Lecture Notes for Oral & Maxillofacial Pathology-KMUOP(陳玉昆老師)

Content

➲References

✠1Oral & Maxillofacial Pathology, Elsevier, 5th edition
✠2Oral Pathology-Clinical Pathologic Correlations, Elsevier, 7th edition
✠3Stuart C. White, and Michael J. Pharoah: Oral Radiology Principles and Interpretation, 8th edition, 2009
✠researchgate.net/figure/The-antegonial-notch-depth-and-the-region-of-interest-10-10-mm-2-in-the-human_fig1_51426212
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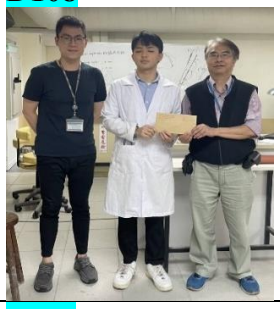
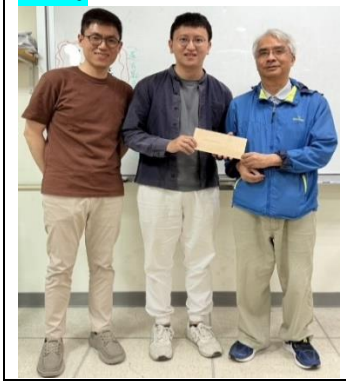
Taiwan Oral Pathology Association Scholarship

D106 	D107 	D108 	D109 
D110 	D111	D112	D113

學 習 目 標

樹貧易空，人惰易鬆

習醫之鑰

戒之以空，戒之以鬆

就從此刻，實踐以終

常被引用的一句話：

聰明人從自己錯誤中學習

智慧人從別人錯誤中學習

Chapter 1 Developmental defects of oral & maxillofacial region

Stafne defect(Stafne bone cyst, lingual mandibular salivary gland depression, static bone cyst, lingual cortical mandibular defect)

➲developmental in nature➔BUT not from birth

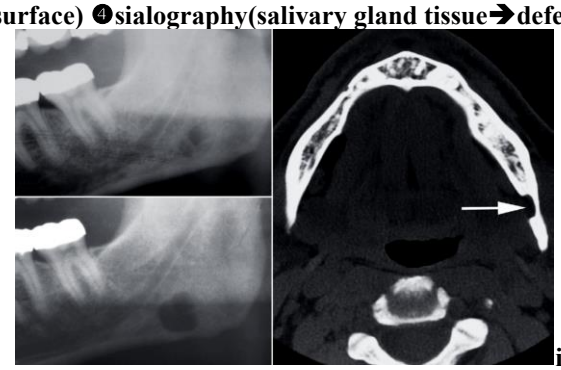
➲most➔middle-age & older adult(child rare)

➲defect content➔❶devoid of tissue ❷contain➔①muscle ②blood vessel ⑤fat ④c.t. ⑤lymphoid tissue

➲male predilection(80-90%)

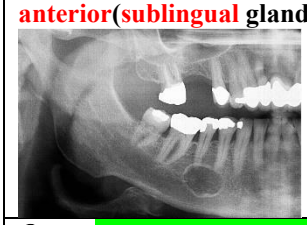
➲asymptomatic RL below mandibular canal➔posterior mandible (between molar & angle)

➲confirm➔❶CT ❷CBCT ❸MRI(WD concavity➔mandible lingual surface) ❹sialography(salivary gland tissue➔defect)

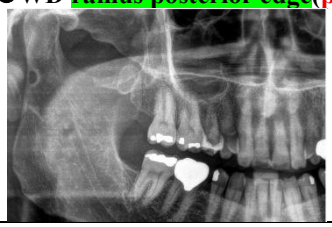


ill-defined(may be)

➲mandibular location➔WD uni(bi)lateral anterior(sublingual gland)

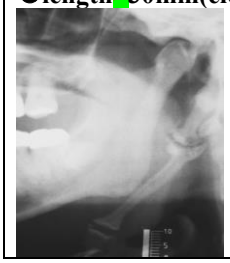


➲WD ramus posterior edge(parotid gland)



Eagle syndrome

➲length>30mm(elongated stylohyoid process, SP)



➲symptom

❶swallowing➔tissue in throat rub on SP➔pain along glosso-pharyngeal nerve

❷pain upon turning head/extending tongue

Developmental cysts(non-odontogenic)

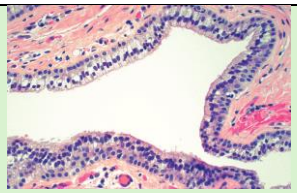
Palatal cysts of new born(Epstein's pearl, Bohn's nodule)

➔also describe gingival cyst of newborn)

➲small keratin-filled cyst (junction of hard & soft palates)

Nasolabial cyst

➲pseudostratified columnar epithelium with goblet cell & cilia

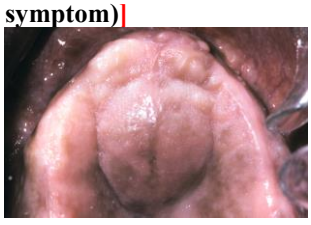


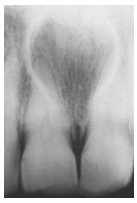
Nasopalatine duct cyst(incisive canal cyst)

➲most common nonodontogenic cyst(1%)

➲arise from remnant of nasopalatine duct

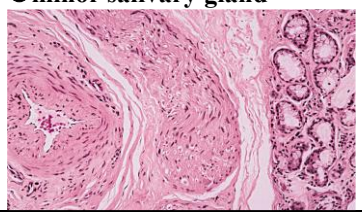
➲incisive foramen normal diameter➔6mm [RL≤6mm➔normal(unless with sign/ symptom)]





➲cystic lining➔transition from pseudostratified columnar to stratified squamous epithelium

➲cyst wall➔❶neurovascular bundle ❷hyaline cartilage ❸minor salivary gland

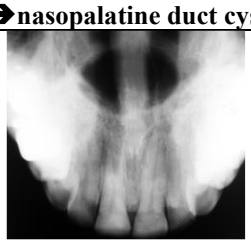


➲develop➔soft tissue of incisive papilla➔cyst of incisive papilla

Median palatal cyst

➲**true median palatal cyst➔palatal enlargement[(N.B.)midline RL without palatal expansion➔nasopalatine duct cyst]**

❶**occlusal radiograph➔hard palate➔WD oval-shaped midline RL**
❷**posterior to palatine(incisive) papilla**
❸**not related to non-vital tooth**
❹**not communicate with incisive canal**
❺**cystic wall➔no[❶neurovascular bundle ❷hyaline cartilage ❸minor salivary gland]**

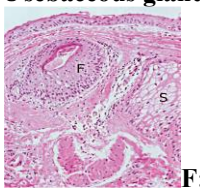



1. Which cyst is *not* an odontogenic cyst?
   (A) dentigerous cyst
   (B) primordial cyst
   (C) median palatal cyst
   (D) lateral periodontal cyst

Dermoid cyst➔most➔midline of mouth floor(under mylohyoid muscle)

➲**above geniohyoid muscle➔sublingual swelling➔ displace tongue toward mouth floor➔❶eat ❷speak ❸breath difficulty**
➲**below geniohyoid muscle➔submental swelling (double-chin)**

❶**orthokeratinized stratified squamous epithelial lining➔ prominent granular cell layer**
❷**lumen➔abundant keratin**
❸**respiratory epithelium(rare)**
❹**cyst wall➔skin appendages**
①**sebaceous gland ②hair follicle ③sweat gland**

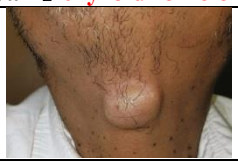
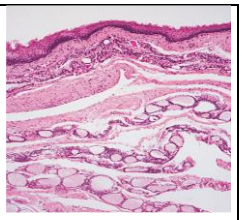


F: hair follicle; S: sebaceous gland

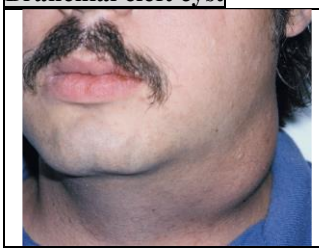
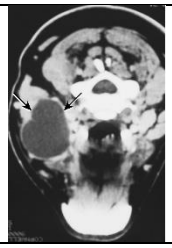
2. With which cyst may the patient complain of **dysphagia**?
   (A) thyroglossal tract cyst (dermoid cyst)
   (B) median palatal cyst
   (C) static bone cyst
   (D) traumatic bone cyst

Thyroglossal duct cyst

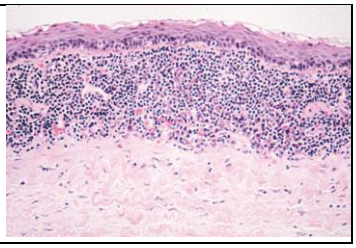
➲**swelling➔neck anterior midline(anywhere➔foramen cecum of tongue↔suprasternal notch)**
➲**tongue base➔laryngeal obstruction** | ➲**75% below hyoid bone** | ➲**cyst wall➔thyroid follicle**
➲**attach hyoid bone/tongue➔swallow➔cyst 垂直移動➔protrude tongue**
➲**suprahyoid➔submental➔dysphagia(?)**
➲**arise thyroglossal carcinoma(papillary thyroid adenocarcinoma)(1-3%)➔ metastasis rare**

Branchial cleft cyst

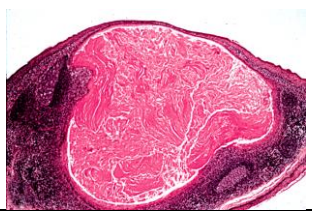
➲**2nd arch➔upper lateral neck (anterior/deep to sternocleidomastoid muscle)**
➲**cyst wall➔lymphoid tissue**
➲**most➔children & young adult(10-40 y/o)**



Oral lymphoepithelial cyst

➲**micro➔like branchial cleft cyst(BUT much smaller size)** | ➲**site➔tonsillar fossa, posterior lateral border of tongue**
➲**cyst wall➔lymphoid tissue(with germinal center)**





Synopsis➔midline & lateral neck masses

soft tissue mass➔midline neck	
thyroid gland enlargement	goiter, thyroid tumor
thyroglossal duct cyst	may move up & down with tongue motion
dermoid cyst	soft & fluctuant
plunging ranula	soft & compressible
soft tissue mass➔lateral neck	
reactive lymphadenopathy	2^0 to oral & maxillofacial infection; often tender to palpation
epidermoid cyst	soft & movable
lipoma	soft mass
metastatic carcinoma	from oral & pharyngeal carcinomas; usu. indurated & painless; may fixed
lymphoma	may uni(bil)lateral; usu. painless; Hodgkin & non-Hodgkin types
infectious mononucleosis	fatigue; sore throat; tender lymph node
salivary gland tumors	arise from submandibular gland/tail of parotid gland
submandibular sialadenitis	2^0 to sialolithiasis
branchial cleft cyst	soft & fluctuant; most young adult
granulomatous diseases	tuberculosis, sarcoidosis
cat-scratch disease	history of exposure to cat
cystic hygroma	infant; soft & fluctuant
plunging ranula	soft & compressible
other mesenchymal tumors	neurofibroma, carotid body tumor

Crouzon syndrome(Craniofacial dysostosis)

➲FGFR2(fibroblast growth factor receptor) gene point mutation(chromosome 10q26)

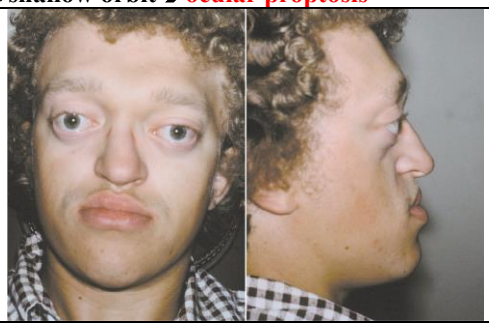
➲rare marked mental deficiency ➲sense symptoms➔❶visual impairment ❷total blindness ❸hearing deficit

➲premature sutural closure➔❶brachycephaly(short) ❷scaphocephaly(boat-shaped) ❸trigonocephaly ▲-shaped)

➲skull film➔increased digital markings(beaten-metal pattern)

➲under-develop maxilla➔❶midface hypoplasia ❷crowded upper teeth ❸occlusal disharmony

➲shallow orbit➔ocular proptosis



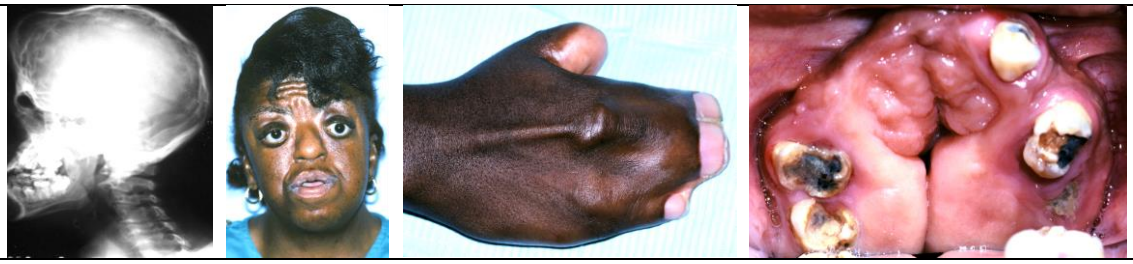
Apert syndrome

➲FGFR2 gene point mutation(chromosome 10q26)(like Crouzon syndrome)

➲syndactyly(併指) of hand phalanges & feet(2nd, 3rd & 4th digits)

➲skull film➔❶tower skull ❷midface hypoplasia(like Crouzon syndrome) ❸digital markings

➲❶ocular proptosis(like Crouzon syndrome) ❷short height ❸pseudocleft ❹梯形 appearance lips as relaxed

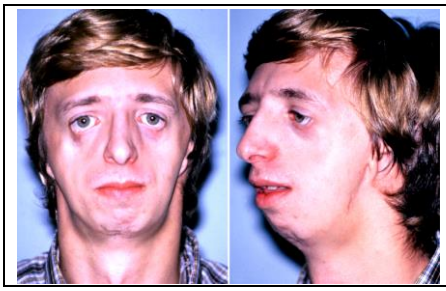


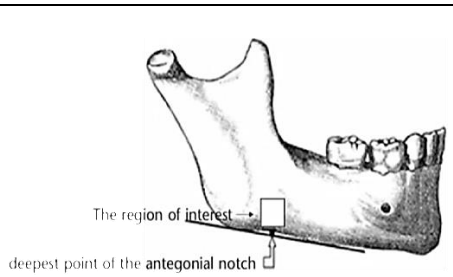
Treacher Collins syndrome(Mandibulofacial dysostosis)➔autosomal dominant➔1st & 2nd branchial arches defect

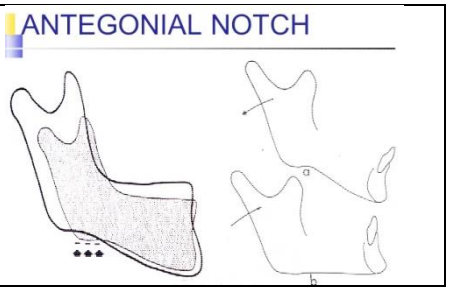
➲parotid gland➔hypoplastic(total absent)

➲radiograph➔❶condylar & coronoid processes hypoplasia ❷prominent antegonial notch ❸cleft palate

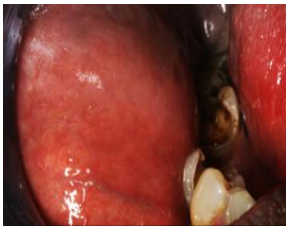
➲clinic➔❶hypoplastic mandible ❷downward-slanting palpebral fissures ❸ear deformities

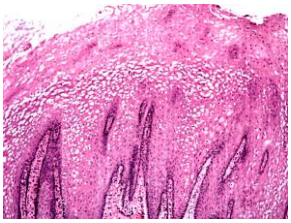






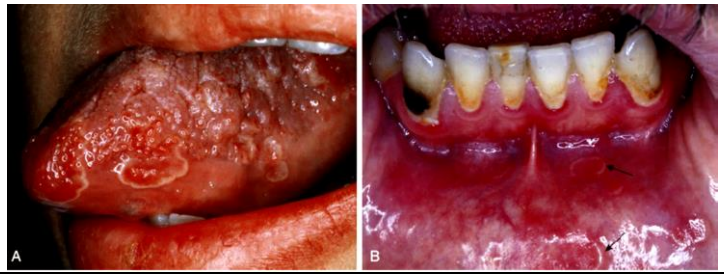
3. The benign anomaly, as shown in the left and middle figures below, has a **diffuse gray-to-white opaque** appearance on the **buccal mucosa** (**less opaque on stretching of mucosa**) with histopathological features of parakeratosis & **intracellular edema of spinous layer** (as shown in the right figure below), and is most commonly seen in adult black individuals. What is the most like diagnosis?



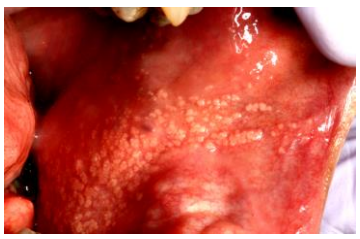


(A) leukoedema
(B) linea alba
(C) lichen planus
(D) ectopic geographic tongue

➲**(Fig. A) geographic tongue➔erythema migrans ➲(Fig. B) ectopic geographic tongue(非舌之 erythema migrans)**

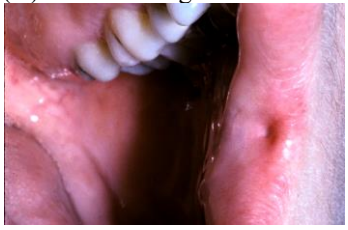


4. The condition (the left picture below) is most often seen on the buccal mucosa with histopathological features as shown in the right figure below? Which of the following is the most likely diagnosis?



(A) melanin pigmentation
(B) Fordyce granules
(C) nicotine stomatitis
(D) angular cheilitis

5. Which location is the most common for **lip pits**(as shown the figure below)?
(A) commissure
(B) philtrum
(C) nasolabial groove
(D) labiomental groove



6. The **paramedian lip pit (congenital lip pits)** occurs:
(A) in the commissure
(B) either side of the midline of vermilion of lower lip
(C) in the center of the upper lip
(D) on the mucosa of the upper lip

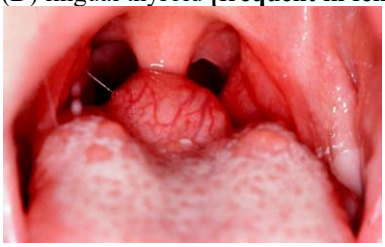
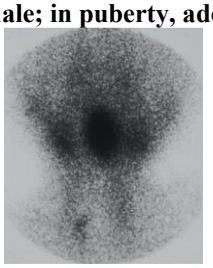
Paramedian lip pit(Congenital lip pits)

➲**van der Woude syndrome**➔❶**paramedian lip pit** ❷**most common syndromic clefting(2% of all CL+CP)**


➲**popliteal pterygium syndrome**➔❶**paramedian lip pit** ❷**CL and/or CP** ❸**popliteal webbing (pterygia)** ❹ **congenital bands connect upper & lower jaws(syngnathia)** ❺**genital abnormalities**

➲**Kabuki syndrome**➔❶**eversion of lower lateral eyelids** ❷**paramedian lip pit** ❸**CL and/or CP** ❹**large ears** ❺**hypodontia** ❻**joint laxity** ❼**skeletal abnormalities** ❽**intellectual disability**

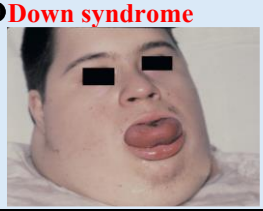
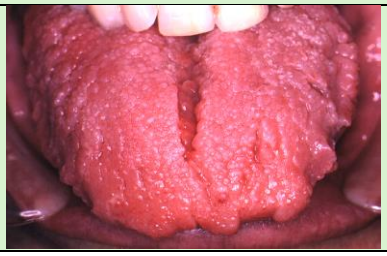
7. Which term refers to an **ectopic mass of thyroid tissue** on **posterior dorsal tongue (lower left figure) between foramen cecum & epiglottis with scan showing central dark zone of iodine/technetium-99m isotope in tongue mass & minimal uptake in neck (lower right figure) with risk of malignant transformation & causing dysphagia, dysphonia, dyspnea**?
(A) thyroid cyst
(B) thyroid tumor
(C) lingual tonsil
(D) lingual thyroid **[frequent in female; in puberty, adolescence, pregnancy, menopause; only thyroid tissue(70%)]**

Macroglossia

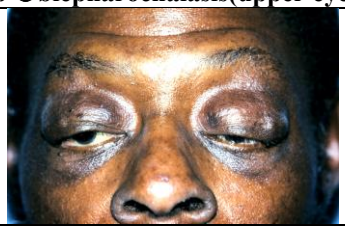
causes

➲**congenital & hereditary**			➲**acquired**		
❶**vascular malformations(lymphangioma & hemangioma)**			❶**edentulous**	❷**amyloidosis**	❸**myxedema**
❷**hemihyperplasia**	❸**cretinism**	❹**MEN type 2B**	❹**acromegaly**	❺**angioedema**	❻**myasthenia gravis**
❺**Beckwith-Wiedemann syndrome**			❼**amyotrophic lateral sclerosis**		
❻**Duchenne muscular dystrophy**			❽**carcinoma & other tumor**		
❼**mucopolysaccharidoses**	❽**neurofibromatosis type I**				
❾**Down syndrome**					

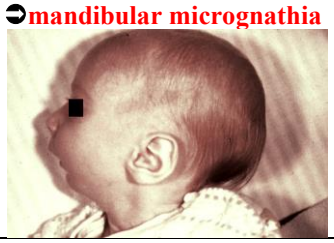



Ascher syndrome

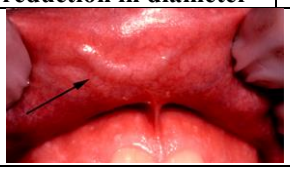
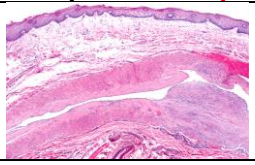
➲**triad features**➔❶**double lip** ❷**blepharochalasis(upper eyelid edema)** ❸**nontoxic thyroid enlargement(50%)**

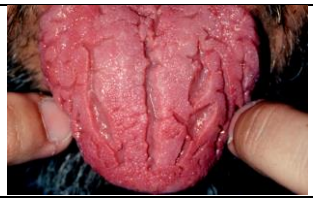
Pierre Robin sequence

➲cleft palate 	➲mandibular micrognathia 	➲glossoptosis(lower, posterior tongue displacement➔ airway obstruction)
➲❶isolated ❷associate syndromes/other anomalies(①Stickler syndrome ②velocardiofacial syndrome)		

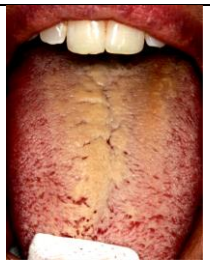
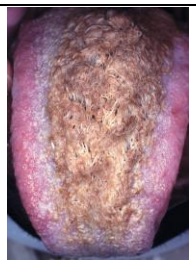
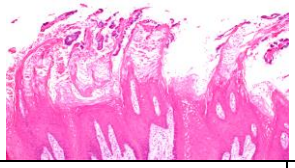
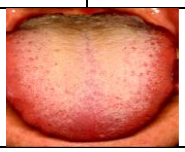
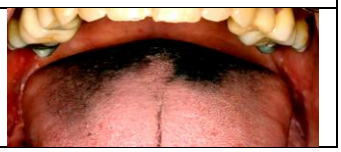
Caliber-persistent artery

➲arterial branch➔superficial submucosal tissue without reduction in diameter		➲unique feature➔pulsation
➲lip(either or both lips/bilateral)(almost exclusively)		
➲pale to normal-bluish color		
➲linear, arcuate, papular elevation		
➲stretch lip➔artery➔inconspicuous		

Fissured tongue(Scrotal tongue)

➲strong associate➔geographic tongue		
➲depth➔2-6mm	➲dorsolateral tongue	
➲component of Melkersson-Rosenthal syndrome		
➲asymptomatic(most); mild burning/soreness(some)		
➲male predilection	➲2-5% overall population	
➲prevalence & severity➔increase with age		

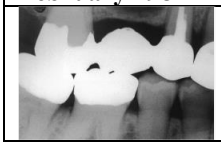
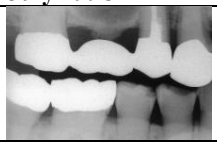
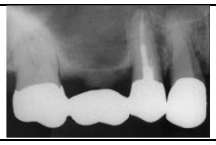
Hairy tongue(Coated tongue)

➲marked keratin accumulated on filiform papillae of dorsal tongue		 
➲0.5% of adult	➲many➔heavy smoker	
➲associate factor➔❶debilitation ❷poor oral hygiene ❸drug➔xerostomia ❹HN RT history		
➲affect midline just anterior to circumvallate papillae(no lateral & anterior)		
➲elongated papillae➔brown, yellow, black(due to pigment-produce bacteria/ tobacco & food stain)		
➲coated tongue➔without hairlike filiform projection		 
➲misdiagnosed➔candidiasis➔treated with antifungal medication		
➲transitory staining of posterior dorsal tongue using bismuth subsalicylate➔react with sulfur in saliva➔bismuth sulfide		

8. **Torus mandibularis** and **torus palatinus** are:
(A) inherited as an autosomal-recessive trait
(B) more prevalent in males
(C) inherited as an autosomal-dominant trait
(D) sporadic traits

Reactive subpontic osseous hyperplasia (exostosis)

➲radiograph ❶increased radiopacity, dense ❷compact without trabecular pattern, cortical, sclerotic ❸trabeculated ❹mottled radiopaque/radiolucent	❺smooth ❻nodular, lobulated, bilobed ❼dome shaped ❽saucer shaped

February 1984	July 1998	
		

Chapter 1: Developmental Defects of the Oral and Maxillofacial Region

1. Which one of the following statements about leukoedema is true?
A. Lesions are seen most commonly on the lateral surface of the tongue
B. Leukoedema is caused by Epstein-Barr virus
C. Malignant transformation occurs in 10% of cases
D. The condition is most common in whites
E. The white appearance disappears when the lesion is stretched

2. The branchial cleft cyst is also known as:
A. cervical lymphoepithelial cyst
B. cystic teratoma
C. dermoid cyst
D. epidermoid cyst
E. thyroglossal duct cyst

3. The favored treatment for Fordyce granules is:
A. conservative excision
B. laser ablation
C. tetracycline rinses
D. topical corticosteroid therapy
E. no treatment is necessary

4. Macroglossia is most likely to be associated with which endocrine problem?
A. Diabetes mellitus
B. Hyperparathyroidism
C. Hyperthyroidism
D. Hypoparathyroidism
E. Hypothyroidism

5. Fordyce granules are:
A. hair follicles
B. minor salivary glands
C. sebaceous glands
D. sweat glands
E. tiny epidermoid cysts

6. Which one of the following sites is the most common location for a caliber-persistent artery?
A. Buccal mucosa
B. Gingiva
C. Lateral soft palate
D. Upper labial mucosa
E. Ventral surface of tongue

7. Which one of the following developmental cysts of the oral cavity is most common?
A. Dermoid cyst
B. Globulomaxillary cyst
C. Median palatal cyst
D. Nasolabial cyst
E. Nasopalatine duct cyst

8. Which one of the following anomalies occurs in approximately 80% of the population?
A. Commissural lip pits
B. Epidermoid cysts of the skin
C. Fordyce granules
D. Hypodontia of one of the third molars
E. Torus palatinus or torus mandibularis

9. The most commonly purported cause of hairy tongue is:
A. cigarette smoking
B. human immunodeficiency syndrome infection
C. long-standing geographic tongue (erythema migrans)
D. misplaced follicular progenitor cells from the first and second branchial arches
E. mouth-breathing associated with a high-arched palate

10. The most common presenting symptom of coronoid hyperplasia is:
A. increasing anterior open bite
B. restriction of mandibular opening

C. subluxation of the temporomandibular joint
D. temporal headaches
E. unilateral cross-bite

11. The least likely site for an oral lymphoepithelial cyst is:
A. floor of mouth
B. palatine tonsil
C. posterior lateral border of tongue
D. tip of tongue

12. The microscopic appearance of a branchial cleft cyst is most similar to:
A. dermoid cyst
B. epidermoid cyst
C. nasolabial cyst
D. nasopalatine duct cyst
E. oral lymphoepithelial cyst

13. Which one of the following statements about the Stafne defect is NOT true?
A. No treatment is recommended for the Stafne defect
B. The Stafne defect also has been known as a static bone cyst
C. The Stafne defect is lined by stratified squamous epithelium
D. The Stafne defect is located beneath the mandibular canal
E. The Stafne defect occurs more commonly in males

14. The most common location for an oral dermoid cyst is:
A. floor of the mouth
B. lateral aspect of the upper lip
C. midline of the hard palate
D. posterior buccal mucosa
E. posterior lateral tongue

15. Torus palatinus and torus mandibularis are best considered as types of:
A. choristoma
B. exostosis
C. hamartoma
D. osteoma
E. all of the above

16. Which one of the following conditions occurs more commonly in blacks?
A. Commissural lip pits
B. Fordyce granules
C. Leukoedema
D. Stafne defects
E. Torus mandibularis

17. Which one of the following developmental anomalies is most likely to be associated with cleft palate?
A. Bifid condyles
B. Condylar hyperplasia
C. Lingual thyroid
D. Nasopalatine duct cyst
E. Paramedian lip pits

18. By definition, a cyst:
A. is caused by infection.
B. is filled with keratin.
C. is lined by epithelium.
D. occurs within bone.
E. will resolve by itself.

19. A Stafne defect is created by:
A. aberrant thyroid tissue
B. elongation of the stylohyoid ligament
C. hyperplasia of the coronoid process of the mandible
D. secondary inflammation of the cervical lymph nodes
E. submandibular gland

20. A simple diagnostic test for leukoedema is everting the cheek. When this is done, the leukoedema will:

A. become whiter
B. disappear
C. form multiple vesicles
D. peel off
E. release milky fluid

21. Fissured tongue is often seen associated with what other tongue condition?
A. Ankyloglossia
B. Geographic tongue
C. Hairy tongue
D. Lingual thyroid
E. Lingual varicosities

Chapter 1: Developmental Defects of the Oral and Maxillofacial Region➔answers
1. ANS: E
2. ANS: A
3. ANS: E
4. ANS: E
5. ANS: C
6. ANS: D
7. ANS: E
8. ANS: C
9. ANS: A
10. ANS: B
11. ANS: D
12. ANS: E
13. ANS: C
14. ANS: A
15. ANS: B
16. ANS: C
17. ANS: E
18. ANS: C
19. ANS: E
20. ANS: B
21. ANS: B

Chapter 2 Abnormalities of teeth

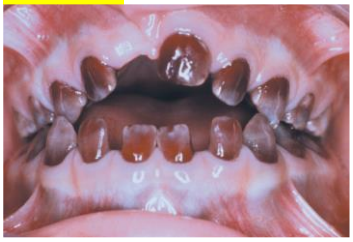
Environmental discoloration of teeth

extrinsic

- ➲bacterial stains
- ➲iron
- ➲tobacco
- ➲foods & beverages
- ➲gingiva hemorrhage
- ➲restorative materials
- ➲medications

intrinsic

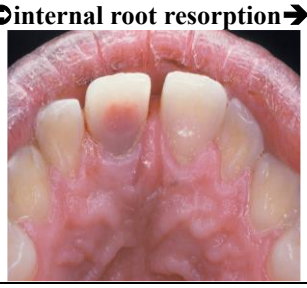
- ➲amelogenesis imperfecta(AI)
- ➲dentinogenesis imperfecta(DI)
- ➲dental fluorosis
- ➲congenital erythropoietic porphyria (紅血球合成性紫質症)(Günther disease)➔ red-brown

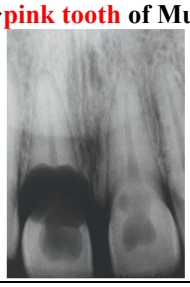


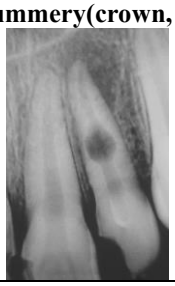
- ➲hyperbilirubinemia(高膽紅素血症)➔ yellow to green color(chlorodontia)
  - ❶deciduous teeth
  - ❷cusp of permanent 1st molar

- ➲ochronosis(黃褐斑病)(alkaptonuria)➔blue color(in conjunction with Parkinson disease)
- ➲trauma➔blood accumulate➔head➔Hb break down➔necrotic pulp
- ➲localized RBC breakdown
- ➲medication➔tetracycline(minocycline)➔brown(gray)(✪ blue alveolar ridge)

- ➲lepromatous leprosy➔pink(red) upper incisor
- ➲internal root resorption➔pink tooth of Mummery(crown, root)

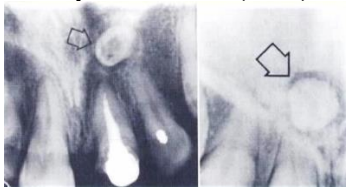




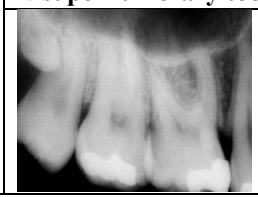


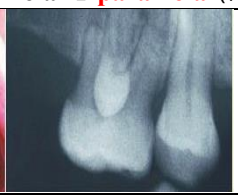
Developmental alterations in number of teeth

- ➲impacted supernumerary tooth➔projected periapical RO
- ➲non-syndromic multiple supernumerary tooth➔ lower premolar area(most)



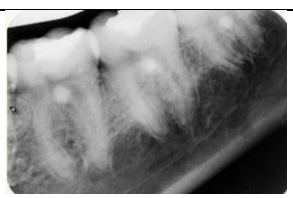
- ➲terms of supernumerary tooth➔location
  - ❶maxillary anterior incisor region➔mesiodens(中圖)
  - ❷accessory 4th molar➔distomolar(distodens) (左圖)
  - ❸supernumerary tooth lingual(buccal) to molar➔paramolar(右圖)

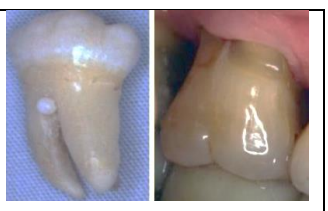




Developmental alterations in shape of teeth

- ➲multiple enamel pearls(1.1-9.7%)
  - ❶round RO➔bifurcation➔3 lower molars(左圖)
  - ❷d.d. pulp stone(within pulp chamber/canal)
  - ❸associate➔delay tooth eruption
  - ❹upper>lower permanet molar
  - ❺ectopic enamel
  - ①enamel pearl(中圖)
  - ②cervical enamel extension(右圖)





Developmental alterations in structure of teeth

Amelogenesis imperfecta(牙釉質發育不全症AI)➔遺傳疾病(autosomal dominant; autosomal recessive; X-linked)(non-syndromic)

➲synopsis➔AI classification

❶牙釉質發育不良型(hypoplasia)➔①牙釉質厚度不足 ②硬度正常(牙釉質沉積量不夠)

❷牙釉質成熟不良型(hypomaturation)(X-linked)➔①牙釉質厚度正常 ②硬度較軟(牙釉質基質蛋白(enamel matrix protein)移除不完全)

❸牙釉質鈣化不足型(hypocalcification)(autosomal dominant)➔①牙釉質厚度正常 ②質地很軟(鈣離子運輸出問題，發生在牙齒萌發後)

✪有學者統稱❷❸為hypomineralization

❹AI with taurodontism[tricho-dento(❶❷)-osseous syndrome]

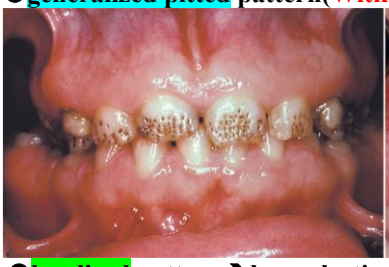
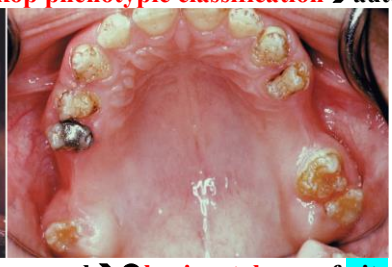
✪summary

➲❷❸➔厚度正常(❶➔厚度不足)

➲❶➔硬度正常(❷❸➔硬度較軟)

❶hypoplastic AI

➲generalized pitted pattern(Witkop phenotypic classification➔autosomal dominant ❶smooth ❷rough pattern)

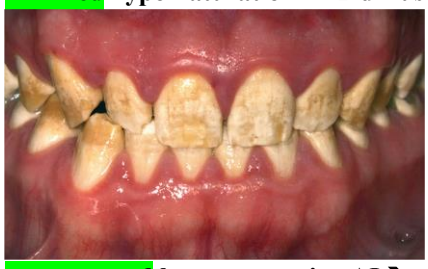
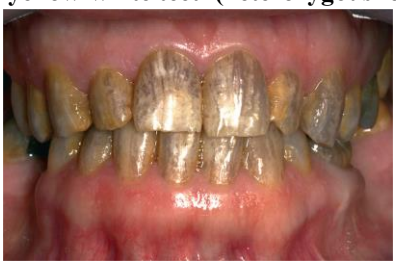



➲localized pattern➔hypoplastic enamel➔❶horizontal row of pits ❷linear depression ❸large area(middle of buccal surface)

❷hypomaturation AI

➲pigmented hypomaturation AI➔mottled & agar-brown enamel

➲X-linked hypomaturation AI➔diffuse yellow-white teeth(heterozygous female, mother➔also has this AI,右下圖)

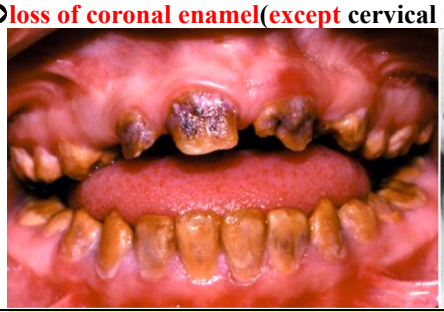
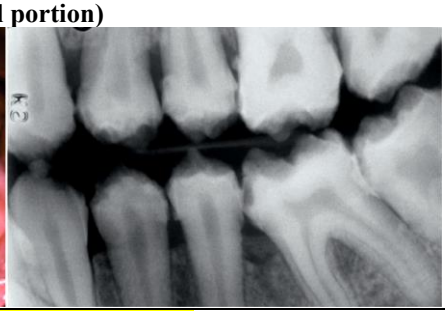



➲snow-capped hypomaturation AI➔white opaque enamel zone(1/4-1/3 incisal & occlusal of crown)

❸hypocalcified AI

➲diffuse yellow-brown discoloration

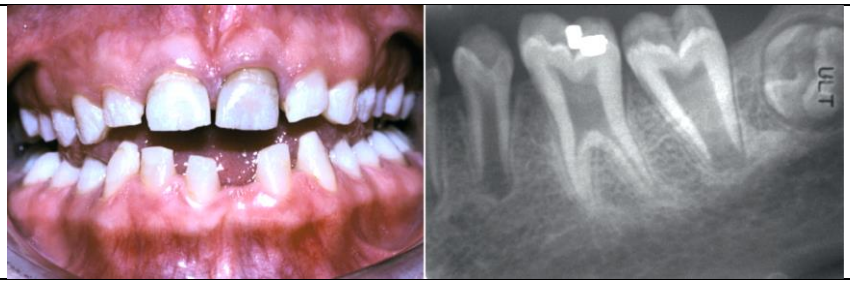
➲loss of coronal enamel(except cervical portion)

❹AI with taurodontism(tricho-dento-osseous syndrome)

➲dentition➔diffuse enamel hypoplasia+hypomaturation(AI with taurodontism)

➲systemic change➔❶kinky(扭結) hair(at birth)➔straighten with age ❷osteosclerosis(skull base & mastoid process) ❸brittle nail ❹mandible(short ramus & obtuse angle)



Dentinogenesis imperfecta(DI)

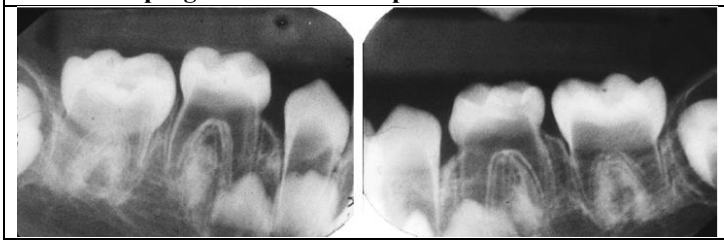
➲**1/2 p't➔with osteogenesis imperfecta**

➲**dentin sialophosphoprotein(DSPP)-associated dental defect➔shell tooth**

Shields	de La Dure-Molla	involved gene/genes
dentinogenesis imperfecta I	osteogenesis imperfecta with opalescent teeth	COL1A1, COL1A2
dentin dysplasia type II dentinogenesis imperfecta II dentinogenesis imperfecta III	dentinogenesis imperfecta mild form moderate form severe form(shell tooth)	DSPP
dentin dysplasia type I(DD-I)	radicular dentin dysplasia	?? SMOC2, VPS4B, SSUH2

1. 關於**殼狀牙(shell tooth)**的敘述，下列何者錯誤？(113)
   (A) 最常見於牙本質形成不良(dentinogenesis imperfecta)之恆齒列
   (B) 與牙本質形成不良(dentinogenesis imperfecta)無關者，稱為孤立型(isolated type)
   (C) 孤立型(isolated type)殼狀牙常有緩慢但持續之牙根吸收
   (D) 孤立型(isolated type)殼狀牙可呈現正常牙齒之外型及顏色

➲**severe form of DI(shell teeth)**
❶**pulp enlarge with normal-thickness enamel➔extreme thin dentin➔entire tooth(isolated to root)**
❷**deciduous teeth(most)➔DI➔pulp expose**
❸**unassociate with DI(isolated type)**
①**both dentitions➔normal tooth shape & coloration**
②**family history(-)**
③**diffuse involvement**
④**slow but progressive root resorption**



❹**kindred(親屬) affected with DI➔evaluate for hear loss**
①**correlate with DSPP mutation**
②**2^0 to 1^0 gnathic change**
[jaw position
①**affect inner ear**
②**premature tooth loss➔hearing deficit]**

2. Loss of tooth structure caused by **chemical action** describes:
   (A) abrasion
   (B) internal resorption
   (C) erosion
   (D) attrition

3. Loss of tooth structure associated with **bulimia** is caused by:
   (A) attrition
   (B) erosion
   (C) bruxism
   (D) abrasion

4. Generalized loss of tooth structure primarily on the **lingual surfaces of maxillary anterior teeth** is associated with:
   (A) erosion
   (B) attrition
   (C) abrasion
   (D) abfraction

5. The wearing away of tooth structure through an **abnormal mechanical action** defines:
   (A) attrition
   (B) abrasion
   (C) erosion
   (D) resorption

6. Which of the following is *not* associated with **attrition**?
   (A) toothpaste
   (B) bruxism
   (C) mastication
   (D) age

7. **Wedge-shaped** defects at **cervical area of teeth** (deep & narrow enamel cervical defect) (figure below) define which of following terms?
   (A) erosion
   (B) abfraction
   (C) attrition
   (D) abrasion

8. **Non-syndromic multiple supernumerary teeth** are most seen in area of:
   (A) maxillary molars
   (B) mandibular molars
   (C) maxillary premolars
   (D) mandibular premolars

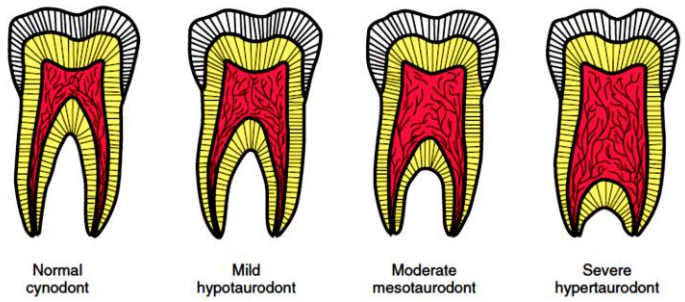
9. The cause of **supernumerary teeth** is most likely:
   (A) genetic
   (B) traumatic
   (C) cystic
   (D) systemic

10. Which term refers to a developmental anomaly in which teeth exhibit **elongated, large pulp chambers** and **short roots**?
    (A) dens invaginatus
    (B) dens evaginatus
    (C) taurodontism
    (D) dilacerations

11. **Taurodontic teeth**:
    (A) are supernumerary
    (B) are pyramidal in shape
    (C) have long roots
    (D) have thistle-shaped pulp chambers

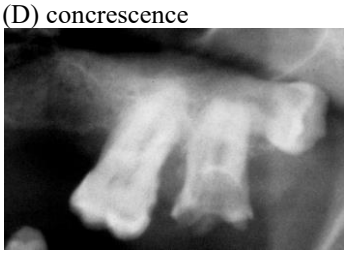
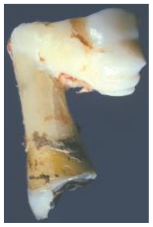
Taurodontism

syndromes associate with taurodontism				
➲amelogenesis imperfecta, hypoplastic type IE		**➲amelogenesis imperfecta-taurodontism type IV**		
➲cranioectodermal dysplasia	**➲Down**	**➲ectodermal dysplasia**	**➲Ellis-van Creveld**	
➲hyperphosphatasia-oligophrenia-taurodontism		**➲hypophosphatasia**	**➲Klinefelter**	**➲Lowe**
➲microcephalic dwarfism-taurodontism		**➲microdontia-taurodontia-dens invaginatus**		**➲Rapp-Hodgkin**
➲oculo-dento-digital dysplasia	**➲oral-facial-digital type II**		**➲scanty hair-oligodontia-taurodontia**	
➲sex chromosomal aberrations(e.g., XXX, XYY)		**➲tricho-dento-osseous types I, II, III**		
➲tricho-onycho-dental		**➲Wolf-Hirschhorn**		



➲type➔❶rectangular ❷pulp chamber➔↑apico-occlusal height ❸bifurcation close to apex
➲uni(bi)lateral➔2^0 teeth frequence>1^0 teeth➔no sex predilection➔prevalence(0.5-46%)
➲field effect(involve all molars)➔1st molar(most severe)➔least with ↑severity in 2nd & 3rd molars

12. Which term refers to the **joining of teeth by cementum** (figure below) *only*?
    (A) fusion
    (B) gemination
    (C) twinning
    (D) concrescence

13. Which teeth are **most often missing**?
    (A) canines
    (B) deciduous second molars
    (C) third molars
    (D) premolars

14. Which tooth is **the most common supernumerary tooth**?
    (A) mesiodens
    (B) distomolar
    (C) paramolar
    (D) Hutchinson incisor

15. Which tooth is the **second most common supernumerary tooth**?
    (A) taurodont
    (B) mesiodens
    (C) paramolar
    (D) distomolar

16. Which teeth most often appear **smaller than normal**?
    (A) mandibular premolars
    (B) maxillary lateral incisors
    (C) mandibular lateral incisors
    (D) mandibular third molars

17. Which term refers to the developmental anomaly that arises when **a single tooth germ attempts to divide** and results in the incomplete formation of two teeth?
    (A) fusion
    (B) gemination
    (C) concrescence
    (D) dilacerations

18. Which term refers to the developmental anomaly that arises from the **union** of two normally separated adjacent tooth germs?
    (A) twinning
    (B) gemination
    (C) fusion
    (D) dilacerations

19. Which developmental anomaly is often associated with a **nonvital** tooth and **periapical lesions**?
    (A) dens invaginatus
    (B) dens evaginatus
    (C) taurodontism
    (D) talon cusp

20. Which of the following teeth most often exhibit **supernumerary roots**?
    (A) maxillary first premolars
    (B) maxillary third molars
    (C) mandibular first molars
    (D) maxillary first molars

21. Which teeth are most often **impacted**?
    (A) distomolars
    (B) maxillary and mandibular first molars
    (C) mandibular cuspids
    (D) mandibular third molars

22. **Natal teeth** are teeth that present:
    (A) 2 months in utero
    (B) at birth
    (C) after 1 month
    (D) at 6 months

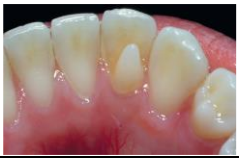
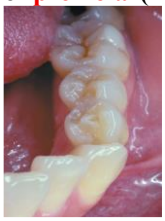
23. When a patient is **missing six teeth** without including third molars, the condition is specifically termed:
    (A) hyperdontia
    (B) oligodontia
    (C) hypodontia
    (D) microdontia

24. Which location is the most likely for an **enamel pearl**?
    (A) maxillary molars
    (B) maxillary second premolar
    (C) mandibular premolars
    (D) mandibular molars

25. Which location is the most likely for a **talon cusp**?
    (A) canines
    (B) incisors
    (C) molars
    (D) premolars

26. Which term refers to an **accessory cusp** located on the occlusal surface of a tooth?
    (A) mulberry cusp
    (B) talon cusp
    (C) dens invaginatus
    (D) dens evaginatus

Accessory cusp

➲**cusp of Carabelli**➔**palatal surface of ML cusp of maxillary molar** 	➲**talon cusp**(前牙lingual surface) ❶上顎恆側門齒(55%) ❷上顎恆正門齒(33%) ❸下顎恆前牙(6%) ❹上顎犬齒(4%) 	➲**dens envaginatus**➔**buccal cusp of premolar(molar)** 

27. Which term refers to the irregular areas of discoloration that result from **fluoride ingestion**?
    (A) pitting defects
    (B) developmental defects
    (C) mottling defects
    (D) extrinsic staining

28. **Fluoride ingestion** causing **enamel hypoplasia** can affect which of the following?
(A) maxillary posterior teeth
(B) all teeth
(C) one tooth
(D mandibular incisors

29. All of the following cause **endogenous staining** of teeth *except* one. Which one is the exception?
(A) tetracycline
(B) rhesus incompatibility
(C) penicillin
(D) neonatal liver disease

30. Which one of the following describes the appearance of **enamel hypoplasia** resulting from a febrile illness or **vitamin deficiency**?
(A) pitting defects
(B) yellowish-brown discoloration
(C) blackish-brown staining
(D) chalky white spots

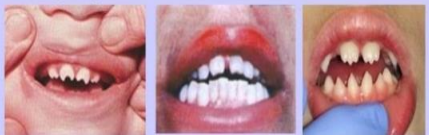
31. Which one of the following describes the appearance of **enamel hypocalcification**?
(A) pitting defects
(B) yellowish-brown discoloration
(C) blackish-brown stains
(D) chalky white spots

32. Which one of the following is associated with **enamel hypoplasia** resulting from **congenital syphilis**?
(A) turner tooth
(B) Hutchinson incisors
(C) taurodont
(D) dens evaginatus

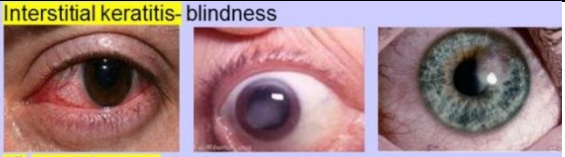
33. Which of the followings are associated with **enamel hypoplasia**?
(1) Ricket (2) Hutchinson incisors (3) congenital syphilis (mulberry molar) (4) Turner tooth
(A) only 1,2,4
(B) only 1,2,3
(C) only 2,3,4
(D) 1,2,3,4

➲**classic Hutchinson triad signs**

1. Hutchinson's incisor- anterior-posterior thickening with notch on narrowed cutting edge



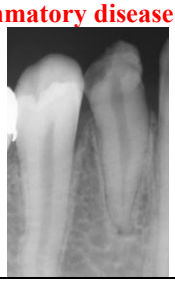
2. Interstitial keratitis- blindness



3. 8th cranial nerve- deafness

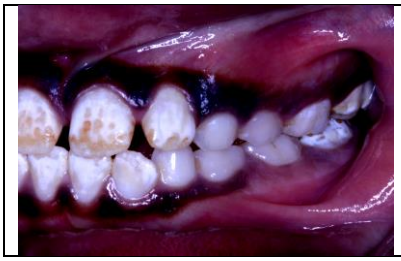
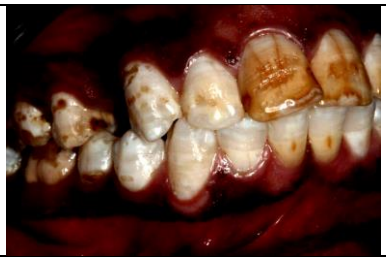
Turner tooth

➲**enamel defect➔periapical inflammatory disease of overlying deciduous tooth**



Dental fluorosis

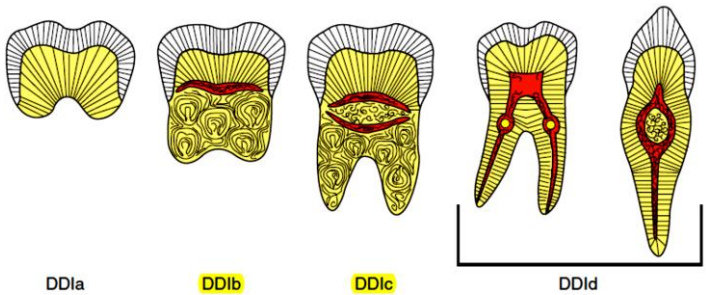
➲**water fluoridation➔recommended concentration➔0.7-1.2ppm**
➲**11, 21 crown➔cosmetic & complete development by 3s➔monitor fluoride intake during 1st 3s**
➲**enamel defect➔❶lusterless, white, opaque ❷brown enamel mottling**

34. Teeth in **snowcapped amelogenesis imperfecta** have:
(A) obliterated pulp chambers
(B) short, blunted roots
(C) a thin, brown enamel
(D) white hypocalcified enamel at the incisal & occlusal thirds

35. Which of the following **tooth is still vital** despite having **apical radiolucency**?
(A) dens in dente
(B) dens evaginatus
(C) dentinal dysplasia
(D) dentinogenesis imperfecta

36. Radiographs of a patient with **radicular dentin dysplasia (dentin dysplasia type I)** show:
(A) pulp chambers with a half-moon (crescent) appearance
(B) taurodontic teeth
(C) internal resorption of teeth
(D) large pulp chambers with long pulp horns

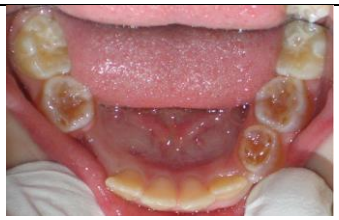
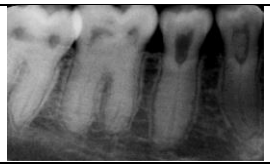


• **Fig. 2-109 Dentin Dysplasia Type I (DD-I).** Illustration demonstrating the variability of the radiographic appearance according to the degree of dentin disorganization within the root.

Dentin dysplasia type I, DDI(radicular dentin dysplasia)

DDIa	**❶no pulp chamber ❷ rootless ❸frequent periapical RL**
DDIb	**❶1 horizontal crescent shaped pulp** **❷root length➔only a few mm(extremely short)** **❸frequent periapical RL**
DDIc	**❶2 horizontal crescent-shaped pulpal remnants surrounding a central dentin island** **❷short root length** **❸variable periapical RL**
DDId	**❶visible pulp chambers & canal(near normal root length)** **❷enlarged pulp stone located in coronal portion of canal➔a localized bulging of canal & root** **❸constriction of pulp canal apical to stone** **❹few periapical RL**

Dentin dysplasia type II(coronal dentin dysplasia)

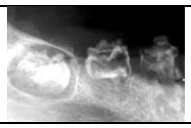
deciduous teeth **❶blue-to-amber-to-brown translucence(like DI)** **❷radiograph** **①bulbous crown** **②cervical constriction** **③thin root** **④early pulp obliteration**	
permanent teeth **❶normal color** **❷radiograph** **①pulp chamber enlargement** **②thistle(flame) tube-shaped apical**	

37. In **dentinogenesis imperfecta type II**, teeth have:
(A) hard, dense dentin
(B) dilacerated roots
(C) markedly brittle enamel
(D) short and thin roots

38. Which of the following radiographic findings of dentinogenesis imperfecta (DI) & amelogenesis imperfecta (AI) are *false*?
(1) DI: crown size is small; AI: crown size is normal (2) DI: root canal cannot be seen；AI: can be seen (3) DI: tooth cervical constriction (4) DI: usually shows tooth open contact
(A) only 1,2
(B) only 2,3
(C) only 1,4
(D) only 3,4

39. Which term refers to **teeth that appear ghostlike** on a dental radiograph?
(A) taurodontism
(B) enamel hypocalcification
(C) regional odontodysplasia
(D) enamel hypoplasia

Regional odontodysplasia

➲**enlarged pulp & extremely thin enamel & dentin** ➲**upper anterior teeth predominant**	

Synopsis➔pathology of teeth

hyperdontia	
idiopathic supernumerary teeth	**mesiodens, paramolar, distomolar**
cleft lip & palate	**extra lateral incisor(canine)**
Gardner syndrome	**osteomas & gastrointestinal polyps**
cleidocranial dysplasia	**hypoplastic(missing) clavicles; failure of tooth eruption**
hypodontia	
idiopathic hypodontia	**missing 3rd molar, lateral incisor**
cleft lip & palate	**missing lateral incisor(canine)**
hereditary hypohidrotic ectodermal dysplasia	**cone-shaped teeth**
incontinentia pigmenti	**cone-shaped teeth**
RT during childhood	**stunted(發育不良) tooth development**
macrodontia	
fusion	**joining of two tooth germs**
gemination	**incomplete splitting of a tooth germ**
idiopathic macrodontia	**—**
facial hemihyperplasia	**affected side only; nondental tissues also enlarged**
gigantism	**abnormal tall stature**
microdontia	
supernumerary teeth	**mesiodens; 4th molars**
peg-shaped lateral incisors	**cone-shaped teeth**
dens invaginatus	**cone-shaped teeth; tendency for pulpal death & periapical pathosis**
idiopathic microdontia	**usually generalized**
hereditary hypohidrotic ectodermal dysplasia	**cone-shaped teeth; sparse, blond hair; diminished sweating**
RT during childhood	**stunted(發育不良) tooth development**
congenital syphilis	**Hutchinson's incisor**
hypopituitarism	**associated dwarfism**
malformed crown	
mesiodens & other supernumeraries	**cone-shaped teeth(microdont)**
environmental enamel hypoplasia	**high fever during tooth development**
peg-shaped lateral incisors	**cone-shaped teeth**
dens invaginatus	**cone-shaped teeth; tendency toward pulpal death & periapical pathosis**
Turner tooth	**infection(trauma) to associate 1^0 tooth**
fusion(gemination)	**double tooth**
talon cusp	**extra cusp on lingual of anterior tooth**
dens evaginatus	**extra cusp on occlusal of premolar**
amelogenesis imperfecta	**hereditary defect in enamel formation**
dentinogenesis imperfecta	**fracturing away of enamel due to hereditary defect in dentin formation; gray-yellow opalescent teeth; calcified pulp chamber**
regional odontodysplasia	**poor tooth formation in focal area; ghost teeth**

congenital syphilis	Hutchinson's incisors; mulberry molars
vitamin D-resistant rickets	hereditary condition; high pulp horn
renal osteodystrophy	abnormal calcium & phosphate metabolism
hypoparathyroidism	possible associated endocrine-candidiasis syndrome
pseudohypoparathyroidism	—
epidermolysis bullosa	hereditary blistering skin disease
RT during childhood	stunted(發育不良) tooth development
globodontia	associated with otodental syndrome
lobodontia	cusp anatomy resembles teeth of carnivores
enamel loss after tooth formation	
caries	—
trauma	fracture tooth
attrition	physiologic loss of tooth structure
abrasion	pathologic loss of tooth structure
erosion	chemical loss of tooth structure
dentinogenesis imperfecta	hereditary defect in dentin formation; poor junction between enamel & dentin
amelogenesis imperfecta	hereditary defect in enamel formation; especially hypocalcified types
extrinsic staining of teeth	
tobacco	black/brown
coffee, tea, cola drinks	brown/black
chromogenic bacteria	brown, black, green, or orange
chlorhexidine	yellow-brown
intrinsic discoloration(staining) of teeth	
aging	yellow-brown; less translucency
death of pulp	gray-black; less translucency
fluorosis	white; yellow-brown; brown; mottled
tetracycline	yellow-brown; yellow fluorescence
internal resorption	pink tooth of mummery
calcific metamorphosis	yellow
dentinogenesis imperfecta	blue-gray; translucent
amelogenesis imperfecta	yellow-brown
congenital erythropoietic porphyria	yellow; brown-red; red fluorescence
erythroblastosis fetalis	yellow; green
abnormally shaped root	
external root resorption	2^0 to infection, cyst, tumor
dilaceration	abnormal curvature
hypercementosis	excessive cementum production
supernumerary roots	—
concrescence	joining of teeth by cementum
taurodontism	enlarged pulp chambers; shortened roots
enamel pearl	ectopic enamel in furcation
cementoblastoma	tumor attached(fusion) to root
radiotherapy during childhood	stunted root development
dentinogenesis imperfecta	shortened roots; obliterated pulps
radicular dentin dysplasia(dentin dysplasia type I)	shortened, pointed roots(rootless teeth); obliterated pulps; periapical pathosis
enlarged pulp chamber or canal	
internal resorption	2^0 to caries/trauma
taurodontism	enlarged pulp chambers; shortened roots
severe form of dentinogenesis imperfecta	shell teeth
regional odontodysplasia	ghost teeth
vitamin D–resistant rickets	high pulp horns
hypophosphatasia	—
mild form of dentinogenesis imperfecta (dentin dysplasia type II)	thistle-tube pulps with pulp stone formation in permanent dentition
pulpal calcification	
pulp stones	asymptomatic radiographic finding
secondary dentin	response to caries
calcific metamorphosis	pulpal obliteration 2^0 to aging/ trauma
dentinogenesis imperfecta (moderate form)	pulpal obliteration by excess dentin
radicular dentin dysplasia(dentin dysplasia type I)	pulpal obliteration by excess dentin; chevron(V)-shaped pulp chamber
mild form of dentinogenesis imperfecta(dentin dysplasia type II)	pulpal obliteration of 1^0 teeth; pulp stone in permanent teeth
thickened periodontal ligament	
periapical abscess	focal thickening at apex of nonvital tooth; painful, esp. percussion of involved tooth
current orthodontic therapy	—
↑occlusal function	—

systemic sclerosis(scleroderma)	generalized widening
sarcoma or carcinoma infiltration	esp. osteosarcoma; localized to teeth in area of tumor
generalized loss of lamina dura	
hyperparathyroidism	calcium removed from bones; bone may have ground glass appearance
osteomalacia	vitamin D deficiency in adults
Paget disease of bone	cotton wool change hides lamina dura
fibrous dysplasia	ground glass change hides lamina dura
premature teeth exfoliation	
trauma	avulsed tooth
aggressive periodontitis	premature alveolar bone loss
immunocompromised states	AIDS, leukemia, chemotherapy
diabetes mellitus	↑susceptibility to infection and severity of periodontitis
osteomyelitis	bone destruction loosening teeth
cyclic/chronic neutropenia	↑susceptibility to infection; premature alveolar bone loss
Langerhans cell histiocytosis	eosinophilic granuloma; premature alveolar bone loss
radicular dentin dysplasia(dentin dysplasia type I)	rootless teeth
regional odontodysplasia	ghost teeth
Papillon-Lefèvre syndrome	palmar and plantar hyperkeratosis; premature periodontitis
Down syndrome	premature periodontitis
hypophosphatasia	lack of cementum production in primary teeth
scurvy	vitamin C deficiency

Chapter 2: Abnormalities of Teeth

1. A Turner tooth may be caused by:
A. excess fluoride in the water supply
B. syphilis
C. too little fluoride in the water supply
D. trauma to the primary dentition
E. viral infection

2. Hypodontia may be a feature of which syndrome?
A. Gardner syndrome
B. Hypohidrotic ectodermal dysplasia
C. McCune-Albright syndrome
D. Neurofibromatosis
E. Peutz-Jeghers syndrome

3. Dens in dente occurs most frequently in which tooth?
A. Mandibular central incisor
B. Mandibular cuspid
C. Mandibular molars
D. Maxillary bicuspid
E. Maxillary lateral incisor

4. Which one of the following is the most common supernumerary tooth?
A. Mandibular premolar
B. Mandibular third molar
C. Maxillary canine
D. Maxillary third molar
E. Mesiodens

5. Which one of the following tooth anomalies is characterized by a tendency for the enamel to fracture away from the dentin?
A. Dentin dysplasia type I
B. Dentinogenesis imperfecta
C. Hypoplastic amelogenesis imperfecta
D. Regional odontodysplasia
E. All of the above

6. Which one of the following is the most common developmentally missing tooth?
A. Central incisor
B. First bicuspid
C. First molar
D. Lateral incisor
E. Third molar

7. Shell teeth represent a clinical variant of:
A. amelogenesis imperfecta
B. dentin dysplasia type II
C. dentinogenesis imperfecta
D. fluorosis
E. regional odontodysplasia

8. Which one of the following tooth problems may be associated with bulimia?
A. Dilaceration
B. Enamel hypoplasia
C. Erosion
D. External resorption
E. Internal resorption

9. All of the following causes of tooth discoloration are classified as intrinsic stains EXCEPT:
A. chlorhexidine therapy
B. erythroblastosis fetalis
C. hyperbilirubinemia
D. porphyria
E. tetracycline therapy

10. The union of the roots of two adjacent teeth by excess cementum is termed:
A. abfraction

B. concrescence
C. dilaceration
D. fusion
E. gemination

11. Which one of the following conditions is characterized by multiple unerupted and supernumerary teeth?
A. Cleidocranial dysplasia
B. Crouzon syndrome
C. Ectodermal dysplasia
D. Taurodontism
E. van der Woude syndrome

12. “Snow-capped teeth” is an example of:
A. amelogenesis imperfecta
B. dens evaginatus
C. dentinogenesis imperfecta
D. the Lyon hypothesis
E. Turner’s hypoplasia

13. Macrodontia can be a clinical feature of:
A. Ascher syndrome
B. hemihyperplasia
C. juvenile diabetes mellitus
D. Pierre Robin sequence
E. radiation therapy during tooth development

14. Which one of the following dental anomalies is inherited as an autosomal dominant trait?
A. Dens invaginatus
B. Dentinogenesis imperfecta
C. Dilaceration
D. Gemination
E. Regional odontodysplasia

15. The most common problem associated with concrescence is:
A. difficulty in extraction
B. frequent association with Paget’s disease of bone
C. high frequency of pulpal necrosis
D. high incidence of pulp stones
E. lack of room for eruption of all of the teeth

16. Which one of the following dental anomalies is found most frequently in patients of Asian heritage?
A. Dens evaginatus
B. Dilaceration
C. Enamel pearls
D. Hypercementosis
E. Taurodontism

17. Obliteration of the pulp chambers by excess dentin formation is a feature of:
A. dentinogenesis imperfecta
B. Gardner syndrome
C. late taurodontism
D. regional odontodysplasia
E. secondary hyperparathyroidism

18. Mulberry molars might be seen in a child who also exhibits:
A. dens evaginatus
B. Hutchinson incisors
C. osteogenesis imperfecta
D. talon cusps
E. taurodontism

19. Riga-Fede disease refers to ulceration of the tongue associated with:
A. elongation of the styloid process
B. large mandibular tori
C. lingual thyroid
D. natal or neonatal teeth
E. persistent ankyloglossia

20. Talon cusps occur most often on which tooth?
A. Mandibular canine
B. Mandibular premolar
C. Mandibular third molar
D. Maxillary first molar
E. Maxillary lateral incisor

21. Which one of the following conditions often results in the development of nonvital teeth?
A. Dentin dysplasia type I
B. Fluorosis
C. Gemination
D. Hereditary hypohidrotic ectodermal dysplasia
E. Taurodontism

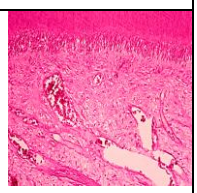
Chapter 2: Abnormalities of Teeth➔answers
1. ANS: D
2. ANS: B
3. ANS: E
4. ANS: E
5. ANS: B
6. ANS: E
7. ANS: C
8. ANS: C
9. ANS: A
10. ANS: B
11. ANS: A
12. ANS: A
13. ANS: B
14. ANS: B
15. ANS: A
16. ANS: A
17. ANS: A
18. ANS: B
19. ANS: D
20. ANS: E
21. ANS: A

Chapter 3 Pulpal & periapical dsease

Pulpitis

➲4 main etiologies
❶mechanical damage➔①trauma ②iatrogenic(dental procedures) ③attrition(abrasion) ④barometric(氣壓) change
❷thermal injury➔①cavity prepare ②polish ③chemical reaction of dental material➔transmit via metallic restoration
❸chemical irritation➔①erosion ②acidic dental material
❹bacterial effect➔toxin➔①direct from caries ②transport via vasculature

➲classification
❶reversible pulpitis➔EPT➔lower current
①cold(sweet) food, heat(sometimes)➔acute pain➔stimulus remove➔discomfort resolve in a few second
②percussion(-), tooth mobility(-), sensitivity(-)
③cracked tooth upon biting
④pulp➔hyperemia & edema

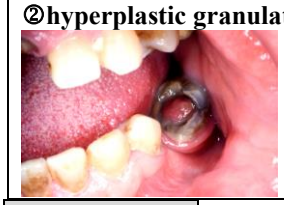
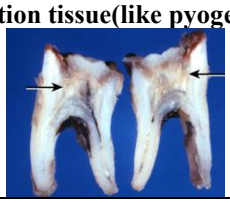
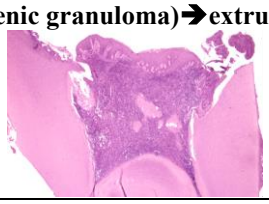


❷irreversible pulpitis➔EPT➔lower current
✪early
①thermal stimulate➔sharp pain➔stimulus remove➔continue a longer time➔easy localized affect tooth
②cold➔esp. uncomfortable(heat/sweet/acidic food➔pain)
③lies down➔pain➔spontaneous/continuous
④pain never cross midline➔can refer from arch to arch➔need EPT(both arches)
✪later➔EPT➔higher current/(-)
①heat➔↑pain intensity➔throbbing pressure➔awake at night(cold➔pain relief)
②percussion(-), tooth mobility(-)

補充(American Association of Endodontists)➔deep caries(❶caries removal➔anticipate pulp exposure ❷carious expose pulp)➔dx to irreversible pulpitis regardless of clinical symptom[(a)symptomatic irreversible pulpitis]

❸pulp necrosis➔EPT(-)
①symptom➔none-acute pain with(out) bite sensitivity & hyperocclusion
②pulse oximetry(血氧測定)➔custom stainless steel adapter➔reliable>traditional method
③partial pulpal necrosis➔pulpal necrobiosis

❹chronic hyperplastic pulpitis(pulp polyp)➔asymptomatic
①children & young adult➔large pulp expose➔deciduous(succedaneous) molar(large pulp chamber)
②hyperplastic granulation tissue(like pyogenic granuloma)➔extrude from pulp chamber

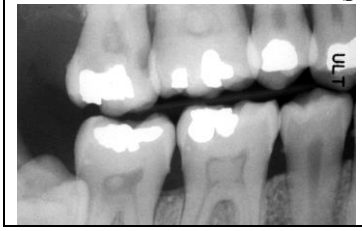
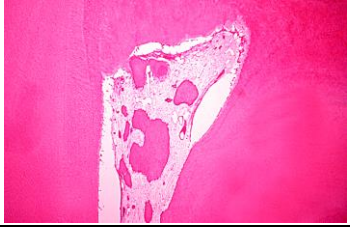
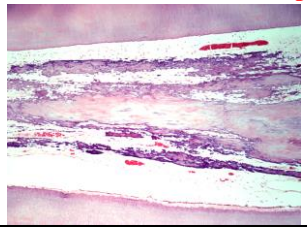
Synopsis➔pulpitis

features	reversible pulpitis	irreversible pulpitis		pulp necrosis
		early	late	
pain	acute	sharp	throbbing	none-acute
EPT	lower current	lower current	higher current/(-)	(-)
stimulus removal	resolve a few second	continue a longer time	—	—
others	❶cold➔acute pain ❷cracked tooth ❸hyperemia & edema	❶cold➔pain ❷easy localized affected tooth ❸lies down➔pain ❹pain never cross midline ❺refer from arch to arch	cold➔pain relief	

Pulp calcification➔pulp stone>200μm➔detected by radiograph

➲carious restored teeth(more frequent)➔inflammatory cause | ➲molar>premolar>incisor | ➲主要在上顎 & female

➲3 types
❶denticle➔epitheliomesenchymal interaction in developing pulp➔core of denticle
❷pulp stone(coronal pulp)➔around central nidus(collagen fibril, ground substance, necrotic cell remnant✖blood thrombi[口胚課本])➔concentric calcified material
❸diffuse linear calcification(pulp chamber/canal)(↑age)➔fine, fibrillar, calcification➔parallel vasculature

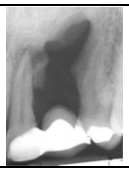
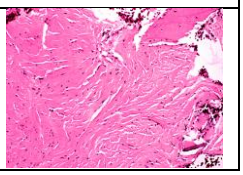
➲associate➔①CVD ②renal stone ③aging ④fluoride ⑤hypervitaminosis D
➲prominent pulpal calcification associate
❶radicular dentin dysplasia(dentin dysplasia type Id)
❷mild form DI
❸pulpal dysplasia
❹tumoral calcinosis
❺calcinosis universalis
❻Ehlers-Danlos syndrome
❼end-stage renal disease

Periapical granuloma➔periapical abscess➔periapical pathosis➔preapical granuloma➔radicular cyst

➲affected teeth➔loss of apical lamina dura➔WD/PD➔RO rim(with/without)
➲lesion>200mm²➔cyst

➲micro➔❶[eosinophilic globule of γ globulin(Russell bodies) ❷cluster of light basophilic particle(pyronine bodies)]➔plasma cell products ❸epithelial rests of Malassez(within granulation tissue) ❹cholesterol cleft

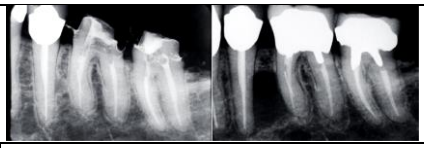
➲periapical scar
❶defect➔dense collagenous tissue➔facial(lingual) cortical plate loss➔inform p't➔form scar➔no need surgery
❷dense fibrotic c.t. with vital bone without significant inflammatory infiltrate

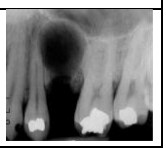
Radicular cyst➔odontogenic, inflammatory➔most common odontogenic cyst

➲2 variations(little postsurgical implication)➔laborious micro & subclassification➔impractical
❶periapical pocket cyst➔apical portion extend into lumen➔incomplete epithelial lining
❷periapical true cyst➔complete epithelium-lined baglike structure➔adjacent to separated from tooth apex
✪d.d. entire tooth & associate soft tissue➔removed *in tot*

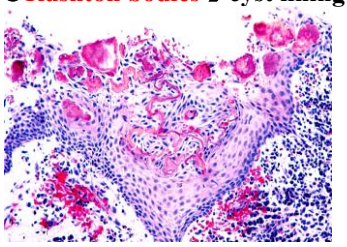
➲lateral radicular cyst➔spread through lateral foramen➔radiograph like lateral periodontal cyst



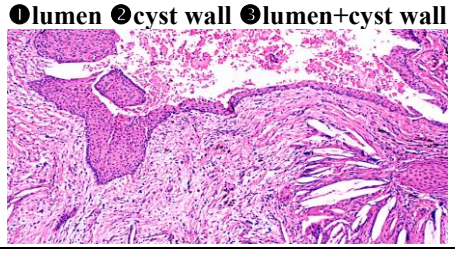
➲periapical inflammatory tissue➔not curetted of tooth removal➔inflammatory residual cyst



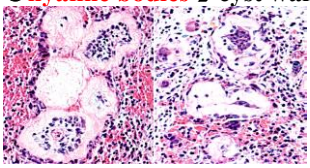
➲Rushton bodies➔cyst lining



➲dystrophic calcification, cholesterol cleft➔❶lumen ❷cyst wall ❸lumen+cyst wall



➲hyaline bodies➔cyst wall

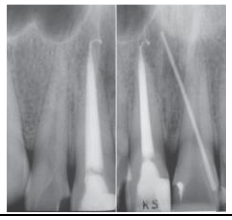


corrugated collagenous ring➔lymphocyte, plasma cell, multinucleated giant cell

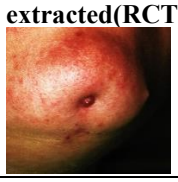
Periapical abscess

➲clinic➔(a)symptomatic➔d.d. acute apical periodontitis(no frank abscess)
➲spread along path of least resistance➔❶medullar space➔osteomyelitis ❷perforate cortex➔soft tissue(cellulitis)

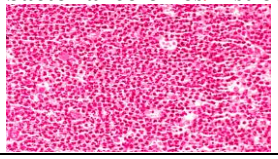
➲parulis(gum boil)➔intraoral sinus tract opening➔subacute granulation tissue mass

➲cutaneous sinus erythematous granulation tissue➔affected tooth extracted(RCT)➔resolve



➲micro➔sea of PMN intermix with inflammatory exudate, cellular debris, necrotic material, bacterial colonies/histiocyte



1. Which of the following cysts is characteristically associated with a tooth that is **nonvital** on pulp testing?
   (A) residual
   (B) radicular
   (C) dentigerous
   (D) dermoid

2. Which of the following cysts results when a **tooth is extracted without removing the periapical cystic sac**?
   (A) radicular
   (B) primordial
   (C) residual
   (D) periodontal

3. Which of the following statements is *false*?
   (A) a periapical cyst develops from a periapical granuloma
   (B) a periapical abscess always causes radiographic periapical changes
   (C) a periapical granuloma is a circumscribed area of chronically inflamed tissue
   (D) a periapical cyst is also called a radicular cyst

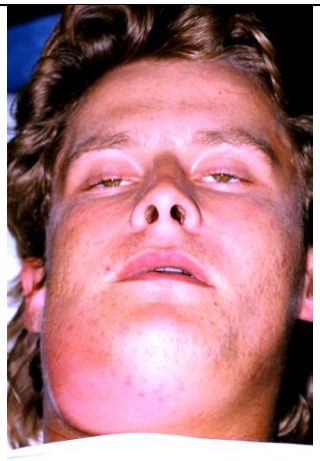
4. A **pink protruding mass** in the occlusal surface of a severely carious **mandibular first or second molar** is most likely a(n):
   (A) irritation fibroma
   (B) pyogenic granuloma
   (C) pulp polyp
   (D) pulpal granuloma

5. **Condensing osteitis** is diagnosed mainly through which type of diagnostic process?
   (A) clinical
   (B) radiographic
   (C) laboratory
   (D) therapeutic

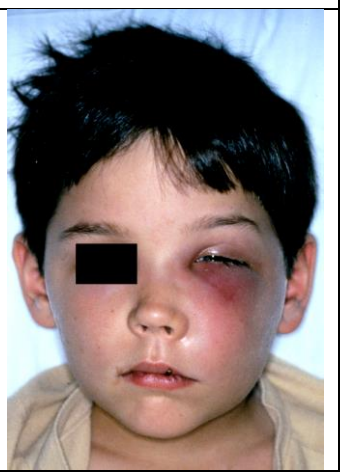
Cellulitis

➲**2 dangerous forms**

❶**Ludwig angina**
unilateral➔bilateral
①sublingual space[massive neck swelling➔clavicle➔tongue elevation, posterior enlargement, protrusion(woody tongue)➔ compromise airway]
②submandibular space[neck enlarge & tender above hyoid bone (bull neck)] ③submental space➔④lateral pharyngeal space[respiratory obstruction 2^0 to laryngeal edema]
➔⑤retropharyngeal space➔ mediastinum➔erect position



❷**cavernous sinus thrombosis**
①edematous periorbital enlargement+involve eyelid(眼瞼) & conjunctiva(結膜)
②canine space➔ swelling➔nose (lateral border)➔ eye & periorbital (medial aspect)



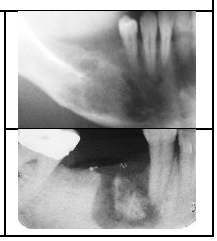
6. Which of the following description about **head and neck cellulitis** is *false*?
   (A) woody tongue is noted in Ludwig angina
   (B) bull neck is noted in infection involved submandibular space
   (C) supine position is needed for patient with retropharyngeal space infection
   (D) canine space is involved for cavernous sinus thrombosis

Osteomyelitis

Acute suppurative osteomyelitis

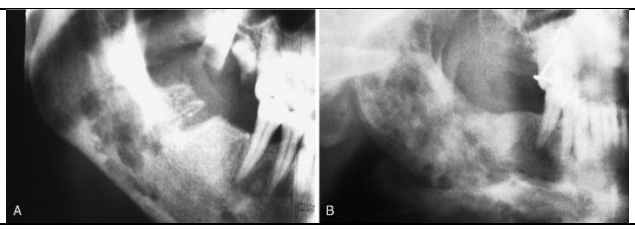
➲**acute inflammation➔spread via medullar space of bone➔insufficient time react to inflammatory infiltrate**
➲**mandible(most)➔poor vascular supply & dense cortical bone➔more susceptible to infection than maxilla**
➲**maxilla➔①主要於 pediatric ②arise from necrotizing gingivitis/noma(壞疽性口腔潰爛➔迅速惡化口腔和臉部感染➔組織壞死、骨骼損傷，嚴重臉部殘疾)**

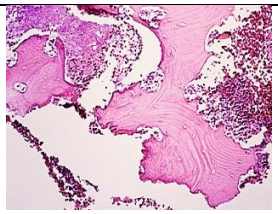
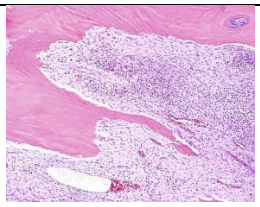
➲**radiograph**
❶**PD-RL➔(occasion with➔①PDL widening ②lamina dura loss ③loss of IAN canal/mental foramen)**
❷**periosteal new bone formation➔response to subperiosteal spread of infection**
❸**plain radiograph➔loss up to 50% bone mineral density➔才呈現 obvious pathosis➔CT(CBCT) better to detect early infection course**
❹**necrotic bone(sequestrum)➔separate from vital bone➔surround by new vital bone(involucrum)➔**
圍繞壞死骨形成反應性新生骨殼➔提供感染(壞死區域)隔離屏障➔防止炎症擴散至周圍健康組織



Chronic suppurative osteomyelitis

➲**chronic inflammation➔swelling, pain, sinus tract formation, purulent, sequestrum, tooth loss, pathologic fracture(lower lip paresthesia➔advance case)**
➲**defend response➔granulation tissue➔dense scar tissue(wall off infected area)➔encircled dead space(reservoir for bacteria)**
➔antibiotic medication difficulty reaching



➲micro ❶acute ①necrotic bone➔(1)lacuna without osteocyte (2)periphery resorption (3)bacterial colony ②bone periphery & haversian canal➔ necrotic debris & acute inflammatory infiltrate (polymorphonuclear leukocyte; PMN)		❷chronic(subacute) ①inflamed fibrous c.t. filling intertrabecular area ②scattered sequestra & abscess	
➲tx ❶acute➔①resolve infection source ②drainage ③infect bone removal ④culture ⑤antibiotic sensitivity test ❷chronic➔antibiotic medications(like used in acute form) BUT IV(high dose)			

Diffuse sclerosing osteomyelitis(DSO)

➲clinic
❶adult exclusive(no sex predominant)
❷主要於 mandible
❸develop 於 chronic infection(periodontitis, pericoronitis, apical inflammatory disease) site
❹sclerosis➔center of crestal(alveolar) bone(alveolar crest) of tooth bearing alveolar ridge
❺not area of attachment of masseter(digastric) muscle
❻not from RL fibro-osseous lesion
❼no black female predilection
❽pain & swelling➔yes but not typical

➲micro
❶sclerosis & bone remodeling➔adjacent to inflammation area➔bone not intermix with inflammatory soft tissue
※(IF)adjacent inflammation➔extend to sclerotic bone➔necrotic bone➔separate from adjacent vital tissue➔surround by subacute inflamed granulation tissue
❷haversian canal(scatter widely)➔little marrow tissue
❸secondary bacteria colony

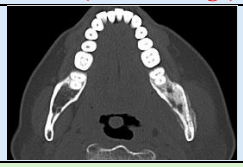
➲tx➔best via chronic infection resolution➔sclerosis remodeling(some p't) but remain in others

Chronic nonbacterial osteomyelitis(1^0 chronic osteomyelitis)

➲clinic
❶no obvious bacterial infection; no suppuration & sequestrum; culture(-); no response to long-term antibiotics
※d.d. chronic suppurative osteomyelitis & DSO)(no➔fever, purulence, sequestrum, sinus formation, odontogenic infection; nonsuppurative➔不同於 DSO & chronic suppurative osteomyelitis)
❷onset 2 peaks➔[①adolescence ②adult(>5th decade of life)]➔female predominant
❸recurrent episode➔pain, swelling, local induration, trismus(not associate dental infection)
❹enlarge & tender of overlying soft tissue & masseter muscle
❺regional lymphadenopathy & ↓sensation of IAN

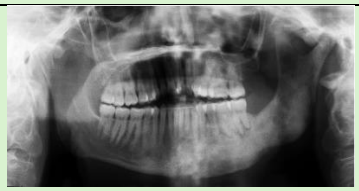
➲lab➔①↑erythrocyte sedimentation rate(ESR)(發炎指標)& C-reactive protein(CRP)肝臟分泌(急性發炎指標) ②WBC(normal range)

➲radiograph
❶early stage➔mixed RL(osteolysis) intermingle with sclerosis(RO)➔osteolytic area discontinue & alternate with zone of sclerosis(不同於 suppurative osteomyelitis)
❷affect bone thicken➔periosteal proliferation(more solid than laminated proliferative periostitis of inflammatory origin)



➲SAPHO➔Synovitis Acne Pustulosis Hyperostosis [Osteitis➔1^0 chronic osteomyelitis CRMO(chronic recurrent multifocal osteomyelitis)]➔autoimmune disturbance 2^0 exposure to acne bacteria(Propionibacterium acnes)
➲sternocostoclavicular hyperostosis(SCCH)

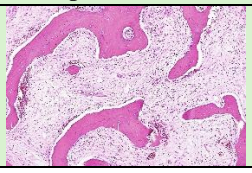
➲chronic tendoperiostitis
❶reactive bone change➔chronic overuse of masseter & digastric muscles➔ parafunctional muscle habit(bruxism, clenching, nail biting, co-contraction(共同收縮), inability to relax jaw musculature)
❷attachment of masseter muscle➔single quadrant(center on anterior angle & posterior body of mandible)



❸attachment of digastric muscle➔cuspid-premolar & anterior mandible(occasion)
❹inferior border(anterior to angle) of mandibular body➔erosion(上圖)

➲micro➔similar➔chronic nonbacterial osteomyelitis, SAPHO syndrome, CRMO, SCCH, chronic tendoperiostitis

❶dense bone, reactive bone, few inflammation signs
❷periosteal proliferation(parallel & interconnect thin bone trabeculae with intervening strip of loose c.t.)
❸medulla area➔fill with thin curvilinear trabeculae of cellular woven bone with hypocellular fibroblastic stroma➔confuse with immature fibrous dysplasia

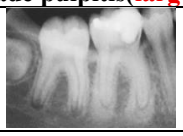


7. Which of the following description about **osteomyelitis** is *false*?
   (A) acute suppurative osteomyelitis➔bacterial infection, pustulate formation, without sequestrum
   (B) chronic suppurative osteomyelitis➔dense scar tissue wall off infected area causing antibiotic medication difficulty
   (C) primary chronic osteomyelitis➔mixed radiolucency with radiopacity noted at early stage
   (D) primary chronic osteomyelitis➔no suppuration & sequestrum; no bacterial colonies; no response to long-term antibiotics

Condensing osteitis(Focal sclerosing osteomyelitis)

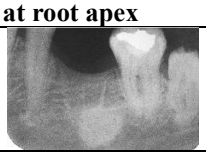
➲localize bone sclerosis➔❶teeth apex with low-grade pulpitis(large caries/deep coronal restoration) ❷pulp necrosis

➲clinic
❶children & young adult(most)➔also older adult
❷no clinical expansion
❸non-vital lower (pre)molar➔pulpitis/necrosis



➲radiograph➔no RL rim
at(not fused) root apex➔RO with thicken PDL
✠focal cemento-osseous dysplasia➔RL rim
✠idiopathic osteosclerosis➔not at root apex

➲tx
❶infection resolution(extraction/RCT)➔regress(85%)(partial/total)➔back to normal PDL width
❷residual RO after infection resolution➔bone scar➔root resorption on ortho tx(sclerotic bone in path of tooth movement)



8. Which of the following description about **condensing osteitis** is *true*? It is
   (A) a radiolucent lesion
   (B) attached to root of the affected tooth
   (C) caused by an acute pulpitis
   (D) usually associated with the large carious lesion

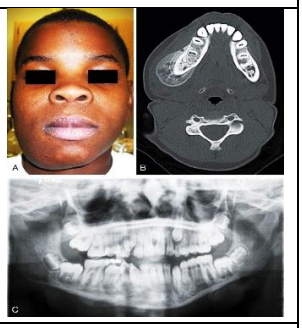
Osteomyelitis with proliferative periostitis(Periostitis ossificans, Ossifying periostitis)

➲Garrè osteomyelitis(often use synonymous)➔improper designation➔suggest not use

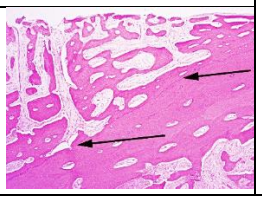
➲cause
❶osteomyelitis, trauma(tooth extraction, fracture), cyst(buccal bifurcation cyst), infantile cortical hyperostosis, fluorosis, avitaminosis C, hypertrophic osteoarthropathy, congenital syphilis, neoplasm(①Ewing sarcoma ②Langerhans cell histiocytosis ③osteogenic sarcoma), pericoronitis, non-odontogenic infection
❷most frequent➔①osteomyelitis & malignant neoplasm ②caries with periapical inflammatory disease
❸$2^0$ to periodontal infection

➲clinic➔parallel rows(lamination) of reactive vital bone➔surface expand
❶primarily child & young adult(no sex predominant)➔mean 13s
❷lower (pre)molar(most)
❸locate➔①lower border of mandible(most) ②buccal cortex(also common) ③isolated lingual cortex(infrequent)
❹unifocal(most)➔multiple quadrants(may be)

➲radiograph
❶RO lamination(1-12 片)➔parallel➔cortical surface➔RL between new bone & original cortex
❷new bone➔consolidation➔fine bony projection➔perpendicular from intact periosteum
❸in new bone➔small sequestra/osteolytic RL



➲micro
❶parallel rows(cellular & reactive woven bone)➔individual trabeculae perpendicular to surface(右圖箭頭)
❷trabeculae➔interconnect meshwork of bone(scatter widely)➔like immature fibrous dysplasia
❸between trabeculae➔uninflamed fibrous c.t.



