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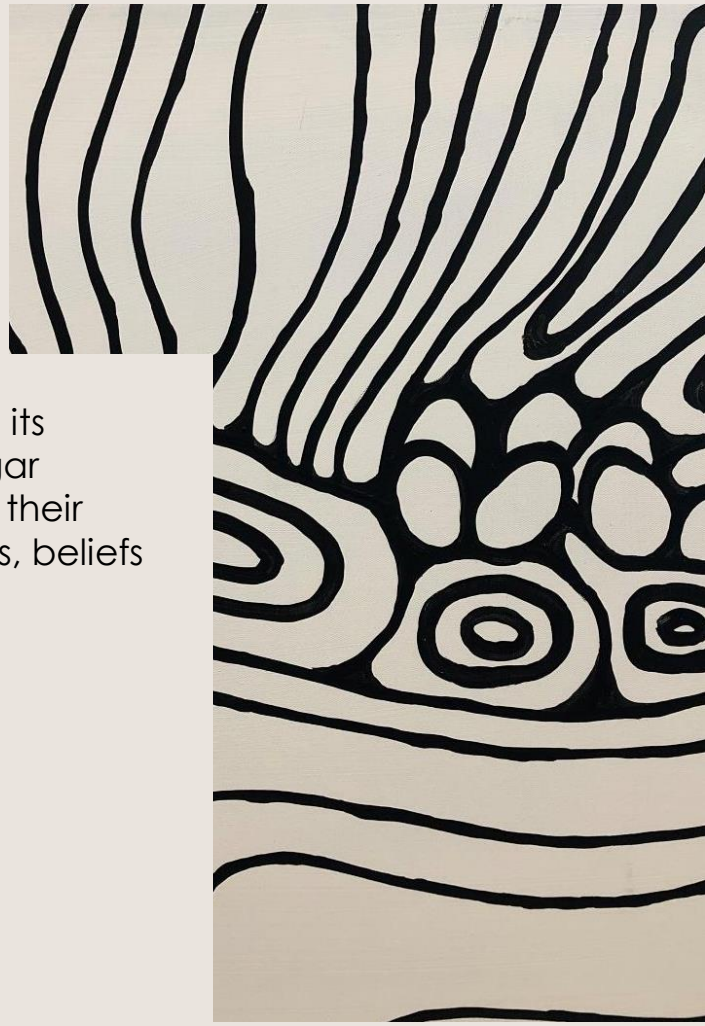
Oral Pathology module

Connective Tissue disorders

DENT4217

Acknowledgement
of country

The University of Western Australia acknowledges that its campus is situated on Noongar land, and that Noongar people remain the spiritual and cultural custodians of their land, and continue to practise their values, languages, beliefs and knowledge.

