Benign and Malignant lesions of oral cavity

- Benign –
  - The term "benign" refers to a condition, tumor, or growth that is NOT cancerous.
  - This means that it does not spread to other parts of the body or invade and destroy nearby tissue.
  - Benign tumors usually grow slowly.
  - In general, a benign tumor or condition is not harmful. However, this is not always the case. If a benign tumor is big enough, its size and weight can press on nearby blood vessels, nerves, or organs, or otherwise cause problems.
- Malignant (Neoplasm)
  - A tumor is a growth of tissue that forms an abnormal mass. Tumors generally provide no useful function and grow at the expense of healthy tissues.

- Epithelial pathology
- Connective tissue pathology

Epithelial pathology

Benign lesions

- Squamous papilloma
- Melanocytic nevus
- Leukoplakia
- Erythroplakia
- Smokeless tobacco keratosis
- Oral sub mucous fibrosis
- Nicotine stomatitis
- Actinic keratosis
- Actinic cheilosis
- Keratoacanthoma

Malignant lesions

- Squamous cell carcinoma
- Verrucous carcinoma
- Spindle cell carcinoma
- Adenosquamous carcinoma
- Carcinoma of maxillary sinus
- Nasopharyngeal carcinoma
- Basal cell carcinoma
- Melanoma

Connective tissue pathology

Benign lesions

- Fibroma
- Giant cell fibroma
- Inflammatory papillary hyperplasia
- Pyogenic granuloma
- Peripheral giant cell granuloma
- Peripheral ossifying fibroma
- Neural lesions
- Hemangioma

Malignant lesions

- Fibrosarcomas
- Malignant fibrous histiocytoma
- MPNST
- Angiosarcoma
- Kaposis sarcoma
- Leiomyosarcoma
- Rhabdomyosarcoma
- Metastasis to oral soft tissues.

Terminologies

- Precancerous lesion
- Precancerous condition
- Malignant transformation potential
- Relative risk

Precancerous lesion

- Also called Precancer, Premalignancy
- A benign, morphologically altered tissue that has a greater than normal risk of malignant transformation.

Precancerous condition

- A disease or patient habit that does not necessarily alter the clinical appearance of local tissue but is associated with greater than normal risk of precancerous lesion or cancer development in that tissue.

Malignant transformation potential

- The risk of cancer being present in a precancerous lesion or a condition either at initial diagnosis or in the future.
- Usually expressed as a percentage
- The potential for mucosa without precancerous lesion or condition is called normal.

Relative risk

- A specific epidemiologic measure of the association between exposure to a particular factor and the risk of acquiring a disease, expressed as a ratio of the incidence or prevalence of a disease among those exposed and those not exposed to the factor.

Leukoplakia

- Leuko – white, plakia – patch
- WHO def - a white patch or plaque that cannot be characterized clinically or pathologically as any other disease.
- Could be due to thickened keratin layer or thick spinous layer masking the normal vascularity
- Considered to be a precancerous lesion

Etiology

- Tobacco – 80% in smokers,
  - increase in number and larger lesions
  - Disappear or smaller when stopped
- Alcohol - Synergistic effect with tobacco
- uv radiation – lower lip
- Micro-organisms
  - Tertiary syphilis
  - Candida albicans
  - HPV 16 & 18
- Trauma –
  - Nicotine stomatitis, Frictional keratosis – if persists for one month duration after stoppage of the habit.
- Sanguinaria – herbal extract

Leukoplakia

- Older than 40 years with strong male predilection
- Involves lip vermilion, buccal mucosa, gingiva, tongue and floor of mouth
- Varied clinical appearance and tend to change over time.
- Slightly elevated, gray to grayish white, plaques, translucent, fissured or wrinkled, sharply demarcated

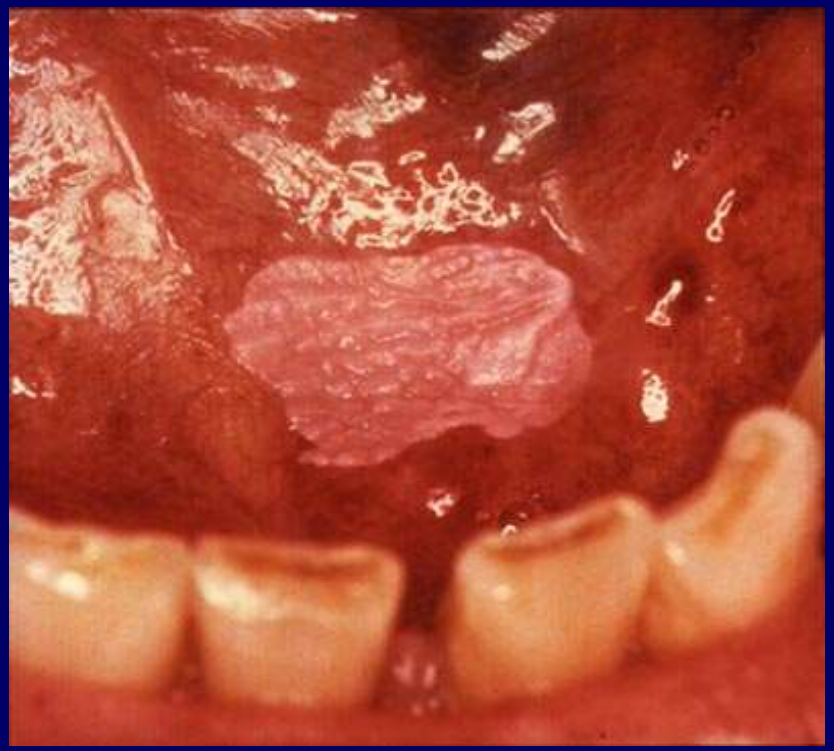
Leukoplakia

- LSCP classification
  - L – Lesion extent - <2cm, 2-4cm, >4cm
  - S – Site of lesion – Floor of mouth/ or tongue, other sites
  - C – Clinical aspect – Homogenous/Non-homogenous
  - P – Histopathology of biopsy – No/mild/moderate/severe dysplasia

Leukoplakia

- Mild / Thin / Pre-leukoplakia – soft and flat
- Homogeneous / Thick – thicker, white, leathery, deep fissures
- Granular / Nodular – surface irregularities
- Verrucous / Verruciform – sharp or blunt projections
- Erythroleukoplakia / Speckled – scattered patches of redness
  - Greatest risk for malignant transformation

Homogeneous leukoplakia

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Erythroleukoplakia

Proliferative verrucous leukoplakia

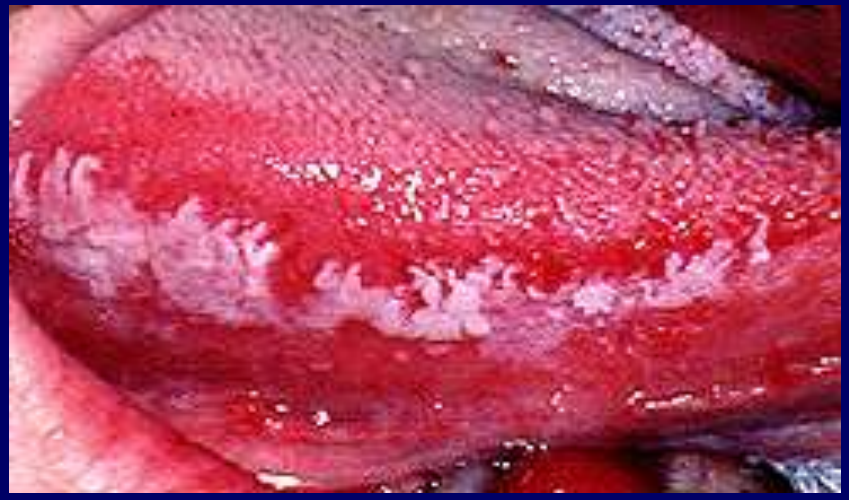
- Multiple, keratotic plaques
- Rarely regress
- In females
- No history of tobacco
- Slowly spreads
- Passes thru phases of verrucous carcinoma and OSCC.