➲tx
❶eliminate infection source(extraction/RCT)➔bone layer consolidate(6-12-mon)➔muscle remodel bone➔original state
❷periosteal reaction without inflammation source➔biopsy

Alveolar osteitis(Dry socket; Fibrinolytic alveolitis)

➲most associate➔❶↑age(40-45s) ❷preoperative infection ❸difficulty of extraction
➲other associate➔❶oral contraceptive ❷tobacco ❸inexperience surgeon ❹flap design(envelope flap rather modified triangular flap) ❺local anesthetic with vasoconstrictor ❻postoperative irrigation inadequate

➲clinic➔S/S(last 10-40 days)
❶posterior mandible(higher frequency)
❷no significant sex predilection(without oral contraceptive)
❸prevalence(1 & 3%)➔25-30% impacted lower 3rd molar
❹prevalence highest➔20 & 40s(when majority of teeth extracted)
❺3-4-day after extraction➔severe pain, foul odor, swelling(less frequent) & lymphadenopathy
❻pain radiate(occasion)➔ipsilateral ear, temporal region, eye
❼trismus(rare)

Chapter 3: Pulpal and Periapical Disease

1. Which of the following is NOT true about chronic hyperplastic pulpitis?
A. Associated with grossly carious tooth
B. Because the pulp is still vital, root canal therapy (or extraction) is not necessary
C. Granulation tissue grows out of the pulp to fill the carious defect
D. The tooth is often asymptomatic
E. Usually occurs in children and young adults

2. The most likely source of the epithelium for the periapical cyst is:
A. crevicular epithelium
B. oral mucosa
C. rests of Malassez
D. sinus mucosa
E. vascular endothelium

3. Which one of the following lesions may contain Rushton bodies?
A. Chronic osteomyelitis
B. Parulis
C. Periapical abscess
D. Periapical cyst
E. Pulp stones

4. The site of a draining abscess on the gingival/alveolar mucosa is termed:
A. ephelis
B. epulis
C. Ludwig's angina
D. nevus
E. parulis

5. A tooth that is sensitive to cold after having a restoration placed recently would probably represent an example of:
A. acute pulpitis
B. chronic hyperplastic pulpitis
C. chronic pulpitis
D. pulpal necrosis
E. reversible pulpitis

6. Which one of the following histopathologic patterns best characterizes the periapical granuloma?
A. Caseous necrosis
B. Epithelium-lined cavity
C. Fibrous scar tissue
D. Granulation tissue
E. Periosteal bone production

7. Which one of the following infections is an example of a cellulitis?
A. Ludwig's angina
B. Primary syphilis
C. Pyogenic granuloma
D. Sarcoidosis
E. Scarlet fever

8. A piece of dead bone in a case of osteomyelitis is best termed a(n):
A. cementoma
B. exostosis
C. osteoma
D. Russell body
E. sequestrum

9. The characteristic radiographic pattern seen in proliferative periostitis is:
A. "Cobweb" trabeculation
B. "cotton-wool" bone
C. "ground-glass" bone
D. "onionskin" laminations
E. widened periodontal ligament spaces

10. The predominant inflammatory cell in an abscess is the:
A. histiocyte

B. Langerhans cell
C. neutrophil
D. plasma cell
E. T-lymphocyte

Chapter 3: Pulpal and Periapical Disease➔answers
1. ANS: B
2. ANS: C
3. ANS: D
4. ANS: E
5. ANS: E
6. ANS: D
7. ANS: A
8. ANS: E
9. ANS: D
10. ANS: C

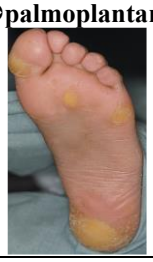
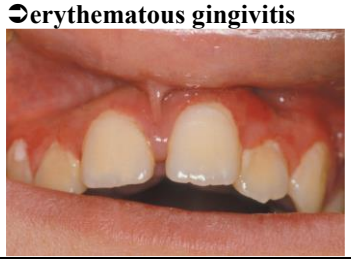
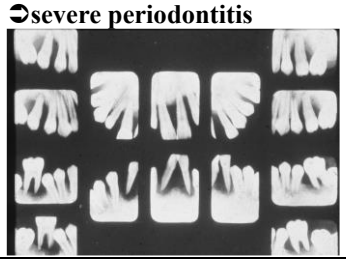
113-2 midterm exam
1. Which of the following statement about radicular cyst is *false*? (Chapter 3)
(A) it is associated with a tooth that is nonvital on pulp testing
~~(B) Russell bodies can be detected in cystic wall microscopically.~~(Russel bodies➔periapical granuloma)
(C) Rushton bodies can be detected in cystic lining microscopically
(D) hyaline bodies can be detected in cystic wall microscopically

2. Which of the following statement about pulpal calcification is *false*? (Chapter 3)
(A) prominent pulp stone can be found in patients with Ehlers-Danlos syndrome
(B) concentric pulp stone can be detected in ~~root canal~~ pulp chamber
(C) diffuse linear calcification can be detected in pulp chamber(also in root canal)
(D) pulp stone < 200 μm in diameter cannot be detected by radiographic examination

3. Which of the following statement about reversible and irreversible pulpitis is *false*? (Chapter 3)
(A) pain never cross midline for early irreversible pulpitis
(B) higher EPT current is usually noted in later irreversible pulpitis
(C) ~~dull~~ acute pain and resolves in a few seconds being noted in reversible pulpitis
(D) crack tooth upon biting is noted in reversible pulpitis

Chapter 4 Periodontal diseases

Papillion-Lefevre syndrome

➲palmoplantar hyperkeratosis	➲erythematous gingivitis	➲severe periodontitis
		

1. Which of the following features of patients with **Papillon-Lefevre syndrome** are *true*:
   (1) autosomal recessive pattern (2) autosomal dominant pattern (3) severe periodontal disease (4) palmoplantar hyperkeratosis
   (A) only 1,3,4
   (B) only 2,3,4
   (C) only 3,4
   (D) only 1,4

2. A 9-year-old boy exhibits markedly swollen red and bleeding gingiva. In addition, he has tooth mobility, and the intraoral radiographs show marked alveolar bone atrophy with vertical periodontal pockets. Which of the following will be found in this child if has been to have Papillon-Lefevre syndrome?
   (A) blue sclerae
   (B) lack of anterior vestibular sulcus
   (C) diminished sweating
   (D) palmar and plantar hyperkeratosis

3. Which of the following is *not* a clinical characteristic of **necrotizing ulcerative gingivitis**?
   (A) painful gingiva
   (B) xerostomia
   (C) foul odor
   (D) metallic taste

Drug-induced gingival hyperplasia

anticonvulsant➔❶phenytoin ❷carbamazepine	Ca channel blocker➔nifedipine	cyclosporine➔GVHD(50%)	➲erythromycin ➲oral contraceptive
			

Desquamative gingivitis

➲superficial peeling of epithelium➔rupture of mucosal vesicles➔mucous membrane pemphigoid

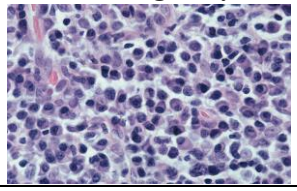
➲atrophic & erosive gingiva without peeling of epithelium
❶lichen planus(most frequent)
❷linear IgA disease
❸pemphigus vulgaris
❹epidermolysis bullosa acquisita
❺systemic lupus erythematosus(SLE)
❻chronic ulcerative stomatitis
❼paraneoplastic pemphigus(less frequent)
❽coronavirus disease-2019

Plasma cell gingivitis

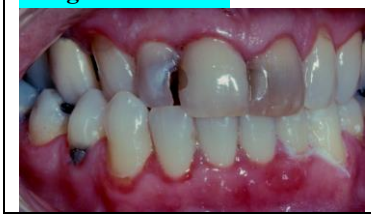
➲hypersensitivity➔❶chewing gum ❷herbal toothpaste ❸mint candy ❹pepper

➲entire free & attached gingiva➔❶diffuse enlargement with bright erythema ❷loss of normal stipple





3 atypical of periodontal diseases associated with HIV infection

❶linear gingival erythema➔linear band of erythema➔free gingival margin往下2-3mm	❷necrotizing ulcerative gingivitis➔ ulcer & necrosis of interdental papillae without attachment loss	❸necrotizing ulcerative periodontitis ➔deep pocket not seen
		

Synopsis➔dermal disease associate periodontitis➔Chapter 16

❶dyskeratosis congenital
❷Ehlors-Danlos syndrome
❸multiple hamartoma syndrome(Cowden syndrome)
❹lupus erythematous
❺junctional epidermolysis bullosa

Chapter 4: Periodontal Diseases

1. Which one of the following drugs has NOT been associated with gingival hyperplasia?
A. Amoxicillin
B. Cyclosporine
C. Dilantin
D. Nifedipine
E. Phenytoin

2. Hyperkeratosis of the palms and soles is a feature of:
A. Apert syndrome
B. Crouzon syndrome
C. Papillon-Lefèvre syndrome
D. Treacher Collins syndrome
E. tricho-dento-osseous syndrome

3. Hypertrichosis (excess body hair) can be associated with:
A. aggressive periodontitis
B. granulomatous gingivitis
C. hereditary gingival fibromatosis
D. necrotizing ulcerative gingivitis
E. plasma cell gingivitis

4. A 25-year-old white male presents to you with classic necrotizing ulcerative gingivitis. Which of the following underlying conditions should be considered?
A. Acquired immune deficiency syndrome
B. Parkinson's disease
C. Patent ductus arteriosus
D. Posttraumatic stress syndrome
E. Tetralogy of Fallot

5. Desquamative gingivitis is a clinical term used to describe the vesiculoerosive lesions of the gingiva that occur in association with dermatologic disorders. Which one of the following conditions would NOT be expected to present in the mouth as a desquamative gingivitis?
A. Erosive lichen planus
B. Pemphigoid
C. Pemphigus
D. Psoriasis

6. "Desquamative gingivitis" is most likely to occur in a:
A. 15-year-old female
B. 25-year-old male
C. 35-year-old female
D. 45-year-old male
E. 55-year-old female
ANS: E

7. Aggressive periodontitis in young persons most frequently involves:
A. bicuspids
B. cuspids
C. incisors and first molars
D. third molars
E. unerupted teeth

8. Which of the following is the inheritance pattern of Papillon-Lefèvre syndrome?
A. Autosomal dominant
B. Autosomal recessive
C. Multifactorial
D. X-linked dominant
E. X-linked recessive

Chapter 4: Periodontal Diseases➔answers

1. ANS: A
2. ANS: C
3. ANS: C
4. ANS: A
5. ANS: D
6. ANS: E

7. ANS: C
8. ANS: B

113-2 midterm exam
1. Which of the following features of patients with Papillon-Lefevre syndrome are *true*: (Chapter 4)
① autosomal recessive pattern ② autosomal dominant pattern ③ severe periodontal disease ④ palmoplantar hyperkeratosis
(A) only ①③④
(B) only ②③④
(C) only ③④
(D) only ①④

2. Desquamative gingivitis *cannot* be noted in: (Chapter 4)
(A) mucous membrane pemphigoid
(B) erosive lichen planus
(C) coronavirus disease-2019
(D) erythroplakia

Chapter 5 Bacterial infections

Synopsis➔terminology

➲macule(斑)(e.g. freckle雀斑)➔focal area of color change➔not elevate/depress in relation to its surrounding
➲patch[(與周圍不同的)小塊斑]➔small area➔different in some way from area that surrounds it
➲plaque(丘斑)➔lesion➔slightly elevated & flat on its surface
➲papule(丘疹)➔solid raised lesion➔<5mm in diameter
➲nodule(結節)➔solid raised lesion➔>5mm in diameter

➲papillary(乳突狀)➔tumor/growth➔numerous surface projections
➲verrucous(疣狀)➔tumor/growth➔rough, warty surface

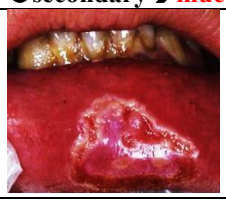
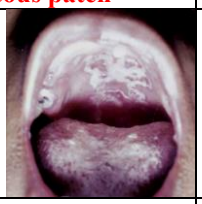
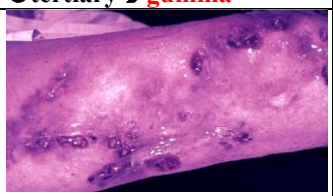
➲vesicle(小水泡)➔superficial blister<5mm in diameter, usu. filled with clear fluid
➲bulla(水皰)➔large blister➔>5mm in diameter
➲pustule(膿包)➔blister filled with purulent exudate

➲fissure(裂縫)➔narrow slitlike ulceration/groove

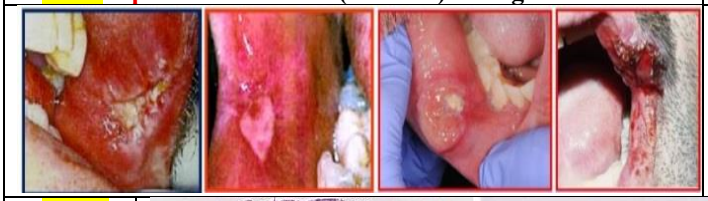
➲petechia(紫癜)➔round, pinpoint area of hemorrhage
➲ecchymosis(瘀斑)➔nonelevated area of hemorrhage>petechia
➲telangiectasia(毛細血管擴張)➔vascular lesion of small superficial blood vessel dilatation

Syphilis(Lues)➔spirochete Treponema pallidum

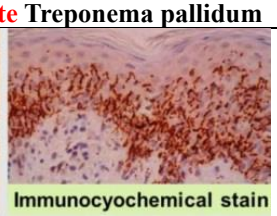
➲oral syphilis stages

❶primary➔chancre	❷secondary➔mucous patch	❸tertiary➔gumma	❹latent➔none
	 		none

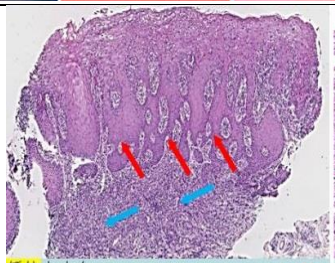
➲clinic➔painless oral ulcer(chancer)➔diagnostic criteria

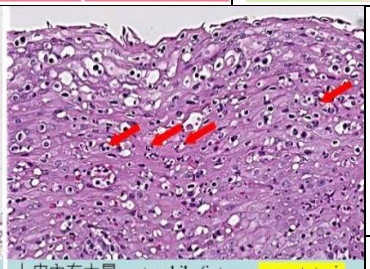


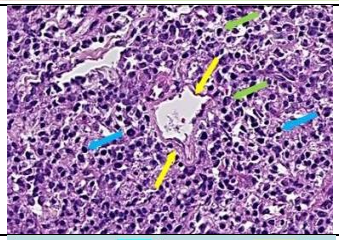
➲detection of spirochete Treponema pallidum



➲micro


低倍上皮有elongated, blunt rete ridges(red↑) lamina propria有大量發炎細胞 (blue↑)


上皮內有大量neutrophils (intense exocytotosis of neutrophils into epithelium) (red↑)


大量lymphocyte(blue↑)與plasma cell (green↑)在lamina propria 圍繞在血管週邊(yellow↑) (perivascular inflammatory infiltrate)

1. Which statement is *false*?
   (A) the primary lesion of syphilis is called a chancre
   (B) the secondary lesion of syphilis occurs at the site of inoculation with the organism
   (C) the tertiary lesion of syphilis is called a gumma
   (D) syphilis is caused by the spirochete *Treponema pallidum*

2. Which of the following is the name of the oral lesions of **primary syphilis**?
   (A) gumma
   (B) mucous patch
   (C) chancre
   (D) verruca vulgaris

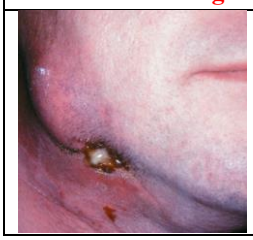
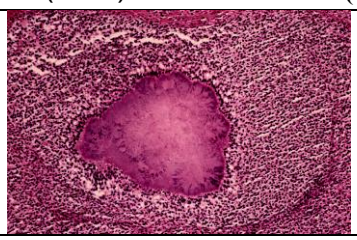
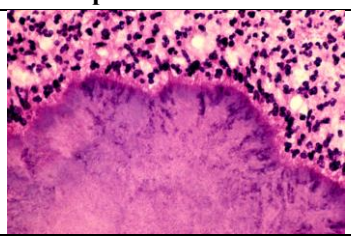
3. Which of the following stages of **syphilis** is *not* infectious?
   (A) primary
   (B) secondary
   (C) tertiary
   (D) all stages are equally infectious

4. Which of the following is *not* associated with **syphilis**?
   (A) mucous patch
   (B) venereal Disease Research Laboratories and fluorescent treponemal antibody
   (C) dark-field microscopy detecting spirochete
   (D) hypodontia

5. **Hutchinson incisors** and **mulberry molars** are associated with
   (A) odontodysplasia
   (B) congenital syphilis
   (C) neonatal liver disease
   (D) febrile illnesses

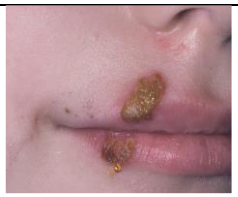
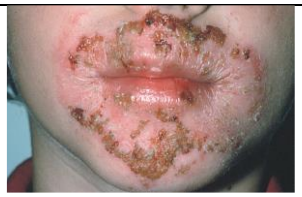
6. A specific clinical characteristic found in **actinomycosis** is:
   (A) periapical radiolucency
   (B) filamentous bacteria
   (C) fungal infection
   (D) sulfur granules present in exudate

Actinomycosis(放線菌病)➔gram(+) anaerobic bacteria(filamentous, branching)

➲**clinic➔ yellowish flecks(斑點) discharge(下左圖)**
➲**micro➔sulfur granule(下中圖)➔bacteria colonies(club-shaped filament➔radiating rosette) (下右圖)**
  

7. Perioral lesions of **impetigo** may resemble:
   (A) syphilis
   (B) herpes labialis
   (C) herpes zoster
   (D) actinomycosis

Impetigo(膿庖病)➔staphylococcus(葡萄球菌)(group A β-hemolytic)

➲**clinic➔superficial skin infection➔❶nonbullous ❷bullous pattern**	
❶nonbullous pattern(S. aureus/S. pyogenes)➔facial(nose, mouth) ➔red macule(papule)➔vesicle➔rupture➔amber(琥珀色) crust➔ like exfoliative cheilitis/recurrent herpes simplex	 
❷bullous pattern(S. aureus)➔infant & newborn➔❶extremities ❷trunk ❸face➔vesicle➔large flaccid bullae(clear serous fluid➔ turbid(混濁)➔purulent)➔rupture➔thin brown crust(右圖)	

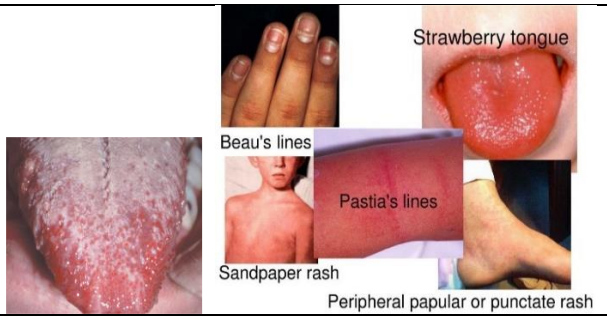
8. Which type of infection is involved when **normal components of the oral microflora** can cause disease?
   (A) chronic inflammatory
   (B) opportunistic
   (C) hyperplastic
   (D) granulomatous

9. Which of the following is *not* associated with **group A, β-hemolytic streptococcal infection**?
   (A) tonsillitis
   (B) syphilis
   (C) scarlet fever
   (D) rheumatic fever

10. "**Strawberry tongue**" is associated with which condition?
    (A) herpangina
    (B) scarlet fever
    (C) rheumatic fever
    (D) tuberculosis

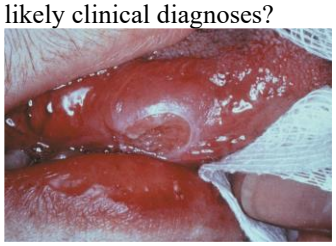
Scarlet fever(猩紅熱)➔group A streptococci(A型鏈球菌)

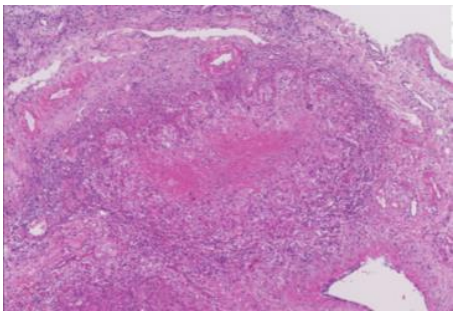
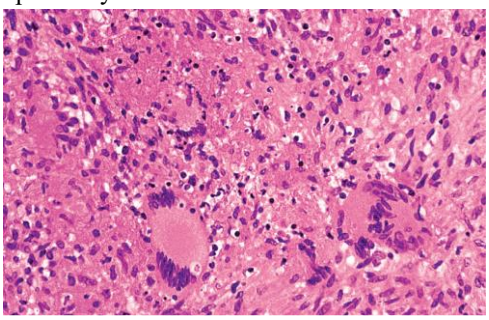
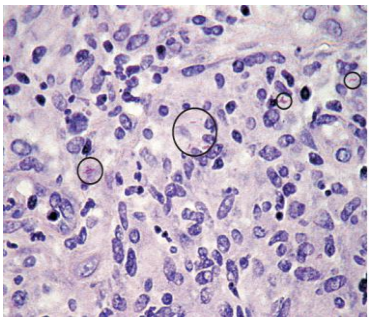
➲**clinic➔tonsillitis(pharyngitis)➔erythrogenic toxin➔attack blood vessel➔skin rash**

❶**dorsal tongue➔white strawberry tongue(white fungiform papillae coating)➔red strawberry tongue(4th/5th day)➔ erythematous hyperplastic fungiform papillae** ❷**classic rash➔sunburn with goose pimple(青春痘)➔normal color pinhead punctate project through erythema➔skin of trunk & extremities➔sandpaper texture** ❸**Pastia lines➔transverse red streaks(條痕)(skin folds 2^0 to capillary fragility in stress zone)**	

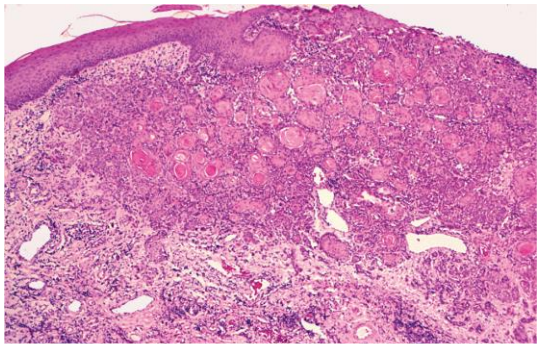
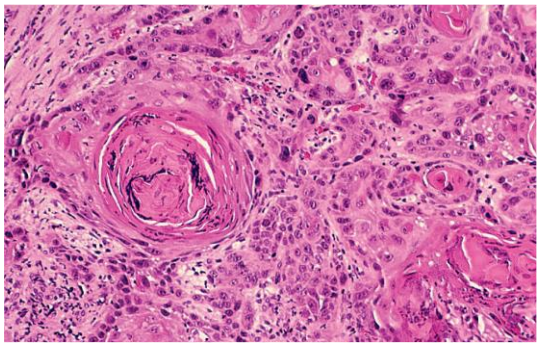
11. A positive skin reaction to **PPD** indicates:
(A) active tuberculosis
(B) contagious tuberculosis
(C) if a person has ever been infected with the tuberculosis bacteria
(D) need for antibiotic therapy

12. Which of the following microorganisms causes **tuberculosis**?
(A) *Mycobacterium israelii*
(B) *Actinomycosis israelii*
(C) *Mycobacterium tuberculosis*
(D) *Treponema pallidum*

13. A patient suffered from a painful ulceration with indurated border over right tongue border (Figure below); what are the most likely clinical diagnoses?

(1) minor oral aphthous ulcer (2) oral tuberculosis (3) oral squamous cell carcinoma
(A) 1,2,3
(B) only 1,2
(C) only 1,3
(D) only 2,3

14. Following the question 13 above, patient received **chest X-ray showing cloudy appearance of lung** as well as biopsy with the histopathological figures depicted as below. What is the most likely histopathological diagnosis, and what kind of special stain used for the most-right figure below respectively?



(1) hematoxylin stain (2) acid-fast stain (3) oral squamous cell carcinoma (4) oral tuberculosis
(A) only 1,4,
(B) only 1,3
(C) only 2,3
(D) only 2,4

15. Following the question 13 above, patient received **chest X-ray showing cloudy appearance of lung** as well as **oral biopsy with histopathological picture depicted in lower left** and **lung biopsy with histopathological picture depicted in lower right**. What is the most likely histopathological diagnosis, grade, and stage of the oral disease respectively if both oral and lung biopsies were **negative for TTF (thyroid transcription factor)-1 (a marker of lung carcinoma)** & **positive for CK** upon immunohistochemical stainings?

(1) primary oral squamous cell carcinoma (2) metastatic oral squamous cell carcinoma to lung 3) grade 1 (4) grade 3 (5) stage I (6) stage IV

(A) only 1,2,3,5

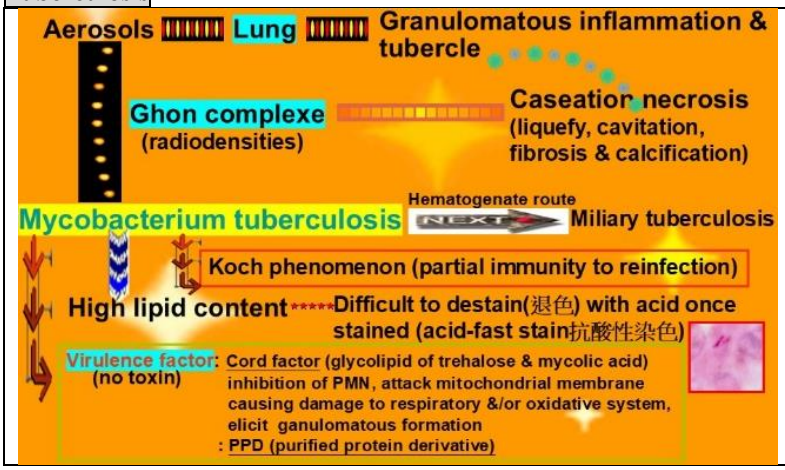
(B) only 1,2,4,6

(C) only 1,2,4,5

(D) only 1,2,3,6

oral ulcer	chest X-ray	biopsy for oral ulcer	diagnosis of oral ulcer
+	+	not done	❶$1^0$ SCC ❷$1^0$ TB ❸metastatic lung SCC ❹$2^0$ TB
+	-	not done	❶$1^0$ SCC ❷$1^0$ TB
+	-	+(OSCC)	1^0 SCC
+	+	+(TB)	2^0 TB
+	-	+(TB)	1^0 TB

Tuberculosis



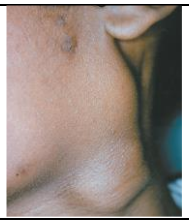
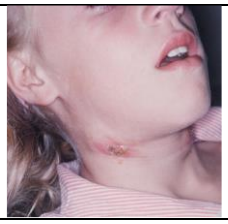
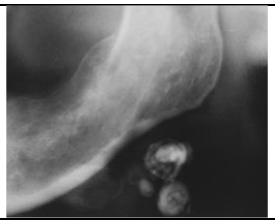
分枝桿菌屬(genus *Mycobacterium*)，結核菌綜合群(*Mycobacterium tuberculosis* Complex)

- 結核菌 (*Mycobacterium tuberculosis*)
- 牛型結核菌 (*Mycobacterium bovis*)
- 非洲型結核菌 (*Mycobacterium africanum*)

結核桿菌不具鞭毛、也不會移動，是一種好氧性的抗酸性細菌。目前尚無研究指出其會製造內毒素或外毒素，所以受到感染之後，不會立即產生反應其細胞壁含有許多脂質和蛋白質，對外界抵抗力甚強，在陰暗處痰液內的結核菌可以生存6-8 個月不死。侵入人體後可引發宿主產生遲發型過敏反應 (delayed-type hypersensitivity，DTH) 及引發乾酪性壞死 (Caseous necrosis)

Scrofula(頸部淋巴腺結核)➔nontuberculous mycobacteria

➲contaminate milk➔❶oropharyngeal lymphoid tissue ❷cervical LN enlarge(左圖) (calcified➔like sialolith radiograph)(右圖)➔caseous necrosis➔skin sinus tract(中圖)

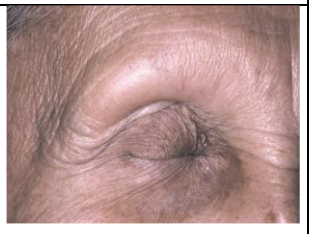




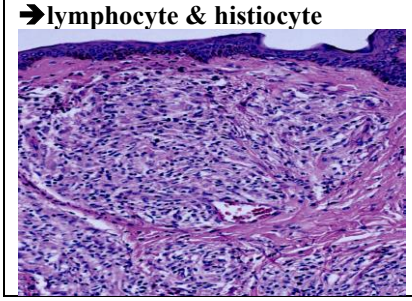
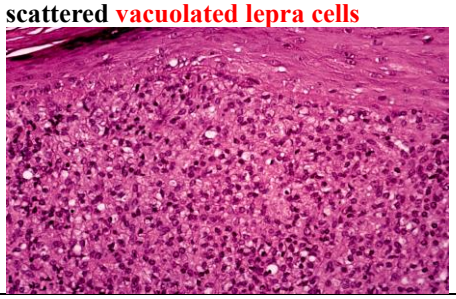
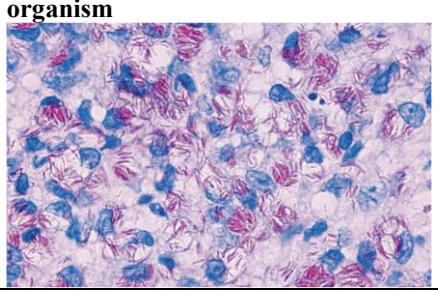
Leprosy(Hansen disease)➔mycobacterium leprae

➲temperature-dependent(?)➔lesion in cooler parts of body(skin, nasal cavity, palate)

➲tuberculoid leprosy
❶well-circumscribed hypopigmented skin lesion
❷nerve involve(anesthesia of skin, loss of sweating)
❸oral lesion(rare)

➲lepromatous(multibacillary) leprosy
❶numerous thickened facial nodule ❷distorted facial appearance(leonine facies)(右圖)
❸hair, eyebrow, lashes loss(右圖) ❹facial, trigeminal nerve involve(loss of sweat & ↓light touch, pain, temperature sensor) ❺nosebleed, stuffiness(鼻塞), smell loss
❻nose bridge collapse ❼dental pulp infection➔internal resorption(pulpal necrosis)➔intrapulpal vascular damage➔pink tooth
❽palatal perforation

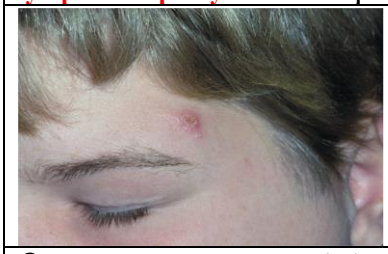
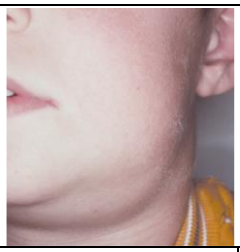


➲granulomatous inflammation ➔lymphocyte & histiocyte	➲sheet of lymphocyte & histiocyte➔ scattered vacuolated lepra cells	➲acid-fast stain➔small mycobacterial organism
		

16. Which of the following lesion show mycobacterial organism upon acid-fast-stain?
(1) cat-scratch disease (2) tuberculosis (3) Hansen disease (4) oral candidiasis
(A) only 1,4,
(B) only 1,3
(C) only 2,3
(D) only 2,4

Cat-scratch disease➔Barotonella henselae

➲contact with cat(cat flea)
❶intraerythrocytic parasite
❷human via saliva
❸from a scratch➔skin(papule, along scratch line)➔heal(1-3-wk)➔adjacent LN[most cause of chronic regional lymphadenopathy in children]➔nodal necrosis➔surrounded by band of epithelioid histiocyte & lymphocyte


➲immunocompetent
❶necrotizing granuloma
❷vasoproliferative disorder
①bacillary angiomatosis
②bacillary peliosis hepatis

➲person-to-person transmission➔not documented	➲dog, monkey, porcupine quill & thorn(豪猪刺)(rare)

Chapter 5: Bacterial Infections

1. Scrofula refers to a form of:
A. cat-scratch disease
B. gonorrhea
C. lymphoma
D. syphilis
E. tuberculosis

2. Which one of the following infections is NOT caused by a fungus?
A. Actinomycosis
B. Blastomycosis
C. Candidiasis
D. Histoplasmosis
E. Phycomycosis

3. Tuberculosis is classically characterized by which type of necrosis?
A. Aspiration necrosis
B. Caseous necrosis
C. Coagulative necrosis
D. Fat necrosis
E. Liquefactive necrosis

4. Most intraoral lesions of tuberculosis are thought to be secondary to:
A. dental treatment with infected instruments
B. kissing a person with active tuberculosis
C. lupus vulgaris
D. pulmonary tuberculosis
E. scrofula

5. Which one of the following infections is caused by an acid-fast mycobacterium?
A. Cat-scratch disease
B. Leprosy
C. Noma
D. Scarlet fever
E. Syphilis

6. Which one of the following infections often affects nerves resulting in loss of sensation?
A. Actinomycosis
B. Leprosy
C. Primary syphilis
D. Sarcoidosis
E. Scarlet fever

7. “Split papules” at the commissures may be seen in patients with:
A. actinomycosis
B. erysipelas
C. impetigo
D. noma
E. secondary syphilis

8. Which one of the following is a characteristic oral lesion that has been described in patients with scarlet fever?
A. Chancre
B. Gumma
C. Mucous patch
D. Strawberry tongue
E. Sulfur granules

9. Many examples of noma represent a progression of which infection?
A. Necrotizing ulcerative gingivitis
B. Primary herpetic gingivostomatitis
C. Pyogenic granuloma
D. Scarlet fever
E. Syphilis

10. Hutchinson incisors are associated with:
A. congenital syphilis
B. diphtheria

C. gonorrhea during pregnancy
D. multibacillary leprosy
E. oral cat-scratch disease

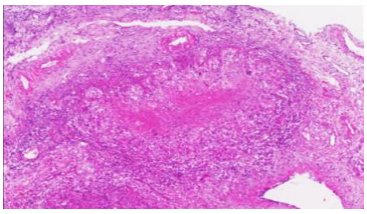
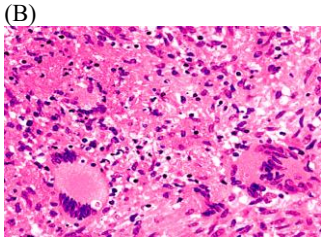
Chapter 5: Bacterial Infections➔answers
1. ANS: E
2. ANS: A
3. ANS: B
4. ANS: D
5. ANS: B
6. ANS: B
7. ANS: E
8. ANS: D
9. ANS: A
10. ANS: A

113-2 midterm exam
1. Which statement about syphilis is *false*? (Chapter 5)
(A) the primary lesion of syphilis is called a chancre
(B) the secondary lesion of syphilis occurs at the (site of inoculation with the organism➔primary lesion)
(C) the tertiary lesion of syphilis is called a gumma
(D) syphilis is caused by the spirochete Treponema pallidum

2. Which of the following matching of the clinical sign with the corresponding disease is *false*? (Chapter 5)
(A) Beaue line with hand-foot-mouth disease
(B) Pastia lines with scarlet fever
(C) linear gingiva erythema with AIDS
(D) Warthin-Finkeldey giant cell in ~~Rubella~~ measles(rubeola)

3. "Strawberry tongue" is associated with which condition? (Chapter 5)
(A) herpangina
(B) scarlet fever
(C) rheumatic fever
(D) tuberculosis

4. A patient with painful ulceration over tongue border received chest X-ray showing cloudy appearance of lung and biopsy with histopathological features depicted in the Figures A-C. (Chapter 5)
What is the most likely histopathological diagnosis? What kind of special stain is used for Figure (C)?

(A)

(B)

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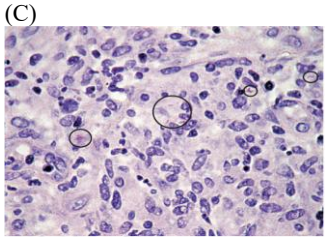


① hematoxylin eosin stain ② acid-fast stain ③ oral squamous cell carcinoma ④ oral tuberculosis
(A) only ①④
(B) only ①③
(C) only ②③
(D) only ②④

Chapter 6 Fungal & protozoal(原生動物) diseases

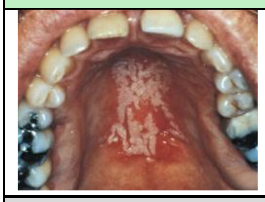
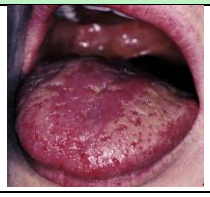
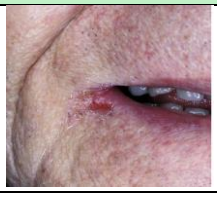
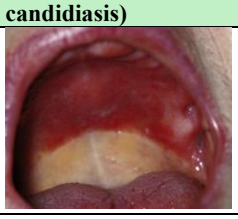
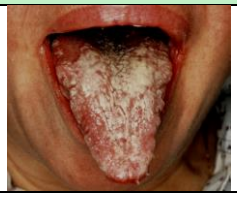
Candidiasis[Candidosis(英式), Moniliasis(過時)]➔most oral fungal infection in human

➲dimorphism➔❶yeast(酵母)➔relative innocuous ❷hypha(菌絲)➔host tissue invasion

➲types of oral candidiasis

clinical type	appearance & symptoms	common sites	associated factors & comments
❶pseudomembranous(thrush)	creamy-white plaque(丘斑), removable; burning sensation, foul taste	buccal mucosa, tongue, palate	Ab therapy, immunosuppression
❷erythematous	red macule, burning sensation	posterior hard palate, buccal mucosa, dorsal tongue	Ab therapy, xerostomia, immunosuppression, idiopathic
❸central papillary atrophy (median rhomboid glossitis)	red, atrophic mucosal area; asymptomatic	midline posterior dorsal tongue	idiopathic, immunosuppression
❹chronic multifocal	red area, often with removable white plaque; burning sensation, asymptomatic	posterior palate, posterior dorsal tongue, mouth angle	immunosuppression, idiopathic
❺angular cheilitis	red, fissured lesion; irritated, raw feeling	mouth angle	idiopathic, immunosuppression, vertical dimension loss
❻denture stomatitis(chronic atrophic candidiasis, denture sore mouth)	red, asymptomatic	confined➔palatal denture-bearing mucosa	probably not true infection; denture often is positive on culture but mucosa is not
❼hyperplastic(candidal leukoplakia)	white plaque➔not removable; asymptomatic	anterior buccal mucosa	idiopathic, immunosuppression; not to confuse with other keratotic lesions with superimposed candidiasis
❽mucocutaneous	white plaque, some may be removable; red area	tongue, buccal mucosa, palate	rare; inherited/sporadic idiopathic immune dysfunction
❾endocrine-candidiasis syndromes	white plaque➔most not removable	tongue, buccal mucosa, palate	rare; endocrine disorder develops after candidiasis

➲clinic pictures➔oral candidiasis

❶peudomembranous	❷erythematous	❺angular cheilitis	❻denture stomatitis (chronic atrophic candidiasis)	❼chronic hyperplastic (candida leukoplakia)
				

Mucocutaneous candidiasis

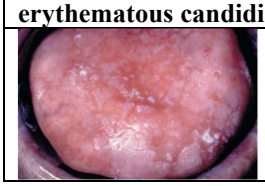
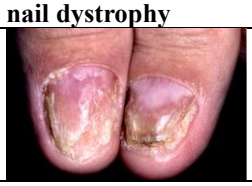
➲severe type➔component of rare group of immunologic disorders

➲candidal infection➔❶mouth ❷nail ❸skin ❹other mucosa

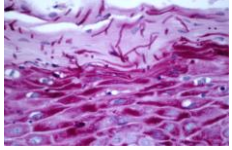
➲oral lesion(chronic hyperplastic candidiasis)➔thick, white plaque(not rub off)

Endocrine-candidiasis syndrome(autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy[APECED]) syndrome/autoimmune polyendocrinopathy syndrome, type 1)

➲endocrine disturbance➔❶hypothyroidism ❷hypoparathyroidism ❸hypoadrenocorticism(Addison disease) ❹DM

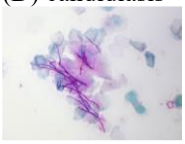
erythematous candidiasis	nail dystrophy	corneal keratopathy
		

1. **Oral candidiasis** is caused by a:
   (A) bacterium
   (B) yeastlike fungus
   (C) spirochete
   (D) protozoan



2. Which statement is *false*?
   (A) angular cheilitis may be caused by *Candida albicans*
   (B) white lesions resulting from candidiasis may not rub off the mucosal surface
   (C) erythematous candidiasis is usually completely asymptomatic
   (D) denture stomatitis may be a form of oral candidiasis

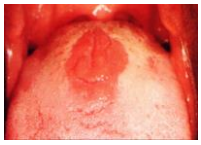
3. A **cytologic smear** may be helpful in the diagnosis of:
   (A) coxsackievirus infection
   (B) human papillomavirus infection
   (C) tuberculosis
   (D) candidiasis



4. Which of the following is the **best diagnostic test** for **oral candidiasis**?
   (A) a mucosal smear (cytologic preparation) showing fungal hyphae
   (B) a mucosal smear (cytologic preparation) showing Tzanck cells
   (C) a positive culture for *Candida albicans*
   (D) a blood test for *Candida* antibodies

5. Which of the following is *not* associated with the development of **oral candidiasis**?
   (A) antibiotic therapy
   (B) HIV infection
   (C) xerostomia
   (D) herpangina

6. Which one of the following occurs as an **erythematous** area, is **devoid of filiform papillae**, is **oval to rectangular** in shape, and is on the **midline of dorsal tongue**?



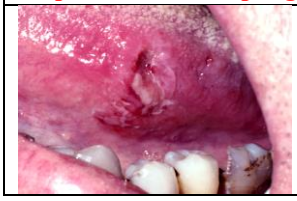
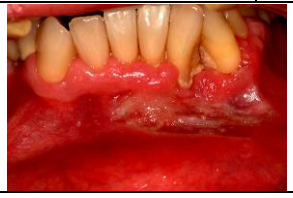
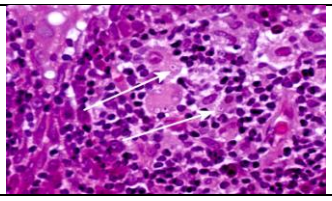
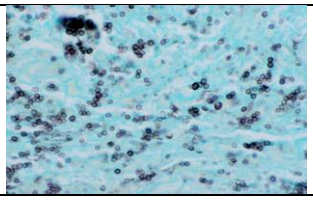
   (A) median rhomboid glossitis
   (B) geographic tongue
   (C) fissured tongue
   (D) lingual thyroid

7. Another term for **geographic tongue** is:
   (A) allergic tongue
   (B) median rhomboid glossitis
   (C) migratory glossitis
   (D) white hairy tongue

8. Which one of the following is considered a **deep fungal infection**?
   (A) median rhomboid glossitis
   (B) angular cheilitis
   (C) histoplasmosis
   (D) herpangina

Histoplasmosis(組織胞漿菌病)

➲acute histoplasmosis(1%)➔low spore no.➔self-limited pulmonary infection
➲chronic histoplasmosis➔lung➔clinic like TB➔chest X-ray➔upper lobe infiltrate & cavitation
➲disseminated histoplasmosis➔AIDS ➲oral➔ulcer➔tongue, palate, buccal mucosa➔mistaken OSCC
➲micro➔granulomatous inflammation➔macrophage➔multinucleated giant cell
➲epithelioid macrophage contain yeast(酵母) ➲Grocott-Gomori methenamine silver stain, PAS➔small yeast

Aspergillosis(曲霉菌)➔2 most common species in medical setting➔❶A. flavus ❷A. fumigatus(most)

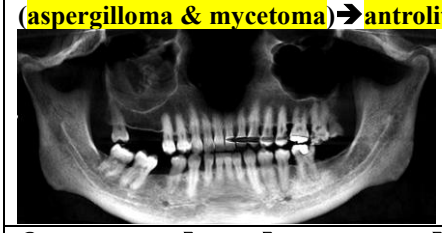
❶noninvasive➔normal host➔allergic reaction/cluster of hyphae➔no tissue invasion
❷localized invasive➔normal host➔infection of damaged tissue
❸extensive invasive➔immunocompromise(❶chemotherapy ❷AIDS ❸solid-organ ❹bone marrow transplant)

➲saprobic(腐生 live in breakdown, recycle dead plant & animal material)➔❶soil ❷water ❸decaying organic debris

➲resistant spore(孢子)➔air➔human inhale➔opportunistic fungal infection(2nd in frequency to candidiasis)

➲most cannot grow at 37° C➔only pathogenic species➔replicate at body temperature

➲low-grade infection➔maxillary sinus➔fungus ball (aspergilloma & mycetoma)➔antrolith

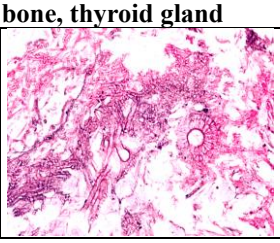


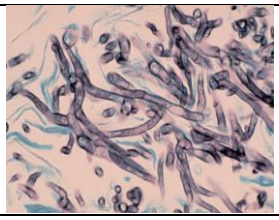
➲immunocompromise➔tooth extraction/endoTx➔oral aspergillosis➔yellow/black ulcer

➲disseminate➔lung➔bloodstream➔CNS, eye, skin, liver, GI tract, bone, thyroid gland

➲micro➔branching(at acute angle), septate hyphae(3-4μm)(右圖)

➲fruiting body➔fungus ball(左圖)➔invade adjacent small blood vessel ➔occult vessel➔necrosis





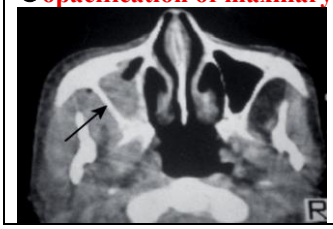
Mucormycosis(毛霉菌病)(Zgomycosis, Phycomycosis)

➲rhinocerebal form➔oral health care provider

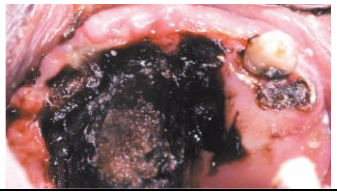
➲Fe(Fe-chelating agent for thalassemia)➔fungi growth

➲resistant spore➔air➔human(uncontrolled DM) hale

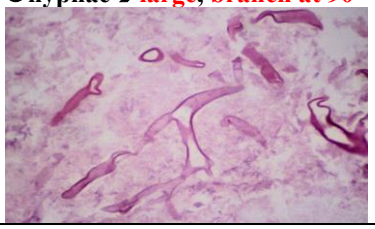
➲opacification of maxillary sinus



➲invade small blood vessel➔ massive tissue destruction



➲hyphae➔large, branch at 90^0

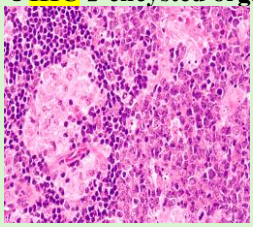


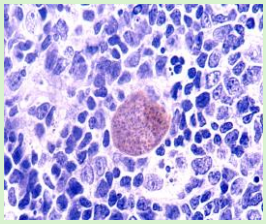
Toxoplasmosis(弓形蟲)➔protozoal(原蟲) infection(Toxoplasma gondii)

➲micro➔LN

❶germinal center➔eosinophilic macrophage

❷IHC➔encysted organism





➲congenital toxoplasmosis➔non-immune mother

❶cross placenta barrier

❷1st trimester of pregnancy

①blind ②intellectual impairment(智力障礙)

③delayed psychomotor development(動作心理發展遲緩)

➲immunosuppress➔1^0infection/reactivation➔encysted organism

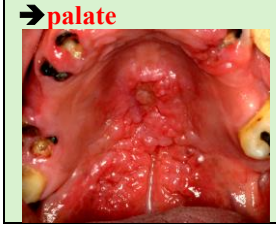
➲normal

❶asymptomatic

❷like infectious mononucleosis(❶low-grade fever ❷cervical lymphadeno-pathy ❸fatigue ❹muscle/joint pain)

Leishmaniasis(利什曼病;黑熱病) ➔protozoal infection➔transmit to human by (certain species)sandfly(蠓蟲) bite

➲ulcer & granulomatous enlargement ➔palate



➲dog & other mammals➔1^0 reservoir➔parasite

➲3-presentation

❶cutaneous(most)➔Old/(New World➔Leishmania mexicana)➔heal with scar

❷mucocutaneous➔New World➔Leishmania braziliensis➔more destructive

❸visceral➔Old➔Leishmania donovan/New World➔Leishmania braziliensis➔ black fever➔grayish discoloration of skin

Chapter 6: Fungal and Protozoal Diseases

1. The most common fungal infection of the oral cavity is:
A. actinomycosis
B. blastomycosis
C. candidiasis
D. histoplasmosis
E. zygomycosis

2. Candidiasis infections are often associated with patients taking which of the following drugs?
A. Antibiotics
B. Anticoagulants
C. Antihistamines
D. Calcium-channel blockers
E. Diet pills

3. Median rhomboid glossitis actually represents what lesion microscopically?
A. Arteriovenous malformation
B. Candidiasis
C. Erythema migrans
D. Erythroplakia
E. Remnants of lingual thyroid tissue

4. Rhinocerebral mucormycosis infections are classically associated with:
A. cocaine abuse
B. ipsilateral herpes zoster
C. overfilled canals during root canal therapy
D. uncontrolled diabetes
E. none of the above

5. Which one of the following infections classically presents with white lesions of the oral mucosa that can be rubbed off?
A. Actinomycosis
B. Candidiasis
C. Histoplasmosis
D. Primary herpetic gingivostomatitis
E. Primary syphilis

6. Which one of the following infections is considered to be endemic in the regions drained by the Ohio and Mississippi Rivers?
A. Coccidioidomycosis
B. Cryptococcosis
C. Histoplasmosis
D. Mucormycosis
E. Paracoccidioidomycosis

7. Mucormycosis infections would most likely occur in which location?
A. Floor of mouth
B. Liver
C. Maxillary sinus
D. Submandibular gland
E. Tongue

8. Which animal is the most common host for toxoplasmosis?
A. Armadillo
B. Bird
C. Cat
D. Dog
E. Elephant

9. Allergic fungal sinusitis is related to which organism?
A. Aspergillus
B. Blastomyces
C. Candida
D. Histoplasma
E. Mucor

10. Which one of the following organisms often is related to angular cheilitis?

A. Herpes simplex, type 1
B. Candida albicans
C. Streptococcus mutans
D. Actinomyces israelii
E. Tinea versicolor

Chapter 6: Fungal and Protozoal Diseases➔answers

1. ANS: C
2. ANS: A
3. ANS: B
4. ANS: D
5. ANS: B
6. ANS: C
7. ANS: C
8. ANS: C
9. ANS: A
10. ANS: B

Chapter 7 Viral infections

Synopsis➔diseases matched viruses

virus	disease
herpes simplex virus (HSV-1/HHV-1; HSV-2/HHV-2)	❶acute herpetic gingivostomatitis(primary herpes) ❷recurrent(secondary) herpes simplex infections➔herpes labialis ❸recurrent intraoral herpes(recurrent herpetic stomatitis) ❹herpetic whitlow(herpetic paronychia) ❺herpes gladiatorum(scrumpox)➔wrestler & rugby player ❻herpes barbae ❼eczema herpeticum(Kaposi varicelliform eruption)
varicella-zoster virus(VZV/HHV-3)	❶varicella(chickenpox)➔1^0 infection ❷herpes zoster(shingles)➔recurrent infection(1/3 person of lifetime)
Epstein-Barr virus(EBV/HHV-4)	❶infectious mononucleosis ❷NPC ❸Burkitt lymphoma/extranodal NK/T-cell lymphoma ❹hairy leukoplakia
cytomegalovirus(CMV/HHV-5)	non-specific(immunosuppressive)
enteroviruses(echovirus, coxsackieviruses, polioviruses)	❶herpangina ❷hand-foot-and-mouth disease ❸acute lymphonodular pharyngitis
morbillivirus	❶measles(rubeola)
rubulavirus	❶mumps(epidemic parotitis)
rubivirus	❶rubella(German measles)
human immunodeficiency viurus(HIV)	❶AIDS
covid-19	❶coronavirus disease 2019

Human herpesvirus(HHV) family➔double-stranded DNA viruses

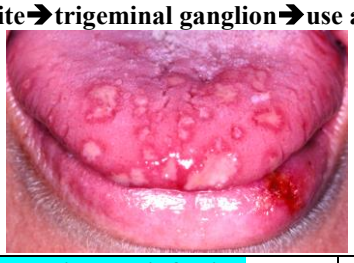
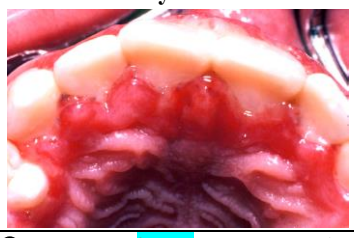
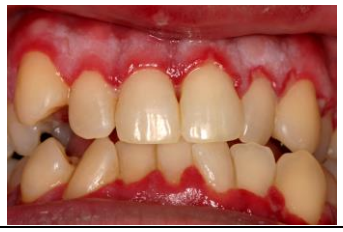
❶herpes simplex virus(HSV) type 1(HSV-1/HHV-1) ❷HSV type 2(HSV-2/HHV-2) ❸varicella-zoster virus(VZV/HHV-3) ❹Epstein-Barr virus(EBV/HHV-4) ❺cytomegalovirus(CMV/HHV-5)	❻human herpesvirus 6(HHV-6) ❼human herpesvirus 7(HHV-7) ❽human herpesvirus 8(HHV-8) ①Kaposi sarcoma-associated herpesvirus(KSHV) ②lymphoma(certain types) ③Castleman disease(a benign lymphoid proliferation)

Herpes simplex virus(HSV)

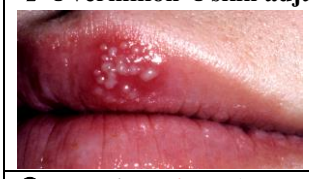
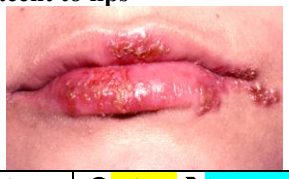
➲HSV-1➔[spread via ❶infected saliva ❷active perioral lesion]➔adapt to oral, facial, ocular region➔❶pharynx ❷oral mucosa ❸lip ❹eye ❺skin above waist

➲HSV-2➔sexual contact➔❶genitalia ❷skin below waist(腰)

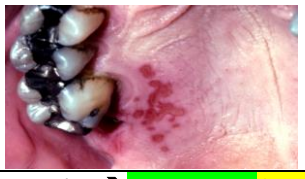
➲clinic➔❶primary(HSV-1, 90%)➔acute herpetic gingivostomatitis(primary herpes)➔peak(2-3s); range(6-mon↔5s)
❷most common latency site➔trigeminal ganglion➔use axon of sensory neuron travel back & forth to skin/mucosa

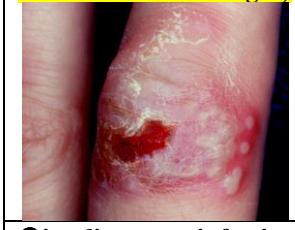
❷recurrent secondary herpes simplex infection (HSV-1,most)➔herpes labialis(cold sore/fever blister)➔①vermilion ②skin adjacent to lips

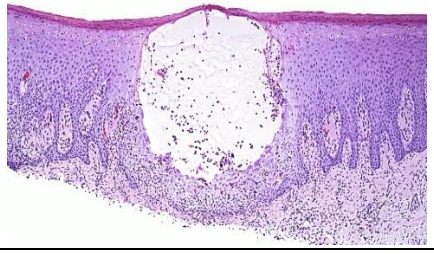
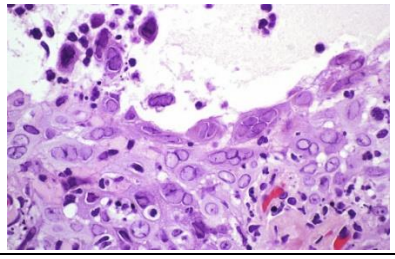
❸recurrent intraoral herpes(recurrent herpetic stomatitis)➔keratinized mucosa bound to bone(①attached gingiva ②hard palate)

❹herpetic whitlow(herpetic paronchia)(primary/recurrent HSV infection of finger)



➲micro➔intraepithelial vesicle➔ballooning degeneration➔Tzanck cell(acantholytic epithelial cell)➔chromatin margination➔multinucleation

➲implicate noninfectious process➔erythema multiforme➔trigger by HSV

1. Painful oral ulcers, gingivitis, fever, malaise, and cervical lymphadenopathy in a **child younger than 6 years old** would suspect which of the following diseases?
   (A) herpangina
   (B) Heck disease
   (C) primary herpes simplex infection
   (D) herpetic whitlow

2. The most affected **peak prevalence of primary herpetic gingivostomatitis(原發性疱疹齦口炎)** occurs between ages of:
   (A) birth and 5 years
   (B) before 6 months
   (C) 2 years and 3 years
   (D) 50 years and 60 years

3. The most common form of **recurrent herpes simplex** infection is:
   (A) herpes zoster
   (B) herpetic whitlow
   (C) herpangina
   (D) herpes labialis

4. Which of the following statements is *false* concerning **primary herpetic gingivostomatitis**?
   (A) after primary herpes simplex infection, the latent infection is usually in the trigeminal ganglion
   (B) the virus is able to survive outside body & hence easily transmitted by fomites[(非動植物，可傳播疾病給生物的)病媒，污染物]
   (C) the initial oral infection is usually due to HSV type 1
   (D) the HSV altered epithelial cell is called a Tsanck cell

5. Which of the following clinical features would help **differentiate** between **recurrent oral mucosal simplex infection** and **recurrent aphthous stomatitis**?
   (A) location of ulcers; herpes simplex ulceration occurs on keratinized epithelium and aphthous ulcers occur on nonkeratinized epithelium
   (B) systemic signs & symptoms accompany recurrent herpes simplex infection, but do not accompany recurrent aphthous ulcers
   (C) recurrent herpes simplex ulceration is painful; recurrent aphthous ulcers are usually asymptomatic
   (D) recurrent aphthous ulcers take much longer to heal than recurrent herpes simplex ulceration

Comparison of clinical features➔recurrent minor aphthous ulcer & recurrent herpes simplex ulceration

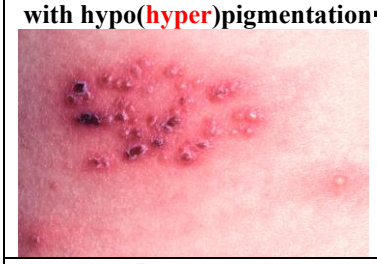
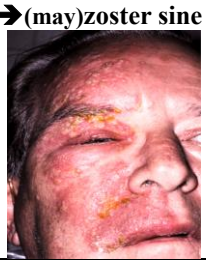
features	recurrent minor aphthous ulcer	recurrent herpes simplex ulceration
➲location	nonkeratinized mucosa	keratinized mucosa
➲number	one to several	multiple(crops)
➲vesicle precedes ulcer	no	yes
➲pain	yes	yes
➲size	<1cm	1-2mm
➲borders	round to oval	cluster of ulcer coalesce➔large irregular ulcer
➲recurrent	yes	yes

6. The **primary infection** with the **varicella-zoster virus** is called:
   (A) primary herpetic gingivostomatitis
   (B) chickenpox
   (C) shingles
   (D) measles

7. An adult being affected by painful vesicles over skin of external auditory canal with involvement of ipsilateral facial and auditory nerves showing facial paralysis and hearing deficits, vertigo as well as loss of taste in anterior two-thirds of tongue, what is the most possible clinical diagnosis?
   (A) Sjogren syndrome(修格蘭氏症候群)
   (B) Behçet's syndrome(貝謝氏症候群)
   (C) auriculotemporal syndrome(耳顳神經症候群)
   (D) Ramsay Hunt syndrome(侖謝亨特症候群)

8. The most characteristic clinical feature of **herpes zoster (shingles)** is:
   (A) ulcer formation
   (B) pain
   (C) unilateral distribution of lesions
   (D) abscesses that drain through fistula

Herpes zoster

➲after 1^0 infection(recur) with varicella-zoster virus(chickenpox)	➲3 phases➔❶prodrome ❷acute ❸chronic
❶prodrome➔pain➔epithelium innervated by affected sensory nerve(dermatome) with fever, malaise, headache	
❷acute➔cluster of vesicles with skin rash➔along affected nerve stop at midline➔contagious until crust➔scar with hypo(hyper)pigmentation➔(may)zoster sine herpete[zoster(pain) without rash]   	
❸chronic➔postherpetic neuralgia(15%)	
➲oral➔vesicle on movable/bound mucosa➔pulpitis, pulp necrosis, calcified pulp, root resorption➔osteonecrosis	
➲ocular lesion(25%)➔blindness	➲nose tip lesion(Hutchinson sign)➔trigeminal nerve➔severe ocular risk
➲Ramsay Hunt syndrome➔reactivation(herpes zoster) in geniculate ganglion(顏面神經進入內聽道後往前彎一小段距離形成膝狀神經節)➔skin lesion on external auditory canal➔ipsilateral(同側) facial & auditory nerve➔❶facial paralysis ❷hearing deficit(不足) ❸vertigo(眩暈) ❹taste loss➔anterior 2/3 tongue	

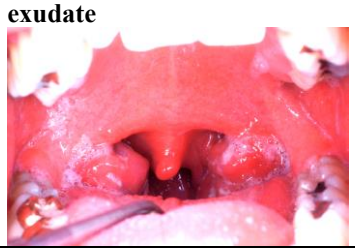
9. 下列那個臨床表現與相關病毒或疾病的配對組合是錯誤的？(114)
   (A) 感染性單核白血球增多症(infectious mononucleosis)和巨細胞病毒(cytomegalovirus)
   (B) 手足口病(hand-foot-and-mouth disease)和腸病毒(enterovirus)
   (C) 柯普里克氏斑(Koplik's spots)和麻疹病毒(Morbillivirus)
   (D) 佛斯克海默爾斑(Forchheimer sign)和德國麻疹病毒(Rubivirus)

10. Which condition is *not* associated with the **Epstein-Barr virus (EBV)**?
   (A) hairy leukoplakia
   (B) herpangina
   (C) nasopharyngeal carcinoma
   (D) infectious mononucleosis

EBV implicated in 4 diseases occurred in oral region

❶infectious mononucleosis	❷nasopharyngeal carcinoma(NPC)	❸Burkitt lymphoma	❹hairy leukoplakia

Infectious mononucleosis(Kissing disease)

➲hyperplastic tonsil➔yellowish crypt exudate 	➲petechiae on hard(soft) palate (25%) in 1-2-day 	➲lymphoid enlargement(symmetrical) (>90%) ➲oral➔necrotizing gingivitis

Cytomegalovirus(巨細胞病毒)➔coinfect➔HIV, HSV, EBV

➲latent➔❶salivary gland cell ❷endothelium ❸macrophage ❹lymphocyte	
➲found➔body fluid(❶saliva blood ❸urine ❹tears ❺respiratory secretion ❻genital secretion ❼breast milk)	
➲clinic➔❶neonate(via placenta, delivery, breast-feeding)(most) ❷immunosuppress adult(輸血、器官移植) ❸sexual contact	
➲neonatal infection➔❶enamel hypoplasia(hypomaturation) ❷attrition yellow ❸coloration from underly dentin	
➲micro➔change in vascular endothelial cell/salivary duct epithelial cell➔owl eye cell	
➲Grocott-Gomori methenamine silver & periodic acid-Schiff(PAS) stains➔cytoplasmic inclusion(not intranuclear change)	

11. **Herpangina** is caused by:
   (A) coxsackievirus
   (B) herpes simplex virus
   (C) varicella-zoster virus
   (D) Epstein-Barr virus

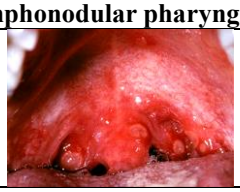
12. All of the following are characteristic features of **hand-foot-and-mouth disease** except one. Which **one is the exception**?
(A) occurs in epidemics in children younger than 5 years
(B) is caused by Epstein-Barr virus
(C) is characterized by painful oral vesicles
(D) is characterized by multiple papules on the skin

Enterovirus(腸病毒)

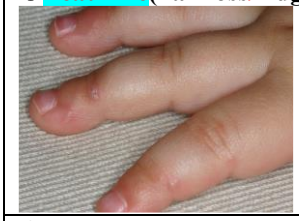
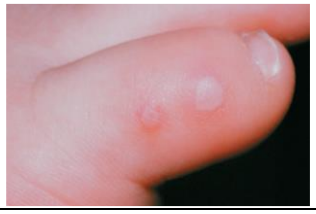
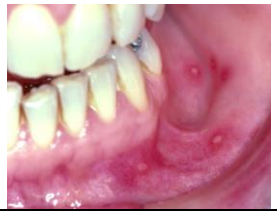
➲❶echovirus ❷coxsackievirus A & B ❸poliovirus | ➲acute➔❶saliva ❷air droplet | ➲chronic➔fecal-oral

➲clinic➔❶herpangina ❷hand-foot-and-mouth disease ❸acute lymphonodular pharyngitis

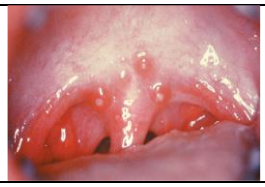
➲herpangia(皰疹性咽峽炎)❶echoviruses ❷coxsackieviruses A & B
①ulcer(2-4mm)➔resolve in a few days
②ulcer➔heal in 7-10-day



➲hand-foot-and-mouth disease(手足口病)❶echovirus ❷coxsackievirus A
①ulcer(2-7mm; >1cm)➔heal within a wk
②Beau line(nail loss/ridges)

➲acute lymphonodular pharyngitis❶coxsackieviruses A
①1-5 yellow-pink nodule(lymphoid hyperplasia)➔soft plate/tonsillar pillar



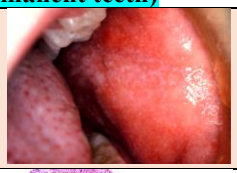
13. Koplik spots(柯普里克氏斑點) are oral manifestation (buccal, labial mucosa) of:
(A) chickenpox(水痘)
(B) measles(麻疹)
(C) mumps(腮腺炎)
(D) herpetic stomatitis(疱疹性口炎)

Measles(rubeola)➔effective measles vaccine

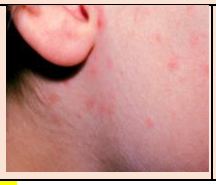
➲RNA virus➔family paramyxoviridae & genus Morbillivirus | ➲lingual & pharyngeal tonsil enlargement

➲3 stages➔each stage last 3-day➔9-day measles | ➲child➔pitted enamel hypoplasia(permanent teeth)

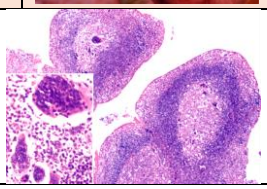
➲1st stage(fever)
❶3 Cs➔①coryza(流鼻水) ②cough ③conjunctivitis(結膜炎red watery, photophobic eye)
❷Koplik spots(buccal, labial mucosa)➔epithelial necrosis[foci, blue-white macule(grain of salt) encircled by erythema]➔①hyperparakeratosis ②spongiosis ③dyskeratosis ④epithelial syncytial giant cell



➲2nd stage(fever continue)
❶Koplik spot fade
❷skin rash(face先出現➔往下至trunk & extremities)



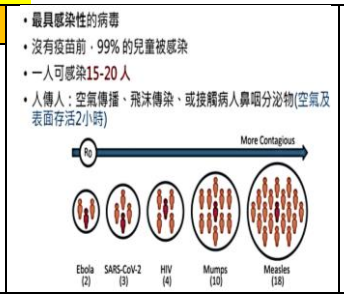
➲3rd stage(fever end)➔rash fade➔brown pigment (desquamation of skin affected by rash)➔腦炎➔subacute sclerosing panencephalitis(SSPE)➔甚至最初感染11年後

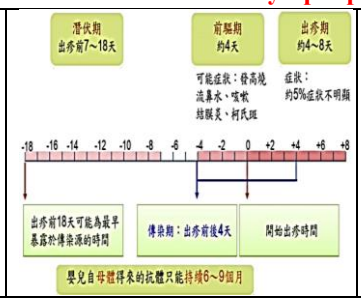


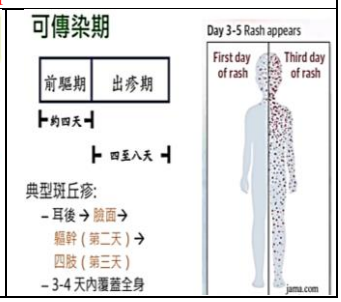
➲Warthin-Finkeldey giant cell➔亦在❶淋巴癌 ❷Kimura disease ❸AIDS-related lymphoproliferative disease ❹LE

<補充>
◆致病原 (Infectious agent)
RNA病毒，麻疹病毒 (Measles virus) ，副黏液病毒屬(Paramyxoviridae, Morbillivirus)

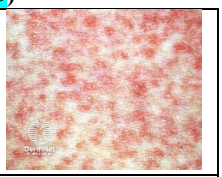
◆傳染特性
-人是唯一感染宿主
-空氣、飛沫或是直接接觸而感染
-潛伏期約兩週，可傳染期為發疹前後四天。
-好發於冬末及春季。







Rubella(German measles)➔family Togavirus & genus Rubivirus➔congenital rubella syndrome(CRS)

➲triad of CRS➔❶deaf(bilateral)(80%)➔evident till 2s ❷heart disease ❸cataract	
➲transmission(~100%)➔respiratory droplet➔close living condition➔incubate time(12↔23-day)	
➲contagious➔1-wk before↔1-wk after exanthem(acute rash)➔pink macule(右圖)➔papule➔fade	
➲developing fetus➔birth defect➔late winter & early spring	
➲infant➔congenital infection➔release virus up to 1s➔intraocular virus for decades	
➲prodromal symptom(1↔5-day before exanthem)➔fever, headache, malaise, anorexia, myalgia, mild conjunctivitis, coryza, pharyngitis, cough, lymphadenopathy(persist for wks)➔suboccipital, postauricular, cervical chains	
➲complication(subsequent to rash)➔❶arthritis(most)➔↑frequency with age ❷encephalitis ❸thrombocytopenia(rare)	
➲rash➔1st sign➔face & neck➔entire body(1-3-day)➔facial rash clear before spread to lower body➔complete resolve by day 3(3-day measle)	
➲oral ❶Forchheimer sign(~20%)➔small, discrete, dark-red papule➔soft(hard) palate➔6h after 1st symptom➔not last longer than 12-14h ❷palatal petechiae	

Mumps(Epedemic parotitis)➔family Paramyxoviridae & genus Rubulavirus➔diffuse swelling of exocrine gland

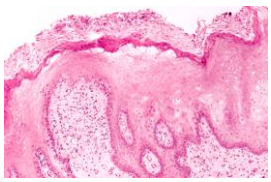
➲site➔❶salivary gland(parotid gland) ❷pancreas ❸choroid plexus(脈絡叢)➔CSF ❹mature ovary ❺teste(frequent)	
➲transmit➔❶respiratory droplet ❷saliva ❸urine➔incubation time➔16↔18-day(2↔4-wk)	
➲contagious➔1-day before clinic appear↔14-day after clinic resolution➔most in winter & spring	
➲prodromal symptom➔[low-grade fever, headache, malaise, anorexia, myalgia]develop first➔salivary gland (parotid gland most, sublingual & submandibular glands also)➔enlarge & pain(peak in 2↔3-day)➔begin on one side➔contralateral in a few days(25% unilateral)	
➲epididymo-orchitis(附睪睾丸炎)(2nd most)➔postpubertal male(25%)➔teste(most unilateral)➔❶rapid swelling ❷significant pain ❸tenderness➔atrophy➔❶subfertility ❷permanent sterility(rare)	
➲❶oophoritis(卵巢炎) ❷mastitis(乳腺炎)➔postpubertal female	➲1st trimester of pregnancy➔自發性abortion(25%)
➲less common➔meningoencephalitis, cerebellar ataxia, hearing loss, pancreatitis, arthritis, carditis, ↓renal function ➲CNS involve➔headache(most common) ➲pancreas involve➔nausea & vomiting	
➲oral➔❶Wharton & Stensen duct opening➔red & enlarge ❷sublingual gland➔bilateral mouth floor enlarge	

14. All of the following statements are correct statements concerning **HIV infection** *except one*. Which one is the exception?
    (A) two positive Elisa tests followed by a positive Western blot test confirms HIV infection
    (B) initial infection with HIV can be asymptomatic
    (C) antibodies to HIV are usually detectable in the blood by 2 weeks after infection
    (D) PCR is a test that measures viral load

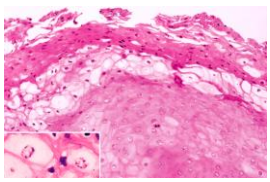
15. **Antibody testing** to determine whether a person has been infected with **human immunodeficiency virus** includes which of the following tests?
    (A) Schilling
    (B) Schirmer
    (C) prothrombin time and partial thromboplastin time
    (D) enzyme-linked immunosorbent assay and Western blot

16. Which one of the following oral conditions is an **early sign** of a deficiency in the immune system and is commonly found in patients with **HIV infection**?
    (A) erythema migrans
    (B) advanced periodontitis
    (C) candidiasis
    (D) histoplasmosis

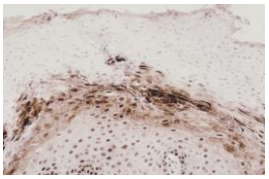
17. **Hairy leukoplakia** most commonly occurs on the:
    (A) buccal mucosa
    (B) dorsal tongue
    (C) lateral tongue
    (D) soft palate



hyperparakeratosis



balloon cell

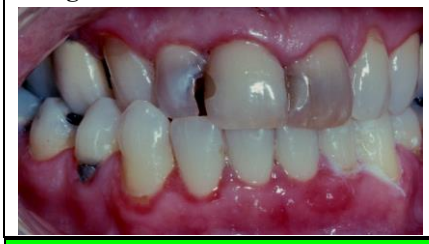
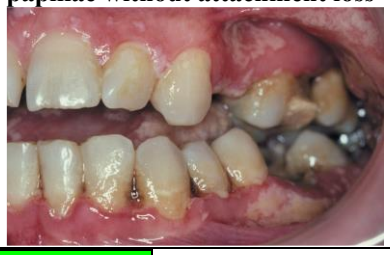


EBV within epithelial cell

18. Which one of the following oral conditions is *not* a lesion associated with **HIV** or **AIDS**?
(A) candidiasis
(B) hairy leukoplakia
(C) Kaposi sarcoma
(D) leukoedema

19. **Linear gingival erythema** has specific characteristics that include spontaneous bleeding, petechiae on the attached gingiva and alveolar mucosa, and a band of erythema at the gingival margin. Which one of the following statements is *true*?
(A) these tissues respond well to scaling and root planning
(B) excellent oral hygiene and home care techniques will eliminate these gingival conditions
(C) this condition will automatically develop into advanced periodontal disease in all patients infected with human immunodeficiency virus
(D) patients with linear gingival erythema do not respond to scaling or oral hygiene techniques; the gingival condition exists independently of the patient's oral hygiene status

3 atypical periodontal diseases associated with HIV infection

❶linear gingival erythema➔linear band of erythema➔free gingival margin往下2-3 mm	❷necrotizing ulcerative gingivitis➔ ulcer & necrosis of interdental papillae without attachment loss	❸necrotizing ulcerative periodontitis ➔deep pocket not seen
		

Oral & maxillofacial manifestations➔HIV infection

strongly associate	less common associate	others
➲candidiasis ❶pseudomembranous(most)➔CD4<200 ❷erythematous(most)➔CD4<400 ❸hyperplastic ❹angular cheilitis	➲mycobacterial infection(TB) ➲hyperpigmentation(focal melanosis) ➔skin, nail, mucosa(melanin in basal cell layer)	➲histoplasmosis ➲aphthous stomatitis ➲molluscum contagiosum ➲oral & oropharyngeal SCC
➲oral hairy leukoplakia	➲thrombocytopenia	
➲Kaposi sarcoma	➲herpes simplex virus(HSV)	
➲persistent generalized lymphadenopathy	➲varicella-zoster virus(VZV)	
➲HIV-associated periodontal disease	➲human papillomavirus(HPV) ❶oral squamous papilloma ❷verruca vulgaris ❸condyloma acuminatum ❹multifocal epithelial hyperplasia	

20. Which of the following statements is *false* concerning **oral human papilloma virus (HPV) infection**?
(A) HPV may be present in the oral mucosa without any signs or symptoms
(B) HPV causes papillary oral mucosal lesions
(C) HPV is transmitted by droplet infection
(D) microscopically, HPV-infected epithelial cells are called koilocytes

21. Another name for a **common wart** is:
(A) papilloma
(B) verruca vulgaris
(C) condyloma acuminatum
(D) fibroma

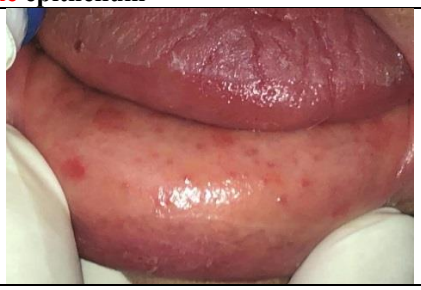
22. Which of the following is caused by a **papillomavirus** and is considered a **sexually transmitted** disease?
(A) actinomycosis
(B) syphilis
(C) condyloma acuminatum
(D) infectious mononucleosis

Coronavirus disease 2019➔severe acute respiratory syndrome coronavirus 2(SARS-CoV-2)➔incubate➔2↔14-day

➲transmitted
❶inhalation of contaminated respiratory droplet/aerosol

❷deposition of respiratory droplet onto oral, nasal, ocular mucous membrane
❸touch mucous membrane with hand➔contact with respiratory fluid/contaminate surface
❹enter host cells➔interact between spike protein & host ACE2(angiotensin-converting enzyme 2) receptor➔lung (type II alveolar cell), myocardium, intestinal lining, renal proximal tubule, tongue epithelium

➲oral condition➔desquamative gingivitis
①ulcer(aphthous-like, herpes-like, necrotic, nonspecific ulcer)
②tongue(lingual papillitis, depapillated tongue)➔taste disturbance
③hemorrhage(petechiae, ecchymosis, hemorrhage, angina bullosa)
④vesiculobullous eruption
⑤halitosis
⑥orofacial pain
⑦salivary gland(sialadenitis, ectasia)➔xerostomia
⑧erythematous plaque/macule



Chapter 7: Viral Infections

1. “Ballooning degeneration” of the nuclei of epithelial cells is a characteristic microscopic finding in:
A. herpangina
B. herpes simplex infections
C. infectious mononucleosis
D. measles
E. mumps

2. The most common site for recurrent intraoral herpes infections is:
A. buccal mucosa
B. dorsal tongue
C. floor of mouth
D. hard palate
E. soft palate

3. Orchitis (testicular inflammation) is a well-known complication of:
A. lymphonodular pharyngitis
B. mumps
C. rubella
D. rubeola
E. all of the above

4. Oral hairy leukoplakia is caused by:
A. candidiasis
B. cytomegalovirus (CMV)
C. Epstein-Barr virus
D. smoking
E. tongue-biting

5. The most common oral infection associated with acquired immune deficiency syndrome (AIDS) is:
A. acute herpetic gingivostomatitis
B. blastomycosis
C. candidiasis
D. CMV
E. human papillomavirus

6. Which one of the following presentations of herpes simplex infection is most common?
A. Herpes labialis
B. Herpetic whitlow
C. Neonatal herpes
D. Primary herpetic gingivostomatitis
E. Recurrent intraoral herpes

7. Which one of the following can be an early oral sign in patients with infectious mononucleosis?
A. Enlargement of the fungiform papillae
B. Forchheimer sign
C. Fordyce spots
D. Koplik spots
E. Palatal petechiae

8. A unilateral distribution of skin lesions would be most suggestive of:
A. CMV dermatitis
B. eczema herpeticum
C. German measles
D. hand-foot-and-mouth disease
E. herpes zoster

9. Kaposi sarcoma is believed to be caused by:
A. cryptococcus neoformans
B. CMV
C. Epstein-Barr virus
D. human herpesvirus type 2
E. human herpesvirus type 8

10. The most common location for Kaposi sarcoma in the mouth is:
A. buccal mucosa
B. hard palate

C. lower lip
D. tongue
E. upper lip

11. In addition to Kaposi sarcoma, which one of the following tumors has the most significantly increased risk in patients with AIDS?
A. Breast cancer
B. Hepatocellular carcinoma
C. Lymphoma
D. Nasopharyngeal carcinoma
E. Prostate cancer

12. For both herpes simplex and varicella-zoster virus, the organism may remain dormant in the body for many years, and later give rise to a recurrence. The most common site for the virus to remain dormant is:
A. bone marro
B. circumvallate papillae
C. liver
D. nerve ganglia
E. sinus mucosa

13. Oral hairy leukoplakia is often associated with:
A. CMV
B. human immunodeficiency virus infection
C. increased risk for squamous cell carcinoma
D. smoking
E. all of the above

14. The "whitlow" phenomenon is an infection of the finger or nail bed caused by which virus?
A. CMV
B. Herpes simplex
C. Human papillomavirus
D. Pox virus
E. Varicella-zoster

Chapter 7: Viral Infections➔answers
1. ANS: B
2. ANS: D
3. ANS: B
4. ANS: C
5. ANS: C
6. ANS: A
7. ANS: E
8. ANS: E
9. ANS: E
10. ANS: B
11. ANS: C
12. ANS: D
13. ANS: B
14. ANS: B

113-2 midterm exam
1. Which of the following clinical manifestation of the disease with the matched virus is *true*? (Chapter 7)
(A) infectious mononucleosis with Epstein-Barr virus
(B) hand-foot-and-mouth disease with ~~cytomegalovirus~~ enteroviruses(echovirus, coxsackieviruses, polioviruses)
(C) Koplik's spots with ~~Rubivirus~~ Morbillivirus(measles, rubeola)
(D) Forchheimer sign with ~~Morbillivirus~~ Rubivirus(German measles, rubella)

2. An adult is affected by painful vesicles over skin of external auditory canal with involvement of ipsilateral facial & auditory nerves showing facial paralysis & hearing deficits, vertigo as well as loss of taste. What is the most possible clinical diagnosis? (Chapter 7)
(A) Sjogren syndrome
(B) Behçet's syndrome
(C) auriculotemporal syndrome
(D) Ramsay Hunt syndrome

3. Which of the following statement is *true*? (Chapter 7)
(A) vesicles of herpes zoster along the nerve not being cross midline

(B) Tzanck cell is noted in ~~lichen planus~~ HSV/VZV(varicella; chickenpox); pemphigus
(C) rubella is also regarded as 3-day measles(Rubeola➔9-day measles)
(D) ~~submandibular gland~~ parotid gland is mostly affected by Rubulavirus(mump)

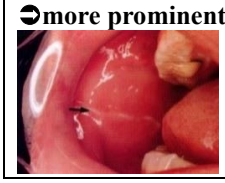
4. Hairy leukoplakia most commonly occurs on the: (Chapter 7)
(A) base of tongue
(B) dorsal tongue
(C) lateral tongue
(D) ventral tongue

5. The peak prevalence of primary herpetic gingivostomatitis occurs between ages of: (Chapter 7)
(A) birth and 5 years
(B) before 6 months
(C) 2 years and 3 years
(D) 50 years and 60 years

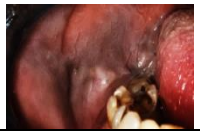
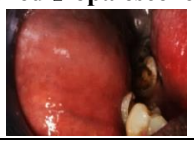
Chapter 8 Physical & chemical injuries

Linea alba➔white line

➲**buccal mucosa**(extend anteroposterior)
➲**bilateral occlusal planes**
➲**more prominent in clenching/bruxing p't**



➲**compare with leukoedema➔generalized opalescence**(乳白色)
❶buccal mucosa ❷gray-white **film**(下左圖)
❸mucosa stretched➔opalescence **less prominent**(下右圖)

1. A **raised, white line** is seen on the **buccal mucosa** at the level of the **occlusal plane (figure below)**. This is best called:

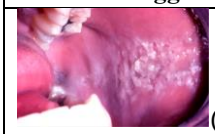
(A) frictional keratosis
(B) leukoplakia
(C) linea alba
(D) a traumatic ulcer

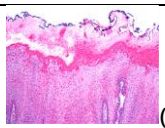
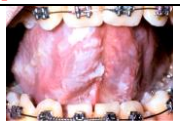
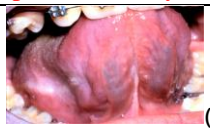
Morsicatio(bite) mucosae oris(Chronic mucosal chewing)➔[❶women ❷>35s]

➲**chronic nibbling**(啃咬)(suction & glassblower)➔bilateral mid-anterior buccal(most)➔**along occlusal plane**

➲**surface**(❶erythema zone ❷erosion ❸ulcer)➔❶white ragged(邊緣參差不齊) ❷thick ❸shred(撕碎)➔**habit push cheek between teeth with finger➔large lesion➔above/below occlusal plane**(圖 1)

➲**micro**
❶like➔①**oral hairy leukoplakia**(圖 2) ②**uremic stomatitis**(圖 4) ③betel chewer mucosa ④**linea alba** ⑤**leukoedema**
❷**HPK**➔ragged surface with keratin projection➔bacterial colony➔**[vacuolated cell➔prickle cell layer**(圖 3)]

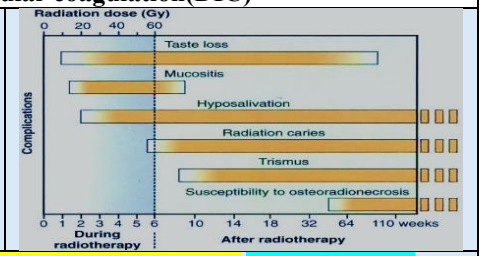

(圖 1)

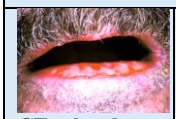
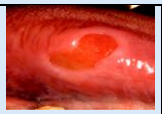
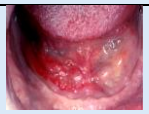
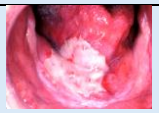
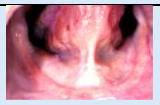
(圖 2)

(圖 3)


(圖 4)

Noninfectious oral complications➔antineoplastic therapy(①RT➔radiotherapy ②CT➔chemotherapy)

➲**hemorrhage➔minor trauma➔petechiae & ecchymosis(any mucosa)➔①labial ②tongue ③gingiva(①②③most)**
❶**bone marrow suppression➔thrombocytopenia**(血小板減少症)
❷**intestinal(hepatic) damage➔↓vitamin K-dependent clotting factor➔↑coagulation time**
❸**therapy➔tissue damage➔↑tissue thromboplastin➔disseminated intravascular coagulation(DIC)**

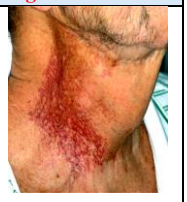
➲**mucositis[clinic(ulcer)➔RT & CT the same**](下圖)
❶**HN RT(almost all)** ❷high-dose CT(80%) ❸systemic CT(20-40%)
①**RT➔begin during 2nd wk of RT**(右圖)
②**CT➔CT 開始後的 a few-day**
③**RT & CT resolve 2-3-wk after Tx(RT & CT) cessation**(右圖)
✪**RT➔mucosa within direct portal**
✪**CT➔nonkeratinized**[①buccal ②舌(ventrolateral) ③軟腭 ❹mouth floor]




CT-related ulcer

CT-related ulcer

SCC before RT

RT-related mucositis

resolution of SCC, mucositis

➲**time course of complications during & after RT**(上圖)
➔persist 2-year pose lifelong risks
❶shaded area(1st 6-wk)➔**accumulated dose(60Gy)**
❷shaded area within bar➔**complication severity**
❸**resolve after RT**➔①**taste recovery**
②**mucositis healing**

➲**dermatitis**
❶**mild**➔erythema, edema, burning, pruritus➔**Tx 停止後 2-3-wk resolve**➔①**hyperpigment** ②**hair loss**
❷**moderate**➔erythema, edema, **erosion, ulcer➔resolve in 3-month**
①**permanent hair loss** ②**scar** ③**hyperpigment**
❸**severe acute**➔necrosis & deep ulcer
❹**chronic**➔dry, smooth, shiny, atrophic, necrotic, telangiectatic, depilated(脫毛), ulcer

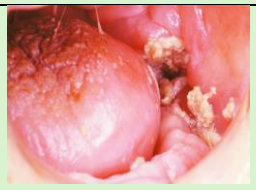


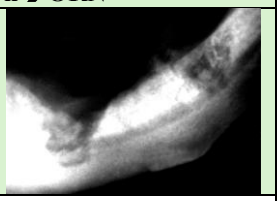
➲**xerostomia➔radiation caries(cervical)**
❶RT **1-wk begin➔RT 6-wk dramatic ↓saliva flow➔further↓up to 3s**(上上圖)
❷**radiosensitivity➔serous gland>mucous gland➔parotid gland affect dramatic(irreversible)**
❸**mucous gland➔partial recover**(over several months)➔flow approach **50% preradiation level**
❹**teeth➔①↓microhardness ②↓resistance to tensile(compressive) stress**

➲taste acuity loss(2nd/3rd wk of RT)➔❶dysgeusia(altered sense of taste) ❷hypogeusia(abnormal low sense of taste)
RT➔❶lost all 4-taste in several-wk➔return in 2-4-month(60-120-day) ❷(some)permanent hypogeusia, dysgeusia(上上圖)

➲osteoradionecrosis(ORN)➔expose nonvital irradiated bone➔persist>3-month without local neoplasm
❶ORN➔≧60Gy➔4 mon-3s after RT(上上圖)
❷2 etiologic theories➔①RT➔hypovascularity, hypoxia, hypocellularity➔persistent hypoxia➔ORN
②RT➔↑fibroblastic activity & dysregulation➔fibrotic tissue breakdown➔ORN

❸ORN➔most➔2^0 to local trauma(tooth extraction)
①spontaneous(minority)➔1st 3s
②mandible(24×)>maxilla➔dentate(3×)>non-dentate
❹radiograph➔PD-RL➔RO(dead bone)zone
❺pain, cortical perforation, fistula, ulcer, pathologic fracture
❻at least 3-wk between dental Tx & RT➔significant ↓bone necrosis





➲trismus(after RT)➔tonic muscle spasm with(out) fibrosis of masticatory muscle & TMJ capsule(上上圖)

➲developmental abnormalities(childhood)➔alter facial bone➔❶micrognathia ❷retrognathia ❸malocclusion
➲developing teeth➔❶root[①root dwarfism ②blunt root ③root dilaceration]
❷pulp canal[①premature pulp canal closure(deciduous teeth ②enlarge canal(permanent teeth)]
❸whole teeth[①microdontia ②hypodontia ③incomplete calcification]

(牙放課本補充)
❶RT➔post. 2/3 tongue➔bitter & acid➔more severe
❷RT➔ant. 1/3 tongue➔salt & sweet➔more severe
❸taste acuity➔↓1000-10000× during RT
❹saliva change➔partly affect taste acuity

➲acute radiation syndrome

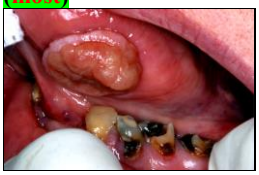
dose(Gy)	manifestation
1-2	prodromal symptoms
2-4	mild hematopoietic symptoms
4-7	severe hematopoietic symptoms
7-15	GI symptoms

2. Which of the followings are typically an **oral complication of antineoplastic therapy**?
①hypogeusia ②cervicofacial emphysema ③xerostomia ④osteoradionecrosis ⑤mucositis
(A) ①②③④
(B) ②③④⑤
(C) ①③④⑤
(D) ①②④⑤

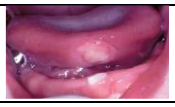
3. 口腔癌病人在接受**放射線治療後的副作用**，下列何者正確？(114)
①味覺喪失且無法恢復 ②味覺喪失但 會逐漸恢復 ③刺激唾液腺分泌，導致唾液變黏稠 ④唾液腺萎縮，且不易完全恢復
(A) ②③
(B) ①④
(C) ①③
(D) ②④

Traumatic ulcerations

➲eosinophilic ulceration(traumatic ulcerative granuloma with stromal eosinophilia [TUGSE])➔like pyogenic granuloma➔tongue (most)



➲Riga-Fede disease➔1-wk & 1s➔natal teeth➔
❶mandibular incisor➔anterior ventral tongue(most)
❷maxillary incisor➔dorsal tongue



❸similar presentation➔neuro condition related to self-mutilation(自殘)
➔[①familial dysautonomia(Riley-Day syndrome) ②congenital indifference to pain ③Lesch-Nyhan syndrome ④Gaucher disease ⑤cerebral palsy ⑥Tourette syndrome]

➲1^0 cutaneous CD30+ lymphoproliferative disorder(oral counterpart)
➔sequential ulcer, necrosis, self-regression(occasion)➔eosinophilic ulcer

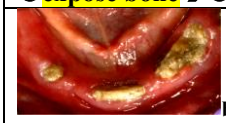
Medication-related osteonecrosis of the jaw(MRONJ)[Bisphosphonate-related osteonecrosis of the jaw(BRONJ)]

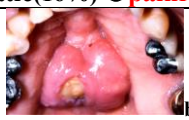
➲definition
❶current/previous antiresorptive(angiogenic) agent Tx
❷exposed bone➔maxillofacial region(>8-wk)
❸no RT history(jaws metastasis)

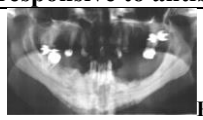
➲stages
stage 0➔no expose necrotic bone➔但有 clinic/radiograph change[①unexplained odontalgia ②dull bone pain ③sinus pain ④neurosensory function 改變 ⑤unexplained loose teeth ⑥sinus tract ⑦alveolar bone loss not associate periapical/periodontal infection ⑧patchy osteosclerosis ⑨lamina dura 變厚 ⑩extraction site 無法 remodeling]

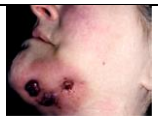
stage 1➔asymptomatic exposed necrotic bone(sinus tract to bone)

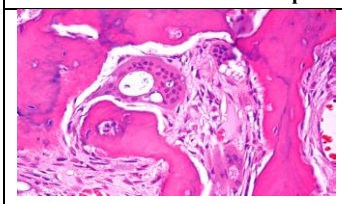
stage 2➔symptomatic exposed necrotic bone(sinus tract to bone) + pain & erythema with(out) purulence
stage 3➔symptomatic exposed necrotic bone(sinus tract to bone) + >1(❶❷❸❹)➔[❶necrotic bone beyond alveolus (①inferior border/ramus ②sinus/zygoma) ❷pathologic fracture ❸extraoral sinus tract ❹oral antral/nasal fistula]
➲antiangiogenic agent➔direct against VEGF(vascular endothelial growth factor) ❶tyrosine kinase inhibitor➔①axitinib(inlyta) ②cabozantinib(carbometyx, cometriq) ③dasatinib(sprycell) ④erlotinib(tarceva) ⑤imatinib(gleevec) ⑥pazopanib(votrient) ⑦sorafenib(nexavar) ⑧sunitinib(sutent) ❷mAb inhibiting VEGF➔①aflibercept(zaltrap, eylea) ②bevacizumab(avastin, mvasi) ③ramuciramab(cyramza)
➲antiresorptive agent & bone metabolism modifier ❶aminobisphosphonate(nitrogen-containing bisphosphonate)➔antineoplastics ❷denosumab➔antineoplastic ❸aminobisphosphonate➔osteoporosis ❹denosumab➔osteoporosis ❺romosozumab➔osteoporosis
★正常➲trauma➔clot➔granulation tissue➔woven(immature) bone➔remodel to lamellar bone➔4-mon(2-8-mon)
★正常➲remodeling➔organized synergism of [❶osteoclast ❷osteoblast ❸local vascular supply]➔basic multicellular unit(BMU)➔moving structure➔continual replace of participate cell at correct time & place[osteoclast➔critical for signaling]
➲mandible(65%)>maxilla(27%)>both jaws(8%)
➲bone necrosis➔❶dental extraction(65%) ❷spontaneous(26%) ❸denture pressure/minor trauma of torus(7%)
➲expose bone➔❶asymptomatic(16%) ❷painful(66%)➔not responsive to antibiotics(18%)

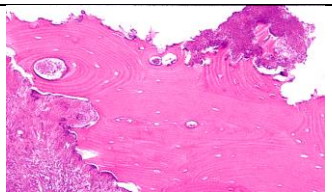

bone expose


bone expose


PD-RL+RO


oro-cutaneous fistula

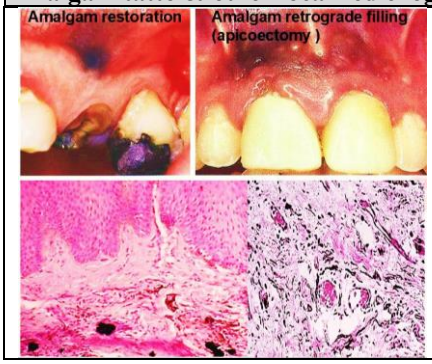




➲micro
❶trabeculae of pagetoid bone➔enlarged osteoclast➔ numerous intracytoplasmic vacuoles(左圖)
❷trabeculae of sclerotic lamellar bone➔sequestrum(no osteocyte within lacunae)➔peripheral resorption with bacterial colonization(右圖)

4. The **amalgam tattoo** represents amalgam particles in the tissue and is **most observed** in the oral cavity on the:
   (A) lateral borders of the tongue
   (B) anterior palate near the rugae
   (C) floor of the mouth
   (D) posterior gingiva and edentulous ridge

Amalgam tatto & other localized exogenous pigmentations➔mistaken for melanoma



➲❶gingiva>❷[alveolar mucosa, buccal]
➲graphite implant➔micro similar to amalgam tatto➔d.d. by ❶ammonium sulfide Tx➔birefringence ❷reticulin stain of fiber(-) ❸energy dispersive x-ray microanalysis➔foreign body material type
➲large particle➔surround by chronic inflamed fibrous tissue ➲smaller particle➔surround by more significant inflammation➔ ❶granulomatous ❷mixture of plasma cell & lymphocytes

Systemic metallic intoxication

lead (plumbism)	➲bluish(marginal) gingival line(Burton line) ➲grey area➔buccal mucosa & tongue	gold	➲metallic taste before oral mucositis(buccal, tongue border, palate, pharynx)
mercury (erethism)	➲neural symptom➔❶excitability ❷tremor ❸memory loss ❹insomnia(失眠) ❺shy ❻weak ❼deliriu(譫妄) ➲oral➔❶metallic taste ❷ulcerative stomatitis ❸enlargement of ①salivary gland(excessive salivation) ②gingiva(blue-gray to black) ③tongue		
silver (argyria)	➲slate(石板)-blue silver line along gingival margin➔1st sign in oral cavity ➲grayish discoloration➔face		bismuth	➲diffuse blue-gray discoloration of skin, conjunctivae, oral cavity ➲blue-gray line along gingival margin
arsenic	➲arterial occlusion➔dry gangrene & spontaneous amputation of extremities➔black foot disease ➲metal & ↑melanin production➔oral mucosa discoloration(變色)(rare)		

Drug-related discolorations➔oral mucosa

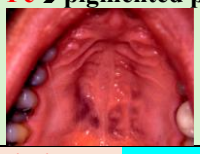
➲phenolphthalein(laxative 瀉藥)➔skin & oral mucosa➔small, well-circumscribed hyperpigmentation

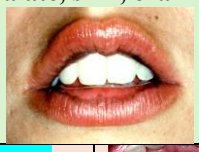
➲peginterferon alfa➔ethnically pigmented hepatitis C p't➔pigmented filiform papillae(dorsal tongue)

➲minocycline
❶linear band➔facial attached gingiva near mucogingival junction
❷hard palate➔broad discoloration zone
❸dental pulp➔dark stain➔darkened teeth

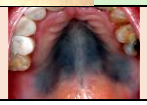
❹alveolar bone➔blue-gray discoloration(原 dark green) visible via thin mucosa

❺melanosis/drug metabolites chelated to Fe➔pigmented palate, skin, oral mucosa





➲antimalarial/tranquilizer(hydroxychloroquine)➔blue-black discoloration➔limited to hard palate

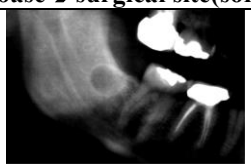


5. Which one of the following **drugs** has been known to result in **palatal hyperpigmentation**?
   (A) botox
   (B) chloroquine
   (C) dilantin
   (D) ephedrine

6. Which one of the following **drugs** may stain bone & result in **blue-gray discoloration of alveolar mucosa** adjacent to teeth?
   (A) clotrimazole
   (B) fluconazole
   (C) fluocinonide
   (D) minocycline

Myospherulosis➔topical antibiotic in petrolatum base➔surgical site(soft tissue/bone)➔foreign body reaction

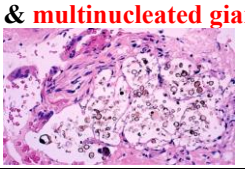
➲antibiotic 方置於 extraction site➔目的 prevent alveolar osteitis
➲radiograph➔asymptomatic WD-RL➔exploration➔black greasy tarlike material
➲clinic➔painful swelling & purulent drainage



❷c.t.➔cystlike space➔numerous brown-black-stain spherule(小球)[這些小球是 RBC➔altered by medication]➔surround by outer membrane (parent body)➔bag of marbles(右圖)
❸dark coloration➔degradation of hemoglobin

➲paranasal sinus➔zygomycetes(aspergillus)

➲micro
❶dense collagenous tissue mixed with granulomatous inflammation➔macrophage & multinucleated giant cell



➲xx cheilitis(唇炎)⇆S/S

❶exfoliative cheilitis⇆↑↑production & desquamation of keratin(allergy, psychiatric & abnormal thyroid function)
❷factitious(人為的) cheilitis⇆chronic injury(lip licking, biting, picking, sucking)
❸allergic contact cheilitis(stomatitis)⇆tooth paste, aluminum chloride
❹angular cheilitis⇆①bacterial/candidal infection of lips ②with plasma cell gingivitis
[Plummer-Vinson syndrome➔(1)Fe deficiency anemia (2)oral/esophageal SCC)] (3)koilonchia(凹甲) (4)angular cheilitis (5)dysphagia (6)esophageal web (7)glossitis[beef tongue➔dorsal papillary atrophy]
❺actinic cheilitis(cheliosis)⇆UV light➔premalignancy➔lower lip vermilion
❻cheilitis granulomatosa of lips alone(of Miescher)⇆orofacial granulomatosis
[Melkersson-Rosenthal syndrome➔①cheilitis granulomatosa ②facial paralysis ③fissured tongue]
❼cheilitis glandularis⇆inflammaton of minor salivary gland➔lower lip vermilion

➲healing of tooth extraction wound(補充)

❶Mangos(1941)
①術後3天➔纖維母細胞(fibroblast)出現於血塊邊緣
②術後7天➔血管開始有機化
③上皮幾乎覆蓋拔牙傷口
④術後14天➔上皮已覆蓋拔牙傷口，並有骨小樑(trabeculae)出現
⑤術後40天➔拔牙槽之上半部有明顯的纖維組織
⑥術後72天➔上皮組織已很整，皮下肉芽組織已不見(被緻密結締組織取代)

❷Amler(1960)有類似發現➔在術後7天的拔牙傷口➔造骨纖維(osteogenic fiber)出現

❸Amler的觀點被Carter等人(1991)證實➔造骨纖維➔新生骨(woven bone/immature bone)生成時的模板(template)架構➔bone modeling生成的新生骨➔成熟的板狀骨(lamellar bone)

❹Boyne(1996)➔tetracycline作fluorochrome bone label
①拔牙傷口內新生骨出現於術後10天
②先出現於socket wall，非過去認為齒槽底部(socket fundus)

➲events(almost simultaneously & dependent on each other) of cutaneous(mucosa) wound healing

injury(epithelium & c.t.)➔bleeding(hemostasis➔clot)➔❶inflammation ❷epithelization(migrating epithelial cells from both ends of ulcer to form a new surface layer) ❸neurovascularization ❹granulation tissue ❺contraction ❻collagen formation ❼scar remodeling ※mucosa➔wet & scab(痂) not form(slight difference from skin)

Chapter 8: Physical and Chemical Injuries

1. Which of the following is not typically an oral complication of antineoplastic therapy?
A. Cervicofacial emphysema
B. Hypogeusia
C. Mucositis
D. Osteoradionecrosis
E. Xerostomia

2. Which one of the following drugs may stain bone and result in blue-gray discoloration of the alveolar mucosa adjacent to the teeth?
A. Amphotericin B
B. Clotrimazole
C. Fluconazole
D. Fluocinonide
E. Minocycline

3. Which one of the following drugs has been known to result in palatal hyperpigmentation?
A. Accutane
B. Botox
C. Chloroquine
D. Dilantin
E. Ephedrine

4. The most common location for the traumatic granuloma (traumatic ulcerative granuloma with stromal eosinophilia) is:
A. buccal mucosa
B. gingiva
C. hard palate
D. lower lip
E. tongue

5. Minute, pinpoint areas of hemorrhage on the skin or mucosa are best termed:
A. ecchymoses
B. hematomas
C. petechiae
D. purpura
E. vesicles

6. Susceptibility to dental caries in a patient with a history of radiation therapy to the head and neck is mostly related to:
A. decreased ability of the patient to brush and floss the teeth
B. direct radiation damage to the hydroxyapatite crystal structure of tooth enamel
C. direct resorption of tooth structure by cancerous cells
D. radiation-induced mutations to caries-causing bacteria (*Streptococcus mutans*)
E. secondary xerostomia due to damage to salivary glands in the field of radiation

7. A pseudocyst of the maxillary sinus will classically appear as:
A. a cavity lined by pseudostratified columnar epithelium
B. a cavity lined by stratified squamous epithelium
C. a dome-shaped radiopacity arising from the floor of the sinus
D. a well-defined radiolucency located between the roots of the maxillary teeth
E. total opacification of the sinus with evidence of peripheral bone resorption

8. Bisphosphonate medications work by:
A. causing renal phosphate excretion
B. decreasing serum calcium levels
C. inhibiting calcitonin activity
D. inhibiting resorptive activity by osteoclasts
E. promoting the action of parathyroid hormone

9. Which one of the following drugs may be used for the treatment of xerostomia?
A. Chlorpromazine
B. Methamphetamines
C. Pamidronate
D. Pilocarpine
E. Zoledronic acid

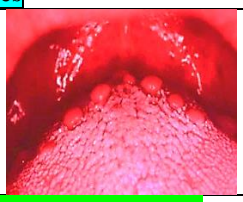
Chapter 8: Physical and Chemical Injuries➔answers

1. ANS: A
2. ANS: E
3. ANS: C
4. ANS: E
5. ANS: C
6. ANS: E
7. ANS: C
8. ANS: D
9. ANS: D

Chapter 9 Allergies & immunologic diseases

➲4 types of tongue papillae(乳頭)

❶fungiform(蕈狀) papillae➔切面似蕈類➔舌尖
❷filiform(絲狀) papillae(右圖)
❸circumvallate(輪狀) papilla(右圖)➔舌根
❹foliate(葉狀) papillae➔舌側緣後



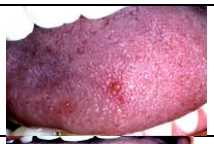
➲stomatitis medicamentosa(systemic drug➔oral mucosa反應)

❶anaphylactic stomatitis(allergen➔circulation➔bind to IgE)
❷intraoral fixed drug eruption
❸lichenoid drug reaction(indirect IF➔string of pearls➔cell membrane of basal cell layer)
❹pemphigoid-like drug reaction ❺lupus erythematosus-like eruption
❻nonspecific erosive(ulcerative) lesion

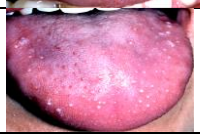
Transient lingual papillitis➔involve fungiform papillae(FP)

➲3 patterns

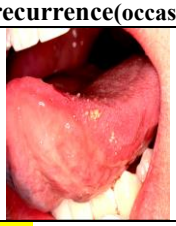
❶first pattern➔female predominance
①localized➔1-several FP➔enlarged & papule➔red with yellow, ulcerated cap
②anterior dorsal(most)➔mild to moderate pain➔resolve spontaneous(hrs-several days)
③transient lingual papillitis(56%)➔single affected papilla(majority)➔associate food allergy



❷second pattern➔FP more generalized➔tip & lateral dorsal
①FP➔sensitive, enlarged, erythematous, focal erosion
②fever & cervical lymphadenopathy➔spread among family members➔possible virus correlated
③~7-day➔spontaneous resolution➔recurrence(occasion)



❸third pattern➔more diffuse
①FP(asymptomatic)➔white-yellow papule
②papulokeratotic variant➔ thickened parakeratotic cap



➲micro
❶first & second patterns➔normal surface epithelium
①focal area➔exocytosis/ulceration
②lamina propria➔↑↑small blood vessel & mixed inflammatory infiltrate
③HPV(-), HSV(-), fungal infestation(大量滋生)(-)

❷papulokeratotic variant(third pattern)➔①marked HPK(ragged)➔bacterial colonization
②superficial lamina propria➔chronic lymphocytic infiltrate➔extend to basal portion of adjacent epithelium

1. Which of the following is not the clinical features of **recurrent aphthous ulcer**?
   (A) most frequently in gingiva and hard palate (bounded mucosa)
   (B) well-demarcated ulceration with red halo
   (C) yellowish or greyish base of ulceration
   (D) most frequently in nonkeratinized, movable mucosa

2. The followings are the inducing factors of **recurrent aphthous ulcer** *except*:
   (A) genetic
   (B) use of beta blocker
   (C) autoimmunity
   (D) smoking cessation

Recurrent aphthous stomatitis(Canker sores)➔❶minor ❷major ❸herpetiform aphthous ulcer