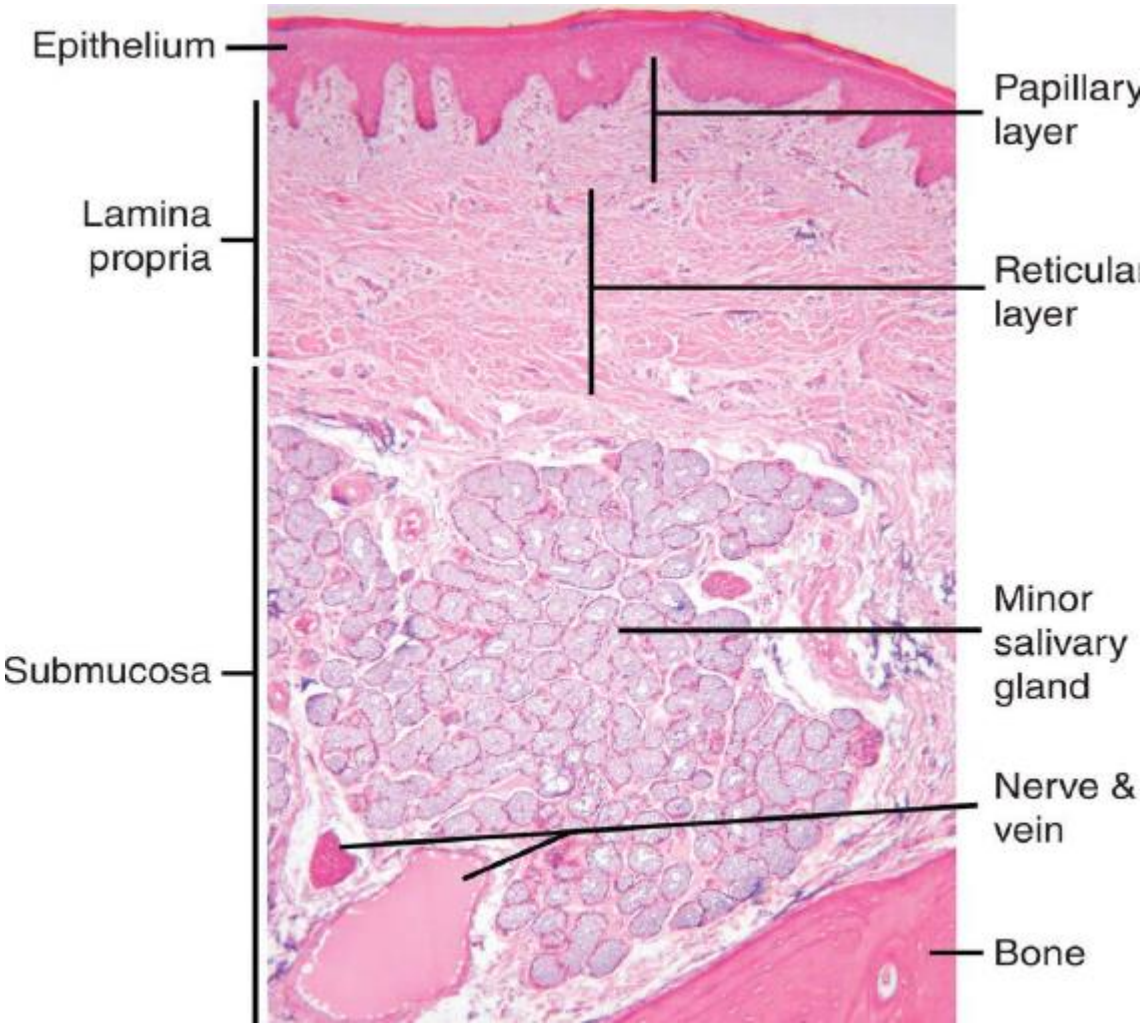


Artist: Dr Richard Barry Walley OAM

Learning outcomes

- To develop a basic knowledge of reactive, benign and malignant connective tissue lesions that may occur in the oral cavity.

- To recognise the common causes of various types of localised gingival lesions



Soft-tissue tumours derived from mesenchymal components of connective tissue

Classification of Connective Tissue Disorders		
Group	**Reactive/congenital**	**Neoplasms**
Fibrous	•Fibroma /fibroepithelialpolyp •Peripheral giant cell granuloma •Peripheral ossifying fibroma •Epulis fissuratum (inflammatory fibrous hyperplasia) •Inflammatory papillary hyperplasia •Generalized gingival hyperplasia	•Giant cell fibroma •Myofibroma •Aggressive Fibromatosis •Solitaryfibrous tumor •Fibrosarcoma •Fibrous histiocytoma, benign and malignant •Nodular fasciitis
Vascular	•Pyogenic granuloma •Varix; other acquired malformations •Benign vascular malformation •Lymphangioma	•Hemangioma •Angiosarcoma •Kaposi's sarcoma •Hemangiopericytoma
Neural	•Traumatic neuroma	•Neurofibroma •Granular cell tumor •Schwannoma (neurilemoma) •Mucosal neuromas of MEN III •Palisaded encapsulated neuroma •Malignant peripheral nerve sheath tumor
Adipose tissue	•Herniated fat pad	•Lipoma and Liposarcoma
Muscle	•Smooth muscle •Striated muscle	•Leiomyoma and Leiomyosarcoma •Rhabdomyoma and Rhabdomyosarcoma

FIBROMA ("BITE" OR "IRRITATION" FIBROMA, FIBROEPITHELIAL OR FIBROVASCULAR POLYP), AND GIANTCELL FIBROMA

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- This occurs at any age group without sex predilection and consists of a dome-shaped nodule or papule that may be white/keratotic, mucosa-colored, or ulcerated. It is located in areas readily traumatized by biting (i.e., buccal mucosa, lateral tongue, and lower lip mucosa) or on the gingiva where plaque accumulates.