PVL

Oral Hairy Leukoplakia

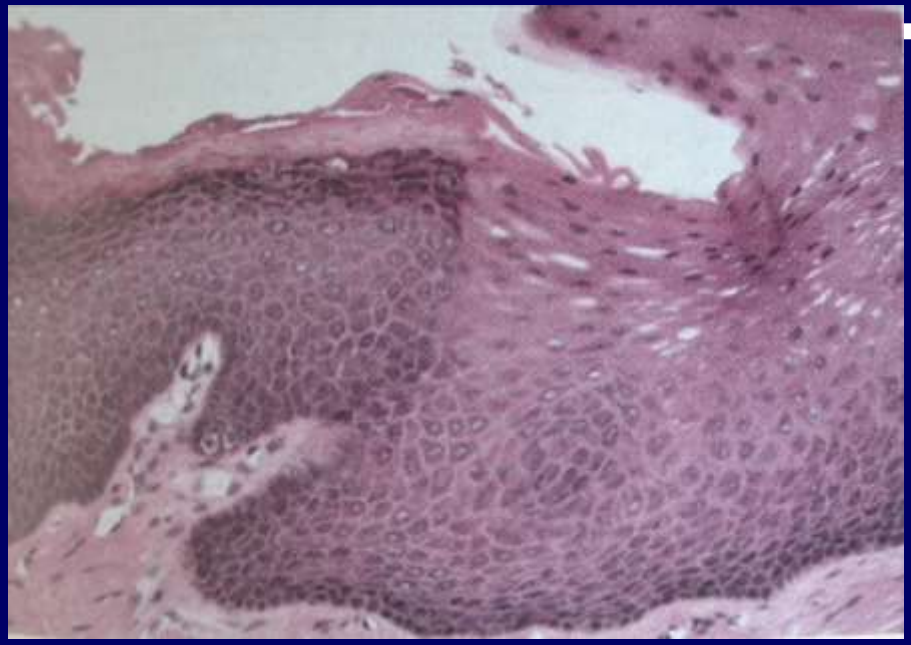
- Seen in lateral borders of tongue
- Vertical fissures
- Associated with HIV infection in AIDS.

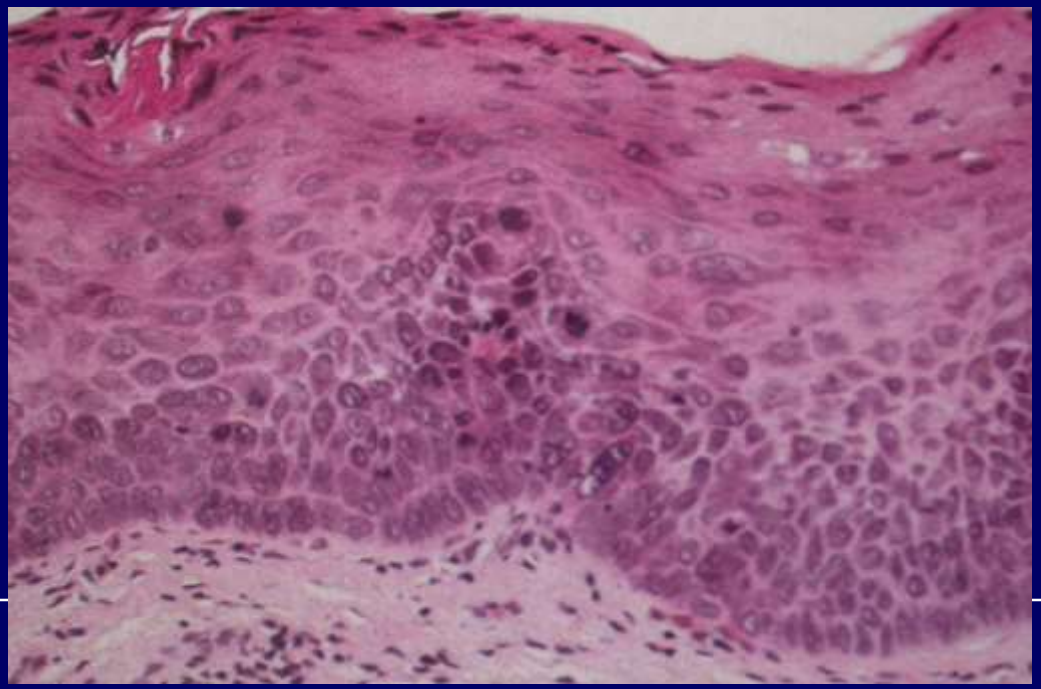
Oral hairy leukoplakia



Histopathology

- Thickened keratin layer on surface epithelium – Hyperkeratosis – para/ortho
- Parakeratin –
  - Nuclei retained in keratin layer
  - No granular cell layer
- Thickened spinous layer – Acanthosis
- Variable inflammatory infiltrate
- PVL – Verrucous Ca - OSCC





Dysplasia – abnormal development

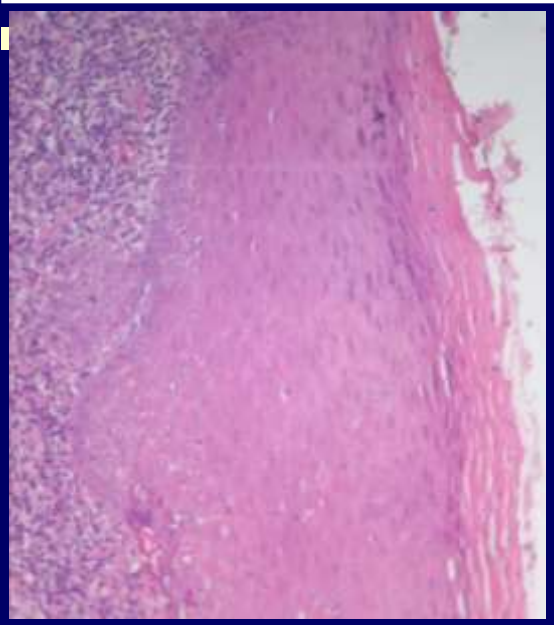
- Enlarged nuclei and cells
- Pleomorphic nuclei and cells
- Large and prominent nucleoli
- Dyskeratosis – Premature keratinization of individual cells
- Increased nuclear and cytoplasmic ratio
- Hyperchromatic nuclei
- Increased mitotic activity
- Abnormal mitotic figures (tripolar or star shaped) or mitotic figures above the basal layer.

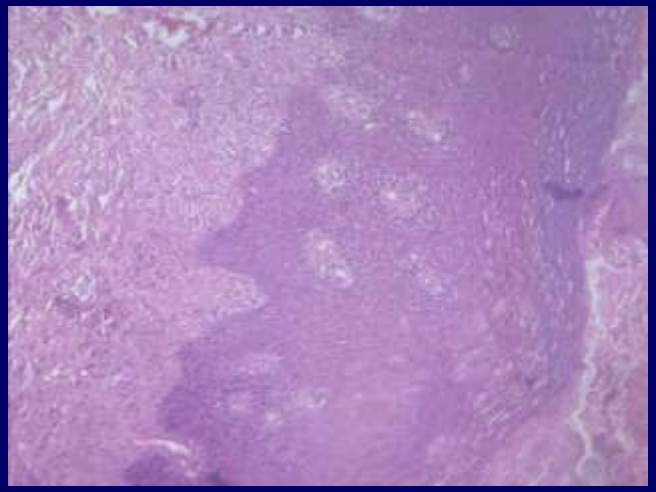
Dysplasia

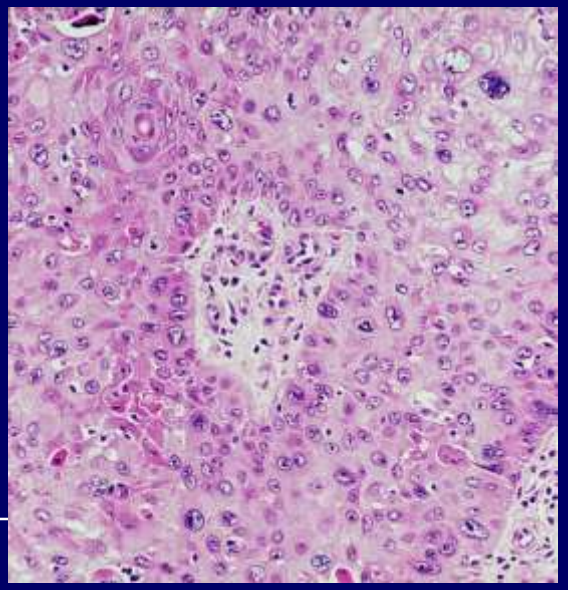
- Bulbous or tear-drop shaped rete ridges
- Loss of polarity – lack of progressive maturation towards the surface
- Keratin or epithelial pearls – focal, round collections of concentrically layered keratinized cells
- Loss of cohesion in epithelial cells

Dysplasia

- Mild – alterations limited to basal and parabasal cells
- Moderate – alterations from the basal layer to the midpoint of the spinous layer
- Severe – alterations from the basal layer to a level above the midpoint of the epithelium
- Ca in situ – entire thickness of epithelium is involved – (top to bottom change), but no invasion.