Comparison of clinical features of recurrent minor aphthous ulcer & recurrent herpes simplex ulceration

features	recurrent minor aphthous ulcer	recurrent herpes simplex ulceration
location	nonkeratinized mucosa	keratinized mucosa
number	one to several	multiple(crops)
vesicle precedes ulcer	no	yes
pain	yes	yes
size	<1cm(3-10mm)	1-2mm
borders	round to oval	clusters of ulcers coalesce➔large irregular ulcer
recurrent	yes	yes

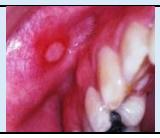
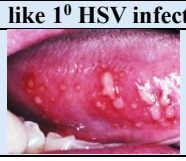
➲mucosa destruction➔T cell-mediated➔TNF(tumor necrosis factor)α(inflammatory cytokine)➔assist cytotoxic T cell(CD8+)➔destruct epithelium

➲systemic disorders associate RAS
①Behcet syndrome ②celiac(腹腔) disease ③cyclic neutropenia
④nutritional deficiencies(Fe, folate, Zn, B1,2,6,12) ⑤IgA deficiency ⑥immunocompromise condition➔HIV
⑦inflammatory bowel(腸) disease ⑧MAGIC syndrome(mouth & genital ulcer with inflamed cartilage)
⑨PFAPA syndrome(periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis) ⑩reactive arthritis
⑪sweet syndrome ⑫ulcus vulvae(外陰) acutum

➲inducing factor➔❶allergies ❷genetic ❸mucosal barrier(nomal)
❶allergies➔①toothpaste(Na lauryl sulfate) ②NSAID ③bisphosphonate ④beta blocker
⑤angiotensin receptor blocker ⑥cyclooxygenase-2 inhibitor ⑦rapamycin inhibitor
⑧trimethoprim-sulfamethoxazole ⑨nicorandil ⑩many food
❷genetic predisposition(hematologic abnormalities)➔child➔①RAS family history➔90% chance
②no RAS family history➔20%

❸hormonal influence➔↑mucosal barrier(nomal)
❹immunologic factor➔immunodysregulation➔abnormal response to normal antigen
❺infectious agent➔①streptococci(L form) ②helicobacter pylori ③HSV ④VZV ⑤adenovirus ⑥CMV
❻nutritional deficiencies➔↓mucosal barrier
❼smoking cessation➔↓mucosal barrier(smoking➔↑mucosal barrier)
❽stress(mental & physical)➔↓mucosal barrier
❾trauma➔↓mucosal barrier

Comparison of clinical features➔❶minor ❷major ❸herpetiform aphthous ulcer

features	minor	major	herpetiform
recurrence	fewest	up to 20-yr or more	most frequent
duration	shortest(7-14-day)	longest(2-6 weeks)	7-10-day
size	3-10mm/episode	1-3cm(larger)	1-3mm(small)➔coalesced➔larger
number	1-5	1-10	greatest no.(as many as 100)
pain	+	++	+
location	buccal & labial(most)	labial, soft palate, tonsillar fauces	nonkeratinized movable mucosa (most); any mucosa
others	heal without scar	❶scar ❷restricted mouth opening	like 1^0 HSV infection
	 		

3. The least likely location for an **aphthous ulcer** is:
   (A) hard palate
   (B) labial mucosa
   (C) lateral tongue
   (D) soft palate

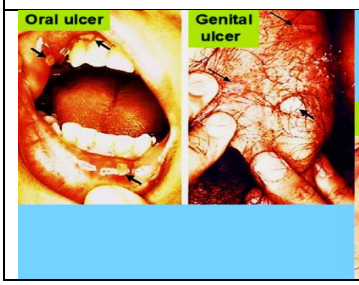
4. Which of the following is the main diagnostic criteria of **Behçet disease**?
   (A) blood routine test
   (B) history and clinical features
   (C) histopathological examination
   (D) titer of autoantibodies

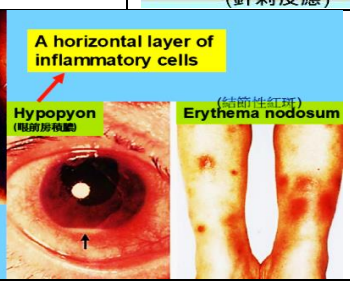
5. **Aphthous ulcers** are seen in each all the following systemic diseases except
   (A) Behcet syndrome
   (B) Langerhans cell histiocytosis
   (C) ulcerative colitis
   (D) cyclic neutropenia

Bechet syndrome(Bechet disease(貝賽特氏病)

➲criteria➔recurrent oral ulcer+
≥2 other findings

Findings	Definitions
Recurrent oral ulceration	Minor aphthous, major aphthous, or hepetiform ulcers observed by the physicians or patients, which have occurred at least three times over a 12-month period
Recurrent genital ulceration	Aphthous ulceration or scarring observed by the physician or patient
Eye lesions	Anterior uveitis, posterior uveitis or cells in the vitreous on slite lamp examination or retinal vasculitis detected by an ophthalmologist
Skin lesions	Erythema nodosum observed by the physician or patient, pseudofolliculitis, or papulopustular lesions or acneriform observed by the physician in a postadolescent patient who is not receiving corticosterioids
Positive pathergy test (針刺反應)	Test interpreted as positive by the physician at 24 to 48 hours





Definition of different grades of skin pathergy test

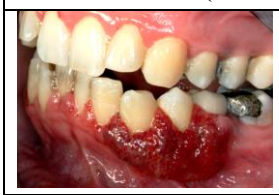
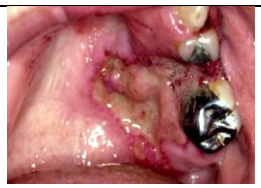
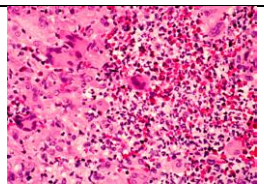
Grade of test	Clinical characteristic of the test at 48 h
Negative (-)	Only erythema < 2 mm
Suspect (+/-)	Only erythema > 3 mm or papule 1-2 mm + erythema < 2 mm
Positive (+)	1+ Papule 2-3 mm + erythema > 3 mm
	2+ Papule > 3 mm + erythema > 3 mm
	3+ Pustule 1-2 mm + erythema > 3 mm
	4+ Pustule > 2 mm + erythema > 3 mm

Erythema/Papule/Pustule--Diameter

Wegener granulomatosis(WG)(Granulomatosis with polyangitis)

➲3 types
❶generalized WG➔①upper & lower respiratory tract ②renal involvement(rapid)
❷limited WG➔①respiratory system involve ②without rapid renal development

❸superficial WG➔①skin ②mucosa involve➔strawberry gingivitis(early manifestation before renal)➔①ulcer with blood vessel 增生(廣泛 RBC extravasation) ②lymphocyte ③neutrophil ④eosinophil ⑤multinucleated giant cell

➲other orofacial signs
①facial paralysis ②labial mucosa nodule
③sinusitis-related toothache
④TMJ pain ⑤jaw claudication
⑥palatal ulcer from nasal extension
⑦oroantral fistula ⑧poor heal extraction site

➲lab markers
❶PR3(proteinase-3)-ANCA(antineutrophil cytoplasm Ab)(90-95%)
❷MPO(myeloperoxidase)-ANCA

Sarcoidosis(結節病)

➲multisystem involve[lung, LN(almost all cases), skin, eye & salivary gland]➔improper antigen degradation➔noncaseating granulomatous inflammation

➲possible antigen➔❶infectious agent[①mycobacterium ②propionibacteria 丙酸菌 ③EBV ④HHV-8]
❷environmental factors(wood dust, pollen, clay, mold, silica)

➲↑prevalence➔female & black
➲asymptomatic(~20%)➔discovered on routine chest radiograph

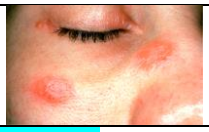
➲acute➔fever, fatigue, anorexia, weight loss+(respiratory symptom, polyarthritis, visual problem & skin lesion)

➲chronic➔pulmonary symptom(dry cough, dyspnea, chest discomfort)

➲salivary gland➔enlargement, xerostomia, keratoconjunctivitis sicca Sjögren syndrome

➲ocular➔anterior uveitis conjunctiva retina lacrimal gland(keratoconjunctivitis sicca)

➲skin(nose, ear, lip, face, lower leg)➔violaceous, indurated lesion(lupus pernio)➔erythema nodosum



➲endocrine system, GI tract, heart, kidney, liver, nervous system & spleen

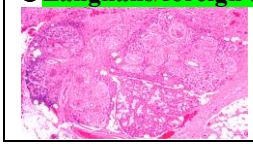
➲intraosseous➔phalange, metacarpal & metatarsal (less frequent➔skull, nasal bone, ribs & vertebrae)

➲oral(2/3 cases before multisystem involvement)
❶submucosal mass(papule, granularity, ulcer)➔mucosa lesion(normal color, brown-red, violaceous, hyperkeratotic)➔buccal mucosa(most)
❷PD-RL(occasion eroded cortex; never expansion)

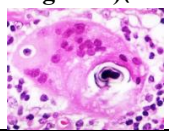
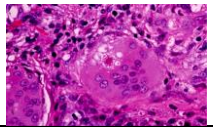
➲associate(acute)➔❶Lofgren syndrome(①erythema nodosum ②bilateral hilar lymphadenopathy ③arthralgia)
❷Heerfordt syndrome(uveoparotid fever)➔①parotid enlargement ②anterior uveitis ③facial paralysis ④fever

➲micro

❶aggregate of
①epithelioid histiocyte
②surrounding rim of lymphocyte
③Langhans/foreign body giant cell



❷Schaumann bodies(degenerated lysosome)➔laminated basophilic calcification(下左圖)
❸stellate inclusion➔intracytoplasmic asteroid bodies(entrapped collagen fragment)(下右圖)

Orofacial granulomatosis➔biopsy➔nonspecific granulomatous inflammation

➲associate with systemic diseases

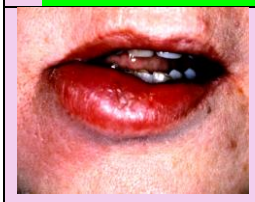
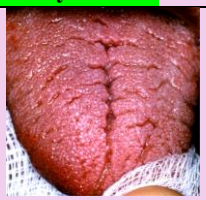
systemic cause	preliminary screening procedure
systemic drug reaction	review medication➔checkpoint inhibitor, highly active antiretroviral therapy, interferon, TNFα antagonist➔trigger sarcoid-like reaction
chronic granulomatous disease	neutrophil nitroblue tetrazolium reduction test(if medical history of chronic infections)
Crohn disease	hematologic➔GI malabsorption(low albumin, Ca, folate, Fe, RBC count; ↑ESR), serum IgA Ab to Saccharomyces cerevisiae, leukocyte scintigraphy using ^{99m}Tc-HMPAO(hexamethyl propylene amine oxime), fecal calprotectin➔initial screen(+)➔[esophagogastroduodenoscopy, ileocolonoscopy, small-bowel radiograph]
sarcoidosis	serum angiotensin-converting enzyme & chest X-ray(hilar lymphadenopathy)
tuberculosis	skin test & chest X-ray[acid-fast fast stain(-) on biopsy specimen➔not R/O mycobacterial infection]

➲R/O local causes

local cause	intervention
chronic oral infection	eliminate all oral foci of infection
foreign material	①debris➔in foreign body gingivitis➔difficult to associate definite with diffuse inflammation ②lesion➔isolated to gingiva➔local excision evaluated
allergy	①cosmetic, food & food additive(aspartate, benzoate, carbone piperitone, carmoisine, carvone, chocolate, cinnamon(肉桂), cocoa, dairy product, egg, monosodium glutamate, peanut, sun yellow dye, tartrazine,

	wheat) ②flavor ③OH product(toothpaste & mouth rinse) ④dental restorative metal ⑤patch test(contact dermatitis standard series with oral battery) eliminate diet may discover antigen

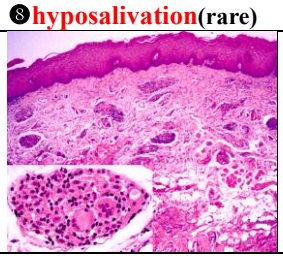
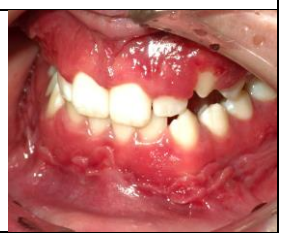
➲clinic➔majority adult➔most frequent lip(s)➔nontender swelling
❶Melkersson-Rosenthal syndrome➔①orofacial granulomatosis combine ②facial paralysis ③fissure tongue(左下1-2圖)

❷cheilitis granulomatosa (of Miescher)➔lips alone

❸tongue➔fissure, edema, erosion, paresthesia, altered taste
❹gingiva➔swelling, erythema, pain, erosion
❺buccal➔cobblestone mucosa
❻linear hyperplastic fold(右下圖)
❼palate➔papule
❽hyposalivation(rare)

➲micro
❶edema➔lamina propria➔lymphatic dilatation
❷lymphocyte➔diffuse & cluster
❸fibrosis➔long-term lesion
❹noncaseating granulomatous inflammation➔lymphocyte & epithelioid histiocyte with(out) multinucleated giant cell(右圖inset)
❺granuloma➔around scattered vessel

6. All the following are examples of **hypersensitivity reactions** *except*
   (A) systemic lupus erythematosus
   (B) urticaria(蕁麻疹)
   (C) angioedema
   (D) contact dermatitis and mucositis

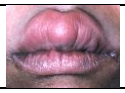
7. Which of the following orofacial structures could create a life-threaten situation for patient from **angioedema** involvement?
   (A) lips
   (B) mucosa
   (C) eyelids
   (D) epiglottis

8. Which of the following about **angioedema** is *true*?
   (A) angioedema is formed on using ACE inhibitors
   (B) it is an IgG induced allergic reaction
   (C) the second generation of angiotensin II receptors blocker prongs to cause angioedema
   (D) antihistamine can treat all types of angioedema

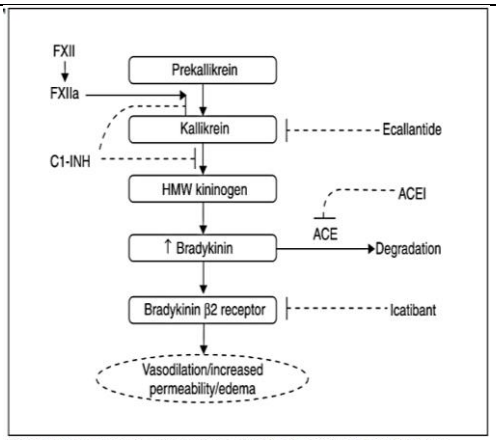
Angioedema(Quincke disease)➔IgE-mediated hypersensitivity➔mast cell degranulation➔histamine

➲FXII(a)➔kalikrein pathway➔↑bradykinin(激肽釋放酶 pathway➔↑緩激肽)

➲clinic➔diffuse edematous subcutaneous(mucosa) swelling



➲causes
❶allergen(drug, food, plant, dust, inhalant)➔contact allergic reaction(cosmetic, topical medication, rubber dam)
❷physical stimuli(heat, cold, exercise, stress, solar exposure, vibration ➔prolong snore/use of musical instrument with mouthpiece)
❸angiotensin converting enzyme(ACE)inhibitor(ACEI) (antihypertensive drug➔captopril, enalapril, lisinopril)➔severe form (not mediated by IgE)➔swelling not respond to antihistamine[⊠excess bradykinin]
⊠blockage of bradykinin degradation by ACE inhibitor➔accelerate the process(右圖)
✪angiotensin II receptor blocker(2nd generation)➔specific avoid bradykinin degradation inhibition➔↓angioedima frequency



Kallikrein Pathway in Angioedema . Diagram demonstrating the kallikrein pathway with the over-production of bradykinin in angioedema. Note the blockage of bradykinin degradation by ACE inhibitors and the three medical interventions that can halt the process (C1-INH, ecallantide, icatibant).

➲3 hereditary types➔①type I hereditary angioedema(HAE I) ②HAE II(major)(autosomal dominant)
③hereditary angioedema with normal C1 esterase inhibitor(C1-INH)(rare)(右圖)➔FXII mutation➔trigger kalikrein pathway

➲ACEI+3 medical interventions(上圖)(①C1-INH ②ecallantide ③icatibant)➔blockage of bradykinin degradation➔halt the process

➲acquired type
①associate lymphoproliferative diseases(Caldwell syndrome)/p't with specific autoAb
②clot buster tissue plasminogen(tPA, alteplase) for stroke➔ intraoral angioedema
③↑Ag-Ab complex(LE & viral/bacterial infection)
④↑peripheral blood eosinophil count p't

Chapter 9: Allergies and Immunologic Diseases

1. The least likely location for an aphthous ulcer is:
A. buccal mucosa
B. hard palate
C. labial mucosa
D. lateral tongue
E. soft palate

2. Which one of the following is a typical feature of an aphthous ulcer?
A. Caused by herpes simplex
B. Grayish yellow ulcer located on the maxillary gingiva
C. Painful ulcer surrounded by a red halo
D. Starts as a fluid-filled blister that ruptures
E. Usually associated with inflammatory bowel disease

3. "Strawberry gingivitis" is a characteristic oral presentation of:
A. aspergillosis
B. histoplasmosis
C. scarlet fever
D. tertiary syphilis
E. Wegener granulomatosis

4. Which of the following conditions is NOT associated with granulomatous inflammation?
A. Cheilitis granulomatosa
B. Leprosy
C. Recurrent aphthous stomatitis
D. Sarcoidosis
E. Tuberculosis

5. The clinical appearance of contact stomatitis on the lateral tongue from chewing cinnamon-flavored gum is most likely to resemble which of the following?
A. Black hairy tongue
B. Erythema migrans (geographic tongue)
C. Fissured tongue
D. Leukoedema
E. Oral hairy leukoplakia

6. Oral mucosal contact reactions to dental materials, such as amalgam, may appear clinically and histopathologically similar to:
A. candidiasis
B. lichen planus
C. morsicatio buccarum
D. orofacial granulomatosis
E. pemphigus vulgaris

7. Which one of the following classes of drugs is most likely to produce a severe form of angioedema?
A. Angiotensin-converting-enzyme inhibitors
B. Antifungals
C. Calcium-channel blockers
D. Nonsteroidal antiinflammatory drugs
E. Statins

8. Which one of the following oral lesions is classically associated with Behçet syndrome?
A. Aphthous ulcers
B. Diffuse enlargement of the upper lip
C. Fissured tongue
D. Superficial peeling of the oral mucosa
E. White plaques that do not rub off

Chapter 9: Allergies and Immunologic Diseases➔answers

1. ANS: B
2. ANS: C
3. ANS: E
4. ANS: C
5. ANS: E
6. ANS: B
7. ANS: A

8. ANS: A

Chapter 10 Epithelial pathology

1. All of the following neoplasms arise from **squamous epithelium** *except* one. Which one is the exception?
   (A) squamous cell carcinoma
   (B) verrucous carcinoma
   (C) adenoid cystic carcinoma
   (D) papilloma

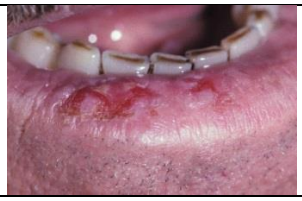
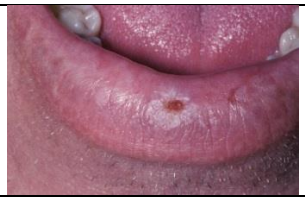
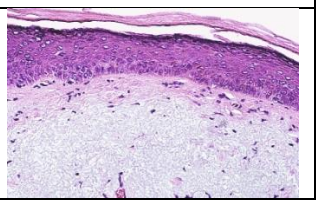
2. Which of the following is *false* concerning **actinic cheilitis (cheilosis)**?
   (A) it affects the vermilion of the lips
   (B) it is caused by sun exposure
   (C) it usually involves the upper lip more severely than the lower lip
   (D) it can be identified by clinical changes in the appearance of the lips

3. Which one of the following concerning **solar cheilitis** is *false*?
   (A) there is distinct demarcation between vermilion border and skin
   (B) it appears as mottled grayish-pink discoloration of lower lip
   (C) linear fissures are seen at right angles to the vermilion border
   (D) it is caused by excessive exposure to sunlight

Actinic cheilosis(Actinic cheilitis; Solar cheilosis)➔chronic UV light➔premalignancy lower lip vermilion

➲<45s	➲M:F=10:1	➲leukoplakic appearance➔extend near wet line of lower lip➔ulcer➔SCC

➲micro➔surface epithelium➔atrophic/acanthotic➔varying degrees of dysplasia
❶hyperkeratosis
❷c.t.➔solar elastosis(amorphous, acellular, basophilic band)➔UV induce change of collagen & elastic fiber
❸chronic inflammatory cell infiltrate & dilated blood vessel

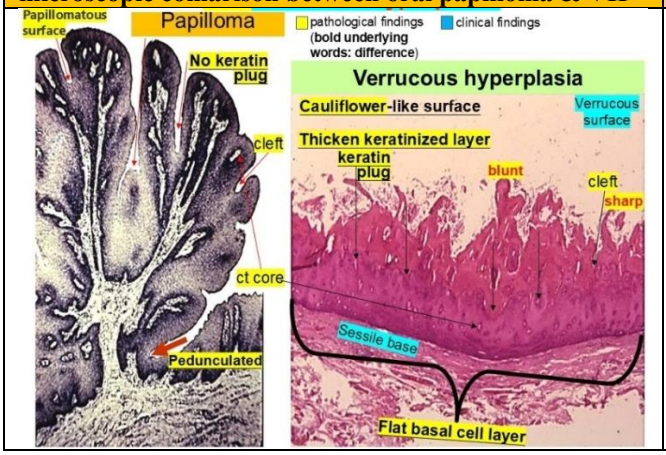
4. Which of the following types of human papilloma virus (HPV) are mostly associated with oral squamous papilloma?
   (A) type 6, 11
   (B) type 3, 32
   (C) type 16, 18
   (D) type 3, 10

5. All the following diseases are caused by **HPV infection**; however, which one with the HPV type distinct to the other three diseases?
   (A) oral squamous papilloma
   (B) recurrent respiratory papillomatosis
   (C) verruca vulgaris
   (D) condyloma acuminatum

site	lesion	major HPV types
oral/head & neck mucosa	oral squamous papilloma	6, 11
	recurrent respiratory papillomatosis	6, 11
	exophytic sinonasal papilloma	6, 11
	inverted sinonasal papilloma	6, 11, 16, 18
	multifocal epithelial hyperplasia	13, 32
	oropharyngeal SCC	16
	conjunctival papilloma	6, 11
Skin	verruca vulgaris	2
	verruca plana	3, 10
	palmoplantar wart	1, 4
	Butcher's wart	2, 7
Anogenital region	condyloma acuminatum	6, 11
	intraepithelial neoplasia	6, 11, 16, 18, 31, 33
	cervical SCC	16, 18

6. A **small white exophytic** lesion on the palate is a benign lesion composed of squamous epithelium. **Papillary projections** are arranged in a cauliflower-like appearance. It is most likely a:
   (A) congenital epulis
   (B) neurofibroma
   (C) granular cell tumor
   (D) papilloma

microscopic comarison between oral papilloma & VH



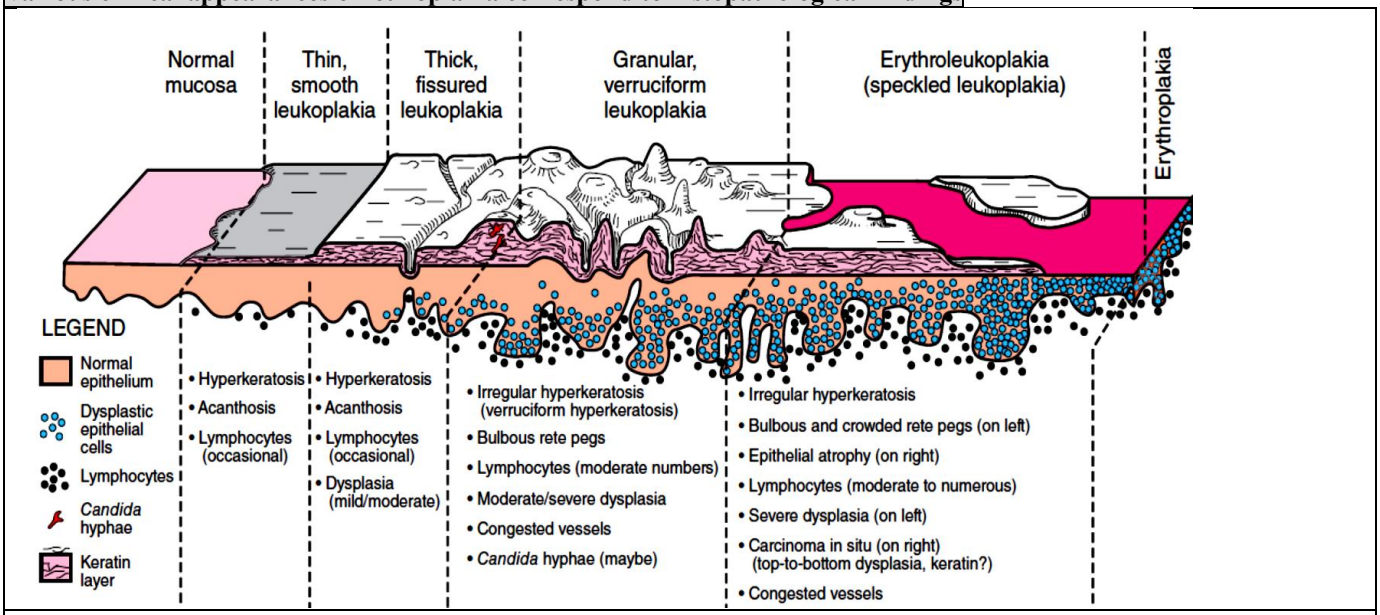
comparison of oral papilloma & verrucous hyperplasia

DIFFERENCES	
Histopathogical	
Papillomatous surface	Cauliflower-like surface
Normal (para)keratinized layer	Thick (para)keratinized layer
No keratin plug	With (para)keratin plug
Pedunculated stalk	Flat broad basal layer
Clinical	
Papillomatous surface	Verrucous surface
Pedunculated base	Sessile base
Smaller size	Larger size
Etiology: HPV	Etiology: Alcohol, Betel-quid, Cigarette(premalignancy)
SAME	
Histopathogical	
Cleft	Cleft
Connective tissue core	Connective tissue core
Clinical	
White color	White color

7. Which of the following **precancer** lesion has the **highest malignant transformation rate**
   (A) tongue of Plummer-Vinson syndrome➔**(1)Fe deficiency anemia (2) SCC)] (3)koilonchia(凹甲) (4)angular cheilitis**
   (B) thin leukoplakia
   (C) thick leukoplakia
   (D) proliferative verrucous leukoplakia (PVL)

8. A white plaque-like lesion that cannot be rubbed off or diagnosed clinically as a specific disease is called:
   (A) squamous cell carcinoma
   (B) erythroplakia
   (C) leukoplakia
   (D) epithelial dysplasia

Various clinical appearances of leukoplakia correspond to histopathological findings



➲thin(mild/early) leukoplakia➔homogeneous(thick) leukoplakia➔granular (nodular) leukoplakia➔verrucous (verruciform) leukoplakia

➲PVL(❶M:F=1:4 ❷multiple ❸slow spread plaques ❹rough surface)➔VCa➔SCC

➲erythroleukoplakia(specked leukoplakia)➔erythroplakia

9. Which of the following represents an **early clinical example of squamous cell carcinoma**?
   (A) exophytic erythroleukoplakia
   (B) urticaria
   (C) brown macule
   (D) destructive radiolucency

10. The most appropriate treatment for **moderate (severe) epithelial dysplasia** is:
    (A) radiation therapy
    (B) chemotherapy
    (C) surgical excision
    (D) observation

11. What percentage of **erythroplakias** is diagnosed as severe epithelial dysplasia or squamous cell carcinoma?
(A) 10%
(B) 25%
(C) 60%
(D) 90%

Grade of oral epithelial dysplasia(ED)

➲mild ED	dysplastic cell➔basal layer to parabasal layers(1/3 of epithelium thickness)
➲moderate ED	dysplastic cell➔basal layer to midportion of spinous layer(1/2 of epithelium thickness)
➲severe ED	dysplastic cell➔basal layer to level above middle of epithelium(2/3 of epithelium thickness)
➲carcinoma in situ	dysplastic cell➔basal layer to surface of epithelium(top to bottom); intact basal layer

12. Which of the followings are microscopic characteristics of **squamous cell carcinoma**?
(1) tumor cells invade into connective tissue (2) cells with very small nuclei (3) hyperchromatic nuclei (4) keratin pearls (5) individual cell keratinization
(A) only 1,2,3,4
(B) only 1,3,4,5
(C) only 2,3,4,5
(D) only 1,2,4,5

Histopathologic features of oral dysplastic epithelial cells

➲enlarged nuclei & cells	➲abnormal mitotic figures (above basal layer)
➲large & prominent nucleoli	➲pleomorphic nuclei and cells
➲↑nuclear-to-cytoplasmic (N/C) ratio	➲low power(LP)➔bulbous/teardrop-shaped rete ridge
➲hyperchromatic nuclei	➲LP➔loss of polarity(lack progressive maturation toward surface)
➲dyskeratosis(individual cell keratinization)	➲LP➔keratin pearl
➲↑mitotic activity(excessive no. of mitoses)	➲LP➔loss of typical epithelial cell cohesiveness

13. Oral squamous cell carcinoma exhibits **jaw bone invasion**, **lung metastasis**, or **T4 tumor dimension**. What clinical stage correlates with these findings?
(A) stage III
(B) stage 3
(C) stage 4
(D) stage IV

14. **Depth of invasion (DOI)** or **tumor thickness** may predict occult cervical lymph node metastasis indicating elective selective neck dissection since an increased risk for nodal metastasis with a DOI or tumor thickness greater than:
(A) 1-2 mm
(B) 3-5 mm
(C) 6-8 mm
(D) 8-9 mm

Tumor-Node-Metastasis(TNM) Staging for oral cavity carcinoma

primary tumor(T) [❶greatest dimension ❷DOI(depth of invasion)]			
TX	primary tumor cannot be assessed	Tis	carcinoma in situ(CIS)
T1	tumor≤2cm; DOI≤5mm	T2	❶[tumor≤2cm; (DOI>5mm; ≤10mm)) *or* ❷[tumor>2cm; ≤4cm; DOI≤10mm]
T3	❶[(tumor>2cm; ≤4cm); DOI>10mm] ❷[tumor >4cm; DOI≤10mm]		
T4a	❶[tumor>4cm; DOI>10mm] ❷[tumor invade adjacent structure only(through cortical bone of mandible/maxilla)] ❸[involve maxillary sinus/skin of face] ✪superficial erosion of bone/tooth socket alone by gingiva primary➔not as T4		
T4b	tumor invade➔[❶masticator space, pterygoid plate] [❷skull base &/or encase internal carotid artery]		
clinical regional lymph node involvement(cN) [lymph node(LN)➔❶greatest dimension ❷ipsi(contra)(bi)lateral ❸no. ❹ENE]			
NX	regional LN cannot be assessed	N0	no regional LN meta
N1	meta➔single ipsilateral LN≤3cm & extranodal extension(ENE)(-)		
N2a	meta➔ipsilateral LN>3cm; ≤6cm & ENE(-)		
N2b	meta➔multiple ipsilateral LN≤6cm & ENE(-)		
N2c	meta➔bilateral/contralateral LN≤6cm & ENE(-)		
N3a	meta➔a LN>6cm & ENE(-)		
N3b	meta➔any LN & ENE(+)		
distant metastasis(M)			
M0	no distant meta	M1	distant meta

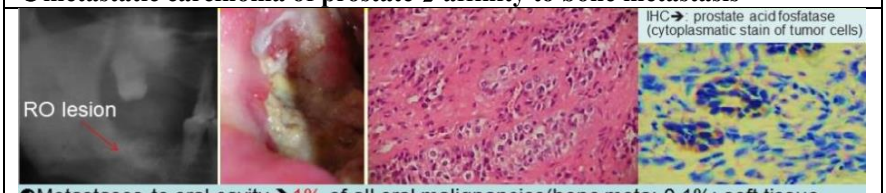
Stage for oral cavity carcinoma

stage	TNM	stage IVA	T4a N0 M0 T4a N1 M0 T1 N2 M0 T2 N2 M0 T3 N2 M0 T4a N2 M0
stage 0	Tis N0 M0		
stage I	T1 N0 M0	stage IVB	any T N3 M0
stage II	T2 N0 M0		T4b Any N M0

stage III	**T3 N0 M0** **T1 N1 M0** **T2 N1 M0** **T3 N1 M0**	**stage IVC**	**any T Any N M1**

15. Which of the followings are *true*?
(1) metastases from tumor from lower parts of body via Batson plexus (2) most common oral soft tissue metastases is gingiva (3) most common site for bone metastasis is breast (4) Numb-chin syndrome involves upper lip paresthesia
(A) 1,2,4
(B) 2,3,4
(C) 1,2,3
(D) 1,3,4

➲metastatic carcinoma of prostate➔affinity to bone metastasis

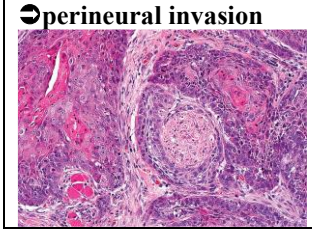


➲Metastases to oral cavity➔1% of all oral malignancies(bone meta: 0.1%; soft tissue meta:0.01%)
➲Metastases from lower parts of body➔blood-borne(filtered out by lung)➔**Batson plexus**(valveless vertebral venous plexus)➔retrograde of tumor cell(bypass filtration through lung)
➲Most common oral soft tissue metastases➔gingiva(54%); next most➔tongue(22.5%)
➲Tumor cell➔vascular network of inflamed gingiva➔fertile site for further growth
➲Lung ca➔1/3 of all oral soft tissue metastases(men)➔followed: renal ca & melanoma
➲Breast ca(women)➔25% of all cases➔followed: malignancies of genital organs, kidney, lung & bone
➲Most common sites for bone metastasis➔breast, lung, thyroid, prostate & kidney
➲Most metastatic bone➔vertebrae, rib, pelvis & skull
➲Jaw metastasis➔mandible(molar)
➲Numb-chin syndrome➔mental nerve involve; lower lip paresthesia
➲Bone metastasis➔stage IV
➲PDL widening➔metastatic to jaws
➲Bone scintigraphy➔sensitive to detect bone metastasis

16. One possible explanation for **blood-borne metastases to head & neck**, especially **absence of pulmonary metastases**, is associated with which of the following?
(A) Batson plexus
(B) tympanic plexus
(C) pterygoid venous plexus
(D) choroid plexus

Invasion pattern➔tumor islands break through basement membrane into subepithelial connective tissues

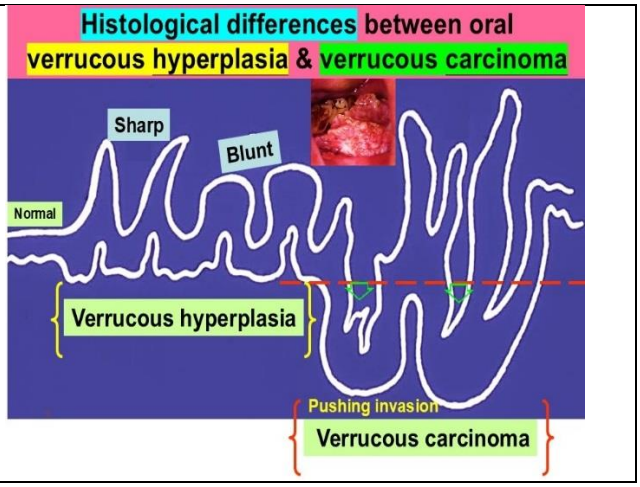
➲superficial/microinvasive(early)

➲perineural invasion	**➲vascular invasion**	**➲desmoplasia(scirrhous change)** **➲angiogenesis**
		

17. **Verrucous carcinoma** (Ackerman tumor) is different from **squamous cell carcinoma** because it:
(A) has pushing down invasion
(B) responds to chemotherapy
(C) often metastasizes
(D) has jawbones invasion having a poor prognosis

Comparison between oral squamous cell carcinoma & oral verrucous carcinoma

Features	Squamous cell carcinoma	Verrucous carcinoma
Macroscopic aspect	Various appearances	Fungating, cauliflower-like tumor
Cellular differentiation	Various degrees	High
Cytologic features of malignancy	Present	Absent or Occasional
Margins	Infiltrating	Pushing
Cellular response	Variable	Prominent
Cleft-like spaces	Usually absent	Present
Grade of malignancy	Moderate/high	Low
Local metastases	Usually present	Absent
Distant metastases	May be present	Absent
Prognosis	Worse than verrucous carcinoma	Better



18. Which of the following has the best long-term prognosis?
    (A) basal cell carcinoma
    (B) intraoral squamous cell carcinoma
    (C) rhabdomyosarcoma
    (D) malignant melanoma

19. All of the following neoplasms occur in **young individuals** *except* one. Which one is the exception?
    (A) ameloblastic fibroma
    (B) basal cell carcinoma
    (C) congenital epulis
    (D) hemangioma

20. Which of the followings about **oral melanoma** are true?
    (1) most (70-80%) common site: palate & maxillary gingiva (2) clinical features ABCDE: E indicates "elevation" (3) 10% amelanotic lesion: confirmed by S100 or HMB45(Human Melanoma Black) (4) mucosal lesion: more aggressive than cutaneous counterpart and male predilection
    (A) 1,2,3,4
    (B) only 1,3,4
    (C) only 2,3,4
    (D) only 1,2,4

Immunohistochemical (IHC) markers (A-O) ➔ Pathological diagnosis of the diseases
(A) stat6 (B) TFE3 (C) CK20 (D) CD117 (E) CD1a (F) TTF1 (G) MDM2 (H) S100 (I) HMB45
(J) CD3 (K) bcl-2 (L) CD34 (M) HHV-8 (N) CK (O) CK19 (P) CK7 (Q) kappa (R) lambda

	Histopathological diagnosis	IHC marker
1	Solitary fibrous tumor	A, K, L
2	Alveolar soft part sarcoma	B
3	Low grade osteosarcoma	G
4	Adenoid cystic carcinoma	D
5	Merkel cell carcinoma	C
6	Metastatic lung carcinoma	F
7	Melanoma	H, I
8	Langerhans cell histocytosis	E, H
9	Pleomorphic adenoma	H
10	T-cell lymphoma	J
11	Neurofibroma, schwannoma (neurilemmoma)	H
12	Kaposi sarcoma	M
13	Squamous cell carcinoma	N
14	Organ of Chieviz	O
15	Salivary gland tumors	P
16	Odontogenic tumors	O
17	Nevus	H, I
18	Multiple myeloma	O,R
	Burkitt lymphoma	Almost 100% Ki67

	Histopathological diagnosis	FISH marker
1	Langerhans cell histiocytosis Melanoma	*B-raf*
2	Fibrous dysplasia	*GNAS*
3	Clear cell carcinoma	*EWSR1*
4	Mucoepidermoid carcinoma *vs* glandular odontogenic cyst	*MAML2*
5	Pleomorphic adenoma	*PLAG1*
6	Odontogenic keratocyst Pindborg tumor	*PTCH1*

FISH: Fluorescence in situ hybridization

S100

➲soluble in 100%(saturated) ammonium sulphate solution at pH 7

present➔❶cells derived from neural crest(Schwann cell, melanocyte) ❷chondrocyte ❸adipocyte ❹myoepithelial cell ❺Langerhans cell ❻dendritic cell ❼nevus cell

21. Among the "**ABCDE**" denoting the clinical features of melanoma, 'D' represent diameter that greater than a pencil eraser being how many mm in length?
    (A) 2
    (B) 4
    (C) 6
    (D) 8

ABCDE➔clinical features of melanoma

Asymmetry	**uncontrolled growth**
Border irregularity	**with notching**
Color variegation	**brown to black, white, red & blue, depend on amount & depth of melanin**
Diameter	**>6mm(diameter of a pencil eraser)**
Evolving	**size, shape, color, surface, or symptoms➔changed over time**

22. For **Clark's definition of level of tumor invasion for cutaneous melanoma**, cells extending into **reticular dermis** represents which level?
(A) II
(B) III
(C) IV
(D) V

Clark's definition for level of melanoma invasion

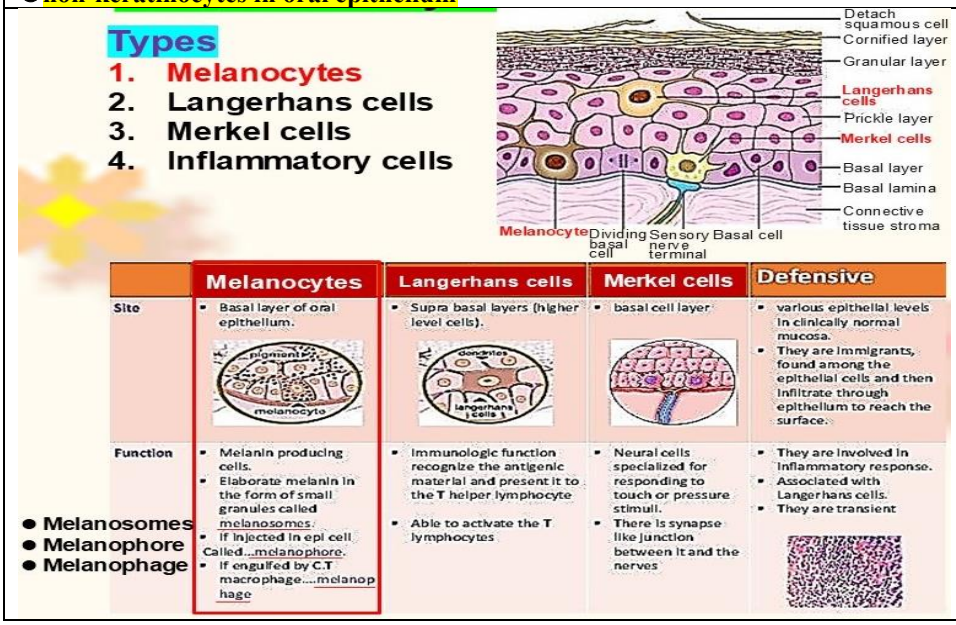
tumor cells	**confined to epithelium**	**Level I**
	penetrating papillary dermis	**Level II**
	filling papillary dermis	**Level III**
	extend into reticular dermis	**Level IV**
	invade subcutaneous fat	**Level V**

23.有關口腔內色斑病灶(pigmented lesion)，若是出現下列何種徵象，必須強烈懷疑黑色素瘤(**melanoma**)的可能？(114)
①外觀呈現非對稱性 ②在同一病灶有多重顏色表現 ③邊緣不規則
(A) 僅①②
(B) 僅①③
(C) 僅②③
(D) ①②③

24. Which of the following marker can be used to confirm **Merkel cell carcinoma**?
(A) CK7
(B) CK20 (perinuclear dot) (neuroendocrine markers: chromogranin A synaptophysin, neuron-specific enolase, CD56)
(C) CK18
(D) CK19

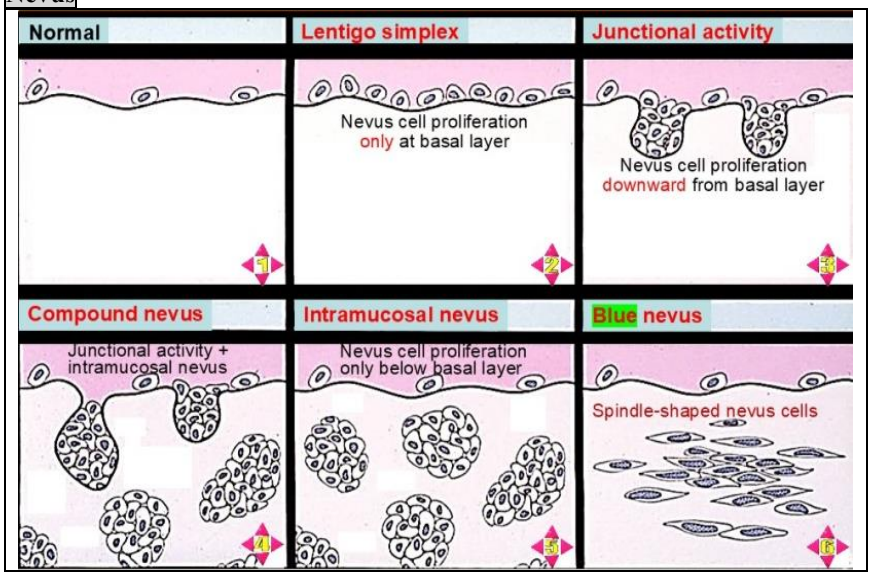
Merkel cell carcinoma➔neuroendocrine carcinoma

➲micro➔small blue round cell(d.d.❶Lymphoma ❷Embryonic rhabdomyosarcoma ❸Ewing sarcoma ❹ Melanoma (amelanotic) ❺Olfactory neuroblastoma ❻Neuroblastoma ❼Sinonasal undifferentiated carcinoma)➔LEMONS		
pseudoglandular	**trabecular**	**cribriform(Swiss cheese)**
➲sheetlike	**➲overlapping nuclei**	**➲scant cytoplasm(indistinct cell border)**
➲fine granular chromatin	**➲Grimelius stain➔intracytoplasmic argyrophilic granules**	**➲brisk mitotic activity**
	➲PCR➔MCPγV DNA (+)➔round nuclei	**➲PCR➔MCPγV DNA(-)➔irregular nuclei**
➲non-keratinocytes in oral epithelium		



25. Which of the following are melanin-producing cells?
(A) nevus cells
(B) squamous cells
(C) granular cells
(D) mesenchymal cells

Nevus



Chapter 10: Epithelial Pathology

1. Which one of the following is NOT caused by one of the human papillomaviruses (HPV)?
A. Condyloma acuminatum
B. Focal epithelial hyperplasia
C. Molluscum contagiosum
D. Squamous papilloma
E. Verruca vulgaris

2. Oral mucosal melanoma most commonly arises on the:
A. buccal mucosa and upper labial mucosa
B. hard palate and maxillary alveolar mucosa
C. mandibular alveolar ridge and floor of mouth
D. soft palate and buccal mucosa
E. ventrolateral tongue and floor of mouth

3. Which one of the following lesions typically shows squamous metaplasia of the minor salivary gland ducts on microscopic examination?
A. Nicotine stomatitis
B. Seborrheic keratosis
C. Squamous papilloma
D. Tobacco pouch keratosis
E. Traumatic neuroma

4. Squamous cell carcinoma represents approximately what percentage of all oral cancer?
A. 10%
B. 30%
C. 50%
D. 70%
E. 90%

5. HPV would most likely be involved in the pathogenesis of a squamous cell carcinoma in which one of the following locations?
A. Floor of mouth
B. Gingiva
C. Lateral tongue
D. Palatine tonsil
E. Upper lip vermilion

6. Which one of the following lesions is LEAST likely to transform into a carcinoma?
A. Actinic keratosis
B. Erythroplakia
C. Proliferative verrucous leukoplakia
D. Seborrheic keratosis
E. Speckled leukoplakia

7. Which of the following is the most common site for the melanotic macule?
A. Buccal mucosa
B. Gingiva
C. Hard palate
D. Lower lip vermilion
E. Tongue

8. Which strain of HPV has most often been associated with an increased risk of oropharyngeal cancer?
A. HPV-1
B. HPV-2
C. HPV-6
D. HPV-11
E. HPV-16

9. A 59-year-old white male presents with a 3×3 cm ^{2} ulcerated carcinoma of the buccal mucosa. No evidence of regional or distant metastasis can be identified clinically or radiographically. This lesion is best classified as:
A. grade I
B. stage I
C. stage II
D. stage III
E. stage IV

10. Which one of the following lesions would be most likely to show malignant or dysplastic changes?
A. Erythroplakia of the floor of the mouth
B. Leukoplakia of the floor of the mouth
C. Leukoplakia of the lateral border of the tongue
D. Nicotine stomatitis
E. Snuff pouch

11. Which one of the following benign dermatologic lesions classically presents as a brown, scaly, greasy plaque that appears to be "stuck onto" the skin surface?
A. Ephelis
B. Lentigo maligna
C. Lentigo simplex
D. Seborrheic keratosis
E. Verruciform xanthoma

12. Which one of the following is the most common site for intraoral cancer?
A. Buccal mucosa
B. Floor of mouth
C. Gingiva
D. Hard palate
E. Lateral border of tongue

13. By definition, carcinoma *in situ* is characterized by:
A. dysplasia involving the entire epithelial thickness, but without invasion
B. metastasis
C. parakeratin production
D. proliferative verrucous leukoplakia
E. tripolar mitoses

14. In the ABCDE warning signs for melanoma, the "A" stands for:
A. acral
B. amelanotic
C. anteverted
D. aplastic
E. asymmetry

15. The most common form of melanoma is:
A. acral lentiginous.
B. lentigo maligna
C. nodular
D. oral
E. superficial spreading

16. Which of the following locations would be the LEAST likely site for squamous cell carcinoma?
A. Floor of mouth
B. Lateral soft palate/palatine tonsil
C. Lateral surface of tongue
D. Lower lip vermilion
E. Midline dorsal surface of tongue

17. The so-called liver spot on the skin is better known as a(n):
A. actinic lentigo.
B. ephelis
C. epulis
D. melanoacanthosis
E. melanotic macule

18. Which one of the following clinical lesions is most likely to become an invasive squamous cell carcinoma?
A. A 1×1 cm ^{2} leukoplakia in the floor of the mouth
B. A 4×2 cm ^{2} wrinkled tobacco pouch keratosis in the lower vestibule
C. A 5×5 mm ^{2} squamous papilloma of the lateral soft palate
D. Generalized nicotine stomatitis involving the entire posterior hard palate
E. Long-standing inflammatory papillary hyperplasia of the midline vault of the hard palate

19. Oral squamous cell carcinoma is more common in men. In which of the following locations does squamous cell carcinoma show the most striking male predilection?
A. Buccal mucosa

B. Floor of mouth
C. Lower lip vermilion
D. Palate
E. Tongue

20. An increase in thickness of the spinous layer of the epithelium is termed:
A. acanthosis
B. dyskeratosis
C. hyperparakeratosis
D. leukoplakia
E. polarity

21. Select the tumor with the worst prognosis.
A. Intraoral melanoma
B. Junctional nevus
C. Lentigo maligna melanoma of the face
D. Superficial spreading melanoma of the back
E. Verrucous carcinoma

22. Nicotine stomatitis is most often associated with:
A. cigar smoking
B. cigarette smoking
C. nicotine gum.
D. pipe smoking
E. snuff dipping

23. Which one of the following clinical features would be a warning sign for a possible malignant alteration in a pigmented lesion?
A. A blue lesion that blanches under direct pressure
B. A blue-pigmented lesion
C. A lesion with multiple different colors
D. A uniform brown color
E. A uniform dark black color

24. The prognosis of melanoma of the skin is most closely related to:
A. age of the patient
B. asymmetry of the borders
C. degree of melanin produced
D. depth of invasion
E. diameter of the tumor

25. Compared to melanoma of the skin, the overall prognosis for oral melanoma is:
A. much better
B. slightly better
C. the same
D. slightly worse
E. much worse

Chapter 10: Epithelial Pathology➔answers
1. ANS: C
2. ANS: B
3. ANS: A
4. ANS: E
5. ANS: D
6. ANS: D
7. ANS: D
8. ANS: E
9. ANS: C
10. ANS: A
11. ANS: D
12. ANS: E
13. ANS: A
14. ANS: E
15. ANS: E
16. ANS: E
17. ANS: A
18. ANS: A

19. ANS: C
20. ANS: A
21. ANS: A
22. ANS: D
23. ANS: C
24. ANS: D
25. ANS: E

Chapter 11 Salivary gland pathology

Frequency with respect to sites(major/minor glands) of salivary gland tumor(SGT)

➲1st common SGT➔parotid gland(61-80%;2/3-3/4)➔其parotid gland當中2/3-3/4 benign(是least common malignant)
➲2nd common SGT➔minor gland(9-28%)➔其minor gland中38-49%malignant(是2nd most common site malignancy)➔[其minor gland malignancy當中1st common➔retromolar(up to 95% mucoepidermoid carcinoma, MEC)]
➲least common SGT➔sublingual gland(<1%)➔其中70-95%malignant(sublingual gland是1st common site malignancy)
➲1st common minor gland SGT(不分benign, malignancy)➔palate(42-54%)➔posterior lateral hard(soft) palate

Frequency of different microscopic SGT with respect to sites(major/minor glands)

➲1st common (benign, all) SGT	pleomorphic adenoma➔❶parotid(50-77%) ❷submandibular(53-72%) ❸minor(~40%)
➲1st common malignant SGT (除SMG是AdCC，其他salivary glands都是MEC)	❶MEC➔all salivary glands ❷MEC➔parotid gland ❸adenoid cystic carcinoma(AdCC)➔submandibular gland(SMG) ❹MEC➔minor gland

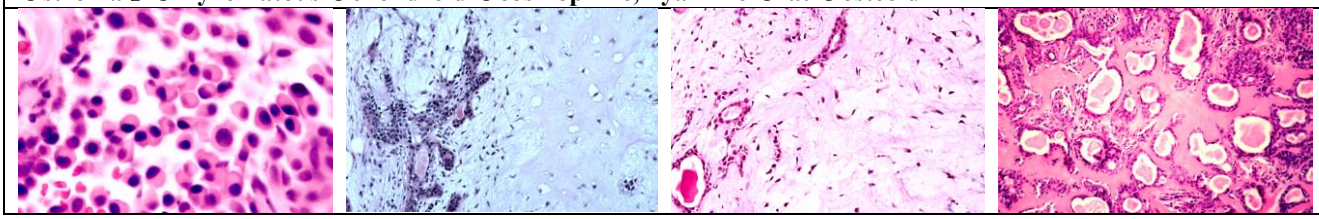
1. The **most common intraoral location of salivary gland tumors** is:
   (A) upper lip
   (B) junction of hard & soft palate
   (C) anterior buccal mucosa
   (D) posterior lateral tongue

2. What is the **most common benign salivary gland tumor**?
   (A) trabecular adenoma
   (B) pleomorphic adenoma
   (C) canalicular adenoma
   (D) Warthin tumor

3. Which of the following probe for **FISH** can confirm **pleomorphic adenoma**?
   (A) *PLAG1*
   (B) *EWSR1*
   (C) *MAML2*
   (D) *HER2*

Pleomorphic adenoma(PA)

➲derived from ductal & myoepithelial cells	➲slight female predilection	➲bilateral[syn(meta)chronous]
➲cytogenetic➔pleomorphic adenoma gene 1(PLAG1) translocation(chromosome 8q12)(~70%)		
➲most common pediatric SGT(不分benign & malignant)		
➲superficial lobe(most)➔swelling over ramus before ear	➲deep lobe(beneath facial nerve)(~10%)	
➲1st common in minor gland➔(posterior lateral)palate(50-60%)➔bound palate mucosa➔non-movable		
➲2nd common in minor gland➔upper lip(movable)	➲3rd common in minor gland➔buccal(movable)	
➲micro ❶capsule➔①incomplete(more in minor gland tumor➔palatal PA beneath epithelial surface) ②infiltrate by tumor cell ❷glandular epithelium+myoepithelial cell in stroma➔①幾乎全是stroma ②highly cellular幾乎無stroma(cellular PA) ❸glandular epithelium➔①duct+cystic structure ② island(sheet) of cell ③keratinize squamous cell & mucus cell ❹myoepithelial cell➔morphology➔①angular/spindle ②plasmacytoid(more prominent in minor gland PA) ✪entire(almost) myoepithelial cell(no ductal cell)➔myoepithelioma ❺stroma➔①myxomatous ②chondroid ③eosinophilic, hyalinize ④fat ⑤osteoid		

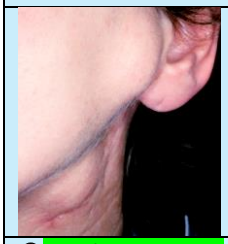
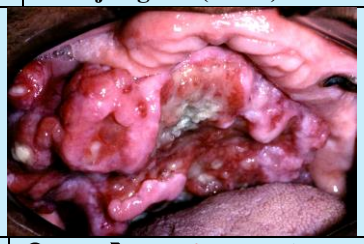
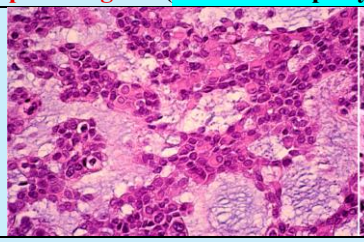
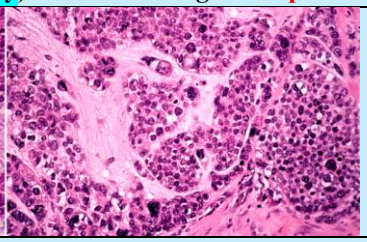


4. Which of the following lesion may undergo **malignant transformation**?
   (A) granular cell tumor
   (B) pleomorphic adenoma
   (C) torus
   (D) hemangioma

Malignant mixed tumors

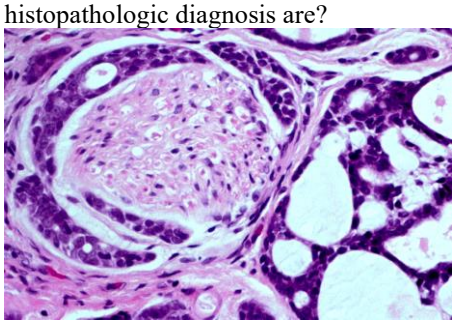
(❶Carcinoma ex(arising from) PA(mixed tumor) ❷Carcinosarcoma ❸Metastasizing mixed tumor)

➲2-4% of all salivary tumors

❶carcinoma ex PA(3-4%)➔malignant change of epithelial component of benign PA ①mean 15s>benign PA ②many-year mass ➔recent rapid growth with pain(ulceration) ③area of benign PA➔epithelial component➔malignant change(cellular pleomorphic & abnormal mitoses)	
❷carcinosarcoma➔carcinoma & sarcoma components	
❸metastasizing PA➔micro benign➔meta(metastatic tumor➔micro benign like 1^0 PA)	
➲clinic	
❶carcinoma ex PA	①major gland(>80%)➔主要在parotid gland(facial nerve palsy) ②近2/3 minor gland➔palate
   	
❷carcinosarcoma	①most➔parotid gland(submandibular gland & minor glands also) ②PA history/arise de novo
❸metastasizing PA	①most➔parotid gland(submandibular gland/minor gland also) ②most meta➔bone/lung(regional LN, skin, liver also) ③most➔PA excised many years earlier ④$1^0$ tumor➔multiple recur before meta
➲micro	
❶carcinoma ex PA	①most➔poor differentiated adenocarcinoma(salivary duct carcinoma)➔myoepithelial carcinoma, polymorphous adenocarcinoma, MEC, AdCC ②3 growth patterns (1)invasive(extracapsular invasion≥1.5mm) (2)minimal invasive(extracapsular invasion≤1.5mm) (3)noninvasive[small malignant focus without extracapsular invasion)]➔carcinoma in situ (intracapsular carcinoma) ex PA
❷carcinosarcoma (biphasic①+②)	①carcinoma(poor differentiated adenocarcinoma/undifferentiated carcinoma) ②sarcoma (1)chondro(osteo)sarcoma (2)fibro(lipo)sarcoma (3)rhabdomyosarcoma (4)malignant fibrous histiocytoma ③arise from PA(some)
❸metastasizing PA	1^0 & meta sites➔micro benign PA

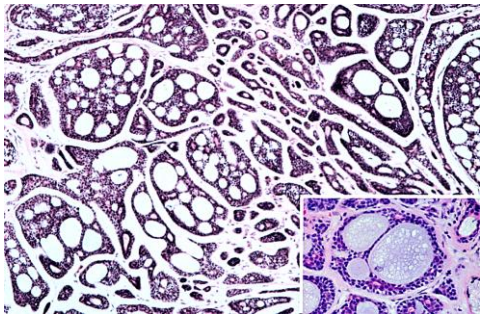
5. **Clear cell carcinoma** can be potentially confirmed using the probe for **FISH** to detect the existence of:
   (A) *PLAG1*
   (B) *EWSR1*
   (C) *MAML2*
   (D) *HER2*

6. Figure below shows **perineural invasion** of the salivary gland tumor, please suggest which of the followings the most likely histopathologic diagnosis are?



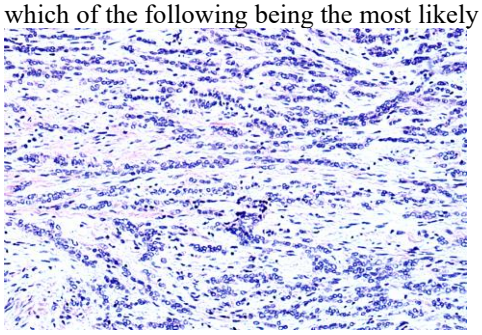
   (1) adenoid cystic carcinoma (2) mucoepidermoid carcinoma (3) polymorphous adenocarcinoma (4) acinic cell carcinoma
   (A) only 1,2
   (B) only 1,3
   (C) only 2,3
   (D) only 1,4

7. Figure below shows **cribriform pattern** of the salivary gland tumor, please identify which of the followings are the most likely histopathological diagnosis?



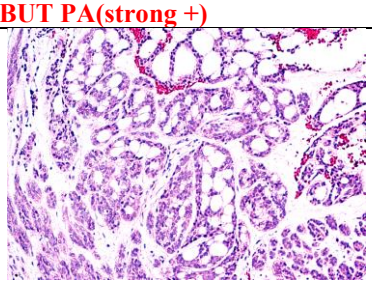
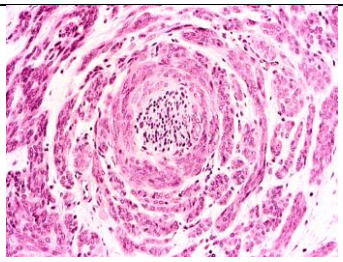
(1) adenoid cystic carcinoma (2) mucoepidermoid carcinoma (3) polymorphous adenocarcinoma (4) acinic cell carcinoma
(A) only 1,2
(B) only 1,3
(C) only 2,3
(D) only 1,4

8. Figure below showing **pale staining** of tumor cell infiltrate of the salivary gland tumor as **single-file cords**, please identify which of the following being the most likely tumor?



(A) pleomorphic adenoma
(B) mucoepidermoid carcinoma
(C) polymorphous adenocarcinoma
(D) acinic cell carcinoma

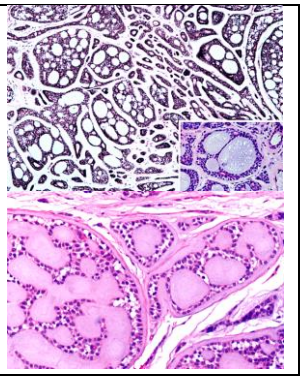
Polymorphous adenocarcinoma(Polymorphous low-grade adenocarcinoma)

➲almost exclusive➔minor salivary gland(65% hard/soft palate)	➲next most➔upper lip & buccal mucosa	
➲major gland(rare)➔❶de novo ❷malignant component of carcinoma ex PA	➲female(2/3 cases)	
➲old adult(most)➔peak 6-8th decades	➲PRKD1 hotspot mutation(>70%)	➲slow painless growth
➲palatal➔papillary hyperplasia➔rough surface		
➲cribriform adenocarcinoma(1999) ❶posterior tongue➔PRKD 1,2,3 gene fusion➔variant(polymorphous adenoma, cribriform subtype)/unique entity(?) ❷vesicular(clear) nuclei➔like papillary thyroid carcinoma		
➲d.d. adenoid cystic carcinoma(AdCC)➔ CD43& c-kit(CD117)(weaker +) (+) BUT AdCC(strong +)		
➲d.d.PA➔glial fibrillary acidic protein(GFAP)(-) BUT PA(strong +)		
➲micro ❶different growth pattern(polymorphous) ①solid pattern ②cord, duct, cystic spaces ③cribriform(mimic AdCC)(左圖) ❷mitosis➔uncommon ❸invade adjacent tissue➔single-file fashion(LP) ❹perineural invasion(like AdCC)(右圖)		

9. Which of the following carcinoma is mostly related to **HPV-related multiphenotypic sinonasal carcinoma** upon histopathological findings?
(A) squamous cell carcinoma
(B) Burkitt lymphoma
(C) adenoid cystic carcinoma
(D) Langerhans cell histiocytosis

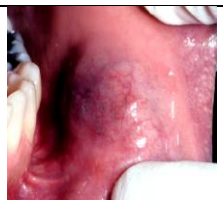
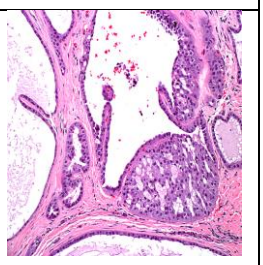
Adenoid cystic carcinoma(AdCC)

➲1st common site➔minor gland(60%)➔palate(most)	➲2nd➔parotid gland	➲3rd➔submandibular gland	
➲in submandibular gland(most common)(11-17%)	➲palate(rel. common)(8-17%)	➲parotid gland(rare)(2%)	
➲pain(common)➔early & important➔before notable swelling	➲slight female predilection	➲<20s(rare)	
➲intraosseous(reported)	➲MYB oncogene overexpression(>80%)➔t(6;9)(q22-23:p22-23)➔MYB:NFIB fusion		

➲micro ❶3 patterns➔①cribriform(Swiss cheese)➔space➔basophilic mucoid material, hyalinize eosinophilic product ②tubular➔ductal & myoepithelial cell ③solid➔cellular pleomorphism, mitosis, central necrosis➔worse prognosis ❷perineural invasion(also polymorphous adenocarcinoma)	
➲IHC ❶CD43(+) & c-kit(CD117)(+) ❷p63+p40➔d.d. AdCC & polymorphous adenocarcinoma ①AdCC➔myoepitheial cell➔p63(+) & p40(+) ②polymorphous adenocarcinoma➔lesional cell➔p63(+); p40(-) ❸Ki-67(proliferation index)➔AdCC(21.4%)>>polymorphous adenocarcinoma(2.4%)	

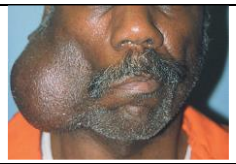
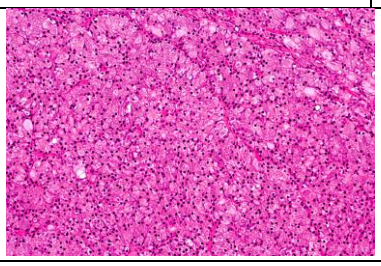
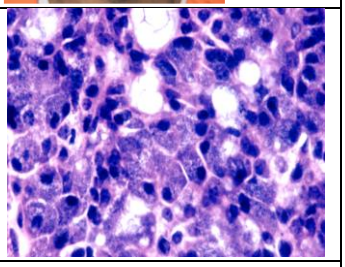
10. **Mammary analogue secretory carcinoma**, a newly recognized salivary gland malignancy, has overlapping microscopic features with which of the following salivary gland tumor?
(A) pleomorphic adenoma
(B) mucoepidermoid carcinoma
(C) acinic cell carcinoma
(D) adenoid cystic carcinoma

Secretory carcinoma(Mammary analogue secretory carcinoma)

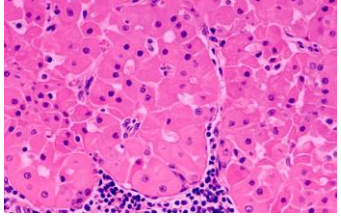
➲FISH/RT-PCR➔chromosome translocation t(12;15)(p13;q25)➔ETV6-NTRK3 fusion gene➔like secretory carcinoma of breast			
➲clinic ❶frequency➔①parotid gland (most;58%) ②minor gland[31% ➔lips, soft palate, buccal(右圖)] ③submandibular gland(9%) ❸mean age➔47s ❹male➔slightly>female ❺slow grow painless mass	 bluish➔mistaken as mucocele	➲micro(mistaken as acinic cell ca.) ❶solid, tubular, micro(macro) cystic structure ❷cystic space➔papillary infolding tumor cell➔hobnail appearance ❸mitoses(rare) ➲IHC➔❶S-100(+)❷vimentin(+) ❸mammaglobin(+)	

11. **Acinic cell carcinoma** may likely be mistaken as which of the following salivary gland tumor?
(A) mucoepidermoid carcinoma
(B) mammary analogue secretory carcinoma
(C) pleomorphic adenoma
(D) adenoid cystic carcinoma

Acinic cell carcinoma

➲malignant cell➔serous acinar differentiation		
➲poor in zymogen(inactive precursor of enzyme; proenzyme) granule➔reclassified➔ mammary analogue secretory carcinoma		
➲parotid gland(most)(85-90%)	➲submandibular gland(2.7- 5%)	
➲minor gland(9%)➔❶palate(most) ❷buccal ❸lips		
➲micro ❶solid➔well-differentiated acinar cell➔like normal parotid gland(右圖) ❷microcystic➔small cystic space➔mucinous/ eosinophilic material ❸papillary cystic➔papillary projection(lined by epithelium)➔into cystic space ❹follicular➔like thyroid tissue		
➲IHC➔❶DOG1(+) ❷NR4A3(+)		

12. Figure below is a case of **oncocytoma** showing sheet of large, eosinophilic oncocytes that can be demonstrated by electron microscopy as an abundance of which of the following?

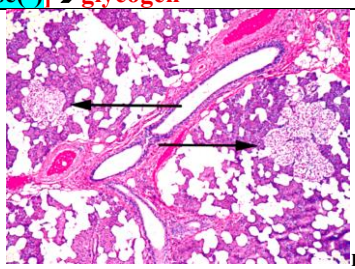


(A) oral keratinocyte

(B) mitochondria
(C) myoepithelial cell
(D) glycogen

13. Following question 12 above, eosinophilic oncocytes show **positive staining with periodic acid-Schiff (PAS)** technique but **negative after digestion with diastase**, suggesting the oncocytes being contained:
(A) osteoid
(B) mucin
(C) amyloid
(D) glycogen

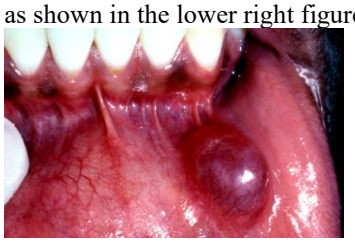
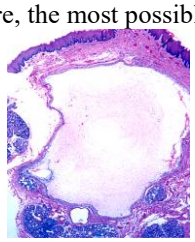
Oncocytoma(Oxyphilic adenoma)

➲~1% of all salivary gland tumor	➲major gland(most)➔parotid(most; 85-90%)	➲minor gland(exceedingly rare)
➲old adult(6-8th decade)	➲painless➔rare>4cm	➲oncocytic carcinoma➔reported(rare)➔poor prognosis
➲clear cell variant➔d.d.❶low-grade salivary clear cell adenocarcinoma ❷metastatic renal cell carcinoma		
➲oncocytoma➔sinonasal gland➔local aggressive(low-grade malignant)		
➲oncocyte➔swollen granular cytoplasm➔abundant mitochondria➔phosphotungstic acid hematoxylin(PTAH)		
➲periodic acid-Schiff (PAS)➔[❶PAS(+) ❷PAS+diastase(-)]➔glycogen		
➲d.d. oncocytois➔parotid(most)➔old adult➔swelling(nodular)(may)➔multifocal➔entire(diffuse hyperplastic oncocytosis)➔benign(metaplastic) ➲focal oncocytic metaplasia of ductal & acinar cell (common)➔age related(uncommon<50s; almost 70s)		mitochondria➔glycogen

14. The most common site for a **mucocele** to occur is the:
(A) floor of the mouth
(B) tongue
(C) buccal mucosa
(D) lower lip

15. Which of the following is the most common cause of a **mucocele**?
(A) acute inflammation
(B) tumor formation
(C) minor salivary gland duct trauma
(D) a sialolith

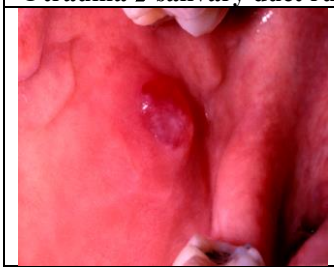
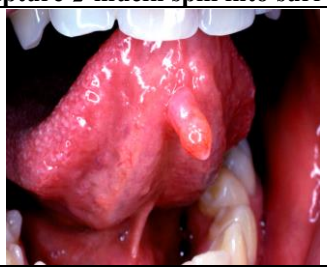
16. A 12 years old boy complained **blue-pigmented nodule on the lower lip** (lower left figure) and received excisional biopsy as shown in the lower right figure, the most possible diagnosis has been which of the following disease?

(A) hemangioma
(B) mucocele
(C) fibroma
(D) lipoma

Mucocele(Mucus extravasation phenomenon)

➲trauma➔salivary duct rupture➔mucin spill into surrounding soft tissue	➲false cyst➔lack epithelial lining

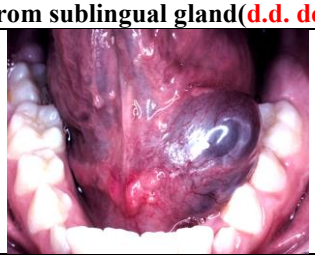
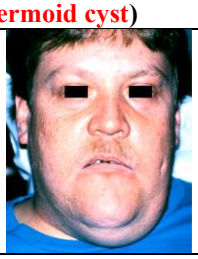



Location	Number of Cases	Percentage of All Cases
Lower lip	1405	81.9
Floor of mouth	99	5.8
Ventral tongue	86	5.0
Buccal mucosa	82	4.8
Palate	23	1.3
Retromolar	9	0.5
Unknown	11	0.6
Upper lip	0	0.0

17. A **ranula** is located on the:

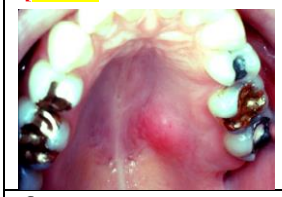
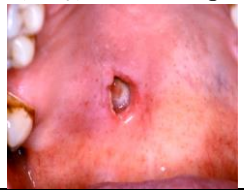
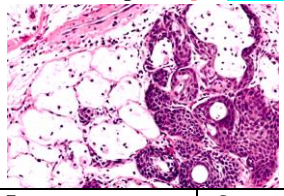
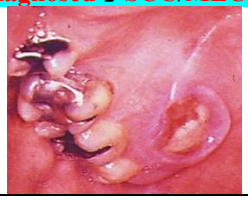
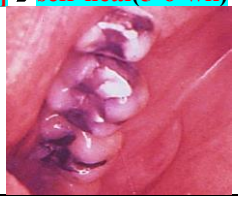
(A) lower lip
(B) buccal mucosa
(C) retromolar area
(D) floor of the mouth

Ranula

➲mouth floor(blue, dome-shape, fluctuant lateral swelling➔arise from sublingual gland(d.d. dermoid cyst)	
➲lesser sublingual gland(15-30 smaller glands)➔short duct of Rivinus to sublingual plica	 
➲greater sublingual gland➔Bartholin duct ❶join Wharton duct ❷open next at sublingual caruncle	
➲clinic variant➔plunging/cervical ranula➔spilled mucin穿越 mylohyoid muscle➔neck swelling➔CT & MRI➔slight extension into sublingual space(tail sign)	

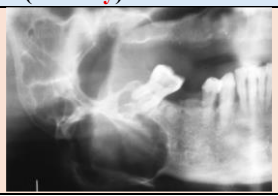
18. Which one of the following is the most likely cause of **necrotizing sialometaplasia**?
(A) loss of blood supply
(B) radiation therapy
(C) smoking
(D) a sialolith

Necrotizing sialometaplasia

➲salivary tissue ischemia➔infarction➔mimic malignancy[(clinic➔nonulcerated swelling➔pain/paresthesia➔(2-3-wk)necrotic tissue slough out➔craterlike ulcer(<1➔>5cm)➔pain subside➔palatal bone destruction(rare)) & [micro➔acinar necrosis(early)➔ductal squamous metaplasia]➔misdiagnosed➔SCC/MEC]➔self-heal(5-6-wk)		
    		
➲posterior palate(>75%)(palate>soft)(others➔minor gland)		➲parotid(reported); sub(mandibular)lingual(rare)
➲support non-malignancy➔❶low p53 & Ki-67 ❷overall lobular architecture preserved		
➲most➔adult(mean 46s)	➲M:F=近2:1	➲palatal➔2/3 unilateral(1/3 bilateral/midline)
➲predispose factor➔❶traumatic injury ❷dental injection ❸ill-fitting denture ❹upper respiratory infection ❺adjacent tumor ❻previous surgery ❼eating disorder with binge-purging(暴食症)		
➲many➔no known predisposing factor		

19. **Central** involvement of the jaws may occur with a:
(A) granular cell tumor
(B) peripheral ossifying fibroma
(D) melanocytic nevus
(D) mucoepidermoid carcinoma

Intraosseous(central) mucoepidermoid carcinoma(MEC)

①➲most common intrabony salivary tumor			
➲other intrabony salivary tumor ❶AdCC❷benign & malignant PA ❸adenocarcinoma ❹acinic cell carcinoma ❺epithelial myoepithelial carcinoma ❻monomorphic adenoma			
➲hypotheses	❶mucus-producing cell➔common in odontogenic cyst lining(esp., dentigerous cyst)➔associate impact teeth(odontogenic cyst) ❷ectopic salivary gland tissue entrap within jaws(unlikely)		
➲clinic	❶middle-age adult(most) ❷female(slight predilection) ❸mandible(molar-ramus)(more) ❹cortical swelling(most frequent symptom)		➲micro ❶low-grade(most) ❷high-grade(also report)
➲radiograph➔❶WD-UL(ML) RL➔odontogenic cyst/tumor ❷irregular PD bone destruction(some)			

Mucoepidermoid carcinoma(MEC)

②➲most common salivary malignancy➔❶4-10% of major gland tumor (parotid gland) ❷13-23% of minor gland tumor(palate)	③➲most common pediatric malignant SGT
➲MAML2 gene rearrangement &/or [CRTC1::MAML2 fusion➔t(11;19)(q21;p13)reciprocal translocation]➔low- & intermediate-grade MEC(more)➔better prognosis	

➲3 histopathologic grades
❶amount of cyst formation
❷degree of cytologic atypia
❸no. of
①mucous cell[mucicarmine stain (+)]
②epidermoid cell
③intermediate cell(progenitor of mucous & epidermoid cell)➔small basaloid cell(ovoid cell with scant pale eosinophilic cytoplasm)

Auclair et al. (1992)

Intracystic component < 20%	2
Neural invasion present	2
Necrosis present	3
Four or more mitoses per 10 high-power fields	3
Anaplasia present	4

Grade	Total Point Score
Low	0-4
Intermediate	5-6
High	7-14

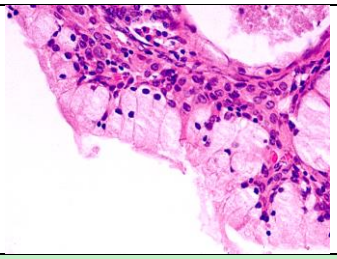
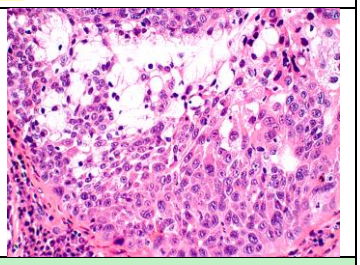
Brandwein et al. (2001)

Intracystic component < 25%	2
Tumor front invades in small nests and islands	2
Pronounced nuclear atypia	2
Lymphatic or vascular invasion	3
Bony invasion	3
Greater than four mitoses per 10 high-power fields	3
Perineural spread	3
Necrosis	3

Grade	Total Point Score
I	0
II	2-3
III	4 or more

➲variants
❶clear cell ❷oncocytic ❸sclerosing(stroma)

➲low-grade➔❶prominent cyst formation ❷minimal cellular atypia ❸high proportion of mucous cell
➲high-grade➔solid island of squamous & intermediate cell(pleomorphism & mitosis)➔mucus-producing cell infrequent➔difficult to d.d from SCC
➲intermediate-grade(between low- & high-grade)➔ cyst less prominent than low-grade➔intermediate cell predominate

➲(補充)histologic subtype➔❶classic ❷Warthin-like ❸sclerosing ❹oncocytic ❺papillary ❻clear cell ❼solid

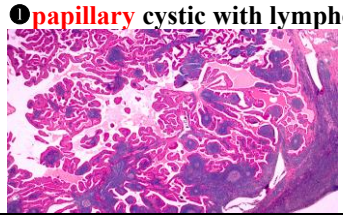
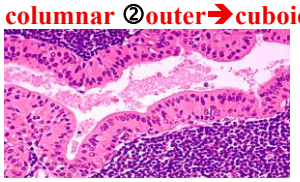
20. Which one of the following is *not* a monomorphic adenoma (Warthin tumor, oncocytoma, basal cell adenoma, and canalicular adenoma➔avoid usage (mentioned its specific name)?
(A) trabecular adenoma
(B) canalicular adenoma
(C) pleomorphic adenoma
(D) papillary cystadenoma lymphomatosum

21. Which of the following salivary gland tumors often occurs in **adult men**?
(A) pleomorphic adenoma
(B) monomorphic adenoma
(C) papillary cystadenoma lymphomatosum
(D) mucoepidermoid carcinoma

Warthin tumor(Papillary cystadenoma lymphomatosum)

➲almost exclusive➔parotid gland(7.7-22.4%)➔2nd most benign parotid tumor	➲bilateral(5-17%)➔metachronous(occur different times)(most)
➲older adult(6-7th decades)	➲M:F=10:1(more equal ratio recently)
➲associate with smoking lesion ❶more equal sex ratio ❷more bilateral tumors	➲risk factor ❶smoking(8× >non-smoker) ❷obesity

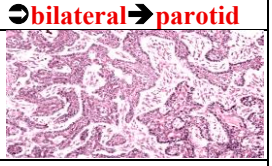
➲malignant Warthin tumor(carcinoma ex papillary cystadenoma lymphomatosum)➔reported(exceedingly rare)

➲micro	❶papillary cystic with lymphoid stroma 	❷epithelial oncocytic lining➔2 rows(①inner luminal➔columnar ②outer➔cuboid) 

22. 關於唾液腺的基底細胞腺瘤**(basal cell adenoma)**，下列敘述何者正確？(114)
(A) 70%以上的病例發生在舌下腺
(B) 如果發生於小唾液腺，以上唇及頰黏膜為主要的好發部位
(C) 基底細胞腺癌多由基底細胞腺瘤惡性轉變而成
(D) 病理組織學亞型中的腺管型(tubular variant)具有高度再發率

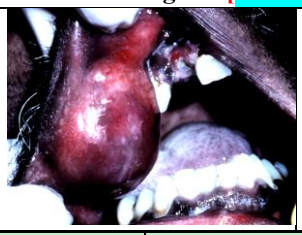
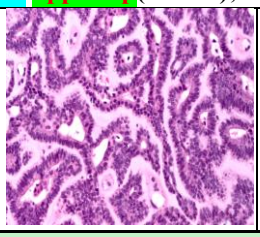
23. The following salivary gland tumors may show microscopic of **cribriform feature** *except*:
(A) adenoid cystic carcinoma
(B) polymorphous adenocarcinoma
(C) basal cell adenoma
(D) canalicular adenoma

Basal cell adenoma➔❶IHC➔nuclear β-catenin(distinguish from AdCC) ❷CTNNB1 mutation(60%)

➲(1-4%)all SGT	➲frequency➔❶1st common in parotid(75%) ❷2nd common➔minor gland(upper lip, buccal)			
➲frequency by age➔❶middle-age(most) ❷older adult(61~70s)		F:M=2:1	most<3cm	➲bilateral➔parotid
➲micro	❶solid type(most)(like basal cell carcinoma) ①multiple islands & epithelial cords ②peripheral cell(hyperchromatic; palisade) ③central cell➔eddies(漩渦)/keratin pearl	❷trabecular type ❸tubular type ❹cribriform pattern(some)➔ like AdCC		
➲basal cell adenocarcinoma➔❶de novo(most) ❷from basal cell adenoma(some) ❸預後佳但常local recur ❹meta rare				
➲membranous basal cell adenoma	❶hereditary ❷combined skin appendage tumor(dermal cylindroma & trichoepithelioma) ❸malignant counterpart➔basal cell adenocarcinoma(good prognosis) ❹multifocal(jigsaw puzzle)➔recur(25-37%) ❺hyaline material between tumor islands ❻hyaline droplets➔among epithelial cells			

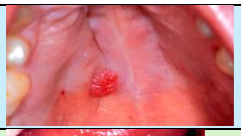
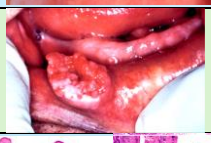
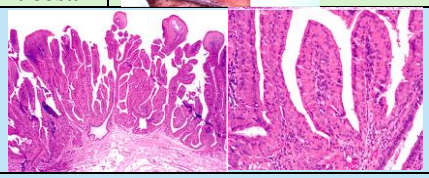
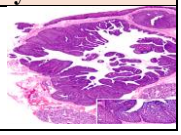
24. Which of the following comparisons between basal cell adenoma (BCA) and canalicular adenoma (CCA) is false?
(A) BCA most common in parotid gland; CCA most common in upper lip
(B) BCA most common in middle-age adult; CCA most common in older adult
(C) BCA more common in female; CCA more common in female
(D) BCA may show *CTNNB1* mutation; CCA may show *PLAG1* translocation

Canalicular adenoma➔almost exclusive➔minor gland[1st most upper lip(近75%); 2nd most upper lip tumor➔PA]

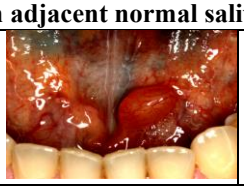
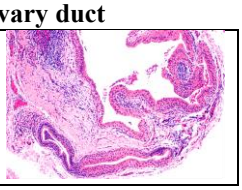
➲2nd most➔buccal mucosa ➲other minor gland sites➔rare ➲older adult(7th decade) ➲F:M=1.2-1.8:1 ➲most➔幾mm-2cm ➲multifocal➔multiple separate ➲bluish color➔like mucocele			➲single(bi)-layer cord (columnar/cuboid)➔canal-like ductal structure ➲papillary projections➔ larger cystic space ➲satellite islands(22-24%)➔ multifocal

➲salivary gland tumor➔micro➔papillomatous	❶papillary cystadenoma lymphomatosum(Warthin tumor)(most) ❷sialadenoma papilliferrum(rare) ❸intraductal papilloma(rare) ❹inverted ductal papilloma(rare)

Ductal papillomas(❶Sialadenoma papilliferrum ❷Intraductal papilloma ❸Inverted ductal papilloma)

➲clinic		
❶sialadenoma papilliferrum	①most➔minor gland(palate)➔also parotid gland ②older adult ③M:F=1.5:1 ④exophytic papillary surface➔clinic➔like squamous papilloma	
❷intraductal papilloma ①adult ②minor salivary gland ③submucosal swelling	❸inverted ductal papilloma ①only➔minor gland of adult ②most➔lower lip & mandibular vestibule ③asymptomatic nodule➔a pit(indentation) in overly mucosa	
➲micro		
❶sialadenoma papilliferrum ✪micro➔like skin syringocystadenoma papilliferum	①exophytic papillary stratified squamous epithelium ②與相鄰papillomatous ductal epithelium ③double-row➔(1)luminal columnar (2)basal cuboid cell ④ductal cell➔oncocytic change(variant)	
	⑤BRAFV600E mutation➔classic type & cutaneous syringocystadenoma papilliferum(52%) ⑥NO BRAFV600E mutation➔oncocytic variant➔distinct/subtype	
❷intraductal papilloma	①dilated, unicystic below mucosal surface ②lined by single/double row of cuboidal/columnar epithelium➔papillary projection into cystic lumen	
❸inverted ductal papilloma	①squamoid epithelium proliferation➔bulbous papillary projection➔fill ductal lumen ②connect overly epithelium➔communicate surface via a small pore-like opening ③luminal lining cell➔cuboid/columnar with scattered mucus cell ④in situ hybridization(ISH)➔HPV type 6 & 11(surface & inverted epithelium)	

Salivary duct cyst➔true developmental cyst➔lined by epithelium separate from adjacent normal salivary duct

➲major gland(most)➔parotid➔❶slow growth ❷asymptomatic swelling ➲intraoral➔mouth floor, buccal, lips(most) ➲ductal obstruction(mucus plug)➔ductal dilation➔mucus retention cyst (salivary ductal ectasia)➔rather than a true cyst		

Cheilitis glandularis

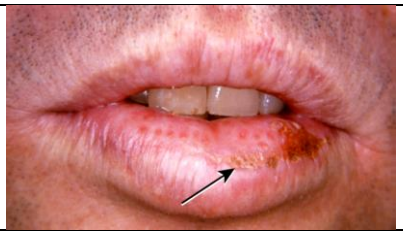
➲inflammatory condition of minor salivary gland

➲etiology➔❶actinic damage ❷tobacco ❸poor hygiene ❹heredity

➲clinic➔lower lip vermilion➔hypertrophic & inflamed swelling➔lower lip eversion(外翻)[albino(白化) patient➔2^0 to sun sensitivity]

➲middle-age & older men(most); also women & children(exfoliative cheilitis)

➲micro➔❶chronic sialadenitis ❷ductal dilatation with mucin accumulation ❸oncocytic ductal metaplasia ❹dysplastic change➔surface epithelium



➲3 types

severity➔❶simple ❷superficial suppurative(Baelz disease) ❸deep suppurative(cheilitis glandularis apostematosa)

IgG4-related disease

➲1st found➔sclerosing inflammation of pancreas(autoimmune pancreatitis)➔↑serum IgG4➔IgG4(+) plasma cell➔後來也發現在salivary & lacrimal gland

➲IgG4➔involved type 2 helper T cell & B cell➔anti-inflammatory(allergic)➔bystander rather than causative

➲serum IgG4 level➔25× normal level [✪20-40% p't➔within normal limit(5% of total IgG)]

➲allergic disorders(asthma, allergic rhinitis, atopic dermatitis)➔common

➲middle-age, older adult(mean➔~60s)

➲men➔affected equally/slight>women(Japan➔female predilection)

➲1st most➔pancreas➔①obstructive jaundice ②weight loss ③abdominal discomfort

➲2nd most➔H&N

➲ocular➔swollen eyelid, lacrimal inflammation, proptosis(眼球突出), pain, diplopia, optic nerve involved➔visual loss

➲IgG4-related sialadenitis

①submandibular gland(most)➔uni(bil)lateral swelling(1.5-5cm)➔like neoplasm

②parotid gland & minor gland(rare)

➲Riedel thyroiditis

➲lymphadenopathy

➲sclerosing cholangitis➔hepatic failure

➲abdominal aortitis➔aneurysm

➲kidney➔inflammatory pseudotumor

➲micro

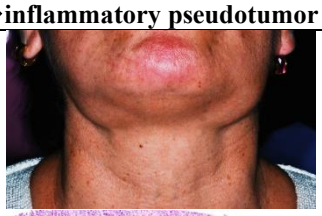
❶sclerosing sialadenitis➔①heavy lymphoplasmacytic infiltrate ②hyperplastic lymphoid follicle ③acinar atrophy

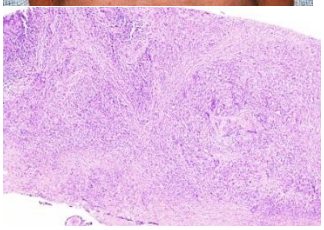
❷IHC➔↑IgG4(+) plasma cell [①>30-50/HP ②(IgG4 (+) plasma cell/total)>40%]

❸interlobular fibrosis➔storiform pattern(LP)

❹obliterative phlebitis(閉塞性靜脈炎)➔elastic stain➔Kuttner tumor

❺labial biopsy➔minimal invasive➔low sensitivity





➲Tx

❶systemic corticosteroid➔prevent organ damage & failure

❷glucocorticoid-sparing agent(①azathioprine ②myophenolate mofetil ③methotrexate)

❸immunosuppressive therapy➔rapid response(good prognosis)

❹recur➔B-cell depletion with rituximab

❺submandibular gland lesion/highly fibrotic orbital pseudotumor➔resection

25. The most characteristic oral manifestation of **Sjogren syndrome** is:

(A) xerostoma

(B) geographic tongue

(C) erythema multiforme

(D) acute disseminated reticulosis

Sjogren syndrome(Sicca syndrome)(SS)➔[xerostomia(dry mouth)+xerophthalmia(dry eyes)]sicca➔dry (1^0 SS➔wt score≥4)

➲chronic systemic autoimmune disorder(2nd most)(✪1st➔rheumatoid arthritis, RA)➔salivary(lacrimal) gland➔xerostomia & xerophthalmia

➲not hereditary disease per se(本身) BUT with genetic influence

➲gene related to➔❶certain histocompatibility antigen(HLA) ❷interferon response ❸B-lymphocyte function

➲population prevalence➔1%(0.1-4.8%)

➲F:M=9:1

➲middle-age adult➔predominant

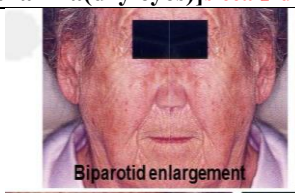
➲children➔rare

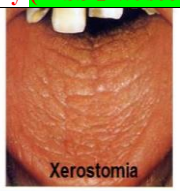
➲↑severity➔↑salivary enlargement

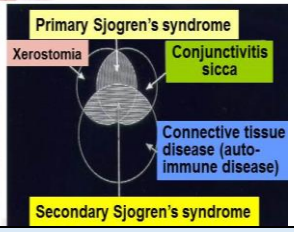
➲↓salivary flow➔↑bacterial sialadenitis

➲RA(~15%)➔Sjögren syndrome

➲SLE(30%)➔2^0 Sjögren syndrome







➲lifetime risk of lymphoma(5-10%)(within salivary gland/LN)➔~15–20×>general population

❶low-grade non-Hodgkin B-cell lymphoma of mucosa-associated lymphoid tissue(MALT lymphoma)

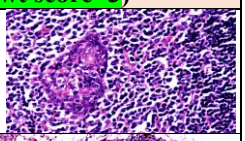
❷extranodal marginal zone B-cell lymphoma

➲keratoconjunctivitis sicca➔↓tear+pathologic effect on ocular surface epithelial cell➔blur vision(aching pain)➔least severe on wakening➔pronounce as daytime

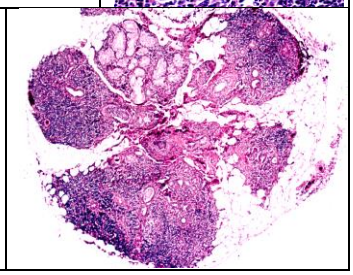
➲sialography➔punctate sialectasia(lack of normal arborization of ductal system)➔fruit-laden branchless tree(snow storm) pattern
➲scintigraphy➔radioactive technetium(Tc)-99m pertechnetate➔↓isotope uptake; ↓delay empty
➲US➔multiple hypo(an)echoic area➔parotid(submandibular) gland
➲Schirmer test➔無菌濾紙➔下眼皮邊緣➔tear(at least 1 eye)➔<5mm/5min➔abnormal(wt score=1)

➲lab
❶↑erythrocyte sedimentation rate(ESR) ❷↑serum IgG level ❸RF factor(+)(~60%)
❹ANA(75-85%)[①anti-SS-A(anti-Ro)(50-76%) ②anti-SS-B(anti-La)(30-60%)]➔1^0 Sjögren syndrome(wt score=3)

➲micro
❶lymphocytic infiltration➔acinar destruction➔benign lymphoepithelial lesion(myoepithelial sialadenitis)➔ductal epithelium persist➔epimyoepithelial island➔germinal enter(may/may not)
❷minor gland➔lymphocytic infiltration➔epimyoepithelial island(rare)



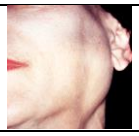
➲labial biopsy(minor salivary gland)(wt score=3)
❶1.5-2cm incision➔lower labial mucosa(平行vermilion border & lateral to midline➔accessory gland)➔focal inflammatory aggregate(≥50 lymphocyte & plasma cell)
❷focus score➔inflammatory aggregate no./4mm^2 glandular tissue
❸focus score≥1➔Sjögren syndrome
❹↑foci no.(up to 12/confluent foci)➔↑correlate with Sjögren syndrome
❺也可檢查IgG gene rearrangement➔lymphoma development marker
➲unstimulated whole saliva flow rate➔≤1ml/min(wt score=1)



Sialadenosis(Sialosis)➔noninflammatory salivary gland enlargement➔parotid gland(particular)

➲cause
❶dysregulated autonomic innervation of acini➔aberrant intracellular secretory cycle➔secretory granule accumulate➔acinar cell enlargement
❷↓myoepithelial cell innervation➔supporting myofilament around acinar cell atrophy

➲clinic
❶slow (non)painful bi(uni)lateral parotid swelling
❷ submandibular gland(may)
❸ minor gland(rare)



➲sialography➔hypertrophic acinar cell comprises finer duct➔leafless tree pattern

➲associate
❶endocrine disorder➔①DM ②diabetes insipidus(尿崩症) ③acromegaly ④hypothyroidism ⑤pregnancy
❷nutritional condition➔①malnutrition ②alcoholism ③cirrhosis ④anorexia nervosa(神經性厭食症) ⑤bulimia(暴食症)
❸neurogenic medication➔①antihypertensive drug ②psychotropic drug ③sympathomimetic drug for asthma

➲micro➔acinar cell hypertrophy➔2-3×normal size
❶nuclei➔displaced to cell base ❷cytoplasm➔engorged with zymogen granule

Adenomatoid hyperplasia of minor salivary glands

➲cause➔local trauma	➲4-6th decades(most)	➲localize swelling(pseudotumor)➔hard(soft) palate (most)
➲soft(firm) sessile painless mass➔normal(red/bluish) color		
➲micro➔lobular aggregates of normal mucous acini(no.>normal)➔↑size➔close to mucosal surface		

26. Which of the following drug will not cause **xerostomia**:
(A) antihistamines
(B) antidepressants
(C) parasympathetic stimulators
(D) decongestants

Xerostomia

cause
➲developmental/hereditary➔❶salivary gland aplasia ❷ectodermal dysplasia
➲water/metabolite loss➔❶dehydration ❷hemorrhage ❸vomiting/diarrhea
➲iatrogenic➔❶medication ❷H&N RT ❸chemotherapy
➲infection➔❶HIV ❷hepatitis C ❸cytomegalovirus
➲autoimmune disorder➔❶Sjögren syndrome ❷rheumatoid arthritis ❸systemic lupus erythematosus ❹systemic sclerosis ❺$1^0$ biliary cirrhosis
➲other systemic disease➔❶DM ❷diabetes insipidus ❸sarcoidosis ❹amyloidosis ❺end-stage renal disease ❻graft-versus-host disease (GVHD) ❼psychogenic disorder
➲local factor➔❶decreased mastication ❷smoking ❸mouth breathing

class of drug➔xerostomia
➲antihistamine➔❶diphenhydramine ❷chlorpheniramine
➲decongestant➔❶pseudoephedrine ❷loratadine
➲antidepressant➔❶amitriptyline ❷citalopram ❸duloxetine ❹fluoxetine ❺paroxetine ❻sertraline ❼bupropion
➲antipsychotic➔❶phenothiazine derivatives ❷haloperidol ❸quetiapine
➲sedative & anxiolytic➔❶diazepam ❷lorazepam ❸alprazolam
➲antihypertensive➔❶reserpine ❷methyldopa ❸chlorothiazide ❹furosemide ❺metoprolol ❻Ca^{2+} channel blocker
➲anticholinergic/antimuscarinic➔❶atropine ❷scopolamine ❸oxybutynin ❹solifenacin ❺tolterodine

Sialorrhea(Ptyalism)

➲cause
❶rabies(狂犬病)
❷heavy-metal poisoning
❸antipsychotic agent➔clozapine, cholinergic agonist(treat Alzheimer dementia & myasthenia gravis)

➲Tx
❶anticholinergic medication➔↓saliva production➔side effect
❷botulinum toxin(肉毒桿菌素)➔intraglandular injection➔↓saliva secretions(維持6wk-6mon)

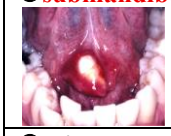
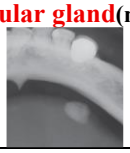
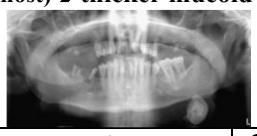
Salivary gland aplasia/hypoplasia

➲M:F=2:1 | ➲❶pilocarpine ❷sugarless gum/sour candy chewing刺激➔residual salivary gland tissue➔saliva

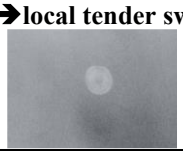
➲associated with
❶mandibulofacial dysostosis(Treacher Collins syndrome)
❷ectodermal dysplasia
❸oculo-auriculo-vertebral spectrum (hemifacial microsomia; Goldenhar syndrome)
❹lacrimo-auriculo-dento-digital(LADD) syndrome➔autosomal dominant➔FGF10,2,3 mutation
①lacrimal & salivary gland a(hypo)plasia
②cup-shaped ears
③hearing los
④hypodontia, microdontia & enamel hypoplasia
⑤digital anomalies
❺Down syndrome

Sialolithiasis

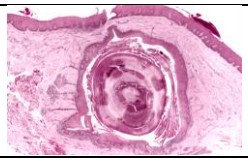
➲submandibular gland(most)➔thicker mucoid secretion➔Wharton duct

➲minor gland➔local tender swelling

➲micro
❶intraductal concentric calcified mass
❷ductal metaplasia

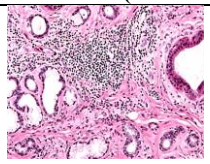
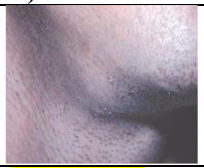
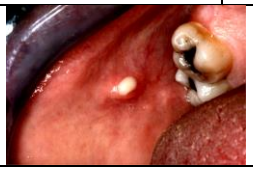
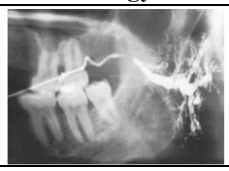


Sialadenitis

➲cause
❶abdominal surgery➔without food/fluid(NPO)+atropine➔acute parotitis(surgical mump)
❷infection
①bacteria(virus) ②sialolithiasis ③↓saliva flow(xerostomia)

❸noninfectious
①Sjögren syndrome
②sarcoidosis
③RT ④allergy

➲micro
❶chronic inflammatory infiltrate
❷acinar atrophy
❸ductal dilatation
❹fibrosis

➲clinic➔❶tender swelling ❷pus from duct orifice

➲sialography➔ductal dilatation proximal to obstruction

Chapter 11: Salivary Gland Pathology

1. Which of the following is the most common intrabony salivary gland tumor?
A. Adenoid cystic carcinoma
B. Malignant pleomorphic adenoma
C. Mucoepidermoid carcinoma
D. Oncocytoma
E. Papillary cystadenoma lymphomatosum

2. Which one of the following locations is the LEAST common site for mucoceles?
A. Buccal mucosa
B. Floor of mouth
C. Lower lip
D. Upper lip
E. Ventral tongue

3. Patients with Sjögren syndrome have a higher risk of developing which tumor?
A. Acinic cell adenocarcinoma
B. Hepatocellular carcinoma
C. Kaposi's sarcoma
D. Lymphoma
E. Melanoma

4. Which one of the following tumors is the most common malignancy arising in minor salivary glands?
A. Acinic cell adenocarcinoma
B. Adenoid cystic carcinoma
C. Mucoepidermoid carcinoma
D. Polymorphous low-grade adenocarcinoma
E. Warthin tumor

5. The most common site for necrotizing sialometaplasia is:
A. anterior tongue
B. lower lip
C. posterior hard palate
D. posterior lateral tongue
E. upper lip

6. Which one of the following features would NOT be associated with Sjögren syndrome?
A. Benign lymphoepithelial lesion
B. Elevated antinuclear antibodies
C. Female predominance
D. Keratoconjunctivitis sicca
E. Sialorrhea

7. Sialadenosis is often associated with:
A. bulimia
B. chewing cinnamon-flavored gum
C. history of recent tooth extraction
D. postsurgical mumps
E. none of the above

8. The most common salivary gland tumor is:
A. adenoid cystic carcinoma.
B. basal cell adenoma
C. canalicular adenoma
D. mucoepidermoid carcinoma
E. pleomorphic adenoma

9. Perineural invasion is most likely to occur in which tumor?
A. Acinic cell adenocarcinoma
B. Adenoid cystic carcinoma
C. Mucoepidermoid carcinoma
D. Pleomorphic adenoma
E. Warthin tumor

10. In which one of the following locations is a salivary gland tumor most likely to be malignant?
A. Hard palate
B. Lower lip

C. Parotid gland
D. Submandibular gland
E. Upper lip

11. The salivary gland neoplasm most closely correlated with cigarette smoking is:
A. adenoid cystic carcinoma
B. mucoepidermoid carcinoma
C. pleomorphic adenoma
D. polymorphous low-grade adenocarcinoma
E. Warthin tumor

12. The canalicular adenoma most commonly occurs in which location?
A. Lower labial mucosa
B. Palate
C. Parotid gland
D. Submandibular gland
E. Upper labial mucosa

13. Minor salivary gland tumors are most common in which location?
A. Buccal mucosa
B. Floor of mouth
C. Lower lip
D. Posterior lateral hard palate
E. Upper lip

14. The best treatment for mucoceles is:
A. aspiration of spilled mucin with a small gauge needle
B. incision and drainage
C. injection with a sclerosing agent
D. surgical excision along with the "feeder" gland
E. no treatment is needed because it is a benign condition

15. Which of the following lesions typically has the worst prognosis?
A. Adenoid cystic carcinoma
B. Canalicular adenoma
C. Necrotizing sialometaplasia
D. Pleomorphic adenoma
E. Polymorphous low-grade adenocarcinoma

16. Which of the following is NOT commonly a cause of xerostomia?
A. Adenomatoid hyperplasia
B. Dehydration
C. Medications
D. Radiation therapy to the head and neck
E. Sjögren syndrome

17. The most common site for the Warthin tumor is:
A. lower lip
B. palate
C. parotid gland
D. submandibular gland
E. tongue

18. Another name for the pleomorphic adenoma is:
A. benign lymphoepithelial lesion.
B. benign mixed tumor
C. Donath-Seifert tumor
D. monomorphic adenoma
E. Warthin tumor

19. Sialoliths occur most frequently in the:
A. minor salivary gland ducts
B. nasopalatine duct
C. parotid duct
D. submandibular duct
E. Donald duct

20. Which one of the following salivary gland tumors has the best prognosis?
A. acinic cell adenocarcinoma
B. adenoid cystic carcinoma
C. mucoepidermoid carcinoma
D. pleomorphic adenoma
E. polymorphous adenocarcinoma

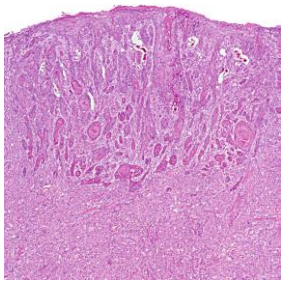
Chapter 11: Salivary Gland Pathology➔answers
1. ANS: C
2. ANS: D
3. ANS: D
4. ANS: C
5. ANS: C
6. ANS: E
7. ANS: A
8. ANS: E
9. ANS: B
10. ANS: B
11. ANS: E
12. ANS: E
13. ANS: D
14. ANS: D
15. ANS: A
16. ANS: A
17. ANS: C
18. ANS: B
19. ANS: D
20. ANS: D

Chapter 12 Soft tissue tumors

1. Epulis fissuratum results from irritation caused by:
   (A) a denture flange
   (B) denture adhesive
   (C) poor suction from the denture in the palatal vault
   (D) an allergic reaction to the acrylic in the denture

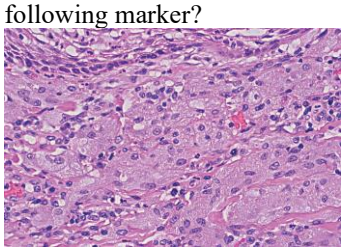
2. Which of the following neoplasms often occurs in the buccal mucosa or vestibule?
   (A) lipoma
   (B) congenital epulis
   (C) lymphangioma
   (D) rhabdomyoma

3. Figure below showing marked **pseudoepitheliomatous hyperplasia** overlying a **granular cell tumor** that may easily be mistaken for which of the following disease?