FIBROMA ("BITE" OR "IRRITATION" FIBROMA, FIBROEPITHELIAL OR FIBROVASCULAR POLYP), AND GIANTCELL FIBROMA

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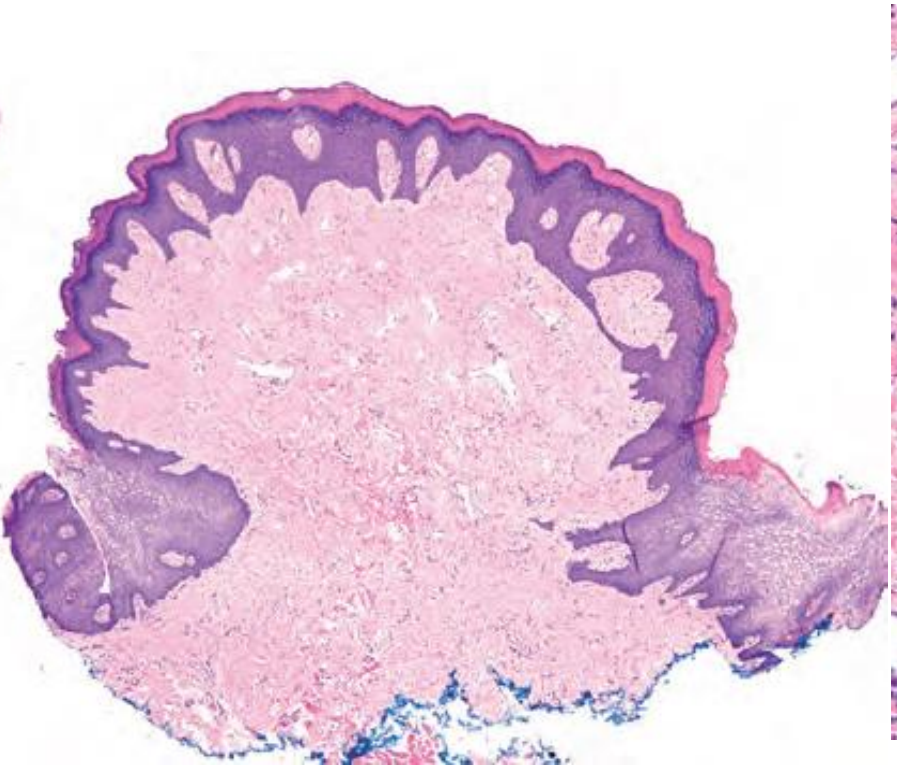
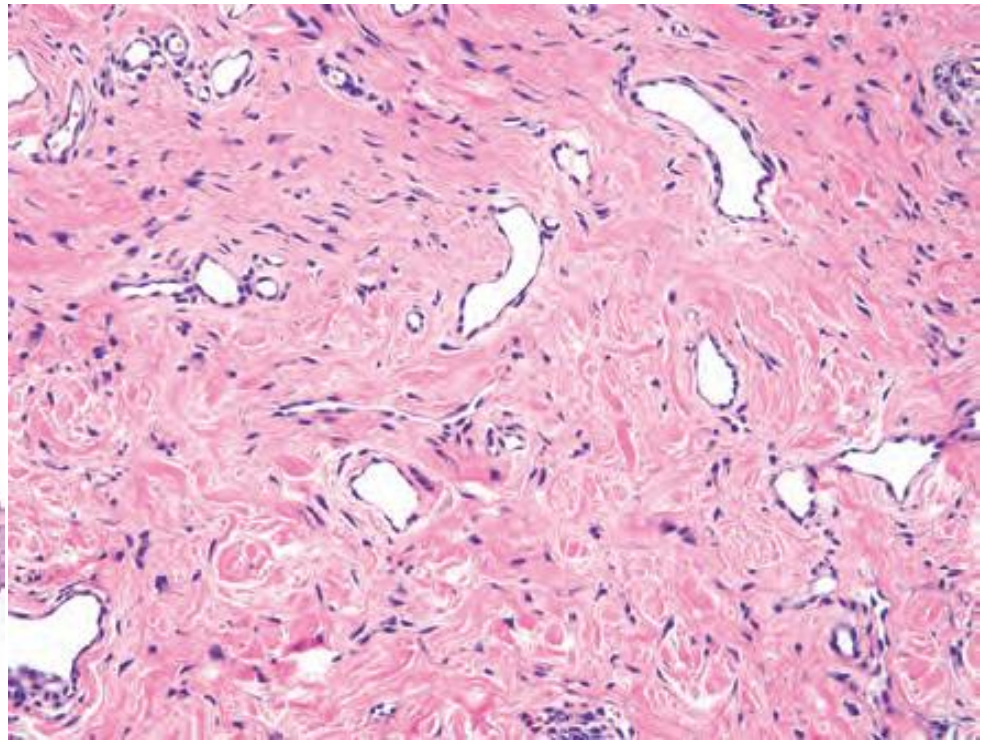




- A nodular mass of dense fibrous connective tissue
- Normal, hyperkeratotic, or ulcerated surface epithelium

Ossifying fibrous epulis (peripheral ossifying fibroma)

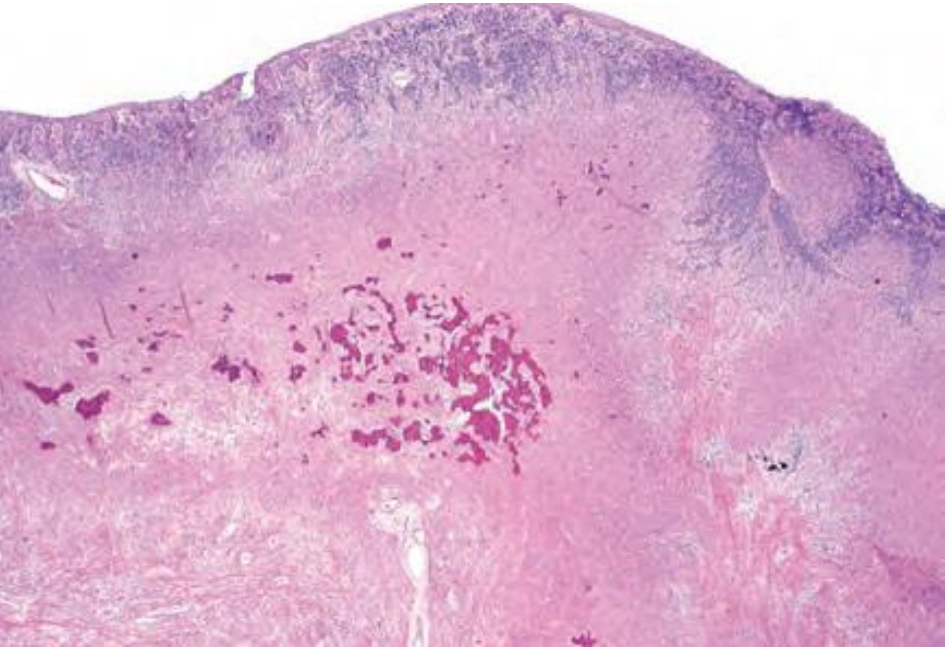
- A common, swelling of the gingiva characterized by a core of fibrous connective tissue exhibiting the formation of variable amounts of amorphous deposits of calcifications
- Mostly seen in children and young adults
- A reactive lesion to local irritation