Ttt and prognosis

- Biopsy is mandatory
- Long term followup
- Risk:
  - Thick = 1 – 7 %
  - Granular = 4 – 15%
  - Erythroleuko = 18 - 47%
  - Floor or ventral tongue = 16 - 39%

Erythroplakia

- Also called Erythroplasia of Queyrat – described a precancerous red lesion in the penis.
- Defined as a red patch that cannot be clinically or pathologically diagnosed as any other condition.
- Almost all show – severe epithelial dysplasia, ca in situ or invasive SCC

Erythroplakia

- Oral lesions occur 1 per 2500 adults
- In older adults involving floor of mouth, tongue and soft palate
- Well demarcated, erythematous macule or plaque with a soft, velvety texture.
- May occur in conjunction with leukoplakia

Erythroplakia

- Lack of keratin production
- Often has atrophic epithelium – Red color
- Associated with chronic inflammation

Differential diagnosis

- Non-specific mucositis
- Candidiasis
- Psoriasis
- Vascular lesion

Treatment

- Biopsy and long term followup
- Recurrence is common
- Multiple lesions are also common.

Smokeless tobacco keratosis

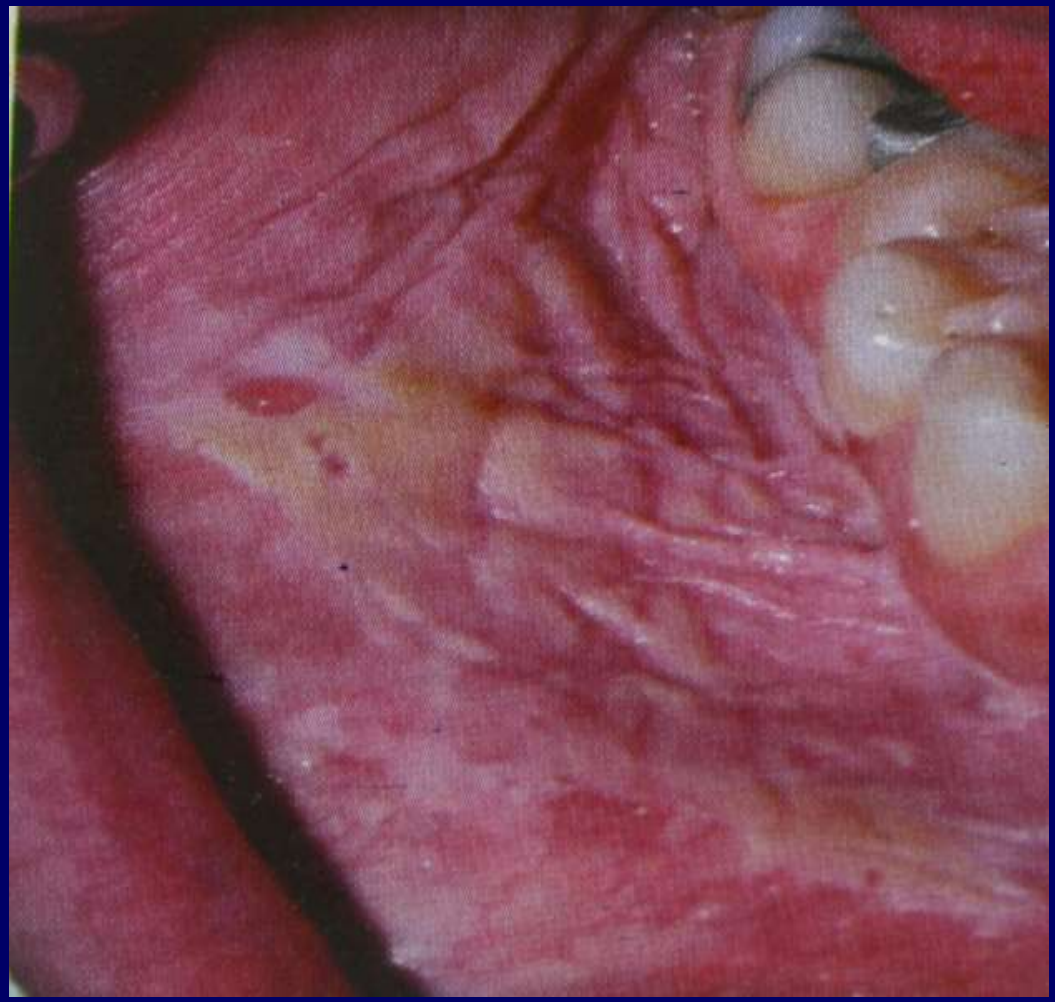
- Seen in patients with the habit of chewing coarsely cut tobacco leaves or other forms of tobacco, betel nuts and slaked lime.
- Influenced by the habit duration and frequency of usage.
- Most common in India and south east Asia
- Because of the absorption of nictotine and other molecules through the oral mucosa

Smokeless tobacco keratosis

- Loss of gingiva, periodontal tissues and alveolar bone
- Wear of occlusal and incisal surfaces
- Extrinsic stains on teeth
- Halitosis