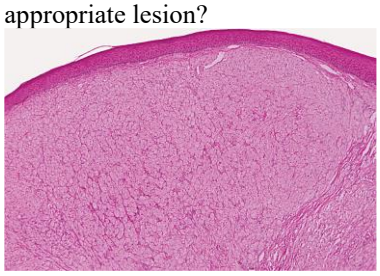
   (A) epithelial hyperplasia
   (B) keratoacanthoma
   (C) congenital epulis
   (D) squamous cell carcinoma, grade 1

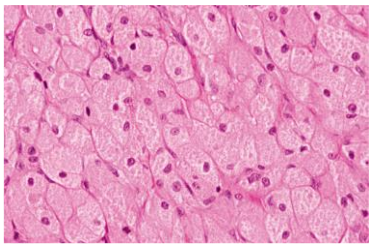
4. Following the question 3 above, the **granular cells** as shown in below figure showing positive staining for which of the following marker?



   (1) S100 (2) CD68(macrophage/histiocyte marker) (3) neuron-specific enolase (D) CK
   (A) only 1,2,3
   (B) only 1,3,4
   (C) only 2,3,4
   (D) 1,2.3.4

5. Figures below showing a nodular tumor mass occurring in **infant** noting the **atrophy of the rete ridges**. What is the most appropriate lesion?



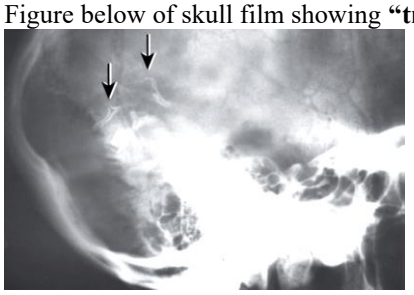


   (A) granular cell tumor
   (B) congenital epulis
   (C) hemangioma
   (D) fibroma

6. What followings are *true* for the lesion of **congenital epulis**?
   (1) more common on maxillary ridge than mandibular ridge (2) most frequently occurs lateral to midline in area of developing lateral incisor & canine (3) strong predilection for females (~ 90%), suggesting a hormonal influence (4) estrogen & progesterone receptors are detected

(A) only 1,2,3
(B) only 1,3,4
(C) only 2,3,4
(D) 1,2.3.4

7. Which of the following lesions characteristically occurs on the **alveolar mucosa** in **newborn girl**?
(A) granular cell tumor
(B) congenital epulis
(C) lymphangioma
(D) plasmacytoma

8. Figure below of skull film showing **"tramline" calcifications (arrows)**; what is the most possible lesion?

(A) Sturge-Weber syndrome
(B) nasopharyngeal angiofibroma
(C) lymphangioma
(D) juvenile (cellular) hemangioma

9. Which of the following tumors is associated with **von Recklinghausen disease**?
(A) neurilemoma
(B) neuroma
(C) fibroma
(D) neurofibroma

10. **Syndrome** involvement may occur with:
(A) neurofibroma
(B) verrucous carcinoma
(C) pleomorphic adenoma
(D) ameloblastic fibroma

11. **Human herpesvirus 8** is associated with:
(A) herpangina
(B) rhabdomyosarcoma
(C) Kaposi sarcoma
(D) schwannoma

12. The most serious clinical manifestation of the MEN 2B syndrome is considered to be:
(A) carcinoma of the colon
(B) carcinoma of the thyroid gland
(C) pheochromocytoma
(D) basal cell carcinoma

13. The most common malignant soft tissue tumor of the head and neck in children is:
(A) squamous cell carcinoma
(B) lymphangioma
(C) rhabdomyosarcoma
(D) osteosarcoma

14. What is the most common intraoral location of tumors of nerve (neurofibroma and schwannoma)?
(A) buccal mucosa
(B) lip
(C) palate
(D) tongue

15. 下列腫瘤的細胞或病變組織何者通常不出現在表皮層下(subepithelial layer)?(113)

(A) 舌背的microcystic lymphatic malformation

(B) 牙齦的verruciform xanthoma

(C) 牙齦的mucous membrane pemphigoid

(D) 舌背的venous malformation

Synopsis➔mucosal & soft tissue pathology➔color changes

lesion/condition	characteristics
white lesions➔can be scraped off	
white-coated tongue	may be scraped off slightly, with difficulty
pseudomembranous candidiasis	milk curd/cottage cheese appearance; may leave red base when rubbed off
morsicatio	surface may appear to be peeling off
toothpaste or mouthwash reaction	filmy whiteness; leaves normal appearing mucosa when rubbed off
thermal burn	e.g. pizza burn
sloughing traumatic lesion	e.g. cotton roll "burn"
chemical burn	e.g. aspirin burn secondary to direct application for toothache
secondary syphilis	mucous patch; may be only partially scraped off
diphtheria	gray-white pseudomembrane of oropharynx
white lesions➔cannot be scraped off	
linea alba	buccal mucosa along occlusal plane
leukoedema	in black; bilateral milky white on buccal mucosa; disappears when stretched
leukoplakia	may show benign hyperkeratosis, epithelial dysplasia, invasive carcinoma
tobacco pouch keratosis	usu. mandibular vestibule; associated with use of snuff/chewing tobacco
white-coated tongue	diffuse involvement of dorsal tongue
lichen planus	Wickham's striae; typical bilateral on buccal mucosa
morsicatio	most on ant. buccal mucosa, labial mucosa, lateral border of tongue; ragged surface
actinic cheilosis	pale, gray-white, scaly lower lip; older men with chronic sun exposure; precancerous
nicotine stomatitis	usu. associated with pipe smoking; occurs on hard palate
hairy leukoplakia	usu. lateral border of tongue; rough surface with vertical fissures; usu. with HIV
hyperplastic candidiasis	most affects anterior buccal mucosa
lupus erythematosus	most on buccal mucosa; mimic lichen planus/leukoplakia; skin lesions usu. present
skin graft	history of previous surgery
submucous fibrosis	more in South Asia; associate betel quid chewing
white sponge nevus	hereditary; onset in childhood; generalized lesions, esp., buccal mucosa
hereditary benign intraepithelial dyskeratosis	hereditary; onset in childhood; generalized, esp. buccal mucosa; ocular possible
pachyonychia congenita	hereditary; childhood; most on dorsal tongue & trauma area; nail, palmar & plantar
dyskeratosis congenita	hereditary; onset in childhood; dystrophic nail changes
uremic stomatitis	renal failure
white & red lesions	
erythema migrans	geographic tongue; continual changing pattern; rare involve other oral mucosal sites
candidiasis	white component may be rubbed off
lichen planus	atrophic/erosive forms; Wickham's striae; typical bilateral on buccal mucosa
burns	e.g. pizza burn, aspirin burn, other chemical burns; white component be rubbed off
actinic cheilosis	pale, gray-white & red on lower lip; usu. in older men with chronic sun exposure
erythroleukoplakia	usu. shows epithelial dysplasia or carcinoma
cinnamon reaction	related to cinnamon-flavored gum; typically on buccal mucosa and lateral tongue
nicotine stomatitis	usu. associated with pipe smoking; on hard palate
lupus erythematosus	most on buccal mucosa; mimic lichen planus/leukoplakia; skin lesions usu. present
scarlet fever	secondary to β-hemolytic streptococcal infection; strawberry/raspberry tongue
verruciform xanthoma	most on gingiva & hard palate; surface may be papillary
red lesions	
pharyngitis	e.g. strep throat, viral pharyngitis
traumatic erythema	caused by local irritation
denture stomatitis	denture-bearing palatal mucosa
erythematous candidiasis	e.g. central papillary atrophy(median rhomboid glossitis)
erythema migrans	geographic tongue; continual changing pattern; rarely involves other mucosal sites
angular cheilitis	erythema & cracking at labial commissures
thermal burn	e.g. caused by hot liquid
erythroplakia	usu. shows epithelial dysplasia/carcinoma
lichenoid and granulomatous stomatitis	most on upper labial mucosa
anemia	atrophic, red tongue; due to pernicious(Fe-deficiency) anemia, hypovitaminosis B
hemangioma	develops in younger patients; may blanch; may show bluish hue
lupus erythematosus	usu. with associated skin lesions
scarlet fever	secondary to β-hemolytic streptococcal infection; strawberry/raspberry tongue
plasma cell gingivitis	allergic reaction usu. related to flavoring agents
radiation mucositis	patient currently undergoing radiotherapy
petechial, ecchymotic & telangiectatic lesions	

nonspecific trauma	history of injury to lesional site
upper respiratory infections	soft palate petechiae
infectious mononucleosis	soft palate petechiae; tonsillitis &/or pharyngitis may be present
idiopathic thrombocytopenic purpura	areas of trauma; gingival bleeding possibly present
trauma from fellatio	posterior palatal petechiae/ecchymosis
hemophilia	hereditary; childhood onset; gingival bleeding may present
leukemia	caused by 2^0 thrombocytopenia; gingival bleeding may present
hereditary hemorrhagic telangiectasia	multiple, pinhead-sized telangiectasias; possible history of nosebleeds/GI bleeding
CREST syndrome	multiple, pinhead-sized telangiectasias; C alcinosis cutis, R aynaud's phenomenon, E sophageal motility defect, S clerodactyly, T elangiectasias
blue &/or purple lesions	
varicosities	esp., >45s; most on ventral tongue & lips
submucosal hemorrhage	
amalgam tattoo	most on gingiva; blue-gray; RO amalgam particle(discovered on x-ray sometimes)
mucocele	esp. on lower labial mucosa; pale blue; cyclic swelling and rupturing often exhibited
eruption cyst	overly an erupting tooth
salivary duct cyst	usu. pale blue
hemangioma	usu. red-purple; may blanch under pressure; onset in younger patients
ranula	pale blue, fluctuant swelling of lateral mouth floor
Kaposi sarcoma	esp., in AIDS; usu. purple; most on palate & maxillary gingiva
nasopalatine duct cyst	midline of anterior palate
salivary gland tumors	esp., MEC & pleomorphic adenoma; usu. pale blue; most on posterior lateral palate
gingival cyst of the adult	most in mandibular bicuspid-cuspid region
blue nevus	most on hard palate
melanoma	most on hard palate & maxillary gingiva; may be mixture of deep blue, brown, black
brown, gray, &/or black lesions	
racial pigmentation	most on attached gingiva in darker complexioned patient
amalgam tattoo	most on gingiva; usu. slate-gray to black; opaque amalgam particle(may be on x-ray)
black/brown hairy tongue	discoloration & elongation of filiform papillae
melanotic macule	brown; most on lower lip
smoker's melanosis	most on anterior facial gingiva
non-amalgam tattoos	e.g. graphite from pencil
melanocytic nevus	most on hard palate; be flat/raised
melanoma	most on hard palate & maxillary gingiva; may be mixture of deep blue, brown, black
oral melanoacanthoma	rapid enlarging pigmented lesion; usu. in black
drug ingestion	e.g. chloroquine, chlorpromazine, minocycline; esp., on hard palate
Peutz-Jeghers syndrome	freckle-like lesion of vermilion & perioral skin; intestinal polyps; hereditary
Addison disease	chronic adrenal insufficiency; associated with bronze skin
neurofibromatosis type I	Café au lait pigmentation; cutaneous neurofibromas
McCune-Albright syndrome	Café au lait pigmentation; polyostotic fibrous dysplasia; endocrine disorders
heavy metal poisoning	typical along marginal gingiva (lead, bismuth, silver)
melanotic neuroectodermal tumor of infancy	anterior maxilla; destroys underlying bone
H. yellow lesions	
Fordyce granules	sebaceous gland; multiple submucosal papules on buccal mucosa/upper lip vermilion
superficial abscess	e.g. parulis from nonvital tooth
accessory lymphoid aggregate	most in oropharynx & mouth floor; may be orange hue
lymphoepithelial cyst	most on lingual & palatine tonsils, mouth floor; may be yellow-white
lipoma	most on buccal mucosa; soft to palpation
jaundice	generalized discoloration, esp., involve soft palate & mouth floor; sclera usu. affected
verruciform xanthoma	most on gingiva & hard palate; surface may be rough/papillary
pyostomatitis vegetans	"snail-track" pustule; associated with inflammatory bowel disease

Chapter 12: Soft Tissue Tumors

1. The microscopic appearance of the congenital epulis most closely resembles:
A. congenital melanocytic nevus
B. epulis fissuratum
C. granular cell tumor
D. peripheral giant cell granuloma
E. pyogenic granuloma

2. The cystic hygroma is a type of:
A. leiomyoma
B. leukoplakia
C. lymphangioma
D. lymphoepithelial cyst
E. lymphoma

3. Medullary thyroid carcinoma is a common feature of which condition?
A. Graves' disease
B. Multiple endocrine neoplasia type 2B
C. Neurofibromatosis type I
D. Nevoid basal cell carcinoma syndrome
E. PHACES syndrome

4. Epilepsy is frequently a feature associated with:
A. bisphosphonate-related osteonecrosis of the jaws
B. multiple endocrine neoplasia type 2B
C. primary herpetic gingivostomatitis
D. primary syphilis
E. Sturge-Weber syndrome

5. Lisch nodules are associated with:
A. embryonal rhabdomyosarcoma
B. granular cell tumor
C. Kaposi sarcoma
D. Neurofibromatosis type I
E. Sturge-Weber syndrome

6. The oral cavity is the most common location in the body for which one of the following tumors?
A. Granular cell tumor
B. Kaposi sarcoma
C. Leiomyoma
D. Lipoma
E. Schwannoma

7. Which one of the following is one of the diagnostic criteria for neurofibromatosis type I?
A. Axillary freckling
B. Complex seizure disorder
C. Mental retardation
D. Merrick sign
E. Schwannoma

8. Which one of the following is the most common site for the granular cell tumor?
A. Buccal mucosa
B. Gingiva
C. Hard palate
D. Lower lip
E. Tongue

9. A peripheral giant cell granuloma is most likely to mimic what other lesion clinically?
A. Epulis fissuratum
B. Inflammatory papillary hyperplasia
C. Lymphangioma
D. Pyogenic granuloma
E. Schwannoma

10. Which one of the following lesions is often associated with pregnancy?
A. Non-Hodgkin lymphoma
B. Oral papillomas

C. Peripheral giant cell granuloma
D. Proliferative verrucous leukoplakia
E. Pyogenic granuloma

11. The most common site for metastatic tumors to the oral cavity is:
A. buccal mucosa
B. gingiva
C. hard palate
D. lower lip
E. upper lip

12. Which one of the following tumors is often painful?
A. Irritation fibroma
B. Neurofibroma
C. Pleomorphic adenoma
D. Pyogenic granuloma
E. Traumatic neuroma

13. Which one of the following tumors has the most striking predilection for males?
A. Congenital epulis
B. Kaposi sarcoma
C. Nasopharyngeal angiofibroma
D. Peripheral ossifying fibroma
E. Pyogenic granuloma

14. Which one of the following malignancies would most likely develop secondary to immunosuppressive therapy used to prevent rejection of an organ transplant?
A. Carcinoma ex pleomorphic adenoma
B. Embryonal rhabdomyosarcoma
C. Kaposi sarcoma
D. Lentigo maligna melanoma
E. Malignant peripheral nerve sheath tumor

15. What is the inheritance pattern for neurofibromatosis type I?
A. Autosomal dominant
B. Autosomal recessive
C. Multifactorial
D. X-linked dominant
E. X-linked recessive

16. The port wine nevus is:
A. a capillary vascular malformation
B. a congenital malformation of melanocytes limited to the left side of the body
C. a congenital melanocytic nevus that occurs in a patient with partial albinism
D. a form of congenital melanocytic nevus with a high malignant transformation rate
E. a rare, congenital form of blue nevus

17. Which tumor is characterized by Antoni A tissue with Verocay bodies?
A. Blue nevus
B. Congenital epulis
C. Fibrous histiocytoma
D. Peripheral giant cell granuloma
E. Schwannoma

18. What is the inheritance pattern for multiple endocrine neoplasia type 2B?
A. Autosomal dominant
B. Autosomal recessive
C. Multifactorial
D. X-linked dominant
E. X-linked recessive

19. In classic Kaposi sarcoma, the lesions usually begin to develop in which location?
A. Chest wall
B. Inguinal region
C. Lower extremities
D. Neck
E. Scalp

20. Which of the following conditions is often associated with intellectual disability?
A. Dermatosis papulosa nigra
B. Multiple endocrine neoplasia type 2B
C. Sialadenosis
D. Sturge-Weber syndrome
E. All of the above

21. By definition, an epulis refers to a tumor or growth that:
A. develops on the gingiva or along the alveolar ridge.
B. has a rough, pebbly surface
C. is associated with an ill-fitting denture
D. is composed of epithelium
E. is related to an underlying infection

22. Which one of the following tumors shows a striking predilection for females?
A. Congenital epulis
B. Granular cell tumor
C. Inverted papilloma
D. Lymphangioma
E. Schwannoma

23. Kaposi sarcoma is believed to be caused by which of the following?
A. Arthropod bites
B. Chronic ultraviolet light exposure
C. Epstein-Barr virus
D. Hepatitis C virus
E. Human herpes virus, type 8

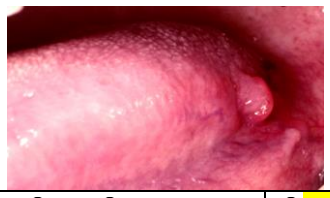
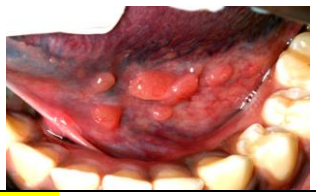
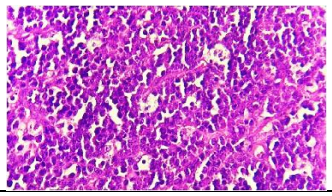
24. The most common site for angiosarcoma is:
A. scalp
B. upper lip
C. lower lip
D. neck
E. back

Chapter 12: Soft Tissue Tumors➔answers
1. ANS: C
2. ANS: C
3. ANS: B
4.ANS: E
5. ANS: D
6. ANS: A
7. ANS: A
8. ANS: E
9. ANS: D
10. ANS: E
11. ANS: B
12. ANS: E
13. ANS: C
14. ANS: C
15. ANS: A
16. ANS: A
17. ANS: E
18. ANS: A
19. ANS: C
20. ANS: D
21. ANS: A
22. ANS: A
23. ANS: E
24. ANS: A

Chapter 13 Hematologic disorders

Lymphoid hyperplasia

➲foreign antigen(virus, fungi, bacteria)➔↑lymphoid cell no.➔lymphoid enlarge [<1cm➔❶LN ❷Waldeyer ring ❸lymphoid aggregate➔①oropharynx ②soft palate ③lateral tongue ④mouth floor]➔significant asymmetry➔R/O lymphoma

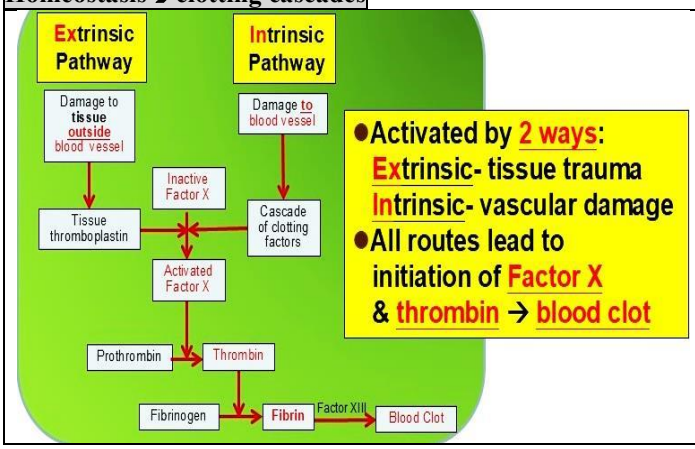
❶acute enlarge LN➔①tender ②soft ③movable	❷chronic enlarge LN➔①nontender ②rubbery firm ③movable

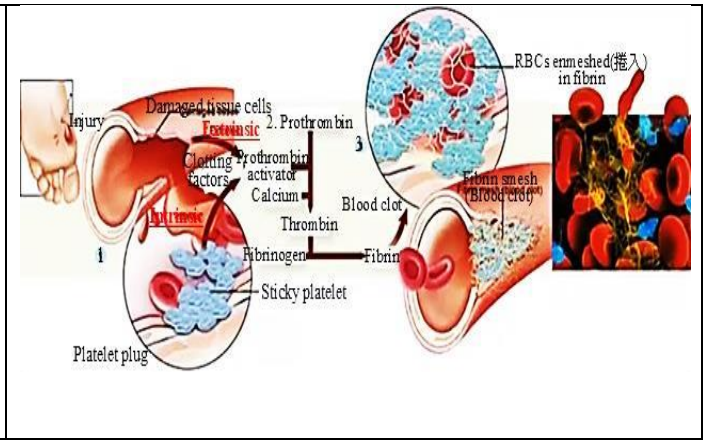
❸LN➔[①multiple ②persistent enlarge ③nontender]➔suspect HIV infection

➲micro(sheet of small, well-differentiated lymphocytes)
- ❶germinal center➔reactive lymphoblast➔transformed B lymphocyte➔numerous mitoses
- ❷tingible body(易染体巨噬细胞)➔macrophage(engulf nuclear debris from lymphocyte in cytoplasm)

1. **Waldeyer ring** is composed of:
   (A) epithelial cells
   (B) melanocytes
   (C) lymphoid tissue
   (D) adipose tissue

Homeostasis➔clotting cascades





Hemophilia(血友病)➔abnormal partial thromboplastin time(PTT)➔alteration of coagulation➔clotting factor deficiencies

type	defect	inheritance	findings
hemophilia A (classic hemophilia)	Factor VIII deficiency	X-linked recessive	abnormal PTT
hemophilia B (Christmas disease)	Factor IX deficiency	X-linked recessive	abnormal PTT
von Willebrand disease	Abnormal von Willebrand factor, abnormal platelets	autosomal dominant	abnormal PFA, abnormal PTT

PFA➔platelet function assay(replaces bleeding time test)

➲clinic(% of normal factor VIII level)
- ❶≥25% normal level➔normal function
- ❷<5%➔minor trauma➔bruise

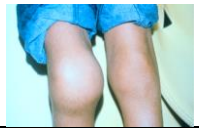
➲Tx guide lines
- ❶mild(5-40% normal level)➔no need special Tx for normal activities(但surgery➔ replace clotting factor)
- ❷severe(<1% normal level)➔clotting factor injection➔prevent crappie(蹩腳) knee joint deformities

➲von Willebrand factor(a transport molecule)
- ❶aid palate adhesion ❷bind to Factor VIII

➲X-linked
- ❶female➔carrier(trait carrier)
- ❷male➔1^0 express(1/5000)

➲aspirin(adverse effect on platelet function)➔strict contraindicate

➲pseudotumor[hemarthrosis(knee)]
- ❶hemophilia A(most)
- ❷hemophilia B & von Willebrand disease(rare)

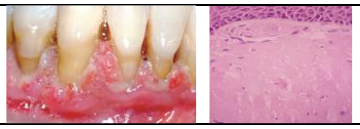
Plasminogen deficiency(纖維蛋白溶酶原缺乏症)(Ligneous conjunctivitis; Hypoplasminogenemia)

➲autosomal recessive

➲normal➔plasminogen(纖維蛋白溶酶原)➔plasmin(纖溶酶)➔degrade clot➔fibrinolysis

➲abnormal➔↓plasminogen➔↑clot➔↑fibrin➔plaque(nodule) ➔conjunctival mucosa➔ligneous(woodlike) conjunctivitis

➲affected mucosa➔①ocular(80%) ②oral(gingiva,34%) ③laryngeal(vocal cord➔raspy(刺耳), hoarse voice)(16%) ④vaginal(8%)

➲patchy ulcerated papule(nodule) with irregular surface➔ few(all) quadrants➔wax & wane(起伏不定) severity	

2. Please matching the **classification (A) macrocytic normochromic**, **(B) microcytic hypochromic**, or **(C) normocytic normochromic** with respect to:
   (2-1) pernicious anemia
   (2-2) iron deficiency
   (2-3) thalassemia
   (2-4) aplastic anemia
   (2-5) sickle cell anemia

Anemia(貧血)(縱論)➔↓RBC➔↓production/↑destruction/↑loss

➲**classic symptom**(based on severity & compensation)➔❶fatigue ❷weakness ❸dyspnea(呼吸困難) ❹pallor(蒼白)

➲**classification**➔❶[**RBC size**➔①macrocytic ②microcytic ③normocytic] ❷[**Hb content**➔①normochromic ②hypochromic]
❶macrocytic normochromic(**megaloblastic**)➔①pernicious anemia[folic acid(vitamin B12) deficiency➔RBC的DNA合成問題]
❷microcytic hypochromic➔[①Fe deficiency, sideroblastic(鐵粒幼細胞)➔RBC的營養素不足 ②thalassemia(Mediterranean)➔不正常RBC structure & function] anemia
❸normocytic normochromic➔[(①aplastic ②hemolytic)➔RBC總數量不足 ③sickle cell(鐮刀型)➔不正常RBC structure] anemia

➲**lab➔anemia classfication(types)**
❶RBC no.(男-4.0-5.52)(女-3.78-4.99)10^6/μl
❷hematocrit(Ht)(血球容積比)
一定量血液中含RBC的比例(男-36-50%)(女-34-47%)
❸Hb concentration(血紅素濃度)
(男-13.2-17.2g/dl)(女-0.8-14.9g/dl)

❹mean corpuscular volume(平均紅血球體積)(MCV)
MCV=❷Ht/❶RBC×10=80-100➔RBC size
❺mean corpuscular Hb(平均血紅素)(MCH)
MCH=❸Hb含量/❶RBC百萬數=28-34pg➔Hb content
❻mean corpuscular Hb concentration(平均血紅素濃度)(MCHC)
MCHC=❸Hb/❷Ht(❺MCH/❹MCV)×10=32-36%➔縮小貧血的類型

❶綜合MCV值MCHC值	可能問題	❷綜合MCV值MCHC值	可能問題	❸綜合MCV值MCHC值	可能問題
❶MCV值較高 而MCHC值正常 (macrocytic/normochromic)	①維生素(B6、B12)缺乏性貧血 ②葉酸缺乏性貧血 (過量飲酒)	❷MCV值較低 而MCHC值較低 (microcytic/hypochromic)	①鐵缺乏性貧血 ②鐵芽球性貧血 ③地中海貧血 (慢性發炎)	❸MCV值正常 而MCHC值正常 但仍有貧血情況 (normocytic/normochromic)	①再生障礙性貧血 ②溶血性貧血 ③腎性貧血 (急性出血)

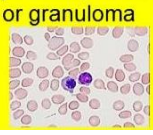
➲**causes**

❶**ANEMIA WITH DISTURBED IRON METABOLISM**
①iron deficiency anemia
②sideroblastic anemia(鐵粒幼細胞):
-Impaired ability of bone marrow to produce normal RBC
-Iron inside RBC is inadequately used to make Hb despite normal amount of iron

❷**MEGALOBLASTIC ANEMIA**
①cobalamin(B_{12}) deficiency(pernicious anemia)
②folic acid deficiency

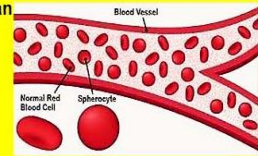
❸**HEMOGLOBIN DISORDER**
①sickle cell anemia
②thalassemia

❹**ANEMIAS ASSOCIATED WITH CHRONIC DISORDER**
①anemia of chronic infection(infective endocarditis, osteomyelitis, lung abscess, pyelonephritis)
②anemia of inflammatory connective tissue (rheumatoid arthritis, lupus erythematosus, sarcoidosis, temporal arteritis, regional enteritis)
③anemia associated with malignancy
-secondary to chronic bleeding
-myelophthisic anemia(myelophthisis): hemopoietic bone-marrow tissue replaced by fibrosis, tumor or granuloma
④anemia of uremia
⑤anemia of endocrine failure
⑥anemia of liver disease



❺**HEMOLYTIC ANEMIAS**
①extrinsic causes
-splenomegaly
-red cell antibodies
-trauma in circulation
-direct toxic effects (microorganisms, Cu salt, snake venom(毒液))

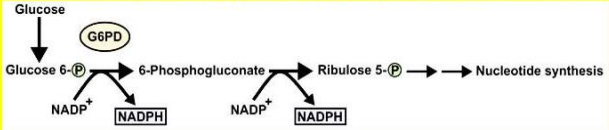
②membrane abnormalities
-spur cell anemia: acquired hemolytic anemia associated with liver cirrhosis; increased large RBC➔covered with spike-like projection
-hereditary spherocytosis
(1)caused by mutations in genes relating to membrane proteins that allow RBC to become sphere-shaped **rather than normal biconcave disk shaped**
(2)dysfunctional membrane proteins interfere with cell's flexibility to travel from arteries to smaller capillaries.
Difference in shape➔RBC more prone to rupture



-Hereditary elliptocytosis
large no. of RBCs are elliptical rather than typical biconcave disc shape

-Paroxysmal nocturnal hemoglobinuria
(陣發性睡眠性血紅蛋白尿)
rare acquired, life-threatening, destruction of RBC, thrombosis, & impaired bone marrow function[not making enough 3 blood components(RBC, WBC, platelet)]

③Disorders of interior of RBC
-Defects in Embden-Meyerhof pathway
紀念研究此過程Gustor Emhden及Otto Meyerthof，命名為醣解作用(glycolysis)。生物細胞藉由一系列酵素催化的反應，將葡萄糖轉變為丙酮酸產生能量的過程
-Defects in hexose monophosphate shunt
a metabolic pathway parallel glycolysis; important in RBC



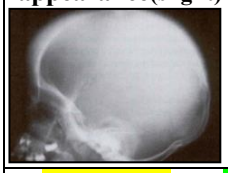
3. Which of the followings are characteristics of **sickle cell anemia**?
   (1) large maxilla (2) osteopetrosis (3) thin cortical plate (4) red blood cells are circular
   (A) only 1,2
   (B) only 1,3
   (C) only 2,3
   (D) only 1,4

4. Which of the following is *not* a characteristic of **sickle cell anemia**?
   (A) it is an inherited blood disorder found predominantly in blacks
   (B) it occurs because of an abnormal type of hemoglobin and decreased oxygen in the red blood cells
   (C) the individual with sickle cell anemia can experience weakness, fatigue, and joint pain
   (D) red blood cells are circular

5. **Hair-on-end bone pattern of skull radiograph** may be occurred in patients with:
   (1) sickle cell anemia (2) thalassemia anemia (3) Ewing sarcoma
   (A) only 1,2
   (B) only 1,3
   (C) only 2,3
   (D) 1,2,3

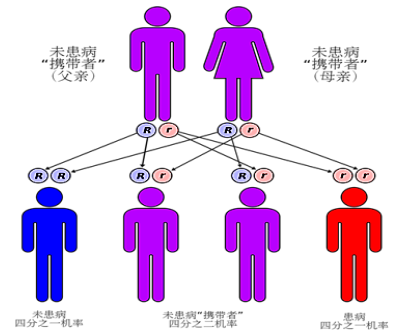
Sickle cell anemia(鐮刀型細胞貧血)➔hemolytic anemia(autosomal recessive)

❶US-African(black)
❷mediterranean South America
❸India➔natural protectve adaptation vs malaria
❹skull X-ray➔hair-on-end appearance(slight)



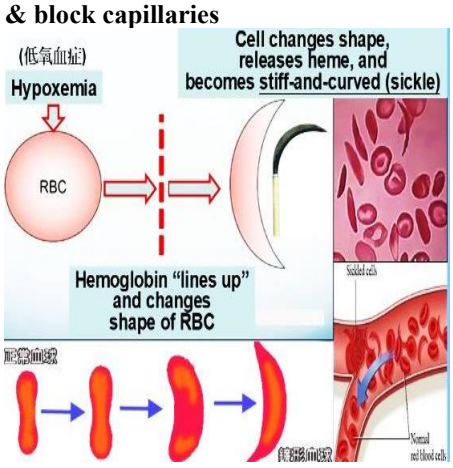
➲2 major forms(❶ & ❷)
❶sickle cell trait(heterozygous)(carrier)
①1 defective gene(40-50% Hb abnormal)
②asymptomatic(carrier)/recur pain & tissue ischemia
❷sickle cell anemia(homozygous)
①defective gene from both parents
②life threaten, pain crisis, organ infarction, profound RBC destruction(aplastic crisis)

➲fragile(sickled) RBC➔short lifespan (12-16-day➔僅1/10 of normal)

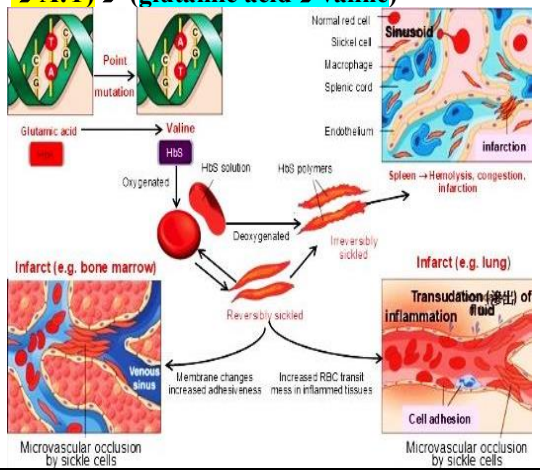


❺radiograph➔①↓trabeculae of mandible(↑hematopoiesis marrow) ②↑osteomyelitis(mandible) ③ infarction(mandible) ④prolonged paresthesia(mandibular nerve) ⑤asymptomatic pulpal necrosis

➲sickled RBC➔stiff-curved➔fragile & block capillaries



➲RBC➔point mutation(Thymine:Adenine ➔A:T)➔ (glutamic acid➔valine)

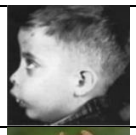


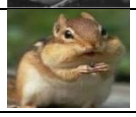
➲clinic
❶sickle cell crisis
①dehydration
②stress/strenuous(費勁) exercise
③infection ④fever ⑤bleeding
⑥acidosis ⑦hypoxia(smoking)
❷bone crisis
❸vaso- occlusive crisis of pulmonary vasculature(acute chest syndrome)➔chest X-ray➔pulmonary infiltrate
❹abdominal crisis
❺joint crisis
❻bleeding
❼jaundice(黃疸), bruising(瘀傷), blood urine

Thalassemia(地中海貧血)➔among the most common human inherited disease

➲Hb➔tetramer(2α+2β chains)➔[❶2 genes encode➔β chain ❷4 genes encode➔α chain]➔one chain with inadequate quantity➔abnormal Hb amount➔excess globin chain in RBC➔abnormal RBC structure & function➔hemolysis by spleen➔❶microcytic ❷ hypochromic anemia

➲β-thalassemia
❶1 defective gene➔thalassemia minor➔no significant clinical manifestation
❷2 defective genes➔thalassemia major(Cooley/Mediterranean anemia)
①maintain oxygenation➔↑hematopoiesis rate(30×normal)(still ineffective)➔bone marrow hyperplasia (extramedullary hematopoiesis)➔hepatosplenomegaly & lymphadenopathy
②bone marrow hyperplasia➔esp. affect jaw➔altered trabecular pattern & mandible & maxilla enlarge (painless)➔chipmunk(花栗鼠) facies(右圖)➔paranasal sinuses(↓size/obliteration)

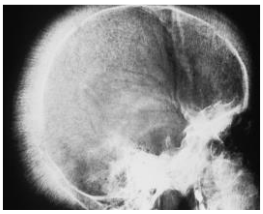




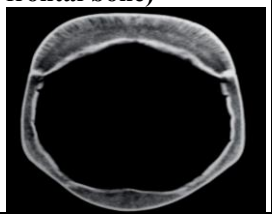
➲α-thalassemia
❶1 defective gene➔thalassemia minor➔no disease(not clinic significant)
❷2 defective genes➔thalassemia trait➔mild anemia & microcytosis
❸3 defective genes➔hemoglobin H(HbH) disease➔hemolytic anemia & splenomegaly➔splenectomy
❹4 defective genes(homozygous)➔hydrops fetalis(severe generalized fetal edema)➔die within a few-hour of birth

➲radiograph

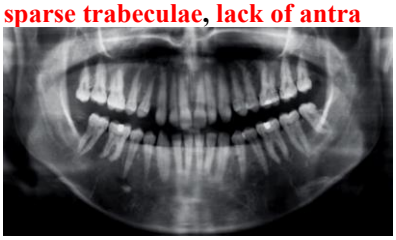
❶hair-on-end



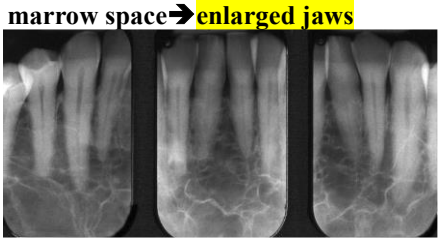
❷linear orientation of trabeculae(esp. frontal bone)



❸thick mandibular body & sparse trabeculae, lack of antra

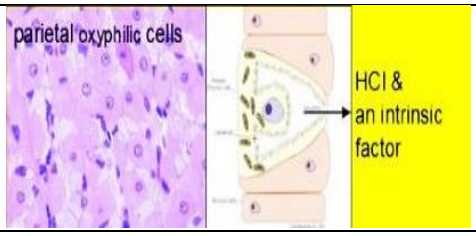


❹thick trabeculae & large bone marrow space➔enlarged jaws



Pernicious anemia(惡性貧血)➔most common➔macrocytic normochromic anemia

➲causes
❶↓vitamin B12
❷intrinsic factor absence➔↓vitamin B12 gastric absorption
❸congenital
❹autoimmune
❺bariatric(減肥) surgery(gastrectomy)➔removal of parietal cell[胃壁細胞 secrete HCl & intrinsic factor➔a compound with vitamin B12]

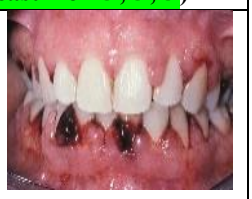


6. Which of the following about **pernicious anemia** is *false*? It is
   (A) caused by vitamin C deficiency
   (B) a macrocytic nomochromic anemia
   (C) associated with gastrectomy
   (D) related to the absence of intrinsic factor of parietal cell of gastric wall

Aplastic anemia(再生障礙性貧血)

➲pancytopenia➔bone marrow(hematopoietic precursor cell)➔not produce all types of blood cell(❶,❷,❸)➔lab Dx➔
❶<500 granulocyte[顆粒(免疫)細胞]/μl ❷<20,000 platelet/μl ❸<20,000 reticulocyte[網狀(未成熟)紅血球)]/μl(at least 2 of ❶,❷,❸)

❶ or ❷➔immune-mediate➔cytotoxic T lymphocyte➔hematopoietic stem cell➔no normal mature
❶arise➔①environment toxin(benzene)
②drug(抗生素chloramphenicol)
③virus感染(non-A, non-B, non-C, non-G hepatitis)
❷associate➔①Fanconi anemia ②dyskeratosis congenita



➲oral(右圖)
❶gingiva➔[①hemorrhage ②ulcer ③hyperplasia]
❷oral mucosa➔①petechiae ②purpura[(紫斑)0.3-1cm] ③ecchymoses ④pale

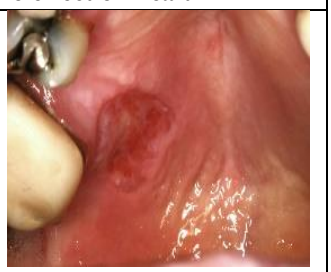
7. Which of the following about **anemia** is *false*?
   (A) red blood cells of sickle cell anemia show point mutation resulting valine to glutamic acid
   (B) aplastic anemia associates with dyskeratosis congenita or Fanconi anemia
   (C) pernicious anemia is the most common macrocytic normochromic anemia
   (D) thalassemia belongs microcytic hypochromic anemia

Neutropenia(嗜中性白血球低下)➔↓neutrophil no.➔❶<1.5×10⁹/l(adult) ❷[0.5×10⁹/l➔pulmonary infection]

➲oral finding➔ulcer(gingiva)(右圖)

➲benign ethnic neutropenia➔低neutrophil no.(1.2×10⁹/l)➔no effect on health

➲causes(❶-❻)➔bone marrow destruction
❶viral/fungal & bacterial infection➔neutrophil➔[①↓no. ②↑destruction(autoimmune➔SLE)]
❷malignancies(①leukemia ②lymphoma ③melanoma ④renal cell carcinoma)
❸drug➔①chemotherapy ②antibiotic ③phenothiazine(antipsychotic) ④tranquilizer ⑤diuretic
❹metabolic disease
①Gaucher disease(高雪氏症)[missing an enzyme that break down lipid➔lipid build up➔spleen & liver]
②osteopetrosis
❺維他命B_{12}/folate deficiencies



❻infant➔①Schwachman-Diamond syndrome ②dyskeratosis congenita ③cartilage-hair syndrome ③嚴重先天neutropenia

Agranulocytosis(粒性白细胞缺乏症)➔①↓no. ②↑destruction➔granulocytic series cells(esp. neutrophil) absent

➲causes
❶drug(most)①anticancer chemotherapeutic agent➔inhibit normal mitosis & hematopoietic stem cell maturation
②trigger immune reaction➔destruct granulocyte)
❷congenital(①congenital agranulocytosis ②Kostmann syndrome)➔↓G-CSF(granulocyte colony-stimulating factor)

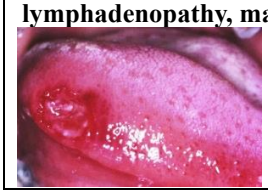
➲clinic
❶bacterial infection(malaise, sore throat, swelling, fever, chill, bone pain, pneumonia, shock)
❷RBC & platelet➔normal(↓slightly)
❸oral➔①necrotizing punched-out ulcer(buccal, tongue, palate)
②necrotizing ulcerative gingivitis(NUG)

Cyclic neutropenia➔regular periodic ↓neutrophil no.

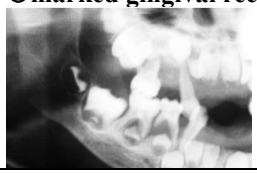
➲cause➔neutrophil elastase(ELA-2/ELANE) gene mutation➔arrested neutrophil develop(promyelocyte stage in marrow)

➲symptom(begin in child)➔correlate with neutrophil no.
❶lowest point➔infection
①present 3-6-day
②↑(blood monocyte & eosinophil)
❷rises toward(less than) normal➔↓S/S

➲clinic➔❶21-day cycle[recurrent of fever, anorexia, cervical lymphadenopathy, malaise, pharyngitis, oral(GI) ulcer]



❷severe periodontal bone loss
①marked gingival recession ②tooth mobility



Platelets disorders➔❶thrombocytopenia ❷thrombocythemia(normal platelet no.➔200,000-400,000/mm^3)

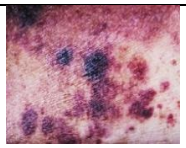
➲thrombocytopenia(血小板減少症)➔platelet no.<150,000/mm^3
❶<50,000➔minor trauma
❷<10,000➔severe bleeding

➲causes➔hypersplenism, autoimmune, hypothermia, viral/bacterial infection➔DIC(disseminated intravascular coagulation), drug-induced, idiopathic

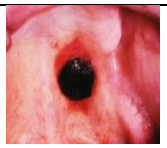
➲↓platelet no.
❶↓production
❷↑destruction➔thrombotic thrombocytopenic purpura(TTP)➔↓von Willebrand factor-cleaving metalloprotease (ADAMTS13)➔thrombi➔gingiva➔fibrin in small blood vessel

❸spleen sequestration(對有害物封存隔離)➔splenomegaly
①portal hypertension 2^0 to liver disease
②$2^0$ to tumor infiltration
③associate Gaucher disease

➲immune thrombocytopenic purpura(ITP)➔autoAb➔spleen sequestration
❶acute➔child(after viral infect)➔[S/S quick, severe]➔
①resolve(4-6-wk) ②recover by 3-6-month(90%)
❷chronic➔20-40s women



petechiae➔ecchymosis



hematoma

➲primary thrombocythemia(血小板增多症)➔JAK2(Janus kinase 2) mutation(>95%)
❶palate no.>600,000/mm^3 ❷disorder of palate precursor cell(megakaryocyte) ❸microvasculature thrombosis

Leukemia(血癌)➔excessive WBC proliferation

➲categories
❶clinical course➔[①acute ②chronic]
❷histogenetic origin➔[①myeloid(骨髓)/lymphocytic ②lymphoblastic]

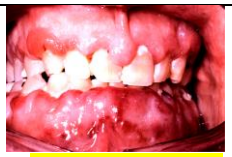
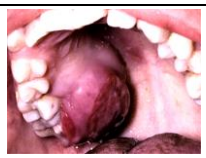
➲myeloid leukemia(differentiate different pathways)➔malignant cell with features
❶granulocyte/monocyte
❷erythrocyte/megakaryocyte(less frequent)

➲manifestation➔anemia, petechiae, ecchymosis, thrombosis, hemorrhage, DIC, infection, weight loss, bone pain, liver, spleen, enlarged LN, pancytopenia[↓(RBC, WBC, platelet)], fatigue

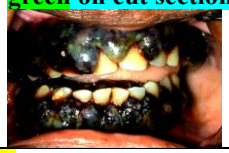
➲acute leukemia
❶clinic
①rapid growth of immature(undifferentiated) blood cell (blast cell)
②onset rapid & abrupt
③↓survival time

➲myelomonocytic type➔oral➔❶diffuse gingival enlargement ❷tumor like growth(ulcer/non-ulcer)

❷classification
①acute lymphoblastic leukemia(ALL)➔least common overall
(1)children(common)(78%)➔~90% cured if Tx
(2)-adult(much lower 5-yr survival rate)➔remission(80%)
②acute myelogenous leukemia(AML)
(1)adult(more common)(broader age range, include children)
(2)5-yr survival rate(40%)
(3)5-yr survival rate(>60s)➔<10%

➲myeloid sarcoma➔tumor cell infiltrate oral soft tissue(gingiva)➔ nontender (non)ulcerated swelling➔ green on cut section ➔chloroma



➲chronic leukemia
❶clinic
①more differentiated/mature cell➔slow growth
②gradual onset
③longer disease course
④longer survival time(mostly 60-80s)
⑤arise from different mature WBC

❷classfication
①chronic lymphoctic leukemia(CLL)(elderly adult more common)
(1)most common type
(2)survival rate(73%)
(3)av. survival>10s; advance(2s)
② chronic myeloid leukemia(CML)
(1)most adult(peak➔3th-4th decades)
(2)5-year survival(80%)

8. The most common **leukemia of childhood** is:
   (A) acute lymphoblastic leukemia
   (B) acute myeloid leukemia
   (C) chronic lymphocytic leukemia
   (D) chronic myeloid leukemia

9. The most common **leukemia of older adults** is:
   (A) acute lymphoblastic leukemia
   (B) acute myeloid leukemia
   (C) chronic lymphocytic leukemia
   (D) chronic myeloid leukemia

10. Which one of the following would be a common feature in a patient with **leukemia**?
   (A) elevated hematocrit
   (B) elevated hemoglobin
   (C) polycythemia
   (D) thrombocytopenia

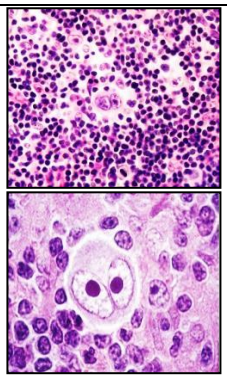
Hodgkin lymphoma(霍奇金氏淋巴癌)

➲neoplastic cell➔Reed-Sternberg(RS) giant cell➔in enlarged LN(~0.1-2% of cell) ➲male predilection

➲ LN(almost)➔❶(supra)cervical(70-75%) ❷axillary & mediastinal(✪縱膈)(5%-10% each) ❸abdominal & inguinal(鼠蹊)(<5%)

➲bimodal➔❶peak➔15-35s ❷peak>50s

Stage	Defining Features
I	Involvement of a single lymph node region (I) or a single extralymphatic organ or site (I_E)
II	Involvement of two or more lymph node regions on the same side of the diaphragm (II) or one or more lymph node regions with an extralymphatic site (II_E)
III	Involvement of lymph node regions on both sides of the diaphragm (III), possibly with an extralymphatic organ or site (III_E), the spleen (III_S), or both (III_{SE})
IV	Diffuse or disseminated involvement of one or more extralymphatic organs (identified by symbols), with or without associated lymph node involvement A: Absence of systemic signs B: Presence of fever, night sweats, and/or unexplained loss of 10% or more of body weight during the 6-month period before diagnosis



➲classification
❶nodular lymphocyte-predominant➔popcorn cell
❷classical
①lymphocyte rich
②nodular sclerosis➔lacunar(RS) cell
③mixed cellularity➔mixture of small lymphocyte, plasma cell, eosinophil & histiocyte+abundant RS cell
④lymphocyte depletion➔numerous bizarre giant RS cell
⑤unclassifiable

✪縱膈(無明顯界限)➔胸腔為中心疏鬆結締組織包圍的構造➔含心臟(含周圍血管)、食道、氣管、膈神經、心臟神經、胸導管、胸腺，胸腔淋巴結

non-Hodgkin lymphoma(非霍奇金氏淋巴癌)

➲initial➔LN➔solid mass ➲異於lymphocytic leukemia➔bone marrow➔malignant cell➔peripheral blood

❶most➔B-lymphocyte series(85%) ❷less common➔T-lymphocyte ❸even rarer➔histiocyte

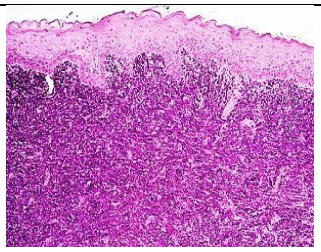
➲EBV-associated lymphoproliferative disorder➔from benign, reactive process through overt malignancies

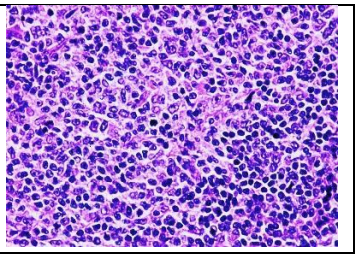
➲HHV-8➔❶Kaposi sarcoma ❷body cavity lymphoma ❸plasmablastic lymphoma

➲human T-cell leukemia/lymphoma virus type I(HTLV-1)➔peripheral T-cell lymphoma

➲bacteria➔mucosa-associated lymphoid tissue(MALT) lymphoma

➲oral lymphoma➔extranodal➔❶oral soft tissue ❷jaws



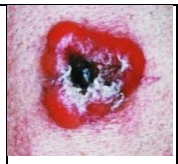


➲micro
❶nodular/follicular
①B-lymphocyte origin ②vague germinal center
❷diffuse
①most➔diffuse large B-cell lymphoma(high grade)(60%)
②destroy normal node architecture
③extranodal➔destroy normal adjacent host tissue

Mycosis fungoides(蕈樣肉芽腫)(Cutaneous T-cell lymphoma) [Dx➔CD4(+)(surface marker of T-helper cell)]

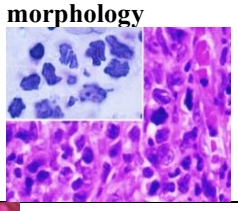
➲derived from T lymphocyte➔T-helper(CD4) cell	➲most➔cutaneous lymphoma	➲mean age➔55-60s
➲epidermotropism➔傾向skin epidermis	➲oral➔infrequent	➲ M:F=2:1 ➲middle-aged adult men

➲clinic➔3-stage
❶eczematous(erythematous)➔well-demarcated, scaly, erythematous patch➔mistaken as psoriasis
❷plaque➔①light elevate ②red
❸tumor➔papule(nodule)(右圖)➔visceral

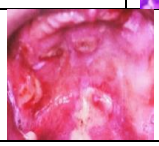


➲micro(plaque stage)➔❶Pautrier microabscess➔atypical lymphocyte (mycosis/Sézary cell)

❷cerebriform(infold nuclear membrane) morphology



➲oral(~60 cases)➔most➔[tongue, palate(右圖), gingiva]➔appear after cutaneous lesion



➲Sézary syndrome➔aggressive➔T-cell leukemia➔generalized exfoliative erythroderma, lymphadenopathy, hepatomegaly, splenomegaly➔lung, kidney, CNS➔death within short period➔median survival 2-3s

11. Which of the following features of patients with **Langerhans cell histiocytosis** are *true*?
(1) derived from eosinophils & mononuclear cells (2) most benign type is eosinophilic granuloma (3) skull view may show multiple punched out lesions (geographic skull) (4) aphthous ulcers are seen
(A) 1,2,3,4
(B) only 1,3,4
(C) only 2,3,4
(D) only 1,2,3

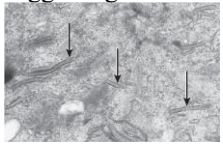
12. Which of the following genetic inhibitor can be used to detect **Langerhans cell histiocytosis**?
(A) *b-raf*
(B) *n-ras*
(C) *k-ras*
(D) *k-raf*

13. The two types that microscopically characterize **Langerhans cell histiocytosis** are:
(A) lymphocytes and plasma cells
(B) fibroblasts and lymphocytes
(C) eosinophils and mononuclear cells
(D) neutrophils and lymphocytes

14. Which one of the following is the form of **Langerhans cell histiocytosis** that is characterized by a **triad of symptoms**?
(A) Letterer-Siew disease
(B) Hand-Schuller-Christian disease
(C) eosinophilic granuloma
(D) Behcet syndrome

15. The most benign type of **Langerhans cell histiocytosis** is:
(A) Hand-Schuller-Christian disease
(B) eosinophilic granuloma
(C) Letterer-Siew disease
(D) chronic disseminated reticulosis

16. Figure below of the malignancy with electron micrograph showing **rod-shaped Birbeck bodies** (arrows) in the cytoplasm, suggesting that it is a lesion of which of the following?



(A) Langerhans cell histiocytosis
(B) squamous cell carcinoma
(C) granular cell ameloblastoma
(D) Pindborg tumor

17. 下列何者不是蘭格罕細胞組織球增生症(**Langerhans cell histiocytosis**)重要的預後因子？(114)

(A) 發病年紀小於2歲

(B) 肺臟、肝臟、脾臟發現腫瘤細胞

(C) 侵犯到皮膚

(D) 首次化療後的腫瘤反應

Langerhans cell histiocytosis蘭格罕細胞組織球增生症(LCH)(Histiocytosis X)

LC(histiocyte-like cell)+(eosinophil, lymphocyte, plasma cell, multinucleated giant cell)

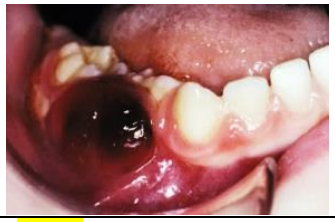
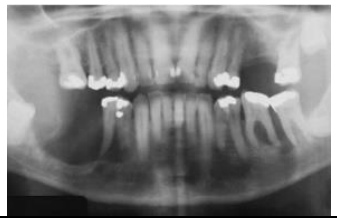
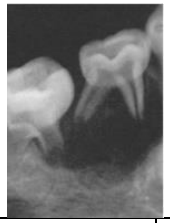
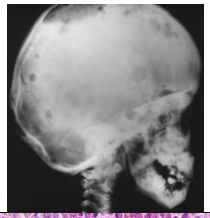
➲<15s(>50%)➔5/million annually	➲adult➔1/million	➲monoclonal proliferation➔neoplastic process

➲LC➔dendritic mononuclear cell➔[❶epidermis ❷mucosa ❸LN ❹bone marrow]➔present antigen to T lymphocyte

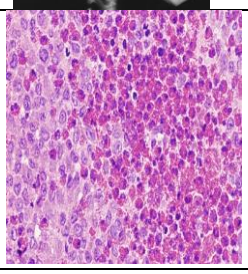
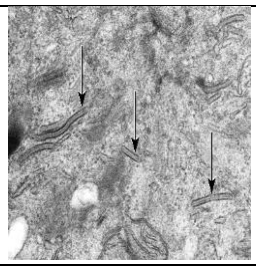
➲BRAF/MAP2K1突變(40-60%)➔[❶early突變➔①more aggressive ②disseminate][❷later➔①more localize ②benign]

➲clinic
❶clinicopathologic spectrum
①eosinophilic granuloma of bone➔solitary/multiple bone lesion(s) without visceral involve
②chronic disseminated histiocytosis(Hand-Schüller-Christian disease)➔bone, skin, viscera
③acute disseminated histiocytosis(Letterer-Siwe disease)➔infant➔cutaneous, visceral, bone marrow
❷Hand-Schüller-Christian triad➔①bone lesion ②exophthalmos ③diabetes insipidus
❸pulmonary LCH(unrelated to jaw lesion)➔①adult with smoking ②reactive process
❹Histiocytic Society➔classification define prognosis
①single organ(bone/skin) ②unifocal ③multifocal ④multi-organ ⑤no organ dysfunction ⑥organ dysfunction
⑦low-risk(skin, bone, LN, &/or pituitary gland) ⑧high-risk(lung, liver, spleen, &/or bone marrow)
❺male predilection/overall sexes equally affected
❻almost any bones➔[skull, rib, vertebrae, mandible(like periapical pathosis)➔most frequent]
❼<10s➔①skull ②femur
❽>20s➔①rib ②shoulder girdle ③mandible
❾adult with solitary/multiple bone lesions➔lymphadenopathy➔no significant visceral
❿bone perforate➔ulcerative gingiva mass(occasion➔only oral soft tissue)(左下圖)

➲radiograph➔punch-out RL without corticated rim/PD-RL(右1下圖)
❶jaws(10-20%)(posterior)(左1下圖)➔scooped out(like severe periodontitis)(下2中圖)➔teeth float in air(右2下圖)

➲micro
❶diffuse infiltration of large, pale-stain mononuclear cell(histiocyte)➔indistinct cytoplasmic border & round/indented vesicular nuclei(左圖)
❷eosinophil➔interspersed among histiocyte, plasma cell, lymphocyte, multinucleated giant cell
❸necrosis & hemorrhage
❹EM➔Birbeck granule(rod-shaped cytoplasmic structure)(右圖)
❺IHC➔①CD1a(+) ②CD207(langerin)(+)

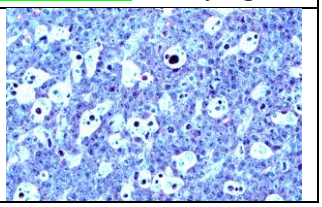
➲Tx
❶accessible bone lesion(maxilla & mandible)➔curettage
❷less accessible bone lesion➔low dose radiation
❸intra-lesion injection➔corticosteroid agent➔effective in localized bone lesion
❹spontaneous regression of localized lesion(infrequent)
❺bone lesion without visceral involve➔good prognosis
❻≥3 bones➔dissemination of disease
❼single-agent chemotherapy(①prednisolone ②etoposide ③vincristine ④cyclosporine)➔good response[①/②/③/④]
❽adult➔low-dose cytarabine(ara-C)➔respond much better
❾induction chemotherapy(1st 6-wk)➔improve significant➔much better prognosis(nearly 90% survival)
❿prognosis➔①poorer➔1st sign develop at very young age ②better➔older at time of onset

18. Which of the following disease can have almost **100% labelling index upon Ki-67 staining** for the tumor cells?
(A) squamous cell carcinoma
(B) Burkitt lymphoma
(C) adenoid cystic carcinoma
(D) Langerhans cell histocytosis

Burkitt lymphoma 伯基特氏淋巴瘤(BL)

➲undifferentiated B-cell lymphoma	➲children➔age related jaw lesions	❶African BL➔sub-Saharan Africa
❷endemic(地方性) BL➔①EBV nuclear antigen(90%) ②NW Brazil & New Guinea➔malaria ③jaws(50-70%)		
❸sporadic(American)➔EBV(↓frequency)➔abdominal mass		❹immunodeficiency-associated➔HIV-related
➲male predilection	➲common➔posterior jaws	➲上顎>下顎(2:1) ➲patchy loss of lamina dura➔early sign

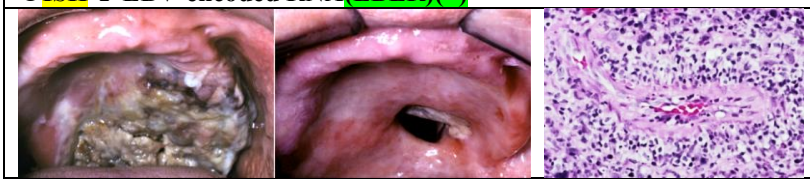
➲micro
❶ Ki-67➔almost 100% labelling index
❷starry[macrophage(histiocyte)➔abundant cytoplasm)]-sky(hyperchromatic neoplastic lymphoid cells)(右圖)
❸similar➔diffuse large B-cell lymphoma
❹t(8;14)(q24;q32) translocation➔ c-myc oncogene



Extranodal NK/T-cell lymphoma, nasal-type(angiocentric T-cell lymphoma; midline lethal granuloma

➲mid-palate & nasal fossa destruction➔oronasal fistula(左下、中圖)	➲EBV➔pathogenesis	➲male predilection

➲micro
❶angiocentric➔infiltrate of inflammatory cell around blood vessel(右下圖)
❷necrosis➔infiltration of blood vessel by tumor cell
❸IHC➔ ①NK-cell[CD56(+)] ②T-lymphocyte[CD3(+)]
❹ISH➔EBV-encoded RNA(EBER)(+)

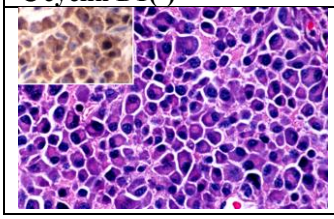
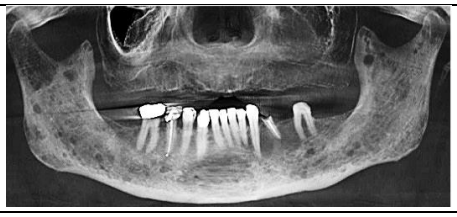
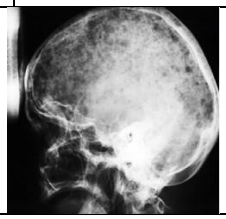
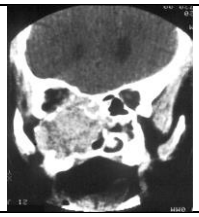


19. The cell type involved in **multiple myeloma** is:
(A) lymphocyte
(B) neutrophil
(C) eosinophil
(D) plasma cell

20. Which of the following malignancies is characterized by a **monoclonal spike** on immunoelectrophoresis?
(A) osteosarcoma
(B) squamous cell carcinoma
(C) multiple myeloma
(D) leukemia

Multiple myeloma多發性骨髓瘤(MM)/Plasmacytoma漿細胞瘤

➲plasma cell malignancy➔derived from B lymphocyte➔ monoclonal κ/λ light chains Ig(immunoglobulin)(最左下圖)	➲multiple➔punch out RL(skull)(下圖)
➲solitary plasmacytoma ❶monoclonal(25-50%)➔amount<MM ❷bone marrow biopsy➔no plasma cell infiltration ❸no signs of [①anemia ②hypercalcemia ③renal failure]	➲50% of all bony malignancy(exclude meta) ➲bone pain ➲renal failure➔excess light chain protein of tumor cell ➲Bence-Jones protein(urine)(30-50%) ➲amyloid➔soft tissue(tongue)(10-15%) ➲metastatic calcification(soft tissue)
➲soft tissue(extramedullary) plasmacytoma ①plasma cell(marked↓) ②CD56(-) ③cyclin D1(-)	

Chapter 13: Hematologic Disorders

1. Which one of the following would be a common feature in a patient with leukemia?
A. Elevated hematocrit
B. Elevated hemoglobin
C. Polycythemia
D. Thrombocytopenia
E. All of the above

2. Which one of the following malignancies is derived from T-lymphocytes?
A. Acute myeloid leukemia
B. Burkitt lymphoma
C. Hodgkin lymphoma
D. Multiple myeloma
E. Mycosis fungoides

3. Which one of the following is the most common site for oral lymphomas?
A. Buccal mucosa
B. Floor of mouth
C. Lower lip
D. Palate
E. Upper lip

4. All of the following are true concerning multiple myeloma EXCEPT:
A. the disease has a relatively good prognosis using local radiation therapy
B. it is a neoplasm of plasma cells
C. it occurs most commonly in middle-aged and older patients
D. it may be associated with amyloidosis
E. tumors characteristically occur in bones

5. The most common leukemia of childhood is:
A. acute lymphoblastic leukemia
B. acute myeloid leukemia
C. chronic lymphocytic leukemia
D. chronic myeloid leukemia
E. hairy cell leukemia

6. The most common leukemia of older adults is:
A. acute lymphoblastic leukemia
B. acute myeloid leukemia
C. chronic lymphocytic leukemia
D. chronic myeloid leukemia
E. hairy cell leukemia

7. Which one of the following conditions should be considered in a child who presents with unexplained severe bone loss around the roots of multiple teeth resembling aggressive periodontitis?
A. Hand, foot, and mouth disease
B. Impetigo
C. Langerhans cell histiocytosis
D. Myospherulosis
E. Primary herpetic gingivostomatitis

8. Which one of the following hematologic conditions is associated with an increased risk of leukemia?
A. Cyclic neutropenia
B. Hemophilia B
C. Idiopathic thrombocytopenic purpura
D. Polycythemia vera
E. Sickle cell trait

9. Birbeck bodies are a characteristic ultrastructural finding of:
A. eosinophils
B. Langerhans cells
C. lymphocytes
D. plasma cells
E. polymorphonuclear leukocytes

10. Amyloidosis is a common secondary manifestation of:
A. acute lymphocytic leukemia

B. Burkitt lymphoma
C. multiple myeloma
D. mycosis fungoides
E. polycythemia vera

11. An elevated hematocrit would be observed in patients with:
A. chronic lymphocytic leukemia
B. cyclic neutropenia
C. myelogenous leukemia
D. pernicious anemia
E. polycythemia vera

12. Bisphosphonate medications are often used in the clinical management of:
A. acute myeloid leukemia
B. Burkitt lymphoma
C. chronic lymphocytic leukemia
D. Hodgkin lymphoma
E. multiple myeloma

13. The neoplastic cell of the so-called eosinophilic granuloma of bone is:
A. eosinophil
B. Langerhans cell
C. natural killer cell
D. T4 lymphocyte
E. T8 lymphocyte

14. Endemic Burkitt lymphoma has been pathogenetically related to:
A. advancing age
B. chemical exposure
C. Epstein-Barr virus
D. human papillomaviruses types 16 and 18
E. PUVA therapy

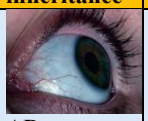
15. Which one of the following conditions may result in jaw enlargement with a “chipmunk” facies?
A. Cyclic neutropenia
B. Hemophilia A
C. Hemophilia B
D. Polycythemia vera
E. Thalassemia major

Chapter 13: Hematologic Disorders➔answers
1. ANS: D
2. ANS: E
3. ANS: D
4. ANS: A
5. ANS: A
6. ANS: C
7. ANS: C
8. ANS: D
9. ANS: B
10. ANS: C
11. ANS: E
12. ANS: E
13. ANS: B
14. ANS: C
15. ANS: E

Chapter 14 Bone pathology

Osteogenesis imperfecta(Brittle bone disease)➔heritable[1/(1萬↔1萬5 birth)]

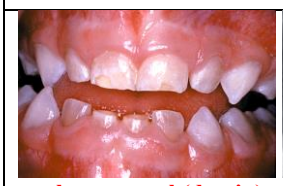
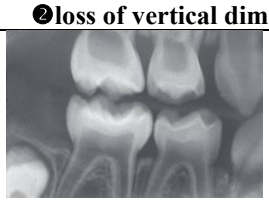
❶autosomal dominant(AD)(~90%)➔COL1A1, A2(encode type I collagen)突變	❷autosomal recessive(AR)突變(10%)
❸可能sporadic	➲type I collagen(triple helix)➔[❶bone ❷dentin ❸sclerae ❹ligament ❺skin]的主成分

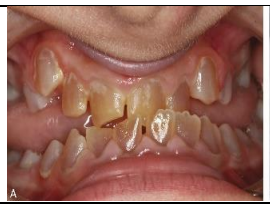
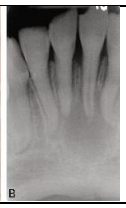
classification	phenotype	inheritance	gene mutated	disease type
OI type 1 (mildest & most common)	❶mild ❷nondeforming disease with persistent blue sclerae	 AD	[COL1A1, A2]➔clinic ❶bone fractures(occur when begins to walk➔↓frequency after puberty) ❷no significant bone deformity ❸essentially normal growth	I
OI type 2 (most severe)	❶severe ❷perinatal lethal disease	AD, AR	[COL1A1, A2, CRTAP, LEPRE1, PPIB]➔clinic ❶extreme bone fragility(deformity) ❷respiratory distress due to multiple rib fractures & small thorax➔die in utero(shortly after birth)	II, VII, VIII, IX
OI type 3	moderate to severe, progressively deforming disease	AD, AR	COL1A1, COL1A2, IFITM5, SERPINF1, CRTAP, LEPRE1, PPIB, SERPINH1, FKBP10, TMEM38B, BMP1, WNT1, CREB3L1, SPARC, TENT5A	III, V, VI, VII, VIII, IX, X, XI, XIII, XIV, XVI, XVII, XVIII
OI type 4	❶moderate disease, ❷normal sclera in adults	AD, AR	COL1A1, COL1A2, WNT1, IFITM5, CRTAP, PPIB, FKBP10, SP7	IV, V, VII, IX, XI, XII, XV
OI type 5	moderate disease with interosseous membrane calcification &/or hypertrophic callus	AD	IFITM5	

➲clinic(additional)➔❶blue sclerae(上圖) ❷hearing loss ❸joint hyperextensibility/contracture
(infrequent)➔❶muscle weakness ❷cardiopulmonary complication

➲radiograph➔❶osteopenia ❷long bone bowing ❸multiple fractures
❹↑skull wormian bone(suture bone in mosaic pattern)(cleidocranial dysplasia also)

➲dental(identical to DI) ❶both dentitions(permanent teeth less prominent)➔severe attrition
❷loss of vertical dimension & tooth loss



opalescent teeth(dentin), shell tooth(thin dentin, normal enamel)



(A)opalescent teeth(class III malocclusion), posterior open bite (B)pulp obliteration

➲other dental findings➔❶pulp stone ❷taurodontism ❸dilaceration ❹hypodontia ❺microdontia

➲craniofacial➔❶▲face ❷frontal bossing ❸macrocephaly ❹flattened vertex & skull base ❺prominent occiput

➲associate➔❶Ehlers-Danlos syndrome ❷Stickler syndrome ❸gnathodiaphyseal dysplasia

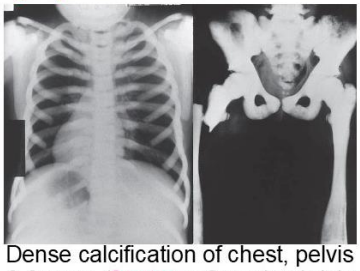
Osteopetrosis(Albers-Schonberg disease, Marble bone disease)

➲↓osteoclast function/differentiation(主要非因no.↓)➔↓bone resorption➔↑bone density

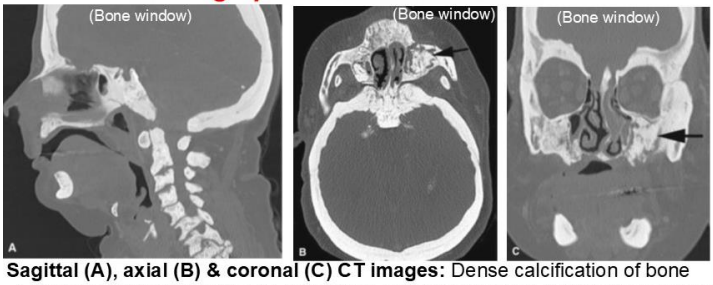
➲3 clinic types(normal serum chemistry level)
❶autosomal recessive infantile(malignant)(die≤20s)➔at birth(early infancy)➔severe & debilitating(虛弱)➔
①neurologic(hematologic) disorders ②pathologic fracture
❷autosomal recessive intermediate
①出生時無症狀➔1st decade末➔輕至中度貧血& extramedulla hematopoiesis(造血)➔bone marrow failure(rare)
②if caused by carbonic anhydrase II deficiency➔renal tubular acidosis &大腦鈣化
❸autosomal dominant adult(benign)(less severe)➔later in life➔minor trauma➔fracture

General Radiographic Features

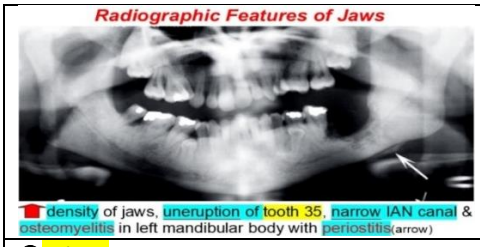

Dense calcification of skull & facial bones (jaws enlargement)
類似HYPERPITUITARISM
類似RENAL OSTEODYSTROPHY

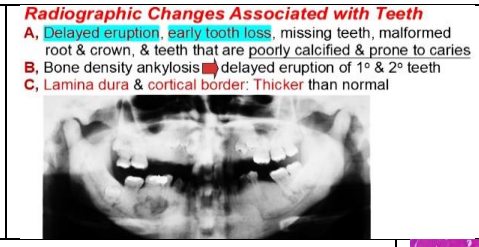

Dense calcification of chest, pelvis & femurs (fracture of proximal right femur)

Radiographic Features of Jaws

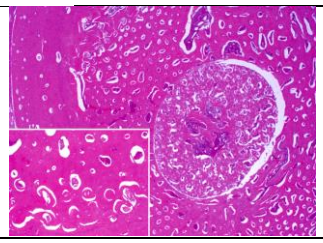


Sagittal (A), axial (B) & coronal (C) CT images: Dense calcification of bone
- Loss of definition of cortical & cancellous bone interfaces & uniformly increased density of all bones
- Complicated by osteomyelitis of left maxilla with sequestra(arrows in B & C)





➲micro
❶tortuous lamellar trabeculae replace cancellous bone
❷globular amorphous bone deposit➔marrow space(右圖)
❸osteophytic bone formation



❹osteoclast no.➔[①↑ ②↓ ③正常]➔non-function➔Howship lacuna➔absent/minimal
❺osteoclast-rich form➔scant residual hematopoetic marrow➔fibrosis➔↑osteoblast no
❻osteoclast-poor form➔scant residual hematopoetic marrow➔non fibrosis

1. Which one of the following is *not* a feature of **Paget disease of bone**?
   (A) deposition of amorphous material
   (B) resorption & osteoblastic repair
   (C) chronic metabolic bone disease
   (D) hypercementosis

2. Which of the following is helpful in the diagnosis of **Paget disease of bone**?
   (A) immunoelectrophoresis
   (B) serum alkaline phosphatase
   (C) serum calcium
   (D) urinalysis

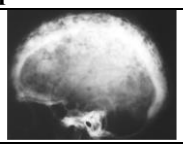
3. Which one of the following is *not* associated with **Paget disease of bone**?
   (A) increased risk of osteosarcoma
   (B) bone pain and bone enlargement
   (C) “cotton-wool” radiographic pattern
   (D) autosomal dominant or X-linked recessive inheritance pattern

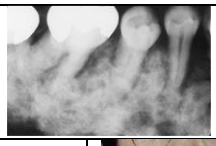
Paget disease of bone(Osteitis deformans)➔autosomal dominant inheritance pattern with incomplete penetrance

➲<40s(rare) | ➲male predilection | ➲slow virus infection➔inclusion body➔paramyxovirus(controversial)

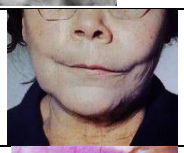
➲oral complication➔❶unfit假牙(bone enlargement) ❷bleeding ❸拔除hypercementosed牙齒➔bone infection

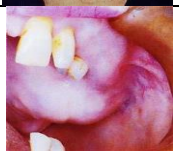
➲radiograph
❶early➔①WD RL(osteoporosis circumscripta) ②loss of lamina dura
③periapical bone resorption➔like infection
❷late(右圖)➔①cotton wool RO ②hypercementosis





➲cause➔osteoclast(❶↑size ❷↑no. ❸↑activity)
❶genetic(~40% familial; 5% sporadic)➔sequestosome 1 gene(SQSTM1; p62) mutation(more severe than cases without such mutation)➔NF-κ pathway[osteoclast precursor➔(①↑RANKL ②↑TNF-α ③↑1,25-dihydroxyvitamin D3)]➔↑osteoclastic activity➔↑haphazard(隨意) bone formation by osteoblast
❷environmental factor(slow virus infection)
➲jaw(17%)➔maxilla:mandible=2:1➔leontiasis facies(右圖)
➲malignant transformation(1%)➔osteosarcoma
➲benign & malignant giant cell tumor➔craniofacial skeleton

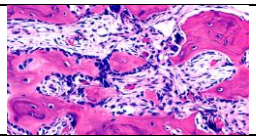




➲lab➔❶high serum alkaline phosphatase level(700 iu/l) ❷normal blood Ca & P

➲limited disease(normal total serum alkaline phosphatase)
❶specialized bone formation marker(serum N-terminal propeptide of type 1 collagen)
❷resorption marker(urinary N-terminal telopeptide of type 1 collagen)

➲micro
❶prominent osteoblastic & osteoclastic activity surround bone trabeculae
❷resting & reversal line
❸benign/malignant giant cell tumor➔facial skeleton



➲start➔❶single bone➔polyostotic(~90%)(common at most 5/6 bones➔❷may occur simultaneously)

➲diseased bone➔❶thicken➔weaken ❷long bone distorted by body weight ❸↑vascularity
❹overlying skin➔warm ❺severe bone pain(active stage)

➲Tx➔bisphosphonate➔❶zoledronic acid(single infusion) ❷oral risedronate/alendronate(daily for several mon)

4. The most characteristic radiographic appearance of **fibrous dysplasia** is described as:
   (A) cotton-wool appearance
   (B) well-circumscribed radiopacity
   (C) ground glass appearance
   (D) well-circumscribed multilocular radiolucency

5. The genetic change of **fibrous dysplasia** is associated with the mutation of:
   (A) *G-nas*
   (B) *N-ras*
   (C) *K-ras*
   (D) *B-raf*

6. Which of the following diseases is associated with **café au lait spots**?
   (A) polyostotic fibrous dysplasia
   (B) Paget disease of bone
   (C) monostotic fibrous dysplasia
   (D) periapical cemento-osseous dysplasia

7. The most characteristic radiographic appearance of **fibrous dysplasia** is described as:
   (A) cotton-wool appearance
   (B) well-defined radiopacity
   (C) orange peel appearance
   (D) well-defined multilocular radiolucency

8. The disease of patient with **smooth cafe au lait pigmentation (coast of California) crossing midline without sexual precocity** is:
   (A) neurofibromatosis type 1 (von Recklinghausen disease)
   (B) polyostotic fibrous dysplasia
   (C) neurofibroma
   (D) giant cell fibroma

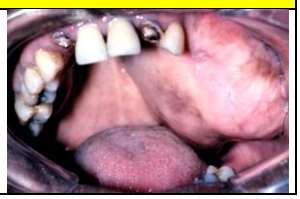
9. What is the disease of the patient with **irregular bordered cafe au lait pigmentation (coast of Maine)**; **NOT crossing midline** over the skin of abdomen with sexual precocity?
   (A) neurofibromatosis type 1(von Recklinghausen disease of the skin)
   (B) Jaffe-Lichtenstein syndrome
   (C) McCune-Albright syndrome
   (D) Mazabraud syndrome

10. Which of the following is characterized by **precocious puberty** in females?
    (A) monostotic fibrous dysplasia
    (B) Jaffe-Lichtenstein-type fibrous dysplasia
    (C) Albright-McCune-type fibrous dysplasia
    (D) focal cemento-osseous dysplasia

11. Which of the following tumors is associated with **von Recklinghausen disease (neurofibromatosis, type 1)**?
    (A) neurilemoma
    (B) neuroma
    (C) fibroma
    (D) neurofibroma

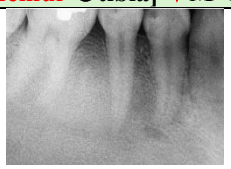
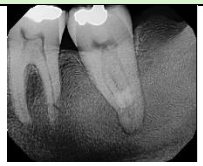
Fibro-osseous lesions of jaws(NOT include cementoblastoma)

❶**fibrous dysplasia(FD)** ①**monostotic FD** ②**polyostotic FD** ❷**cemento-osseous dysplasia(COD)** ①**focal COD** ②**periapical COD** ③**florid COD** ❸**ossifying fibroma** ✪①**idiopathic osteosclerosis** ②**periapical osteosclerosis**
❶**fibrous dysplasia(FD)**
➲**GNAS mutation(encode α subunit G protein)➔❶lesional tissue ❷peripheral blood**
❶**ossifying fibroma/COD➔NOT detected** ❷**occur in early embryonic development(mutation of pluripotent stem cell)➔affect** ①**osteoblast** ②**melanocyte** ③**endocrine cell** ❸**occur in late stage(mutation of skeletal progenitor)➔affect ONLY osteoblast**



➲monostotic FD(~80%)✶limited to single bone➔[①craniofacial bone ②rib ③femur ④tibia] ✶M=F ✶2nd-3rd decades

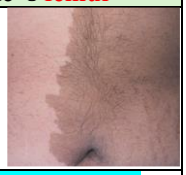
❶[maxilla(右上圖)>mandible](posterior) ❷mean age of jaws➔24↔37s
❸maxilla FD➔[①zygoma ②spenoid ③ethmoid ④frontal bone ⑤temporal bone ⑥occiput]➔craniofacial FD
❹radiograph➔①PD fine ground glass(orange peel) appearance(左圖)
②fingerprint pattern(右圖)

❹clinic➔painless unilateral swelling(most)(最上右圖)
❺mandible FD➔①bucco-lingual expansion ②bulging inferior border
③inferior alveolar canal➔superior displacement
④periapical radiograph➔PDL widening, PD lamina dura
❻maxilla FD➔①superior sinus floor displacemnet ②antrum obliteration ③extensive skull involve

➲polyostotic FD(≥2 bones)➔❶<10s ❷female predilection ❸a few-75% skeleton➔①craniofacial ②pelvic ③femur

➲affected bone➔fibroblast growth factor 23(FGF23)➔renal phosphate wasting➔hypophosphatemia
➲FD associate with syndromes(❶-❷)
❶McCune-Albright syndrome➔①polyostotic FD ②café au lait pigmentation(右圖)
③multiple endocrinopathies(sexual precocity) ④dental anomalites(tooth displacemnet, oligodontia, enamel hypoplasia, enamel hypomineralization, taurodontism, retained 1^0 teeth) [≥2 of ①②③④]



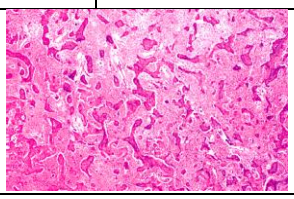
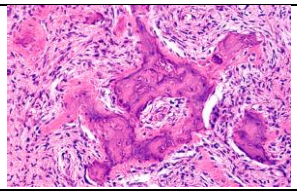
✪①polyostotic FD ②café au lait pigmentation(no endocrinopathy)➔Jaffe-Lichtenstein syndrome(past)(current➔variation of ❶)

❷Mazabraud syndrome➔①polyostotic FD ②intramuscular myxomas

➲café au lait pigmentation➔McCune-Albright syndrome
❶well-defined tan macule
❷unilateral(more or less respect midline➔usu. not cross midline)
❸site➔①skin(most; shortly after birth)
②intraoral mucosa(lips)(adult➔progress with age)
❹congential(may be)

McCune-Albright syndrome	neurofibromatosis (type 1)/von Recklinghausen disease
❶not cross midline	❶cross midline
❷irregular borders	❷smooth borders
❸coast of Maine	❸coast of California

➲micro
❶curvilinear(Chinese characters) shaped trabeculae of immature(woven) bone in cellular fibrous stroma
❷without capsule➔lesion bone fuse with normal bone
❸osteoblastic rim➔absent/minimal
❹$2^0$ ABC formation(reported)

12. **Central giant cell granuloma**:
(A) may occur on the tongue
(B) may present as a multilocular radiolucency
(C) occurs primarily in children less than 6 years of age
(D) is histologically the same as a periapical granuloma

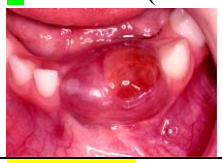
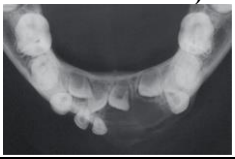
Central giant cell granuloma(CGCG)

➲genetic
[❶TRPV4 ❷KRAS ❸FGFR1]➔somatic mutation(~70%)➔activate Ras-MAPK(mitogen-activated protein kinase)路徑

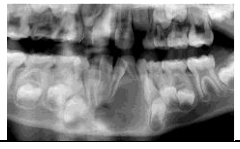
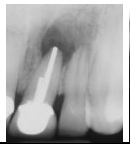
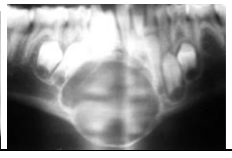
➲long bone nonossifying fibroma & jaw CGCG➔Ras-MAPK路徑➔variant of same entity

➲age(0-86s)➔(~70%<30s) | ➲女性偏高 | ➲mandible(~70%)➔常過中線➔anterior jaws

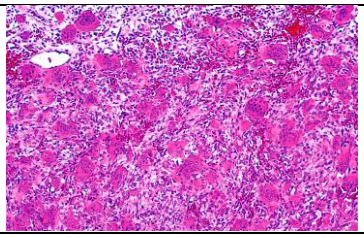
➲2 categories
❶nonaggressive(most)➔①relatively small ②few/no symptoms ③slow growth ④no cortical perforation/root resorption ⑤routine radiograph discover ⑥painless jaw expansion
❷aggressive(下圖)➔①pain ②rapid growth(larger at diagnosis) ③cortical perforation/root resorption ④tooth displacement ⑤paresthesia ⑥extend into soft tissue ⑦overlying mucosa ulcer ⑧younger patient ⑨↑recurrence(recurrence rate➔18%)

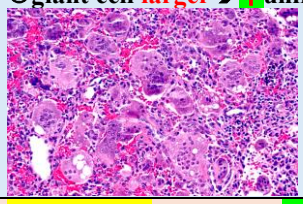
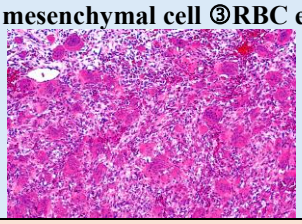
➲radiograph➔WD-UL(small➔like apical granuloma/cyst)/ML-RL(like ameloblastoma)➔no corticated margin➔0.5↔>10cm(destructive)

➲CBCT➔❶bone at periphery➔subtle(細微), granular ❷ML➔wispy(細微) & coarse septa

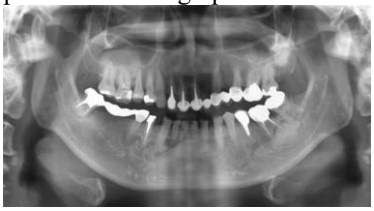
➲micro➔multinucleated giant cell(few to many) ❶stroma(loose & edematous/cellular) ①ovoid to spindle-shaped mononuclear cell➔活化RANK/RANKL路徑➔ monocyte-macrophage precursor➔分化為osteoclastic giant cell ②older lesion➔fibrosis ❷RBC extravasation➔hemosiderin ❸focal bone/osteoid	
❹[①↑vascular density ②↑angiogenesis ③↑MMP(matrix metalloproteinase)]➔aggressive	
➲micro d.d➔①brown tumor ②hyperparathyroidism ③CGCG in aneurysmal bone cyst ④CGCG with central odontogenic fibroma/cemento-ossifying fibroma	
➲radiograph d.d.➔①benign fibro-osseous lesions ②melorheostosis(cortical hyperostosis)➔radiograph like drip candle wax➔MAP2K1 somatic mutation	
➲multiple CGCG➔①cherubism ②Ramon syndrome ③Jaffe-Campanacci syndrome ④RASopathies(Noonan syndrome, neurofibromatosis type 1)	
➲alternative Tx➔①intralesion corticosteroid injection ②subcutaneous/nasal calcitonin(降血鈣素) ③subcutaneous interferon α2a ④imatinib, denosumab, bisphosphonate	

Giant cell tumor(GCT)

	➲extragnathic GCT	➲gnathic GCT
❶somatic mutation不同	①H3F3A(a histone protein) ②IDH1,2(isocitrate dehydrogenase 1,2)	①TRPV4 ②KRAS ③FGFR1
❷clinic (extragnathic➔較痛，較老)	①epiphyses of long bone ②pain➔more likely ③1-2 decade older on average	①jaws ②pain➔less likely ③young on average
❸micro(extragnathic➔giant cell➔核較多，size較大)	①↑cellular stroma ②↑nuclei no. ③giant cell larger➔↑uniform distributed 	①multinucleated giant cell ②proliferating mesenchymal cell ③RBC extravasation 
❹biologic behavior	extragnathic(較嚴重)➔①↑aggressive ②↑recurrence rate ③pulmonary meta(benign) ④malignant transformation(~2%)	

13. **Florid cemento-osseous dysplasia** tends to affect:
(A) white women in 30s
(B) Hispanic men over 60s
(C) black men under 30s
(D) black women over 40s

14. A 48-year-old **black woman** has multiple **asymptomatic**, radiopaque masses in the **mandible and maxilla**. **No bony expansion** is noted. The most likely diagnosis is:
(A) central cementifying fibromas
(B) florid cemento-osseous dysplasia
(C) periapical cemento-osseous dysplasia
(D) fibrous dysplasia

15. What is the most likely clinical diagnosis for the patient with **neither clinical swelling nor painful sensation** receiving the panoramic radiographic examination as shown in the figure below?

(A) florid cemento-osseous dysplasia
(B) cemento-ossifying fibroma
(C) medication-related osteonecrosis of jaw
(D) central squamous cell carcinoma

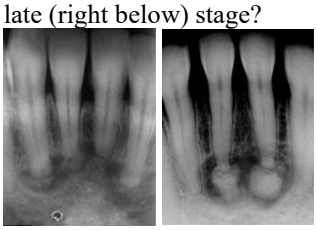
16. Following question 15, what is the most likely clinical diagnosis if the **patient with breast carcinoma having long-term medication of bisphosphonate** having **bilateral ulcerated, painful swellings with pus discharge**?
(A) florid cemento-osseous dysplasia
(B) cemento-ossifying fibroma
(C) medication-related osteonecrosis of jaw
(D) central squamous cell carcinoma

Florid cemento-osseous dysplasia➔multiple RL+RO/multi-focal RO➔2-4 quadrants of jaws

❶restricted to jaws	❷majority>30s	❸female & black predilection	❹mandible>maxilla
❺early/mild➔symptomless(routine X-ray)		❻advanced➔painless expansion(need consistent prosthesis adjust)	

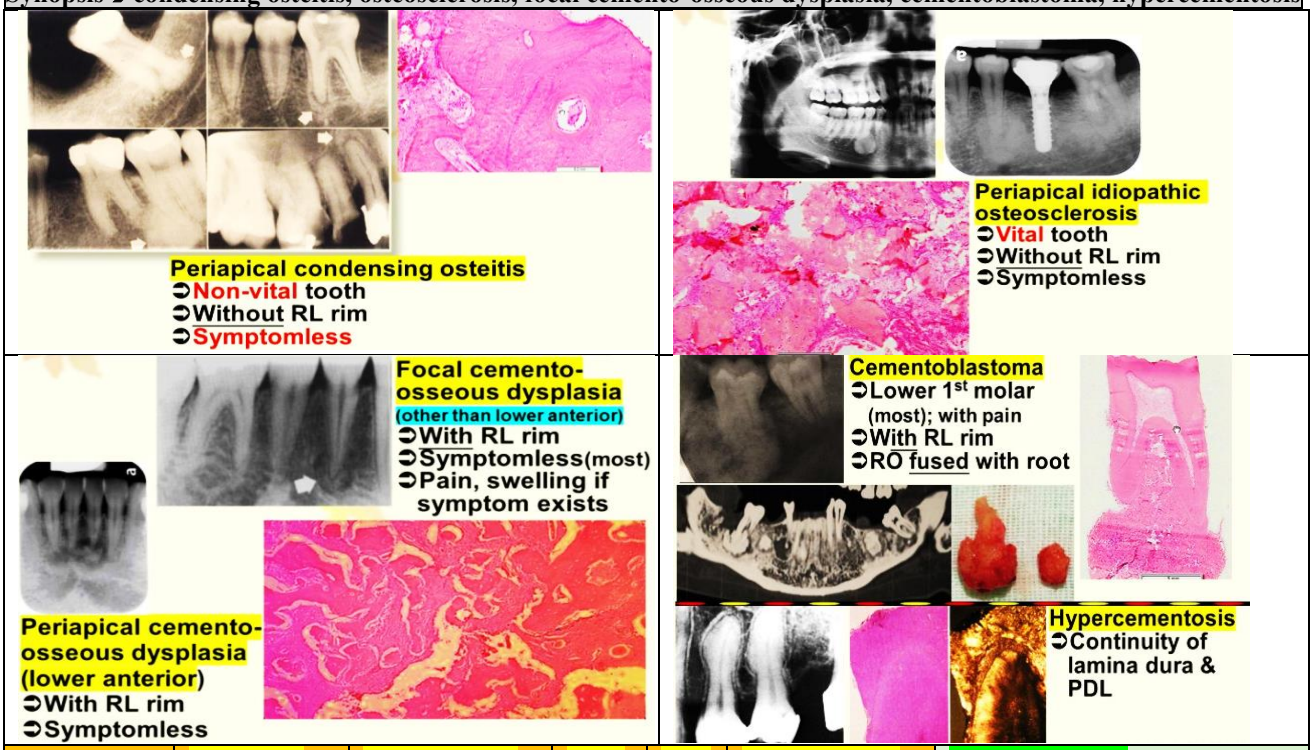
17. **Periapical cemento-osseous dysplasia** is in:
(A) posterior mandible
(B) posterior maxilla
(C) craniofacial bones
(D) anterior mandible

18. What is the disease of the **asymptomatic** patient of the periapical radiographs below suffering from early (left below) and late (right below) stage?