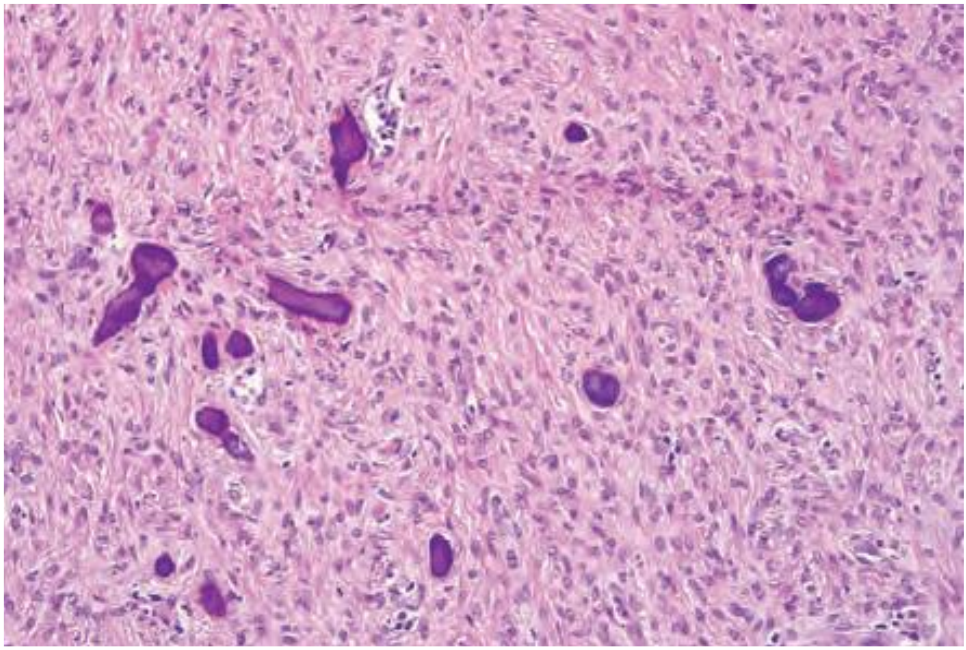
- **Clinically:**
- Red to pink, firm gingival nodule
- typically arise from the interdental papilla
- smooth surfaced, can be ulcerated
- 1 cm in diameter; can be larger

Often shows calcification on radiograph

Ossifying fibrous epulis (peripheral ossifying fibroma)

- A nodular mass of cellular fibrous connective tissue
- contains bone, or cementum-like material
- covered by normal or ulcerated surface epithelium





Angiogranuloma (pyogenic granuloma)

- A common reactive vascular lesion

Aetiology

- A reactive lesion to local irritation or trauma
- Some are attributed to the effect of female hormones
- Tumour-like overgrowth of granulation tissue

Clinical features

- F>M; the prevalence is higher in women during pregnancy
- Most common on the gingiva (75% of all oral cases)
- tongue, lips, and buccal mucosa

Angiogranuloma (pyogenic granuloma)

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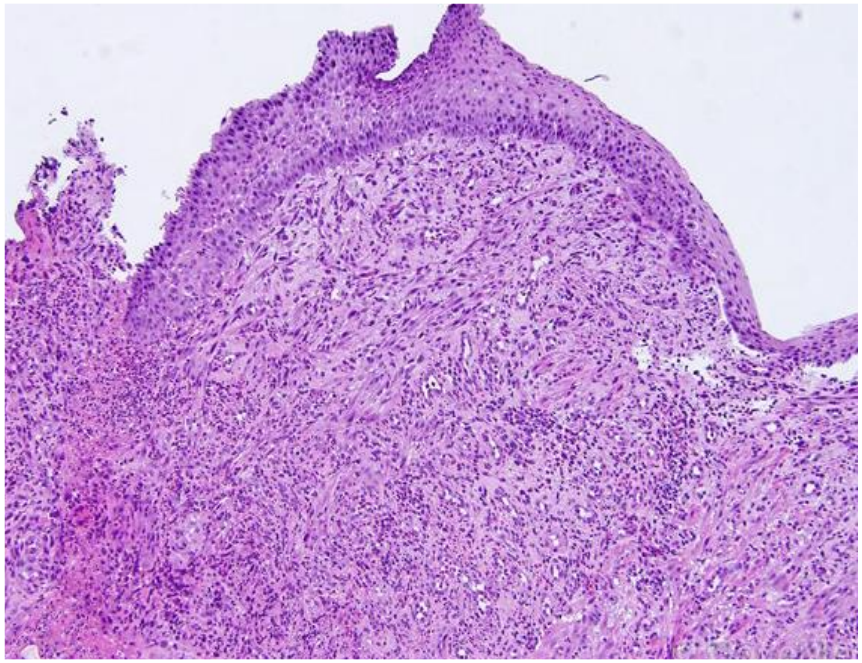
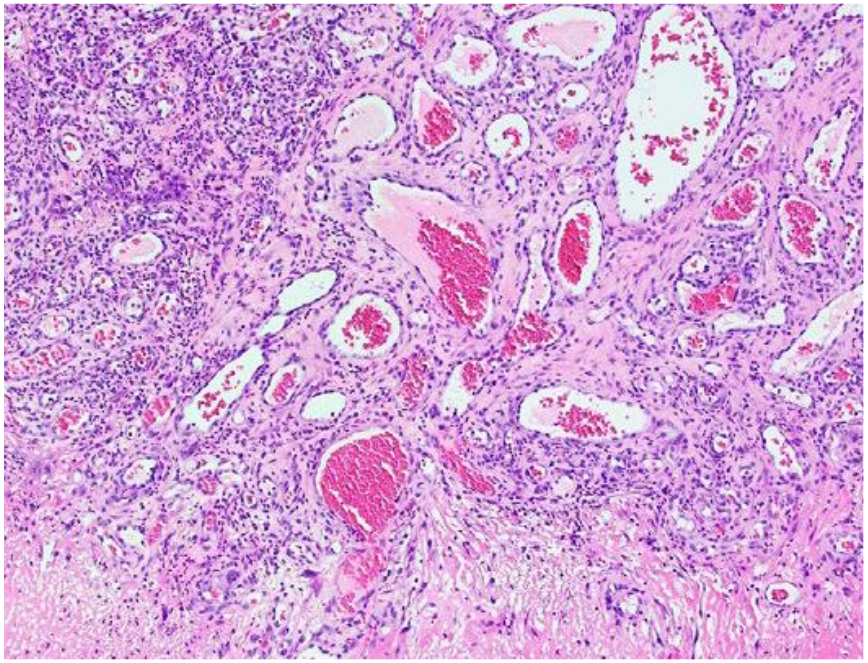
- Bright-red to dark-red, soft nodule
  - smooth or lobulated surface; often ulcerated
  - often bleeds easily
  - <1 cm in diameter; can be larger