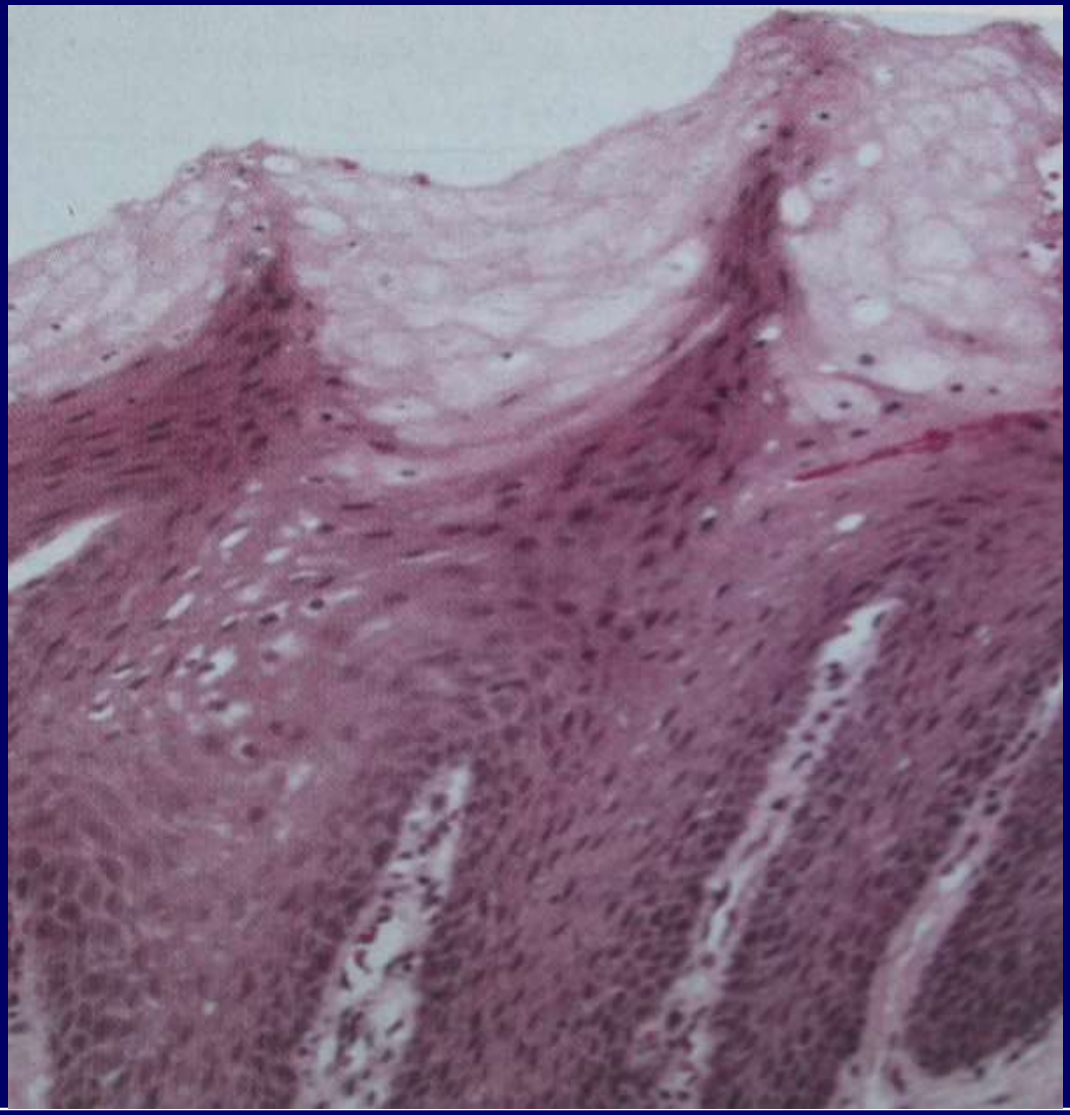
Smokeless tobacco keratosis

- Seen in older women after heavy tobacco use
- Confined to the areas of direct contact with tobacco
- Soft, velvety feel and stretching of mucosa reveals a tobacco pouch – flaccidity of chronically stretched tissues.
- Surface appears fissured or rippled resembling "sand on a beach after an ebbing tide"
- It can thicken and become leathery or nodular.



Histopathology

- Hyperkeratinized, acanthotic epithelium
- Parakeratin chevrons seen as pointed projections above or within the superficial epithelial layers.
- Increase in subepithelial vascularity and vessel engorgement.
- Epithelial dysplasia is uncommon.



Ttt and prognosis

- Stoppage of habit
- Biopsy for more severe cases
- Long term follow up
- Risk of malignant change into SCC and verrucous ca is about 4 – 8%.

Oral sub mucous fibrosis

- First described by Pindborg and Sirsat
- Is a chronic, progressive, high risk precancerous condition of oral mucosa
- Characterized by juxta-epithelial inflammatory reaction, followed by fibro-elastic change in the lamina propria and is associated with epithelial atrophy.
- About 5 million are affected in india.

Oral sub mucous fibrosis

- Associated with the placement of quid in the oral mucosa
- Quid – a substance or mixture of substances placed in the mouth or chewed and remaining in contact with the mouth, usually containing one or both of the two basic ingredients, tobacco and/or areca nut, in raw or any manufactured or processed form.

Oral submucous fibrosis

- Collagen metabolic disorder - Disturbance in the homeostatic equilibrium between synthesis and degradation of extra cellular matrix –
- Increase in TGFβ stimulates production and deposition of extra cellular matrix
- Increase in cross linking of collagen and reduction in collagenase activity.

Oral sub mucous fibrosis

- Characterized by mucosal rigidity of varied intensity
- Submucosal changes due to arecanut with abnormal accumulation of collagen in the sub-epithelial layers
- Epithelial changes and carcinogenesis due to tobacco

Causes

- Multifactorial
  - Areca nut
  - Chillies – capsaicin
  - Immunologic reaction
  - Nutritional deficiency – Vit B12, Iron
  - Genetic predisposition

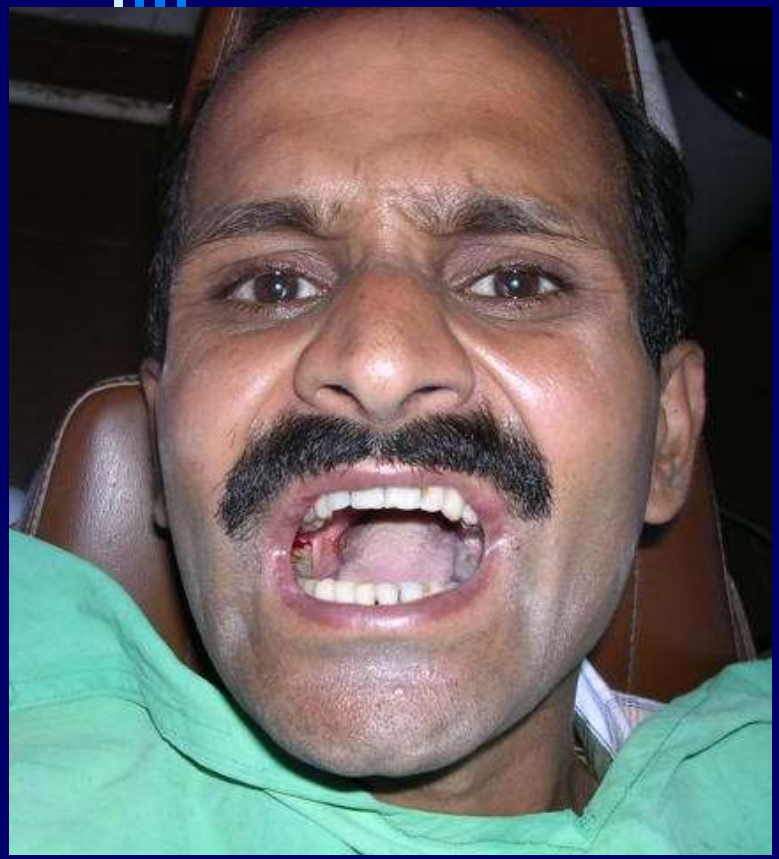
Oral sub mucous fibrosis

- Areca nut alkaloids – arecoline, arecaidine, arecolidine, guyacoline and guacine
- Flavanoids – tannins, catechins
- Arecoline – main factor for inducing fibrosis
- Arecaidine – feeling of euphoria

Clinical features

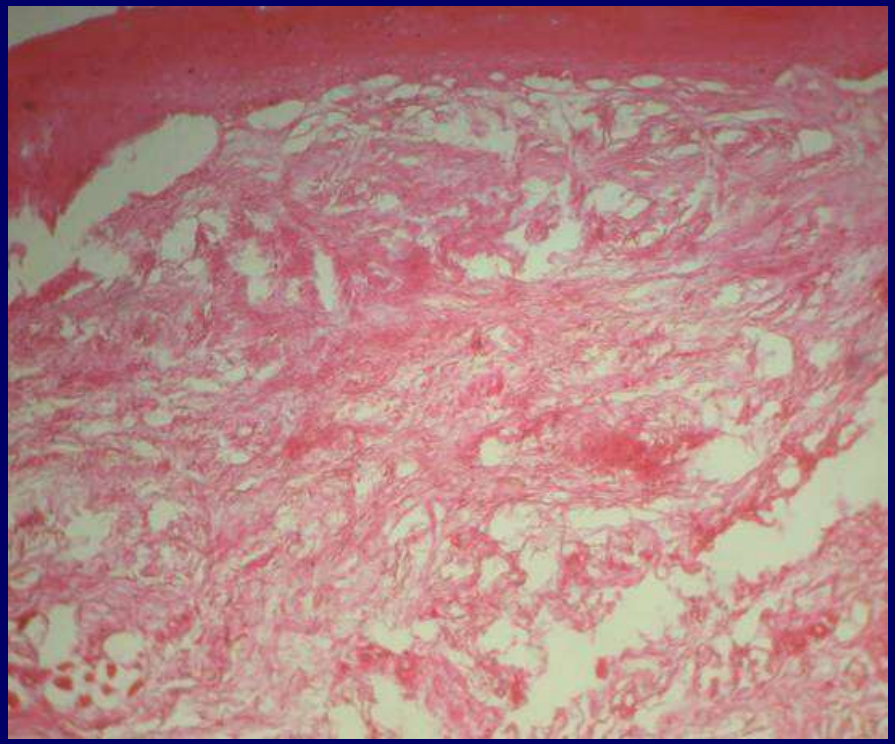
- Inability to open the mouth – Trismus
- Mucosal pain on intake of spicy food
- Reduction in inter-incisal distance
- Generalized burning sensation in the mouth – Stomatopyrosis
- Mobility of tongue and soft palate is reduced.
- Loss of papillae in the tongue.
- Mucosa has a marble-like pallor
- Submucosal fibrous bands can be palpated.
- Betel chewers mucosa – brownish-red discoloration with an irregular surface, that tends to desquamate.