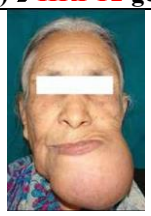
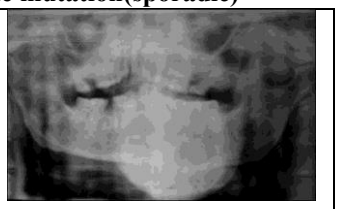
(A) florid cemento-osseous dysplasia
(B) periapical cemento-osseous dysplasia
(C) focal cemento-osseous dysplasia
(D) fibrous dysplasia

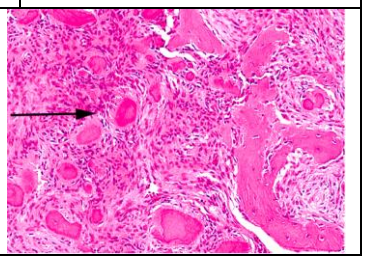
Synopsis➔condensing osteitis, osteosclerosis, focal cemento-osseous dysplasia, cementoblastoma, hypercementosis



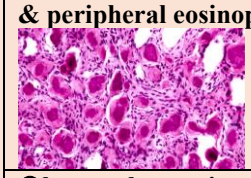
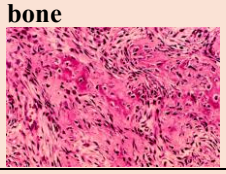
features	condensing osteitis	focal(periapical) osteosclerosis	florid	focal	periapical(單/多)	cementoblastoma	
			cemento-osseous dysplasia				
disease type	inflammatory	idiopathic	fibro-osseous lesions			benign odontogenic tumor	
tooth vitality	non-vital	vital	vital			vital	
RL rim	without	without	with			with(thin)	
tooth position	apical	apical	------		下顎前牙根尖	36/46(fusion with root)(50%)	
symptom	no	no	no			pain	
stage	no	no	early/intermediate/late			no	
age	most young	peak(3rd decade)	中老年	mean 40s	30-50s	20s(1/2 of cases)	30s(3/4 cases)

Cemento-ossifying fibroma(COF)/Ossifying fibroma(true tumor➔osteogenic)➔HRPT2 gene mutation(sporadic)

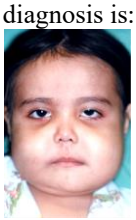
➲clinic➔solitary(most)➔mandible>maxilla(左圖) ❶like focal cemento-osseous dysplasia(x-ray & micro) ❷multiple synchronous(rare) ①isolated ②hyperparathyroidism-jaw tumor syndrome (1)parathyroid adenoma/carcinoma (2)jaw ossifying fibroma (3)renal cyst (4)Wilms tumor	➲radiograph ❶UL-RL(small) ❷mixed RL+RO ❸RO(右圖) ❹ML-RL➔ with ABC		

➲micro ❶most➔①WD(unencapsulated) ②capsule(some) ❷①osteoid(woven bone) ②bone(trabeculae/lamellar) ❸acellular(cementum-like) spherule➔brush border(radiating collagen fiber) blend into connective tissue(like Sharpey fiber within PDL) ❸osteoblastic rimming ❹heterogeneous mineralized product➔differ FD(more uniform osseous pattern) ❺combined with CGCG(COF+CGCG)	

Juvenile ossifying fibroma(Juvenile aggressive ossifying fibroma)

➲2 variants➔❶trabecular ❷psammomatoid>trabecular(in craniofacial skeleton)		
➲[❶MDM2(E3 ubiquitin-protein ligase) gene ❷RASAL1(RAS protein activator like 1) gene amplification]➔ local aggressive➔↑frequency>COF & craniofacial FD		
➲no GNAS/HRPT2 mutation➔distinct from FD & COF	➲often➔❶children ❷adolescents ❸young adult	
➲comparison between psammomatoid & trabecular		
	psammomatoid	trabecular
age range	broader(3 mon-72s)	narrower(1-33s)
mean age	older(~19s)	younger(~12s)
gender	both slight male/no gender predilection	
favor site	paranasal sinus & orbital	jaws
gnathic involvement	both slight favor maxilla	
craniofacial	more frequent	less frequent
radiograph	❶WD-RL/mixed RL+RO(ground glass appearance) ❷sclerotic border(some cases) ❸ML(honeycomb)(may be)	
micro	fibrous stroma➔spherical ossicle(basophilic center & peripheral eosinophilic rim) 	fibrous stroma➔trabeculae of woven bone 
	❶hemorrhage, giant cell➔grossly brown ❷hemorrhagic cystic degeneration➔like ABC	

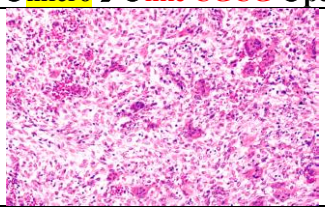
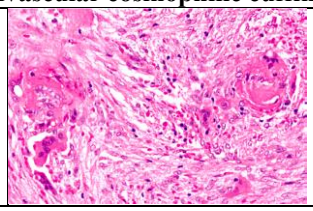
19. A **10-12-year-old** girl is seen in consultation because of **bilateral symmetric painless mandibular expansions (angles, ascending rami & coronoid processes)**. A panoramic radiography is shown as the figure below. The mother of the patient has similar findings. The most likely diagnosis is:

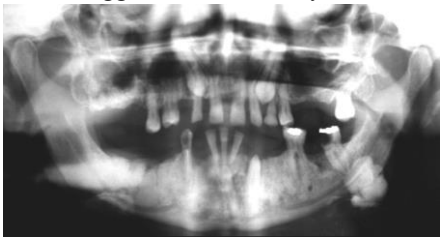
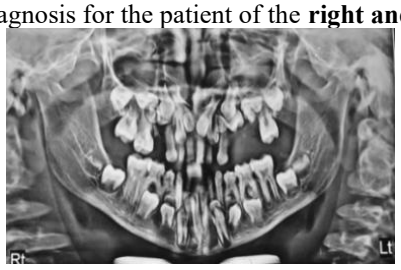
(A) cherubism
(B) cleidocranial dysplasia
(C) nevoid basal cell carcinoma syndrome
(D) Ellis-van Creveld syndrome

Cherubism➔inherited developmental jaw condition[❶autosomal dominant ❷de novo(some)]

➲SH3BP2 gene(chromosome 4p16) mutation➔↑3BP2 adaptor protein stability➔↑signal transduction pathway(gain-of-function)➔↑osteoclastogenesis➔lytic bone lesion
➲mouse model➔macrophage➔↑TNF-α➔inflammation➔口腔共生細菌+幼童牙萌發➔rapid bone remodeling➔ hypothesize primarily affect jaws

➲maxilla tuberosities/entire maxilla(possible)➔V-shaped palatal arch		
➲rib involvement(reported)	➲bilateral ML-RL(most)	➲UL-RL(less common; may be)
➲blood test➔❶serum Ca^{2+} & P^{3-}➔normal ❷↑serum alkaline phosophatase➔active disease		
➲children(bilateral giant cell jaw lesions)➔lab data➔not suggest hyperparathyroidism➔ ❶cherubism(most likely) ❷others ①Ramon syndrome ②Jaffe-Campanacci syndrome ③RASopathies(Noonan syndrome, neurofibromatosis type 1)		
➲most➔regress spontaneous after puberty➔4th decade➔normal facial feature		
➲micro➔❶like CGCG ❷perivascular eosinophilic cuffing(28%)		
		

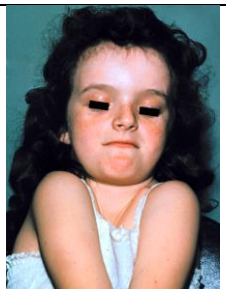
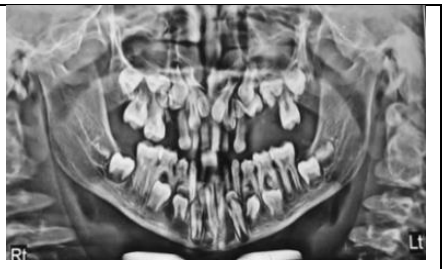
20. Please suggest the most likely clinical diagnosis for the patient of the **right and left panoramic radiography** respectively.

(A) right: Papillion Levere syndrome; left: Cushing syndrome
(B) right: Gardner syndrome; left: cleidocranial dysplasia
(C) right: Cushing syndrome; left: Papillion Levere syndrome
(D) right: cleidocranial dysplasia; left: Gardner syndrome

21. A 19-year-old woman, diagnosed with **cleidocranial dysplasia**, has **absent clavicles and a mushroom-shaped skull**. Which of the following conditions is she also most likely to have?
(A) taurodontism
(B) supernumerary teeth
(C) pegged lateral incisors
(D) large pulp chambers

Cleidocranial dysplasia(Cleidocranial dysplasia)

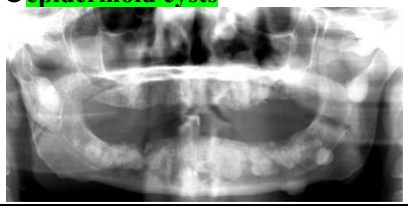
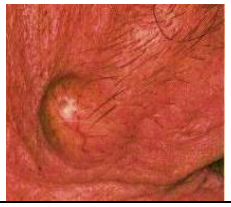
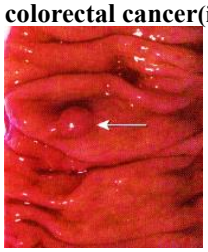
➲early craniofacial signs(❶↔❹)		
❶extraoral sign(左圖) ①frontal bossing ②hypoplastic midface ③prognathic mandible ④quatermoon-physiognomy		
❷intraoral sign➔①erupted 2nd molars ②spacing of lower incisors		
❸panoramic sign(右圖)➔①supernumerary germ ②parallel ramus		
❹cephalometric sign➔①nasal bone missing ②kyphotic(後凸) sphenoid bone ③marked round gonion ④wormian bone		
➲RUNX2(CBFA1) gene(chromosome 6p21) mutation ❶autosomal dominant ❷spontaneous(40%) ❸autosomal recessive form & germline mosaicism(possible)		
❹osteoblastic differentiation, chondrocyte maturation, bone formation ①membranous bone(clavicle, skull, flat bone) ②endochondral ossification ❺odontogenesis ①odontoblast differentiation ②enamel organ formation		

③dental lamina proliferation	
anatomic region	**features**
craniofacial/oral	large skull frontal & parietal bossing brachycephaly ocular hypertelorism nose with depressed bridge & broad base delayed closure of sutures & fontanels wormian bones small/absent paranasal sinuses narrow, high-arched palate; cleft palate numerous unerupted/misshapen(畸形) permanent & supernumerary teeth retention of primary dentition; delayed eruption of permanent dentition mandible➔prognathism, coarse trabeculation, narrow & parallel-sided rami, slender & pointed coronoid processes with distal curvature, patent(明顯) symphysis hypoplastic maxilla
thorax	hypoplastic, discontinuous, absent clavicles hypoplastic scapulae narrow upper thorax absent ribs
pelvis	hypoplastic iliac wings widening of the pubic symphysis and sacroiliac joints delayed ossification of the pubic bone
extremities	genus valgus(knock knees) pes planus(flat feet) brachydactyly tapered fingers & short, broad thumbs short terminal phalanges long second metacarpals short and deformed middle phalanges
other	short stature scoliosis(脊柱側凸)

22. Which of the following is the most **serious component** of **Gardner syndrome**?
(A) mandibular odontomas
(B) multiple osteomas
(C) teeth hypercementosis
(D) intestinal polyposis

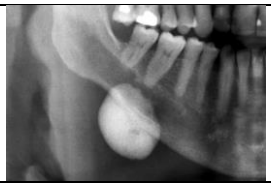
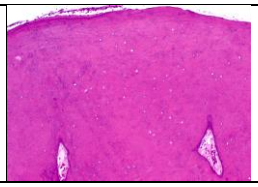
23. Which of the following diseases are most likely having **intestinal polyposis**?
(1) Gardner syndrome (2) cleidocranial dysplasia (3) Addison disease (4) Peutz-Jeghers syndrome
(A) only 1,2
(B) only 2,3
(C) only 2,4
(D) only 1,4

Gardner syndrome

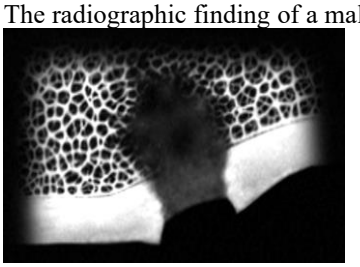
➲frequency➔~1:1,000,000	➲autosomal dominant	➲osteoma precedes intestinal polyposis➔10s➔early Dx
➲extracolonic manifestations ❶osteomas ❷dental anomalies(①odontoma ②supernumerary teeth) ❸epidermoid cysts  		➲familial adenomatous polyposis➔intestinal adenomatous polyp(hundreds-thousands)➔premalignancy➔~100% colorectal cancer(if untreated) 

Osteoma➔mature compact/cancellous bone➔1^0 involve craniofacial skeleton

➲paranasal sinus osteoma➔~gnathic lesion	➲multi-lesion➔Gardner syndrome

➲3 types ❶bone surface(①periosteal ②peripheral ③exophytic) ❷within medullary bone(endosteal/central) ❸extraskeletal[within muscle/dermis(osteoma cutis)]		

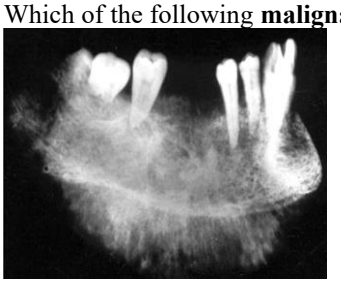
24. The radiographic finding of a malignant neoplasm shown in the **figure below** is so called:



(1) sunray (2) periosteal reaction (3) bony spicules (4) Codman triangle
(A) 1,2
(B) 2,4
(C) 1,3
(D) 1,4

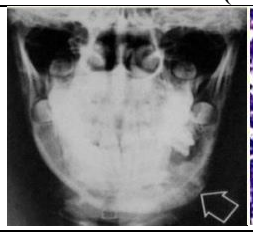
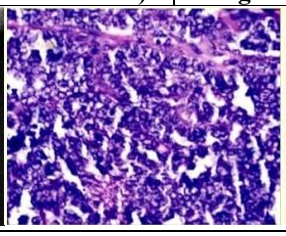
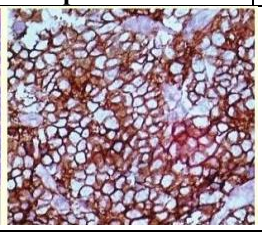
25. Following question 23, malignant neoplasia shown in the **figure** in question 23 are most likely:
(1) osteosarcoma (2) Ewing sarcoma (3) squamous cell carcinoma (4) lymphoma
(A) 1,2
(B) 2,4
(C) 1,3
(D) 1,4

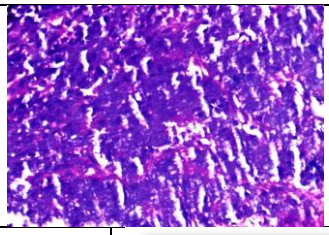
26. Which of the following **malignant tumors** most likely show **radiographic pattern** as shown in the figure below?



(1) melanoma (2) osteosarcoma (3) lymphoma (4) Ewing sarcoma
(A) only 1,2
(B) only 3,4
(C) only 2,4
(D) only 1,4

Ewing sarcoma(EW)➔❶2nd most[after osteosarcoma(1st most)] bone malignancy ❷$1^0$ pediatric bone malignancy

➲type ❶classical EW of bone(long bone, pelvis, rib)(jaw/craniofacial➔1-2%) ❷extraosseous EW(primary case rare) ❸primitive neuroectodermal tumor(EW with neuronal differentiation) ❹Askin tumor(small round cell tumor of chest wall)➔same tumor type	➲clinic➔❶pain, swelling, fever, leukocytosis, (↑ESR➔advanced disease) ❷penetrate cortex➔soft tissue mass over affected bone ❸tooth displacement(mobility), root resorption, paresthesia
➲histogenesis ❶(past)neural crest ❷(current)➔mesenchymal stem cell(MSC)➔neural differentiation➔molecular level➔EWS::FLI1 fusion protein (>85%)[RNA-binding protein EWS fusion with ETS family transcription factor(FLI1, ERG, ETV1, ETV4, FEV)]	
➲Ewing-like sarcoma➔(now)distinct entities➔undifferentiated small round cell sarcomas of bone & soft tissue ❶EWSR1-non-ETS fusion ❷CIC-rearranged sarcoma ❸sarcoma with BCOR genetic alteration	
➲most➔adolescent(median➔15s) ➲slight male predominance ➲majority➔white ➲mandible>maxilla	
  	➲radiograph➔❶PD-RL(most) ❷mixed RL+RO(possible) ❸onionskin periosteal reaction(①long bone EW 常見 ②jaw EW少見) ✠Codman triangle & sunray/hair-on-end speculation; laminar periosteal new bone formation(similar to osteomyelitis)-牙放課本

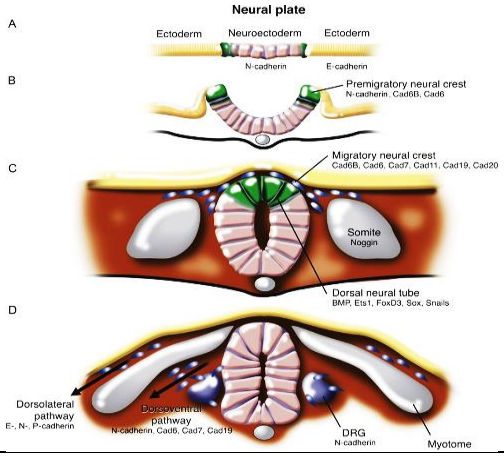


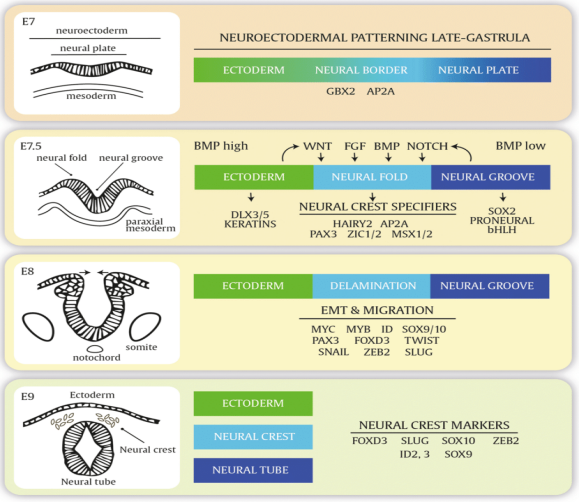
➲micro➔small blue round cell
❶IHC
①CD99(MIC2)➔membrane stain
②NKX2.2➔nuclear stain
❷PAS➔intra-cytoplasmic glycogen

➲most metastatic sites➔①lung ②bone

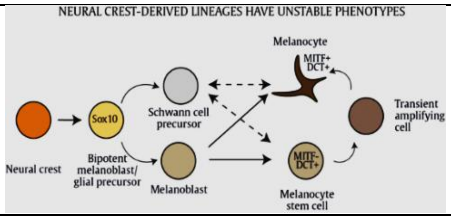
➲extrapulmonary meta➔prognosis worse

補充➲neuroectoderm➔derived from ectoderm
➔神經系統發展第一步





➲neural crest➔multipotent stem cell➔side of neural tube proximal to epidermal layer after neurulation➔migrate throughout embryo ➔large range of cell type



Osteosarcoma➔❶central(most)➔medullar cavity ❷[(surface)juxacortical也有)]

➲most➔bone malignancy | ➲clinic➔swelling & pain(most)

➲risk factor➔❶radiation ❷alkylating agent ❸Paget disease of bone
❹heritable syndrome(①Li-Fraumeni syndrome ②retinoblastoma ③Rothmund-Thompson syndro ④Bloom syndrome ⑤Werner syndrome ⑥Diamond-Blackfan anemia)

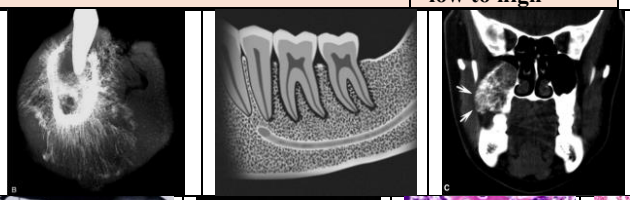
➲genetic profile➔❶TP53 ❷RB1 ❸MDM2 ❹CDKN2A ❺ATRX ❻DLG2

➲extragnathic➔bimodal age distribution➔[❶major peak(adolescence) ❷lesser peak(adult>60s➔Paget disease of bone/irradiation)]

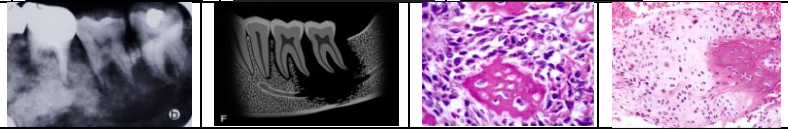
➲gnathic(~6%)➔❶no gender predilection ❷broad age range ❸peak(3rd↔5th decade)
❹mean age(~35-41s) [~2 decade>mean age of long bone lesion]

type		grade
❶central(intramedullary)	conventional ①osteoblastic ②chondroblastic ③fibroblastic	high
	other rare variants ①telangiectatic ②small cell ③epithelioid ④giant cell-rich ⑤osteoblastoma-like ⑥chondroblastoma-like	high
	low-grade central	low
❷surface(juxtacortical)	parosteal	low
	periosteal	intermediate
	high-grade surface	high
❸extraskeletal		low to high

➲radiograph➔mixed RL+RO/PD-RL
❶cortical destruction(expansion)
❷periosteal reaction
①sunburst/sunray(~25%➔jaw)
②Codman▲(▲periosteum elevation)
③spiculated new bone

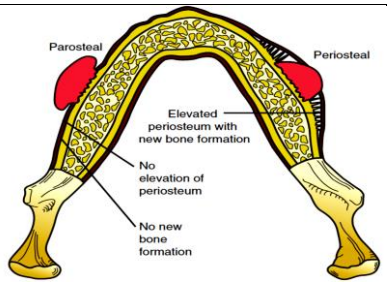


❸spiking root/floating tooth
❹Garrington sign(symmetric PDL widening)➔clue for early diagnosis



➲micro
❶conventional type(>90%)➔①osteoid(右上第三張圖)(osteoblastic) ②chondroid(最右上圖)(chondroblastic)
③fibrous(collagen) tissue(fibroblastic)
❷low-grade➔uniform, round/spindle-shaped cell➔minimal cellular atypia
❸high-grade➔marked pleomorphic cell with bizarre nuclear & cytoplasmic shape
❹①IHC➔MDM2 & CDK4
②FISH➔MDM2 amplification➔d.d. low-grade from benign fibro-osseous lesion & benign bone tumor
❺chondroblastic➔①almost malignant cartilage(foci of osteoid)➔osteosarcoma rather than chondrosarcoma
②lack isocitrate dehydrogenase(IDH)1,2 gene mutation(such mutation➔chondrosarcoma & chondroma frequent)

➲surface(juxtacortical osteosarcoma)➔3 types(❶↔❸)
❶parosteal(骨膜外面的)
①nodule➔short, broad stalk➔attached cortex
②no periosteum elevation
③no periosteal reaction
④X-ray➔RL line(string sign)➔periosteum between tumor & cortex
⑤low-grade➔low recurrence & metastasis
❷periosteal(骨膜裡面的)➔sessile mass➔↑periosteal reaction
❸high-grade surface osteosarcoma



27. Which one of the following radiographic patterns may be an early sign of **osteosarcoma**?
(A) cotton-wool opacity
(B) ground-glass opacity
(C) radiolucency with scalloped borders
(D) widening of the periodontal ligament space

Post-radiation bone sarcoma➔↑radiation dose➔↑risk➔median dose➔43↔64Gy

➲ RT3↔55-yr後產生➔mean latency period➔~4↔17-yr➔post-irradiation bone/soft tissue sarcoma(0.03↔0.2%)

➲日本原子彈生還者(dose as low as 0.85Gy)➔↑bone sarcoma

➲type➔❶most➔osteosarcoma(49-85%)
❷others
①undifferentiated pleomorphic sarcoma(malignant fibrous histiocytoma)
②fibrosarcoma
③chondrosarcoma

28. Which of the following is most likely associated with **chronic osteomyelitis**?
(1) Paget's disease (2) radiation treatment involving bone (3) long term usage of bisphosphonates (4) osteopetrosis
(A) only 2,3
(B) only 1,3
(C) only 1,2,3
(D) 1,2,3,4

29. Which of the following does *not* describe the **aneurysmal bone cyst**? It is:
(A) radiographic honey comb appearance
(B) a true cyst
(C) associated with other primary bony lesions
(D) usually treated with curettage or enucleation

Aneurysmal bone cyst(ABC)➔no epithelial lining➔pseudocyst➔1^0(de novo)/2^0[associate➔其他bone lesions(20-30%)]

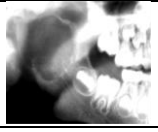
➲pathogenesis➔❶reactive ❷traumatic ❸vascular malformation
❹neoplasm➔disrupt osseous hemodynamic➔hemorrhage & osteolysis

➲cytogenetic➔1^0 ABC➔neoplastic
❶translocation of USP6(ubiquitin-specific protease 6; Tre-2/TRE17)(chromosome 17p13)➔[t(16;17)(q22;p13)](few craniofacial lesions)➔fusion with➔[①cadherin 11(CDH11) ②zinc-finger 9(ZNF9) ③collagen 1A1(COL1A1) ④thyroid receptor-associated protein(TRAP150) ⑤osteomodulin gene(OMD)]
❷downstream dysregulation of BMP(bone morphogenetic protein)➔disrupt osteoblastic maturation
❸nuclear factor-kappa B(NF-κB)-mediated induction of matrix metalloproteinase(MMP)➔angiogenesis & inflammation

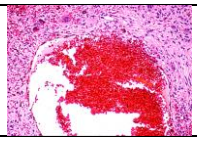
➲long bone/vertebrae➔<30s | ➲jaws(2%) | ➲most➔rapid enlarging swelling

➲gnathic➔❶young patient(peak➔2nd decade) ❷no sex/slight female predilection ❸mandible>maxilla
❹posterior jaws[mandible➔①ramus & posterior body ②condyle & coronoid process(infrequent)]

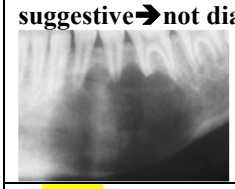
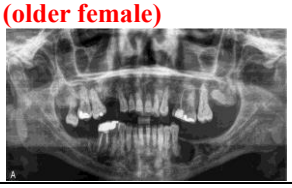
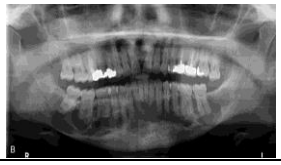
➲radiograph➔WD/PD-UL/ML-RL
❶marked cortical expansion & thinning
❷ballooning/blow-out distention
❸small RO foci➔reactive bone trabeculae➔within RL



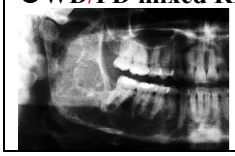
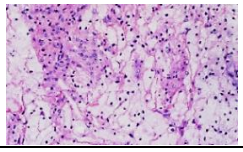
➲micro➔blood-filled space➔no endothelial-epithelial lining
❶fibroblastic/myofibroblastic spindle cell
❷multinucleated giant cell, osteoid, woven bone
❸associate➔①COF(cemento-ossifying fibroma) ②FD ③CGCG



Simple bone cyst(Traumatic bone cyst)➔pseudocyst(no epithelial lining)

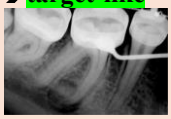
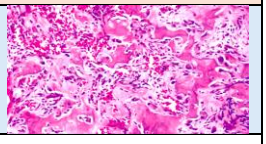
➲empty/fluid-containing bone	➲subset of extragnathic case➔FUS::NFATC2/EWSR1::NFATC2 fusion
➲radiograph(1↔10cm)➔ ❶scallop between roots of teeth➔ suggestive➔not diagnostic 	❷WD-UL RL(most), PD & ML-RL(possible) ❸most➔solitary(multifocal reported) ❹associate➔cemento-osseous dysplasia (older female)  
➲clinic ❶mandible predominant➔①(pre)molar ②symphysis ❷maxilla➔anterior region ❸most➔young patient➔peak➔2nd decade ❹jaw➔no gender bias(BUT extragnathic➔male predilection)	

Central xanthoma of jaws➔reactive process/benign neoplasm➔lipid-laden macrophages[xanthoma(foamy)cell]

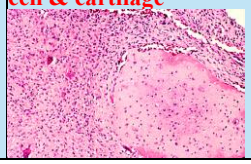
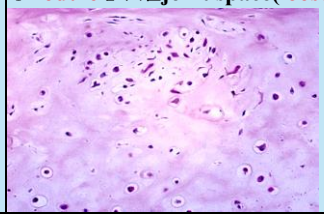
➲local trauma/hemorrhage➔lipid leak from blood vessel➔lipid phagocytosis	
➲not metabolic/endocrine disorders(hyperlipidemia/DM)➔unlike ①soft tissue xanthoma ②extragnathic bone	
➲clinic➔❶broad age range(peak➔2nd-3rd decade) ❷no gender predilection ❸ mandible(posterior)>maxilla	
➲radiograph➔1-11cm(median 2cm) ❶solitary ❷WD/PD(pouch out/sclerotic)-UL/ML RL ❸WD/PD mixed RL+RO(ground-glass) 	➲micro➔abundant foamy cell ❶IHC➔CD68(+) ❷CD1a(-), CD207(-)➔not Langerhans cell histiocytosis ❸d.d➔①Erdheim-Chester disease ②lipid reticuloendothelioses 

Osteoblastoma(Giant osteoid osteoma) & Osteoid osteoma

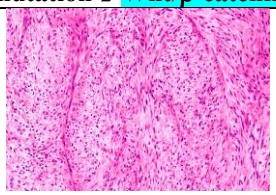
➲osteoid osteoma➔3% all 1^0 bone tumor	➲osteoblastoma➔~1%(rare) of all 1^0 bone tumor
➲osteoid osteoma➔nidus有高密度周邊神經及prostaglandin➔夜間疼痛➔NSAID舒緩(顎外➔較可)	
➲comparison of gnathic osteoblastoma & osteoid osteoma	

	osteoblastoma	osteoid osteoma
clinic	❶mandible predilection➔posterior ❷ 85%<30s ❸slight female predominance ❹2↔4cm➔10cm ❺夜間dull疼痛➔NSAID no舒緩 ❻tender swelling	❶slight mandible➔posterior ❷peak➔2nd↔3rd decade ❸no gender predilection(顎外➔male較多) ❹<1.5/2cm ❺夜間dull疼痛➔NSAID舒緩(顎外➔較會) ❻more limited growth potential
radiograph	❶WD/PD-round to oval RL with patchy mineralization ❷surrounding sclerosis➔less prominent ❸most➔medullary bone[periosteal/ intracortical origin(possible)]	❶WD-round to ovoid RL(nidus<1.5cm)➔small central RO ➔target-like  ❷surrounding sclerosis➔variable ❸most➔cortical bone(medullary/periosteal possible)➔ periosteal reaction(occasion)
micro	❶bony trabeculae➔prominent osteoblastic rimming & osteoclast ❷vascularity➔osteoblastoma>osteoid osteoma ❸periphery zone of dense sclerotic bone➔osteoid osteoma>osteoblastoma ❹FISH➔FOS/FOSB rearrangement➔ neoplastic➔variant of same lesion	
➲aggressive osteoblastoma(d.d. low-grade osteosarcoma➔difficult) ❶atypical histopathologic feature➔①large(epithelioid) osteoblast ②mitosis ③lacelike osteoid(blue bone matrix) ❷local aggressive behavior ❸>30s ❹severe pain ❺radiographic larger(>4 cm)		

Synopsis➔chondroma, chondromyxoid fibroma, synovial chondromatosis

	chondroma	chondromyxoid fibroma	synovial chondromatosis
genetic	❶IDH1,2(isocitrate dehydrogenase 1,2 gene) mutation ❷COL2A1 &YEATS2 mutation/結構改變(chondrosarcoma也有) ✪CDKN2A amplification➔分辨chondrosarcoma/chondroma	❶↑glutamate receptor metabotropic-1 gene (GRM1)(6q24.3)➔tumor development	❶FN1(fibronectin 1) &/or ACVRA2(activin receptor 2A) gene rearrangement
others	❶Ollier disease(enchondromatosis)➔單側appendicular skeleton ❷Maffucci syndrome (enchondromatosis)➔extraskeletal angioma ❸micro➔區分chondroma & low-grade chondrosarcoma of jaws➔difficult	❶mandible>maxilla ❷myxoid stroma with giant cell & cartilage 	❶nodule➔atypia➔low-grade chondrosarcoma ❷3 stages(nodule position) ①(osteo)cartilaginous nodule➔synovial lining ②nodule➔(1)detach在joint space (2)在synovial membrane ③nodule➔只在joint space(loose bodies) 

Desmoplastic fibroma➔jaws➔associate tuberous sclerosis

➲local aggressive	➲<30s	➲most➔[❶mandible ❷femur ❸pelvis ❹tibia ❺radius]
➲counterpart of soft tissue fibromatosis(desmoid tumor)➔CTTNB1 & APC mutation➔Wnt/β-catenin pathway		
➲micro➔potentially malignant ❶↑fibroblast➔interlacing fascicle➔like well-differentiated fibrosarcoma ❷IHC ①smooth muscle(muscle specific) actin(+) ②Ki-67≤5% ③β-catenin[variable(+)]		

Chondrosarcoma

➲frequency➔❶half as osteosarcoma ❷2× as Ewing sarcoma

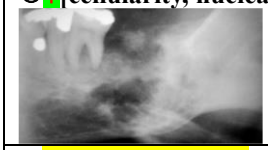
➲11%➔all 1^0 malignant bone tumor➔jaws rare[(~1-12%)H&N; (0.1%)all HN malignancies]

➲↑risk➔[❶Ollier disease ❷Maffucci syndrome]➔associate IDH1,2(isocitrate dehydrogenase 1,2) gene mutation(such mutation also frequent in chondroma & chondrosarcoma)

➲site➔❶maxilla(anterior) ❷mandible(posterior) | ➲pain➔unusual➔contrast to osteosarcoma

➲radiograph➔❶PD RL+RO foci ❷root resorption ❸symmetric PDL space widening

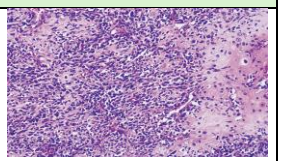
➲micro➔grade I-III(most gnathic chondrosarcoma➔grade I/II)
❶low-grade➔like normal cartilage➔difficult d.d. chondroma
❷↑grade
①↓cartilaginous matrix
②↑[cellularity, nuclear size, nuclear pleomorphism, bi(multi)nucleate chondrocyte, cellular spindling, mitosis, necrosis]




➲4 variants(❶↔❹)
❶clear cell➔low-grade➔difficult d.d. metastatic clear cell carcinoma
❷dedifferentiated➔high-grade➔mixture of well-differentiated & high-grade sarcoma
❸myxoid➔soft tissue tumor(central possible)➔↑clear vacuolated cell/↑cell with eosinophilic cytoplasm in mucoid material

❹mesenchymal(2-9% of all chondrosarcoma types)➔high-grade(aggressive)➔2nd-3rd decade➔jaw often(22-27% of cases); soft tissue(30-60% of cases)
①HEY1-NCOA2 fusion(~90%); IRF2BP2-CDX1 fusion(possible); NO IDH1(isocitrate dehydrogenase 1) mutation
②clinic➔(1)swelling (2)pain(often short duration)
③radiograph➔PD-RL with(out) calcification(maxilla➔predominant RO)

④2 distinct micro elements(biphasic)
(1)well-differentiated cartilaginous nodule(chondroma to low-grade chondrosarcoma)➔S100 (+)
(2)undifferentiated small spindle/round cell[branching vascular pattern➔like solitary fibrous tumor("hemangiopericytoma"); rhabdomyosarcoma, Ewing sarcoma, lymphoma, metastatic small cell carcinoma]➔CD99(+), SOX9(+), NKX3.1(+)



30. Which of the following features for mesenchymal chondrosarcoma is *true*? It
(A) is an intraosseous neoplasm only
(B) shows biphasic microscopical features
(C) is a low-grade malignancy
(D) usually occurred in the 7-8th decade

Metastatic tumors to oral cavity➔1% of all oral malignancies[❶bone meta(0.1%) ❷soft tissue meta(0.01%)]

➲**metastasis(meta) to oral soft tissue**
❶meta to H&N from lower part of body➔blood-borne(should be filtered out by lung)➔Batson plexus(valveless vertebral venus plexus)➔retrograde of tumor cell(bypassing lung filtration)
❷site➔①most➔gingiva(54%) ②next most➔tongue(22.5%)
❸lung carcinoma(men)➔1/3 of all oral soft tissue meta➔followed(renal carcinoma & melanoma)
❹breast carcinoma(women)➔25% of all cases➔followed (malignacies of genital organs, kidney, lung & bone)
❺25% oral soft tissue meta➔1st sign of malignancy

➲**metastatic carcinoma(most common cancer involving bone)**
❶most common 1^0 sites for carcinoma meta to bone(①breast ②lung ③thyroid ④prostate ⑤kidney)
❷most common bone be meta(①vertebrae ②rib ③pelvis ④skull)

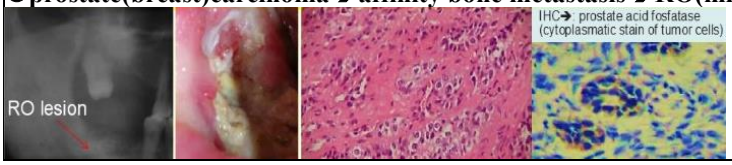
➲**meta to jaws(stage IV disease)**➔hematogenous route
❶jaw meta➔mandible(molar)
❷Numb-chin syndrome
①mental nerve involve
②lower lip paresthesia
❸radiograph
①PD/moth-eaten RL(most)
②others➔like PAP/periodontal disease, cortical erosion, pathologic fracture, PDL widening
❹bone scintigraphy➔sensitive to detect bone meta

➲**IHC markers(A-P)**➔(A)stat6 (B)TFE3 (C)CK20 (D)CD117 (E)CD1a (F)TTF1 (G)MDM2 (H)S100 (I)HMB45 (J)CD3 (K)bcl-2 (L)CD34 (M)HHV-8 (N)CK (O)CK19 (P)CK7 (FISH➔fluorescence in situ hybridization)
➲**Burkitt lymphoma**➔almost 100% Ki67
➲**multiple myeloma**➔kappa/lambda Ab

	Histopathological diagnosis	IHC marker
1	Solitary fibrous tumor	A, K, L
2	Alveolar soft part sarcoma	B
3	Low grade osteosarcoma	G
4	Adenoid cystic carcinoma	D
5	Merkel cell carcinoma	C
6	Metastatic lung carcinoma	F
7	Melanoma	H, I
8	Langerhans cell histocytosis	E, H
9	Pleomorphic adenoma	H
10	T-cell lymphoma	J
11	Neurofibroma, schwannoma (neurilemmoma)	H
12	Kaposi sarcoma	M
13	Squamous cell carcinoma	N
14	Organ of Chieviz	O
15	Salivary gland tumors	P
16	Odontogenic tumors	O
17	Nevus	H, I

	Histopathological diagnosis	FISH marker
1	Langerhans cell histiocytosis Melanoma	B-raf
2	Fibrous dysplasia	GNAS
3	Clear cell carcinoma	EWSR1
4	Mucoepidermoid carcinoma *vs* glandular odontogenic cyst	MAML2
5	Pleomorphic adenoma	PLAG1
6	Odontogenic keratocyst Pindborg tumor	PTCH1

➲**prostate(breast)carcinoma**➔affinity bone metastasis➔RO(mixed RL+RO)



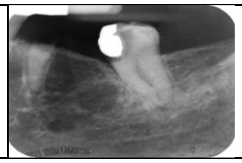
✪**FISH marker**➔**BRAF**
❶Langerhans cell histiocytosis
❷melanoma
❸ameloblastma
❹ameloblastic (fibro)sarcoma

Focal osteoporotic marrow defect➔hematopoietic marrow➔RL➔not pathologic➔confuse with intraosseous neoplasm

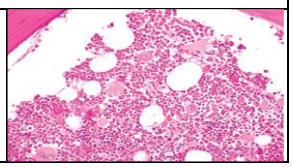
➲**pathogenesis**
❶aberrant bone regeneration after tooth extraction
❷persistence of fetal marrow
❸marrow hyperplasia due to ↑RBC demand

➲**clinic**
❶adult female(~75%)
❷posterior mandible(~70%) ❸most➔edentulous area
❹asymptomatic ❺nonexpansile

➲**WD-RL with fine central trabeculation**



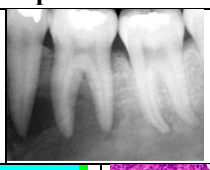
➲**cellular hematopoietic &/or fatty marrow**



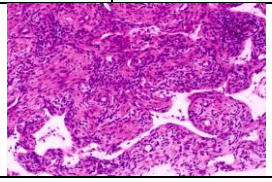
Massive osteolysis(Gorham disease)➔destroyed bone➔replaced by vascular proliferation➔dense fibrous tissue

➲**proposed mechanism(no underlying metabolic/endocrine imbalance)**
❶trauma-induced➔①proliferation of vascular granulation tissue ②activation of previous silent hamartoma
❷IL-6 mediated ↑osteoclastic activity
❸VEGF & PDGF(platelet-derived growth factor) mediated lymphangiogenesis
❹thyroid C cell agenesis/dysfunction
❺dilated vessel➔↓blood flow➔hypoxia & ↓pH➔活化hydrolytic enzyme➔bone resorption

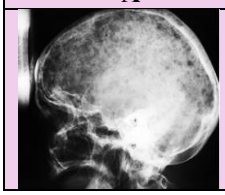
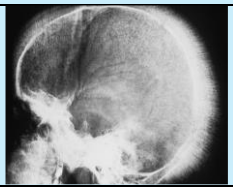
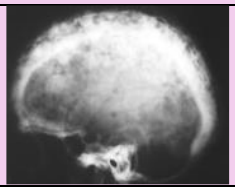
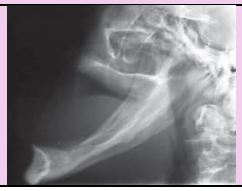
➲**clinic**➔trauma(~50%)
❶children & young adult predilection
❷gnathic➔mandible(most)
❸early➔RL foci➔coalesce➔enlarge➔[①lamina dura loss ②cortex thinning]➔bone loss



➲**micro**➔early➔vascular proliferation{❶blood vessel &/or ❷[lymphatic vessel D2-40(+)] predominate} intermixed with fibrous tissue & chronic inflammatory cell



Synopsis➔radiographic pathology	
mixed RL/RO lesion➔poorly demarcated borders	
medication-related osteonecrosis of jaw(MRONJ)	exposed necrotic bone; most often associated with bisphosphonate drug
osteomyelitis	with sequestrum formation/with sclerosing type; often painful
metastatic carcinoma	esp., prostate & breast carcinomas; may be painful
osteosarcoma/chondrosarcoma	may be painful
mixed RL/RO lesion➔multifocal/generalized	
florid cemento-osseous dysplasia	intermediate-stage lesion; esp. middle-aged black women; usu. mandible
medication-related osteonecrosis of jaw(MRONJ)	exposed necrotic bone; most associated with bisphosphonate drug
Paget disease of bone	in older patients; more common in maxilla
ground glass RO	
fibrous dysplasia	onset usu. younger patient
hyperparathyroidism	may cause loss of lamina dura
central xanthoma of jaws	reactive process/benign; lipid-laden macrophage[xanthoma(foamy)cell]
cotton wool RO	
cemento-osseous dysplasia	esp., middle-aged black women; usu. mandible
Paget disease of bone	in older patients; more common in maxilla
Gardner syndrome	multiple osteomas; epidermoid cysts; GI polyp➔malignant change; hereditary
gigantiform cementoma	hereditary; facial enlargement may be present
sunburst (ray) RO	
osteosarcoma	often painful; usu. young adult
intraosseous hemangioma(教課書 5th p. 549)	esp. younger patient
odontogenic myxosma	large lesion may be
onion-skin RO	
proliferative periostitis	younger patient; often associate nonvital tooth; best seen with occlusal radiograph
Ewing sarcoma	young children
punch-out RL	
multiple myeloma	painful; in older adults; “punched-out” lesions
Langerhans cell histiocytosis	histiocytosis X; usu. children/young adults
central xanthoma of jaws	reactive process/benign; lipid-laden macrophage[xanthoma(foamy)cell]

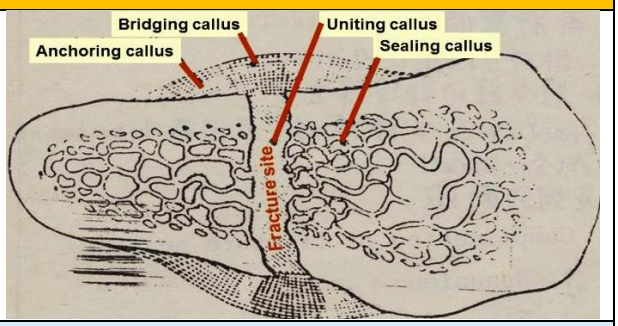
A	B	C	D	E
				

31. Which of the lateral skull images **A-E** above is most likely respectively for **(31-1) Paget disease of bone; (31-2) sickle cell anemia/thalassemia; (31-3) multiple myeloma/Langerhans cell histiocytosis; (31-4) acromegaly; (31-5) osteopetrosis**?

➲bone fracture healing(補充)

❶blood clotting & hematoma formation(6-8hr)
❷organization of hematoma(10-day complete)
①fibrin
②phagocytic activity
③granulation tissue
❸fibrous callus formation

❹primary bony callus formation(10-30-day) complete(右圖)
①stages of primary bony callus
(1)anchoring callus (2)sealing callus
(3)bridging callus (4)uniting callus
②low calcium➔no radiographic image



❺secondary bony callus formation(20-60-day)
①irregular bone➔influx of calcium
②radiographic image
③removal of cast(4-5-wk for jaw bones)

❻reconstruction & remodeling
①alignment to stress
②removal of excess

Chapter 14: Bone Pathology

1. Which one of the following is not a true cyst because it is not lined by epithelium?
A. Epidermoid cyst
B. Nasopalatine duct cyst
C. Oral lymphoepithelial cyst
D. Periapical cyst
E. Simple (traumatic) bone cyst

2. Failure of eruption of the permanent teeth is a clinical feature of:
A. cleidocranial dysplasia
B. Gardner syndrome
C. hemifacial hyperplasia
D. multiple endocrine neoplasia type 2B
E. thalassemia

3. A patient with a jaw tumor diagnosed as a central giant cell granuloma should be evaluated to rule out the possibility of:
A. hyperparathyroidism
B. multiple sclerosis
C. stomach cancer
D. systemic lupus erythematosus
E. ulcerative colitis

4. What is the inheritance pattern of cherubism?
A. Autosomal dominant
B. Autosomal recessive
C. X-linked dominant
D. X-linked recessive
E. It is not hereditary

5. Which of the following types of fibro-osseous lesions of the jaws is most often encountered by dental practitioners?
A. Cemento-osseous dysplasia
B. Familial gigantiform cementoma
C. Fibrous dysplasia
D. Juvenile active ossifying fibroma
E. Ossifying fibroma

6. *Café au lait* pigmentation may be associated with which one of the following conditions?
A. Cherubism
B. Hypohidrotic ectodermal dysplasia
C. Polyostotic fibrous dysplasia
D. Secondary hyperparathyroidism
E. Sickle cell trait

7. Which one of the following is NOT associated with Paget's disease of bone?
A. Autosomal dominant or X-linked recessive inheritance pattern
B. Bone pain
C. Bony enlargement
D. "Cotton-wool" radiographic pattern
E. Increased risk of osteosarcoma

8. Precocious puberty may be a feature of:
A. cleidocranial dysplasia
B. florid cemento-osseous dysplasia.
C. Gardner syndrome
D. McCune-Albright syndrome
E. osteopetrosis

9. Which one of the following conditions occurs most frequently in black women?
A. Chronic myelogenous leukemia
B. Paget's disease
C. Periapical cemento-osseous dysplasia
D. Polycythemia vera
E. Polyostotic fibrous dysplasia

10. Which one of the following lesions is characteristically attached to the roots of a tooth?
A. Cementoblastoma

B. Central ossifying fibroma
C. Complex odontoma
D. Fibrous dysplasia
E. Juvenile ossifying fibroma

11. What is typically the most appropriate management for a simple bone cyst of the jaws?
A. Curettage followed by peripheral ostectomy
B. Interferon alfa-2a, alone or in combination with surgical enucleation
C. Intralesional steroid injection
D. Segmental resection
E. Surgical exploration to establish the diagnosis followed by periodic radiographic examination to monitor for resolution

12. The most likely complication of florid cemento-osseous dysplasia is:
A. fracture of the mandible
B. secondary hyperparathyroidism
C. secondary hypocalcemia
D. secondary infection
E. transformation into osteosarcoma

13. Which one of the following radiographic patterns may be an early sign of osteosarcoma?
A. Cotton-wool opacity
B. Dome-shaped radiopacity in the maxillary sinus
C. Ground-glass opacity
D. Radiolucency with scalloped borders
E. Widening of the periodontal ligament space

14. Which one of the following is the most significant feature of Gardner syndrome?
A. Development of colon cancer
B. Development of insulin-resistant diabetes
C. Development of melanoma
D. Disorderly eruption of the teeth
E. Hypercalcemia leading to kidney stones

15. What is the treatment of choice for periapical cemento-osseous dysplasia?
A. Apicoectomy and periapical curettage
B. Broad-spectrum antibiotics
C. Extraction of the involved teeth
D. Root canal therapy
E. No treatment is indicated

16. Microscopically, the bony lesions of cherubism most closely resemble:
A. central giant cell granuloma
B. simple bone cyst
C. odontogenic keratocyst
D. cemento-osseous dysplasia
E. Paget disease

Chapter 14: Bone Pathology➔answers
1. ANS: E
2. ANS: A
3. ANS: A
4. ANS: A
5. ANS: A
6. ANS: C
7. ANS: A
8. ANS: D
9. ANS: C
10. ANS: A
11. ANS: E
12. ANS: D
13. ANS: E
14. ANS: A
15. ANS: E
16. ANS: A

Chapter 15 Odontogenic tumors

Classification of odontogenic tumor

➲tumors of odontogenic epithelium	➲mixed odontogenic tumors	➲tumors of odontogenic ectomesenchyme
❶ameloblastoma & ameloblastoma, unicystic type ①metastasizing(malignant) ameloblastoma ②ameloblastic carcinoma ❷clear cell odontogenic carcinoma ❸adenomatoid odontogenic tumor ❹calcifying epithelial odontogenic(Pinborg) tumor ❺squamous odontogenic tumor	❶ameloblastic fibroma ❷ameloblastic fibro-odontoma ❸ameloblastic fibrosarcoma ❹odontoameloblastoma ❺odontoma ①compound ②complex odontoma ❻primordial odontogenic tumor	❶odontogenic fibroma ①central ②peripheral ❷granular cell odontogenic tumor ❸odontogenic myxoma ❹cementoblastoma

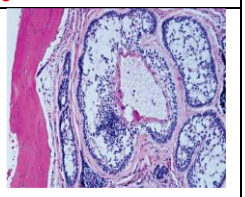
Tumors of odontogenic epithelium

Ameloblastoma➔BRAF p.V600E mutation(80%)➔MAPK kinase pathway

➲most common odontogenic tumor➔frequency=frequency of all other odontogenic tumors(exclude odontoma)

➲classification➔3 subtypes
❶conventional solid/multicystic(~75↔86%)
❷unicystic(~13↔21%)➔ameloblastic-like cells➔①luminal ②intraluminal ③mural(tumor cell infiltrate cyst wall)➔whether a truly ML-RL➔arguable(值得商榷)
❸peripheral(extraosseous)(~1↔4%)
✪adenoid ameloblastoma➔epithelial feature(❶conventional ameloblastoma) with duct-like structure

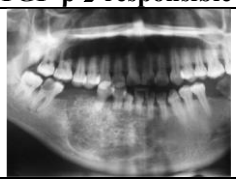
➲micro
❶ameloblastic-like cell(nuclei➔reverse polarity)
①follicular(cystic degeneration)(右圖) ②plexiform(stroma degeneration)➔①,②most common
❷stellate reticulum-like cell➔①acanthomatous(squamous metaplasia) ②granular cell ③basal cell
❸stroma➔desmoplasia
❹cystic degeneration➔central zone(stellate-like reticulum like cell area)

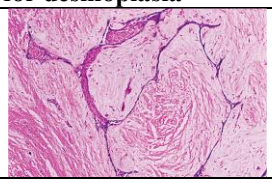


Desmoplastic ameloblastoma

➲anterior jaws predilection ➲mandible:maxilla=1:1 ➲IHC➔↑TGF-β➔responsible for desmoplasia

➲radiograph(like fibro-osseous lesion)➔mixed RL & RO(osseous metaplasia in dense fibrous septa)➔NOT tumor itself ➔mineralized product



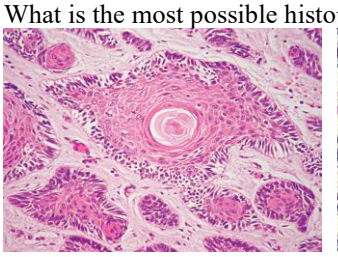


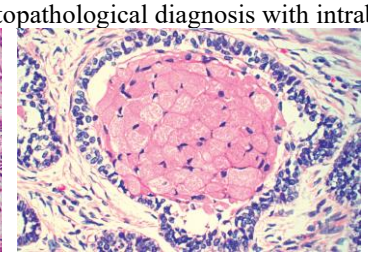
1. 有關**造釉細胞瘤**的組織特性，下列何者正確？(114)
   (A) 最常見的型態為濾泡型(follicular type)及角質型(keratosis type)
   (B) 可見柱狀(columnar)及立方形(cuboidal)的外層上皮細胞(outer epithelial cell)排列在結締組織邊緣
   (C) 外層上皮細胞(outer epithelial cell)的細胞核偏向基底膜(basement membrane)
   (D) 內層上皮細胞(inner epithelial cell)常會出現dysplasia現象

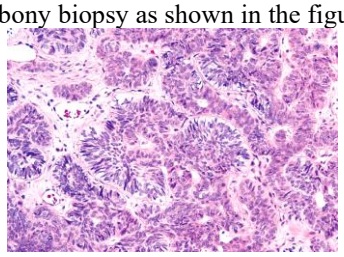
2. Which of the following is *not* a characteristic feature of **ameloblastoma**? It is:
   (A) a benign tumor
   (B) most often occurred in mandible
   (C) usually radiographic multilocular
   (D) encapsulated

3. Which of the following concerning ameloblastoma is *false*? It:
   (A) can present as a multilocular radiolucency
   (B) is a benign & locally aggressive lesion
   (C) often occurs in mandibular molar & ramus
   (D) should be treated with radiation therapy

4. What is the most possible histopathological diagnosis with intrabony biopsy as shown in the figures below respectively?







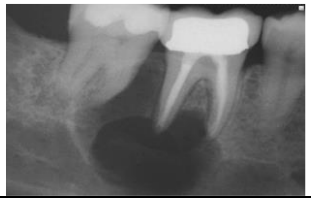
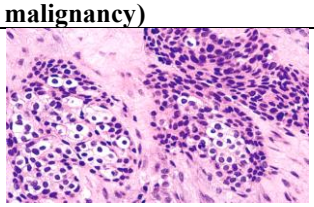
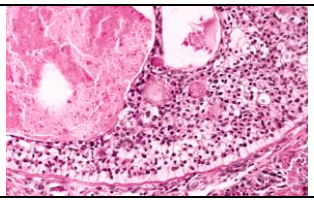
(1) ameloblastoma, plexiform (2) ameloblastoma, follicular (3) acanthomatous (4) granular cell (5) basal cell
(A) right: 1,3; middle: 1,4; left: 2,5
(B) right: 1,5; middle: 2,4; left: 2,3
(C) right: 1,3; middle: 2,4; left: 1,5
(D) right: 2,3; middle: 1,4; left: 1,5

5. What are true for **malignant ameloblastoma**?
(1) with abnormal mitosis (2) with lung metastasis (3) no metastasis (4) no abnormal mitosis in both primary AND metastatic lesions
(A) only 1, 2
(B) only 2, 4
(C) only 1, 3
(D) only 2, 3

6. What are true for **ameloblastic carcinoma**?
(1) with abnormal mitosis in primary OR in metastatic lesions (2) must with lung metastasis (3) possible with lung metastasis (4) no abnormal mitosis
(A) only 1, 2
(B) only 2, 4
(C) only 1, 3
(D) only 2, 3

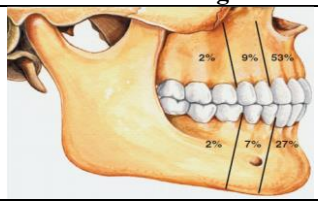
7. 關於**齒源性腫瘤(odontogenic tumors)**的敘述，下列何者錯誤？(114)
(A) 轉移性造釉細胞瘤(metastasizing ameloblastoma)最常轉移的部位是肺
(B) 造釉細胞癌(ameloblastic carcinoma)不一定會合併遠端轉移的病灶
(C) 亮細胞齒源性癌(clear cell odontogenic carcinoma)好發於成年女性
(D) 亮細胞齒源性癌(clear cell odontogenic carcinoma)較好發於上顎骨

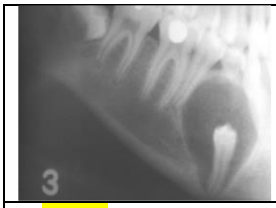
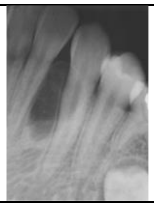
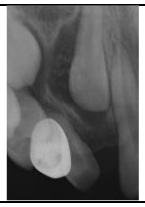
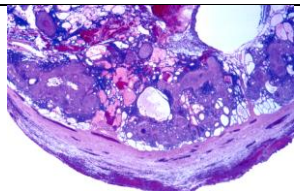
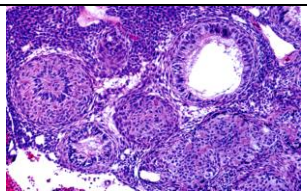
Clear cell odontogenic carcinoma➔EWSR1 gene translocation(fuse with ATF1 gene)➔also in hyalinizing clear cell carcinoma(a rare salivary gland malignancy)

➲**clinic** ❶**female(65%)** ❷**mandible(slight>80%)** ❸**pain/lower lip paresthesia** ❹**bony swelling(80%)** ❺**PD-UL/ML RL** 		➲**micro➔3 patterns** ❶**biphasic➔[①clear(faint) eosinophilic cytoplasm+ ②eosinophilic polygonal] epithelial cell** ❷**monophasic➔only clear cell➔nest & cord** ❸**like ameloblastoma➔palisading clear cell island**
		❹**nuclear/cytologic pleomorphism➔not significant** ❺**mitoses➔sparse** ❻**necrosis➔not prominent** ❼**clear cell➔small amount glycogen➔mucin stain(-)**

8. The odontogenic tumor that characteristically appears as a well-circumscribed radiolucency located in anterior maxilla of an adolescent girl is:
(A) ameloblastic fibro-odontoma
(B) adenomatoid odontogenic tumor
(C) peripheral ossifying fibroma
(D) odontogenic myxoma

Adenomatoid odontogenic tumor(AOT)➔2-7% of all odontogenic tumors

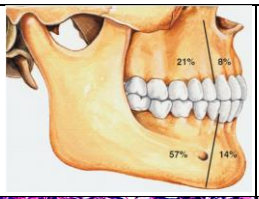
➲**histogenesis** ❶**enamel organ epithelium** ❷**reduced enamel epithelium** ❸**rests of Malassez** ❹**dental lamina remnant associate gubernacular cord**		➲**clinic➔2/3 patient➔10↔19s** ❶**>30s(uncommon)** ❷**anterior jaw(common)** ❸**maxilla:mandible(F:M)=2:1** ❹**seldom>3cm** ❺**extraosseous(rare)➔maxilla(facial gingiva)**
gubernacular cord(in gubernacular canal)➔link tooth follicle to gingiva➔in lingual/palatal surface of 1^0 teeth		
➲**radiograph➔UL-RL➔unerupt tooth(canine)** ❶**follicular type(like dentigerous cyst)➔d.d. as RL extends apical along root past CE junction** ❷**extrafollicular type(less common)➔not relate to unerupt tooth➔between roots of erupted teeth** ❸**nevus sebaceus syndrome(Schimmelpenning syndrome)➔multiple AOTs associate impacted teeth** ❹**calcification (snowflake)➔d.d. dentigerous cyst**		

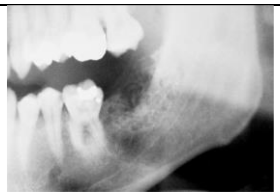







➲micro➔spindle-shaped epithelial cell(sheet, strand, whorled)➔scant stroma
❶epithelial cell➔rosette about a central space➔empty(small amount eosinophilic material➔stain for amyloid)
❷tubular(ductlike) structure(NOT true duct➔no glandular element)➔central space surrounded by columnar(cuboid) epithelial cell
❸small calcification foci➔abortive enamel formation
❹larger calcification➔dentinoid/cementum
❺focal area➔resemble CEOT(Pindborg tumor)/COT(Gorlin cyst)

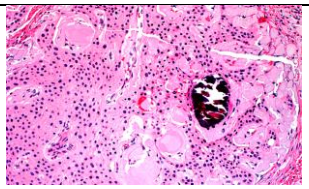
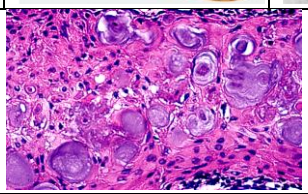
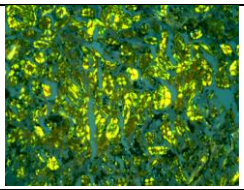
Calcifying odontogenic tumor(Pindborg tumor)➔PTCH1 gene➔mutation

➲arise➔dental lamina	➲posterior mandible(most)
➲ painless, slow-growing swelling (most common)	
➲UL(maxilla more)/MLRL➔calcification(driven-snow pattern)(some)	
➲peripheral(extraosseous) counterpart(sessile gingival mass, anterior)	
➲malignant with metastasis to regional LN & lung(rare)	
➲micro➔clear cell variant	





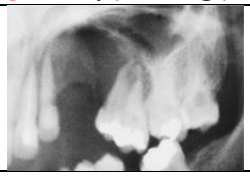
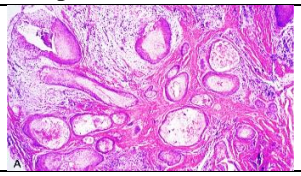
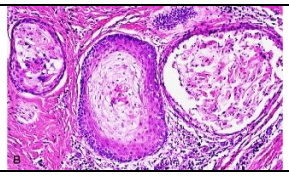
❶amorphous, eosinophilic, hyalinized (amyloid-like) extracellular material
❷calcification(develop within amyloid)
❸concentric Liesegang ring calcifications
❹Congo red stain➔amyloid➔apple-green birefringence with polarized light

9. Which of the following description of **squamous odontogenic tumor** is *false*? It:
(A) may be diagnosed as ameloblastoma leading to radical surgery
(B) shows the peripheral cells of epithelial islands demonstrate reverse polarization
(C) may contain globular eosinophilic structures that do not stained for amyloid
(D) may arise from rest of dental lamina or rests of Malassez

Squamous odontogenic tumor(SOT)➔misdiagnosed as ameloblastoma➔unnecessary radical surgery

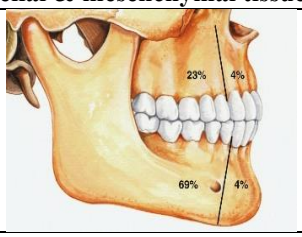
➲arise ❶dental lamina rest ❷epithelial rests of Malassez ❸within PDL➔associate lateral root surface of erupted tooth	➲clinic➔painless(mild pain) gingival swelling associate teeth mobility(most) ❶9↔67s(mean➔34s) ❷no site & sex predilection ❸involved several quadrants [1 family(3 siblings)➔multiple lesions]
➲radiograph ❶▲RL(PD/WD) lateral to teeth root ❷vertical periodontal bone loss ❸seldom>1.5cm	

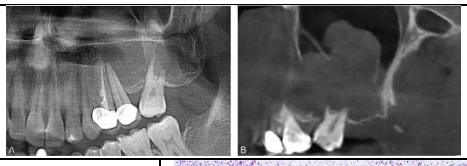
➲micro
❶bland squamous epithelium island(vacuolization & individual cell keratinization) in mature fibrous c.t.
❷peripheral cells of epithelial islands➔no reverse polarization(as in ameloblastoma)
❸small microcyst within epithelial island(may be)
❹within epithelium➔laminated calcified bodies(dystrophic calcification) & globular eosinophilic structure(not stain for amyloid)(reported)
❺dentigerous(radicular) cyst wall➔epithelium island like SOT(not relate to cyst behavior)➔SOT-like proliferation

Mixed odontogenic tumors

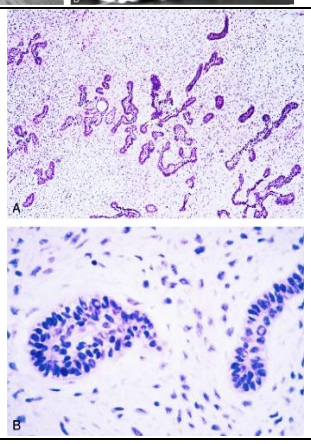
Ameloblastic fibroma(AF)➔true mixed tumor(epithelial & mesenchymal tissues➔both neoplastic)

➲clinic➔1↔2 decade(most)(mean 15s) ❶middle-age(occasion) ❷male(slight more common) ❸small➔asymptomatic(larger➔ jaws swelling) ❹posterior mandible(70%) ❺gingival soft tissue(rare)		❻conservative Tx➔substantial recur risk ❼ameloblastic fibrosarcoma(~26%) develop in recur AF➔aggressive surgical excision for recur AF

➲radiograph
❶WD-UL(small lesion)/ML-RL with corticated margin
❷associate unerupt tooth(75%)
❸large size(may be)➔large portion of body & ramus of mandible/posterior maxilla

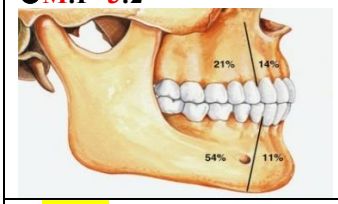


➲micro➔solid, soft tissue mass with a smooth outer surface with(out) definite capsule
❶cell-rich mesenchymal tissue(like primitive dental papilla)+proliferating odontogenic epithelium
❷odontogenic epithelium➔2-pattern
①long, narrow anastomosing cords(2-cell thick➔cuboid/columnar cell)(most)
②small, discrete islands(like follicular stage of developing enamel organ)➔peripheral columnar cells surround loosely arranged epithelial cells(like stellate reticulum)➔seldom microcyst formation(contrast to follicular ameloblastoma)
❸mesenchymal tissues
①plump stellate & ovoid cells in loose matrix(like developing dental papilla)
②inconspicuous collagen
③juxtaepithelial hyalinization(sometimes)
④hyalinized acellular lesional tissue(occasion)
❹coexist with COC(reported)

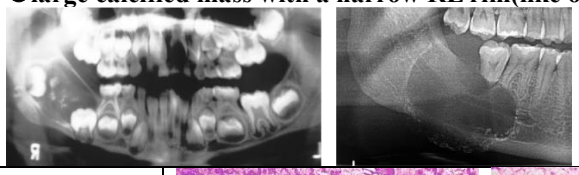


Ameloblastic fibro-odontoma(AFO)➔AF➔also contain enamel & dentin

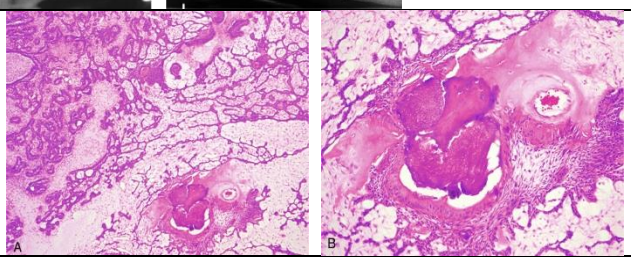
➲clinic➔painless swelling of posterior jaws (majority➔mandible)
❶most➔children(mean 10s)(adult rare)
❷M:F=3:2



➲radiograph
❶WD-UL/ML(infrequent) RL with RO(tooth structure)
❷unerupt tooth➔lesion margin/crown of unerupt tooth within
❸RL(~5%)➔minimal enamel & dentin matrix
❹large calcified mass with a narrow RL rim(like odontoma)(some)



➲micro
❶soft tissue component➔identical to AF(narrow cord & small island of odontogenic epithelium in primitive c.t. like dental papilla)
❷calcifying element
①foci of enamel & dentin matrix
②more calcified lesion➔rudimentary small teeth/ conglomerate mass of enamel & dentin



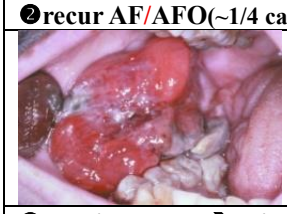
➲recur after conservative removal(~7%)
➲ameloblastic fibrosarcoma after curettage of AFO(exceedingly rare)

Ameloblastic fibrosarcoma(Ameloblastic sarcoma)➔malignant counterpart of AF(only mesenchymal➔malignancy)

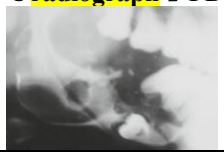
➲arise
❶de novo
❷recur AF/AFO(~1/4 cases)

➲molecular analysis
❶BRAF mutation
❷NRAS mutation(less common)

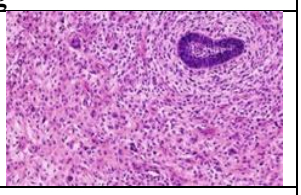
➲clinic➔mandible(80%)
❶male(slight more) ❷younger p't(mean ~30s)
❸pain & rapid growth swelling



➲radiograph➔PD-RL



➲micro
❶epithelial component➔benign
❷mesenchymal portion
①cellular hyperchromatic bizarre cell
②mitoses prominent



❸multiple recur➔epithelial component(less conspicuous)➔poor differentiated fibrosarcoma
❹malignant change of both epithelial & mesenchymal componets➔ameloblastic(odontogenic) carcinosarcoma

10. Which of the following description of **odontoameloblastoma** is *false*? It:
(A) is formerly named as ameloblastic odontoma
(B) shows the ameloblastic component that is closely related to the component of odontoma
(C) more often occurs in young age patient
(D) has same biological potential as that of ameloblastoma

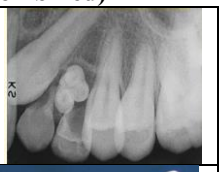
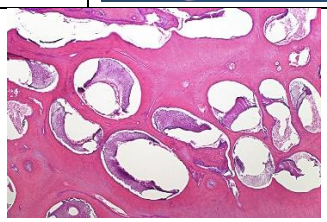
Odontoameloblastoma

➲formerly➔called ameloblastic odontoma(confused with AFO)
➲ameloblastoma➔in conjunction with an odontoma(2 lesions being otherwise unrelated)
➲biologic potential➔same as ameloblastoma➔multiple recur after local curettage

➲clinic➔either jaw affected ❶younger p't(more often) ❷pain, delayed teeth eruption, bone expansion	➲radiograph➔RL with RO contain calcified structure➔miniature teeth(complex odontoma)
➲micro ❶proliferating epithelial portion➔features of ameloblastoma(plexiform/follicular) ❷ameloblastic component➔intermingle(混在一起) with immature(more mature) dental tissue➔like odontoma	

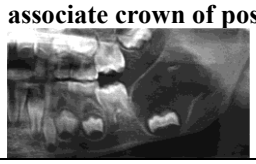
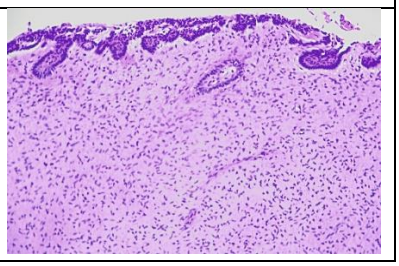
11. **Compound odontoma differs from complex odontoma** in that a compound odontoma. It:
(A) is composed of several toothlike structures
(B) has unlimited growth potential
(C) presents as a radiopaque mass
(D) is most in the posterior mandible

Compound & complex odontoma➔most common odontogenic tumor(>all other odontogenic tumors combined)

➲clinic ❶odontoma(all)➔maxilla>mandible ❷compound type➔anterior maxilla ❸complex type➔molar region of either jaw ❹may develop in gingiva(peripheral)	➲radiograph➔diagnostic ❶compound type➔seldom confused with other lesion(toothlike structure with RL rim) ❷complex type➔calcified mass	
➲micro ❶compound type ①multiple small single-rooted teethlike structures in loose fibrous matrix➔loss of mature enamel cap during decalcification for slide preparation➔enamel matrix(varying amount) ②pulp tissue➔coronal & root portions of toothlike structure		
❷complex type ①mature tubular dentin(cleft/hollow circular space➔mature enamel removed during decalcification)➔enamel matrix/immature enamel(small amount) ②islands of epithelial ghost cells(eosinophilic; small)(~20%)➔odontogenic epithelium remnant(local anoxia➔keratinization & cell death) ③periphery➔thin cementum layer ④dentigerous cyst(occasion)➔arise from epithelial lining of fibrous capsule		

12. Which of the following description of **primordial odontogenic tumor** is *false*? It:
(A) often shows a well-defined unilocular posterior mandibular radiolucency
(B) shows myxoid-cellular ectomesenchymal tissue microscopically
(C) may show calcification like enamel matrix microscopically
(D) is a benign tumor of odontogenic epithelium

Primordial odontogenic tumor

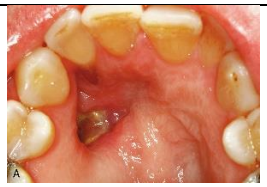
➲clinic➔firm painless swelling ❶1st/2nd decade ❷posterior mandible(most) ❸maxilla(less common) ❹3rd molar & 1^0molar(most) ❺greatest dimension➔1.5-9cm	➲radiograph➔WD-UL(BL)-RL associate crown of posterior tooth 	➲Tx➔enucleation/conservative excision include involved tooth ➲24 reported cases➔1 recur
➲micro➔encapsulate ❶myxoid-cellular ectomesenchymal tissue➔lobulated/undulating(起伏) periphery ❷tumor edge➔thin cuboid-columnar epithelium(like inner enamel epithelium of developing tooth) ❸stellate reticulum-like differentiation adjacent to columnar epithelium(1/2 cases) ❹epithelium➔prominent dipping between ectomesenchymal lobules of tumor ❺eosinophilic mineralized tissue(enameloid) ❻basophilic calcification(like enamel matrix)		

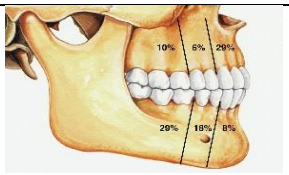
Tumors of odontogenic ectomesenchyme

13. Which of the following description of **central odontogenic fibroma** is *false*? It:
(A) may show well-defined multilocular radiolucency with corticated margin containing radiopaque flecks
(B) may be associated with giant cell granuloma
(C) may show amyloid substance microscopically
(D) has been classified as the simple type that is occurred most often compared to the WHO type

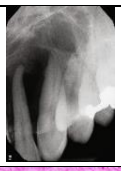
Central odontogenic fibroma

➲clinic➔palatal mucosa overlies tumor➔a defect/groove(occasion)
❶range➔3↔77s(mean 33s)
❷F:M=1.35:1(strong female predilection)
❸maxilla(anterior-1st molar)=mandible(~1/2 posterior to 1st molar)
❹associate unerupt tooth(~5%)
❺smaller➔asymptomatic; larger➔bony expansion/teeth loosening

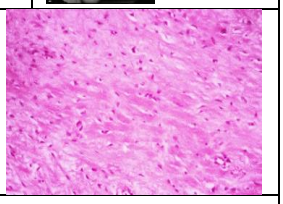




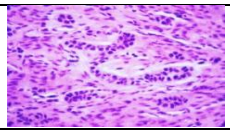
➲radiograph
❶smaller➔WD-UL RL with corticated border(periradicular area of erupted teeth)➔root divergence
❷larger lesion➔ML RL with corticated border
❸root resorption(common)
❹RO flecks(斑點)(~12%)



➲micro➔no definite capsule BUT limited growth potential(esp. in anterior jaws)
❶simple type(rare)
①stellate fibroblast➔whorled fine collagen fibril & considerable ground substance
②foci of odontogenic epithelial rests(may be)
[spindle cell collagenous lesion without epithelial rest➔desmoplastic fibroma, myo(neuro)fibroma]
③foci of dystrophic calcification(occasion)

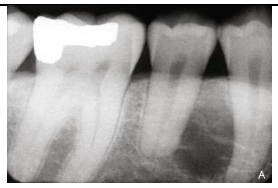


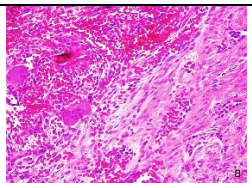
❷epithelium-rich(WHO type)(more common)
①cellular fibrous c.t. with collagen fiber➔interlacing bundle
②odontogenic epithelium➔long strands/isolated nests
③fibrous component➔myxoid to densely hyalinized



❸calcification(cementum-like material/dentinoid)(some cases)
①focal deposits of odontogenic ameloblast-associated protein(ODAM)➔amyloid
②Langerhans cell➔non-calcifying Langerhans cell-rich CEOT cannot be excluded

❹associated giant cell granuloma(40 cases)
①recur(several)➔exhibit both components
②3 possibilities of giant cells
(1)odontogenic fibroma induced giant cell response
(2)giant cell granuloma triggered odontogenic fibroma formation
(3)biphasic





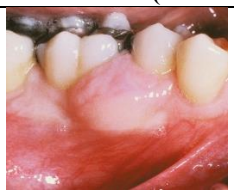
➲Tx➔enucleation & vigorous curettage➔a few recur documented

14. Which of the following diseases may have **Langerhans cells** microscopically?
(1) histiocytosis X (2) central odontogenic fibroma (3) Pindborg tumor (4) adenomatoid odontogenic tumor
(A) only 1,2,3
(B) only 2,3,4
(C) only 1,2,4
(D) only 1,3,4

15. **Peripheral odontogenic tumors** are located on:
(A) palate
(B) gingiva
(C) lower lip
(D) buccal mucosa

Peripheral odontogenic tumor➔soft tissue counterpart of central(intraosseous) odontogenic fibroma

➲clinic➔facial lower gingiva sessile mass(most)
❶firm, slow-grow, covered by normal mucosa
❷multifocal/diffuse lesions(rare)
❸0.5↔1.5 cm(most)
❹teeth displacement(infrequent)
❺2nd↔4th decades(most)



➲radiograph
❶soft tissue mass(calcification➔some cases)
❷not involve bone➔cupped out appearance (occasion)
❸root/crown resorption caused by tumor (rare)

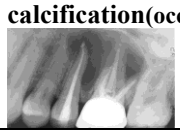
➲micro➔like central odontogenic fibroma(WHO type)
❶cellular fibrous c.t.➔interspersed with myxoid tissue(①granular cell change ②giant cell granuloma-like area)
❷islands/strands of odontogenic epithelium(may show vacuolization)➔scattered throughout c.t
❸①dysplastic dentin ②cementum-like calcification(morphous ovoid) ③osteoid trabeculae(may present)

➲Tx➔local surgical excision➔prognosis good BUT recur documented

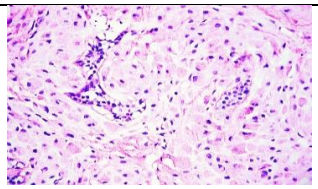
Granular cell odontogenic tumor(Granular cell odontogenic fibroma)

➲clinic➔mandible(premolar & molar)
❶>40s(more than half)
❷women(>70%)
❸gingival soft tissues(few cases)

➲radiograph➔WD-RL(UL/ML)➔small calcification(occasion)

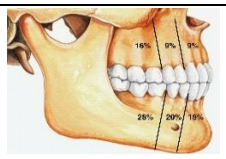
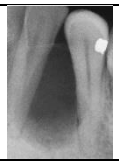
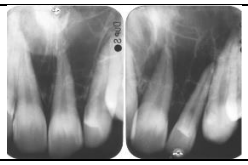
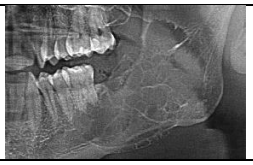
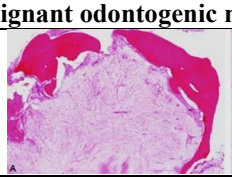
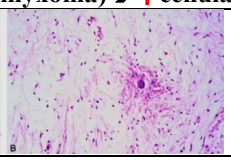


➲benign➔respond well to curettage
➲only 1 recur
➲only 1 malignant reported

➲micro ❶large eosinophilic granular cells(like soft tissue granular cell tumor/granular cell ameloblastoma) ❷narrow cords(small islands) of odontogenic epithelium ❸small cementum-like/dystrophic calcifications		❹granular cell nature(controversial) ①EM➔mesenchymal cell(lesional cell cytoplasm➔bodies consistent with lysosomal structure) ②IHC➔S-100(-)[contrast to S-100(+) of granular cell tumor]

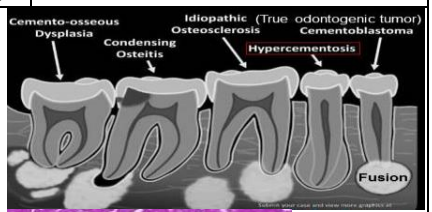
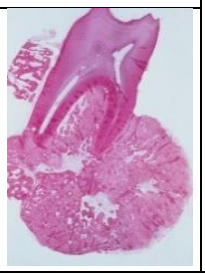
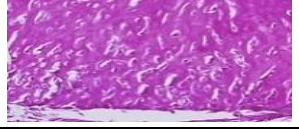
16. Which odontogenic tumor most closely resembles the **mesenchyme of dental follicle**?
(A) cementoblastoma
(B) odontogenic myxoma
(C) compound odontoma
(D) ameloblastoma

Odontogenic myxoma➔arise from odontogenic ectomesenchyme➔like mesenchymal portion of developing tooth

➲myxoma of jaws➔odontogenic origin				
➲clinic ❶young adult predominant ❷average age➔25-30s ❸slight female sex predilection ❹mandible>maxilla				
➲radiograph➔UL/ML RL(displace/teeth resorption)➔wispy trabeculae➔at right angle to one another ❶large lesion➔①soap bubble RL(indistinguish from ameloblastoma) ②sun-burst(ray)(like osteosarcoma)				
➲micro(gross➔gelatinous, loose structure) ❶haphazard arranged stellate, spindle-shaped, round cell➔abundant loose myxoid stroma(a few collagen fibril) ❷histochemical➔ground substance➔glycosaminoglycan➔①hyaluronic acid ②chondroitin sulfate ❸IHC➔①vimentin(+) ②muscle-specific actin(+) ❹odontogenic epithelial rest(inactive)➔in myxoid ground substance ❺cementum-like calcification(rare)				
➲fibromyxoma/myxofibroma/chondromyxoid fibroma/myxoid neurofibroma ➲myxoid change in enlarged dental follicle(papilla)➔like myxoma ➲sinonasal myxoma(1st 2s)➔like odontogenic myxoma➔β-catenin(+)(unlike odontogenic myxoma)				
➲small myxoma➔curettage➔periodic reevaluation(at least 5s) ➲larger lesion➔extensive resection➔not encapsulated➔infiltrate surrounding bone ➲myxosarcoma(malignant odontogenic myxoma)➔↑cellularity & cellular atypia➔death➔distant meta(not reported)				
				

17. Which one of the following best describes **cementoblastoma**? It is a:
(A) well-circumscribed radiopaque lesion with a radiolucent halo fused to root of a vital tooth
(B) radiolucent multilocular lesion
(C) radiolucent lesion surrounding the crown of an impacted tooth
(D) lesion composed of numerous toothlike structures

Cementoblastoma(True cementoma)➔fused to tooth root➔distinguish osteoblastoma

➲下顎(近80%)➔(小)大臼齒➔下顎恆牙1st大臼齒(近半)➔阻生,unerupt,乳牙(rare)➔EPT(+)/(-, 20%)			➲<1% of all odontogenic tumor
➲pain & swelling(~70%)	➲mean size➔~2cm(0.5-8cm)		
➲主要在年輕人(mean 24s)➔peak➔2nd-3rd decade		➲no sex predilection	
➲bony expansion/cortical perforation➔↑recurrent(~12%)			
➲infiltrate pulp chamber & root canal(may)			
➲micro➔like osteoblastoma ❶mineralized trabeculae ①lacunae & basophilic reversal line ②multinucleated giant cell & prominent cementoblast-like cell(周邊) ③stroma➔cellular fibrovascular tissue ❷radiating uncalcified matrix(周邊)➔RL rim			

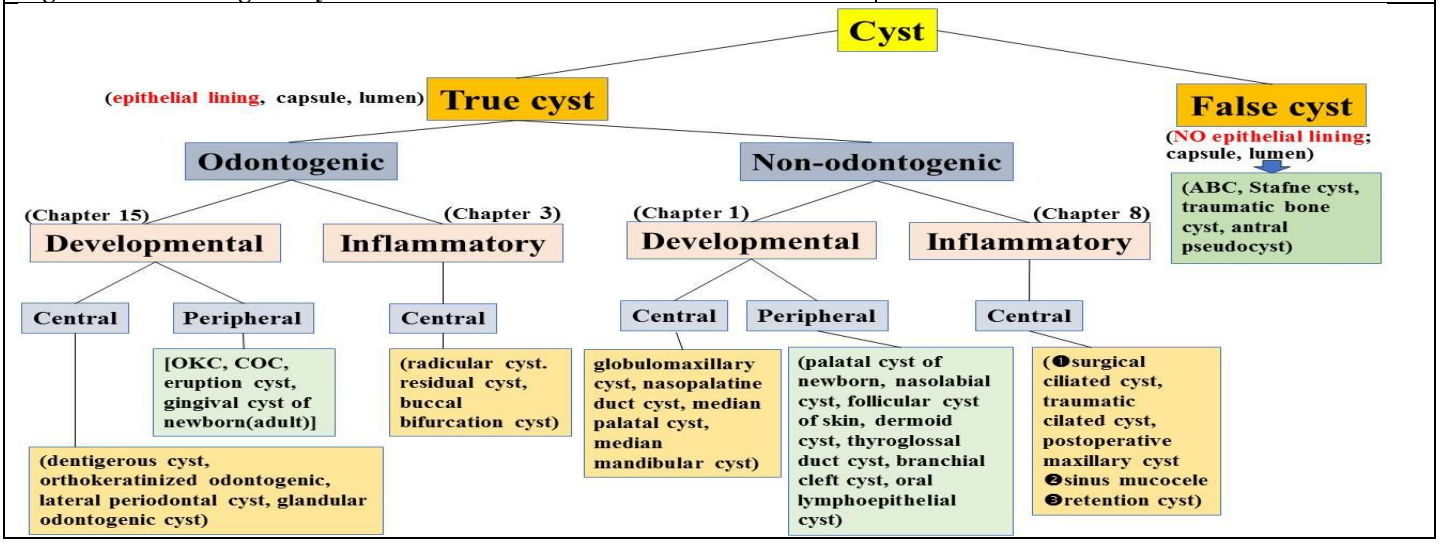
18. Pain is most often a symptom of:
(1) amputation (traumatic) neuroma (2) cementoblastoma (3) osteoid osteoma (osteoblastoma) (4) osteosclerosis
(A) only 1,2,3
(B) only 2,3,4
(C) only 1,2,4
(D) only 1,3,4

19. Which of the following tumors may contain **central radiopacities**?
(1) desmoplastic ameloblastoma (2) adenomatoid odontogenic tumor (3) peripheral odontogenic tumor (4) Pindborg tumor
(A) only 1,2,3
(B) only 2,3,4
(C) only 1,2,4
(D) 1,2,3,4

Chapter 15 Odontogenic cysts

➲**classification**

❶**developmental**(#also has soft tissue counterpart; ✶soft tissue cyst)	❷**Inflammatory**
①dentigerous cyst ②eruption cyst ③odontogenic keratocyst(OKC)# ④orthokeratinized odontogenic cyst ⑤gingival(alveolar) cyst of newborn* ⑥gingival cyst of adult(counterpart of ⑦)* ⑦lateral periodontal cyst ⑧calcifying odontogenic cyst(COC)# ⑨glandular odontogenic cyst	①periapical(radicular) cyst ②residual cyst ③buccal bifurcation cyst



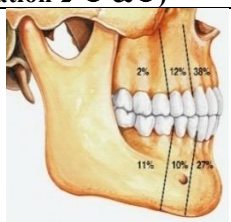
20. 關於**鈣化齒源性囊腫**(calcifying odontogenic cyst)的敘述，下列何者正確？(114)
(A) 好發於上顎
(B) 若伴生齒瘤(odontoma)，多發生於年輕人
(C) 好發於臼齒區，尤其是阻生齒
(D) 一般需以骨切除手術(resection)治療

Calcifying odontogenic cyst(COC; Gorlin cyst; Calcifying cystic odontogenic tumor)

➲**WHO classification(2022)➔3-type ghost cell lesion**
❶cystic(COC) ❷solid(dentinogenic ghost cell tumor) ❸malignant nature(ghost cell odontogenic carcinoma)

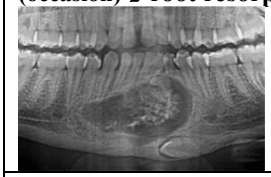
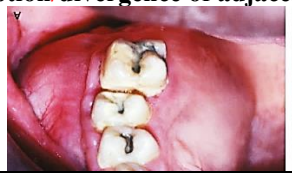
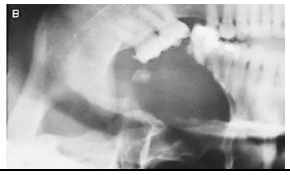
➲**COC❶➔CTNNB1mutation➔encode β-catenin(similar mutation➔❷ &❸)**

➲**clinic➔maxilla=mandible**
❶incisor & canine areas(65%)
❷mean 30s(2nd↔4th decade)
❸combined with
①compound/[complex odontoma(most)]➔younger(mean 17s)
②AOT
③ameloblastoma



➲intraosseous ghost cell odontogenic lesion➔cystic lesion
➲solid dentinogenic ghost cell tumor/ ghost cell odontogenic carcinoma(<5%)
➲~1/3 peripheral lesion➔solid in nature➔not aggressive as intraosseous counterpart

➲**radiograph(2↔4cm➔12cm)➔WD-UL with RO(1/3↔1/2 case)➔calcification/toothlike(1/3 case, unerupt canine)/WD-ML (occasion)➔root resorption/divergence of adjacent teeth**

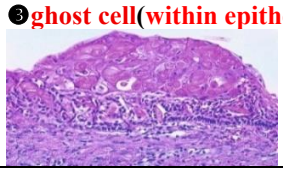




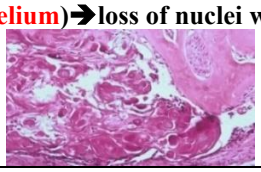
➲**intraosseous dentinogenic ghost cell tumor➔3rd↔5th decade(most)➔posterior jaws➔more aggressive➔root resorption, cortical plate perforation, sinus destruction**

➲ghost cell odontogenic carcinoma(maxilla>mandible)➔aggressive➔de novo/malignant change from COC/dentinogenic ghost cell tumor➔❶cellular pleomorphism ❷↑mitotic activity ❸necrosis ❹invade surround tissue

➲extraosseous odontogenic ghost cell lesion (5-17%)➔peak(6th-8th decade) ➔gingiva➔like fibroma, cyst, peripheral giant cell granuloma

➲micro➔lumen with capsule & odontogenic epithelium(4↔10 cell thick)
❶basal cell of epithelial lining(cuboid/columnar)➔like ameloblasts
❷epithelium➔stellate reticulum of ameloblastoma
❸ghost cell(within epithelium)➔loss of nuclei with basic cell outline





➲ghost cell➔❶coagulative necrosis/enamel protein accumulation ❷normal/aberrant keratinization of odontogenic epithelium ❸fuse to form sheet of amorphous, acellular material ❹calcification(fine basophilic granule➔extensive calcified mass) ❺eosinophilic matrix➔dysplastic dentin(dentinoid) adjacent to epithelium(inductive effect by odontogenic epithelium adjacent mesenchymal tissue)

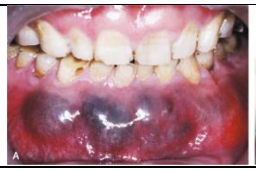
➲variant➔❶epithelial lining proliferates into lumen➔filled with ghost cell & dystrophic calcification
❷multiple daughter cysts➔fibrous wall➔foreign body reaction
❸uni(multi)focal epithelial proliferation(mixed with ghost cell) into lumen➔resemble ameloblastoma

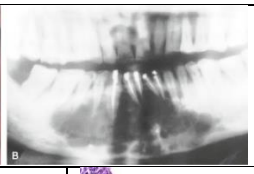
➲solid dentinogenic ghost cell tumor[intraosseous/extraosseous(more)]➔nest of ghost cells & juxtaepithelial dentinoid➔ d.d. peripheral ameloblastoma

Glandular odontogenic cyst(GOC, Sialo-odontogenic cyst)➔developmental odontogenic cyst

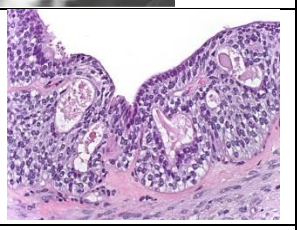
➲glandular(salivary) feature➔pluripotential of odontogenic epithelium

➲clinic➔mandible(68↔75%)➔anterior(mandible➔cross midline)
❶middle-aged adult(most)➔mean 46↔48s(rare<20s)
❷small(<1cm; asymptomatic)
❸large(destructive➔most of jaw; pain/paresthesia expansion)
➲radiograph➔WD-UL(ML) RL with a corticated rim





➲micro➔epithelium(cuboid-columnar; vary thickness; may papillary)➔flat interface between epithelium & c.t. wall
❶epithelium➔①mucin-producing goblet cell with cilia ②glandular, ductlike space➔ mucicarmine(+) fluid ③spherical nodule(like seen in lateral periodontal cyst)
❷fibrous cyst wall➔no inflammatory cell infiltrate
❸features of intraosseous, low-grade mucoepidermoid carcinoma(MEC)
❹MAML2 gene rearrangement(-) vs [central MEC➔MAML2 gene rearrangement(+)]



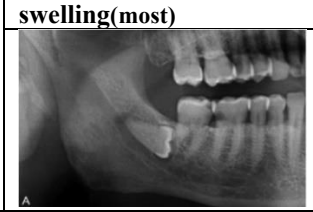
➲enucleation/curettage➔recur(~22-30%)(more in ML RL)➔aggressive➔en bloc resection
➲marsupialization & decompression➔promote shrinkage prior to surgery
➲central MEC arise from recur GOC(1 reported)

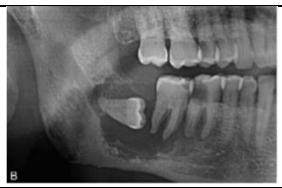
21. Which of the following lesions may have **ghost cell** microscopically?
(1) adenomatoid odontogenic tumor (2) Gorlin cyst (3) complex odontoma (4) central odontogenic fibroma
(A) only 1.2
(B) only 2.3
(C) only 1,4
(D) only 3,4

Carcinoma arising in odontogenic cysts

➲odontogenic carcinoma
❶de novo➔ameloblastoma(rare from other odontogenic tumors)
❷arise from epithelial lining of odontogenic cyst➔(central MEC arise from mucous cell of dentigerous cyst lining)
①from residual periapical cyst(60%)
②from dentigerous cyst(16%)
③from lateral periodontal cyst(one case)
④from orthokeratinized odontogenic cyst ⑤from OKC

➲older p't(mean 60s)➔>2× in men➔pain & swelling(most)

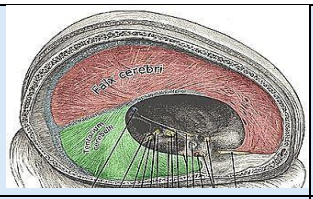




Nevoid basal-cell carcinoma syndrome(NBCCS ; Gorlin syndrome)➔autosomal dominant

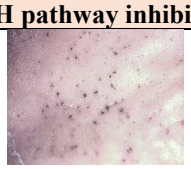
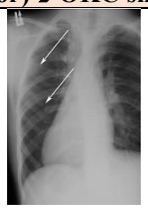
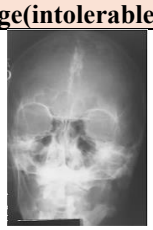
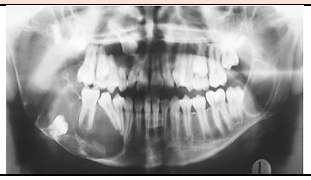
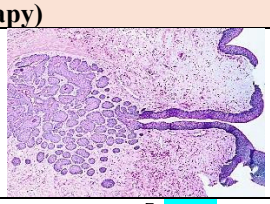
➲major clinic features➔mild mandibular prognathism

❶≥50% frequency		❷15-49% frequency
①multiple basal cell carcinomas of skin ②odontogenic keratocysts(OKCs)(90%)➔early Dx [1st OKC(<19s) removed➔significant younger than isolated OKC]		①calcified ovarian fibromas ②short 4th metacarpal(掌骨)

③epidermal cysts of skin ④palmar/plantar pits ⑤calcified falx cerebri (大腦鐮➔硬腦膜的一部分 ➔形狀似鐮刀)※tentorium cerebellum			③kyphoscoliosis(先天性肌肉病變)/other vertebral anomalies ④pectus excavatum(漏斗胸)/carinatum(雞胸) ⑤strabismus(斜視)(exotropia)
⑥enlarged head circumference ⑦rib(splayed, fused, partial missing &/or bifid)		⑧mild ocular hypertelorism ⑨spina bifida occulta of cervical/thoracic vertebrae	

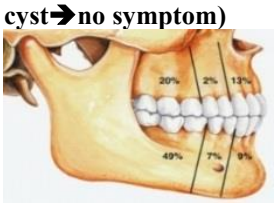
❸<15% frequency(but not random)		➲mutation
①medulloblastoma(髓母細胞瘤)➔MRI➔syndrome child(↑prognosis) ②meningioma ③lymphomesenteric cysts ④cardiac fibroma	⑤fetal rhabdomyoma ⑥marfanoid build ⑦cleft lip &/or palate ⑧hypogonadism in male ⑨intellectual disability	❶patched(PTCH)➔tumor suppressor gene(chromosome 9q22.3-q31)➔sonic hedgehog(SHH) pathway ❷suppressor of fused(SUFU)(PTCH2)(much smaller %)➔SHH pathway (SUFU mutation➔①OKCs(may not) ②↑medulloblastoma) ❸new mutations(~20-30%)

➲vismodegib(SHH pathway inhibitor)➔OKC shrinkage(intolerable side effect➔discontinue therapy)

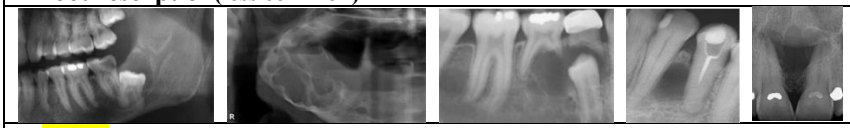
 basal cell carcinoma	 plantar pits	 bifid ribs	 falx cerebri calcification	 ➲multiple OKCs(up to 10)➔fibrous capsule➔more ❶satellite cysts ❷solid islands of epithelial proliferation ❸odontogenic epithelial rests than isolated OKC	