- Pregnancy tumour (granuloma gravidarum): a pyogenic granuloma that develops on the gingiva during pregnancy
- Epulis Granulomatosa: a pyogenic granuloma that develop in a healing extraction socket


Angiogranuloma (pyogenic granuloma)

- Nodular mass of granulation tissue
- dilated blood vessels in a loose fibrous stroma, with acute and chronic inflammatory infiltrate
- normal or ulcerated overlying surface epithelium





Peripheral Giant Cell Granuloma (Giant Cell Epulis)

- A relatively common growth on the gingiva or the alveolar ridge characterized by a proliferation of multinucleated giant cells that resemble osteoclasts.

Aetiology

- A reactive lesion to local irritation or trauma

Clinical features

- Exclusively on the gingiva or edentulous alveolar ridge
  - ❑Red to blue-purple, firm gingival nodule
  - ❑typically arise from the interdental papilla
  - ❑smooth surface; may or may not be ulcerated
  - ❑typically <1 cm in diameter; can be larger
  - ❑may cause cupping resorption of the underlying alveolar bone

Peripheral Giant Cell Granuloma (Giant Cell Epulis)

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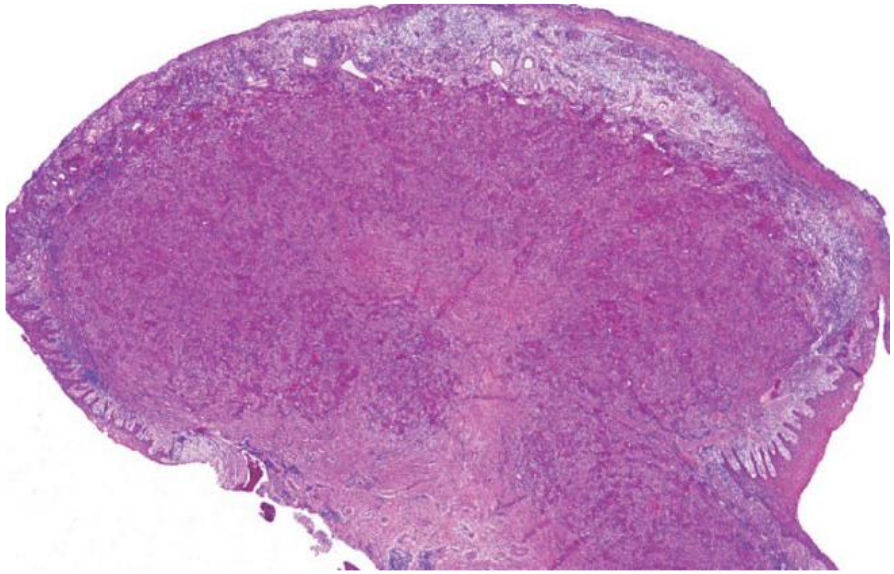
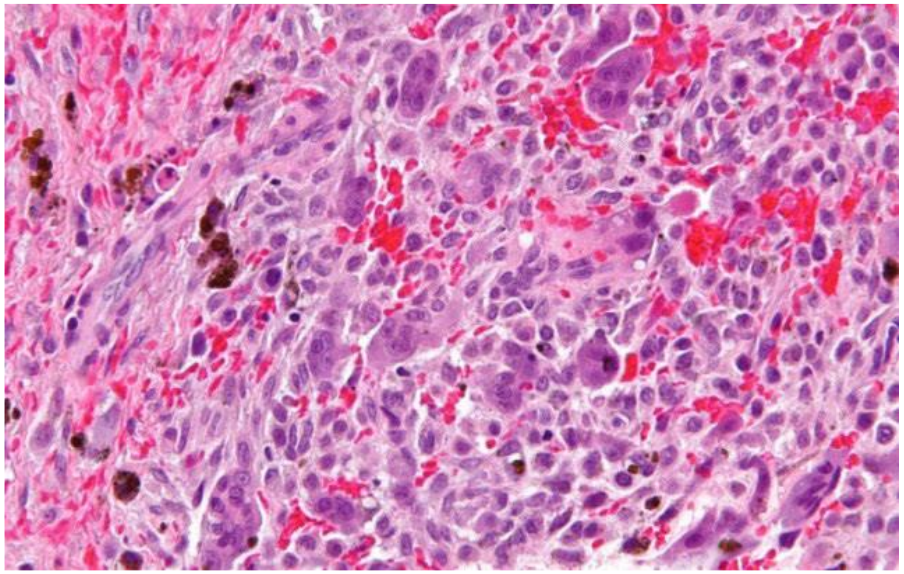
- **Microscopy**
- A nodular proliferation composed of osteoclast-like multinucleated giant cells in a cellular and haemorrhagic background
- osteoclast-like multinucleated giant cells
- cellular fibrous stroma
- extravasated RBCs, and haemosiderin pigmentation
- normal or ulcerated overlying surface epithelium