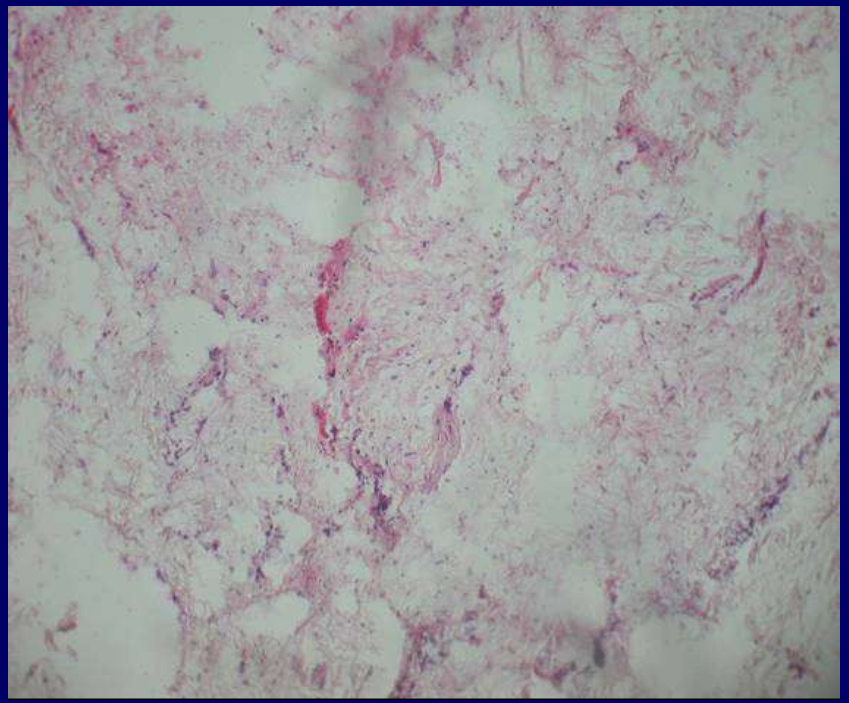
Sub mucous fibrosis



Histopathology

- Submucosal deposition of extremely dense and avascular collagenous connective tissue with variable numbers of chronic inflammatory cells
- Marked atrophy of epithelium in older lesions





Ttt and prognosis

- Does not regress with habit cessation
- Intralesional injection of corticosteroids, interferon-γ
- Long term followup
- 19 times risk than normal for cancer development.

Nicotine stomatitis

- Also called smoker's palate
- Common in the hard palate of smokers, especially pipes and cigars.
- Develops in response to heat
- Not premalignant
- Can also occur in long term usage of extremely hot beverages.

Nicotine stomatitis

- In men, older than 45 years
- Palatal mucosa is diffusely gray or white, numerous slightly elevated papules with punctate red centers
- Papules represent inflamed minor salivary glands and their ductal orifices
- Thick palatal keratin has a fissured or dried mud appearance
- Brown or black stains on teeth.

Histopathology

- Hyperkeratosis and acanthosis of palatal epithelium
- Mild, patchy chronic inflammation
- Squamous metaplasia of excretory ducts and inflammatory exudate within the lumina
- Correlates with the level of heat exposure.
- Epithelial dysplasia is rare.

Ttt and prognosis

- Completely reversible
- Encouraged to stop smoking
- Not a precancerous lesion
- If it persists after one month of habit cessation, it should be managed as leukoplakia.

Reverse smoking

- Burning end is kept inside the mouth
- Pronounced palatal keratosis
- Has a significant potential to develop dysplasia or carcinoma

Actinic keratosis

- Also called solar keratosis
- Cutaneous, premalignant lesion caused by uv exposure of sun-exposed areas in fair-skinned people.
- Causes mutations in p53 – tumor suppressor gene

Actinic keratosis

- Involves face and neck, dorsum of hands and fore arms
- Irregular, scaly plaques – normal to white, gray or brown
- Sandpaper texture on palpation
- Keratin horn production may be seen.

Histopathology

- Hyperparakeratosis and acanthosis
- Tear drop shaped rete ridges with dysplasia
- Full thickness dysplasia is termed as bowenoid actinic keratosis
- Band of amorphous, acellular, pale, basophilic change in the connective tissue – solar elastosis – four fold increase in amount of elastic fibers due to uv rays.

Ttt and prognosis

- Precancerous in nature
- Recurrence is rare
- Long term followup is required

Actinic cheilosis / cheilitis

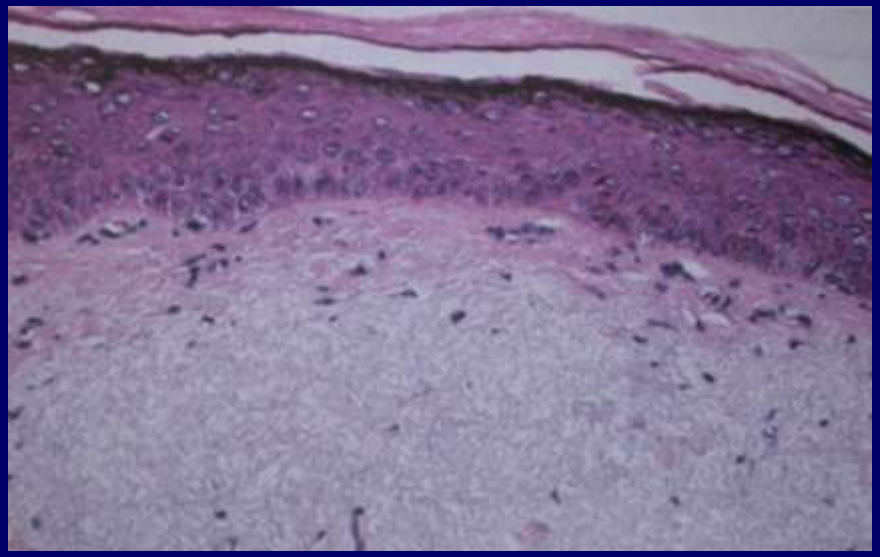
- Common premalignant alteration of lower lip vermilion due to long term exposure to uv light
- Seen in light complexioned people who sunburn easily
- Also called farmer’s lip or sailor’s lip
- Is a precancerous lesion.

Clinical features

- Strong male predilection, Older than 45 years
- Atrophy of lower lip vermilion with a smooth surface and blotchy pale areas
- Blurring of margin between vermilion and cutaneous zones of lips
- Progresses to a rough, scaly area on drier portions of vermilion and can thicken
- Scaly material can be peeled off but reforms again.
- Focal ulceration can develop.

Histopathology

- Atrophic, stratified squamous epithelium
- Marked keratin production
- Varying degrees of epithelial dysplasia
- Mild chronic inflammatory infiltrate
- Solar elastosis is evident in the connective tissue



Ttt and prognosis

- Irreversible
- Areas of induration, thickening, ulceration or leukoplakia should be biopsied.
- Lip shave procedure/vermilionectomy can be done
- Long term follow up
- 6-10% risk for malignant transformation.

Kerato acanthoma

- Also called self healing carcinoma, pseudocarcinoma
- Is a self limiting, epithelial proliferation with a strong clinical and histopathological similarity to WDSCC.
- Cause is unknown, attributed to HPV26,37 and sun damage
- Genetic predisposition in association with muir-torre syndrome.

Clinical features

- Older than 45 years, in males
- In sun exposed skin and outer edge of vermilion border of the lips
- Firm, non-tender, well demarcated, sessile, dome-shaped nodule with a central plug of keratin
- The keratin plug is yellow, brown or black with an irregular, crusted, often verruciform surface.

Clinical features

- Rapid enlargement to a diameter of 1-2cm within six weeks (d/d SCC)
- regress spontaneously within 6-12 months of onset
- Leaves a depressed scar in the area.
- Ferguson-smith type – early life, multiple lesions, hereditary
- Eruptive grzybowski type – hundred of papules in skin and upper digestive tract and associated with internal malignancy.

Histopathology

- Epithelium shows dyskeratosis with deeply located, individually keratinizing lesional cells and keratin pearls.
- Surface epithelium lateral to the edge of the tumor is normal and forms a characteristic acute angle with the lesion.
- Crater is filled with keratin and the epithelium at the base of the crater proliferates downward
- Pronounced chronic inflammatory cell infiltrate
- Downward proliferation does not extend below the muscles or sweat glands.