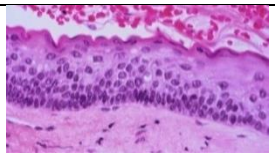
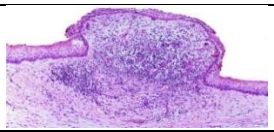
22. Which of the syndromes may have **epidermal cyst of skin**?
(1) Gorlin syndrome (2) Sjogren syndrome (3) Gardner syndrome (4) Nevoid basal-cell carcinoma syndrome
(A) only 1.2,3
(B) only 2.3,4
(C) only 1,3,4
(D) only 1,2,4

Odontogenic keratocyst(OKC, Keratocystic odontogenic tumor)➔developmental odontogenic cyst

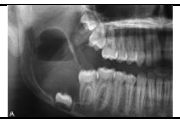
➲❶sporadic OKC(93%) ❷OKCs associate NBCCS(90%)➔PTCH1 gene mutation ➲↑proliferating cell nuclear antigen(PCNA) & Ki-67(esp., suprabasilar layer) ➲loss of heterozygosity(LOH)➔tumor suppressor gene(p16, p53, MCC, TSLC1, LATS2 , FHIT)	➲clinic➔mandible(60-80%)➔posterior body & ramus ❶infancy-old age➔10-40s(60%) ❷slight male predilection ❸small➔asymptomatic(note routine radiograph) ❹larger➔pain, swelling, or drainage(some extremely large cyst➔no symptom)
➲3 significances vs other odontogenic cysts ❶↑growth potential ❷↑recur rate(5-62%) ❸associate NBCCS	

➲radiograph➔multiple➔nevoid basal cell carcinoma(Gorlin) syndrome(1st/2nd decade)
❶AP grow➔no obvious bone expansion➔d.d. dentigerous(radicular) cyst(comparable size with bony expansion)
❷WD-RL with corticated margin
❸large lesion(posterior body & ramus of mandible)➔ML-RL
❹with unerupted tooth(25-40%)
❺root resorption(less common)



➲micro➔thin friable wall➔difficult to enucleate from bone in one piece ❶lumen➔①clear liquid(like transudate of serum)②cheesy material➔keratinaceous debris ❷fibrous wall(no overt inflammation)➔small satellite cyst, cord, odontogenic epithelium island, cartilage ❸epithelial lining(6-8 cells thick)➔wavy(corrugated) parakeratotic squamous epithelium	
❹basal layer➔palisaded cuboid/columnar hyperchromatic epithelial cells ❺epithelium & c.t. interface➔flat & inconspicuous rete ridge (cyst-lining detach from wall) ❻inflammation➔epithelium proliferate to form rete ridges(loss of palisaded basal layer) ❼carcinoma *ex* OKC(reported)	

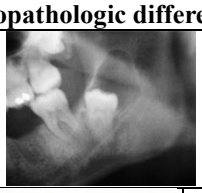
➲Tx➔enucleation & curettage➔recur due to(①original cyst fragment not removed ②new cyst from dental lamina rest)➔long-term follow-up
➲decompression➔↓cystic cavity size➔thicken cyst lining➔easier removal➔↓recur rate



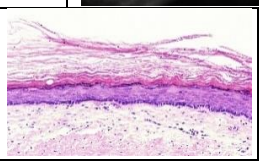
Orthokeratinized odontogenic cyst➔7↔17% of all keratinizing jaw cysts➔clinicopathologic different from OKC

➲clinic
❶young adults
❷male:female=2.6:1
❸posterior jaws
❹mandible:maxilla=3:1

➲radiograph➔UL-RL(<1↔>7cm)
❶ML-RL(occasion)
❷clinic & radiograph➔dentigerous cyst(~2/3 case)
❸unerupted lower 3rd molar(most)
❹multiple(occasion)



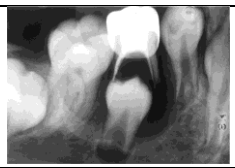
➲micro➔prominent keratohyaline granule➔subjacent orthokeratin
❶cyst lining➔stratified squamous epithelium➔orthokeratotic surface (vary thickness)
❷focal sebaceous differentiation(rare)
❸palisaded basal layer not present(feature of OKC)



➲Tx➔enucleation with curettage
➲recur(2%)➔OKC (≥30%)
➲not associate NBCCS

Dentigerous cyst(Follicular cyst)➔most common developmental odontogenic cyst(~20%)

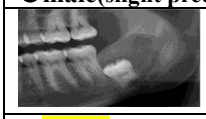
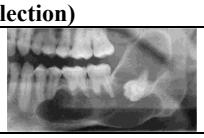
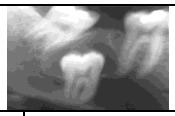
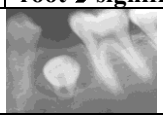
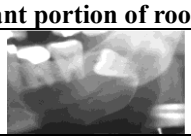
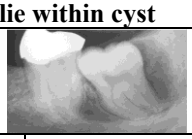
➲enclose unerupted tooth crown➔attached to cementoenamel junction
➲fluid accumulate between reduced enamel epithelium & tooth crown



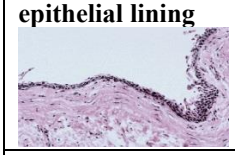
➲inflammatory pathogenesis(2 occasions)
❶periapical inflammation from overlying 1^0 tooth➔around unerupted 2^0 tooth crown(右圖)
❷partial erupted lower 3rd molar➔inflamed cyst along distal(buccal) aspect(paradental cyst)

➲clinic➔lower 3rd molar(~65%)➔other frequent site ➔upper canine(3rd molar), lower 2nd premolar
❶unerupted 10 teeth(rare)
❷supernumerary teeth or odontoma(occasion)
❸multiple(reported)
❹10↔30s(frequent)
❺male(slight predilection)

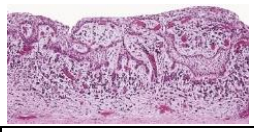
➲radiograph➔WD UL-RL(at least 3↔4 mm)with unerupted tooth crown with corticated border[infected➔PD]
❶cyst-to-crown relationship➔3 patterns
①central➔surround tooth crown➔project into cyst
②lateral➔along root surface➔partial surround crown
③circumferential➔surround crown➔extend some distance along root➔significant portion of root lie within cyst

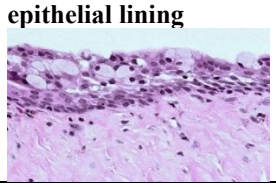
➲micro
❶noninflamed➔thin nonkeratinized epithelial lining



❷inflamed
①thicker lining with hyperplastic rete ridge
②wall➔diffuse chronic inflammatory infiltrate



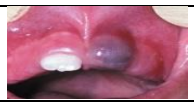
❸scattered mucous cell➔within epithelial lining



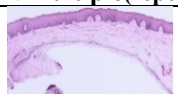
❹neoplastic change➔ameloblastoma
❺lining(malignant change)➔SCC
❻mucous cell in epith. lining➔central MEC

Eruption cyst(Eruption hematomas)➔soft tissue analogue of dentigerous cyst

➲dental follicle separates from around erupting tooth crown➔in soft tissue overlying alveolar bone



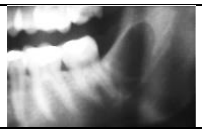
➲clinic➔central incisor & 1st molar(both dentitions)(most)
❶soft translucent swelling➔gingiva overlying erupting tooth
❷<10s(most)
❸multiple(reported)



➲micro(if no tooth erupt➔permit tooth erupt)
❶thin nonkeratinizing squamous epithelial cavity below oral mucosa
❷excised roof of cyst➔facilitate(speedy) tooth eruption
➲Tx(no need)➔cyst rupture spontaneous

Primordial cyst➔a cyst develops in place of a tooth

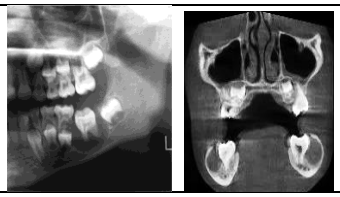
➲no 3rd molar extraction history➔a cyst(micro revealed an OKC) in 3rd molar area(右圖)
➲1972 WHO classification➔primordial cyst as preferred term
➲1992 WHO classification➔OKC as preferred term



Buccal bifurcation cyst(Inflammatory collateral cyst)➔inflammatory odontogenic cyst➔buccal of lower 1st(2nd) 2^0 molar

➲clinic➔children(5↔13s)
❶slight-to-moderate tenderness➔buccal of lower 1st(2nd) permanent molar
❷swelling & foul-tasting discharge
❸pocket on buccal of involved tooth
❹bilateral 1st molars(~1/3 cases)

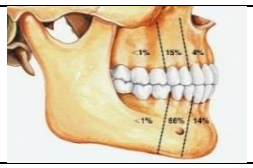
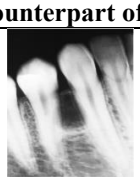
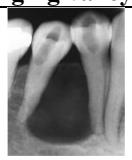
➲radiograph➔WD-RL of buccal bifurcation & root area
❶mean(1.2cm)➔2.5 cm(may be)
❷occlusal radiograph(CBCT)➔buccal site
❸root apices of lower molar➔tipped toward lingual cortex



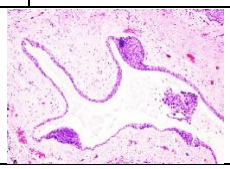
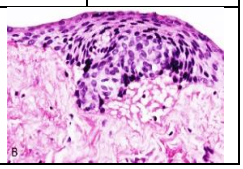
➲micro ❶nonkeratinize hyperplastic stratified squamous epithelium lining ❷prominent chronic inflammatory cell infiltrate➔c.t. wall	➲Tx➔enucleation(tooth extraction unnecessary) ➲resolve without surgery(no Tx➔daily irrigation of buccal pocket with saline & H_2O_2)

Lateral periodontal cyst(Botryoid odontogenic cyst)➔developmental odontogenic cyst(<2%)

➲along lateral root surface of tooth➔arise from rests of dental lamina➔intrabony counterpart of gingival cyst of adult

➲clinic➔asymptomatic ❶5th↔7th decades ❷lower(75↔80%)(upper)➔premolar-canine-lateral incisor		➲radiograph➔WD-RL laterally to roots of vital teeth (<1cm) ❶large lesion➔root divergent ❷botryoid➔ML-RL(often)			

➲micro➔thin noninflamed fibrous wall with epithelial lining(1↔3 cell thick)
❶lining epithelial cell➔foci of glycogen-rich clear cell
❷nodular thickening of lining epithelium(swirling)➔chiefly clear cell
❸malignancy➔1 case reported

➲Tx➔enucleation➔recur unusual(botryoid variant may recur➔polycystic)

Gingival(alveolar) cyst of newborn➔small superficial keratin-filled cyst➔alveolar mucosa of newborn infant(25↔53%)

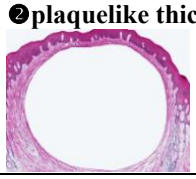
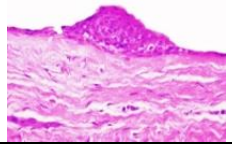
➲arise➔dental lamina remnant	➲inclusion cyst(Epstein's pearl & Bohn's nodule)➔midline/lateral hard(soft) palate

➲clinic➔small(2-3mm) multiple whitish papule➔neonate alveolar mucosa(maxilla>mandible)

	➲micro➔❶thin flatten parakeratotic epithelial lining ❷lumen➔keratin debris	➲no Tx➔spontaneous involute➔rupture of cyst (rare after 3 mon)

Gingival cyst of adult➔soft tissue counterpart of lateral periodontal cyst

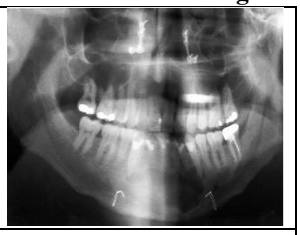
➲arise➔❶dental lamina rest(rest of Serres) ❷gingival graft➔epithelial inclusion cyst(result of surgical procedure)

➲clinic➔bluish painless domelike swelling (>0.5cm) ❶lower canine(premolar) facial gingiva (alveolar mucosa)(60-75%) ❷upper incisor, canine, premolar area ❸5th↔7th decades		➲micro➔❶thin flatten epithelial lining➔with(out) nest of glycogen-rich clear cell➔dental lamina rest(also in c.t.) ❷plaquelike thickening of epithelial lining  

23. What is the difference between **gingival cyst of new born** and **gingival cyst of adult**?
(A) gingival cyst of new born (bluish in color); gingival cyst of adult (whitish in color)
(B) gingival cyst of new born (small papule); gingival cyst of adult (larger dome shaped swelling)
(C) gingival cyst of new born (mandible predominant); gingival cyst of adult (maxilla predominant)
(D) gingival cyst of new born (lining with glycogen-rich clear cell); gingival cyst of adult (lumen with keratin debris)

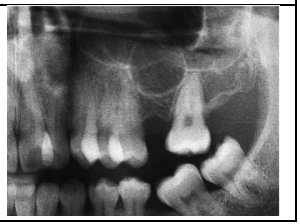
Chapter 8

True cysts of sinuses➔arise ❶subepithelial edema fluid accumulation true epithelium-lined cyst ❷sinonasal mucosa & gland

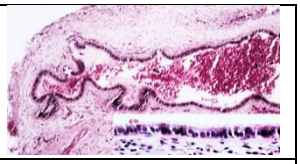
➲3 types➔❶ ❷ ❸ ❶surgical ciliated cyst(traumatic ciliated cyst;postoperative maxillary cyst)(10↔30s postsurgery) ①trauma(surgery)➔detached sinus lining➔epithelium-lined cavity(contain mucus) ②radical surgery➔block drainage passage➔expanding cyst-like structure ③(1)Caldwell-Luc operation(most) (2)upper tooth extraction➔sinus floor damaged ✪genioplasty(chin augmentation, sagittal split osteotomy)➔sinus(nasal) epithelium accidental transplant to mandible➔ectopic ciliated cyst(右圖)	

❷sinus mucocele➔sinus ostium obstruction➔block normal drainage
①blocked sinus➔cyst-like structure lined by epithelium(contain mucus)➔enlarge➔↑intraluminal pressure➔distend sinus wall➔bone erode➔mimic sinus malignancy(unrelated to mucocele of minor salivary gland)

❸retention cyst➔(1)partial blockage of seromucous gland duct in sinus wall (2)invagination of respiratory epithelium
①around ostium/within antral polyp(most)
②most small➔noted during micro exam of antral polyp

➲radiograph ❶surgical ciliated cyst➔spherical RL(lack dome-shaped RO of pseudocyst from sinus floor)➔enlarge➔sinus wall perforation ❷sinus mucocele➔entire cloudy sinus➔enlarge➔thin(eroded)sinus wall ❸retention cyst➔rarely reach a size that produce detectable radiographic change ✪mandibular postoperative cyst 2^0 to genioplasty/chin augmentation➔midline WD-RL ✪2^0 to sagittal split osteotomy➔arise in ascending ramus	

➲**micro**
❶**surgical ciliated cyst & sinus mucocele➔ciliated pseudostratified columnar epithelium with mucous cell**
❷**retention cyst➔duct dilation of seromucous glands of sinus lining**
❸**lumen➔contain thick mucus intermixed with chronic inflammatory cell**



➲**Tx➔surgical ciliated cyst & sinus mucocele➔expansile destructive➔surgical removal**
❶**large mandible cyst➔curettage with marsupialization➔reduce size prior to removal**
❷**maxilla cyst➔①Caldwell-Luc operation ②close to nasal cavity➔best with transnasal endoscopic marsupialization**
❸**sinus mucocele from ostial obstruction➔no need surgery➔①endoscopic middle meatal antrostomy ②marsupialization**

24. Which of the following concerning **cysts of maxillary sinuses** is false?
(A) consist of surgical ciliated cyst, sinus mucocele, sinus retention cyst
(B) surgical ciliated cyst & sinus mucocele show ciliated pseudostratified columnar epithelium with mucous cell
(C) surgical ciliated cyst shows dome-shaped radiopacity from floor of maxillary sinus
(D) size of retention cyst is smaller than that of surgical ciliated cyst and sinus mucocele

Chapter 15: Odontogenic Tumors and Cysts

1. Which one of the following odontogenic lesions is more common in the maxilla than the mandible?
A. Adenomatoid odontogenic tumor
B. Ameloblastic fibroma
C. Calcifying epithelial odontogenic tumor
D. Lateral periodontal cyst
E. Odontogenic keratocyst

2. Which one of the following is the most common presenting sign/symptom of the compound odontoma?
A. Bluish swelling of the gingiva
B. Failure of eruption of a permanent tooth
C. Pain upon mastication
D. Spontaneous abscess formation
E. Spontaneous crevicular bleeding

3. What is the inheritance pattern of the nevoid basal cell carcinoma syndrome?
A. Autosomal dominant
B. Autosomal recessive
C. Multifactorial
D. X-linked dominant
E. X-linked recessive

4. Which one of the following odontogenic tumors is most common?
A. Adenomatoid odontogenic tumor
B. Ameloblastoma
C. Odontogenic fibroma
D. Odontogenic myxoma
E. Squamous odontogenic tumor

5. The nevoid basal cell carcinoma syndrome is caused by a mutation of which gene?
A. Enamelin gene
B. Keratin 6a or keratin 6b
C. Patched (PTCH) gene
D. Ras
E. RET proto-oncogene

6. The most common location for the lateral periodontal cyst is:
A. mandibular bicuspid area
B. mandibular molar area
C. maxillary bicuspid area
D. maxillary incisor area
E. maxillary molar area

7. By definition, a dentigerous cyst must occur:
A. after the age of 25 when all odontogenic activity should have ceased
B. in a periapical location
C. in association with the crown of an unerupted tooth
D. in the place of a tooth that failed to develop
E. in the third molar area

8. The lateral periodontal cyst is most closely related to what other odontogenic cyst?
A. Buccal bifurcation cyst
B. Dentigerous cyst
C. Gingival cyst of the adult
D. Odontogenic keratocyst
E. Paradental cyst

9. The most so-called primordial cysts are microscopically diagnosed as:
A. dentigerous cysts
B. glandular odontogenic cysts
C. odontogenic keratocysts
D. paradental cysts
E. unicystic ameloblastomas

10. The botryoid variant of the lateral periodontal cyst got its name because:
A. it grossly resembles a cluster of grapes
B. it has a high recurrence rate

C. it was first described by Thomas Botry
D. the epithelial lining is ulcerated
E. the original description of the cystic fluid compared it to the slimy trail left by a snail

11. The most common site for the glandular odontogenic cyst is:
A. anterior mandible
B. anterior maxilla
C. parotid gland
D. posterior mandible
E. posterior maxilla

12. Approximately what percentage of ameloblastomas occur in the mandible?
A. 33%
B. 55%
C. 67%
D. 85%
E. 98%

13. Which microscopic variant of ameloblastoma often presents radiographically as a mixed radiolucent and radiopaque lesion?
A. Desmoplastic ameloblastoma
B. Follicular ameloblastoma
C. Granular cell ameloblastoma
D. Plexiform ameloblastoma
E. Unicystic ameloblastoma

14. A microscopically typical ameloblastoma that happens to metastasize to regional lymph nodes is known as:
A. ameloblastic carcinoma
B. ameloblastic fibrosarcoma
C. clear cell odontogenic carcinoma
D. malignant ameloblastoma
E. squamous cell carcinoma

15. Which one of the following odontogenic cysts has the highest recurrence rate?
A. Calcifying odontogenic cyst
B. Dentigerous cyst
C. Glandular odontogenic cyst
D. Lateral periodontal cyst
E. Periapical cyst

16. The adenomatoid odontogenic tumor is frequently associated with an impacted tooth. Which impacted tooth is most likely to be involved?
A. Tooth #1
B. Tooth #6
C. Tooth #17
D. Tooth #27
E. Tooth #30

17. Which one of the following microscopic variants of ameloblastoma has the lowest recurrence rate?
A. Acanthomatous
B. Desmoplastic
C. Follicular
D. Plexiform
E. Unicystic

18. Which one of the following odontogenic cysts is often associated with an odontoma?
A. Calcifying odontogenic cyst
B. Gingival cyst of the adult
C. Gingival cyst of the newborn
D. Glandular odontogenic cyst
E. Orthokeratinizing odontogenic cyst

19. If left untreated, an ameloblastic fibro-odontoma would most likely evolve into which lesion?
A. Adenomatoid odontogenic tumor
B. Ameloblastic carcinoma
C. Ameloblastoma
D. Calcifying epithelial odontogenic tumor

E. Complex odontoma

20. Which odontogenic cyst may sometimes be associated with the nevoid basal cell carcinoma syndrome?
A. Glandular odontogenic cyst
B. Gorlin cyst
C. Lateral periodontal cyst
D. Odontogenic keratocyst
E. Residual cyst

21. Which one of the following is NOT a feature of the nevoid basal cell carcinoma syndrome?
A. Bifid ribs
B. Calcification of the falx cerebri
C. Diabetes insipidus
D. Frontal and parietal bossing
E. Pitting defects on the palms and soles

22. All of the following statements about ameloblastoma are true EXCEPT:
A. Ameloblastoma may present as either a unilocular or multilocular radiolucency
B. Ameloblastomas are more common in the mandible than the maxilla
C. Ameloblastomas are more common in the posterior jaw than the anterior jaw
D. Ameloblastomas are most common in young adults
E. Ameloblastomas are usually best treated with curettage and have a low recurrence rate

23. Which one of the following odontogenic tumors occasionally is associated with a central giant cell granuloma?
A. Adenomatoid odontogenic tumor
B. Ameloblastoma
C. Calcifying epithelial odontogenic tumor
D. Central odontogenic fibroma
E. Squamous odontogenic tumor

24. Which one of the following odontogenic lesions has the highest recurrence rate?
A. Adenomatoid odontogenic tumor
B. Ameloblastic fibro-odontoma
C. Complex odontoma
D. Dentigerous cyst
E. Odontogenic myxoma

25. Which one of the following lesions is also known as a Pindborg tumor?
A. Adenomatoid odontogenic tumor
B. Ameloblastic fibro-odontoma
C. Calcifying odontogenic cyst
D. Odontogenic keratocyst
E. None of the above

26. The eruption cyst is really a variant of the:
A. dentigerous cyst
B. lateral periodontal cyst
C. odontogenic keratocyst
D. periapical cyst
E. none of the above

27. In addition to amyloid that is deposited in various body tissues in systemic amyloidosis, amyloid-like proteins sometimes are discovered within certain tumors. Which one of the following odontogenic tumors often contains amyloid?
A. Ameloblastic fibroma
B. Ameloblastoma
C. Calcifying epithelial odontogenic tumor
D. Complex odontoma
E. Odontogenic myxoma

28. Recurrence after surgery is LEAST likely with which one of the following lesions?
A. Ameloblastic fibro-odontoma
B. Ameloblastoma
C. Odontogenic keratocyst
D. Odontogenic myxoma
E. Pindborg tumor

29. The microscopic hallmark of the calcifying odontogenic cyst is:
A. amyloid production
B. ghost cell keratinization
C. orthokeratin production
D. plexiform epithelium
E. reverse polarization

30. The radiographic appearance of the odontogenic myxoma is most likely to mimic:
A. ameloblastoma.
B. complex odontoma
C. fibrous dysplasia
D. osteosarcoma
E. periapical cemental dysplasia

Chapter 15: Odontogenic Tumors and Cysts➔answers
1. ANS: A
2. ANS: B
3. ANS: A
4. ANS: B
5. ANS: C
6. ANS: A
7.ANS: C
8. ANS: C
9. ANS: C
10. ANS: A
11. ANS: A
12. ANS: D
13. ANS: A
14. ANS: D
15. ANS: C
16. ANS: B
17. ANS: E
18. ANS: A
19. ANS: E
20. ANS: D
21. ANS: C
22. ANS: E
23. ANS: D
24. ANS: E
25. ANS: E
26. ANS: A
27.ANS: C
28. ANS: A
29. .ANS: B
30. ANS: A

Chapter 16 Dermatologic diseases

Synopsis➔terminology

➲macule(斑)(e.g. freckle雀斑)➔focal area of color change➔not elevate/depress in relation to its surrounding
➲patch[(與周圍不同的)小塊斑]➔small area➔different in some way from area that surrounds it
➲plaque(丘斑)➔lesion➔slightly elevated & flat on its surface
➲papule(丘疹)➔solid, raised lesion➔<5mm in diameter
➲nodule(結節)➔solid, raised lesion➔>5mm in diameter

➲papillary(乳突狀)➔tumor/growth➔numerous surface projections
➲verrucous(疣狀)➔tumor/growth➔rough, warty surface

➲vesicle(小水泡)➔superficial blister<5mm in diameter, usually filled with clear fluid
➲bulla(水皰)➔large blister➔>5mm in diameter
➲pustule(膿包)➔blister filled with purulent exudate

➲fissure(裂縫)➔narrow, slitlike ulceration/groove

➲petechia(紫癜)➔round, pinpoint area of hemorrhage
➲ecchymosis(瘀斑)➔nonelevated area of hemorrhage>petechia
➲telangiectasia(毛細血管擴張)➔vascular lesion caused by small, superficial blood vessel dilatation

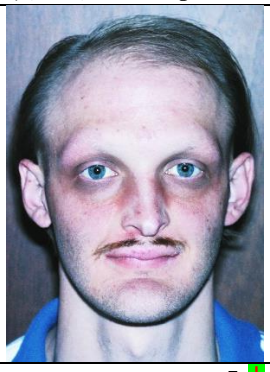
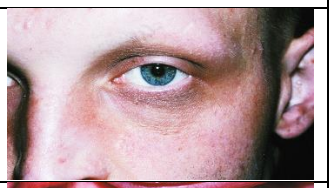
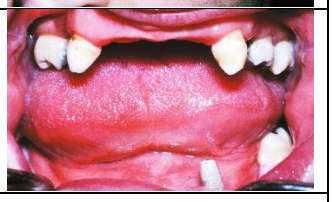
1. Patients with an **X-linked hereditary condition**?
   (A) are always men
   (B) are generally affected more severely if they are men
   (C) are always women
   (D) have cells with many Barr bodies

2. Patents with **hypohidrotic ectodermal dysplasia** characteristically have:
   (A) hypodontia
   (B) multiple tongue nodules
   (C) excessive amounts of hair
   (D) blue sclerae

Ectodermal dysplasia(ED)➔[autosomal dominant(recessive), X-linked]

➲≥2 ectodermal derived structure[❶skin ❷hair ❸nail ❹teeth ❺sweat(salivary) gland]➔a(hypo)plasia
➲hypohidrotic ED(少汗性外胚層發育不良)➔X-linked gene(Xq12-q13.1)(most)➔male predominant

❶autosomal recessive/dominant(few)
❷heat intolerance
❸↓sweat gland
❹fine sparse hair➔↓density of eyebrow眉毛(lash睫毛)
❺periocular skin➔fine wrinkle with hyperpigmentation
❻midface hypoplasia➔protuberant lips
❼salivary gland➔hypoplastic/absent➔xerostomia
❽nail➔dystrophic & brittle
❾oligo(hypo)dontia(anodontia uncommon)➔crown shape abnormal[①incisor crown➔taper(錐), conical(錐形), pointed
②molar crown➔↓diameter]

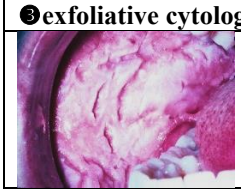
➲female➔Lyon hypothesis➔X-linked recessive(X chromosome➔1 條正常;另 1 條異常)➔↓牙齒no./輕微structure change

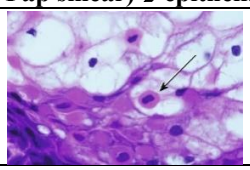
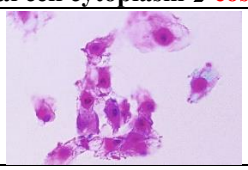
White sponge nevus➔genodermatosis(genetic skin disorder)➔defect in normal keratinization of oral mucosa

➲autosomal dominant➔keratin 4 & 13 pair(spinous cell layer) defect | ➲no need Tx

➲clinic➔at birth(early childhood), adolescence(sometimes)
❶bilateral buccal(most)➔thick white corrugated/velvety(天鵝絨般), diffuse plaque
❷other oral sites(common)➔①ventral tongue ②labial ③soft palate ④alveolar mucosa ⑤mouth floor
❸extraoral➔①nasal ②esophageal ③laryngeal ④anogenital mucosa(less common)

➲micro➔①prominent hyperparakeratosis ②spinous layer➔acanthosis with clear cytoplasm
❶associate➔①leukoedema ②hereditary benign intraepithelial dyskeratosis(HBID)
❷eosinophilic perinuclear condensation(arrow)➔superficial epithelial cell[EM➔tangle mass of keratin tonofilament]
❸exfoliative cytology(Papanicolaou stain, Pap smear)➔epithelial cell cytoplasm➔eosinophilic perinuclear condensation



Hereditary benign intraepithelial dyskeratosis(HBID)➔genodermatosis(genetic skin disorder)

➲autosomal dominant➔affect descendant of triracial(①native American ②black ③white) people➔N. Carolina

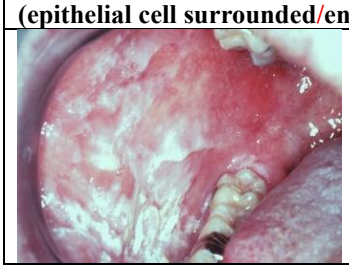
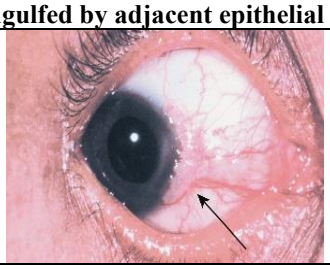
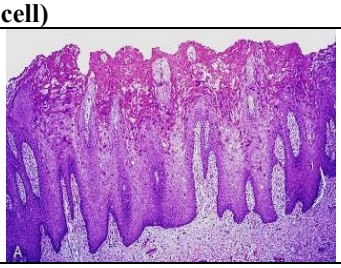
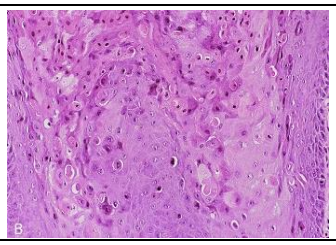
➲clinic➔oral(like white sponge nevus) & conjunctival mucosa of childhood

❶oral➔①buccal & labial[opalescent(乳白色) leukoedema(mild case)]➔superimposed candidiasis
②mouth floor ③lateral tongue

❷ocular➔very early➔thick opaque gelatinous plaque[①spring➔most prominent ②summer/autumn➔regress]➔bulbar conjunctiva adjacent to cornea(active)➔①tearing ②photophobia ③eye itching➔blindness[由於induction of vascularity of cornea 2^0 to shedding(arrow)]

➲micro➔①prominent parakeratin ②marked acanthosis

❶dyskeratosis(like Darier disease)➔scattered throughout upper spinous layer➔cell-within-a-cell phenomenon (epithelial cell surrounded/engulfed by adjacent epithelial cell)

Pachyonychia congenita(先天性厚甲症)(Jadassohn-Lewandowsky type; Jackson-Lawler type)➔genodermatosis(genetic skin disorder)

➲❶autosomal dominant ❷de novo mutation(~45%)➔encode keratin 6a-c,16,17(K6a-c,16,17)

➲nail➔most➔toenail ➲oral➔most K6a mutation ➲type➔based on specific keratin mutation

➲clinic

❶nail change➔birth/neonatal➔①nail free margin lift up(keratin堆積於nail bed)➔pinch(捏), tubular結構➔loss ②palmar-plantar➔↑hyperkeratosis[厚callous(繭)]➔hyperhidrosis➔①blister ②fissure beneath callus➔neuropathic pain with walk

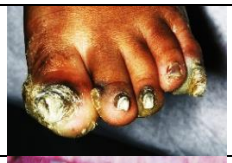
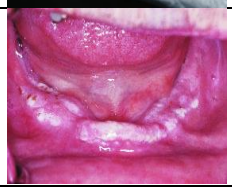
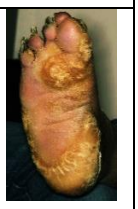
❷skin➔punctate papule➔hair follicle➔abnormal keratin accumulation

❸oral(mild trauma)➔thick white plaque➔①lateral & dorsal tongue
②[palate, buccal, alveolar mucosa]

❹K17 mutation➔①neonatal(新生兒)teeth(time immediate follow birth) ②oral white lesion

❺abnormal keratin➔enamel structure➔↑caries

❻laryngeal mucosa➔①hoarseness ②dyspnea

➲micro➔oral mucosa➔❶marked hyperparakeratosis ❷acanthosis ③perinuclear clear epithelial cell

Dyskeratosis congenita(先天性角化不全)(Cole-Engman syndrome)➔genodermatosis(genetic skin disorder)

➲❶DKC1 gene mutation➔telomere(端粒) disorder➔X-linked recessive➔male predilection

❷autosomal dominant(recessive)(less common) ❸autosomal recessive≠X-linked recessive➔more severe

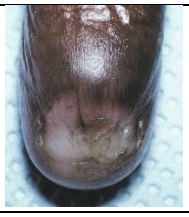
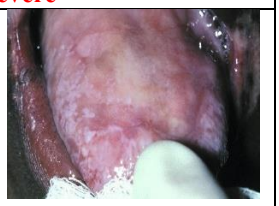
➲clinic➔mild-moderate intellectual disability

❶<10s➔reticular hyperpigment skin➔臉, neck,上胸, nail(dysplastic change)

❷oral➔①tongue & buccal➔bullae➔erosion➔leukoplakia(HOK with epithelial atrophy)➔premalignant(epithelial dysplasia➔1/3➔10-30s癌化)

②rapid progressive periodontal disease

❸thrombocytopenia➔2nd decade➔aplastic anemia(~80%)

Xeroderma pigmentosum(著色性乾皮症)➔genodermatosis(genetic skin disorder)

➲autosomal recessive➔DNA repair defect➔epithelial cell unable to repair UV damage➔mutation➔(non)melanoma skin cancer➔❶10,000×>normal ❷<20s

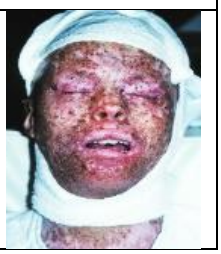
➲clinic➔skin atrophy➔①freckle pigment ②patchy(修修補補) depigmentation(脫色)

❶early childhood➔actinic keratoses(normal not<40s)➔1st decade➔①SCC ②BCC ③melanoma(5%)

❷神經退化(20-30%)➔①subnormal智能 ②ataxia(運動失調) ③sensorineural deaf ④impaired eyesight

❸oral SCC➔lower lip & tongue tip➔<20s

➲micro➔skin (pre)malignancy

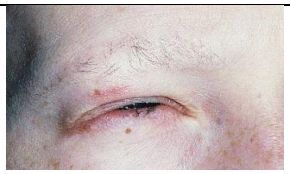


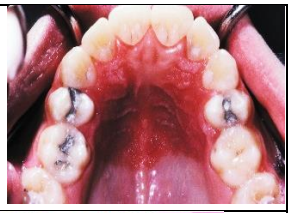
Hereditary mucoepithelial dysplasia➔epithelial cell➔not normal develop➔無↑risk of malignant transformation

➲sporadic/autosomal dominant

➲Pap smear➔epithelial cell➔misinterpret atypical➔hysterectomy(子宮切除術)

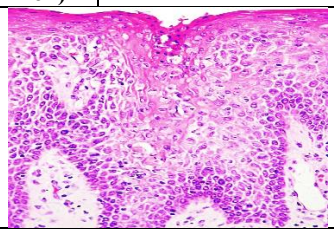
➲clinic➔severe lung complication
❶eyelash睫毛(brow)眼眉➔sparse coarse hair➔nonscar alopecia
❷severe photophobia(early age)➔cataract➔vision impaired
❸rough dry skin➔follicular keratosis(濾泡性角化病)
❹infancy➔prominent perineal(會陰) rash





❺hard palate➔asymptomatic demarcated erythema(attached gingiva & tongue➔less common)

❻[nasal, conjunctival, vaginal, cervical, urethral, bladder mucosa]➔erythematous



➲micro
❶minimal keratinization & disorganized maturation pattern
❷epithelial cell➔↑N/C ratio
❸significant nuclear/cellular pleomorphism➔not observed
❹exfoliative cytology➔cytoplasmic vacuole➔grayish inclusion
❺EM➔↓desmosome no. & internalized gap junction

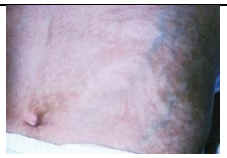
Incontinentia pigmenti(色素失調症)(Bloch-Sulzberger syndrome)➔genodermatosis(genetic skin disorder)

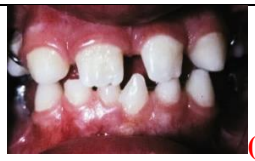
➲Xq28 locus➔IKBKG(inhibitor of kappa B kinase gamma)gene➔X-linked dominant➔F:M ratio=37:1

➲IKBKG gene➔於早期embryogenesis active➔保護embryo from apoptosis➔[❶mutation in female➔less impact(因有2X chromosome) ❷mutated male embryo➔lethal➔if survive➔Klinefelter syndrome(XXY karyotype染色體圖譜)]➔affect ❶skin ❷eye ❸CNS ❹oral

➲clinic➔infancy(1st few-wk)
4 classic stages(❶❷❸❹)➔cutaneous lesion
❶vesicular➔①vesiculobullous➔trunk & limb ②spontaneous resolution➔within 4-month
❷verrucous➔verrucous cutaneous plaque➔limb➔clear by age 6-month
❸hyperpigmentation➔brown macule skin lesion➔swirling pattern➔fade around puberty(下左圖)
❹atrophy & depigmentation➔①skin atrophy ②depigmentation
➲CN(~30%)➔①intellectual disability ②seizure ③motor difficulties
➲ocular(35%)➔①strabismus(斜視) ②nystagmus(眼球震顫) ③cataract(白內障) ④retina血管異常 ⑤optic nerve atrophy
➲oral(70-95%)➔①oligo(hypo)dontia ②delay eruption ③high-arch palate ④hypoplasia/cone shaped crown(下右圖)

➲micro
❶vesicular➔intraepithelial cleft filled with eosinophil
❷verrucous➔hyperkeratosis, acanthosis, papillomatosis
❸hyperpigmentation➔melanin-containing macrophage➔subepithelial connective tissue





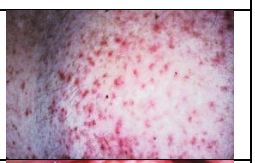
(乳牙及恆牙)

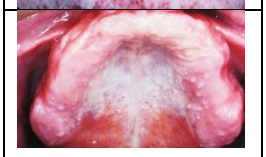
Darier disease(Dyskeratosis follicularis; Darier-White disease)➔genodermatosis(genetic skin disorder)

➲epithelial cell➔lack cohesion➔abnormal desmosomal organization➔↑epithelial cleft

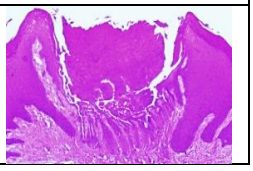
➲autosomal dominant➔ATP2A2 gene mutation➔intracellular Ca^{2+} pump(SERCA2-sarco/endoplasmic reticulum Ca^{2+}-ATPase isoform 2)

➲clinic
❶1st/2nd decade➔trunk & scalp skin➔erythematous, pruritic(搔癢) papule(右上圖)
❷keratin accumulate➔rough texture➔bacterial keratin degradation➔foul odor➔worse in summer[由於①UV light sensitivity ②↑heat in sweating]➔↑epithelial cleft
❸palm & sole➔pit & keratoses➔nail➔①longitudinal(縱的) line ②ridge ③painful split
❹oral(15↔50%)➔hard palate(like inflammatory papillary hyperplasia/nicotine stomatitis) & alveolar mucosa(buccal/tongue occasion)➔asymptomatic➔multiple normal-color/white, flat-topped papule➔confluent to cobblestone(右下圖)
❺recurrent obstructive parotid swelling 2^0 to duct abnormalities





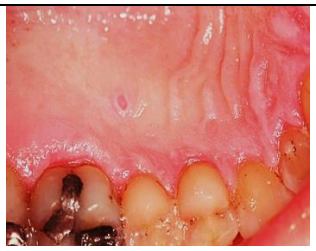
➲micro
❶dyskeratosis➔①central keratin plug ②overly epithelium➔suprabasilar cleft➔acantholysis (also in pemphigus vulgaris)
❷rete ridge➔narrow, elongated, test tube-shaped
❸2-type dyskeratotic cell➔①corps ronds(round bodies) ②grain(resemble cereal grain)

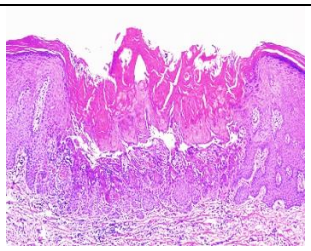


3. 關於**疣狀角化不良(warty dyskeratoma)**的敘述何者錯誤？(113)
(A) 好發於中老年人頭頸區的皮膚
(B) 若發生於口內，則常出現在角質化黏膜區間(keratinized mucosa)
(C) 多數皮膚病灶的直徑大於2 cm
(D) 組織學上可見上皮內陷(invagination)中充滿角質栓(keratin plug)

Warty dyskeratoma疣状角化不良(**Isolated Darier disease**)micro➔**identical to Darier disease**

➲**clinic**➔solitary skin/oral mucosa
❶HN skin(older adult)➔**asymptomatic**, **umbilicated papule**➔older adult(multiple reported)
❷**oral**➔>40s➔slight male predilection➔**pink/white umbilicated papule**➔①**hard palate** ②alveolar ridge➔warty surface➔most**≤0.5cm**
➲**micro**➔❶like **dyskeratosis follicularis** ❷dyskeratosis, **basilar hyperplasia**, **suprabasilar cleft**(**acantholysis**)

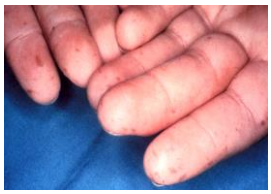




4. Which of the following is a component of **Peutz-Jeghers syndrome**?
(A) multiple jaw cysts
(B) multiple supernumerary teeth
(C) multiple pigmented macules in lower lip
(D) multiple nodules on the tip of tongue

Peutz-Jeghers syndrome

➲hand, perioral skin, oral➔**freckle**-like lesion



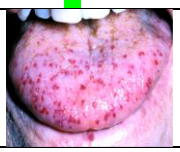
➲**intestinal polyposis**➔intestinal glandular epithelium **overgrowth** supported by smooth muscle core➔**epithelial atypia NOT prominent**(**not premalignant**)
➲**predisposition to develop GI cancer**(**not from polyp**)
➲↑other tumors(❶pancreas ❷breast ❸ovary ❹male & female genital tract)
➲**oral lesion**(>90%)(1↔4mm brown to blue-gray **macule**)
❶vermilion ❷labial ❸buccal mucosa ❹tongue

5. The major concern when treating a patient with **Osler -Rendu syndrome** should be:
(A) gingival hemorrhage
(B) spontaneous ulcerations
(C) severe infections
(D) epithelial desquamation

Hereditary hemorrhagic telangiectasia(**HHT**)(**Osler-Weber-Rendu syndrome**)

➲autosomal dominant➔mutation[❶**HHT1**➔endoglin(ENG) gene(chromosome 9) ❷**HHT2**➔activin receptor-like kinase-1(ALK1; ACVRL1) gene(chromosome 12)]➔affect blood vessel wall integrity➔[❶skin & mucosa➔①vascular hamartoma ②arteriovenous fistula ❷lung(15↔45%)➔brain abscess(由於R-L shunt of bacteria➔bloodstream) ❸liver(30%) ❹brain(10-20%)]
➲HHT1➔❶pulmonary ❷cerebral involvement
➲HHT2➔❶later onset of telangiectasias ❷hepatic involvement
➲**MADH4** gene mutation(less common)➔❶HHT ❷**juvenile polyposis**➔上&下GI tract➔↑risk of early **colorectal ca.**

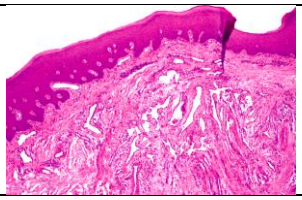
➲epistaxis(鼻出血)➔nasal & oropharyngeal mucosa➔scattered red papule (1↔2mm)➔blanch(發白)when **diascopy**(玻片壓診法)



➲telangiectasia close to mucosa(①vermilion zone of lips ②tongue ③buccal)➔red color

➲telangiectasias➔❶hand & feet ❷GI mucosa➔rupture➔significant blood loss
❸genitourinary mucosa ❹conjunctival mucosa
➲**iron-deficiency anemia**
➲**periodontal vascular malformation**➔septic lung emboli➔**resolve after extract teeth with periodontal abscess**

➲**3 out of ❶-❹➔HHT diagnosis**
❶recurrent spontaneous epistaxis
❷telangiectasias of mucosa & skin
❸arteriovenous malformation➔①lung ②liver ③CNS
❹HHT family history



➲**micro**➔superficial thin-walled vascular space➔RBCs

➲d.d. **CREST syndrome**(**c**alcinosis cutis, **R**aynaud phenomenon, **e**sophageal dysfunction, **s**clerodactyly, **t**elangiectasia)➔anti**c**entromere auto**a**ntibodies➔**ONLY** in CREST syndrome

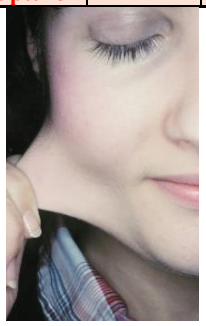
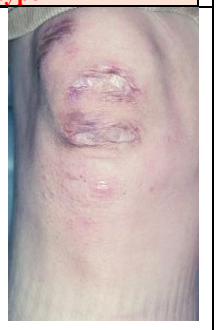
Ehlers-Danlos syndromes➔abnormal collagen(connective tissue main structural component) production

➲**common type**➔autosomal dominant(AD)

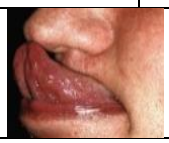
type	clinic	genetic	collagen mutation
❶classic(**severe**)	①**hyper**extensible skin ②**easy bruising** ③**hyper**mobile joint ④**papyraceous scar** of skin ⑤**pulp stone**	AD	**type V**
❶classic(**mild**)➔normal life span	less severe classical manifestation	AD	**type V**

❷hypermobility	①soft skin ②no scarring ③marked joint hyperextensibility	AD	not known
❸vascular(ecchymo(tic)sis)	①severe bruising ②risk for arterial, bowel, uterine rupture	AD	type III

➲clinic➔4 types(❶↔❹)
❶classical(~80%)➔①hyperelasticity of skin(左圖) ②skin fragility
③minor injury➔papyraceous scar➔like crumple(皺巴巴) cigarette paper(右圖)
❷hypermobility➔①remarkable joint hypermobility➔no scar
②greater degree chronic musculo-skeletal pain
❸vascular➔①extensive bruise➔trauma(everyday)
②aortic aneurysm rupture➔↓life expectancy➔sudden death➔aorta rupture 2^0 to weaken collagen of vessel wall
❹periodontal variant(rare)➔①marked periodontal disease at early age
②↓/no attached gingiva ③C1R & C1S mutation

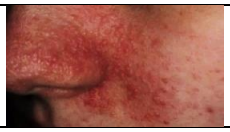
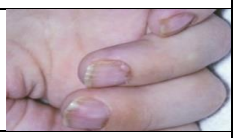
➲oral➔❶nose tip touch with tongue(Gorlin sign)(50% vs<10% general population)(右圖)
❷bruise & bleed ❸mucosa friability ❹TMJ recurrent subluxation
❺teeth➔①malformed ②stunted root
③pulp stone ④enamel hypoplasia



Tuberous sclerosis(結節性硬化症)➔❶intellectual disability ❷seizures ❸skin angiofibroma

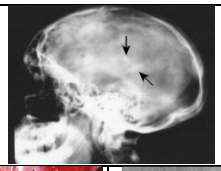
➲❶autosomal dominant ❷sporadic mutation(2/3 cases)➔tumor suppressor genes[①TSC1(chromosome 9)
②TSC2 (chromosome 16)(more common➔2/3 cases)]➔target of Rapamycin(mTOR)路徑➔multiple hamartomas

➲clinic
❶facial angiofibroma➔multiple smooth papules➔nasolabial fold(左圖)
❷(peri)ungual(指(趾)甲fibromas➔nail margins(右圖)

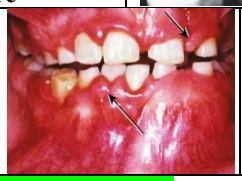
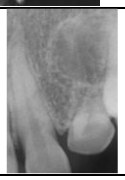



❸ash-leaf spots(90↔98%)➔shagreen(鯊革➔表面粗糙又有粒狀的生皮)patch & ovoid hypopigmentation(UV lamp)
❹confetti(五彩纸屑) spots➔1↔3mm pale macules➔trunk-extremities(symmetrical distribute)

❺CNS➔T_2W MRI(80↔95%)➔potato-like growth(tuber) hamartoma➔patchy calcification➔subependymal giant cell astrocytoma(benign brain tumor)(10%)
❻cardiac rhabdomyoma(30↔50%, child)➔hamartoma(非neoplasm)➔①spontaneous regression
②myocardial function
❼kidney➔angiomyolipoma(bilateral)➔large dilated blood vessel➔spontaneous rupture



❽oral
①enamel pitting➔facial of anterior permanent dentition(50↔100%)
②fibrous papule(11↔56%)➔anterior gingiva(左圖)(lips, buccal, palate, tongue可能有)
③diffuse fibrous gingiva enlargement(even without phenytoin)
④RL of jaws➔dense fibrous c.t. proliferations(右圖)

➲dx➔≥2 major features
❶facial angiofibromas/(peri)ungual fibromas
❷hypomelanotic macules(≥3)/shagreen patch CNS hamartomas
❸subependymal nodules/subependymal giant cell astrocytoma
❹cardiac rhabdomyoma/renal angiomyolipoma
❺multiple retinal nodular hamartomas
❻lymphangioleiomyomatosis of lung

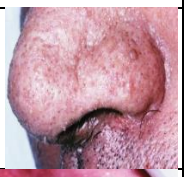
➲dx➔1 major & 2 minor features
❶multiple, randomly distributed enamel pits
❷gingiva fibromas
❸bone cysts(actually fibrous proliferations)
❹confetti skin lesions
❺multiple renal cysts
❻non-renal hamartomas

Multiple hamartoma syndrome(Cowden syndrome; PTEN hamartoma-tumor syndrome)

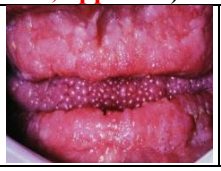
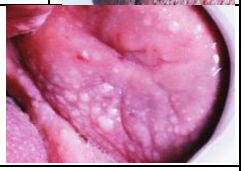
❶autosomal dominant ❷phosphatase & tensin homolog deleted on chromosome 10(PTEN)基因突變(45%)(chromosome 10)

❶Lhermitte-Duclos disease ❷Bannayan-Riley-Ruvalcaba syndrome ❸Proteus-like syndrome➔PTEN基因突變

➲clinic
❶cutaneous(2nd decade)
①multiple papules(≤1mm)➔skin around mouth, nose, ear➔hair follicle hamartoma(trichilemmoma)
②acral keratosis(光化性角化)➔warty➔hand dorsal surface, palmoplantar keratosis(腳底明顯callus)
③hemangioma, sclerotic fibroma, neuroma, xanthoma, lipoma ✻BCC(see Chapter 10; appendix)



❷thyroid➔①goiter(thyroid adenoma) ②papillary/follicular adenocarcinoma
❸breast➔①fibrocystic disease ②breast cancer
❹GI tract➔multiple benign hamartomatous polyps
❺oral➔①multiple papules➔gingiva, dorsal tongue(左圖), buccal mucosa(右圖)
②high-arched palate ③periodontitis ④caries

➲dx
❶2 out of ①②③pathognomonic signs[①facial trichilemmoma ②oral papule ③acral keratosis]

❷PTEN gene mutation➔20%(-)➔(-)not preclude multiple hamartoma syndrome

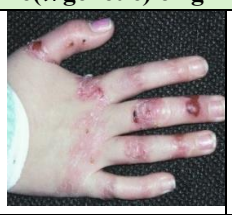
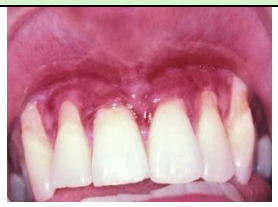
6. What is the **target structure** of **epidermolysis bullosa acquisita**?
   (A) desmoglein 3 of desmosome
   (B) hemidesmosome
   (C) type VII collagen of anchoring fibrils
   (D) basement membrane zone

Epidermolysis bullosa(EB)表皮溶解水皰➔inherited blistering mucocutaneous disorders

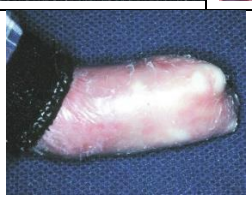
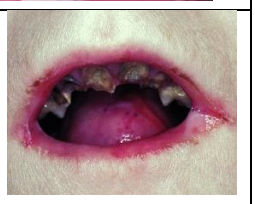
➲4 categories(❶↔❹)
❶simplex➔①hand & feet blister(mucosa uncommon)➔heal without scar➔癒後good ②keratin 5,14 mutations
❷junctional➔①death at birth➔skin sloughing during passage via birth canal ②[laminin-332, collagen XVII, α6β4 integrin]➔mutation(hemidesmosome) ③↑significant dental abnormalities(anodontia, enamel hypoplasia, enamel pit, neonatal teeth, severe periodontitis, severe caries)
❸dystrophic➔①collagen VII mutation ②oral lesion➔most common
❹Kindler syndrome➔hemidesmosome attachment protein, kindlin-1 mutation

✹EB acquisita➔similar name(BUT unrelated condition)➔autoimmune(非genetic) origin

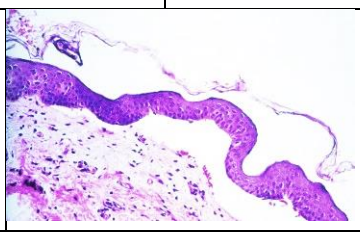
➲clinic
❶dominant dystrophic➔disfiguring➔not life threat
①vesicles/bullae(early in life)(左圖)➔low-grade chronic trauma ➔knuckle(關節)/knee➔rupture➔erosion(ulcer)➔heal with scar➔fingernail loss
②oral➔gingiva erythema(recession)(右圖), ↓buccal vestibule depth

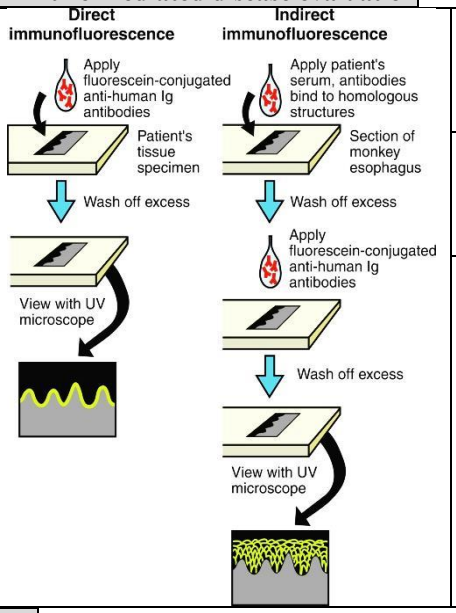
❷recessive dystrophic
①generalized recessive EB➔severe mucosa involve; hand & feet mittenlike(像連指手套) scar(deformities)(左圖); die early adulthood
②oral➔food with some degree of texture(even soft diet➔caries) ➔vesicles/bullae➔cycle of scar➔microstomia & ankyloglossia➔ severe esophagus stricture(右圖)

➲micro
①simplex form➔intraepithelial cleft(左圖)
②junctional, dystrophic, Kindler forms➔subepithelial cleft
EM
①junctional form➔cleft at level of lamina lucida of basement membrane
②dystrophic form➔cleft below lamina densa of basement membrane
③Kindler form➔cleft just below basal cell layer(interface with lamina lucida)

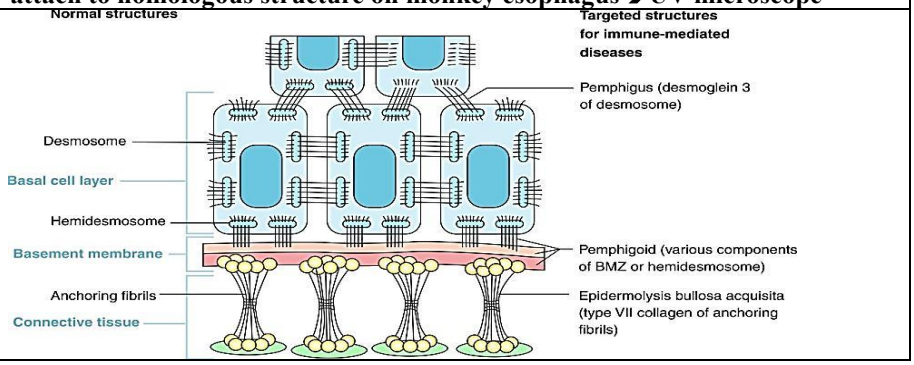


Immune-mediated disease evaluation



➲direct immunofluorescence(IF)
❶detect autoAb bound to p't tissue
❷frozen section➔incubate fluorescein-conjugated goat antihuman Ab➔ bind to human Ig➔UV microscope

➲indirect immunofluorescence(IF)
❶detect autoAb bound to monkey esophagus(like human oral mucosa)
❷frozen section➔incubate patient's serum autoAb *vs* epithelial structure➔ attach to homologous structure on monkey esophagus➔UV microscope



Synopsis

➲X-linked recessive➔male predominant ❶ectodermal dysplasia(ED) ❷dyskeratosis congenita(先天性角化不全)	➲risk of SCC & epithelial dysplasia/other malignancy ❶dyskeratosis congenita(先天性角化不全) ①leukoplakia (epithelial dysplasia)➔SCC

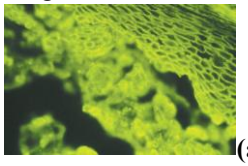
➲X-linked dominant➔female predominant ❶incontinentia pigmenti(色素失調症)➔male lethal➔if survive➔ Klinefelter syndrome	❷aplastic anemia ❷xeroderma pigmentosum(著色性乾皮症) ①SCC ②BCC ③melanoma ❸GVHD➔SCC & epithelial dysplasia ❹hereditary hemorrhagic telangiectasia(HHT) (Osler-Weber-Rendu syndrome) ①colorectal carcinoma➔MADH4➔juvenile polyposis ②iron-deficiency anemia
➲eyebrow眉毛(lash睫毛) ❶ED➔fine sparse hair ❷hereditary mucoepithelial dysplasia➔coarse sparse hair	
➲micro➔HPK+acanthosis ❶white sponge nevus ❷hereditary benign intraepithelial dyskeratosis ❸incontinentia pigmenti(色素失調症)➔verrucous stage ❹pachyonychia congenita(先天性厚甲症)	➲micro➔keratin plug+suprabasilar cleft(acantholysis➔ Tzanck cell)+basilar hyperplasia ❶Darier disease(dyskeratosis follicularis) ❷warty dyskeratoma(疣状角化不良)
➲micro➔HPK+atrophy ❶dyskeratosis congenita(先天性角化不全)	➲micro➔intraepithelial cleft(acantholysis) ❶incontinentia pigmenti(色素失調症)(vesicular stage) ❷(paraneoplastic) pemphigus ❸epidermolysis bullosa(simplex form) ❹erythema multiforme
➲keratin mutation ❶white spongy nevus➔K4,13 ❷achyonychia congenita(先天性厚甲症)➔K6,16,17 ❸epidermolysis bullosa(simplex form)➔K5,14	➲micro➔subepithelial cleft ❶pemphigoid ❷paraneoplastic pemphigus ❸epidermolysis bullosa(junctional, dystrophic, Kindler forms) ❹epidermolysis bullosa acquisita ❺erythema multiforme

Chronic vesicuoulcerative diseases➔ ❶pemphigus vulgaris ❷paraneoplastic pemphigus ❸mucous membrane pemphigoid ❹mucous membrane pemphigoid ❺erythema multiforme ❻lichen planus

chronic vesicuoulcerative diseases	av. age	sex	clinic	micro	direct IF	indirect IF
❶pemphigus vulgaris (desquamative gingivitis)	4th-6th decade	equal	vesicle, erosion & ulcer on any oral mucosa/skin	intraepithelial cleft	(+)intercellular	(+)
❷paraneoplastic pemphigus	6th-7th decade	equal	vesicle, erosion, & ulcer on any oral mucosa/skin	subepithelial & intraepithelial cleft	(+)intercellular & basement membrane zone(BMZ)	(+)rat bladder
❸mucous membrane pemphigoid (desquamative gingivitis)	6th-7th decade	female	1^0 mucosa lesions	subepithelial cleft	(+)BMZ	(-)
❹bullous pemphigoid	7th- 8th decade	equal	1^0 skin lesions	subepithelial cleft	(+)BMZ	(+)
❺erythema multiforme	3rd-4th decade	male	skin & mucosa involve; target lesion(skin)	sub(intra)epithelial cleft & perivascular inflammation	nondiagnostic	(-)
❻lichen planus (erosive type➔ desquamative gingivitis)	5th-6th decade	female	oral &/or skin may/may not erosive	hyperkeratosis, saw-tooth rete ridge, lymphocytic band basal liquefaction	(+)fibrinogen, BMZ (not specific for lichen planus)	(-)

7. **Tzanck cells** are seen in which of the following conditions?
   (A) pemphigus vulgaris
   (B) erythema multiforme
   (C) systemic lupus erythematosus
   (D) Behcet syndrome

8. What is the **target structure** of **pemphigus**?
   (A) desmoglein 3 of desmosome
   (B) hemidesmosome
   (C) type VII collagen of anchoring fibrils
   (D) basement membrane zone

9. Figure below depicting **histopathological** finding (left) & **direct immunofluorescence** pattern in intercellular areas between the epithelial cells, resulting in a **"chicken wire" pattern** (right); what is the most adequate histopathological diagnosis?
   
   
   (also called "fishnet" pattern)
   (A) pemphigus vulgaris

(B) mucous membrane pemphigoid
(C) lichen planus
(D) epidermolysis bullosa acquisita

Pemphigus➔oral lesion➔1st to show & last to go

➲flaccid bulla➔quick rupture(within hours-few day)➔erythematous denuded surface➔untreated➔death

➲ocular➔bilateral conjunctivitis➔no scar(symblepharon 瞼球粘連)➔unlike mucous membrane pemphigoid

➲Nikolsky sign➔firm lateral pressure➔normal skin➔acantholysis(Tzanck cell)➔cell of spinous layer➔fall apart

➲5 types

(1) 尋常性天皰瘡 (pemphigus vulgaris)/
增殖性天皰瘡 (pemphigus vegetans)
(2) 葉狀天皰瘡 (pemphieus foliaceus)/
紅斑性天皰瘡 (pemphigus erythematosus)
(3) 藥物引起天皰瘡 (drug-induced pemphigus)
(4) IgA天皰瘡 (IgA-pemphigus)
(5) 伴腫瘤天皰瘡 (paraneoplastic pemphigus)

Variants	Antigens location	Main antigens	Antibody class	Oral lesions
Pemphigus vulgaris	Desmosomes	Dsg3	IgG	Common
Pemphigus foliaceus	Desmosomes	Dsg3	IgG	Uncommon
Drug-induced pemphigus	Desmosomes	Dsg1	IgG	Common
IgA pemphigus	Desmosomes	Dsg3 Desmocollin 1 Desmocollin 2	IgA	Uncommon
Paraneoplastic pemphigus	Desmosomes or hemidesmosomes	Dsg3 Desmocollin 1 Desmocollin 2 BP230 Periplakin	IgG or IgA	Common

➲causes of acantholysis

* Primary
Pemphigus
Darier's disease
Transient acantholytic dermatosis
Warty (疣) dyskeratoma

* Secondary
Impetigo (膿皰瘡)
Viral infections
Carcinoma

Paraneoplastic pemphigus➔cytotoxic T lymphocyte

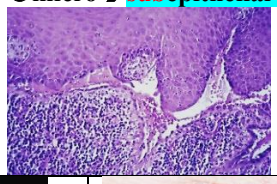
➲伴隨 lymphoma/chronic lymphocytic leukemia(CLL)➔↑(cytokine, IL-6)➔↑Ab attack desmosome & BMZ

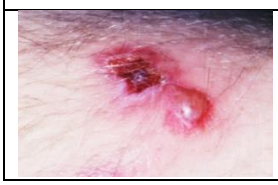
➲伴隨 benign lymphoproliferative disorder➔angiofollicular LN hyperplasia(Castleman disease➔associate HHV-8)

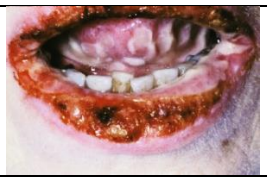
➲clinic
❶multiple vesiculobullous lesions➔skin & oral mucosa(下右 2 圖)
❷palmar/plantar bullae➔a feature uncommon in pemphigus vulgaris
❸skin lesion➔more papular & pruritic➔like skin lichen planus (下左 1 圖)
❹lip➔hemorrhagic crusting ➔like erythema multiforme(下左 2 圖)
❺conjunctiva➔cicatrizing conjunctivitis➔like mucous membrane pemphigoid(下右 1 圖)

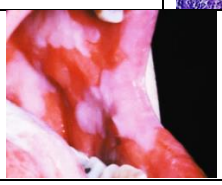
❻anogenital, nasopharyngeal, esophageal, respiratory tract mucosa➔involved
❼lung➔bronchiolar mucosa➔slough➔occlude bronchiolar lumina & alveoli➔bronchiolitis obliterans

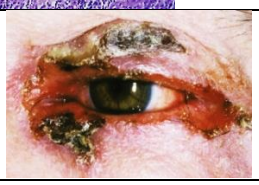
➲micro➔subepithelial & intraepithelial cleft









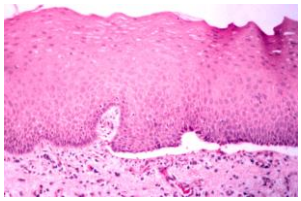
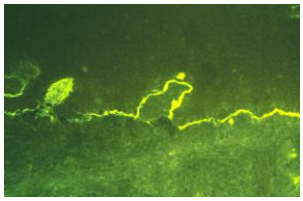


10. **Mucous membrane pemphigoid** not only affecting **oral cavity and skin,** it also likely involves which of the following region?
(A) ocular
(B) brain
(C) intestine
(D) bone

11. **Mucous membrane pemphigoid** most often affect:
(A) oral mucosa
(B) skin
(C) ocular
(D) gastrointestinal tract

12. What is the **target structure** of **pemphigoid**?
(1) desmoglein 3 of desmosome (2) hemidesmosome (3) type VII collagen of anchoring fibrils (4) basement membrane zone
(A) only 1,2
(B) only 2,3
(C) only 3,4
(D) only 2,4

13. Figure below depicting histopathological finding (left) and **direct immunofluorescence pattern** of immunoreactants **deposited in basement membrane zone** of the epithelium (right); what is the most adequate histopathological diagnosis?

(A) pemphigus vulgaris
(B) mucous membrane pemphigoid
(C) lichen planus
(D) epidermolysis bullosa

14. What are true for **bullous pemphigoid (BP)**?
(1) direct immunofluorescence shows a linear band of IgG & C3 at basement membrane (BM)
(2) BP antigens (BP180 & BP230); immunoelectron microscopy showed BP180 in upper portion of lamina lucida of BM
(3) BP resembles mucous membrane pemphigoid (MMP)
(4) clinical course in BP patients has periods of remission followed by relapse; MMP is protracted and progressive
(A) only 1,3
(B) only 2,4
(C) only 1,2,3
(D) 1,2,3,4

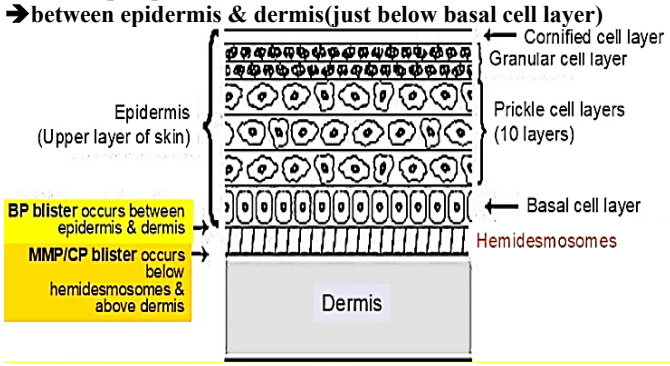
15. Which of the following statements about autoimmune disease with oral manifestations is considered *false*?
(A) the bullae in pemphigus vulgaris are more fragile than those in bullous pemphigoid
(B) acantholysis of the epithelium is seen in pemphigus vulgaris
(C) in pemphigoid the separation of the epithelium from the connective tissue occurs at the basement membrane
(D) skin lesions are common in mucous membrane pemphigoid

16. Which is the most distinct and definite characteristic that distinguishes **pemphigus from pemphigoid**?
(A) size of the ulcerations
(B) age and gender of the patient
(C) microscopic findings
(D) Nikolsky sign

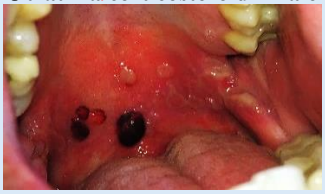
17. **Desquamative gingivitis** may be present in all of the following *except*:
(A) cicatricial pemphigoid
(B) pemphigus vulgaris
(C) lichen planus
(D) aggressive periodontal disease

Pemphigoid➔❶Mucous membrane pemphigoid(Cicatricial pemphigoid) ❷Bullous pemphigoid

➲**2 major types**
❶**mucous membrane pemphigoid(MMP)/cictricial phemphigoid**
➔**below hemidesmosome; above dermis(blister roof)**
❷**bullous pemphoid(BP)**
➔**between epidermis & dermis(just below basal cell layer)**



➲**other conditions(micro like pemphigoid)**
❶**linear IgA bullous dermatosis**
①**linear deposition only IgA➔BMZ ②skin predominant**
❷**angina bullosa hemorrhagica➔middle-aged/older adult**
①**oral mucosa➔soft palate➔pain blood-filled vesicle/bulla**
②**blister➔rupture spontaneous➔heal without scar➔subepithelial cleft**
③**trauma/corticosteroid inhale**

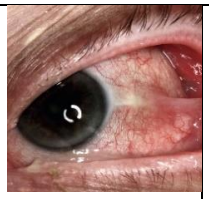


❸**epidermolysis bullosa acquisita**
①**autoAb➔type VII collagen(ancho fibril bind epithelium to c.t.)➔bulla(minimal trauma)➔middle-aged/older adult**
②**oral(50%)➔uncommon without skin lesion**
③**perilesional skin➔incubate in concentrated salt solution ➔epithelium separate from c.t.➔artificial bulla➔IHC➔IgG autoaAb deposit**
✪**bulla floor(c.t.)➔type VII collagen ✪blister roof➔MMP**

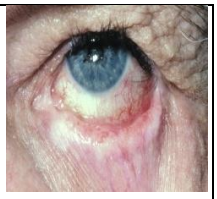
❶Mucous membrane pemphigoid(Cicatricial pemphigoid)

➲**ocular➔oral lesion patient(25%)**	➲**ocular lesion➔affect one eye before the other**

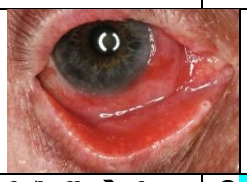
❶earliest➔subconjunctival fibrosis (ophthalmologist➔slit-lamp micro exam)➔ inflamed & eroded conjunctiva➔scar between bulbar(lining eye globe) & palpebral(lining eyelid inner surface)conjunctivae➔symblepharons(瞼球粘連)

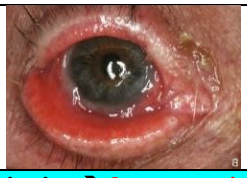


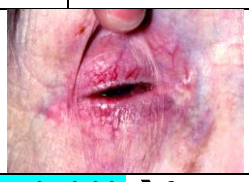
❷severe➔scar➔eyelid (眼瞼)內翻(entropion) ➔eyelash(睫毛)rub cornea(角膜) & globe (trichiasis)(倒睫)



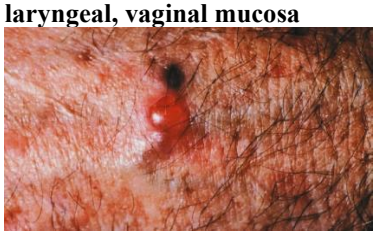
❸scar➔close off lacrimal gland opening➔loss of tear➔dry eye➔cornea➔keratin➔ blindness(上下眼瞼adhesion)



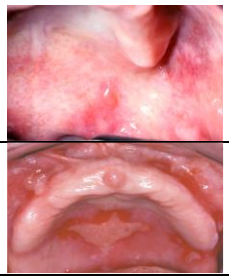




➲skin(20%)➔tense bullae
➲conjunctiva, nasal, esophageal, laryngeal, vaginal mucosa



➲oral➔vesicle/bulla➔ulcer

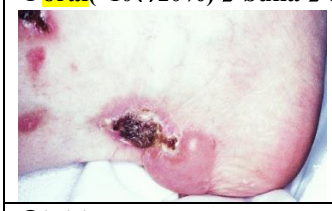


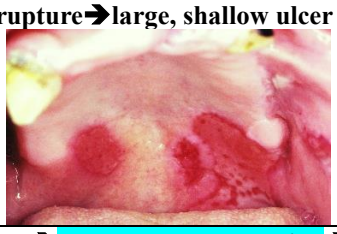
➲gingiva➔desquamative gingivitis ➔also erosive lichen planus & pemphigus vulgaris

Bullous pemphigoid

➲skin➔pruritus➔tense bullae➔正常/erythematous➔rupture(after few days)➔superficial crust➔heal without scar

➲oral(~10↔20%)➔bulla➔rupture➔large, shallow ulcer





➲micro
❶direct IF➔linear band(IgG & C3)➔BMZ➔ hemidesmosomes➔BP180 &230
❷EM➔BP180➔upper portion of lamina lucida of BM
❸indirect IF➔serum circulate autoAb(50-90%)➔titer➔ not correlate disease activity

❹initiate complement cascade➔mast cell degranulation➔neutrophil & eosinophil➔elastase & matrix metalloproteinase(MMP)➔BM damage

18. The most common precipitating factors of **erythemal multiforme** are
(A) bacterial infection
(B) hereditary
(C) autoimmunity
(D) virus infection and drug

19. **Erythema multiforme major** not only affecting mucosa, and skin, it also involves which of the following region?
(A) ocular
(B) brain
(C) intestine
(D) bone

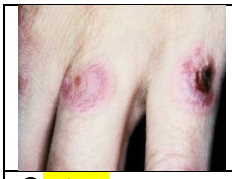
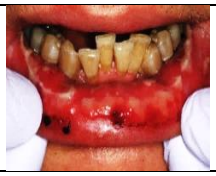
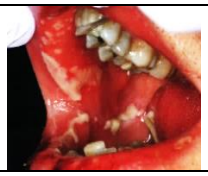
20. A **target lesion on skin** is associated with which of the following diseases?
(A) Behcet syndrome
(C) systemic lupus erythematosus
(C) lichen planus
(D) erythema multiforme

Erythema multiforme(EM)(多形性紅斑)➔electron microscope➔spectrum of severity➔❶EM minor ❷EM major

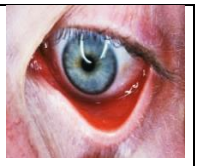
➲cell-mediated(非humoral) immune-attack➔oral mucosa &/or epidermis(mucocutaneous condition)➔blister, ulcer

➲precipitating cause(trigger attack)➔❶infection(herpes simplex, mycoplasma pneumoniae) ❷antibiotic/analgesic

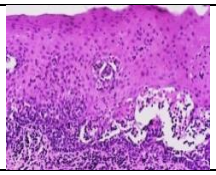
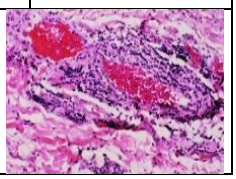
➲clinic➔20s/30s➔prodromal(前驅) symptom(onset前1-wk)➔fever, malaise(身體不適), headache, cough, sore throat
❶EM minor
①skin➔slight↑round dusky(昏暗)-red patch➔extremities➔concentric erythematous ring➔target lesion(like bull eye)➔bullae with necrotic center(下左圖)
②oral➔erythematous patch➔necrosis➔large, shallow erosion & ulceration➔hemorrhagic crust➔lip vermilion (common➔lip(下中圖), labial, buccal(下右圖), tongue, mouth floor, soft palate; spare➔gingiva & hard palate)
③mouth pain➔cannot ingest liquid➔dehydrated

❷EM major
①≥2 mucosa+skin+ocular/genital
②ocular➔scar(symblepharon瞼球粘連)➔ like mucous membrane pemphigoid



➲micro
❶subepithelial/intraepithelial vesicle➔basal keratinocyte(necrotic)(左圖)
❷perivascular inflammatory infiltrate(lymphocyte, neutrophil, eosinophil)(右圖)

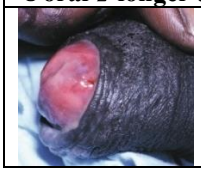
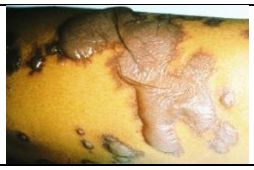
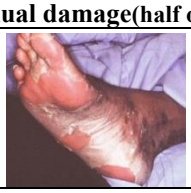



Stevens-Johnson syndrome & toxic epidermal necrolysis➔drug exposure trigger➔↑apoptosis➔epithelium damage

➲clinic➔female predilection

difference	Stevens-Johnson syndrome	toxic epidermal necrolysis
affect body surface	<10%	>30%
average rate	1-7case/million/year	1 case/million/year
age	younger	60s(older)

❶flu-like prodromal symptom➔fever, malaise, sore throat, headache, appetite loss
❷skin(幾天內)➔trunk(unlike EM)➔skin erythematous macule(within 1-14天內)➔skin slough➔flaccid(弛緩) bullae
❸all➔mucosa involve(esp. oral)➔diffuse slough➔badly scald(燙傷)➔if survive➔①skin resolve(in 3-5 wk)
②oral➔longer to heal ③ocular➔residual damage(half of patient)

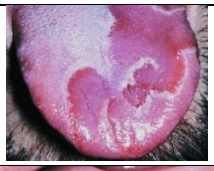
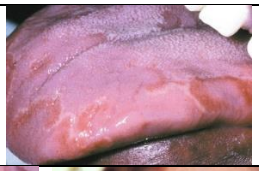
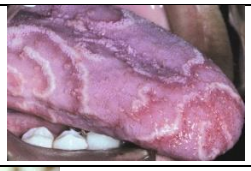




➲micro
❶subepithelial blister➔degenerate, necrotic basal keratinocyte
❷underlying c.t.➔sparse chronic inflammatory cell

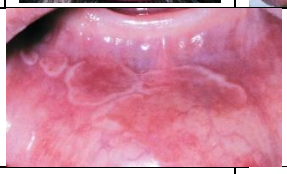
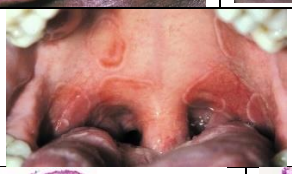
Erythema migrans遊走性紅斑(Geographic tongue; Benign migratory glossitis)➔tongue➔無症狀(燒灼感/熱/辣食物)

➲❶1↔3% population ❷not frequent➔cigarette smoker ❸unrelate➔age, sex, oral contraceptive, allergy, DM, psycho (dermal) conditions

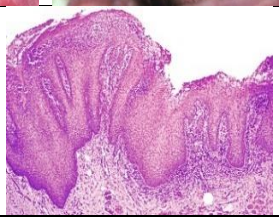
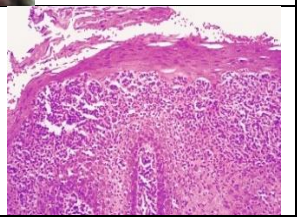
➲clinic➔filiform papillae atrophy➔multiple well-demarcated erythema➔anterior 2/3 dorsal tongue(tip & lateral)(~1/3 with fissured tongue)➔heal(in a few days/wks)➔develop in very different areas

➲other oral sites
❶buccal(labial)
❷soft palate/mouth floor(less frequent)
❸confuse with candidiasis/erythroplakia

➲micro
❶hyperparakeratosis, spongiosis, acanthosis, elongated rete ridge
❷neutrophil(munro abscess)➔superficial epithelium destruction ➔atrophic, red mucosa
❸lymphocyte & neutrophil➔lamina propria
❹reminiscent of psoriasis➔psoriasiform mucositis

21. **Reactive arthritis** is known for being
(A) an infectious disease
(B) an immunodeficiency disease
(C) an immunologic disorder
(D) more common in women than in men

22. The oral lesions in **Reiter syndrome** may resemble:
(A) pemphigus vulgaris
(B) lichen planus
(C) angioedema
(D) geographic tongue

Reactive arthritis(Reiter syndrome)➔immune-mediated(with mucocutaneous/oral component)➔HIV infection

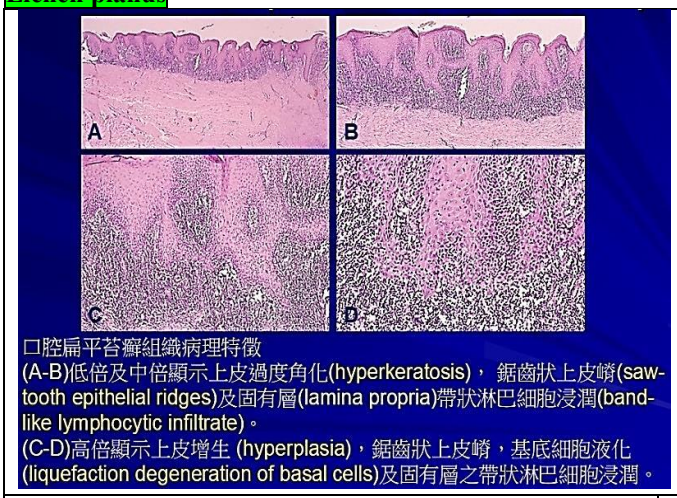
➲classic triad signs(❶↔❸)
❶nongonococcal urethritis➔1st sign(male & female)
❷arthritis➔joint of lower extremities➔TMJ(1/3)(condylar head erosion)
❸conjunctivitis➔伴隨urethritis
✹American Rheumatism Association definition➔arthritis(>1 month)+urethritis &/or cervicitis(子宮頸炎)

➲clinic
❶prevalent➔young adult men ❷HLA-B27(+)(60↔80%) ❸develop 1↔4wk after dysentery(痢疾)/venereal(性病) disease
❹uterine cervix inflammation ❺skin➔glans penis[balanitis circinate(20↔30%)]➔well-circumscribe(scallop, white linear) erythematous erosion
❻oral(微少於20%)➔①painless erythematous papule➔buccal & palate ②shallow, painless ulcer➔tongue, buccal, palate, gingiva ③geographic tongue➔like balanitis circinate(螺旋狀環dermatitis of glans penis-one of most common cutaneous manifestations of reactive arthritis)

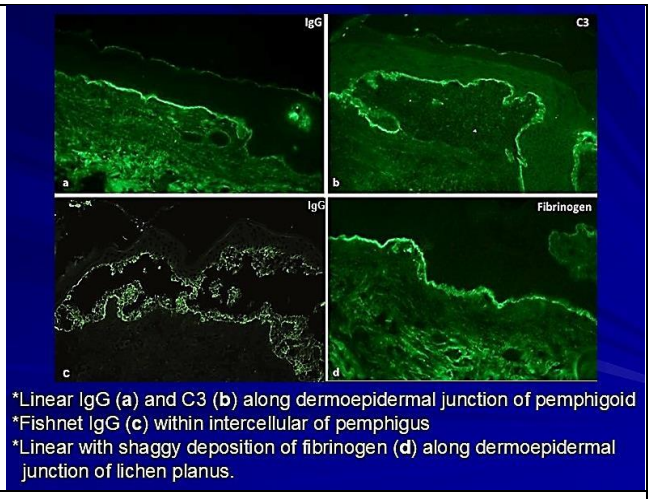
➲micro➔like psoriasis
❶hyperparakeratosis with elongate, thin rete ridge ❷microabscess➔epithelium surface

23. **What is the most common location for Wickham striae in the intraoral region?**
(A) dorsal surface of tongue
(B) floor of mouth
(C) buccal mucosa
(D) vermilion border

Lichen planus

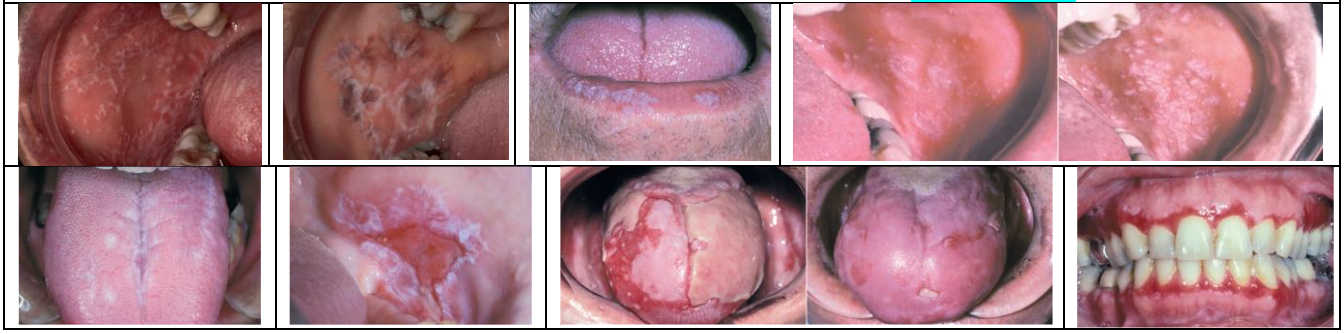


口腔扁平苔癬組織病理特徵
(A-B)低倍及中倍顯示上皮過度角化(hyperkeratosis)， 鋸齒狀上皮嵴(saw-tooth epithelial ridges)及固有層(lamina propria)帶狀淋巴細胞浸潤(band-like lymphocytic infiltrate)。
(C-D)高倍顯示上皮增生 (hyperplasia)，鋸齒狀上皮嵴，基底細胞液化(liquefaction degeneration of basal cells)及固有層之帶狀淋巴細胞浸潤。

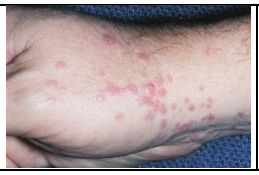
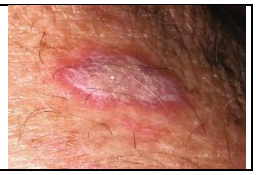


*Linear IgG (a) and C3 (b) along dermoepidermal junction of pemphigoid
*Fishnet IgG (c) within intercellular of pemphigus
*Linear with shaggy deposition of fibrinogen (d) along dermoepidermal junction of lichen planus.

➲T細胞免疫異常的局部自體免疫疾病➔血清有自體抗體(60.9%) | ➲與C型肝炎病毒感染有關聯，C型肝炎病毒感染易致口腔扁平苔癬
➲全人口成年人發生率約1↔2% | ➲好發中老年(>40歲)女性(男女比1：1.5)
➲6種型態➔❶網狀型(reticular) ❷丘疹型(papular) ❸斑狀型(plaque) ❹萎縮型(atrophic) ❺糜爛型(erosive) ❻大泡型(bullous type)
➲好犯之口腔黏膜：頰黏膜、舌及牙齦，口腔病變通常發生於兩側口腔黏膜，呈對稱性
➲❶~15%患者同時有皮膚病變 ❷~20%同時有生殖器病變 ❸~60%皮膚扁平苔癬同時會有口腔病變 ❹很少發生於兒童
➲網狀型➔❶好犯兩側後方頰黏膜 ❷白色線條(Wickham striae)呈網狀交錯排列 ❸常無症狀 ❹可同時在舌側緣(背)、牙齦、唇黏膜及唇紅緣
➲斑狀型➔❶常侵犯舌背 ❷白色斑塊 ❸無舌乳頭(lingual papillae) ❹和口腔白斑相似，不易區分
➲非糜爛型(網狀型、丘疹型、斑狀型)➔較無惡性轉變
➲糜爛型➔侵犯牙齦➔牙齦發炎紅腫、上皮萎縮和潰瘍➔脫屑性牙齦炎(desquamative gingivitis)(pemphigoid也有)



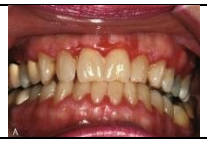
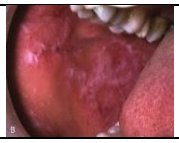
➲skin➔purple, pruritic, polygonal papule(Wickham striae)➔ extremities flexor surface➔no excoriation(表皮脫落)➔itch(癢)
➲other extraoral site➔❶glans penis ❷vulvar

Chronic ulcerative stomatitis慢性潰瘍性口炎(CUS)➔immune-mediated disorder➔oral mucosa

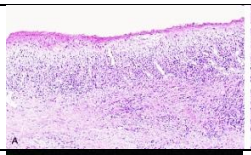
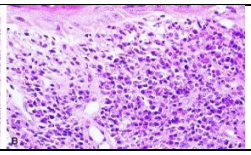
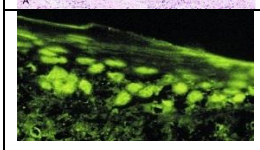
➲autoAb *vs* 70kD nuclear protein(ΔNp63α➔p63 isoform)➔中斷epithelium/connective tissue交接處的正常維護

➲clinic
❶like erosive lichen planus➔d.d. lichen planus(CUS without Wickham striae) ➔CUS not respond to corticosteroid➔CSU improve with antimalarial drug[like lupus erythematosus(LE)]

❷adult(av. late 6th decade) women➔desquamative gingivitis➔tongue/buccal ulcer/erosion also common➔heal without scar➔migrate around oral mucosa➔severity[wax & wane(起伏不定)]➔伴隨lichenoid skin lesion(<20%)

➲micro(右上圖)
❶like lichen planus ❷epithelium more atrophic
❸inflammatory infiltrate➔significant plasma cell, lymphocyte
❹artefactual epithelial separation from underlying connective tissue
❺direct IF➔autoAb(IgG)➔nuclei of (para)basal epithelial cell
❻indirect IF➔stratified epithelium-specific ANA(+)
❼ELISA➔screening➔much more cost-effective
✪direct IF➔systemic sclerosis & LE(immune-mediated condition)➔ nuclei throughout entire epithelium thickness(+)(右下圖)

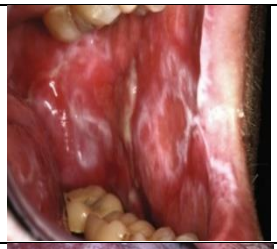
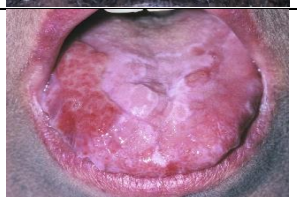
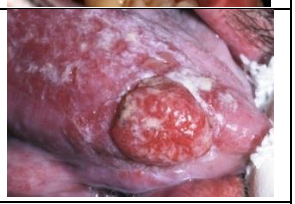




Graft-versus-host-disease移植物對抗宿主疾病(GVHD)➔devastating(毀滅性) to patient

➲allogeneic bone marrow transplantation(BMT) recipient➔HLA-matched donor➔not exact➔grafted cell➔not in native environment➔attack as a foreign body➔GVHD

➲❶graft-versus-leukemia effect➔donor cell➔leukemic cell as foreign body ❷mini-allograft(nonmyeloablative allogenic hematopoietic cell transplantation)➔not all WBC destroyed➔donor cell➔attack leukemic cell
❸autologous stem cell transplantation➔cell derived from patient➔no GVHD risk

➲clinic➔depend what organ involved & acute/chronic [①better histocompatibility match ②較年青 ③cord blood ④female]➔milder
❶acute[①1st few-wk after BMT(50%) ②任意defined➔within 100 day after BMT]➔skin➔mild rash to diffuse severe slough➔like toxic epidermal necrolysis➔①diarrhea(腹瀉) ②nausea(噁心) ③vomit ④腹痛 ⑤liver dysfunction
❷chronic(30-70%)➔延續acute GVHD(>100-day/not appear several years after BMT)➔mimic➔①SLE ②Sjögren syndrome ③$1^0$ biliary cirrhosis ④skin lichen planus/systemic sclerosis
❸salivary gland➔①xerostomia(immune-response) ②superficial mucocele➔soft palate

❹oral(only sign)➔[①acute(33↔75%) ②chronic(≥80%)]➔①like lichen planus(tongue, gingiva, labial, buccal) ②candidiasis ③mucosa atrophy ④ulcer(chemotherapy & neutropenia in 1st 2wk after BMT)➔>2-wk➔acute GVHD➔ small但↑ risk of oral & skin epithelial dysplasia & SCC

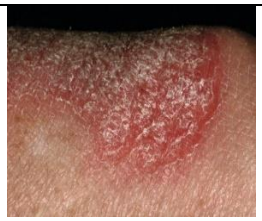
➲micro➔❶lichen planus(GVHD less intense inflammation)➔hyperorthokeratosis, short pointed rete ridge, basal cell degeneration➔↑collagen deposition(advanced)➔like systemic sclerosis ❷minor salivary gland➔periductal inflammation(early)➔acinar destruction & periductal fibrosis(later)

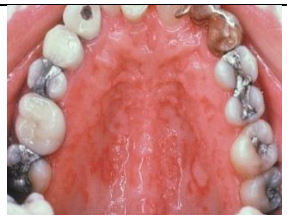
➲psoralen & ultra violet A(PUVA) therapy➔improve skin & oral lichenoid form GVHD

Psoriasis➔itching➔活化T淋巴球, cytokine, adhesion molecule, chemotactic polypeptides, GF➔↑skin keratinocyte繁殖

➲oral➔❶white to red plaque to ulcer ❷erythema migrans➔intraoral psoriasis

➲clinic➔well-demarcated, erythematous plaque (symmetric) with silvery scale➔①scalp ②elbow ③knee
❶2nd/3rd decade➔persist yrs➔惡化-靜止➔夏季改善↔冬季惡化 (related to UV expose)
❷psoriatic arthritis(25↔30%)➔TMJ
❸其他co-madidities➔inflammatory bowel disease, non-alcoholic liver disease, mood disorder(心境障礙), CVD
❹more prevalent with periodontitis



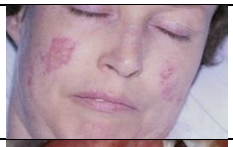


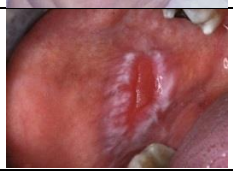
➲micro
❶↑parakeratin(Munro abscess➔neutrophil)
❷elongated rete ridge ❸connective tissue papilla➔ dilated capillaries➔close to epithelial surface
❹perivascular chronic inflammatory cell infiltrate

24. Which of the following is a pathologic condition producing a characteristic **butterfly-shaped lesion on the face** and **oral ulcers occurs more frequently in females than males**, and for which the result of a blood test is important in its diagnosis?
(A) pemphigus
(B) erosive lichen planus
(C) desquamative gingivitis
(D) lupus erythematosus

Lupus erythematosus紅斑狼瘡(LE)➔immuno-mediated➔↑B淋巴球活性+不正常T淋巴球功能➔基因與環境基因子交互作用

➲systemic LE(SLE)(全身性紅斑狼瘡)➔multisystem with oral/cutaneous manifestation
❶women>men(近8↔10×) ❷average age➔31s ❸common finding➔fever, weight loss, arthritis, fatigue, malaise ❹butterfly rash(40-50%)➔malar & nose➔spare nasolabial fold
❺sunlight➔lesion worsen
❻kidney(~40↔50%)➔kidney failure
❼cardiac➔pericarditis(Libman-Sacks endocarditis)
❽oral(5↔25%)➔palate, buccal, gingiva, vermilion of lower lip(lupus cheilitis)➔lichenoid granulomatous area➔ulcer, pain, erythema, hyperkeratosis
❾other oral complaint➔xerostomia, stomatodynia, candidiasis, periodontal disease



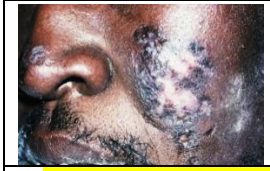


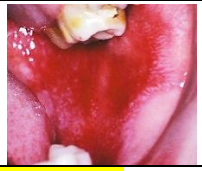
Prevalence of clinical & lab manifestations of SLE

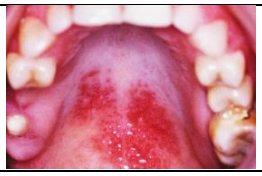
findings	frequency
systemic signs & symptoms: fatigue, malaise, fever, anorexia, weight loss	95%
MUSCULOSKELETAL SYMPTOMS	95%
arthralgia/myalgia	95%
nonerosive polyarthritis	60%
CUTANEOUS SIGNS	80%
photosensitivity	70%
malar rash	50%
oral ulcers	40%
discoid rash	20%
HEMATOLOGIC SIGNS	85%
anemia(chronic disease)	70%
leukopenia(<4000/μL)	65%
lymphopenia(<1500/μL)	50%

findings	frequency
thrombocytopenia(<100,000/μL)	15%
hemolytic anemia	10%
NEUROLOGIC SIGNS AND SYMPTOMS	60%
cognitive disorder	50%
headache	25%
seizures	20%
CARDIOPULMONARY SIGNS	60%
pleurisy, pericarditis, effusions	30-50%
myocarditis, endocarditis	10%
RENAL SIGNS	30-50%
proteinuria >500mg/24h, cellular casts	30-50%
nephrotic syndrome	25%
end-stage renal disease	5-10%

➲chronic cutaneous LE(CCLE)➔skin & oral mucosa➔good prognosis
❶few/no systemic symptom➔skin/mucosa➔discoid LE➔scaly, round (discoid) erythematous patch➔sun-expose HN skin➔heal spontaneous in one area➔appear another area➔healing➔skin atrophy➔scar & hypo(hyper) pigmentation(下左圖)
❷conjunctiva(結膜)➔cicatrizing(瘢痕) conjunctivitis➔mucous membrane pemphigoid
❸oral➔erosive lichen planus(下右圖)

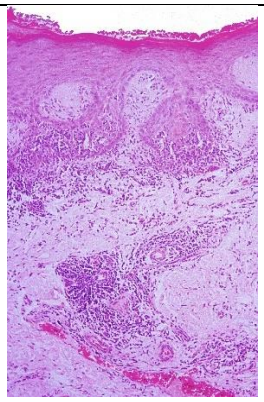


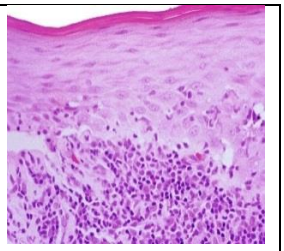




➲subacute cutaneous LE(SCLE)➔clinic➔intermediate between SLE & CCLE
❶photosensitive➔sun-exposed area➔no induration & scar
❷oral➔like CCLE
❸no renal/neurologic abnormalities
❹arthritis/musculoskeletal problem

➲micro(右圖)
❶skin➔①hyperkeratosis➔keratin packed into opening of hair follicle(follicular plug) ②basal cell degeneration ③patchy to dense subepithelial lymphocytic infiltration ④perivascular inflammation
❷oral➔①hyperkeratosis ②alternate atrophy & thickening of spinous cell layer ③basal cell degeneration ④subepithelial lymphocytic infiltration
❸d.d. with oral lichen planus
LE
①patchy deposit➔basement membrane zone➔PAS(+)
②subepithelial edema(point of vesicle formation)
③diffuse deep perivascular inflammatory infiltrate
④direct IF/histopathologic exam





➲diagnosis
❶direct IF➔positive lupus band test
❷serum ANA➔①double-stranded DNA➔70% SLE ②directed vs Sm➔30% SLE

Selected abnormal immune-finding in lupus erythematosus(LE)

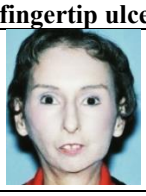
findings	frequency		significance
direct IF, lesional skin	CCLE:90%	SLE:95%	may help distinguish among various types of LE
direct IF, normal skin➔shaggy/granular band➔BMZ(IgM/IgG/C3)	CCLE:0%	SLE:25-60%	lupus band test(①rheumatoid arthritis ②Sjögren syndrome ③systemic sclerosis也會有)
antinuclear Ab(ANA)	CCLE:0-10%	SLE:98%	very sensitive for SLE, not very specific; not useful for CCLE diagnosis
anti-double-stranded DNA Ab	CCLE:0%	SLE:70%	specific for SLE; may indicate disease activity/ kidney involvement
anti-Sm Ab(a protein complexed with small nuclear RNA)	CCLE:0%	SLE: 25(30)%	specific for SLE

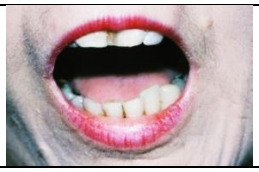
25. 對於**全身性紅斑性狼瘡(systemic lupus erythematous)**的血清檢查，下列何者正確？
(A) 只有少數的患者有antinuclear antibodies(ANAs)
(B) antinuclear antibodies(ANAs)的存在，對於全身性狼瘡的診斷有專一性
(C) Ro/La抗體對於全身性紅斑性狼瘡的診斷有專一性
(D) small nuclear RNA的抗體存在，對於全身性紅斑性狼瘡的診有被高的專一性

26. **Progressive systemic sclerosis** chiefly includes:
(1) skin: thickened, leathery, not mobile (2) mandibular erosions, angles, coronoid process (3) increased periodontal ligament spaces (4) tooth mobility
(A) only 1,3
(B) only 2,4
(C) only 1,2,3
(D) 1,2,3,4

Systemic sclerosis(SSc)硬皮症(Progressive systemic sclerosis; Scleroderma)➔dense collagen➔skin(most body organ)

➲clinic
❶women(5×)>men ❷1st sign➔Raynaud phenomenon➔vasoconstrictive triggered by emotion distress/cold
❸finger➔①terminal phalange resorption(acro-osteolysis) ②clawlike finger➔flexion contracture➔shortened ③vascular event& abnormal collagen deposition➔fingertip ulceration



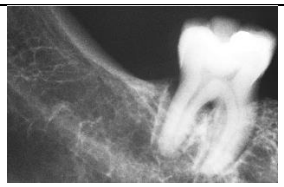


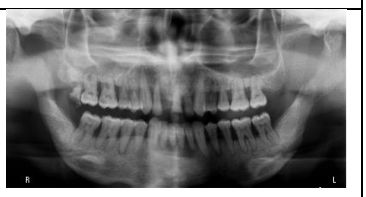
❹skin➔diffuse smooth hard texture
①facial➔subcutaneous collagen deposition➔smooth, taut(繃緊), masklike face
②nasal ala➔atrophy➔pinch nose➔mouse face
③hand, face, feet, limb(lower portion)➔limited cutaneous SSc➔pulmonary hypertension later
④trunk, proximal limbs➔diffuse cutaneous SSc(③④different prognoses)➔lung(hypertension & heart failure➔death), heart, kidney, GI tract➔organ failure(1st 3s)

❺oral
①microstomia➔collagen deposit➔perioral tissue➔trismus(70%)➔furrow(溝) radiate from mouth➔purse string
②attached gingiva➔recession
③firm hypomobile(boardlike) tongue & inelastic esophagus➔dysphagia

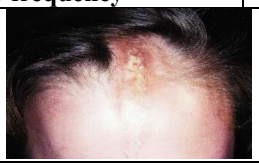
④xerostomia➔concurrent 2nd Sjögren syndrome

➲radiograph
❶diffuse PDL space widening➔throughout dentition
❷pano➔posterior ramus, coronoid process, chin, condyle resorption(10↔20%)➔↑pressure associate ↑collagen deposit
❸individual tooth resorption➔higher frequency

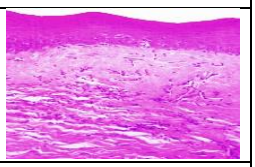




➲milder➔localized scleroderma/ morphea➔solitary patch➔like scar➔en coup de sabre(strike of sword)➔cosmetic problem➔rare life threatening➔unrelated to SSc



➲micro
❶diffuse deposition of dense collagen➔replace & destroy normal tissue➔loss of normal tissue function



➲diagnosis
❶anticentromere Ab➔limited cutaneous SSc(include CREST syndrome)➔late-onset lung hypertension
❷anti-topoisomerase I(Scl 70) & anti-RNA polymerase III Ab➔diffuse cutaneous SSc➔lung fibrosis

27. Which one of the following is involved in the **Raynaud phenomenon**?
(A) kidney
(B) ocular components
(C) fingers and toes
(D) joints

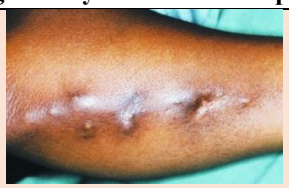
CREST syndrome(limited scleroderma)➔variant of limited cutaneous SSc

➲CREST➔❶Calcinosis cutis ❷Raynaud phenomenon ❸Esophageal dysfunction ❹Sclerodactyly ❺Telangiectasia

➲clinic➔6↔7th decade women

➲sign➔❶synchronous ❷sequential over months to years

❶calcinosis cutis
①multiple movable nontender subcutaneous nodule(0.5↔2cm)(右圖)
②larger more numerous superficial calcification➔removal

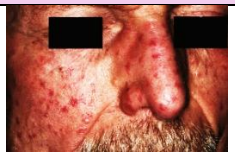


❷Raynaud phenomenon
hands/feet➔cold expose➔blanch of digit➔dead-white color(severe vasospasm)➔bluish color (venous stasis)(few min later)➔warming (dusky-red hue)➔hyperemic blood flow return➔ throbbing pain

❸esophageal dysfunction➔↑collagen deposit
①not note in early phase
②initial sign➔barium swallow radiograph

❹sclerodactyly➔↑collagen deposit➔dermis
①finger➔stiff(smooth shiny skin)➔ permanent flexure➔claw deformity

❺telangiectasia➔like hereditary hemorrhagic telangiectasia(HHT)
①superficial dilated capillary(facial skin & vermilion zone of lips) ➔↑bleeding



➲micro➔like SSc(milder)
❶superficial dilate capillary➔telangiectatic vessel

➲diagnosis➔d.d. HHT
❶anticentromere Ab➔ specific➔CREST syndrome & limited cutaneous SSc

28. **Acanthosis nigricans** is a skin disorder associated with which condition?
(A) anemia
(B) hyperthyroidism
(C) type 2 diabetes
(D) Addison disease

Acanthosis nigricans(黑色棘皮症)➔velvety(絲滑)/像皮革棕色皮膚(下左圖)➔cytokine-like peptide➔表皮細胞➔伴隨GI cancer

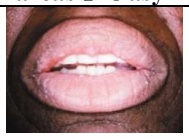
➲cutaneous(benign)➔cutaneous marker for internal malignancy

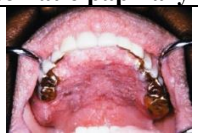
➲benign acanthosis nigricans(without malignancy)[like pseudoacanthosis nigricans(obese)]➔❶DM ❷Addison disease ❸hypothyroidism ❹acromegaly ❺Crouzon syndrome ❻drug(oral contraceptive/corticosteroid)

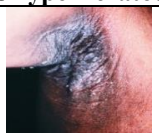
➲malignant acanthosis nigricans➔GI tract adenocarcinoma

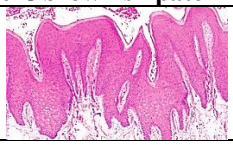
➲both forms➔intertriginous & flexural skin areas➔❶asymptomatic papillary ❷hyperkeratotic ❸brownish patch

➲oral(25↔50%)➔malignant form
❶diffuse papillary patch➔①tongue ②lips(upper) ③buccal
❷brown pigment➔not seen in oral lesion









➲micro(上最右圖)
❶hyperorthokeratosis & papillomatosis
❷oral lesion➔①↑more acanthosis ②minimal↑melanin(rather mild)

Chapter 16: Dermatologic Diseases

1. Which one of the following is not a feature of CREST syndrome?
A. Calcinosis cutis
B. Raynaud phenomenon
C. Esophageal motility problems
D. Splenomegaly
E. Telangiectasias

2. Widening of the periodontal ligament spaces may be associated with:
A. discoid lupus erythematosus.
B. hereditary hypohidrotic ectodermal dysplasia
C. psoriasis
D. systemic lupus erythematosus
E. systemic sclerosis

3. Xerostomia is a common finding in patients with:
A. Ascher syndrome.
B. cleidocranial dysplasia
C. dentin dysplasia type II
D. Gardner syndrome
E. hypohidrotic ectodermal dysplasia

4. Which one of the following vesiculobullous diseases is the most serious and will usually be fatal if left untreated?
A. Bullous lichen planus
B. Erosive lichen planus
C. Mucous membrane pemphigoid
D. Pemphigus vulgaris
E. Primary herpetic gingivostomatitis

5. The recommended mode of therapy for most patients with benign migratory glossitis (erythema migrans) is:
A. multivitamin therapy.
B. low-dose systemic corticosteroid therapy
C. surgical removal of lesions as they occur
D. topical corticosteroid therapy
E. no treatment is indicated

6. The most common site for oral lichen planus is:
A. dorsum of tongue
B. gingiva
C. hard and soft palate
D. lower lip vermilion
E. posterior buccal mucosa

7. Which one of the following vesiculobullous disorders is characterized by the so-called target lesions on the skin?
A. Bullous pemphigoid
B. Cicatricial pemphigoid
C. Erosive lichen planus
D. Erythema multiforme
E. Pemphigus vulgaris

8. Which of the following conditions may be associated with a positive Nikolsky sign?
A. Candidiasis
B. Erythema migrans
C. Major aphthous stomatitis
D. Pemphigus vulgaris
E. Traumatic granuloma

9. Which of the following conditions is associated with the development of oral premalignant lesions?
A. Dyskeratosis congenita
B. Ectodermal dysplasia
C. Erythema multiforme
D. Pachyonychia congenita
E. White sponge nevus

10. Hemorrhagic, crusting lip lesions are most characteristic of:
A. dyskeratosis congenita
B. erosive lichen planus

C. erythema multiforme
D. hereditary benign intraepithelial dyskeratosis
E. pemphigus

11. Which one of the following diseases typically has an acute, explosive onset?
A. Erosive lichen planus
B. Erythema multiforme
C. Mucous membrane pemphigoid
D. Pemphigus vulgaris
E. Psoriasis

12. Which one of the following conditions is least likely to show oral involvement?
A. Erythema multiforme
B. Lichen planus
C. Mucous membrane pemphigoid
D. Pemphigus
E. Psoriasis

13. All of the following are typical features of systemic lupus erythematosus EXCEPT:
A. elevated antinuclear antibodies.
B. skin rash
C. more common in males
D. joint pain
E. glomerular damage

14. The most common site for skin lesions of lichen planus is:
A. chest
B. flexor surface of the forearms
C. malar eminence
D. scalp
E. soles of the feet

15. Which one of the following vesiculobullous disorders is characterized by suprabasilar epithelial separation with acantholysis?
A. Epidermolysis bullosa
B. Erythema multiforme
C. Mucous membrane pemphigoid
D. Pemphigus vulgaris
E. Recurrent aphthous stomatitis

16. Indirect immunofluorescence is performed using the patient's:
A. biopsy tissue
B. blood
C. saliva
D. sputum
E. urine

17. Oral lesions of lupus erythematosus are most likely to mimic what other condition?
A. Erythema migrans
B. Leukoedema
C. Lichen planus
D. Median rhomboid glossitis
E. Traumatic granuloma

18. Pruritis is a common feature of the skin lesions of lichen planus. This feature refers to:
A. bilateral distribution
B. color of the lesions
C. itching of the lesions
D. location on extensor surfaces
E. positive Koebner phenomenon

19. The most typical oral feature of Darier disease is:
A. diffuse white lesions that partially rub off
B. interlacing white striae
C. rough, pebbly hard palate
D. salmon-colored macules
E. wart-like keratotic lesions throughout the mouth

20. Which one of the following conditions is associated with development of intestinal polyps and an increased risk for gastrointestinal adenocarcinoma?
A. Addison disease
B. Darier disease
C. Hereditary mucoepithelial dysplasia
D. Peutz-Jeghers syndrome
E. White sponge nevus

21. The microscopic appearance of erythema migrans (geographic tongue) most closely resembles:
A. lichen planus
B. psoriasis
C. lupus erythematosus
D. white sponge nevus
E. pemphigus vulgaris.