"multinucleated giant cells"
b/c from monocytes





Epulis Fissuratum (Inflammatory fibrous hyperplasia; denture epulis)

A reactive overgrowth of fibrous connective tissue in response to an ill-fitting denture

Aetiology

- Trauma from an overextended or ill-fitting denture

Clinical features

- In the alveolar vestibule adjacent to a denture flange
- more frequently along the anterior vestibule

Epulis Fissuratum (Inflammatory fibrous hyperplasia; denture epulis)

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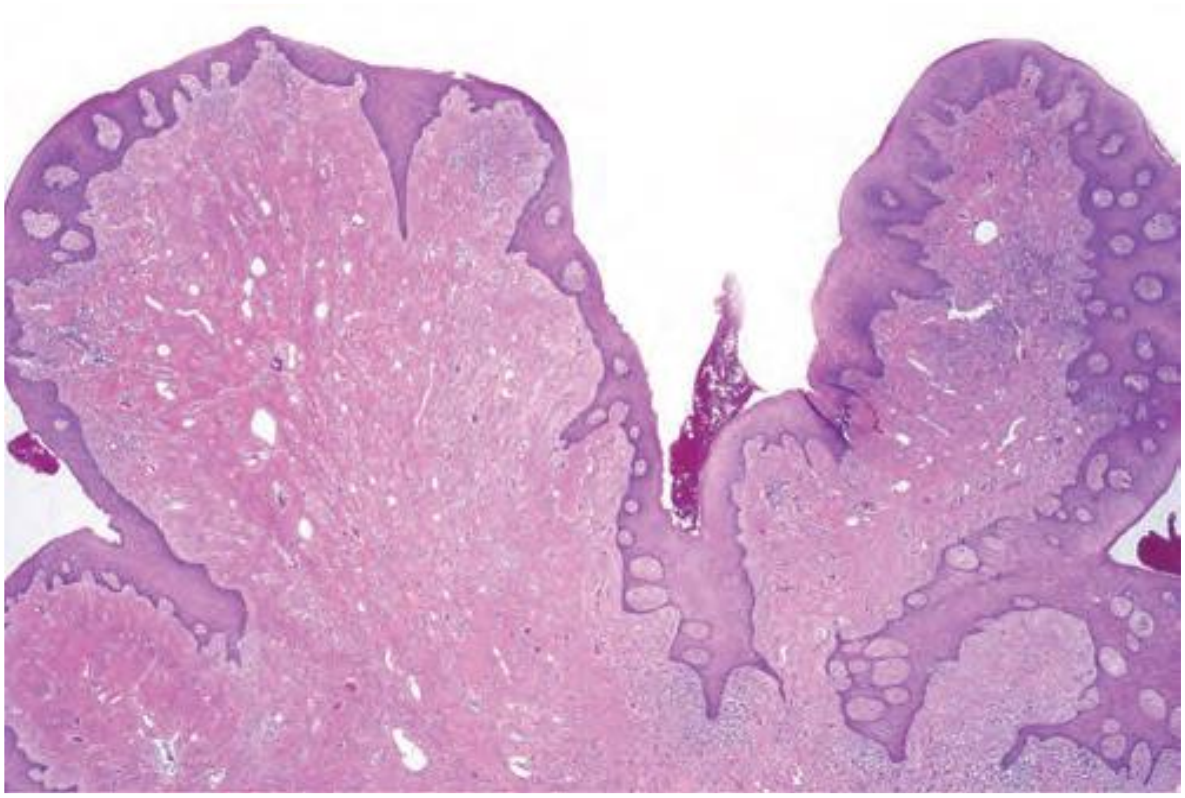
Histopathology

- A hyperplasic mass of fibrous connective tissue
- often with folds and grooves
- Hyperplastic, hyperkeratotic, or ulcerated surface epithelium