Ttt and prognosis

- Surgical excision
- Close similarities to SCC can possibly lead to misinterpretation.

Squamous papilloma

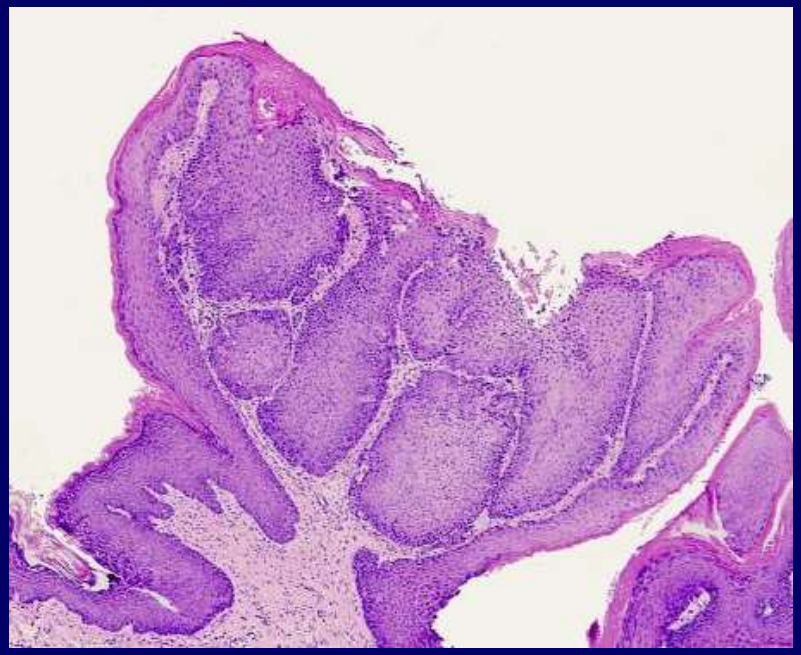
- Benign proliferation of stratified squamous epithelium
- Equal frequency in men and women aged 30-50 years.
- Induced by HPV subtypes 6 & 11
- Involves tongue, lips and soft palate

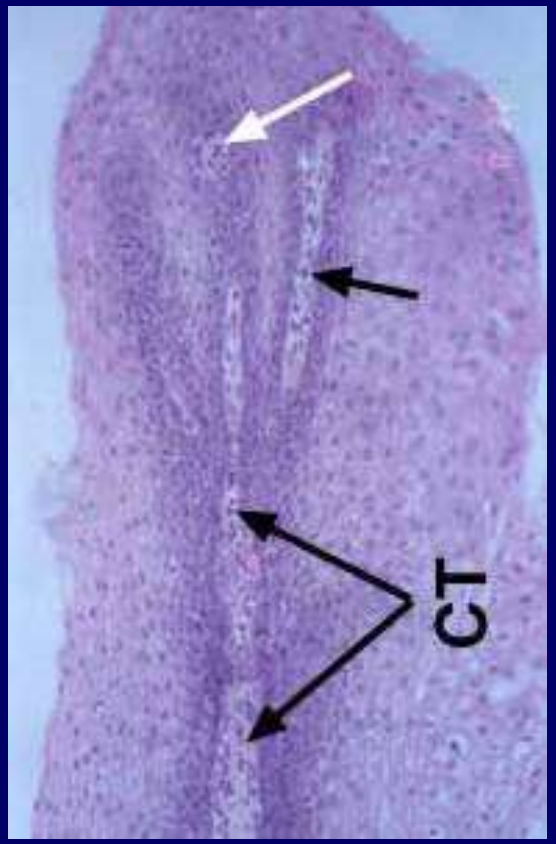
Squamous papilloma

- Soft, painless, pedunculated, exophytic nodule with numerous finger like projections resembling cauliflower or wart like appearance.
- Usually, 0.5cm in diameter.
- Can be white, slightly red or normal in color.
- Papillomatosis – extensive, coalescing papillary lesions in association with skin disorders like acanthosis nigricans, goltz-gorlin syndrome.

H/P

- Proliferation of keratinized squamous epithelium in finger like projections with fibro-vascular connective tissue cores
- Keratin layer is thickened in whiter lesions
- Virus altered epithelial clear cells with small, dark (pyknotic nuclei) are sometimes seen – Koilocytes.

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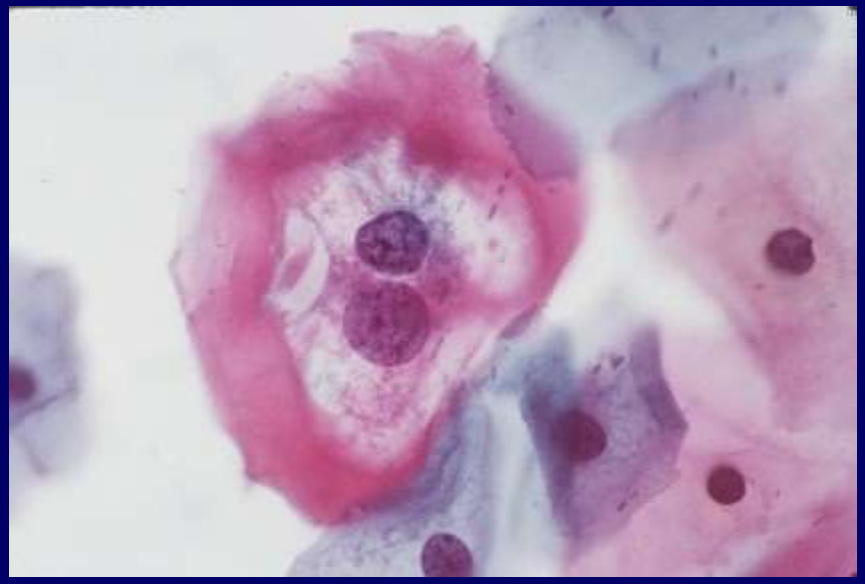
Koilocytes



Squamous papilloma – D/D

- Verruca vulgaris
  - by HPV 2,4,6 & 40,
  - In children
  - Contagious and can spread by auto-innoculation
  - Cutaneous or keratin horn
- Condyloma acuminatum
  - Venereal wart, sexually transmitted disease
  - High risk HPV 16 & 18
  - Sessile, pink mass larger than papillomas

Squamous papilloma – D/D

- Verruciform xanthoma
  - Hyperplastic condition in mouth, skin and genitalia with characteristic accumulation of lipid laden histiocytes (Foam cells / Xanthoma cells) beneath the epithelium.
  - Can be seen in association with lichen planus, LE, EB etc
  - In females aged 40-70 years
- Focal epithelial hyperplasia / Heck's disease
  - In children
  - Multiple, flattened or rounded papules
  - Same color as normal mucosa

Melanocytic nevus

- Nevus refers to malformations of the skin and mucosa that are congenital or developmental in nature.
- Acquired MN represents a benign, localized proliferation of cells from the neural crest called Nevus cells.
- Most common.

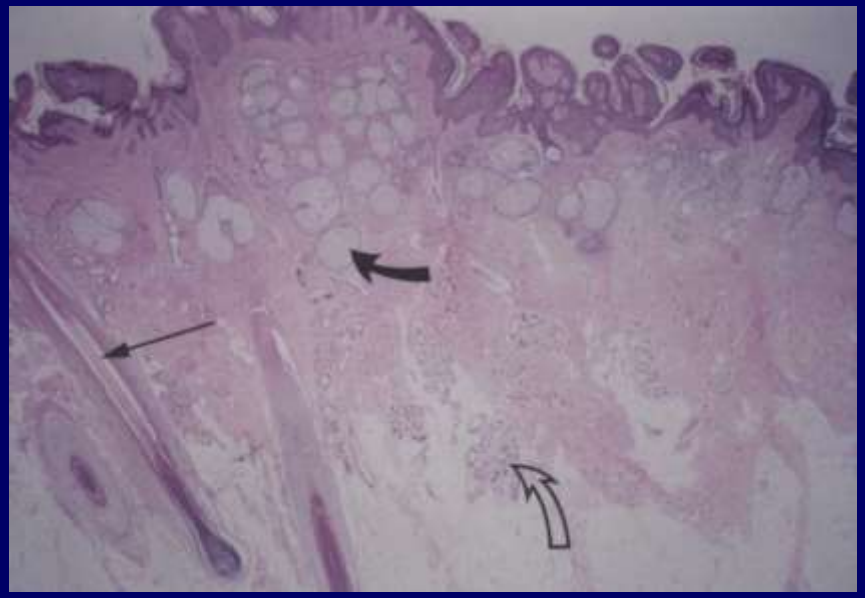
Developmental nevi

- Nevus flammeus / Portwine stain – deep purple in color, unilateral, seen in sturge-weber syndrome.
- Basal cell nevus – associated with nevoid basal cell carcinoma syndrome.
- White sponge nevus - Misnomer
- Epidermal nevus -
- Nevus sebaceus -

Port wine stain

Congenital nevus

Nevus sebaceus



Epidermal nevus

Acquired MN

- Begins to develop during childhood
- More in whites.Intra-oral is usually seen in females.
- Junctional nevus – sharply demarcated, brown or black macule, <6mm dia
- Compound nevus – slightly elevated, soft papule, relatively smooth surface, brown or tan
- Intradermal nevus – papillomatous, loses color, hairs can be seen.
- Risk of malignant transformation is 1 in 1 million.