Chapter 16: Dermatologic Diseases➔answers
1. ANS: D
2. ANS: E
3. ANS: E
4. ANS: D
5. ANS: E
6. ANS: E
7. ANS: D
8. ANS: D
9. ANS: A
10. ANS: C
11. ANS: B
12. ANS: E
13. ANS: C
14. ANS: B
15. ANS: D
16. ANS: B
17. ANS: C
18. ANS: C
19. ANS: C
20. ANS: D
21. ANS: B

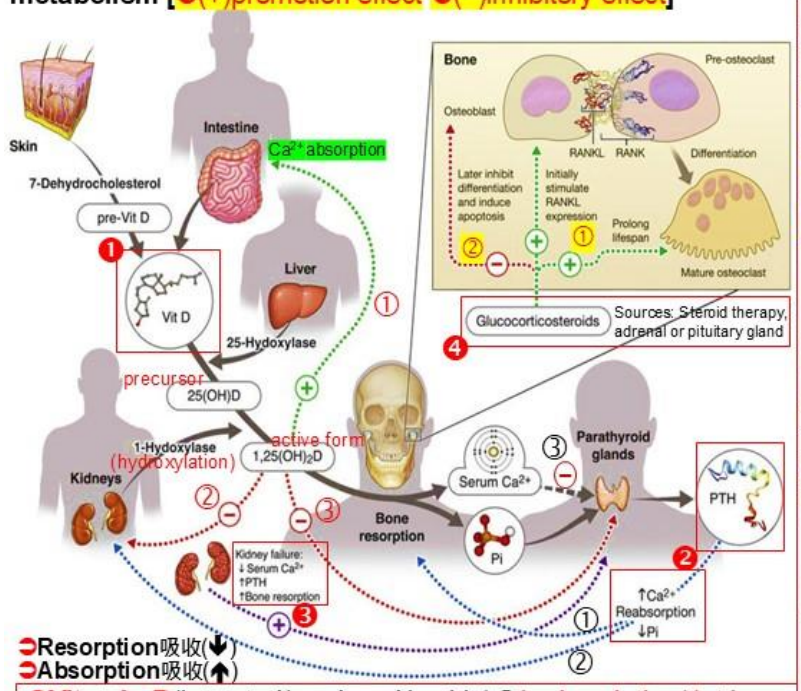
Chapter 17 Oral Manifestations of systemic diseases

Endocrine disorders

- ➲hyperparathyroidism
- ➲hypoparathyroidism
- ➲hyperpituitarism
- ➲hypopituitarism
- ➲hyperthyroidism
- ➲hypothyroidism

- ➲diabetic mellitus
- ➲Cushing syndrome

●Vit D ❷❸parathyroid hormone(PTH) ❹glucocorticosteroid activity➔maintain normal serum Ca^{2+} & P^{3-} levels in bone metabolism [➲(+)promotion effect ➲(−)inhibitory effect]



➲Resorption吸收(↓)
➲Absorption吸收(↑)

❶Vitamin D(ingested/produced in skin)➔hydroxylation(1st in liver➔then in kidney)➔active form 1,25-dihydroxy vitamin D *(1,25(OH)$_2$D)(solid dark gray arrows)*➔①promote Ca^{2+} & P^{3-} absorption in intestine *(dotted green line)*➔imbalance of bone metabolism➔bone resorption➔release Ca^{2+} & P^{3-} from bone to serum

➲Bone resorption*(upper right inset box)*➔via receptor activator of nuclear factor kappa B ligand *(RANKL) expression* by osteoblast➔interact with receptor activator of nuclear factor-kappa B *(RANK)* receptor on preosteoclast➔active osteoclast➔骨吸收
➲(osteoblast)RANKL+RANK(preosteoclast)→active osteoclast→bone resorption
②1,25(OH)$_2$D➔inhibit hydroxylation of precursor (25(OH)D) in kidney*(dashed red arrow)* ③inhibit parathyroid gland to produce PTH*(dashed red arrow)*

❷PTH➔①promote RANKL expression & osteoclast differentiation➔directly increase bone resorption➔increase serum Ca^{2+} *(dashed blue arrow)* ❷PTH➔②(in kidney) increase Ca^{2+} reabsorption & promote vitamin D hydroxylation to active form➔increase serum Ca^{2+}*(dashed blue arrow)* ➲③however, elevated serum Ca^{2+}➔reduce PTH of parathyroid gland*(dashed dark gray arrow)*

❸kidney failure➔upregulate PTH➔increase serum calcium*(dashed purple arrow)*.

❹Glucocorticosteroid➔①initial, through increased osteoblastic expression of RANKL➔increase osteoclast differentiation ➔prolong osteoclast life span➔increase bone resorption ②later, limit differentiation & inducing apoptosis of osteoblast➔reduce bone formation

Hyperparathyroidism➔↑PTH(parathormone)➔↑osteoclastic bone resorption➔↑serum Ca^{2+} level

➲hyperparathyroidism(1)

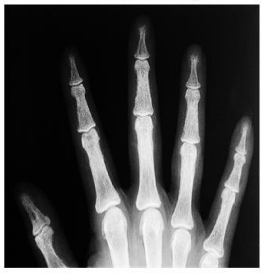
➲↑serum alkaline phosphatase level: A reliable indicator of bone turnover(週轉)

Radiographic Features

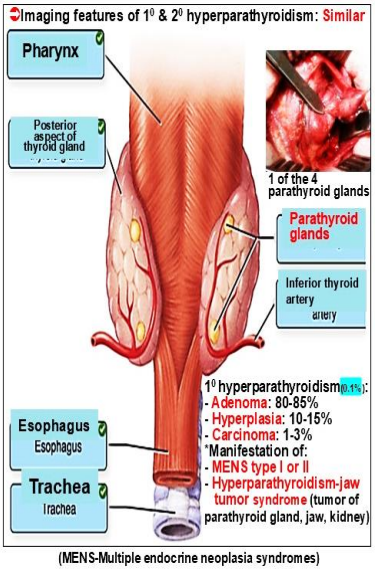
Only ~1/5 p't➡radiographic bone (observable) changes

General Radiographic Features

❶ Earliest & most reliable changes: Bone erosion from subperiosteal surfaces of phalanges of hand



➲Imaging features of 1^0 & 2^0 hyperparathyroidism: Similar



1^0 hyperparathyroidism(0.1%):
- Adenoma: 80-85%
- Hyperplasia: 10-15%
- Carcinoma: 1-3%

*Manifestation of:
- MENS type I or II
- Hyperparathyroidism-jaw tumor syndrome (tumor of parathyroid gland, jaw, kidney)

(MENS-Multiple endocrine neoplasia syndromes)

➲hyperparathyroidism(2)

❷Demineralization of skeleton➡radiolucency(generalized osteopenia)

❸Osteitis fibrosa cystica(most severe): Osteoclastic activity➡localized bone loss➡loss of all apparent bone structure & fibrosis of long-standing brown tumor

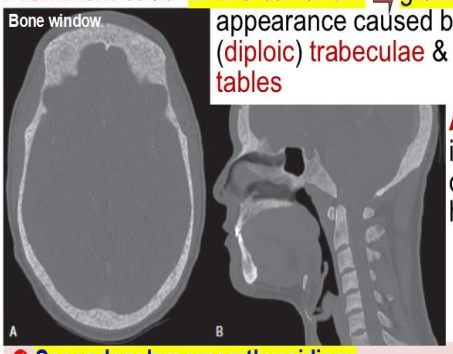
➲Triad of "stone, bone, groan":
Stone -- renal calculi
Bone – include osteoporosis, arthritis, fracture, brown tumor & osteitis fibrosa cystica
Groan(abdominal) – gastrointestinal symptoms including peptic ulcers

❹Brown tumor(giant cell tumor): Occur at late-long standing(~10% of cases)
- Central bone tumor➡radiolucency(any bones; 常見於facial bones & jaws)
- Gross specimen➔Brown/reddish-brown color
- Microscopic features➔Similar to central giant cell granuloma (CGCG/aneurysmal bone cyst(ABC)

❺Pathologic soft tissue calcification(stone): Kidney & joint (punctate/nodular appearance)

➲**hyperparathyroidism(3)**

❻Prominent case: Entire calvarium ➡ granular(salt & pepper skull) appearance caused by loss of central (diploic) trabeculae & thinning of cortical tables

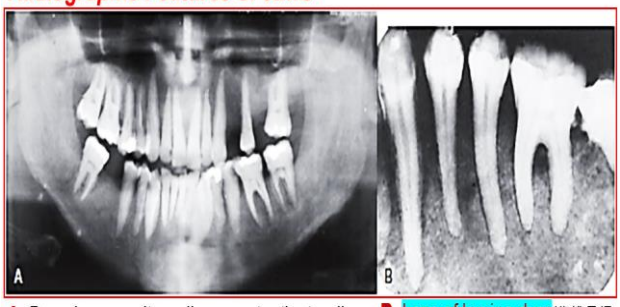


A, Axial, **B**, sagittal CT images of a case of secondary hyperparathyroidism

➲ **Secondary hyperparathyroidism**:
Compensatory PTH increase in response to hypocalcemia due to➔
(1) Inadequate dietary(飲食) intake
(2) Poor intestinal absorption of vitamin D
(3) Deficient metabolism of vitamin D in liver/kidney(renal osteodystrophy)

➲**hyperparathyroidism(4)**

Radiographic Features of Jaws



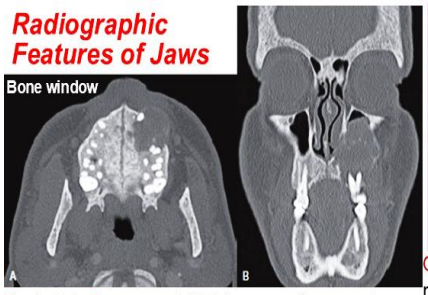
A, Bone loss results radiopaque teeth standing out in contrast to radiolucent jaws

➲ Loss of lamina dura(partial or involve entire tooth): One of the earliest manifestations of hyperparathyroidism(~10% patients)

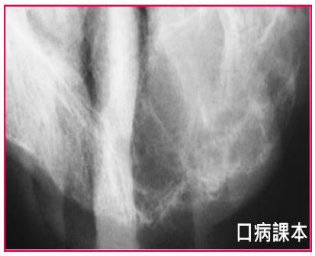
B, Loss of lamina dura(齒槽骨板) & granular texture of bone (ground glass appearance➔ numerous, small, randomly oriented trabeculae replace normal bone)

➲**hyperparathyroidism(5)**

Radiographic Features of Jaws



A, Axial, **B**, coronal CT. A case of secondary hyperparathyroidism with a brown tumor involving maxilla with a granular expanded cortex of maxilla & very subtle(微少) & ill-defined internal septa

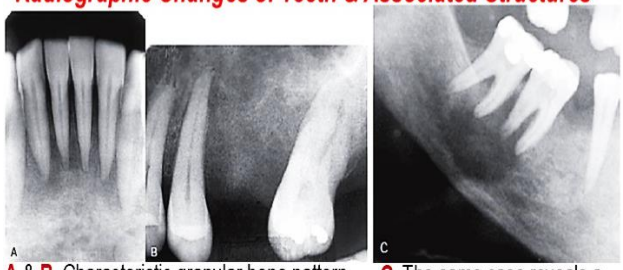


Occlusal radiograph of edentulous maxillary anterior region shows a well-defined multilocular radiolucency of a brown tumor of 1⁰ hyperparathyroidism

➲ Often affect mandible, clavicle, rib & pelvis
➲ May be solitary; often multiple
➲ Long-standing lesions may produce cortical expansion (口病課本)

➲**hyperparathyroidism(6)**

Radiographic Changes of Teeth & Associated Structures



A & **B**, Characteristic granular bone pattern loss of lamina dura & floor of maxillary antrum

➲PTH mobilizes minerals from skeleton (bone resorption) BUT mature teeth➔Immune to this systemic demineralizing process
➲PTH不會影響成熟牙齒的結構，會讓骨頭產生骨吸收(bone resorption)，就是指破骨細胞將硬骨組織分解為礦物質的過程，此機制會將骨中的鈣釋放至血液中

C, The same case reveals a brown tumor in apical region of 2nd & 3rd molars

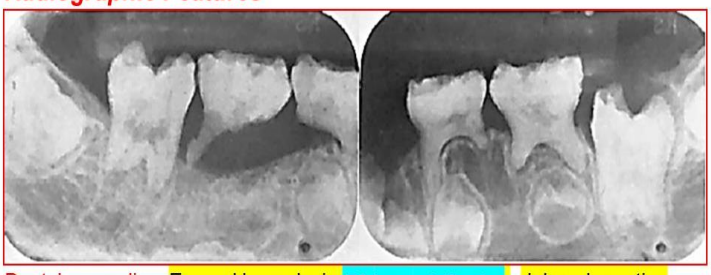
➲ Central giant cell granuloma later than 2nd decade➔ Should screen for an increase in serum Ca, PTH & alkaline phosphatase levels

➲(Osteoblast)RANKL↔RANK(Preosteoclast) → Active osteoclast → Bone resorption

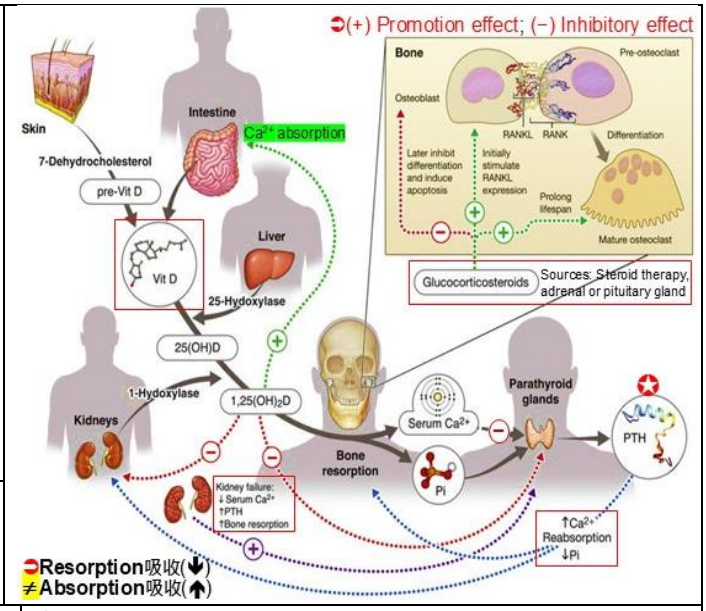
Hypoparathyroidism➔↓secretion of PTH➔↓serum Ca^{2+} level

➲**hypothyroidism(1)**

Radiographic Features



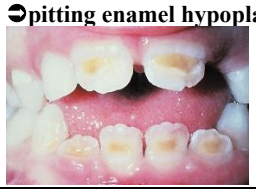
Dental anomalies: Enamel hypoplasia(但無hypocalcification), delayed eruption, external root resorption or root dilacerations
(PTH不影響成熟牙齒的結構，只影響骨頭，但↓PTH會影響成熟牙齒的結構，見右圖)
Skull PA images: Cerebral hemispheres(bilateral) calcification(flocculent絨毛狀)
Basal ganglia神經節 calcification(central)



➲**associate➔❶DiGorge syndrome ❷autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome(endocrine-candidiasis syndrome, autoimmune polyglandular syndrome, type 1)**

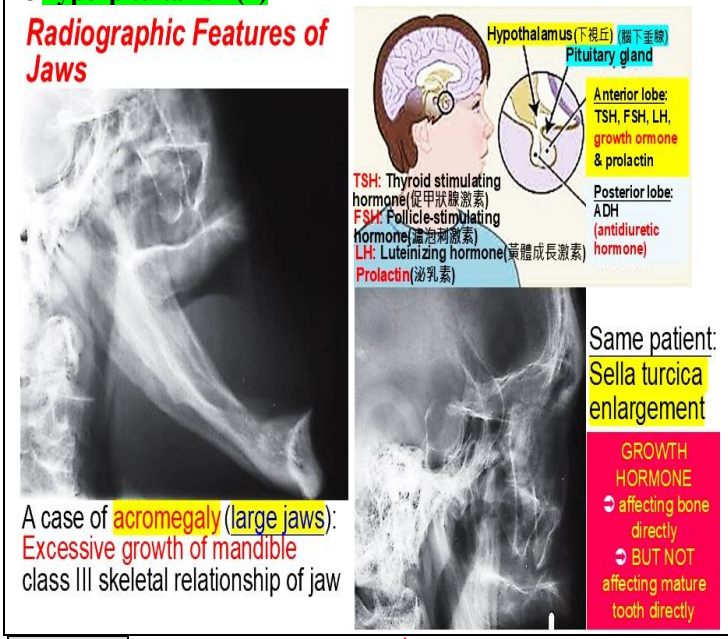
➲**Chvostek sign➔facial nerve tapped(輕拍) just below zygomatic arch➔upper lip twitching(抽搐)➔tetany(痙攣)(latent)**

➲**pitting enamel hypoplasia**

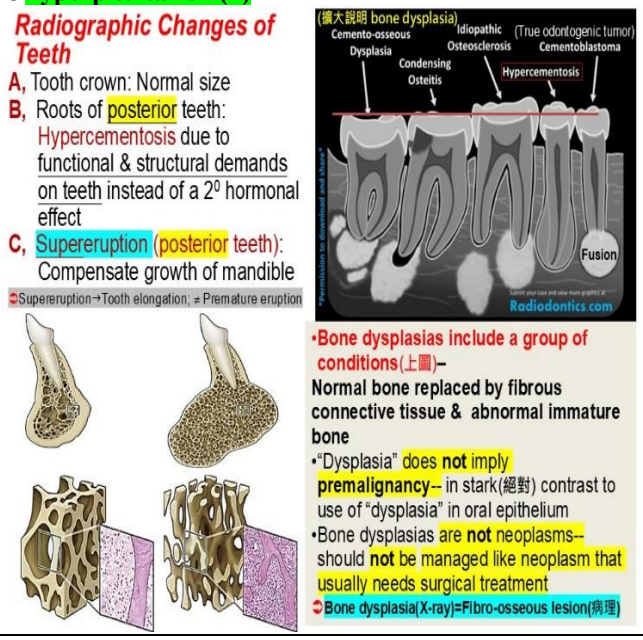


Hyperpituitarism(acromegaly肢端肥大症-adult; gigantism-child)➔↑pituitary gland(anterior lobe)➔↑growth hormone

➲**hyperpituitarism(1)**



➲**hyperpituitarism(2)**



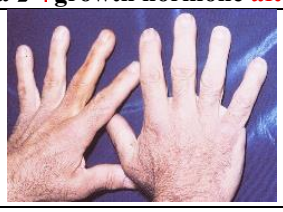
Gigantism➔pituitary adenoma➔↑growth hormone before epiphyseal plate closure➔grow rapid➔abnormal tall

➲**uncorrected ↑growth hormone for prolong period**
❶**extreme height(>7-feet)**
❷**facial soft tissue enlarge➔apparent mandible; hand & feet(like acromegaly)**
❸**true generalized macrodontia**

➲**radiograph(skull)➔enlarge sella(presence of pituitary adenoma)**
➲**adenoma➔compress & destroy remain normal pituitary gland tissue➔hormone deficiencies(hypothyroidism & hypoadrenocorticism)**
➲**20% gigantism➔McCune-Albright syndrome(polyostotic FD & café au lait pigmentation with associate endocrinologic disturbance)**

Acromegaly➔MRI➔pituitary adenoma➔↑growth hormone after epiphyseal plate closure

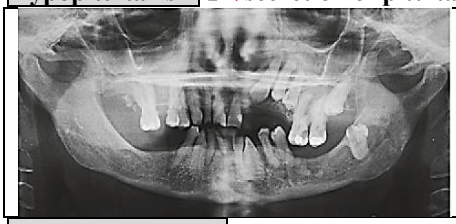
➲**clinic➔no sex predilection**
❶**renewed grow**
①**small bone of hand & feet**
②**membranous bone of skull & jaw**
❷**soft tissue affected➔coarse facial appearance**



➲**radiograph**
❶**mandibular prognathism ➔anterior open bite**
❷**teeth spacing ➔diastema formation**

❸**soft palatal tissue hypertrophy➔accentuate sleep apnea**
❹**average age at diagnosis➔42s ❺ macroglossia**

Hypopituitarism➔↓secretion of pituitary hormones-growth hormone



➲***Radiographic Features***
A, Primary dentition➔❶erupt at normal time ❷delayed exfoliation
B, Permanent teeth➔❶crown form normal ❷delayed eruption
C, Third molar buds➔completely absent(may be)
D, Jaws(esp. mandible)➔small➔crowding & malocclusion

Pituitary dwarfism➔much shorter than normal(body proportions appropriate)

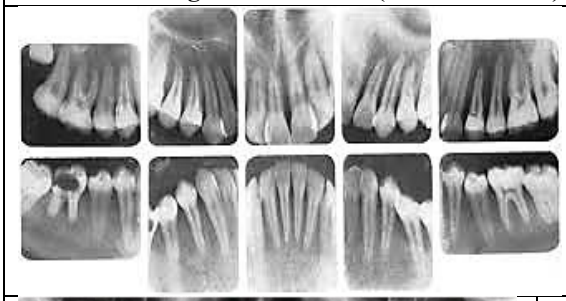
➲**cause**
❶**↓growth hormone by (anterior) pituitary gland**
①**pituitary gland(aplasia/hypoplasia)**
②**destruction of pituitary or hypothalamus by (1)tumor (2)(therapeutic)radiation (3)infection**
✖**IF affected hypothalamus[↓other hormones(thyroid hormone and cortisol)]➔↓growth hormone-releasing hormone(produced by hypothalamus) deficiency➔↓growth hormon**
❷**growth hormone molecule abnormalities**
❸**↓capacity of tissue response to growth hormone**

➲**Some p't(normal/↑growth hormone➔normal growth not proceed➔autosomal recessive trait➔abnormal & ↓growth hormone receptor**

➲clinic➔body proportion normal(smaller face)
❶mental(within normal limit)
❷smaller maxilla & mandible➔delay teeth eruption(delay 1-3s for teeth that normal erupt in 1st decade; 3-10s for teeth that normal erupt in 2nd decade)
❸delay deciduous teeth shedding➔delayed root of permanent teeth development
❹lack development of 3rd molar(common)
❺teeth size➔reduced in proportion to other anatomic structure
❻more severe periodontal disease
✖lack growth hormone receptors➔no tx available

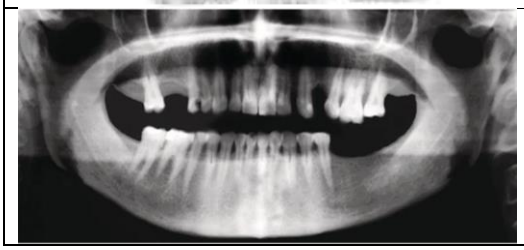
Hyperthyroidism(thyrotoxicosis)➔↑thyroxin in thyroid gland

➲3 most common forms
❶diffuse toxic goiter(甲狀腺腫大)(Graves disease) ❷toxic nodular goiter(Plummer disease) ❸toxic adenoma



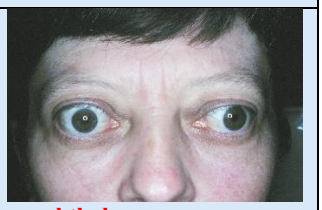
➲*Radiographic Features*
A, ❶advanced rate of dental development
❷early(premature) eruption with premature loss of primary teeth

➲cause➔❶Graves disease(60-90%)➔autoAb➔TSH receptor➔↑thyroxin ❷(benign & malignant) thyroid tumor(hyperplasia)
❸pituitary adenoma➔TSH➔↑↑thyroxin
➲clinic➔❶[F(5-10×)>M]➔3rd-4th decades of life(most)
❷exophthalmos(proptosis)➔glycosaminoglycans➔retro-orbital c.t.



➲*Radiographic Features*
B, ❶↑bone turnover(週轉) rate imbalanced state in favor of excessive bone resorption
❷adults➔generalized loss of bone density (volume)➔edentulous area

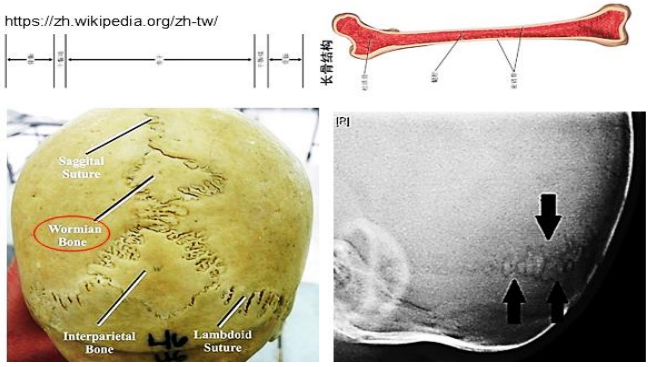
➲affected p't➔❶↑ serum thyroxine(free T4)
❷↓ serum TSH



exophthalmos

Hypothyroidism(myxedema黏液水腫➔coma & cretinism矮呆病)➔↓thyroxine secretion despite TSH presence

➲*Radiographic Features*
A, Children➔delayed closing of epiphyses(骨骺)➔skull sutures➔wormian bones(accessory suture bone縫間骨)



B, Effects on teeth➔❶delayed eruption ❷short root ❸thin lamina dura(1⁰teeth➔delayed exfoliation)

C, Jaws➔relatively small(類似HYPOPITUITARISM)
D, Adult➔❶periodontal disease ❷tooth loss ❸tooth separation due to ①tongue hypertrophy (macroglossia)(↑glycosaminoglycans) ②external root resorption

Diabetic mellitus(DM)

➲type I, insulin-dependent DM➔↓insulin(produced by β-cell of islets of Langerhans in pancreas)

➲type II, non-insulin-dependent DM➔insulin resistance

➲*Radiographic Features*(from text book)
A, Jaws/teeth➔no characteristic radiographic features
B, Periodontal disease with DM➔indistinguishable radiographically from periodontal disease without DM

➲mandibular cortical index(Braz Dent J 28(5 Sep-Oct 2017https://doi.org/10.1590/0103-6440201701523)
C1➔endosteal margin of cortex even & sharp
C2➔endosteal margin with semilunar defect/endosteal cortical residue
C3➔cortical layer clearly porous & with reduced thickness

Cushing syndrome(hypercortisolism)➔↑glucocorticoid by adrenal gland(腎上腺)➔❶↓osteoblastic ❷↑osteoclastic activity

➲clinic➔❶moon face➔fat deposition ❷buffalo hump

➲source➔❶corticosteroid therapy ❷endogenous-adenoma, carcinoma, hyperplasia(bilateral)(adrenal gland) ❸basophilic adenoma(pituitary gland)

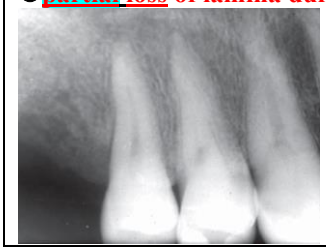
➲*Radiographic Features of Jaws*

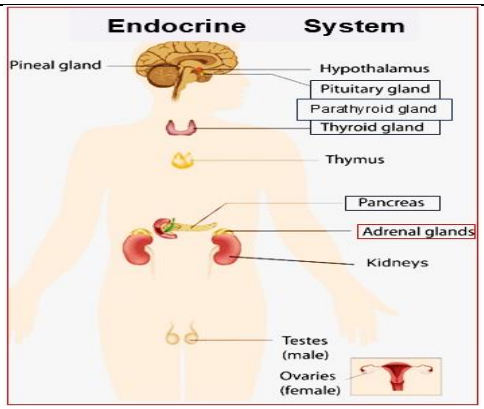
A, Generalized osteoporosis granular bone pattern➔pathologic fracture

B, Skull➔diffuse thinning accompanied by mottled(斑駁) appearance

C, Teeth➔❶premature(early) eruption(類似 HYPERTHYROIDISM)

❷partial loss of lamina dura(類似 HYPERPARATHYROIDISM)





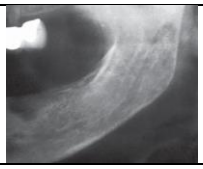
Metabolic bone disorders

➲osteoporosis ➲rickets(infant, child) & osteomalacia(adult)骨軟化病 ➲hypophosphatasia(磷酸鹽酵素過少)	➲hypophosphatemic rickets(血磷酸鹽過少佝僂病) ➲renal osteodystrophy(腎性骨營養不全)(renal rickets) ➲osteopetrosis骨質石化病(Albers-Schönberg & marble bone disease)

Osteoporosis➔↓bone mass but normal bone histology

➲inferior cortex of mandible➔loss of normal thickness & density

➲thin lamina dura than normal(occasion)



Rickets(infant, child) & Osteomalacia骨軟化病(adult)➔

➲↓serum & extracellular ❶calcium & phosphate ❷minerals for normal calcification of bone & teeth

➲↓activity of vitamin D metabolites(esp. 1,25(OH)$_2$D➔require for resorption of calcium in intestine)

➲*Radiographic Features of Jaws*

Rickets

A, Thin mandibular border/IAN(Inferior Alveolar Nerve) canal wall

B, Changes in jaws occur after changes in rib & long bone

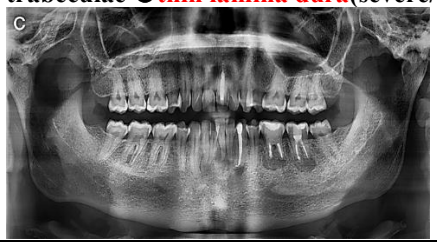
C, Trabeculae of cancellous bone of jaws➔↓density, no. & thickness

D, Severe case➔jaws(RL)➔teeth(bereft 喪失 of bony support)(類似 HYPERPARATHYROIDISM)

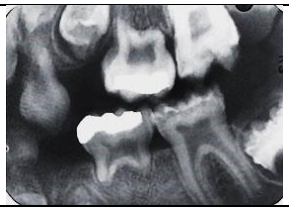
Osteomalacia(❶waddling/"penguin" gait ❷tetany ❸greenstick bone fracture)

A, No radiographic manifestation in jaws & teeth(most)

B, Radiograph(if)➔❶overall RL & sparse(疏鬆) trabeculae ❷thin lamina dura(severe/long-standing case)



➲*Radiographic Changes Associated with Teeth*
A, Enamel hypoplasia & hypocalcification(類似 HYPOPARATHYROIDISM)
B, Early ricket➔delayed tooth eruption
C, Lamina dura & cortical boundary of tooth follicles➔thin/missing(loss)
(✠summary 表➔lamina dura 只寫 thin; P.131)

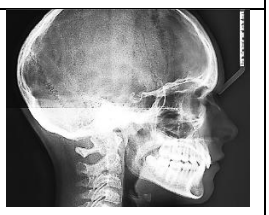


Hypophosphatasia(HPP,磷酸鹽酵素過少)

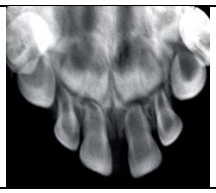
➲inherited disorder➔↓production(defective function) of alkaline phosphatase mineralization of osteoid, teeth
(✠alkaline phosphatase➔produced by osteoblast & odontoblast)

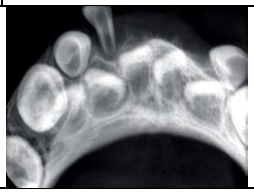
➲6 clinic forms(depend on age)
❶perinatal➔lethal
❷perinatal➔nonlethal(benign)
❸infantile
❹childhood
❺adult
❻odontohypophosphatasia

➲*Radiographic Features of Jaws*
A, Mandible & maxilla➔generalized RL
B, Cortical bone & lamina dura➔thin(summary 表➔loss; P.130)
C, Alveolar bone➔poorly calcified & (may)appear deficient
➲older children➔skull suture premature closure➔inner table of skull 的 gyral impression(大腦迴轉的壓痕)(convolutional markings-multiple RL areas)➔like hammered metal(Cu)
➲skull(may)➔brachycephalic(短頭顱)



➲*Radiographic Changes Associated with Teeth*
A, Primary teeth(~85%)➔premature loss(esp. incisor)
B, Large pulp chamber(root canal) & thin(hypoplastic) enamel layer➔both dentitions
C, Permanent teeth➔delayed eruption

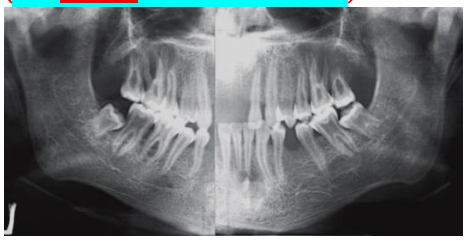




Hypophosphatemic rickets(血磷酸鹽過少佝僂病)(vitamin D-resistant rickets & hypophosphatemia血磷酸鹽過少, mild)

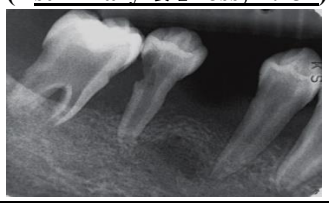
➲[❶distal renal tubules fail to reabsorb P] ❷multiple myeloma➔2^0 renal damage]➔↓serum phosphorus

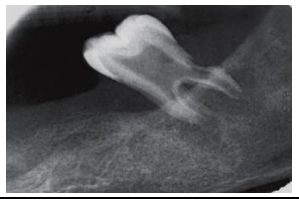
➲*Radiographic Features of Jaws*
A, jaws RL➔❶lack of bone density ❷large pulp chamber (類似 HYPOPHOSPHATASIA)



B, Thin enamel layer(enamel hypoplasia)

➲*Radiographic Changes Associated with Teeth*
A, ❶bone loss around teeth(granular bone pattern) ❷large pulp chamber(root canal) ❸external root resorption ❹sparse(稀疏)lamina dura(may be)
(✠summary 表➔loss; P.131)

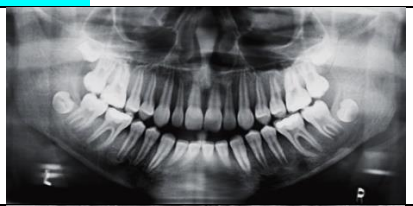




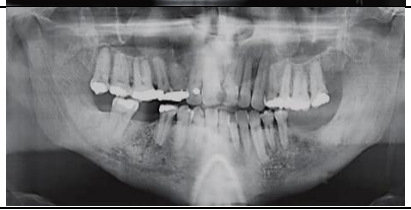
Renal osteodystrophy(腎性骨營養不全)(Renal rickets)

➲renal failure➔interfere renal 25(OH)D hydroxylation to 1,25$(OH)_2$D➔↓intestinal reabsorption➔hypocalcemia & hyperphosphatemia➔parathyroid gland➔↑PTH➔2^0 hyperparathyroidism

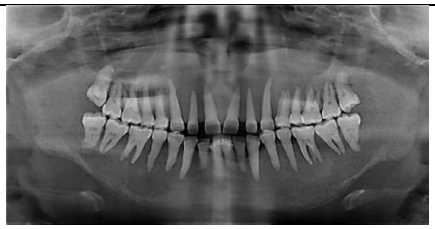
➲*Radiographic Features of Jaws*
A, Jaw enlargement(renal disease)➔due to cancellous bone enlargement; brown tumor(may be; less frequent)(類似 HYPERPARATHYROIDISM)
B, ❶RL area due to loss of bone mass ❷loss of lamina dura ❸(by contrast)sclerotic bone pattern around roots of teeth



C, Diffuse sclerotic (radiopaque) bone pattern throughout jaws(rare)
D, Indistinct lower cortex due to ↑RO of internal aspect of bone



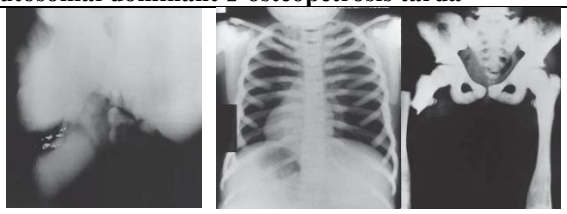
➲*Radiographic Changes Associated with Teeth*
A, Enamel hypoplasia & hypocalcification loss of radiographic evidence of enamel
類似 HYPOPARATHYROIDISM, RICKETS, HYPOPHOSPHATASIA, HYPOPHOSPHATEMIA
(✪HYPOPARATHYROIDISM➔只有 ENAMEL HYPOPLASIA 無 ENAMEL HYPOCALCIFICATION)
B, Lamina dura➔absent(loss)/less apparent in instance of bone sclerosis
(類似 HYPERPARATHYROIDISM, RICKETS, HYPOPHOSPHATASIA, HYPOPHOSPHATEMIA)



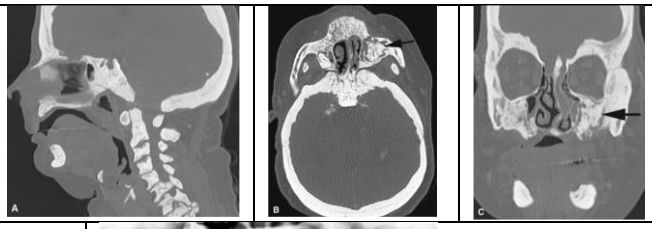
Osteopetrosis骨質石化病(Albers-Schönberg & marble bone disease)➔↓normal function of osteoclast➔↓bone mass

➲3 types➔❶autosomal recessive➔osteopetrosis congenita ❷autosomal dominant➔osteopetrosis tarda

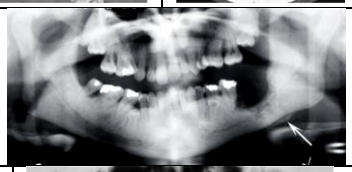
➲*General Radiographic Features*
A, Dense calcification of skull & facial bones(jaws enlargement)
類似 HYPERPITUITARISM
類似 RENAL OSTEODYSTROPHY
B, Dense calcification of chest, pelvis & femurs(fracture of proximal right femur)



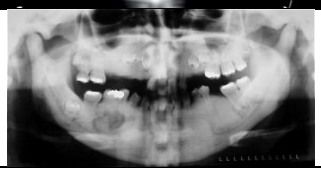
➲*Radiographic Features of Jaws*
A, Sagittal (A), axial (B), & coronal (C) CT images➔dense calcification of bone
❶loss of definition of cortical & cancellous bone interfaces & uniformly increased density of all bones
❷complicated by osteomyelitis of left maxilla with sequestra (arrows in B & C)



➲*Radiographic Features of Jaws*
❶↑density of jaws
❷unabrupt tooth 35
❸narrow IAN canal
❹osteomyelitis in left mandibular body with periostitis(arrow)



➲*Radiographic Changes Associated with Teeth*
A, ❶delayed eruption ❷early tooth loss ❸missing teeth
❹ malformed root & crown ❺teeth➔poorly calcified(prone to caries)
B, Bone density ankylosis delayed eruption of 1^0 & 2^0 teeth
C, Lamina dura & cortical border➔thicker than normal



Changes in Bone Observed in Systemic Diseases

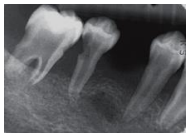
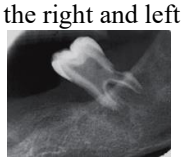
Systemic Disease DM not included	BONES				
	Density	Size of jaws	TRABECULE		
			Increase	Decrease	Granular
Hyperparathyroidism	Decrease	No	Yes	Yes	Yes
Hypoparathyroidism	Rare increase	No	No	No	No
Hyperpituitarism	No	Large	No	No	No
Hypopituitarism	No	Small	No	No	No
Hyperthyroidism	Decrease	No	No	No	No
Hypothyroidism	No	Small	No	No	No
Cushing syndrome	Decrease	No	No	Yes	Yes
Osteoporosis	Decrease	No	No	Yes	No
Rickets	Decrease	No	No	Yes	No
Osteomalacia	Rare decrease	No	No	Rare decrease	No
Hypophosphatasia	Decrease	No	No	Yes	No
Renal osteodystrophy	Decrease; rare increase	Large	Rare	Yes	Yes
Hypophosphatemia	Decrease	No	No	Yes	No
Osteopetrosis	Increase	Large (cancellous bone enlargement)			
Sickle cell anemia	Decrease	Large maxilla (large bone marrow space)			hair-on-end (skull)
Thalassemia	Decrease	Large maxilla			

Effects on Teeth and Associated Structures

DM not included Systemic Disease	Hypocalcification	Hypoplasia	Large Pulp Chamber	Loss of Lamina Dura	Loss of Teeth	Eruption
Hyperparathyroidism	No	No	No	Yes*	Rare	No
Hypoparathyroidism	No	Yes	No	No	No	Delayed
Hyperpituitarism	No	No	No	No	No	Supereruption
Hypopituitarism	No	No	No	No	No	Delayed
*Hyperthyroidism	No	No	No	No	Yes	Early
*Hypothyroidism (教科書兩者寫相反)	No	No	No	Thin	Yes	Delayed
Cushing syndrome	No	No	No	Partial**	No	Premature eruption
Osteoporosis	No	No	No	Thin	No	No
Rickets	Yes, enamel	Yes, enamel	No	Thin (內文: or loss)*	No	Delayed
Osteomalacia	No	No	No	Thin	No	No
Hypophosphatasia	Yes	Yes	Yes	Yes (內文: thin)*	Yes	Delayed
Renal osteodystrophy	Yes	Yes	No	Yes*	No	No
Hypophosphatemia	Yes	Yes	Yes	Yes (內文: sparse)*	Yes	Delayed
Osteopetrosis	Yes	Rare	No	Thick	Yes	Delayed

1. **Large jaws** may be occurred in patients with:
   (1) osteopetrosis (2) hypothyroidism (3) hyperpituitarism (4) renal osteodystrophy
   (A) only 1,2,3
   (B) only 1,2,4
   (C) only 1,3,4
   (D) 1,2,3,4

2. **Small jaws** may be occurred in patients with:
   (1) hypopituitarism (2) hypothyroidism (3) rickets (4) renal osteodystrophy
   (A) only 1,2
   (B) only 1,3
   (C) only 2,3
   (D) 3,4

3. What are the most likely **clinical diagnoses** for patient with periapical radiographs of lower right and lower left posterior teeth as shown in the right and left figures below respectively?
   
   
   (1) hypopituitarism (2) hypothyroidism (3) hypophosphatasia (4) hypophosphatemia
   (A) only 1,2
   (B) only 1,3
   (C) only 2,3
   (D) only 3,4

4. The **most frequently exfoliated teeth** in patients with **hypophosphatasia** are:
   (A) maxillary primary incisors
   (B) maxillary primary molars
   (C) mandibular primary incisors
   (D) mandibular permanent incisors

5. **Loss of lamina dura** of teeth may be occurred in patients:
   (1) hypophosphatasia (2) renal osteodystrophy (3) Cushing syndrome (4) intrabony malignancy (5) hypophosphatemia (6) Rickets
   (A) only 1,2,4,5,6
   (B) only 1,2,3,4,5
   (C) only 1,2,3,5,6
   (D) 1,2,3,4,5,6

6. **Osteomalacia** is usually caused by a **nutritional deficiency** of:
   (A) vitamin B12
   (B) vitamin D
   (C) alkaline phosphatase
   (D) potassium

7. **Osteomalacia in children** is called:
   (A) florid cemento-osseous dysplasia
   (B) osteogenesis imperfecta
   (C) Albright syndrome
   (D) rickets

8. A **brown tumor** may be associated with:
   (1) renal osteodystrophy (2) fibrous dysplasia (3) osteomalacia (4) primary or secondary hyperparathyroidism
   (A) only 1,2
   (B) only 1,4
   (C) only 2,3
   (D) only 3,4

9. Which of the following is *not* characteristic of **primary hyperparathyroidism**?
   (A) osteoclastic resorption
   (B) excessive production of parathyroid hormone
   (C) cotton-wool radiographic appearance
   (D) increased serum calcium

10. What is the most typical **radiographic finding of hyperparathyroidism** related to condition of **tooth**?
    (A) hypercementosis
    (B) loss of lamina dura
    (C) root resorption
    (D) dilated pulp chamber

11. A **multilocular radiolucency** is most likely associated with:
    (A) fibrous dysplasia
    (B) osteomalacia
    (C) Paget's disease
    (D) hyperparathyroidism

12. **Partial loss** or **thin lamina dura** of teeth may be occurred in patients:
    (1) hyperparathyroidism (2) renal osteodystrophy (3) Cushing syndrome (4) osteomalacia (5) hypothyroidism
    (A) only 1,2,4
    (B) only 3,4,5
    (C) only 1,2,3
    (D) only 2,3,5

13. Patients with **hypophosphatasia** characteristically have:
    (A) obliterated pulp chambers
    (B) marked gingival keratinization
    (C) increase in serum alkaline phosphatase levels
    (D) absence of root cementum

14. **Large maxilla** may be occurred in patients with:
    (1) osteoporosis (2) hypothyroidism (3) thalassemia (4) sickle cell anemia
    (A) only 2,3
    (B) only 1,4
    (C) only 3,4
    (D) 1,2

15. **Hypercalcemia**, **hypophosphatemia**, **elevated serum alkaline phosphatase** & **abnormal bone metabolism** are features of:
    (A) Hyperthyroidism
    (B) hypothyroidism
    (C) hyperparathyroidism
    (D) hyperpituitarism

16. Which of the following is *not* characteristic of **primary hyperparathyroidism**?
    (A) osteoclastic resorption
    (B) excessive production of parathyroid hormone
    (C) cotton-wool radiographic appearance
    (D) increased serum calcium

17. **Hyperthyroidism** in **children** can lead to:
    (A) partial anodontia
    (B) amelogenesis imperfecta
    (C) ankyloses
    (D) early exfoliation of deciduous dentition & early eruption of permanent teeth

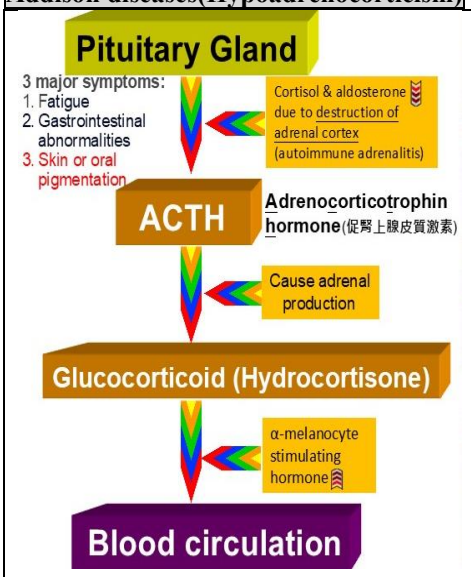
18. Which of the following description about **Graves disease** is *true*? It:
    (A) is more common in female than male
    (B) shows decreased serum thyroxine level
    (C) shows increased serum thyroid stimulating hormone concentration
    (D) usually has autoantibodies

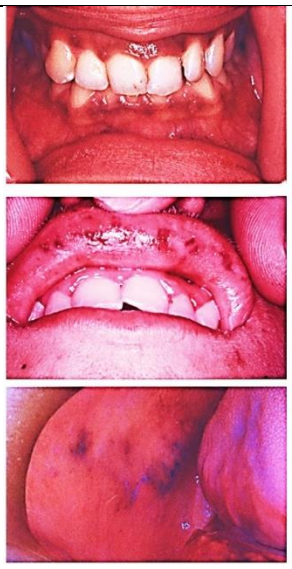
19. Which of the following about **DiGeorge syndrome** is *true*?
    (A) hypercalcemia
    (B) enamel hypoplasia
    (C) enamel hypocalcification
    (D) premature tooth eruption

20. Which one of the following is *false* concerning **Addison disease**?
    (A) also known as primary adrenal cortical insufficiency
    (B) there may be bronzing of skin
    (C) may be caused by a malignant tumor that destroys adrenal gland
    (D) patient may experience pathologic fracture

21. What is the most possible clinical impression for the patient with pigmentation in skin and oral mucosa and has weight loss, low blood pressure and nausea.?
(A) Addison disease
(B) Behcet disease
(C) Crohn disease
(D) Darier disease

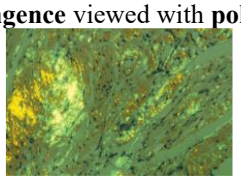
Addison diseases(Hypoadrenocorticism)➔↓cortisol & aldosterone by adrenal gland





➲**causes**
❶**autoimmune destruction**
❷**infection(TB, deep fungal disease[AIDS])**
❸**metastatic tumor, sarcoidosis, hemochromatosis, amyloidosis**
➲**clinic**
oral hyperpigmentation(1st manifest)➔bronze skin after
➲**hypoadrenocorticism(parathyroidism)+mucocutaneous candidiasis➔autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy syndrome**
➲**serum cortisol<16↔18μg/dL➔adrenal insufficiency**
➲**1^0 hypoadrenocorticism➔high plasma ACTH (>100ng/ L)**
➲**2^0 hypoadrenocorticism➔normal plasma ACTH (9↔52 ng/L)➔due to ↓ACTH production by pituitary gland**
➲**pituitary gland(malfunction)➔↓ACTH➔ 2^0 hypoadrenocorticism**

22. Figure below of the patient has an **enlarged and crenated tongue** (left) with biopsy of a **Congo red-stain** demonstrating **apple-green birefringence** viewed with **polarized light** (right). What is the most possible diagnosis?

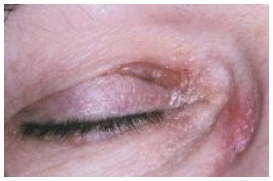
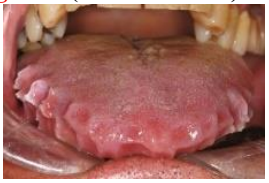
(A) lymphangioma
(B) granular cell tumor
(C) systemic amyloidosis
(D) fibroma

Amyloidosis

➲**clinic classification➔❶organ-limited amyloidosis ❷systemic amyloidosis**

❶**organ-limited amyloidosis(not associate systemic alteration)➔oral soft tissues(infrequent)➔amyloid nodule (solitary, asymptomatic, submucosal deposit)➔Ig light chain aggregate➔produce by monoclonal plasma cell**
❷**systemic amyloidosis➔①primary ②myeloma associated ③secondary ④hemodialysis associated ⑤heredofamilial**

➲**primary amyloidosis & myeloma associated amyloidosis**
❶**affect older adult(av. 65s)**
❷**male(slight predilection)**
❸**light chain molecule deposition(AL)➔①idiopathic(most) ②associate multiple myeloma(~15-20%)**
❹**1st sign➔①fatigue ②weight loss ③paresthesia ④hoarseness ⑤edema ⑥orthostatic hypotension**
❺**amyloid protein deposition➔①carpal tunnel syndrome ②mucocutaneous lesions ③hepatomegaly ④macroglossia**
❻**skin lesion➔smooth-surface, firm, waxy papule & plaque(with petechiae & ecchymoses)➔①eyelid(下左圖) ②retroauricular region ③neck ④lips**
❻**oral lesion➔①macroglossia(10↔40%下右圖) ②ulceration & submucosal hemorrhage ③amyloid nodule(sometimes)**

❼**dry eye(mouth)(infrequent)➔lacrimal(salivary) gland destruction(2^0 to amyloid infiltration)**
❽**significant blood vessel infiltration➔claudication(跛行) of jaw musculature**

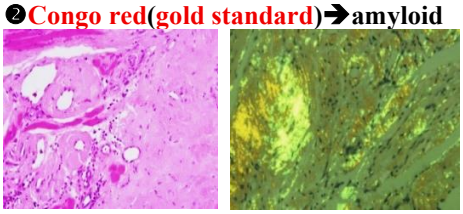
➲**secondary amyloidosis**
❶**due to chronic inflammatory process(①long-standing osteomyelitis ②tuberculosis ③sarcoidosis)**

❷comprise cleavage fragment of circulating acute-phase reactant protein➔designated AA
❸heart(not affected)
❹liver, kidney, spleen, adrenal involvement
➲hemodialysis associated amyloidosis
❶amyloid protein➔β_2-microglobulin($A\beta_2M$)➔normal occurring protein➔not removed by dialysis➔accumulate in plasma➔deposit in bone & joint➔①carpal tunnel syndrome ②cervical spine pain & dysfunction ③tongue involve
❷less problem in future➔dialyzer with larger pore➔remove large β2-microglobulin molecule

➲heredofamilial(遺傳性) amyloidosis
❶autosomal dominant(most)➔sensory & motor nerve polyneuropathy(difficulty walking, bilateral carpel tunnel syndrome, paroxysmal intense pain affect extremities, cardiomyopathy, GI disturbance)
❷autosomal recessive(familial Mediterranean fever)

➲micro
❶gingiva(submucosal c.t.)➔extracellular amorphous eosinophilic material deposition(①perivascular ②entire tissue)
❸thioflavine T(fluorescent dye)➔amyloid
❹crystal violet➔metachromasia(normal purple➔more reddish➔amyloid)
❺EM➔nonbranching linear fibril(7.5↔10nm in diameter)

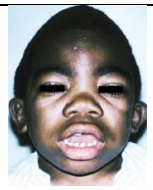
❷Congo red(gold standard)➔amyloid



Mucopolysaccharidoses➔metabolic disorders(autosomal recessive)

➲lack normal enzyme process glycosaminoglycans(mucopolysaccharides)➔
❶heparan sulfate ❷dermatan sulfate ❸keratan sulfate ❹chondroitin sulfate

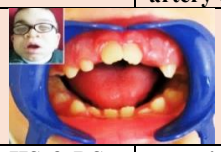
➲clinic(generalized)
❶intellectual disability
❷coarse facial feature(heavy brow ridge右圖)
❸stiff joint
❹cloudy degeneration of cornea➔blindness

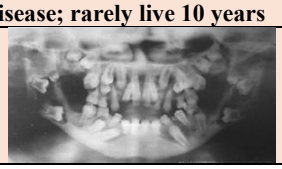


Hunter syndrome

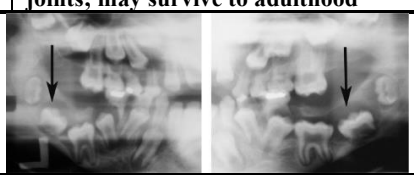
➲selected mucopolysaccharidosis syndromes
(AR, Autosomal recessive; CS, chondroitin sulfate; DS, dermatan sulfate; HS, heparan sulfate; KS, keratan sulfate; R, recessive)

type	eponym	inheritance	enzyme deficiency	stored substrate	clinical features
I-H	Hurler	AR	α- L -Iduronidase	HS & DS	appears in infancy; cloudy cornea, growth impair, ↓intelligence, coronary artery disease; rarely live 10 years
I-S	Scheie	AR	α- L -Iduronidase	HS & DS	onset in late childhood; cloudy cornea, normal intelligence, aortic regurgitation; survive to adulthood
II	Hunter	X-linked R	Iduronate-2-sulfatase	HS & DS	appears at 1↔2s; clear cornea, ↓intelligence, growth impairment, stiff joint
III-A	Sanfilippo-A	AR	Heparan *N* -sulphatase	HS	appears at 4↔6s; clear cornea, reduced intelligence, mild skeletal changes; death in adolescence
III-B	Sanfilippo-B	AR	α- *N*-acetylglucosaminidase	HS	same as Sanfilippo-A
IV-A	Morquio-A	AR	Galactose-6-sulfatase	KS & CS	appears at 1↔2s; cloudy cornea, normal intelligence, lax joints; may survive to middle age
IV-B	Morquio-B	AR	β-Galactosidase	KS	like Morquio-A
VI	Maroteaux-Lamy	AR	Arylsulphatase B	DS & CS	appears at 2-6s; cloudy cornea, normal intelligence, growth impairment, stiff joints; may survive to adulthood





➲oral manifestation
❶macroglossia
❷gingival hyperplasia(anterior➔mouth breath➔drying & irritating effects)
❸dental
①thin enamel with pointed cusp(posterior teeth上頁圖Hurler syndrome)



②impacted teeth(follicular c.t space➔glycosaminoglycans accumulate)[上圖RLs(箭頭)➔unerupt teeth crown, Hunter syndrome]
③multiple impacted teeth congregate in single follicle(radiographic rosette pattern) ④taurodont

❹condylar head➔flattening(distortion)

➲dx➔❶↑glycosaminoglycans(in urine) ❷deficiencies of specific enzyme(in leukocyte & fibroblast)

Lipid reticuloendothelioses➔autosomal recessive➔lack enzyme process lipid➔lipid accumulate in cell(storage disease)

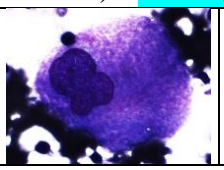
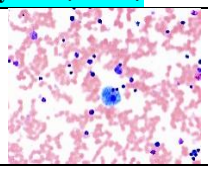
(1)Gaucher disease(most)➔glucocerebrosidase deficiency➔glucosylceramide accumulate➔lysosome(cell with macrophage & monocyte)
❶3-type
①type 1(nonneuronopathic)➔Ashkenazi Jewish(~1/12↔17 p't➔defective gene➔heterozygous➔asymptomatic)
②types 2 & 3(less common)(neuronopathic➔poor prognosis)➔panethnic distribution

(2)Niemann-Pick disease➔acid sphingomyelinase deficiency➔sphingomyelin accumulate in lysosome of macrophage

(3)Tay-Sachs disease➔β-hexosaminidase A deficiency➔ganglioside accumulate in lysosome of neuron

➲clinic
(1)Gaucher disease
❶glucocerebroside-laden macrophage(nonfunction)
①bone marrow accumulate➔displace normal hematopoietic cell➔anemia(thrombocytopenia)➔bone infarct(bone pain)
[✪long bone(esp., femur)➔Erlenmeyer flask deformities]
②liver & spleen➔accumulate(visceral enlargement)➔growth impairment
❷types 2,3➔neurologic deterioration
❸jaw lesion➔PD-RL(usu. mandible)
①cortical bone thinning(without produce non-vital teeth/lamina dura resorption)
②IAN canal wall obliterated
❺↓salivary flow(may not clinic important)
(2)Niemann-Pick disease➔3 types(different clinic expression & prognosis)
❶types A,B(acid sphingomyelinase deficiency)
❷type C(NPC-1,2 gene mutation➔cholesterol processing)
❸types A,C
①neuronopathic(psychomotor impairment, dementia, spasticity痙攣)
②hepatosplenomegaly
③death in 1st/2nd decade of life
❹type B➔survive to adulthood➔visceral sign(①primarily hepatosplenomegaly ②sometimes pulmonary)
(3)Tay-Sachs disease➔genetic heterogeneous(wide clinic range)
❶mild➔survive to adulthood
❷severe(infantile)➔出生不久neuron degenerate(①blindness ②impair development ③seizure)➔death by 3-5s(預後差)

➲micro
❶Gaucher disease(osseous lesion➔lipid-engorged macrophage(Gaucher cell)➔abundant bluish cytoplasm(fine texture like wrinkled silk)(左圖)
❷Niemann-Pick disease(bone marrow aspirate)➔"sea blue" histiocyte(右圖)

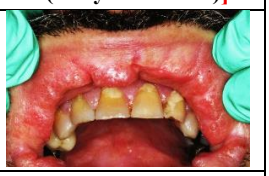
23. Which one of the following matchings of genetic disorder with the corresponding disease is *false*?
(A) Niemann-Pick disease (types A and B)➔alkaline spingomyelinase deficiency
(B) Tay-Sachs disease➔β-hexosaminidase A deficiency
(C) Gaucher disease➔glucocerebrosidase deficiency
(D) vitamin D-resistant➔PHEX deficiency

Lipoid proteinosis(Urbach-Wiethe syndrome)➔autosomal recessive➔waxy material deposit➔dermis & submucosal c.t.

➲ECM1 gene mutation(encode glycoprotein➔extracellular matrix protein 1)

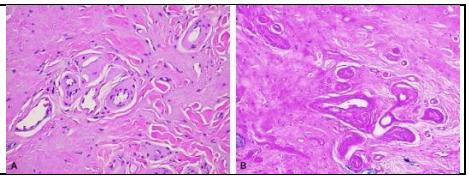
➲clinic➔❶laryngeal mucosa ❷vocal cord➔1st sign[infant❶unable to cry ❷hoarse cry ❸hoarse voice(early childhood)]

❶vocal cord thicken(amorphous material accumulate➔laryngeal mucosa)
(✖also➔pharynx, esophagus, tonsils, vulva, rectum)
❷skin lesion(develop early in life)
①thickened yellowish waxy papule(plaque)
②nodules➔face(lips & eyelid margin左圖)

③dark-crust vesicle➔heal as atrophic hyperpigment patch➔thicken, furrow appearance
④other skin area(neck, palm, axilla, elbow, scrotum, knee, digit)➔chronic trauma➔hyperkeratotic, verrucous surface
❹intracranial calcification(symmetric)➔medial temporal lobes(~70%)➔asymptomatic(a few➔seizure)
❺oral mucosa(2nd decade of life)➔tongue, labial(上右圖), buccal nodule(diffusely enlarge, thicken)
①dorsal tongue papillae destroyed➔smooth surface➔bound to mouth floor(unable protrude tongue)
②gingival enlargement(infrequent)

➲micro
❶lamellar material(A圖)[periodic acid-Schiff(PAS)(+)➔undigest by diastase B圖]➔around blood vessel, nerve, hair follicle, sweat gland
❷material location, stain properties(PAS; diastase)(+), ↑(laminin, type IV,V collagen)➔BM origin



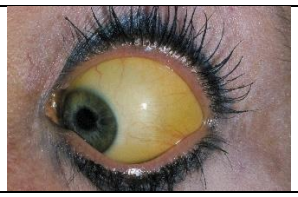
24. Which of the following matchings of genetic disorder with the corresponding lipid disease is *false*?
(A) Niemann-Pick disease(尼曼匹克症) (types A and B)➔alkaline spingomyelinase deficiency
(B) Tay-Sachs disease(戴薩克斯症)➔β-hexosaminidase A deficiency
(C) Gaucher disease(高雪氏症)➔glucocerebrosidase deficiency
(D) lipoid proteinosis(類脂質蛋白沉積症)➔ECM1 mutation

Jaundice(Icterus)➔excess bilirubin in bloodstream➔accumulate➔tissue➔yellow discoloration of skin & mucosa

➲bilirubin metabolism
❶derived from Hb(oxygen-carrying pigment of RBC) breakdown
❷av. life span of RBC in circulation➔120 days➔physiologic breakdown➔degraded Hb(process by cell of reticuloendothelial system)➔bilirubin liberate to bloodstream(unconjugated)➔liver(bilirubin taken up by hepatocyte ➔conjugate with glucuronic acid)➔conjugated bilirubin(soluble product excreted in bile)

➲cause
❶autoimmune hemolytic anemia/sickle cell anemia➔rapid RBC broken down➔liver cannot processing
❷liver not function correct➔①↓bilirubin uptake from circulation ②↓bilirubin conjugation in liver cell
❸frequent present at birth(↓activity of enzyme system conjugate bilirubin)
❹Gilbert syndrome➔defect in bilirubin conjugation enzyme system

➲clinic
❶elastin fiber➔affinity for bilirubin
❷tissue(high elastin content)➔①sclera ②lingual frenum ③soft palate➔sclera of eye (1st site yellow color noted)
※ hypercarotenemia[excess ingest of carotene(vitamin-A precursor in yellow vegetable & fruit)]➔yellow discoloration➔confuse with jaundice BUT sclera not involve



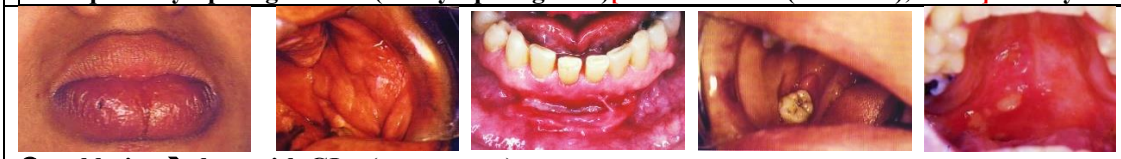
Crohn disease(Regional ileitis; Regional enteritis)➔inflammation & immunologic mediated condition(unknown cause)

➲affect➔❶GI tract(oral to anus)❷extraintestinal site(skin, eye, joint)
➲oral➔significant➔precede GI lesion(30%)
➲cigarette smoking(exacerbate Crohn disease)➔advise to stop

➲familial case➔genetic factor➔pathogenesis

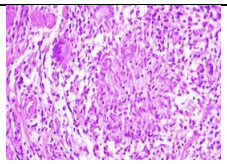
➲clinic➔oral lesion associate condition of orofacial granulomatosis
❶most 1st evident➔teenager vs another diagnostic peak➔>60s
❷GI S/S➔abdomen cramp(pain), nausea, (occasion)fever➔wt loss & malnutrition➔anemia, ↓growth, short stature
❸oral lesion

①(peri)oral nodule(swelling)	②cobblestone mucosa	③linear granulomatous-like ulcer(buccal vestibule)
④patchy erythematous macule(plaque)➔(un)attached gingiva(mucogingivitis)		
⑤soft tissue swelling(like denture-related fibrous hyperplasia)	⑥mucosal tag	⑦aphthous-like ulcer
⑧acquired lymphangiectasias(like lymphangioma)[buccal mucosa(vestibule), labial]➔early childhood		



➲oral lesion➔clear with GI tx(many cases)
➲persistent oral ulcer➔topical(intralesional corticosteroid)
➲systemic thalidomide & infliximab➔refractory oral ulcer

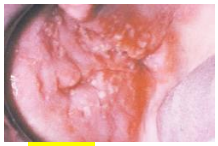
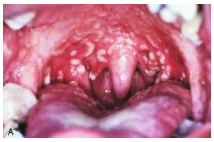
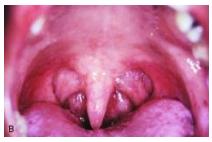
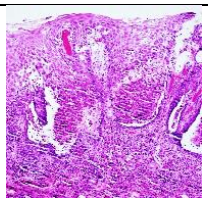
❹recurrent severe buccal space infection➔cutaneous salivary fistula(one instance)
❺pyostomatitis vegetans(infrequent)



➲micro➔nonspecific(like orofacial granulomatosis)
nonnecrotizing granulomatous inflammation➔submucosal c.t.[(-)➔not R/O Crohn disease]➔special stain(R/O deep fungal infection, syphilis, mycobacterial infection)

Pyostomatitis vegetans➔oral expression of inflammatory bowel disease(ulcerative colitis/Crohn disease)

➲clinic➔concurrent liver abnormalities(a few)
❶[buccal(labial) mucosa, soft palate, ventral tongue](erythematous➔"snail track" ulcer下A圖; heal on prednisone下B圖)➔yellow, slight elevate, linear, serpentine(蜿蜒)pustule(下左圖)➔①concurrent bowel symptom ②precede intestinal involvement

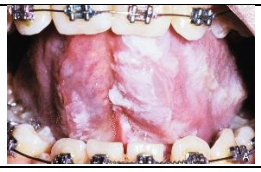
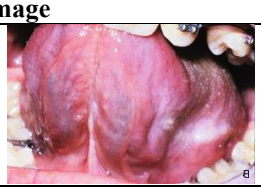
➲micro(上右圖)
❶numerous eosinophil(spinous layer)➔marked edema(acantholytic)➔intraepithelial(subepithelial eosinophilic) abscess
❷c.t.➔①dense inflammatory cell infiltrate(eosinophil, neutrophil, lymphocyte) ②perivascular inflammation

25. Which one of the following about the patient showing an oral "snail track" ulceration is *false*?
(A) it is always concurrent with inflammatory bowel disease (Crohn disease)
(B) biopsy shows intraepithelial abscess containing numerous eosinophil
(C) it may concurrent with liver disorders
(D) it can show positive response upon antibiotic treatment

Uremic stomatitis➔renal failure complication➔painful disorder

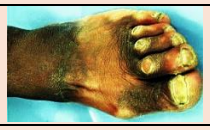
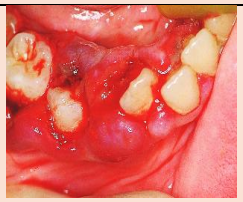
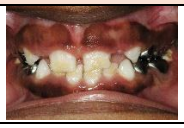
➲cause➔urease(by oral microflora)➔degrade salivary urea➔free ammonia➔oral mucosa damage

➲clinic➔acute renal failure(most)
❶white plaque(like oral hairy leukoplakia)右A圖➔buccal, tongue, mouth floor➔resolution after renal dialysis(a few days↔2-3 wks右B圖)
❷unpleasant taste, oral pain, burning sensation
❸ammonia odor➔①breath ②urine

Vitamin deficiency

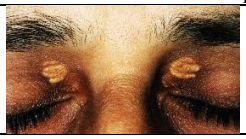
➲vitamin	normal function
①vitamin A(retinol)	❶maintenance of vision ❷growth & tissue differentiation
②vitamin B1(thiamin)	❶maintenance of proper neuron function ❷coenzyme for metabolic reaction
③vitamin B2(riboflavin)	❶cellular oxidation-reduction reaction
④vitamin B3(niacin)	❶coenzyme for oxidation-reduction reaction
⑤vitamin B6(pyridoxine)	❶cofactor associated enzyme➔amino acid synthesis ❷normal neuronal function
⑥vitamin C(ascorbic acid)	❶collagen synthesis
⑦vitamin D	❶hormone ❷calcium absorption from gut
⑧vitamin E(α-tocopherol)	❶fat-soluble ❷antioxidant
⑨vitamin K	❶fat-soluble ❷clotting factor II, VII, IX, X synthesis

➲vitamin	deficiency	
①vitamin A(retinol)	❶infancy➔blindness ❷early occurrence➔night blindness ❸prolong➔skin & conjunctiva dryness➔cornea ulcer➔blindness	
②vitamin B1(thiamin)	beriberi(腳氣病) ❶CV problem(peripheral vasodilation, heart failure, edema) ❷neuro. problem (peripheral neuropathy, Wernicke encephalopathy➔vomit, nystagmus, mental deterioration➔coma & death)	
③vitamin B2(riboflavin)	❶glossitis, angular cheilitis, sore throat, swelling & erythema of oral mucosa ❷normocytic normochromic anemia ❸seborrheic dermatitis	
④vitamin B3(niacin)	❶pellagra(糙皮病)(maize(玉米) as principal diet)➔triad (①dermatitis ②dementia ③diarrhea) ❷oral➔①stomatitis ②glossitis ③tongue(red, smooth, raw) ❸without tx➔dead	
⑤vitamin B6 (pyridoxine)	❶isoniazid(anti-TB drug)➔deficiency ❷weakness, dizziness, seizure disorders ❸cheilitis & glossitis	
⑥vitamin C (ascorbic acid)	❶↓collagen synthesis➔weaken vascular wall➔petechial hemorrhage & ecchymosis ❷delay wound healing ❸childhood➔painful subperiosteal hemorrhage ❹oral➔①gingiva swelling(spontaneous hemorrhage, ulcer, tooth mobility) ➔scorbutic gingivitis ②↑severity of perio infection(bone loss) ❺intracranial hemorrhage➔death	
⑦vitamin D	❶infancy➔rickets(adult➔osteomalacia) ❷costochondral junction(rib) prominence(rachitic rosary)(佝僂病串珠) ❸bowing long bone of leg(poor mineralization) ❹teeth➔hypomineralization	
⑧vitamin E	❶child(chronic cholestatic liver disease)➔severe fat-soluble vitamin malabsorption(esp., vitamin E)	

(α-tocopherol)	❷neurologic signs(CNS & PNS abnormalities)
⑨vitamin K	❶coagulopathy(inadequate synthesis of prothrombin & other clotting factors ❷oral➔gingiva bleeding ❸uncontrol(systemic bleeding)

26. Which one of the following matchings of vitamin B deficiency with disease occurrence is *false*?
(A) thiamin➔beriberi
(B) riboflavin➔microcytic microchromic anemia
(C) niacin➔pellagra
(D) pyridoxine➔angular cheilitis

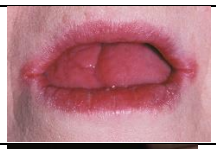
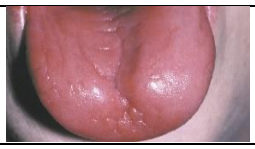
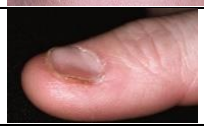
Xanthelasma➔most common cutaneous xanthoma(like cutaneous amyloid deposit)➔↑atherosclerosis & serum lipid risk

➲clinic ❶middle-age(older) adult➔≥1 soft yellow plaque(periocular skin)(medial upper eyelid) ❷soft & yellow color➔distinguish xanthelasma from amyloid deposit	
➲micro➔lipid-laden histiocyte➔superficial to mid-dermal c.t.	

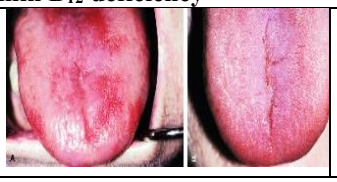
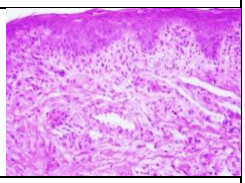
Iron-deficiency anemia➔most common cause of anemia

➲cause➔❶excessi blood loss ❷↑RBCdemand ❸↓iron intake ❹↓iron absorp(①gastrectomy due to celiac sprue➔plant protein, gluten(麩質) sensitivity➔severe chronic diarrhea ②inflammatory bowel disease(Crohn disease)
➲oral➔❶angular cheilitis ❷atrophic glossitis(dorsal tongue papillae atrophy) ❸oral mucosa atrophy(tender/burning sensation)➔candidiasis➔mouth ange & tongue

Plummer-Vinson syndrome(Paterson-Kelly syndrome; Sideropenic dysphagia)

➲oral & esophageal SCC➔premalignant process		
➲clinic➔Fe-deficiency anemia(microcytic hypochromic) ❶burning sensation(tongue & oral mucosa➔cannot worn denture ❷angular cheilitis(左圖) ❸lingual papillae atrophy➔smooth red dorsal(beef) tongue(右圖)		
❹dysphagia(pain on swallow) ❺esophageal web(abnormal band) ❻spoon-shaped configuration nail(koilonychia)➔brittle(右圖)		
➲micro ❶epithelial atrophy submucosal chronic inflammation ❷epithelial dysplasia(advanced)		

Pernicious anemia➔megaloblastic anemia

➲cause(✖vitamin B_{12} cannot absorb unless both extrinsic & intrinsic factors present) ❶↓absorption of cobalamin(vitamin B_{12}, extrinsic factor) ❷lack intrinsic factor(produced by parietal cell of stomach lining➔vitamin B_{12} absorption) ✖ingested cobalamin➔bind to intrinsic factor in duodenum➔cobalamin-intrinsic factor complex ✖cobalamin➔derived from animal source➔strict vegetarian➔vitamin B_{12} deficiency	
➲clinic➔oral ❶burning sensation➔tongue, lip, buccal mucosa ❷oral mucosal erythema & atrophy➔dorsal tongue(A; B healing)	 
➲micro➔epithelial atrophy(loss of rete ridge) ❶epithelial cell ①↑N/C ratio ②prominent nucleoli (misinterprete as epithelial dysplasia) ❷c.t.➔chronic inflammatory cell infiltrate(patchy diffuse)	➲vitamin B 12 deficiency & folate deficiency➔pernicious(megaloblastic) anemia ✖distinguish 2 conditions(important)➔tx of vitamin B_{12} deficiency with folate➔resolve anemia & oral mucosa atrophy BUT ↓myelin production➔further CNS damage

Chapter 17: Oral Manifestations of Systemic Diseases

1. In primary hyperparathyroidism, what abnormal laboratory value would be expected?
A. Decreased adrenocorticotropic hormone levels
B. Increased angiotensin-converting enzyme
C. Increased levels of thyroid stimulating hormone
D. Increased serum calcium levels
E. Increased serum phosphate levels

2. Addison disease is characterized by:
A. excess insulin production
B. insufficient production of adrenal corticosteroids
C. ulcerating oral nodules
D. uncontrollable ("malignant") hypertension
E. none of the above

3. Pernicious anemia is caused by defective absorption of:
A. iron
B. niacin
C. riboflavin
D. vitamin C
E. none of the above

4. Amyloidosis is most likely to present intraorally as:
A. hairy tongue
B. macroglossia
C. palatal ulceration with an associated nasal fistula
D. rapidly progressive periodontitis
E. recurrent aphthous ulcers

5. Pyostomatitis vegetans is most often associated with:
A. deep fungal infections such as blastomycosis
B. diabetes mellitus
C. positive Koebner phenomenon
D. superior vena cava syndrome
E. ulcerative colitis

6. Kidney stones are a common feature of:
A. diabetes mellitus
B. Frey's syndrome
C. hyperparathyroidism
D. hyperthyroidism
E. hypothyroidism

7. Which one of the following special stains is used in the diagnosis of amyloidosis?
A. Congo red
B. GMS
C. PAS
D. PTAH
E. Steiner

8. Which one of the following conditions has been associated with an increased risk for oral squamous cell carcinoma?
A. Addison disease
B. Amyloidosis
C. Pernicious anemia
D. Plummer-Vinson syndrome
E. Pyostomatitis vegetans

9. A 45-year-old white female presents with a 2×2 cm ^{2} radiolucent lesion of the mandible, which is diagnosed as a central giant cell granuloma. Which one of the following conditions should be ruled out?
A. Addison disease
B. Crohn's disease
C. Gigantism
D. Hyperparathyroidism
E. Multiple sclerosis

10. Mandibular prognathism is a clinical feature of:
A. acromegaly

B. beriberi
C. Cushing syndrome
D. scurvy
E. vitamin-D-resistant rickets

11. Which one of these conditions may be associated with delayed tooth eruption?
A. Diabetes mellitus
B. Gigantism
C. Hemifacial hyperplasia
D. Hyperthyroidism
E. Hypothyroidism

12. Pernicious anemia is caused by:
A. autoimmune destruction of the parietal cells in the stomach lining
B. chronic blood loss from the gastrointestinal tract
C. diets that are low in B vitamins
D. gluten sensitivity leading to malabsorption
E. hereditary lack of ferritin production

13. "Secondary" hyperparathyroidism is usually secondary to:
A. chronic renal failure
B. hyperthyroidism
C. pituitary adenocarcinoma
D. primary hyperparathyroidism
E. use of calcium-channel blockers

14. Which one of the following conditions is most likely to be associated with macroglossia?
A. Diabetes mellitus
B. Hyperparathyroidism
C. Hyperthyroidism
D. Hypoparathyroidism
E. Hypothyroidism

15. Exophthalmos is frequently observed in patients with:
A. cretinism
B. Graves' disease.
C. pellagra
D. scurvy
E. all of the above
ANS: B

16. Which one of the following conditions is most strongly associated with an increased risk for systemic amyloidosis?
A. Acromegaly
B. Diabetes mellitus
C. Hunter syndrome
D. Hurler syndrome
E. Multiple myeloma

17. Which one of the following vitamin deficiencies is associated with roughness of sun-exposed areas of the skin?
A. Niacin
B. Riboflavin
C. Thiamin
D. Vitamin A
E. Vitamin C

18. Which one of the following conditions is characterized by granulomatous inflammation?
A. Crohn's disease
B. Lipoid proteinosis
C. Rheumatoid arthritis
D. Trigeminal neuralgia
E. Uremic stomatitis

19. Premature loss of the deciduous teeth is a characteristic dental finding in patients with:
A. celiac sprue
B. hyperthyroidism
C. hypophosphatasia
D. pellagra

E. uremic stomatitis

Chapter 17: Oral Manifestations of Systemic Diseases➔answers

1. ANS: D
2. ANS: B
3. ANS: E
4. ANS: B
5. ANS: E
6. ANS: C
7. ANS: A
8. ANS: D
9. ANS: D
10. ANS: A
11. ANS: E
12. ANS: A
13. ANS: A
14. ANS: E
15. ANS: B
16. ANS: E
17. ANS: A
18. ANS: A
19. ANS: C

Chapter 18 Facial pain & neuromuscular diseases

Frey syndrome(auriculotemporal syndrome)➔[❶facial flushing ❷sweating]➔along auriculotemporal nerve

➲auriculotemporal nerve innervation ❶sensory fiber➔preauricular & temporal region ❷parasympathetic fiber➔parotid gland ❸sympathetic vasomotor(血管運動) & sudomotor(汗腺運動) fiber➔preauricular skin	➲parotid abscess, trauma, 下顎手術, parotidectomy ➔ parasympathetic nerve切斷➔reestablish innervation➔fiber misdirected➔regenerate along sympathetic nerve pathway ➔communicate with sympathetic nerve of sweat gland & blood vessel of facial skin
➲minor starch-iodine test➔1% iodine solution➔ painted on affected skin➔dry➔coated with starch➔ eat➔moisture of sweat➔mix with iodine➔react with starch➔blue color(右圖)	

1. The blood-routine test for the patient with **giant cell arteritis** will reveal:
   (A) increased erythrocyte sedimentation rate
   (B) decreased erythrocyte sedimentation rate
   (C) decreased C-reactive protein
   (D) no change

Giant cell(temporal) arteritis➔immune-mediated➔artery(medium-sized & larger)➔vascular occlusion & ischemia

➲strong genetic predisposition➔express certain human leukocyte antigen(HLA) types➔HLA-DRB1*0 allele		
➲geographic & seasonal variation➔infectious etiology	➲most➔older individual(average 70s)	➲ F:M=2-3:1
➲clinic ❶temporal artery(most)➔new, severe headache & scalp tenderness[other large vessel(30↔70%)➔often asymptomatic] ❷superficial temporal artery➔sensitive to palpation➔erythematous, swollen, tortuous, ulcerated sometimes ❸jaw claudication(跛行)➔cramp(抽筋)(ischemia of masseter & temporalis muscle)➔↑ chewing/talking➔rest relieve ❹❸coexist ocular(frequent)➔HN vasculitis of posterior ciliary artery & ischemic optic neuropathy➔永久性 vision loss ❺visual disturbances(①blurred vision with exercise ②diplopia ③transient vision loss)➔early manifestation ❻systemic S/S➔①fever ②malaise ③fatigue ④anorexia ⑤weight loss ❼polymyalgia rheumatic(風濕性多肌痛)(40%)➔pain & morning stiffness➔①neck ②shoulder ③pelvic girdle(骨盆帶) ❽undetected aortic inflammation➔aneurysm(rupture)➔①↑risk CV accident ②cardiac infarction ③limb 跛行 ④vasculitis		
➲micro➔preferred confirmatory test ❶proper evaluation➔at least 1cm affected vessel ❷tunica intima(media)➔①chronic inflammation(multinucleated giant cell mixed with macrophage & lymphocyte) ②narrow lumen(由於 edema & tunica intima proliferation) ③smooth muscle & elastic lamina necrosis ④thrombosis		
➲lab➔❶↑erythrocyte sedimentation rate(ESR) ❷↑C-reactive protein ❸↑platelet count		
➲diagnosis➔imaging➔vessel wall thickening, occlusion, stenosis(狹窄), non-compressible artery ❶US➔temporal artery➔early diagnosis ❷MRI➔large vessel involvement		

2. **Burning mouth syndrome** is most likely occurred in:
   (A) people with sialorrhea (ptyalism, drooling)
   (B) people with gustatory disturbance
   (C) menopause female
   (D) men more than women

3. **Burning mouth syndrome** is most likely occurred in:
   (A) young men
   (B) young women
   (C) old women
   (D) old men

4. The oral mucosa of **burning mouth syndrome** is usually:
   (A) normal
   (B) hyperplasia
   (C) ulceration
   (D) erosion

5. The first line effective drug for **burning mouth syndrome** is:
   (A) acetaminophen
   (B) NSAID
   (C) clonazepam
   (D) anti-histamine

Burning mouth syndrome

➲local factors	➲systemic factors
❶clinically observable hyposalivation ❷chronic mechanical trauma ❸oral fungal, bacterial, or viral infection ❹contact stomatitis ❺geographic tongue ❻local manifestation of immune-mediated(autoimmune) disease	❶vitamin B deficiency ❷vitamin B1/B2 deficiency ❸pernicious anemia(B12) ❹pellagra(糙皮病)(niacin 維他命 B3 deficiency) ❺folic acid deficiency ❻Fe deficiency ❼DM ❽chronic gastritis/regurgitation(食物回流)

6. Which of the following description for **trigeminal neuralgia** is *false*?
   (A) duration of a single pain "spasm" is more than 2 minutes
   (B) pain is dramatically diminished with carbamazepine
   (C) pain limited to the distribution of one or more branches of trigeminal nerve
   (D) touching the trigger point during refractory period cannot induce additional attacks

7. Which of the following is the most common benign tumor of the synovium of the **temporomandibular joint**?
   (A) osteoblastoma
   (B) osteochondroma
   (C) chondroblastoma
   (D) synovial chondromatosis

8. Which of the following muscles cannot be palpated on clinical examination of **temporomandibular joint disorders**?
   (A) medial pterygoid
   (B) lateral pterygoid
   (C) masseter
   (D) temporalis

9. Which of the following diagnostic modalities should be used for **osteoarthritis of temporomandibular joint**?
   (A) cone-beam computed tomography
   (B) magnetic resonance tomography
   (C) local anesthesia injected into the joint
   (D) arthrography

10. 關於**類風濕性顳顎關節炎**的敘述，下列何者錯誤？(114)
   (A) 膜組織異常增生(pannus formation)
   (B) 發生年齡可能比退化性關節炎早
   (C) 通常侵犯單側
   (D) 可能會造成髁頭-上行枝高度(condylar-ramus height)喪失

11. 關於**顳顎關節 osteoarthritis** 的影像學變化，下列敘述何者錯誤？(114)
   (A) 早期可能出現 joint space 縮小
   (B) 早期可能出現 subchondral bone resorption
   (C) 隨著疾病的進展，articular eminence 可能變平
   (D) 晚期可能出現 condylar head 皮質骨侵蝕

12. **關節穿刺術(arthrocentesis)**之敘述，下列何者錯誤？(114)
   (A) 其作用在沖洗出關節內之發炎物質，達到症狀緩解之目的
   (B) 通常施行在下關節腔
   (C) 沖洗液建議至少 100 毫升
   (D) 第一穿刺點約在關節窩後緣，即在耳珠 - 眼眥線下方 2 mm，耳珠前 10 mm 之位置

13. 55 歲病人，主訴右臉頰陣發性疼痛，具電擊刺痛感，每次發作時間約持續幾秒鐘至 1 分鐘，特別在 吃東西碰到右下第一大臼齒前庭區時。其診斷最可能是下列何者？(114)

(A) 叢發性頭痛

(B) 肌筋膜疼痛

(C) 非典型顏面痛

(D) 三叉神經痛

Dysgeusia(味覺障礙) & Hypogeusia(味覺減退)	
➲local factors **❶oral candidiasis** **❷oral galvanism** **❸periodontitis/gingivitis** **❹chlorhexidine rinse** **❺xerostomia**	**➲systemic factors** **vitamin A deficiency, vitamin B $_{12}$ deficiency, zinc deficiency, iron deficiency** **nutritional overdose(zinc, vitamin A, or pyridoxine), food sensitivity/allergy** **Sjögren syndrome, chorda tympani nerve damage, anorexia, cachexia, or bulimia** **severe vomiting during pregnancy, liver dysfunction, Crohn disease, cystic fibrosis** **familial dysautonomia, Addison disease, Turner syndrome, alcoholism, medications(200 types), sychosis/depression, pesticide ingestion, lead, copper, or mercury poisoning, temporal arteritis, brainstem ischemia/infarction, migraine headach, temporal lobe central nervous system(CNS) tumor, nerve trauma(gustatory nerve), herpes zoster(geniculate ganglion), upper respiratory tract infection, chronic gastritis/ regurgitation, Bell palsy, COVID-19 infection, HN RT**

Chapter 18: Facial Pain and Neuromuscular Diseases

1. An increased prevalence of trigeminal neuralgia is seen in patients with:
A. Bell palsy.
B. congenitally missing teeth
C. diabetes mellitus
D. multiple sclerosis
E. Sturge-Weber syndrome

2. Burning mouth syndrome would be most likely to occur in which patient?
A. 15-year-old female
B. 25-year-old male
C. 35-year-old female
D. 45-year-old male
E. 55-year-old female

3. Which nerve is affected by Bell palsy?
A. Auriculotemporal
B. Vidian
C. V
D. VII
E. VIII

4. The most common cause of Frey syndrome is:
A. eating overly spicy foods
B. exposure to cold weather
C. exposure to hot weather
D. sarcoidosis
E. surgery of the parotid gland

5. Nerve paralysis similar to Bell palsy may be seen in patients with:
A. migraine
B. multiple endocrine neoplasia type 2B
C. Ramsay Hunt syndrome
D. rheumatoid arthritis
E. systemic lupus erythematosus

6. The most significant complication associated with temporal arteritis is:
A. Bell palsy.
B. encephalitis
C. loss of hearing
D. loss of taste
E. permanent loss of vision

7. The starch-iodine test can be used in the diagnosis of:
A. diabetes mellitus.
B. Frey's syndrome
C. hyperparathyroidism
D. hyperthyroidism
E. hypothyroidism

8. In Frey syndrome, sweating of the temporal region is stimulated by:
A. closing the eyes tightly
B. eating.
C. exposure to cold
D. sleep apnea
E. yawning

9. Which one of the following medications can be most beneficial for patients with idiopathic burning mouth syndrome?
A. Albuterol
B. Barbiturates
C. Clonazepam
D. Diltiazem
E. Etanercept