Reactive Gingival Nodules

Diagnosis	Histopathology
Fibroma (inflammatory fibrous hyperplasia)	• Nodule of densely collagenous fibrous tissue with scattered vessels and variable edema and inflammation; crevicular epithelium with underlying plasma cells are often seen; when uninflamed, it is indistinguishable from a traumatic fibroma (see Fig. 5.12A–C)
Pyogenic granuloma (lobular capillary hemangioma) (see also Chapter 6)	• Lobular or more frequently, nonlobular proliferation of endothelial cells and small, dilated capillaries; often ulcerated and inflamed (see Figs. 5.13A) • Endothelial cells show reactive atypia sometimes with focal "hobnail" pattern and hyperchromatic nuclei (see Fig. 5.13B–C); mitotic figures are often present • May see fibrosis depending on stage of organization (Fig. 5.13D–E)
Peripheral ossifying fibroma (fibroma with osseous metaplasia)	• Cellular proliferation of spindled fibroblast-like cells with deposition of osteoid, woven bone with variable osteoblastic rimming, cementum droplets or cementicles (psammoma body–like) (see Figs. 5.14 and 5.15); sometimes lamellar bone is present • Spindle cells have ovoid nuclei, dispersed chromatin, and inconspicuous nucleoli and the spindle cell proliferation may have a storiform pattern (Fig. 5.16); the amount of calcified material is variable (Fig. 5.17) • There may be clusters of multinucleate giant cells similar to peripheral giant cell granuloma (see Fig. 5.18) • Bone morphogenetic protein has been identified in the spindled fibroblast-like cells
Peripheral giant cell granuloma	• Proliferation of monocytic and multinucleate giant cells (osteoclast-like or foreign body type) usually in sheets; giant cells contain 20–30 evenly distributed nuclei; mitoses may be seen in monocytic cells; fresh hemorrhage and hemosiderin deposits are usually present especially beneath the grenz zone (see Figs. 5.19 and 5.20) • May see concomitant osseous metaplasia similar to peripheral ossifying fibroma • Giant cells are positive for TRAP, RANK, and osteoprotegrin

Inflammatory Papillary Hyperplasia
(Denture Papillomatosis)

- A pebbly overgrowth of the oral mucosa, usually occurs beneath a denture

Aetiology

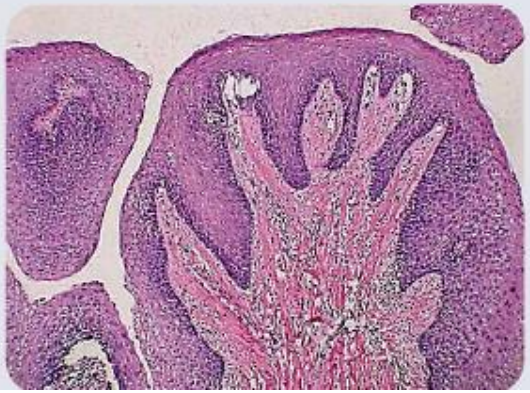
- Ill-fitting denture, a denture that is worn 24 hours a day, or denture stomatitis

Clinical features

- Multiple, pink to red, edematous or fibrous papules
- On the hard palate beneath a denture base
  - mainly the palatal vault

Microscopy

- Multiple papules of edematous fibrous connective tissue
- Normal or hyperplastic surface epithelium



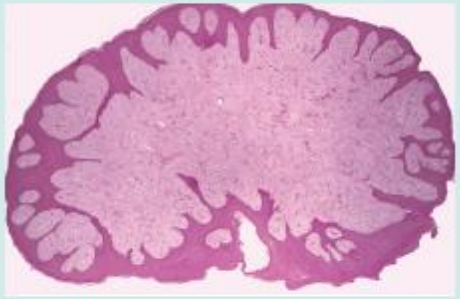
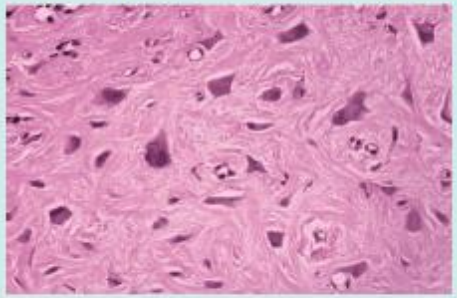
- Epulis = a growth arising from the gingiva
  - it means "on the gum"
- Often used to describe localized hyperplastic gingival lesions
  - Fibrous epulis (firm mass on the gingiva)
  - Vascular epulis (angiogranuloma on the gingiva)
  - Fibrous epulis with calcification (peripheral ossifying fibroma)
  - Giant-cell epulis (peripheral giant cell granuloma)
  - Denture epulis (epulis fissuratum)

Generalized gingival enlargements

Lesion or condition	Special characteristics
Hyperplastic gingivitis	Examples: associated with puberty, pregnancy, diabetes
Drug-related gingival hyperplasia	Examples: phenytoin, calcium-channel blockers, cyclosporine; may be fibrotic
Gingival fibromatosis	May be hereditary; onset in childhood
Leukemic infiltrate	Gingival swelling and bleeding
Wegener's granulomatosis (granulomatosis with polyangitis)	'Strawberry gingivitis' ; may have palatal ulceration and destruction, kidney, lung or nasal septum involvement; often with a skin rash, conjunctivitis or hearing loss
Scurvy	Vitamin C deficiency

Giant Cell Fibroma

- A variant of fibroma with distinctive features
- Compared to the common "irritation" fibroma:
  - does not appear to be caused by trauma
  - occurs most frequently on the gingiva
  - many demonstrate rough, papillary surface
    - can be mistaken for a papilloma
  - large stellate, multinucleated fibroblasts microscopically


Retrocuspid Papilla

- Small, pink papules on the lingual gingiva of the lower cuspids
  - frequently bilateral lesions
  - microscopic features similar to giant cell fibroma
  - do not require excision

Vascular Anomalies [Hemangiomas and Vascular Malformations]