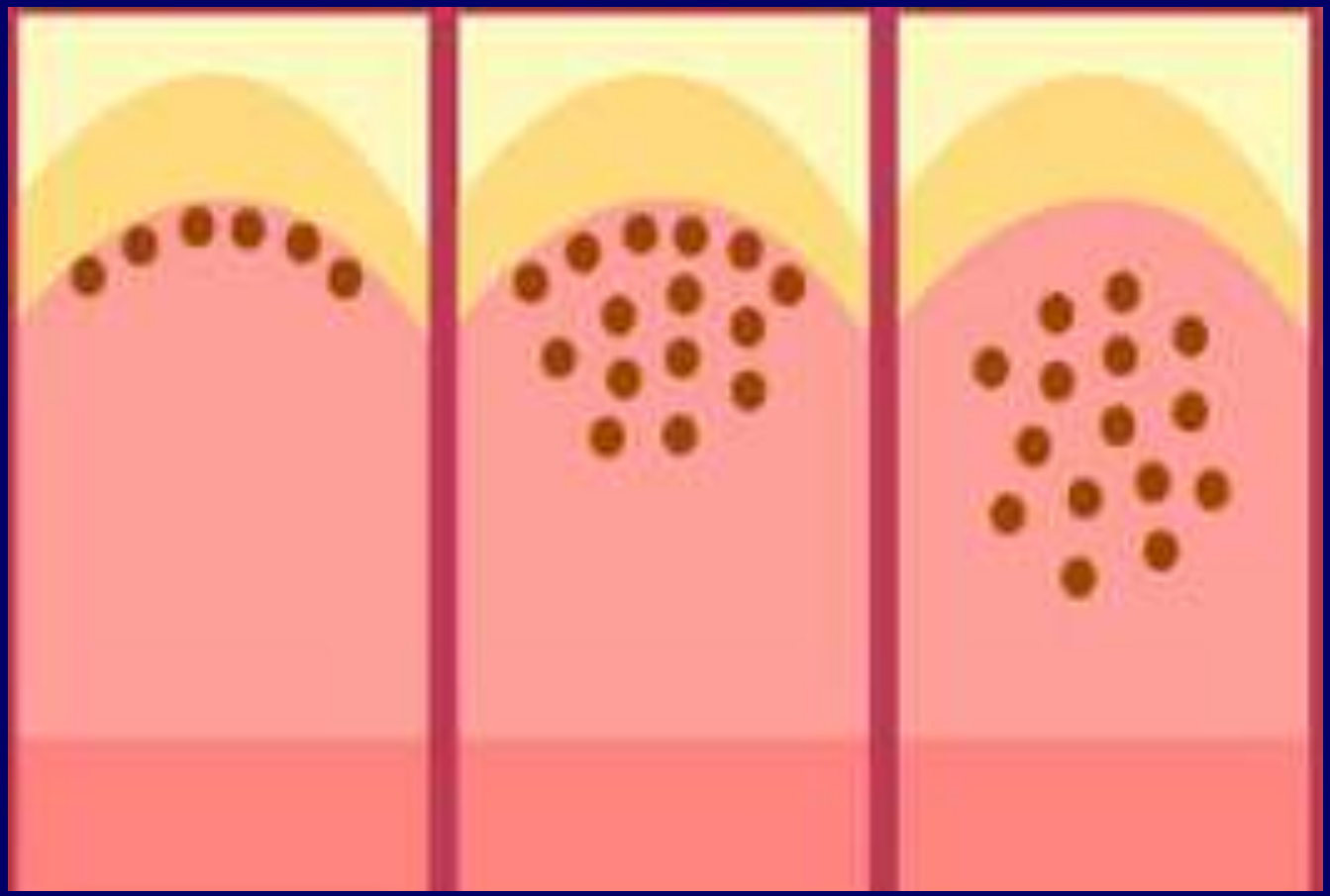
Acquired MN

- Benign, unencapsulated proliferation of small, ovoid cells (nevus cells).
- Small, uniform nuclei and moderate amount of eosinophilic cytoplasm with indistinct cell boundaries.
- Lack dendritic processes – D/D Melanocytes
- Superficial cells organized into small, round aggregates (theques).

Acquired MN

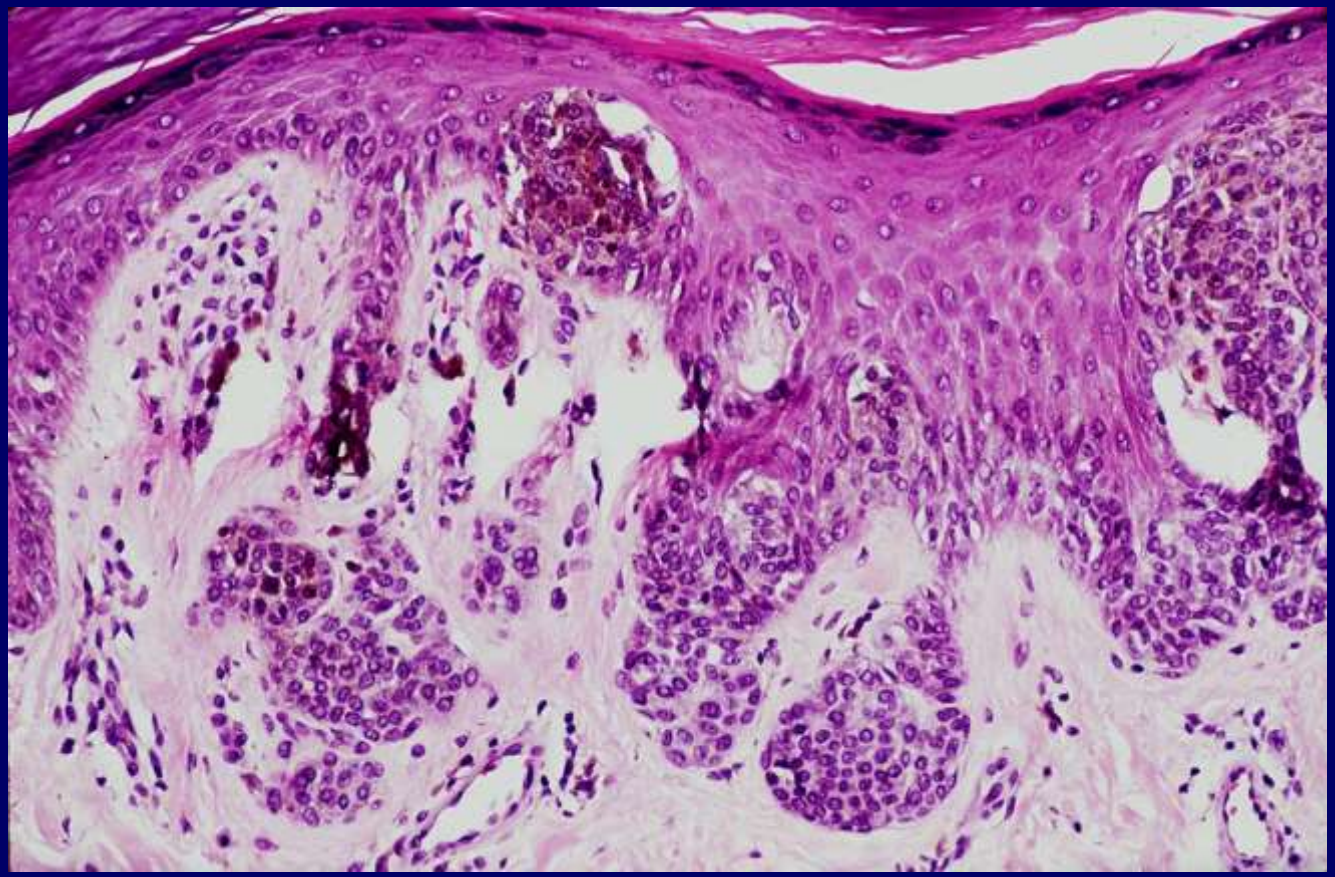
- Junctional nevus – theques seen in the junction between epi & CT.
- Compound nevus – as nevus cell proliferate, they begin to drop off into underlying lamina propria. Cells present both along jn and CT.
- Intradermal / Intramucosal nevus – nevus cells present only in underlying CT.

