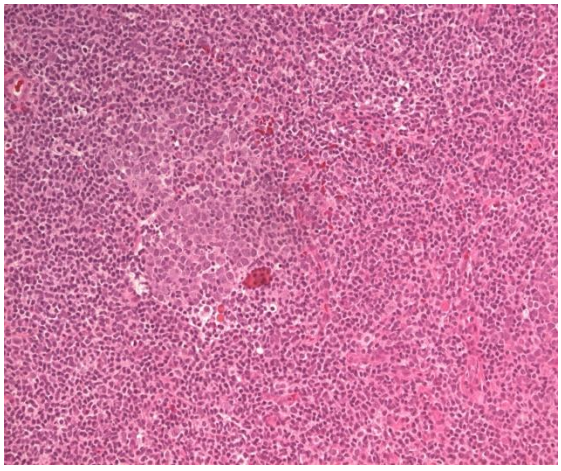
Neurofibroma

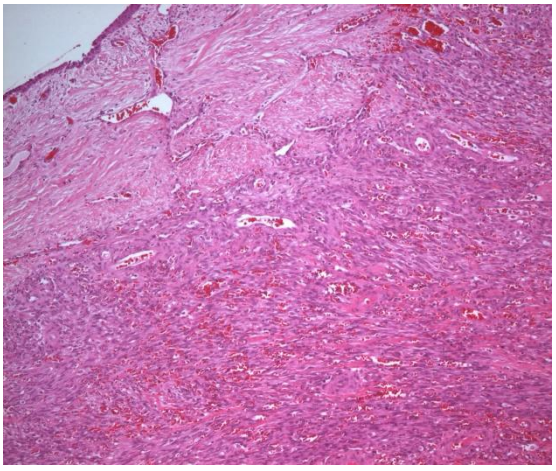




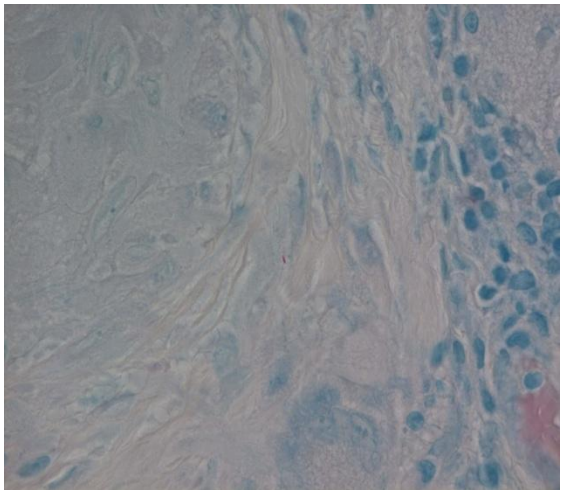


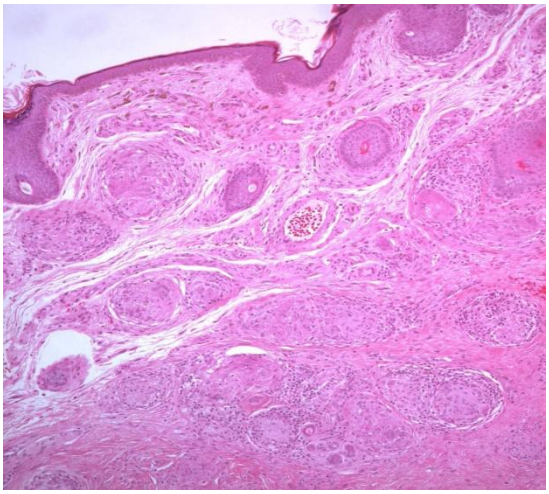






Leprosy





PATHOLOGY OF EYELIDS

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