Major types: ▪vascular tumours and vascular malformations

Classification of Vascular Anomalies

Vascular Tumours

- Infantile Hemangioma
  - Superficial
  - Deep
- Congenital Hemangioma▪
  - Noninvoluting congenital hemangioma (NICH)
  - Rapidly involuting congenital hemangioma (RICH)

Vascular Malformations

▪Capillary malformation
▪Venous malformation
▪Arteriovenous malformation
▪Lymphatic malformation

General Features

Hemangiomas

- Benign tumors
  - the most common tumors of infancy
- Most lesions are not present at birth (arise during the first 8 weeks of life)
  - few present at birth
- Display a rapid growth phase (endothelial cell proliferation)
  - typically followed by gradual involution
  - some show rapid involution or do not undergo involution

Vascular Malformations

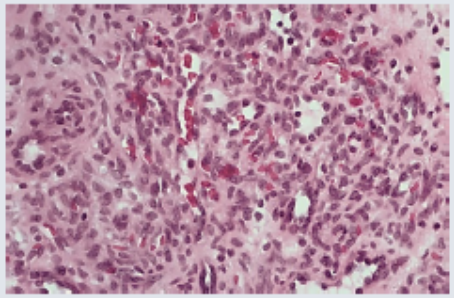
- Hamartomatous growths composed of blood or lymphatic vessels with normal endothelial cell turnover
- Present at birth and persist throughout life
- Categorized according to the type of vessel involved into:
  - capillary, venous, or arteriovenous, or lymphatic
- Categorized according to the hemodynamic features into:
  - low-flow vs. high-flow

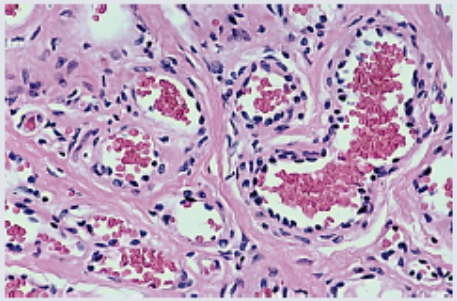
Congenital Hemangioma

- Present at birth
- Subtypes:
  - Rapidly involuting congenital hemangioma (RICH)
    - shows rapid regression, with full involution by 9 to 14 months of age
  - Noninvoluting congenital hemangioma (NICH)
    - does not undergo involution

Microscopy

- Early phase – a proliferation of plump endothelial cells forming indistinct vascular lumina
- Mature phase – capillary-sized vascular spaces lined by flattened endothelial cells
- Involution phase – get replaced by fibrous connective tissue





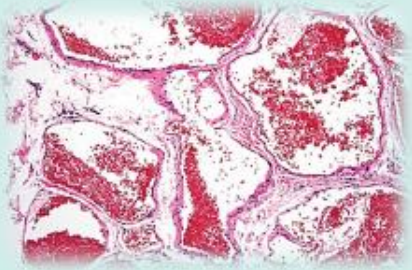
Venous Malformation

- Low-flow anomaly

Clinical features

- Blue-purple mass
  - present at birth
  - thrombi and phleboliths can form within (because of slow blood flow)





Microscopy

- Dilated thin-walled veins

Treatment

- Observation, sclerotherapy, or surgical excision
- Sclerotherapy: injection of sclerosing agents into the lesion to induce fibrosis

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Kaposi Sarcoma

- A vascular malignancy caused by human herpes virus 8

Etiology

- Human herpesvirus 8 (HHV-8)/Kaposi sarcoma–associated herpesvirus (KSHV)

Subtypes

I. Classic
II. Endemic
III. Iatrogenic (transplant-associated)
IV. Epidemic (AIDS-related)

AIDS-Related Kaposi Sarcoma

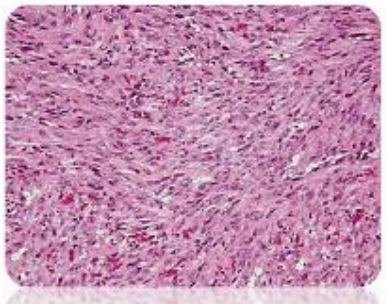
Clinical

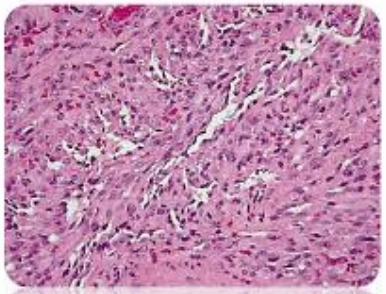
- Mainly manifests as multiple lesions on the skin or oral mucosa
  - oral lesions are seen in more than 50% of patients
- Predilection for adult homosexual males
- Considered as an AIDS-defining cancer

- Oral lesions
  - strong predilection for the palate and gingiva
  - early lesions appear as purple macules ⇨ plaques and nodules

Microscopy

- A cellular proliferation of spindle cells surrounding slit-like vascular spaces





Treatment

- Often regresses with combined antiretroviral therapy (cART)
- Other options include surgery, irradiation, intralesional chemotherapeutic agents (e.g. vinblastine), intralesional sclerosing agents (sodium tetradecyl sulfate), and systemic chemotherapy

References

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- Woo SB. 2023. Oral Pathology. A Comprehensive Atlas and Text
- Sapp JP, Eversole LR, Wysocki GP. 2004. Contemporary oral and maxillofacial pathology.