Nevus



Acquired MN

- Superficial cells –
  - larger and epithelioid with
  - abundant cytoplasm and melanin and
  - cluster into theques.
- Middle portion –
  - less cytoplasm,
  - seldom pigmented, like lymphocytes
- Deeper cells –
  - elongated and spindle shaped
  - like schwann cells or fibroblasts.



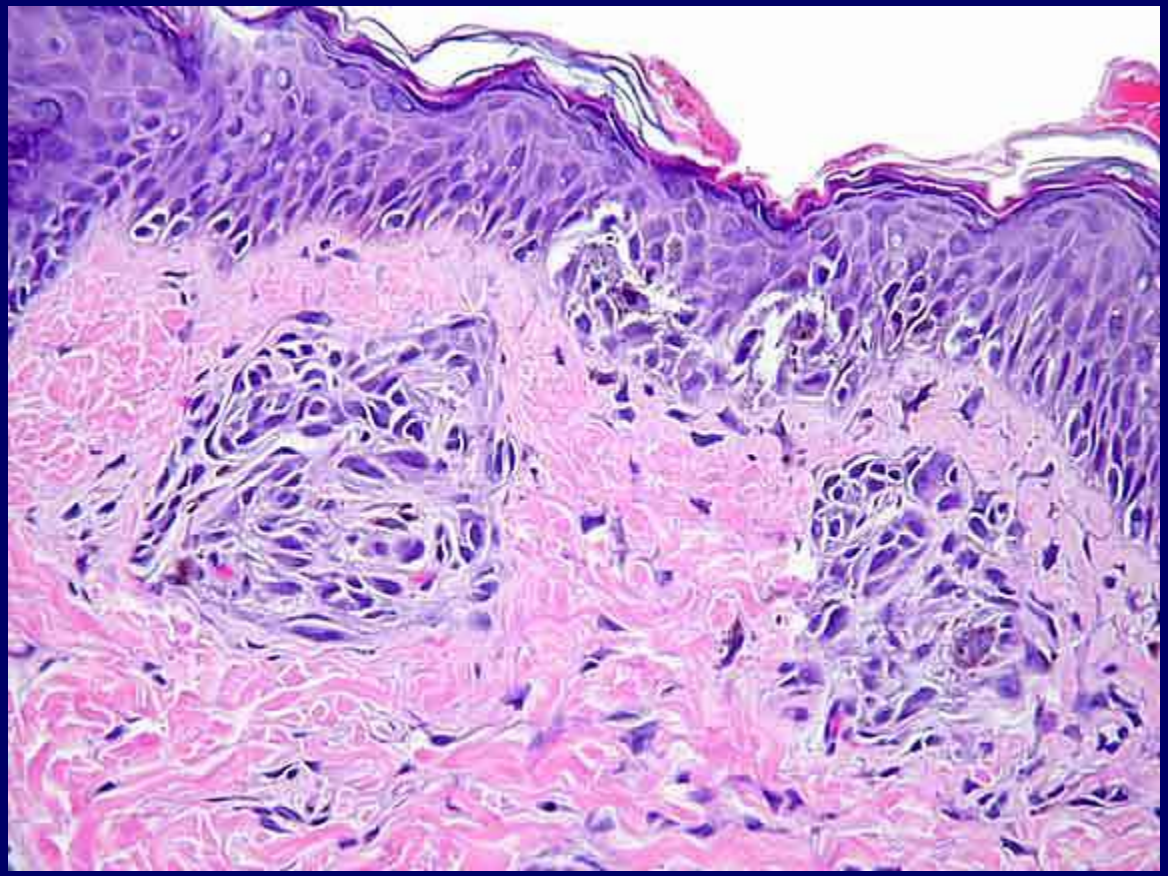
Congenital melanocytic nevus

- Two types
  - Small - <20cm dia
  - Large - >20cm dia
- Larger in dia than acquired nevi.
- Brown to black plaques,
- Associated with hypertrichosis – Giant hairy nevus
- Bathing trunk or Garment nevus

Hairy nevus

Congenital melanocytic nevus

- H/P is similar to acquired nevi.
- Nevus cells extend into the deeper levels of dermis with infiltration of cells between the collagen bundles.
- Seen intermingled with neurovascular bundles and adnexal structures like hair follicles, sebaceous glands.



Halo nevus

- Melanocytic nevus with pale, hypopigmented border or halo of surrounding epithelium, as a result of nevus cell destruction by immune system.
- Seen in skin of trunk especially, in patients with recent excision of melanoma
- Pigmented papule with 2-3mm zone of hypopigmentation.
- H/P shows intense inflammatory infiltrate which surrounds and infiltrates the nevus cells.

Halo nevus

Spitz nevus

- Uncommon type
- In skin of extremities
- Solitary, dome shaped, pink to reddish brown papule, <6mm dia
- H/P like compound nevus with spindle shaped or epithelioid cells.
- Ectatic superficial blood vessels
- S100 and NSE positivity

Spitz nevus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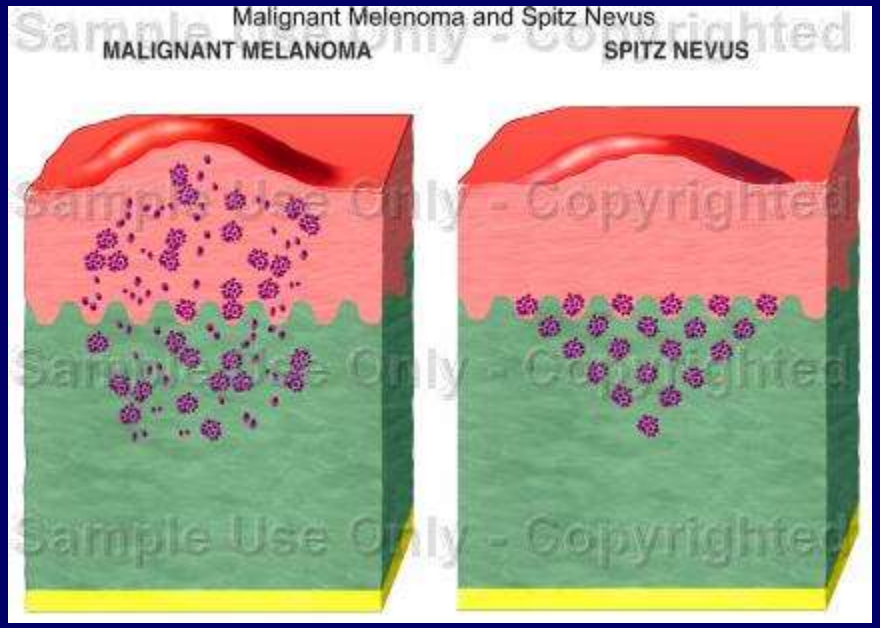
Malignant Melenoma and Spitz Nevus
MALIGNANT MELANOMA
SPITZ NEVUS
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Blue nevus

- Also called Jadassohn-tiecke nevus
- Benign proliferation of dermal melanocytes deep within sub-epi CT.
- Two types
  - Common
  - Cellular
- Blue color is due to tyndall effect – interaction of light due to absorption of red and blue by the tissues and reflection of blue light.

Blue nevus

- Shows elongated, slender melanocytes with branching dendritic extensions and numerous melanin globules.
- Cells located deep in lamina propria
- Aligned parallel to surface epithelium
- Blue nevus along with overlying melanocytic nevus – Combined nevus.