Chapter 18: Facial Pain and Neuromuscular Diseases➔answers

1. ANS: D

2. ANS: E
3. ANS: D
4. ANS: E
5. ANS: C
6. ANS: E
7. ANS: B
8. ANS: B
9. ANS: C

ANSWERS FOR REVISION QUESTIONS	
	Topics
Chapter 1	**Developmental defects of oral & maxillofacial region** **(1)C (2)A (3)A (4)B (5)A (6)B (7)D (8)C**
Chapter 2	**Abnormalities of teeth** **(1)A (2)C (3)B (4)A (5)B (6)A (7)B (8)D (9)D (10)C (11)B (12)D (13)C (14)A (15)D (16)B (17)B (18)C (19)A (20)B (21)D (22)B (23)B (24)A (25)B (26)D (27)C (28)B (29)C (30)A (31)D (32)B (33)D (34)D (35)C (36)A (37)D (38)C (39)C**
Chapter 3	**Pulpal & periapical disease** **(1)B (2)C (3)B (4)C (5)B (6)C (7)A (8)D**
Chapter 4	**Periodontal diseases** **(1)A (2)D (3)B**
Chapter 5	**Bacterial infections** **(1)B (2)D (3)C (4)D (5)B (6)D (7)B (8)B (9)B (10)B (11)C (12)C (13)D (14)D (15)D (16)C**
Chapter 6	**Fungal & protozoal diseases** **(1)B (2)C (3)D (4)A (5)D (6)A (7)C (8)C**
Chapter 7	**Viral infections** **(1)C (2)C (3)D (4)B (5)A (6)B (7)D (8)C (9)A (10)B (11)A (12)B (13)B (14)C (15)D (16)C (17)C (18)D (19)D (20)C (21)B (22)C**
Chapter 8	**Physical & chemical injuries** **(1)C (2)C (3)D (4)D (5)B (6)D**
Chapter 9	**Allergies & immunologic diseases** **(1)A (2)C (3)A (4)B (5)B (6)A (7)D (8)A**
Chapter 10	**Epithelial pathology** **(1)C (2)C (3)A (4)A (5)C (6)D (7)D (8)C (9)A (10)C (11)D (12)B (13)D (14)B (15)C (16)A (17)A (18)A (19)B (20)B (21)C (22)C (23)D (24)B (25)A**
Chapter 11	**Salivary gland pathology** **(1)B (2)B (3)A (4)B (5)B (6)B (7)B (8)C (9)C (10)C (11)B (12)B (13)D (14)D (15)C (16)B (17)D (18)A (19)D (20)C (21)C (22)B (23)D (24)D (25)A (26)C**
Chapter 12	**Soft tissue tumors** **(1)A (2)A (3)D (4)A (5)B (6)D (7)B (8)A (9)D (10)A (11)C (12)B (13)C (14)D (15)A**
Chapter 13	**Hematologic disorders** **(1)C (2-1)A (2-2)B (2-3)B (2-4)C (2-5)C (3)B (4)D (5)D (6)A (7)A (8)A (9)C (10)D (11)D (12)A (13)C (14)B (15)B (16)A (17)C (18)B (19)D (20)C**
Chapter 14	**Bone pathology** **(1)A (2)B (3)D (4)C (5)A (6)A (7)C (8)A (9)C (10)C (11)D (12)B (13)D (14)B (15)A (16)C (17)D (18)B (19)A (20)D (21)B (22)D (23)D (24)B (25)A (26)C (27)D (28)D (29)B (30)B (31-1)C (31-2)B (31-3)A (31-4)E (31-5)D**
Chapter 15	**Odontogenic tumors & cysts** **(1)B (2)D (3)D (4)B (5)B (6)C (7)D (8)B (9)B (10)B (11)D (12)D (13)D (14)A (15)B (16)B (17)A (18)A (19)D (20)B (21)B (22)B (23)C (24)C**
Chapter 16	**Dermatologic diseases** **(1)B (2)A (3)C (4)C (5)A (6)C (7)A (8)A (9)A (10)A (11)A (12)D (13)B (14)D (15)D (16)C (17)D (18)D (19)A (20)D (21)C (22)D (23)C (24)D (25)D (26)C (27)C (28)C,D**
Chapter 17	**Oral manifestations of systemic diseases** **(1)C (2)A (3)D (4)A (5)D (6)B (7)D (8)B (9)C (10)B (11)D (12)B (13)D (14)B (15)C (16)C (17)D (18)A,D (19)B (20)D (21)A (22)C (23)A (24)A (25)D (26)B**
Chapter 18	**Facial pain & neuromuscular diseases** **(1)A (2)C (3)C (4)A (5)C (6)A (7)B (8)B (9)B (10)C (11)B (12)B (13)D**

Appendix(quick revision)➔feature/test⇆disease(different chapters)

➲xx sign⇆diseases

❶Forchheimar sign⇆German measles(rubella)(oral small dark-red papule)
❷Gorlin sign⇆Ehler-Danos syndrome(nose tip touch with tongue)
❸Hutchinson sign⇆herpes zoster(nose tip lesion➔severe ocular risk)
❹Nikolsky sign⇆pemphigus
❺Crowe sign⇆neurofibromatosis type I(von Recklinghausen disease of skin)(freckle of axilla腋下/other intertriginous皺摺間 zone)
❻string sign⇆parosteal osteosarcoma(RL line➔periosteum between tumor & cortex)
❼Chvostek sign⇆hypoparathyroidism(facial nerve tapped輕敲 just below zygomatic arch➔upper lip twitching(抽搐)[latent tetany(痙攣)])

➲Gorlin xx⇆diseases

❶Gorlin cyst⇆calcifying odontogenic cyst
❷Gorlin syndrome⇆nevoid nasal cell carcinoma syndrome
❸Gorlin sign⇆Ehler-Danos syndrome
✶Gorham disease⇆massive osteolysis

➲pink tooth⇆diseases

❶pink tooth⇆internal root resorption
❷pink tooth(upper incisor)⇆leprosy
✶darkened tooth⇆minocycline discoloration

➲multinucleated giant cell⇆diseases

❶giant cell fibroma(unrelated to trauma)
❷giant cell arteritis
❸pleomorphic lipoma(liposarcoma)
❹cherubism/central giant cell granuloma
❺radicular cyst(associate cholesterol cleft)
❻epidermal/dermal cyst(associate keratin)
❼tertiary syphilis
❽blastomycosis
❾paracoccidioidomycosis blastomycosis(Mickey mouse ear)
❿orofacial granulomatosis
⓫myospherulosis
⓬Wegener granulomatosis
⓭fibrous histiocytoma/peripheral giant cell(ossifying) granuloma/peripheral odontogenic tumor
⓮rhabdomyosarcoma/Langerhans cell histiocytosis/giant-cell rich ostosarcoma
⓯aneurysmal bone cyst/juvenile ossifying fibroma/cementoblastoma/chondromyxoid fibroma/central odontogenic fibroma

➲xx multinucleated giant cell⇆diseases

❶Warthin-Finkeldey giant cell(tonsil)/epithelial syncytical giant cell(epithelium)⇆measles(rubeola)
❷Reed Sternberg cell⇆Hodgkin lymphoma
❸Langhans giant cell⇆tuberculosis/sarcoidosis
❹foreign body type giant cell⇆foreign body(granulomatous) gingivitis/sarcoidosis
❺multinucleated giant cell with intracytoplasmic asteroid body ⇆sarcoidosis

➲Tzanck cell(acantholytic cell)⇆diseases

❶Tzanck cell⇆pemphigus, Darier disease, warty dyskeratoma
❷Tzanck cell⇆HSV/VZV(varicella; chickenpox) infection

➲amyloid⇆diseases(Congo red➔apple-green birefringence with polarized light)

❶amyloid⇆amyloidosis
❷amyloid⇆multiple myeloma
❸amyloid⇆calcifying odontogenic tumor(Pindborg tumor)
❹amyloid(odontogenic ameloblast-associated protein(ODAM)) ⇆odontogenic fibroma
✶plasminogen deficiency⇆like amyloid(fibrin)
✶xanthelasma(cutaneous xanthoma)⇆like amyloid(lipid)

➲desquamative gingivitis⇆diseases

❶desquamative gingivitis⇆lichen planus(most frequent)
❷desquamative gingivitis⇆linear IgA disease
❸desquamative gingivitis⇆pemphigus vulgaris
❹desquamative gingivitis⇆mucous membrane pemphigoid
❺desquamative gingivitis⇆epidermolysis bullosa acquisita(EBA)
❻desquamative gingivitis⇆systemic lupus erythematosus(SLE)
❼desquamative gingivitis⇆chronic ulcerative stomatitis(CUS)
❽desquamative gingivitis⇆paraneoplastic pemphigus(less frequent)
❾desquamative gingivitis⇆coronavirus disease-2019

➲xx facies⇆diseases

❶leonine facies⇆①leprosy ②Paget disease of bone
❸chipmunk(花栗鼠) facies⇆β-thalassemia major
❹masklike face⇆systemic sclerosis(scleroderma)
❺moon face⇆hypercortisolism(Cushing syndrome)

➲strawberry xx⇆diseases

❶strawberry tongue⇆scarlet fever
❷strawberry gingivitis⇆Wegner granulomatous

➲xx bodies⇆periapical granuloma

❶Russell bodies(plasma cell product)
❷pyronine bodies(plasma cell product)

xx body⇆periapical(radicular) cyst

❶Rushton bodies(cyst lining)
❷hyaline body(cyst wall)

➲xx line⇆diseases

❶Beau line⇆hand-foot-&-mouth disease(nail loss or ridges)
❷Pastia line⇆scarlet fever(transverse red streak➔skin fold)
❸Burton line(gingiva)⇆lead intoxication
❹slate-blue line(gingiva)⇆silver intoxication
❺blue-gray line(gingiva)⇆bismuth intoxication

➲linear xx⇆diseases

❶linear alba⇆white line➔occlusal plane of buccal mucosa
❷linear scleroderma⇆progressive hemifacial atrophy
❸linear gingiva erythema⇆HIV infected periodontitis
❹linear band(facial attached gingiva➔mucogingival junction)⇆ minocycline discoloration

➲granular cell⇆diseases

❶granular cell⇆granular cell tumor
❷granular cell⇆congenital epulis
❸granular cell⇆granular cell ameloblastoma
❹granular cell⇆peripheral odontogenic fibroma(rare)
❺granular cell⇆granular cell odontogenic tumor
❻granular cell⇆rhabdomyoma➔spider web

➲ghost cell⇆diseases

❶ghost cell⇆Gorlin cyst(calcifying odontogenic cyst)
❷ghost cell⇆dentinogenic ghost cell tumor
❸ghost cell⇆ghost cell odontogenic carcinoma
❹ghost cell⇆complex odontoma(residual odontogenic epithelial rest)
✶ghost tooth⇆regional odontodysplasia

➲hyaline body⇆diseases

❶hyaline body(pulse granuloma/giant cell hyaline angiopathy) ⇆radicular cyst
❷hyaline body⇆lichen planus

➲triad features(signs)⇆diseases

❶Ascher syndrome
①double lip ②blepharochalasis ③nontoxic thyroid enlargement
❷congenital syphilis(Hutchinson triad)
①Hutchinson teeth ②ocular interstitial keratitis➔blindness
③8th nerve deafness
❸leprosy
①atrophy of ANS ②atrophy of anterior maxillary alveolar ridge
③endonasal inflammatory changes
❹congenital rubella syndrome(CRS)➔①deafness ② heart disease ③cataracts
❺lead intoxication➔①red, pain desquamating finger & toe
②neurologic symptom ③hypertension
❻Behcet syndrome(disease)➔①oral ②genital ③ocular lesions
❼Hand-Schüller-Christian triad➔①bone lesion ②exophthalmos ③diabetes insipidus
❽Reiter arthritis(syndrome)➔
①nongonococcal urethritis ②arthritis③conjunctivitis
❾pellagra(糙皮病)(↓niacin維生素B_3)
①dermatitis ②dementia ③diarrhea
❿hyperparathyroidism
①stone(renal calculi)
②bone(subperiosteal resorption of phalanges of index & middle finger; loss of lamina dura; ground glass; brown tumor; osteitis fibrosa cystica) ③abdominal groan(duodenal ulcer)

➲xx spots⇆diseases

❶Koplik spots⇆measles(rubeola)
❷ash-leaf spots(hypopigmentation)⇆tuberous sclerosis
❸Monospot(Paul-Bunnell test & rapid slide agglutination)⇆infectious mononucleosis
❹café-au-lait spots⇆①neurofibromatosis type I ②polyostotic FD[⊠McCune-Albright syndrome, Jaffe-Lichtenstein syndrome(variant of ⊠)]

➲ xx test⇆diseases

❶nucleic acid amplification test(NAAT)⇆gonorrhea
❷tuberculin/purified protein derivative(PPD) skin test⇆tuberculosis
❸lepromin skin test⇆leprosy
❹Paul-Bunnell test⇆infectious mononucleosis
❺neutrophil nitroblue tetrazolium reduction test⇆chronic granulomatous disease
❻patch test⇆allergy
❼PR3-ANCA+ELISA test⇆Wegener granulomatosis(granulomatosis with polyangitis)
❽Schirmer test⇆tear secretion
❾autoantibodies to Ro(SS-A) and/or La(SS-B) antigens test⇆Sjogren syndrome
❿Schilling test(vitamin B12 deficiency)⇆pernicious anemia
⓫partial thromboplastin time(PPT) test⇆hemophilia
⓬lupus band test⇆lupus erythematosus; rheumatoid arthritis; Sjögren syndrome; systemic sclerosis
⓭Minor starch-iodine test⇆Frey syndrome
⓮Kveim test(not used now)⇆sarcoidosis(inject of sterilized suspension of human sarcoid tissue➔difficulty to acquire, accuracy? prion contaminate)

➲EBV⇆diseases

❶EBV⇆infectious mononucleosis
❷EBV⇆NPC
❸EBV⇆Burkitt lymphoma/extranodal NK/T-cell lymphoma
❹EBV⇆hairy leukoplakia

Cushing syndrome(hypercortisolism)⇆features

❶moon face➔fat deposition ❷ buffalo hump ❸osteoporosis➔pathologic fracture ❹premature tooth eruption➔partial loss of lamina dura

➲xx cell⇆diseases

❶owl eye cell⇆cytomegalovirus(CMV)
❷Sézary cell⇆mycosis fungoides(cutaneous T-cell lymphoma)
★Sézary syndrome⇆T-cell leukemia
❸popcorn cell⇆Hodgkin lymphoma(nodular lymphocyte-predominant)
❹balloon cell⇆oral hairy leukoplakia
❺mast cell⇆angioedema

➲goblet cell⇆diseases

❶goblet cell⇆nasolabial cyst/nasopalatine duct cyst
❷goblet cell⇆glandular odontogenic cyst
❸goblet cell⇆inverted papilloma

➲metallic taste⇆diseases

❶metallic taste⇆mercury intoxication
❷metallic taste⇆gold intoxication

➲xx cheilitis⇆S/S

❶exfoliative cheilitis⇆↑↑production & desquamation of keratin(allergy, psychiatric & abnormal thyroid function) of lips
❷allergic contact cheilitis(stomatitis)⇆tooth paste, aluminum chloride
❸factitious cheilitis⇆chronic injury(lip licking, biting, picking, sucking)
❹angular cheilitis⇆①bacterial/candidal infection of lips ②with plasma cell gingivitis
[Plummer-Vinson syndrome➔(1)Fe deficiency anemia (2)oral/esophageal SCC)] (3)koilonchia(凹甲) (4)angular cheilitis (5)dysphagia (6)esophageal web (7)glossitis[beef tongue➔dorsal papillary atrophy]
❺actinic cheilitis(cheliosis)⇆UV light➔premalignancy➔lower lip vermilion
❻cheilitis granulomatosa of lips alone(of Miescher)⇆orofacial granulomatosis
(Melkersson-Rosenthal syndrome➔①cheilitis granulomatosa ②facial paralysis ③fissured tongue)
❼cheilitis glandularis⇆inflammation of minor salivary gland➔lower lip vermilion

➲diseases⇆intrinsic discoloration of teeth

❶aging⇆yellow-brown; less translucency
❷death of pulp⇆gray-black; less translucency
❸fluorosis⇆white; yellow-brown; brown; mottled
❹tetracycline⇆yellow-brown; yellow fluorescence
❺internal resorption⇆pink tooth of mummery
❻calcific metamorphosis⇆yellow
❼dentinogenesis imperfecta⇆blue-gray; translucent
❽amelogenesis imperfecta⇆yellow-brown
❾congenital erythropoietic porphyria[(紅血球合成性紫質症)(Günther disease)]⇆yellow; brown- red; red fluorescence
❿erythroblastosis fetalis[Rh(-)母親先後有兩個Rh(+)胎兒➔第二胎Rh(+)胎兒➔溶血]⇆yellow; green
⓫hyperbilirubinemia(高膽紅素血症)⇆yellow-green(chlorodontia)
⓬ochronosis(黃褐斑病)(alkaptonuria)⇆blue(Parkinson disease)

➲multiple CGCG⇆diseases

❶multiple CGCG⇆cherubism
❷multiple CGCG⇆Ramon syndrome
❸multiple CGCG⇆Jaffe-Campanacci syndrome
❹multiple CGCG⇆RASopathies
[①Noonan syndrome ②neurofibromatosis type 1]

➲CGCG⇆in(with) other diseases

❶CGCG⇆brown tumor
❷CGCG⇆hyperparathyroidism
❸CGCG⇆in aneurysmal bone cyst(ABC)
❹CGCG⇆with central odontogenic fibroma/cemento-ossifying fibroma

➲ABC⇆with other diseases

❶ABC⇆cemento-ossifying fibroma(ML-RL)
❷ABC⇆fibrous dysplasia
❸ABC⇆CGCG

➲bone disease⇆maxilla(most)

❶Paget disease of bone⇆maxilla(most)
❷fibrous dysplasia⇆maxilla(most)
❸juvenile aggressive ossifying fibroma⇆maxilla(most)
❹adenomatoid odontogenic tumor⇆maxilla(most)

➲bone disease⇆↑serum alkaline phosphatase

❶Paget disease of bone⇆↑serum alkaline phosphatase
❷cherubism(active)⇆↑serum alkaline phosphatase

➲urine VMA⇆dsiease

❶urine VMA⇆neuroblastoma
❷urine VMA⇆melanotic neuroectodermal tumor of infancy
❸urine VMA⇆MEN2B

➲BBC(basal cell carcinoma)⇆genodermatoses

❶nevoid basal cell carcinoma syndrome
❷xeroderma pigmentosum ❸Cowden syndrome
❹epidermolysis(Dowling-Meara subtype)
❺others(albinism, Rombo syndrome, Werner syndrome, Rothmund-Thomson syndrome, Muir-Torre syndrome, Brooke-Spiegler syndrome)

➲ABCDE of melanoma⇆features

A➔Asymmetry⇆uncontrolled growth
B➔Border(irregularity)⇆notching
C➔Color(variegation)⇆brown-black, white, red, blue(melanin amount & depth)
D➔Diameter⇆>6mm(diameter of pencil eraser)
E➔Evolving⇆(size, shape, color, surface, symptom)➔change over time

➲sarcoidosis(acute)⇆syndromes

❶Lofgren syndrome⇆①erythema nodosum ②bilateral hilar lymphadenopathy ③arthralgia
❷Heerfordt syndrome(uveoparotid fever)⇆①parotid enlargement ②anterior uveitis ③facial paralysis ④fever

➲anemia⇆classification(RBC size; Hb content)

❶pernicious anemia⇆macrocytic normochromic
❷iron deficiency anemia⇆microcytic hypochromic
❸thalassemia(Mediterranean anemia)⇆microcytic hypochromic
❹aplastic anemia⇆normocytic normochromic
❺sickle cell anemia⇆normocytic normochromic

➲diseases⇆with component of malignancy

❶acanthosis nigricans⇆GI adenocarcinoma
❷Gardner syndrome⇆colorectal carcinoma
❸Peutz-Jeghers syndrome⇆GI adenocarcinoma(other tumors➔pancreas; breast; ovary; male & female genital tract)
❹Gorlin syndrome⇆BCC
❺Plummer-Vinson syndrome⇆oral/esophageal SCC
❻Cowden syndrome⇆thyroid adenocarcinoma; BCC; breast cancer; female genitourinary tract cancer

➲congenital(hereditary)⇆macroglossia

❶vascular malformations(hemangioma, lymphangioma)⇆macroglossia
❷hemihyperplasia⇆macroglossia
❸cretinism((hypothyroidism; myxemema)⇆macroglossia(↑glycosaminoglycans)
❹Beckwith-Wiedemann syndrome⇆macroglossia
❺MEN type 2B⇆macroglossia
❻Duchenne muscular dystrophy⇆macroglossia
❼mucopolysaccharidoses⇆macroglossia
❽neurofibromatosis type I⇆macroglossia
❾Down syndrome⇆macroglossia

➲acquired⇆macroglossia

❶edentulous⇆macroglossia
❷amyloidosis⇆macroglossia
❸myxedema⇆macroglossia
❹acromegaly⇆macroglossia
❺angioedema⇆macroglossia
❻amyotrophic lateral sclerosis⇆macroglossia
❼carcinoma & other tumor⇆macroglossia
❽myasthenia gravis⇆macroglossia

➲xx nodules(solid raised lesion >5mm)⇆diseases

❶Bohn's nodules⇆palatal cysts of new born(Epstein's pearl)
❷Lisch nodules⇆neurofibromatosis type I(brown-pigmented spots➔iris)
❸amyloid nodules⇆limited form of amyloidosis(not associate systemic alterations)
❹rheumatoid nodules⇆rheumatoid arthritis(beneath skin of affected joint➔well-demarcated area of amorphous eosinophilic necrosis surround by thick layer of monocuclear cells)

➲bone diseases⇆genetic changes(Chapter 14 Bone pathology)

❶osteogenesis imperfecta⇆COL1A1, A2 mutation
❷CGCT⇆①TRPV4 ②KRAS ③FGFR1 mutation
❸cemento-ossifying fibroma⇆HRPT2 mutation
❹juvenile ossifying fibroma⇆①MDM2 ②RASAL1 mutation
❺fibrous dysplasia⇆GNAS mutation
❻cherubism⇆SH3BP2 mutation
❼cleidocranial dysplasia⇆RUNX2(CBFA1) mutation
❽Ewing sarcoma⇆EWS::FLI1 fusion protein
❾osteosarcoma⇆①P53 ②RB1 ③MDM2 ④CDKN2A ⑤ATRX ⑥DLG2
❿chondrosarcoma⇆①MDM2 amplification ②IDH1,2 mutation
⓫ABC⇆①USP6 translocation ②BMP dysregulation ③NF-κB-mediated MMP induction
✶Ewing-like sarcoma⇆①EWSR1-non-ETS fusion ②BCOR genetic change

✠chondroma⇆❶IDH1,2 mutation ❷COL2A1 &YEATS2 mutation ❸CDKN2A amplification➔分辨chondrosarcoma/chondroma
✠chondromyxoid fibroma⇆↑GRM1(glutamate receptor metabotropic-1)
✠synovial chondromatosis⇆FN1(fibronectin 1) &/or ACVRA2(activin receptor 2A) gene rearrangement

	histopathological diagnoses	IHC or other markers	
1	solitary fibrous tumor	stat6, bcl-2, CD34	
2	alveolar soft part sarcoma	TFE3	
3	granular cell tumor	S100, CD68, neuron-specific enolase ✠granular cell odontogenic tumor➔S100(-)	
4	Burkitt's lymphoma	Ki-67(100%)	
5	low grade osteosarcoma	MDM2	
6	Langerhans cell histiocytosis	CD1a, S100, BRAF, CD207	
7	Merkel cell carcinoma	CK20, chromogranin A	
8	metastatic lung carcinoma	TTF1	
9	melanoma	HMB45, S100, BRAF, CDKN2A, CDK4(high risk)	
10	adenoid cystic carcinoma	CD117, CD43(strong +)	myoepitheial cell➔p63 & p40(+)
11	polymorphous adenocarcinoma	CD117, CD43(weaker +)	myoepitheial cell➔p63(+); p40(-)
12	pleomorphic adenoma	S100	
13	basal cell adenoma	nuclear β-catenin distinguish from adenoid cystic carcinoma	
14	mucoepidermoid carcinoma	mucin(+)	
15	acinic cell carcinoma	DOG1, NR4A3	
22	mammary analogue secretory carcinoma	S-100, vimentin, mammaglobin	
16	clear cell odontogenic carcinoma	mucin(-), amyloid(-)	
17	Pindborg tumor	amyloid(+)	
18	T-cell lymphoma	CD3	
19	neurofibroma, schwannoma(neurilemmoma)	S100	
20	Kaposi sarcoma	HHV-8	
21	odontogenic keratocyst	↑Ki-67, ↑PCNA	
22	squamous cell carcinoma	CK	
23	oropharyngeal SCC	p16(with HPV)	
24	organ of Chieviz	CK19	
25	salivary gland origin	CK7	
26	epithelium of odontogenic epithelial origin	CK19	

	histopathological diagnosis	genes
1	Langerhans cell histiocytosis	BRAF
2	Burkitt lymphoma	c-MYC
3	ameloblastoma	BRAF
4	ameloblastic fibrosarcoma	BRAF, NRAS(less common)
5	melanoma	BRAF
6	acquired melanocytic nevus	BRAF
7	blue nevus	BRAF, GNAQ
8	ductal papilloma(sialadenoma papilliferrum)	BRAF
9	adenoid cystic carcinoma	MYB➔MYB:NFIB fusion
10	clear cell carcinoma	EWAR1-ATF1
11	clear cell odontogenic carcinoma	EWAR1-ATF1
12	mammary analogue secretory carcinoma	ETV6-NTRK3
13	mucoepidermoid carcinoma	CRTC1-MAML2
14	glandular odontogenic cyst	MAML2(-)
15	pleomorphic adenoma	PLAG1
16	basal cell adenoma	CTNNB1 mutation
17	Cowden syndrome	PTEN
18	Gardner syndrome	APC(tumor suppresser gene)
19	Peutz-Jeghers syndrome	STK11(LKB1)
20	Gorlin syndrome	PTCH1. SUFU(PTCH2, much smaller %), SMO(smoothened)
21	basal cell carcinoma(sporadic)	PTCH1. SUFU(PTCH2, much smaller %), SMO(smoothened)
22	odontogenic keratocyst(sporadic)	PTCH1
23	Pindborg tumor	PTCH1
24	Sturge-Weber syndrome➔tramline(X-ray)	GNAQ, PI3KCA
25	vascular malformation	GNAQ, PI3KCA
26	lymphangioma	PI3KCA
27	seborrheic keratosis	PI3KCA, FGFR3
28	nodular fasciitis	USP6
29	simple bone cyst	NFATC2
30	hypophosphatasia	alkaline phosphatase
31	vitamin D-resistant rickets	PHEX(phosphate-regulating gene with endopeptidase activity on X-chromosome)
32	Gaucher disease(lipid reticuloendothelioses)	glucocerebrosidase deficiency
33	Niemann-Pick disease(lipid reticuloendothelioses)	NPC-1,2(type C) ⊠type A,B➔acid sphingomyelinase deficiency
34	Tay-Sachs disease(lipid reticuloendothelioses)	β-hexosaminidase A deficiency
35	lipoid proteinosis	ECM1 mutation

	histopathological diagnosis	HLA related
1	rheumatoid arthritis	HLA-DRB1, PADI4
2	reactive arthritis(Reiter syndrome)	HLA-B27
3	Langerhans cell histiocytosis	HLA-DR
4	Heck disease	HLA-DR4
5	giant cell(temporal) arteritis	HLA-DRB1
6	Sjogren syndrome	certain HLA, interferon response, B-lymphocyte function

➲disease⇆bacteria

❶syphilis(Lues)⇆spirochete treponema pallidum

❷actinomycosis(放線菌病)⇆gram(+) anaerobic bacteria(filamentous, branching)

❸impetigo(膿庖病)⇆staphylococcus(葡萄球菌)(group A β-hemolytic)

❹scarlet fever(猩紅熱)⇆group A streptococci(A 型鏈球菌)

❺tuberculosis⇆mycobacterium tuberculosis

❻scrofula(頸部淋巴腺結核)⇆nontuberculous mycobacteria

❼leprosy(Hansen disease)⇆mycobacterium leprae

❽cat-scratch disease⇆barotonella henselae

virus	disease
herpes simplex virus (HSV-1/HHV-1; HSV-2/HHV-2)	❶acute herpetic gingivostomatitis(primary herpes) ❷recurrent(secondary) herpes simplex infections➔herpes labialis ❸recurrent intraoral herpes(recurrent herpetic stomatitis) ❹herpetic whitlow(herpetic paronychia甲周炎) ❺herpes gladiatorum(scrumpox)➔wrestler & rugby player ❻herpes barbae ❼eczema herpeticum(Kaposi varicelliform eruption)
varicella-zoster virus(VZV/HHV-3)	❶varicella(chickenpox)➔1^0 infection ❷herpes zoster(shingles)➔recurrent infection(1/3 person of lifetime)
Epstein-Barr virus(EBV/HHV-4)	❶infectious mononucleosis ❷NPC ❸Burkitt lymphoma/extranodal NK/T-cell lymphoma ❹hairy leukoplakia
cytomegalovirus(CMV/HHV-5)	non-specific(immunosuppressive)

enteroviruses(echovirus, coxsackieviruses, polioviruses)⇆❶herpangina ❷hand-foot-and-mouth disease ❸acute lymphonodular pharyngitis

morbillivirus⇆measles(rubeola) | rubulavirus⇆mumps(epidemic parotitis) | rubivirus⇆rubella(German measles)

human immunodeficiency virus(HIV)⇆AIDS | covid-19⇆coronavirus disease 2019

comparison of clinic features➔❶minor ❷major ❸herpetiform aphthous ulcer			
features	**minor**	**major**	**herpetiform**
recurrence	fewest	up to 20-yr or more	most frequent
duration	shortest(7-14-day)	longest(2-6 weeks)	7-10-day
size	3-10mm/episode	1-3cm(larger)	1-3mm(small)➔coalesced➔larger
number	1-5	1-10	greatest no.(as many as 100)
pain	+	++	+
location	buccal & labial(most)	labial, soft palate, tonsillar fauces	nonkeratinized movable mucosa(most); any mucosa
others	without scar	❶scar ❷restricted mouth opening	like 1^0 HSV infection

➲salivary gland tumor➔micro➔papillomatous

❶papillary cystadenoma lymphomatosum (Warthin tumor)(most)
❷sialadenoma papilliferrum(rare)
❸intraductal papilloma(rare)
❹inverted ductal papilloma(rare)

➲hematologic diseases⇆lab value

❶hemophilia⇆
①25% normal level(normal function)
②<5% normal level(minor trauma➔bruise)
※<1% normal level➔clotting factor injection
❷neutropenia⇆neutrophil no.≤1.5×10^9/l
※0.5×10^9/l➔肺部infection
❸thrombocytopenia⇆platelet no.≤150,000/mm^3
※<50,000➔minor trauma
※<10,000➔severe bleeding

➲synopsis for features of dermatologic diseases

➲X-linked recessive➔male predominant
❶ectodermal dysplasia(ED)
❷dyskeratosis congenita(先天性角化不全)

➲X-linked dominant➔female predominant
❶incontinentia pigmenti(色素失調症)➔male lethal(if survive➔Klinefelter syndrome)

➲eyebrow眉毛(lash睫毛)
❶ED➔fine sparse hair
❷hereditary mucoepithelial dysplasia➔coarse sparse hair

➲SCC & epithelial dysplasia/other malignancy risk
❶dyskeratosis congenita(先天性角化不全)
①leukoplakia (epithelial dysplasia)➔SCC
②aplastic anemia
❷xeroderma pigmentosum(著色性乾皮症)
①SCC ②BCC ③melanoma
❸GVHD➔SCC & epithelial dysplasia
❹hereditary hemorrhagic telangiectasia(Osler-Weber-Rendu syndrome)
①colorectal carcinoma➔MADH4➔juvenile polyposis
②iron-deficiency anemia

➲micro➔HPK+acanthosis
❶white sponge nevus
❷hereditary benign intraepithelial dyskeratosis
❸incontinentia pigmenti(色素失調症)➔verrucous stage
❹pachyonychia congenita(先天性厚甲症)

➲micro➔keratin plug+suprabasilar cleft(acantholysis➔Tzanck cell)+basilar hyperplasia
❶Darier disease(dyskeratosis follicularis)
❷warty dyskeratoma(疣状角化不良)

➲micro➔HPK+atrophy
❶dyskeratosis congenita(先天性角化不全)

➲micro➔intraepithelial cleft(acantholysis)
❶incontinentia pigmenti(色素失調症)(vesicular stage)
❷(paraneoplastic) pemphigus
❸epidermolysis bullosa(simplex form)
❹erythema multiforme

➲keratin mutation
❶white spongy nevus➔K4,13
❷achyonychia congenita(先天性厚甲症)➔K6,16,17
❸epidermolysis bullosa(simplex form)➔K5,14

➲micro➔subepithelial cleft
❶pemphigoid
❷paraneoplastic pemphigus
❸epidermolysis bullosa(junctional, dystrophic, Kindler forms)
❹epidermolysis bullosa acquisita
❺erythema multiforme

chronic vesicuoulcerative diseases	av. age	sex	clinic	micro	direct IF	indirect IF
❶pemphigus vulgaris (desquamative gingivitis)	4th-6th decade	equal	vesicle, erosion & ulcer on any oral mucosa/skin	intraepithelial cleft	(+)intercellular	(+)
❷paraneoplastic pemphigus	6th-7th decade	equal	vesicle, erosion, & ulcer on any oral mucosa/skin	subepithelial & intraepithelial cleft	(+)intercellular & BMZ	(+)rat bladder
❸mucous membrane pemphigoid (desquamative gingivitis)	6th-7th decade	female	1^0 mucosa lesions	subepithelial cleft	(+)BMZ	(-)
❹bullous pemphigoid	7th- 8th decade	equal	1^0 skin lesions	subepithelial cleft	(+)BMZ	(+)
❺erythema multiforme	3rd-4th decade	male	skin & mucosa involve; target lesion(skin)	sub(intra)epithelial cleft & perivascular inflammation	nondiagnostic	(-)
❻lichen planus(erosive type➔desquamative gingivitis)	5th-6th decade	female	oral &/or skin may/may not erosive	hyperkeratosis, saw-tooth rete ridge, lymphocytic band, basal liquefaction	(+)fibrinogen➔BMZ (not specific for lichen planus)	(-)

site	lesion	major HPV types
oral/head & neck mucosa	oral squamous papilloma	6, 11
	recurrent respiratory papillomatosis	6, 11
	exophytic sinonasal papilloma	6, 11
	inverted sinonasal papilloma	6, 11, 16, 18
	multifocal epithelial hyperplasia	13, 32
	oropharyngeal SCC	16
	conjunctival papilloma	6, 11
Skin	verruca vulgaris	2

	verruca plana	3, 10
	palmoplantar wart	1, 4
	Butcher's wart	2, 7
Anogenital region	condyloma acuminatum	6, 11
	intraepithelial neoplasia	6, 11, 16, 18, 31, 33
	cervical SCC	16, 18

synopsis➔soft tissue mass➔midline neck masses	
thyroid gland enlargement	goiter, thyroid tumor
thyroglossal duct cyst	may move up & down with tongue motion
dermoid cyst	soft & fluctuant
plunging ranula	soft & compressible
synopsis➔soft tissue mass➔lateral neck	
reactive lymphadenopathy	2^0 to oral & maxillofacial infection; often tender to palpation
epidermoid cyst	soft & movable
lipoma	soft mass
metastatic carcinoma	from oral & pharyngeal carcinomas; usu. indurated & painless; may fixed
lymphoma	may uni(bil)lateral; usu. painless; Hodgkin & non-Hodgkin types
infectious mononucleosis	fatigue; sore throat; tender lymph node
salivary gland tumors	arise from submandibular gland/tail of parotid gland
submandibular sialadenitis	2^0 to sialolithiasis
branchial cleft cyst	soft & fluctuant; most young adult
granulomatous diseases	tuberculosis, sarcoidosis
cat-scratch disease	history of exposure to cat
cystic hygroma	infant; soft & fluctuant
plunging ranula	soft & compressible
other mesenchymal tumors	neurofibroma, carotid body tumor

synopsis➔mucosal & soft tissue pathology➔color changes	
lesion/condition	**characteristics**
white lesions➔can be scraped off	
white-coated tongue	may be scraped off slightly, with difficulty
pseudomembranous candidiasis	milk curd/cottage cheese appearance; may leave red base when rubbed off
morsicatio	surface may appear to be peeling off
toothpaste or mouthwash reaction	filmy whiteness; leaves normal appearing mucosa when rubbed off
thermal burn	e.g. pizza burn
sloughing traumatic lesion	e.g. cotton roll "burn"
chemical burn	e.g. aspirin burn secondary to direct application for toothache
secondary syphilis	mucous patch; may be only partially scraped off
diphtheria	gray-white pseudomembrane of oropharynx
white lesions➔cannot be scraped off	
linea alba	buccal mucosa along occlusal plane
leukoedema	in black; bilateral milky white on buccal mucosa; disappears when stretched
leukoplakia	may show benign hyperkeratosis, epithelial dysplasia, invasive carcinoma
tobacco pouch keratosis	usu. mandibular vestibule; associated with use of snuff/chewing tobacco
white-coated tongue	diffuse involvement of dorsal tongue
lichen planus	Wickham's striae; typical bilateral on buccal mucosa
morsicatio	most on ant. buccal mucosa, labial mucosa, lateral border of tongue; ragged surface
actinic cheilosis	pale, gray-white, scaly lower lip; older men with chronic sun exposure; precancerous
nicotine stomatitis	usu. associated with pipe smoking; occurs on hard palate
hairy leukoplakia	usu. lateral border of tongue; rough surface with vertical fissures; usu. with HIV
hyperplastic candidiasis	most affects anterior buccal mucosa
lupus erythematosus	most on buccal mucosa; mimic lichen planus/leukoplakia; skin lesions usu. present
skin graft	history of previous surgery
submucous fibrosis	more in South Asia; associate betel quid chewing
white sponge nevus	hereditary; onset in childhood; generalized lesions, esp., buccal mucosa
hereditary benign intraepithelial dyskeratosis	hereditary; onset in childhood; generalized, esp. buccal mucosa; ocular possible
pachyonychia congenita	hereditary; childhood; most on dorsal tongue & trauma area; nail, palmar & plantar
dyskeratosis congenita	hereditary; onset in childhood; dystrophic nail changes
uremic stomatitis	renal failure
white & red lesions	
erythema migrans	geographic tongue; continual changing pattern; rare involve other oral mucosal sites
candidiasis	white component may be rubbed off
lichen planus	atrophic/erosive forms; Wickham's striae; typical bilateral on buccal mucosa
burns	e.g. pizza burn, aspirin burn, other chemical burns; white component be rubbed off
actinic cheilosis	pale, gray-white & red on lower lip; usu. in older men with chronic sun exposure
erythroleukoplakia	usu. shows epithelial dysplasia or carcinoma
cinnamon reaction	related to cinnamon-flavored gum; typically on buccal mucosa and lateral tongue
nicotine stomatitis	usu. associated with pipe smoking; on hard palate
lupus erythematosus	most on buccal mucosa; mimic lichen planus/leukoplakia; skin lesions usu. present
scarlet fever	secondary to β-hemolytic streptococcal infection; strawberry/raspberry tongue
verruciform xanthoma	most on gingiva & hard palate; surface may be papillary

red lesions	
pharyngitis	e.g. strep throat, viral pharyngitis
traumatic erythema	caused by local irritation
denture stomatitis	denture-bearing palatal mucosa
erythematous candidiasis	e.g. central papillary atrophy(median rhomboid glossitis)
erythema migrans	geographic tongue; continual changing pattern; rarely involves other mucosal sites
angular cheilitis	erythema & cracking at labial commissures
thermal burn	e.g. caused by hot liquid
erythroplakia	usu. shows epithelial dysplasia/carcinoma
lichenoid and granulomatous stomatitis	most on upper labial mucosa
anemia	atrophic, red tongue; due to pernicious(Fe-deficiency) anemia, hypovitaminosis B
hemangioma	develops in younger patients; may blanch; may show bluish hue
lupus erythematosus	usu. with associated skin lesions
scarlet fever	secondary to β-hemolytic streptococcal infection; strawberry/raspberry tongue
plasma cell gingivitis	allergic reaction usu. related to flavoring agents
radiation mucositis	patient currently undergoing radiotherapy
petechial, ecchymotic & telangiectatic lesions	
nonspecific trauma	history of injury to lesional site
upper respiratory infections	soft palate petechiae
infectious mononucleosis	soft palate petechiae; tonsillitis &/or pharyngitis may be present
idiopathic thrombocytopenic purpura	areas of trauma; gingival bleeding possibly present
trauma from fellatio	posterior palatal petechiae/ecchymosis
hemophilia	hereditary; childhood onset; gingival bleeding may present
leukemia	caused by 2^0 thrombocytopenia; gingival bleeding may present
hereditary hemorrhagic telangiectasia	multiple, pinhead-sized telangiectasias; possible history of nosebleeds/GI bleeding
CREST syndrome	multiple, pinhead-sized telangiectasias; C alcinosis cutis, R aynaud's phenomenon, E sophageal motility defect, S clerodactyly, T elangiectasias
blue &/or purple lesions	
varicosities	esp., >45s; most on ventral tongue & lips
submucosal hemorrhage	
amalgam tattoo	most on gingiva; blue-gray; RO amalgam particle(discovered on x-ray sometimes)
mucocele	esp. on lower labial mucosa; pale blue; cyclic swelling and rupturing often exhibited
eruption cyst	overly an erupting tooth
salivary duct cyst	usu. pale blue
hemangioma	usu. red-purple; may blanch under pressure; onset in younger patients
ranula	pale blue, fluctuant swelling of lateral mouth floor
Kaposi sarcoma	esp., in AIDS; usu. purple; most on palate & maxillary gingiva
nasopalatine duct cyst	midline of anterior palate
salivary gland tumors	esp., MEC & pleomorphic adenoma; usu. pale blue; most on posterior lateral palate
gingival cyst of the adult	most in mandibular bicuspid-cuspid region
blue nevus	most on hard palate
melanoma	most on hard palate & maxillary gingiva; may be mixture of deep blue, brown, black
brown, gray, &/or black lesions	
racial pigmentation	most on attached gingiva in darker complexioned patient
amalgam tattoo	most on gingiva; usu. slate-gray to black; opaque amalgam particle(may be on x-ray)
black/brown hairy tongue	discoloration & elongation of filiform papillae
melanotic macule	brown; most on lower lip
smoker's melanosis	most on anterior facial gingiva
non-amalgam tattoos	e.g. graphite from pencil
melanocytic nevus	most on hard palate; be flat/raised
melanoma	most on hard palate & maxillary gingiva; may be mixture of deep blue, brown, black
oral melanoacanthoma	rapid enlarging pigmented lesion; usu. in black
drug ingestion	e.g. chloroquine, chlorpromazine, minocycline; esp., on hard palate
Peutz-Jeghers syndrome	freckle-like lesion of vermilion & perioral skin; intestinal polyps; hereditary
Addison disease	chronic adrenal insufficiency; associated with bronze skin
neurofibromatosis type 1	Café au lait pigmentation; cutaneous neurofibromas
McCune-Albright syndrome	Café au lait pigmentation; polyostotic fibrous dysplasia; endocrine disorders
heavy metal poisoning	typical along marginal gingiva (lead, bismuth, silver)
melanotic neuroectodermal tumor of infancy	anterior maxilla; destroys underlying bone
H. yellow lesions	
Fordyce granules	sebaceous gland; multiple submucosal papules on buccal mucosa/upper lip vermilion
superficial abscess	e.g. parulis from nonvital tooth
accessory lymphoid aggregate	most in oropharynx & mouth floor; may be orange hue
lymphoepithelial cyst	most on lingual & palatine tonsils, mouth floor; may be yellow-white
lipoma	most on buccal mucosa; soft to palpation
jaundice	generalized discoloration, esp., involve soft palate & mouth floor; sclera usu. affected
verruciform xanthoma	most on gingiva & hard palate; surface may be rough/papillary
pyostomatitis vegetans	"snail-track" pustule; associated with inflammatory bowel disease

synopsis➔radiographic pathology	
lesion/condition	**characteristics**

mixed RL/RO lesion➔poorly demarcated borders	
medication-related osteonecrosis of jaw(MRONJ)	**exposed necrotic bone; most often associated with bisphosphonate drug**
osteomyelitis	**with sequestrum formation/with sclerosing type; often painful**
metastatic carcinoma	**esp., prostate & breast carcinomas; may be painful**
osteosarcoma/chondrosarcoma	**may be painful**
mixed RL/RO lesion➔multifocal/generalized	
florid cemento-osseous dysplasia	**intermediate-stage lesion; esp. middle-aged black women; usu. mandible**
medication-related osteonecrosis of jaw(MRONJ)	**exposed necrotic bone; most associated with bisphosphonate drug**
Paget disease of bone	**in older patients; more common in maxilla**
ground glass RO	
fibrous dysplasia	**onset usu. younger patient**
hyperparathyroidism	**may cause loss of lamina dura**
central xanthoma of jaws	**reactive process/benign; lipid-laden macrophage[xanthoma(foamy)cell]**
cotton wool RO	
cemento-osseous dysplasia	**esp., middle-aged black women; usu. mandible**
Paget disease of bone	**in older patients; more common in maxilla**
Gardner syndrome	**multiple osteomas; epidermoid cysts; GI polyp➔malignant change; hereditary**
gigantiform cementoma	**hereditary; facial enlargement may be present**
sunburst (ray) RO	
osteosarcoma	**often painful; usu. young adult**
intraosseous hemangioma(教課書 5th p. 549)	**esp. younger patient**
odontogenic myxosma	**large lesion may be**
onion-skin RO	
proliferative periostitis	**younger patient; often associate nonvital tooth; best seen with occlusal radiograph**
Ewing sarcoma	**young children**
punch-out RL	
multiple myeloma	**painful; in older adults; "punch-out" lesion**
Langerhans cell histiocytosis	**histiocytosis X; usu. children/young adults**
central xanthoma of jaws	**reactive process/benign; lipid-laden macrophage[xanthoma(foamy)cell]**

113-2 midterm exam

1. Which of the following statement about radicular cyst is *false*? (Chapter 3)
(A) it is associated with a tooth that is nonvital on pulp testing
~~(B) Russell bodies can be detected in cystic wall microscopically~~(Russel bodies➔periapical granuloma)
(C) Rushton bodies can be detected in cystic lining microscopically
(D) hyaline bodies can be detected in cystic wall microscopically

2. Which of the following statement about pulpal calcification is *false*? (Chapter 3)
(A) prominent pulp stone can be found in patients with Ehlers-Danlos syndrome
(B) concentric pulp stone can be detected in ~~root canal~~ pulp chamber
(C) diffuse linear calcification can be detected in pulp chamber(also in root canal)
(D) pulp stone < 200 μm in diameter cannot be detected by radiographic examination

3. Which of the following statement about reversible and irreversible pulpitis is *false*? (Chapter 3)
(A) pain never cross midline for early irreversible pulpitis
(B) higher EPT current is usually noted in later irreversible pulpitis
(C) ~~dull~~ acute pain and resolves in a few seconds being noted in reversible pulpitis
(D) crack tooth upon biting is noted in reversible pulpitis

4. Which of the following features of patients with Papillon-Lefevre syndrome are *true*: (Chapter 4)
① autosomal recessive pattern ② autosomal dominant pattern ③ severe periodontal disease ④ palmoplantar hyperkeratosis
(A) only ①③④
(B) only ②③④
(C) only ③④
(D) only ①④

5. Desquamative gingivitis *cannot* be noted in: (Chapter 4)
(A) mucous membrane pemphigoid
(B) erosive lichen planus
(C) coronavirus disease-2019
(D) erythroplakia

6. Which statement about syphilis is *false*? (Chapter 5)
(A) the primary lesion of syphilis is called a chancre
(B) the secondary lesion of syphilis occurs at the (site of inoculation with the organism➔primary lesion)
(C) the tertiary lesion of syphilis is called a gumma
(D) syphilis is caused by the spirochete Treponema pallidum

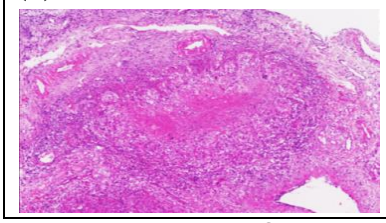
7. Which of the following matching of the clinical sign with the corresponding disease is *false*? (Chapter 5)
(A) Beaue line with hand-foot-mouth disease
(B) Pastia lines with scarlet fever
(C) linear gingiva erythema with AIDS
(D) Warthin-Finkeldey giant cell in ~~Rubella~~ measles(rubeola)

8. "Strawberry tongue" is associated with which condition? (Chapter 5)

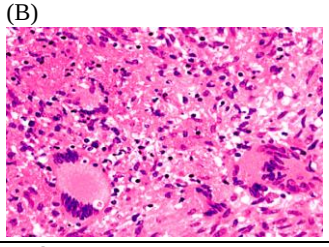
(A) herpangina
(B) scarlet fever
(C) rheumatic fever
(D) tuberculosis

9. A patient with painful ulceration over tongue border received chest X-ray showing cloudy appearance of lung and biopsy with histopathological features depicted in the Figures A-C. (Chapter 5)
What is the most likely histopathological diagnosis? What kind of special stain is used for Figure (C)?

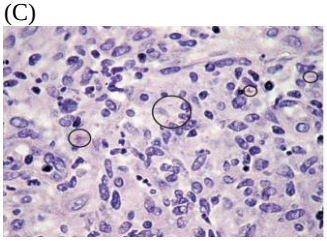
(A)



(B)



(C)



①hematoxylin eosin stain ②acid-fast stain ③oral squamous cell carcinoma ④ oral tuberculosis
(A) only ①④
(B) only ①③
(C) only ②③
(D) only ②④

10. Which of the following clinical manifestation of the disease with the matched virus is *true*? (Chapter 7)
(A) infectious mononucleosis with Epstein-Barr virus
(B) hand-foot-and-mouth disease with ~~cytomegalovirus~~ enteroviruses(echovirus, coxsackieviruses, polioviruses)
(C) Koplik's spots with ~~Rubivirus~~ Morbillivirus(measles, rubeola)
(D) Forchheimer sign with ~~Morbillivirus~~ Rubivirus(German measles, rubella)

11. An adult is affected by painful vesicles over skin of external auditory canal with involvement of ipsilateral facial & auditory nerves showing facial paralysis & hearing deficits, vertigo as well as loss of taste. What is the most possible clinical diagnosis? (Chapter 7)
(A) Sjogren syndrome
(B) Behçet's syndrome
(C) auriculotemporal syndrome
(D) Ramsay Hunt syndrome

12. Which of the following statement is *true*? (Chapter 7)
(A) vesicles of herpes zoster along the nerve not being cross midline
(B) Tzanck cell is noted in ~~lichen planus~~ HSV/VZV(varicella; chickenpox); pemphigus
(C) rubella is also regarded as 3-day measles(Rubeola➔9-day measles)
(D) ~~submandibular gland~~ parotid gland is mostly affected by Rubulavirus(mump)

13. Hairy leukoplakia most commonly occurs on the: (Chapter 7)
(A) base of tongue
(B) dorsal tongue
(C) lateral tongue
(D) ventral tongue

14. The peak prevalence of primary herpetic gingivostomatitis occurs between ages of: (Chapter 7)
(A) birth and 5 years
(B) before 6 months
(C) 2 years and 3 years
(D) 50 years and 60 years

Appendix 2➔Mucosal (surface) lesions

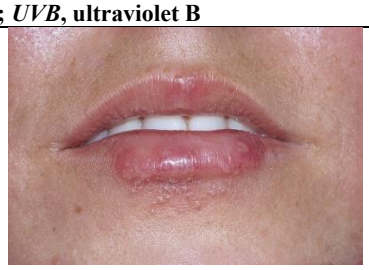
❶Clinical overview➔Vesiculobullous diseases

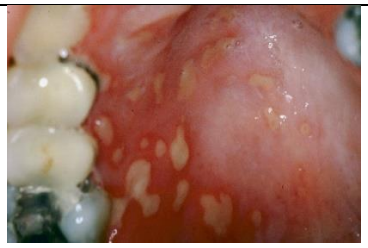
Disease	Clinical Features	Cause	Significance
Herpes Simplex Infections			
Primary herpetic gingivostomatitis	❶multiple painful oral ulcers preceded by vesicles ❷similar perioral & skin lesions ❸fever & gingivitis usually present ❹affect children < 5 years	❶herpes simplex virus type 1 (occasionally type 2)	❶self-limited➔heal in about 2 weeks ❷reactivation of latent virus➔ secondary infection ❸circulating antibodies➔only partial immunity
Secondary herpes simplex infection	❶multiple small ulcers preceded by vesicles; prodromal symptoms of tingling, burning, or pain at site of developing lesion(s) ❷most common on lip, intraorally on palate & attached gingiva; adults and young adults usually affected ❸very common ❹herpetic whitlow➔around fingernail	❶herpes simplex virus➔ reactivation of latent virus and not reinfection ❷precipitated by stress, sunlight, cold temperature, low resistance, & immunodeficiency	❶self-limited➔heal in about 2 weeks without scar ❷lesions infectious during vesicular stage ❸cautioned against autoinoculation ❹herpes type 1 infections➔not link convincingly to oral cancer ❺immunosuppressed patient➔any site affected
Varicella	❶painful pruritic vesicles and ulcers in all stages on trunk and face ❷few oral lesions ❸common childhood disease	❶varicella-zoster virus	❶self-limited➔recover uneventful in several weeks ❷vaccine available
Herpes zoster	❶unilateral multiple ulcers preceded by vesicles along sensory nerve ❷very painful ❸usually on trunk, head, and neck ❹rare intraorally ❺adults	❶reactivation of varicella-zoster virus	❶self-limited ❷may have a prolonged, painful course (post herpetic neuralgia) ❸seen in debilitation, trauma, neoplasia, and immunodeficiency
Hand-foot-and-mouth disease	❶painful ulcers preceded by vesicles on hands, feet, & oral ❷usually in children ❸communicable➔oro-fecal transmit ❹rare	❶coxsackie viruses (A16, others) (enterovirus family)	❶self-limited➔recover uneventful in about 2 weeks
Herpangina	❶multiple painful ulcers in posterior oral cavity and pharynx ❷lesions preceded by vesicles ❸children most commonly affected ❹seasonal occurrence ❺rare	❶coxsackie viruses types A1, 6, 8, 10, 22, others (enterovirus family)	❶self-limited➔recover uneventful in less than a week
Measles (rubeola)	❶oral Koplik's spots precede maculopapular skin rash ❷fever, malaise, plus other symptoms of systemic viral infection	❶measles virus	❶self-limited➔recover uneventful in about 2-week ❷vaccine available
Pemphigus vulgaris	❶multiple painful ulcers preceded by bullae ❷middle age onset ❸positive Nikolsky sign ❹progressive ❺remission /control with therapy ❻rare	❶autoimmune➔antibodies directed vs desmosome-associated protein (desmoglein 3)	❶without treatment➔may be fatal ❷significant morbidity from steroid therapy ❸oral lesions precede skin lesions in over half of cases ❹prognosis improved when treated early
Mucous membrane pemphigoid	❶multiple painful ulcers preceded by vesicles & bullae ❷may heal with scar ❸positive Nikolsky sign ❹may affect oral mucous membranes, eyes, & genitals ❺middle-aged or elderly	❶autoimmune➔antibodies directed against basement membrane antigens, laminin 332, BP180, others	❶protracted course ❷may cause significant morbidity if severe ❸ocular scarring➔symblepharon or blindness ❹death uncommon

	women ❻uncommon ❼clinical➔may confuse with LP, chronic LEof gingiva, pemphigus vulgaris and hypersensitivity		
Bullous pemphigoid	❶skin lesion (trunk & extremities) with infrequent oral lesions ❷ulcers preceded by bullae➔no scarring ❸elderly persons	❷basement membrane autoantibodies➔in tissue and serum	❶chronic course ❷remissions ❸uncommon
Dermatitis herpetiformis	❶skin disease with rare oral involvement ❷vesicles and pustules ❸pruritic exacerbations and remissions typical ❹young and middle-aged adults	❶unknown ❷IgA deposits in sites of lesions ❸usually associated with gluten enteropathy	❶chronic course➔require diet restriction or drug therapy
Epidermolysis bullosa	❶multiple ulcers preceded by bullae ❷positive Nikolsky sign ❸inheritance pattern determines age of onset during childhood & severity ❹may heal with scar ❺primarily a skin disease, but oral lesions often present ❻rare	❶hereditary➔autosomal dominant or recessive ❷acquired adult form also exists	❶severe, debilitating disease that may be fatal in recessive form ❷simple operative procedures may elicit bullae ❸acquired form less debilitating

Abbreviations: *AIDS*, Acquired immunodeficiency syndrome; *BP*, bullous pemphigoid antigen; *GI,* gastrointestinal; *HSV,* herpes simplex virus; *HHV8*, human herpesvirus 8; *HIV*, human immunodeficiency virus; *HLA*, human leukocyte antigen; *Ig*, immunoglobulin; *MEN III* , Multiple endocrine neoplasia syndrome type III; *NK*, natural killer; *SDHD*, succinic dehydrogenase; *STD*, sexually transmitted disease; *UV*, ultraviolet; *UVB*, ultraviolet B

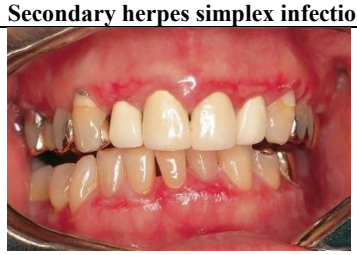

Primary herpes simplex infection


Secondary herpes simplex infection of lips


Secondary herpes simplex infection of palate


Pemphigus vulgaris


Pemphigus vulgaris

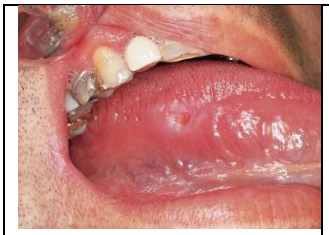
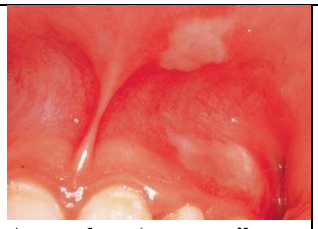
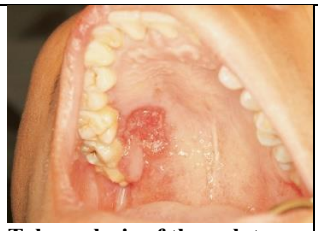
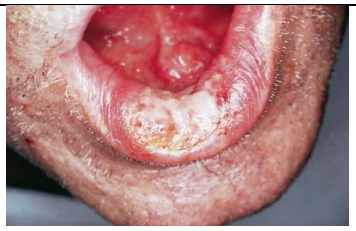
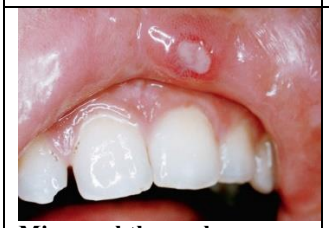
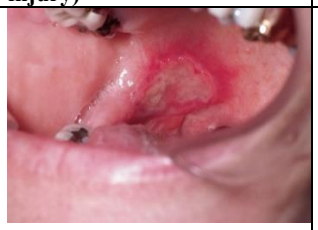
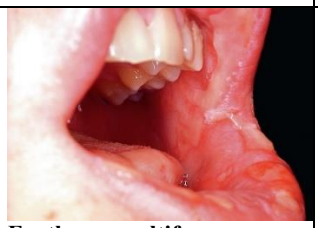
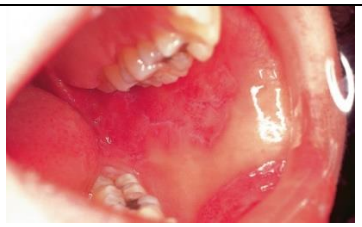
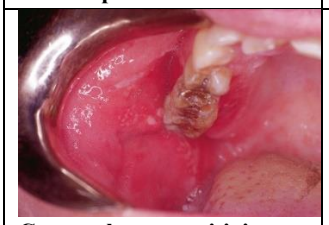
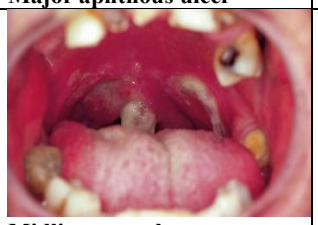
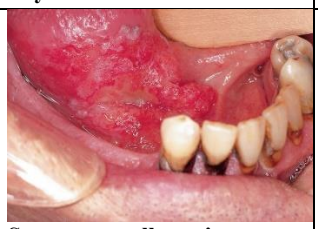
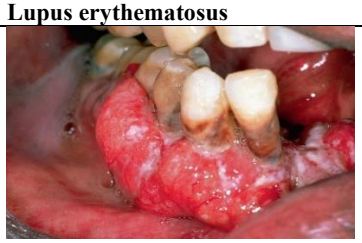

Mucous membrane pemphigoid

❷Clinical overview➔Ulcerative conditions

Disease	Clinical Features	Cause	Significance
Reactive lesions	❶painful ulcer covered by yellow fibrin membrane ❷diagnosis usually evident from appearance & history ❸common ❹traumatic factitial(人工) injuries➔diagnostic challenge	❶trauma, chemicals, heat, radiation	❶self-limited➔heals in days to weeks ❷factitial injuries follow unpredictable course
Syphilis	❶primary (chancre)➔ ①single, indurated, nonpainful ulcer at site of spirochete entry ②spontaneously heals in 4-6 weeks ❷secondary➔①maculopapular rash on skin ②oral ulcers covered by membrane (mucous patch) ❸tertiary➔gumma, cardiovascular & CNS lesion ❹congenital➔dental	❶spirochete➔*Trepo nema pallidum*	❶primary and secondary forms➔highly infectious ❷mimics other diseases clinically ❸untreated➔secondary type develops in 2-10 weeks ❹a minority of patients develop tertiary lesions ❺latency periods➔no clinically apparent disease seen between primary and secondary stages and between secondary and tertiary stages

	abnormalities (mulberry molars, notched incisors), deafness, interstitial keratitis (Hutchinson's triad)		❻untreated➔30% progress to tertiary stage
Gonorrhea	❶typically, genital lesions, with rare oral manifestations, painful erythema or ulcers, or both	❶*Neisseria gonorrhoeae*	❶may be confused with many oral ulcerative diseases
Tuberculosis	❶indurated, chronic ulcer that may be painful➔on any mucosal surface	❶*Mycobacterium tuberculosis*	❶lesions are infectious ❷oral lesions almost always a result of lung lesions ❸differential diagnosis includes oral cancer and chronic traumatic ulcer
Leprosy	❶skin disease, with rare oral nodules/ulcers	❶*Mycobacterium leprae*	❶rare in United States but relatively common in Southeast Asia, India, South America
Actinomycosis	❶typically seen in mandible, with draining skin sinus ❷wood-hard nodule with yellow, "sulfur" granules	❶*Actinomyces israelii*	❶infection follows entry through a surgical site, periodontal disease, or open root canal
Noma	❶necrotic, nonhealing ulcer of gingiva or buccal mucosa ❷rare; affects children	❶anaerobes in patient whose systemic health is compromised	❶often associated with malnutrition ❷may result in severe tissue destruction
Deep fungal diseases	❶indurated, nonhealing, frequently painful, chronic ulcer➔following implantation of organism from lung	❶*Histoplasma capsulatum*, *Coccidioides immitis*, others	❶oral lesions are a result of systemic lesions ❷some types are endemic
Subcutaneous fungal diseases	❶nonspecific ulcers of skin and, rarely, mucosa	❶usually *Sporothrix schenckii*	❶sporotrichosis usually follows inoculation via thorny plants(多刺植物)
Opportunistic fungal infections	❶occurs in compromised host; necrotic ❷nonhealing ulcer(s)	❶*Mucormycosis, Rhizopus,* others	❶known collectively as *phycomycosis* ❷mimic syphilis, midline granuloma ❸frequently fatal
Aphthous ulcers	❶recurrent, painful ulcers ➔tongue, vestibular mucosa, floor of mouth, soft palate and faucial pillars ❷not found on skin, vermilion, attached gingiva, or hard palate ❸usually round or oval ❹ulcers not preceded by vesicles ❺minor type➔solitary, <1.0 cm in diameter; common ❻major type➔severe, heals in up to 6 weeks with scar >1.0 cm in diameter ❼herpetiform type➔ multiple, recurrent crops of ulcers (0.1-0.3 cm diameter) ❽complex aphthosis➔ concurrent recurrent oral aphthae and genital lesions without other Behçet's disease components	❶unknown➔probably an immune defect mediated by T cells ❷may be associated with hypersensitivity, deficiencies, malabsorption, or family history ❸not caused by virus➔ precipitated by stress, trauma, hormonal changes, certain foods ❹autoinflammatory disease recently suggested	❶painful nuisance disease➔rarely debilitating, except major type ❷recurrences are the rule ❸more severe in AIDS ❹may associate with Crohn's disease, or gluten-sensitive enteropathy (celiac sprue)
Behçet's syndrome	❶minor aphthae ❷eye lesions (uveitis, conjunctivitis) ❸genital lesions (ulcers) ❹arthritis occasionally seen	❶probably immune defect ❷hereditary➔presence of HLA-B51 may be factors ❸autoinflammatory disease recently suggested	❶biopsy shows vasculitis and laboratory studies give nonspecific results ❷complications may be significant
Reactive arthritis (formerly Reiter's syndrome)	❶arthritis, urethritis, conjunctivitis, or uveitis ❷oral ulcers; usually in white men in 3rd decade	❶unknown ❷immune response to bacterial antigen ❸usually follows STD or *Shigella* dysentery (痢疾) ❹HLA-B27	❶duration of weeks to months ❷may be recurrent
Erythema multiforme	❶sudden onset ❷painful, widespread, superficial ulcers ❸crusted ulcers ➔vermilion of lips	❶unknown ❷may be associated with hypersensitivity ❸may follow drug ingestion or infection	❶cause should be investigated ❷can be debilitating, esp. severe forms, erythema multiforme major (Stevens-Johnson syndrome) and toxic epidermal necrolysis

	❹usually self-limited ❺young adults ❻target/iris lesions of skin➔may ❼may be recurrent, esp. in spring and fall ❽some cases become chronic ❾uncommon	(herpes labialis or *Mycoplasma* pneu monia)	
Lupus erythematosus	❶Usually painful erythematous and ulcerative lesions on buccal mucosa, gingiva, and vermilion ❷radiating white keratotic areas may surround lesions ❸chronic discoid type➔ affects skin and mucous membrane only ❹acute systemic type➔skin lesions may be erythematous with scale (classic sign➔ butterfly rash across nasal bridge) ❺may have joint, kidney, and heart lesions ❻middle-aged women ❼uncommon	❶immune defect➔ develops autoantibodies, especially antinuclear antibodies	❶discoid type may cause discomfort and cosmetic problems ❷systemic type has variable prognosis from good to poor
Drug reactions	❶may affect skin or mucosa ❷erythema, white lesions, vesicles, ulcers may be seen ❸history of recent drug ingestion	❶potentially any drug via stimulation of immune system	❶reactions, such as anaphylaxis or angioedema, may require emergency care ❷highly variable clinical picture can make diagnosis difficult
Contact allergy	❶lesions caused by direct contact with foreign antigen ❷erythema, vesicles, ulcers may be seen	❶potentially any foreign antigen contact skin/mucosa ❷cinnamon(肉桂) frequent cited	❶patch testing may be helpful for diagnosis ❷history important
Wegener's granulomatosis (granulomatosis with polyangiitis)	❶inflammatory lesions (necrotizing vasculitis) of lung, kidney & upper airway ❷may affect gingiva ❸rare	❶unknown➔possibl y immune defect or infection	❶may become life threatening as a result of tissue destruction in any of the 3 involved sites
Midline granuloma (ulcerating midline lymphoma)	❶destructive, necrotic, nonhealing lesions of nose, palate, and sinuses ❷biopsy shows nonspecific inflammation ❸distinct from Wegener's granulomatosis ❹rare	❶represents NK/T-cell lymphoma	❶poor prognosis ❷death may follow erosion into major blood vessels
Chronic granulomatous disease	❶recurrent infections in various organs ❷oral ulcers ❸males ❹rare	❶genetic disease (X linked)	❶altered neutrophil and macrophage function➔inability to kill bacteria & fungi
Cyclic neutropenia	❶oral ulcers with periodicity (every 3-6 weeks) ❷infection ❸lymphadenopathy ❹3-5 day duration ❺periodontal disease	❶mutations in neutrophil elastase gene ELA2 ❷autosomal dominant or new mutation	❶rare blood dyscrasia
Squamous cell carcinoma of oral cavity	❶indurated, nonpainful ulcer with rolled margins ❷most commonly found on lateral tongue & mouth floor ❸male affected 2× as female ❹clinical➔white/red patch or mass	❶DNA alterations due to carcinogens such as tobacco, UV light, oncogenic HPV type 16 or 18 (oropharynx) ❷alcohol acts as cocarcinogen	❶overall 5-year survival rate is about 50% ❷improved prognosis if found in early stages, poor prognosis if metastasis to regional lymph nodes
Carcinoma of maxillary sinus	❶may have symptoms of sinusitis or referred pain to teeth ❷may cause malocclusion or mobile teeth ❸may be ulcerative mass in palate or alveolus	❶unknown➔some occur in woodworkers	❶prognosis only fair ❷metastases are not uncommon

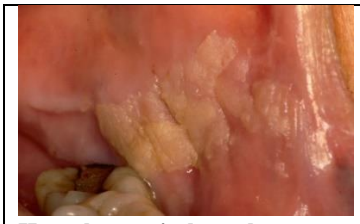
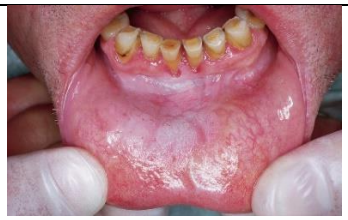
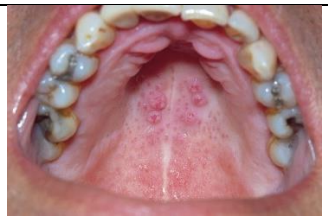
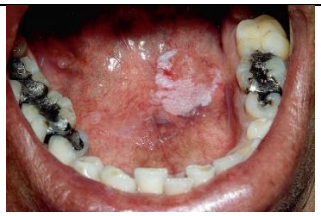
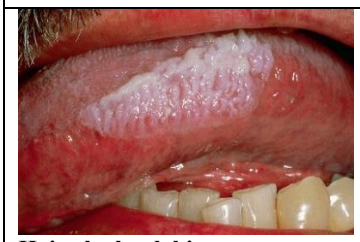
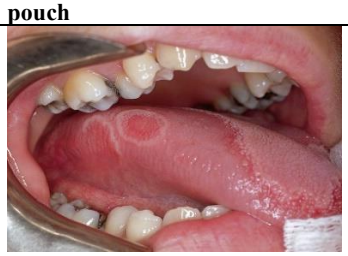
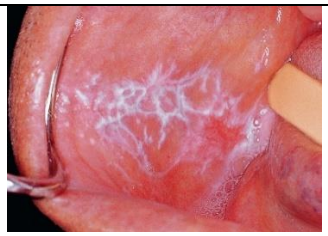
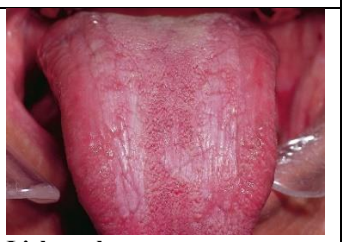
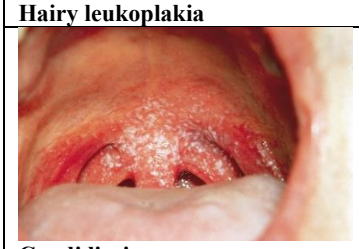
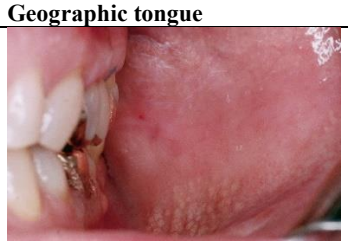
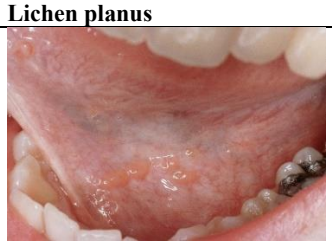
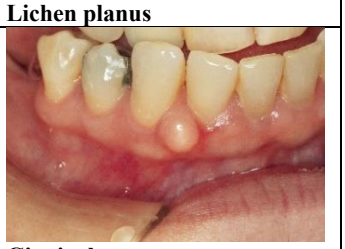
 Chronic traumatic ulcer	 Acute ulcers(cotton rail injury)	 Tuberculosis of the palate	 Histoplasmosis of the lip
 Minor aphthous ulcer	 Major aphthous ulcer	 Erythema multiforme	 Lupus erythematosus
 Contact hypersensitivity, buccal and palatal gingiva	 Midline granuloma	 Squamous cell carcinoma, floor of mouth	 Squamous cell carcinoma, gingiva

❸Clinical overview➔White lesions

Disease	Clinical Features	Cause	Significance
Leukoedema	❶common uniform opacification of buccal mucosa bilaterally	❶unknown	❶remains indefinitely ❷no ill effects
White sponge nevus	❶asymptomatic, bilateral, dense, shaggy, white or gray, generalized opacification ❷primarily buccal mucosa affected, but other membranes may be involved ❸rare	❶hereditary, autosomal dominant (keratin 4 and/or 13 genes)	❶remains indefinitely ❷no ill effects
Hereditary benign intraepithelial dyskeratosis	❶asymptomatic, diffuse, shaggy white lesions of buccal mucosa, and other tissues ❷eye lesions➔white plaques surrounded by inflamed conjunctiva (pannus) ❸rare	❶hereditary, autosomal dominant, duplication of chromosome 4q35	❶remains indefinitely
Follicular keratosis	❶keratotic papular lesions of skin and, infrequently, mucosa ❷lesions are numerous and asymptomatic	❶genetic, autosomal dominant, mutation in *ATP2A2* gene	❶chronic course with occasional remissions
Focal (frictional) hyperkeratosis	❶asymptomatic white patch, commonly on edentulous ridge, buccal mucosa, & tongue ❷does not rub off ❸common	❶chronic irritation, low-grade trauma	❶may regress if cause eliminate
White lesions associated with smokeless tobacco	❶asymptomatic white folds surrounding area where tobacco is held ❷usually in labial & buccal vestibules ❸common	❶chronic irritation from snuff or chewing tobacco	❶increased risk for development of verrucous and squamous cell carcinoma after many years
Nicotine stomatitis	❶asymptomatic, generalized opacification of palate with red dots representing salivary gland orifice ❷common	❶heat & smoke associated with combustion of tobacco	❶rarely develops into palatal cancer
Actinic cheilitis	❶lower lip➔atrophic epithelium, poor definition of vermilion-skin margin, focal zones of keratosis ❷common	❶UV light (especially UVB, 2900-3200 nm)	❶may result in squamous cell carcinoma
Idiopathic leukoplakia	❶asymptomatic white patch ❷cannot be wiped off ❸males affected more than females	❶unknown➔may relate to tobacco and alcohol use	❶may recur after excision ❷5% are malignant and 5% become malignant ❸dysplasia➔higher ca. risk
Hairy leukoplakia	❶filiform to flat patch on lateral	❶Epstein-Barr virus infection	❶20% of HIV-infected patients

	tongue, often bilateral, occasionally on buccal mucosa ❷asymptomatic		❷marked increase in AIDS ❸occur in non-AIDS-affected immunosuppressed patients
Hairy tongue	❶elongation of filiform papillae ❷asymptomatic	❶unknown➔may follow antibiotic, corticosteroid use, tobacco habit	❶Benign process ❷may cosmetical objectionable
Geographic tongue (erythema migrans)	❶white annular lesions with atrophic red centers ❷pattern migrates over dorsum of tongue ❸varies in intensity and may spontaneously disappear ❹occasionally painful ❺common	❶unknown	❶completely benign ❷spontaneous regression after months to years
Lichen planus	❶bilateral white striae (Wickham's) ❷asymptomatic except when erosive type ❸seen in middle age ❹buccal mucosa most commonly affected ❺occasional on tongue, gingiva, and palate ❻skin/genital lesions occasional present ➔purple pruritic papules ❼forearm and lower leg most commonly affected skin sites	❶unknown➔may be precipitated by stress ❷may be hyperimmune condition mediated by T cells	❶may regress after many years ❷treatment may only control disease ❸rare malignant transformation
Dentifrice-associated slough	❶asymptomatic, slough of filmy parakeratotic cells	❶mucosal reaction to components in toothpaste	❶none
Candidiasis	❶painful elevated plaques➔can wiped off, leaving eroded, bleeding surface ❷associated with poor hygiene, systemic antibiotics, systemic disease, debilitation, reduced immune response ❸chronic infection➔erythematous mucosa without obvious white colonies ❹common	❶opportunistic fungus➔*Candida albicans* & rarely other *Candida* species	❶usually disappears 1-2 weeks after treatment ❷some chronic cases require long-term therapy
Mucosal burns	❶painful white fibrin exudate covering superficial ulcer with erythematous ring ❷common	❶chemicals (aspirin, phenol), heat, electrical burns	❶heals in days to weeks
Submucous fibrosis	❶areas of opacification with loss of elasticity; any oral region affected ❷rare	❶may be due to hypersensitivity to dietary constituents➔areca (betel nut), capsaicin	❶irreversible ❷predisposes to oral cancer in about 10% of cases
Fordyce granules	❶multiple asymptomatic, yellow, flat or elevated spots➔buccal mucosa and lips ❷in a majority of patients ❸a variation of normal	❶developmental	❶ectopic sebaceous glands (choristoma) of no significance
Ectopic lymphoid tissue	❶asymptomatic elevated yellow nodules <0.5 cm in diameter ❷usually found on tonsillar pillars, posterolateral tongue, and mouth floor ❸covered by intact epithelium ❹common	❶developmental	❶no significance➔remain indefinitely and are usually diagnostic clinically
Gingival cyst	❶small, usually white to yellow nodule ❷multiple in infants, solitary in adults ❸common in infants ❹rare in adults	❶proliferation and cystic change of dental lamina rests	❶in infants, lesions spontaneously rupture or break ❷recurrence not expected in adults
Parulis	❶yellow-white gingival swelling caused by submucosal pus accumulation	❶periodontitis or dental abscess	❶periodic drainage until primary cause is eliminated
Lipoma	❶asymptomatic, slow-grow, well-circumscribe, yellow/yellow-white mass ❷benign neoplasm of fat ❸occurs in any area	❶unknown	❶seems to have limited growth potential intraorally ❷recurrence not expected after removal

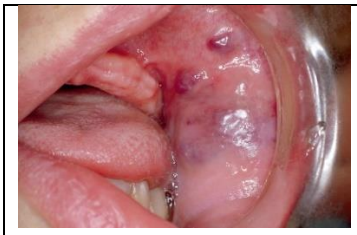
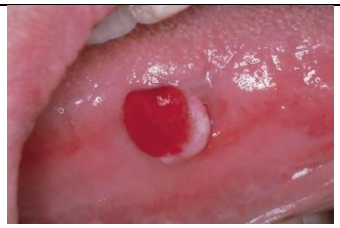
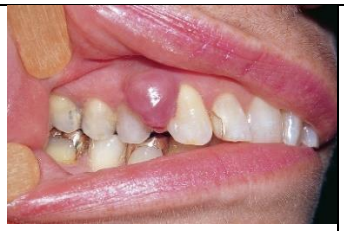
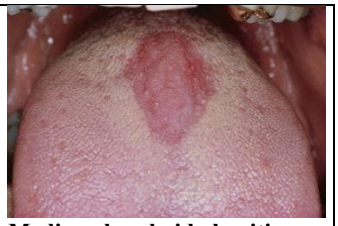
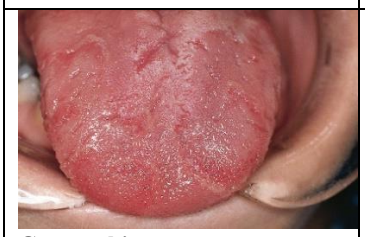
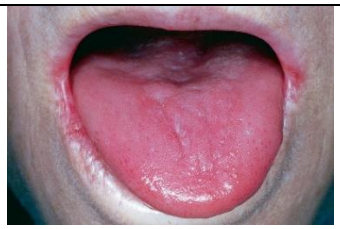
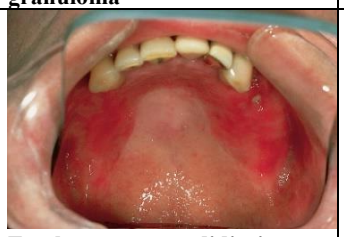
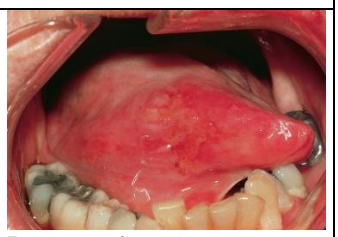
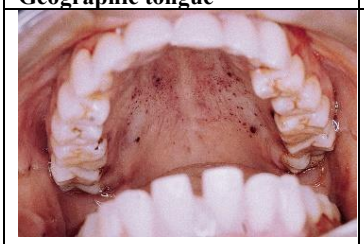
AIDS, Acquired immunodeficiency syndrome; *HIV,* human immunodeficiency virus; *UV,* ultraviolet; *UVB,* ultraviolet B

 Hyperkeratosis, buccal mucosa	 Hyperkeratosis, snuff dipper's pouch	 Nicotine stomatitis	 Idiopathic leukoplakia
 Hairy leukoplakia	 Geographic tongue	 Lichen planus	 Lichen planus
 Candidiasis	 Fordyce's granules *(bottom)*	 Ectopic lymphoid tissue, floor of mouth	 Gingival cyst

❹Clinical overview➔Red-blue lesions

Disease	Clinical Features	Cause	Significance
Congenital hemangiomas and vascular malformations	❶red or blue lesion that blanches when compressed ❷extent of lesion usually difficult to determine ❸skin, lips, tongue, and buccal mucosa➔most common ❹common on skin, uncommon in mucous membrane, rare in bone ❺part of Sturge-Weber syndrome ❻telangiectasias (small focal dilations of terminal blood vessels) blanch as compressed ❼common in sun-damaged skin & hereditary hemorrhagic telangiectasia (HHT)	❶some are benign congenital neoplasms ❷others are caused by abnormal vessel morphogenesis (vascular malformation) ❸HHT➔autosomal dominant ❹venous varix ❺congenital or induced by UV light	❶may remain quiescent or may gradually enlarge ❷hemorrhage may be a significant complication ❸often a cosmetic problem ❹HHT➔epistaxis and GI bleeding may be a problem
Pyogenic granuloma	❶asymptomatic red mass composed of granulation tissue ❷most common➔ gingiva ❸may occur during pregnancy ❹may secondarily ulcerated ❺common	❶trauma or chronic irritation ❷size modified by hormonal changes	❶remains indefinitely ❷recurrence if incompletely excised ❸reduction in size if cause removed or after pregnancy
Peripheral giant cell granuloma	❶asymptomatic red mass of gingiva composed of fibroblasts and multinucleated giant cells ❷most often in adults➔former area of deciduous teeth ❸cup-shaped radiolucency when in edentulous areas ❹uncommon	❶trauma or chronic irritation	❶remains indefinitely if untreated ❷a reactive lesion ❸clinical appearance similar to pyogenic granuloma
Erythroplakia	❶asymptomatic red velvety patch➔in mouth floor or retromolar area in adults ❷seen in older adults ❸red lesions may have foci of white hyperkeratosis (speckled erythroplakia)	❶tobacco and alcohol	❶most (90%)➔in situ or invasive squamous cell carcinoma
Kaposi's sarcoma	❶may be seen in AIDS ❷usually on skin, but may be oral, especially in palate ❸red-blue macules or nodules ❸rare, except in immunodeficiency	❶endothelial cell proliferation in the setting of HHV8 infection	❶fair prognosis➔poor when part of AIDS ❷incidence decline in AIDS under HAART treatment

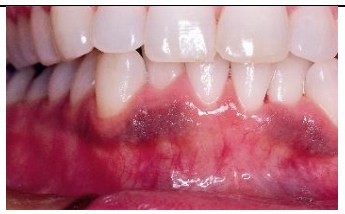
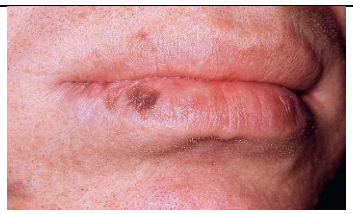
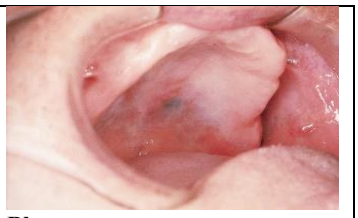
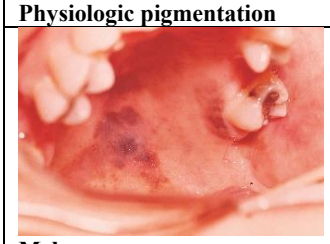
Median rhomboid glossitis	❶red lobular elevation anterior to circumvallate papillae in midline	❶chronic *Candida* infection	❶little significance ❷treat *Candida albicans* infection
Geographic tongue	❶white annular lesions with atrophic, red centers ❷white (keratotic) areas may be poorly developed, leaving red patches on dorsum of tongue ❸occasionally painful ❹common	❶unknown	❶little significance except when painful ❷not premalignant
Psoriasis	❶chronic skin disease with rare oral lesions ❷red skin lesion covered with silvery scales ❸oral lesion red to white patch	❶unknown	❶must have skin lesions to confirm oral disease ❷exacerbation &remission are typical
Vitamin B deficiency	❶generalized redness of tongue caused by atrophy of papillae ❷may be painful ❸may have associated angular cheilitis	❶B complex deficiency	❶remains until therapeutic levels of vitamin B are administered
Anemia (pernicious and iron deficiency)	❶generalized redness of tongue caused by atrophy of papillae ❷may be painful ❸may have angular cheilitis ❹females > males ❺Plummer-Vinson syndrome (sideropenic dysphagia) ❻anemia (iron deficiency), mucosal atrophy, predisposition for oral cancer	❶some forms acquired, some hereditary	❶some types may be life threatening ❷oral manifestations disappear with treatment ❸complication of oral cancer with Plummer-Vinson syndrome
Burning mouth syndrome	❶wide range of oral complaints, usually without any visible tissue changes ❷especially middle-aged women ❸uncommon in males	❶multifactorial (e.g., *C. albicans,* vitamin B deficiency anemias, xerostomia, idiopathic, psychogenic peripheral neuropathy), chronic trauma	❶may persist despite treatment
Scarlet fever	❶pharyngitis, systemic symptoms, strawberry tongue	❶group A streptococci	❶complications of rheumatic fever and glomerulonephritis
Erythematous candidiasis	❶painful, hyperemic palate under denture ❷angular cheilitis ❸red, painful mucosa	❶chronic *C.albicans* infection ❷poor oral hygiene & ill-fitting denture➔predisposing factors	❶discomfort may prevent wearing denture ❷not allergic or premalignant
Plasma cell gingivitis	❶red, painful tongue ❷angular cheilitis ❸red swollen attached gingiva	Possible allergic reaction to dietary antigen such as mint- or cinnamon-flavored chewing gum; certain toothpastes	Gingival lesions similar to lupus, lichen planus, and pemphigoid lesions
Drug reactions and contact allergies	❶red, vesicular, or ulcerative eruption	❶hypersensitivity reaction to allergen	❶hypersensitivity reactions to drugs or HSV may produce erythema multiforme
Petechiae and Ecchymoses			
Traumatic lesions	❶hemorrhagic spot (red, blue, purple, black) composed of extravasated blood in soft tissue ❷not blanch with compression ❸may be anywhere in skin or mucous membranes after trauma ❹changes color as blood is degraded and resorbed	❶follows trauma such as that caused by tooth extraction, tooth bite, fellatio(口交), chronic cough, vomiting	❶resolves in days to weeks ❷no sequelae
Blood dyscrasias(血液疾病)	❶hemorrhagic spots (small➔ petechiae, large➔ecchymoses) on mucous membranes resulting from extravasated blood ❷may be spontaneous or may follow minor trauma ❸spots do not blanch with compression ❹color varies with time ❺uncommon in general practice, but dental personnel may be first to observe	❶lack of clotting factor, reduced numbers of platelets for various reasons, or lack of vessel integrity	❶may be life threatening ❷must be investigated, diagnosed, and treated

 Vascular malformation	 Pyogenic granuloma	 Peripheral giant cell granuloma	 Median rhomboid glossitis
 Geographic tongue	 Vitamin B deficiency	 Erythematous candidiasis	 Drug reaction
 Petechiae, blood dyscrasia			

❺Clinical overview➔Pigmented lesions

Disease	Clinical Features	Cause	Significance
Physiologic pigmentation	❶symmetric distribution ❷not change in intensity ❸not alter surface morphology	❶normal melanocyte activity	❶none
Smoking-associated melanosis	❶gingival pigmentation ❷especially women taking birth control pills	❶component in smoke stimulates melanocytes	❶cosmetic ❷may have smoking-associated lesions elsewhere
Oral melanotic macule	❶flat oral pigmentation < 1 cm in diameter ❷lower lip, gingiva, buccal mucosa, palate usually affected ❸may represent oral ephelis(雀斑), perioral lesions associated with Peutz-Jeghers syndrome, Addison's disease, or post inflammatory pigmentation	❶unknown ❷post inflammatory or traumatic	❶remains indefinitely ❷no malignant potential
Neuroectodermal tumor of infancy	❶pigmented, radiolucent, benign neoplasm in maxilla, usually of newborn ❷pigment is melanin ❸rare ❹children and those <25 years old	❶unknown ❷neural crest origin	❶recurrence unlikely
Melanocytic nevus	❶elevated pigmentations ❷often nonpigmented when intraoral ❸uncommon orally ❹blue nevi➔palate	❶unknown ❷due to nests of nevus cells	❶remains indefinitely ❷oral nevi often cannot be separated from melanoma clinically
Melanoma	❶malignancy of melanocytes ❷some have radial growth phase of years (in situ) before vertical growth phase, but invasive type➔only vertical growth phase ❷oral melanoma➔first as insignificant spot, especially on palate and gingiva ❸adults affected	❶UV light may be carcinogenic on skin ❼unknown for oral lesions	❶skin➔65% 5-year survival ❼oral➔20% 5-year survival ❸in situ melanoma➔better prognosis than invasive melanoma ❹unpredictable metastatic behavior
Amalgam tattoo	❶asymptomatic gray-pigmented macule in gingiva, tongue, palate, or buccal mucosa adjacent to amalgam restoration ❷large particle➔seen radiographically ❸no associated inflammation; common	❶traumatic implantation of amalgam	❶remains indefinitely and changes little ❷no ill effects
Heavy-metal pigmentation	❶dark line along marginal gingiva due to precipitation of metal ❷rare	❶intoxication by metal vapors (lead, bismuth, arsenic, mercury)➔ occupational exposure	❶exposure may affect systemic health ❷gingiva pigmentation of cosmetic significance

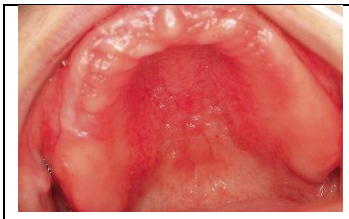
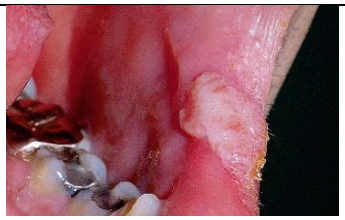
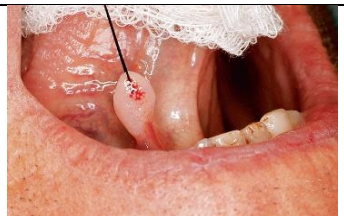
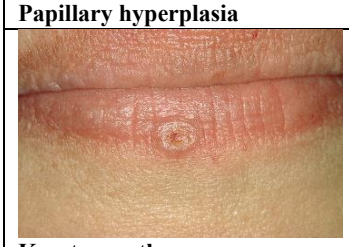
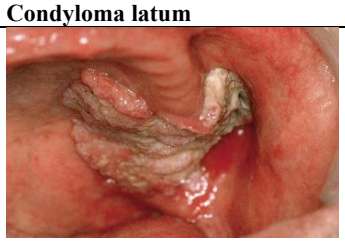
Minocycline pigmentation	❶gray pigmentation of palate, skin, scars, and bone, and rarely, of formed teeth	❶ingestion of minocycline	❶must differentiate from melanoma ❷may cause intrinsic teeth staining

 Physiologic pigmentation	 Smoking-associated melanosis	 Melanotic macule	 Blue nevus
 Melanoma	 Amalgam tattoo		

❻Clinical overview➔Verrucal-papillary lesions

Disease	Clinical Features	Cause	Significance
Papillary hyperplasia	❶painless papillomatous "cobblestone" lesion of hard palate in denture wearers ❷usually red as a result of inflammation ❸common	❶soft tissue reaction to ill-fitting denture and probable fungal overgrowth	❶lesion is not premalignant ❷may show significant regression if denture taken away from patient ❸topical antifungals may help
Condyloma latum	❶clinically similar to papillary hyperplasia ❷part of secondary syphilis	❶*Treponema pallidum*	❶prognosis good with treatment
Squamous papilloma	❶painless exophytic granular to cauliflower-like lesions ❷predilection for tongue, mouth floor, palate, uvula, lips, faucial pillars ❸generally solitary ❹soft texture ❺white or same color as surrounding tissue ❺young adults and adults ❻common	❶most caused by nononcogenic human papillomavirus (HPV) ❷some unknown	❶lesion has no known malignant potential ❷recurrence rare
Oral verruca vulgaris	❶painless papillary lesion➔ white surface projections caused by keratin production ❷may be regarded as a type of papilloma ❸children and young adults ❹common on skin, uncommon intraorally	❶human papillomavirus (HPV)	❶little significance ❷may be multiple & cosmetic problem
Condyloma acuminatum	❶painless, pedunculated to sessile, exophytic, papillomatous lesion ❷adults ❸same color/lighter than surrounding tissue ❹sexual partner has similar lesions ❺rare in oral cavity	❶Human papillomavirus (HPV)	❶oral lesions acquired through autoinoculation or sexual contact with infected partner ❷recurrence common
Focal epithelial hyperplasia (Heck's disease)	❶multiple soft nodules on lips, tongue, buccal mucosa ❷transmissible ❸asymptomatic	❶papillomavirus (HPV 13 and 32)	❶little significance ❷may include in differential diagnosis of mucosal nodules
Keratoacanthoma	❶well-circumscribed, firm, elevated lesion with central keratin plug ❷may cause pain ❸develops rapidly over 4-8 weeks and involutes in 6-8 weeks ❹found on sun-exposed skin and lips ❺rare intraorally ❻ men predilection	❶unknown ❷pilosebaceous(毛囊皮脂腺) origin	❶probably a self-healing squamous cell carcinoma ❷Difficult to differentiate clinically and microscopically from squamous cell carcinoma ❸may heal with scar
Verrucous carcinoma	❶broad-based, exophytic, indurated ❷buccal mucosa or vestibule ❸men most frequently affected ❹uncommon	❶may be associated with use of tobacco	❶slow-growing malignancy ❷well differentiated, better prognosis than squamous cell carcinoma ❸growth➔more expansile than invasive ❸metastasis uncommon

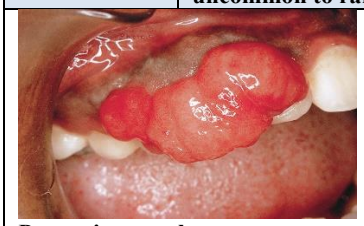
Pyostomatitis vegetans	**❶multiple small pustules in oral mucosa ❷males more than females**	**❶unknown**	**❶may be associated with bowel disease such as ulcerative colitis or Crohn's disease**
Verruciform xanthoma	**❶solitary, pebbly, elevated or depressed lesion➔anywhere in oral mucous membrane ❷color ranges from white to red ❸rare**	**❶unknown**	**❶limited growth potential ❷does not recur**

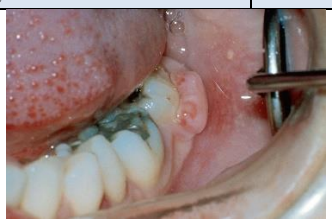
 **Papillary hyperplasia**	 **Condyloma latum**	 **Papilloma**	 **Focal epithelial hyperplasia**
 **Keratoacanthoma**	 **Verrucous carcinoma**		

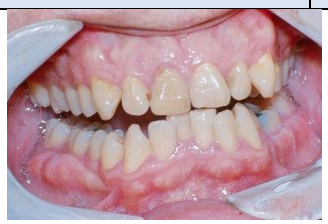
Appendix 2➔Submucosal swelling (by region)

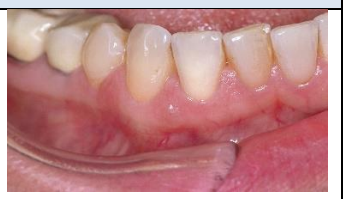
❶Clinical overview➔Gingival swellings

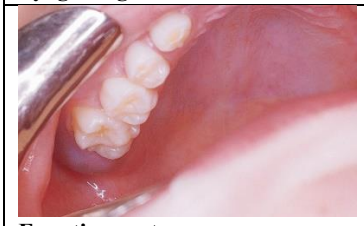
Disease	Clinical Features	Cause	Significance
Pyogenic granuloma	❶asymptomatic red mass➔primarily on gingiva but may be found anywhere on skin or mucous membrane where trauma has occurred ❷common	❶reaction to trauma or chronic irritation	❶may recur if incompletely excised ❷usually does not cause bone resorption
Peripheral giant cell granuloma	❶asymptomatic red mass of gingiva ❷cannot be clinically separated from pyogenic granuloma ❸uncommon	❶reaction to trauma or chronic irritation	❶completely benign behavior ❷unlike central counterpart; ❸recurrence not anticipated
Peripheral fibroma (focal fibrous hyperplasia)	❶firm mass ❷color same as surrounding tissue ❸no symptoms ❹common ❺pedunculated or sessile	❶reaction to trauma or chronic irritation	❶overexuberant repair process with proliferation of scar ❷occasional recurrence seen with peripheral ossifying fibroma
Parulis	❶red mass (or yellow if pus filled)➔buccal gingiva of children and young adults ❷usually without symptoms	❶sinus tract from periodontal or periapical abscess	❶cyclic drainage occurs until underlying problem is eliminated
Exostosis	❶bony hard nodule(s) covered by intact mucosa attached to buccal alveolar bone ❷asymptomatic ❸common ❸usually appears in adulthood	❶unknown	❶no significance except in denture construction
Gingival cyst	❶small, elevated, yellow to pink nodule(s) ❷multiple in infants, solitary in adults ❸common in infants, rare in adults	❶proliferation and cystic change of dental lamina rests	❶known as Bohn's nodule or Epstein's pearls in infant ❷unroofed during mastication ❸adult lesions do not occur
Eruption cyst	❶bluish (fluid- or blood-filled) sac over crown of erupting tooth ❷uninflamed and asymptomatic ❷uncommon	❶hemorrhage into follicular space between tooth crown and reduced enamel epithelium	❶none ❷should not be confused with neoplasm
Congenital epulis of newborn	❶firm, pedunculated or sessile mass attached to gingiva in infants ❷same color or lighter than surrounding tissue ❸rare	❶unknown	❶benign neoplasm of non-neural granular cells ❷different cells to those in a granular cell tumor of adult ❸does not recur
Generalized soft tissue hyperplasia	❶firm, increased bulk of free and attached gingiva ❷usually asymptomatic ❸pseudopockets ❹nonspecific type common, others (drug induced, hormone modified, leukemia induced, genetically influenced) uncommon to rare	❶local gingival irritants plus systemic drugs (phenytoin [Dilantin], nifedipine, cyclosporine), hormone imbalance, leukemia, or hereditary factors/syndromes	❶cosmetic and hygienic, problem ❷causative factors should be eliminated if possible ❸control of local factors can lead to improvement

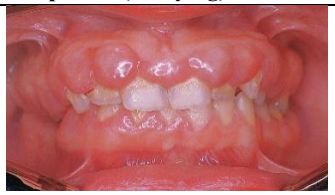

Pyogenic granuloma


Peripheral (ossifying) fibroma


Exostoses


Gingival cyst (canine↔lateral incisor)

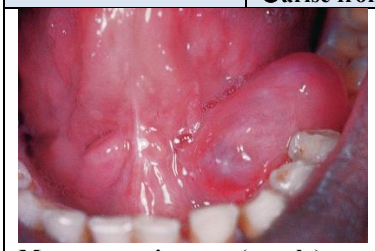

Eruption cyst

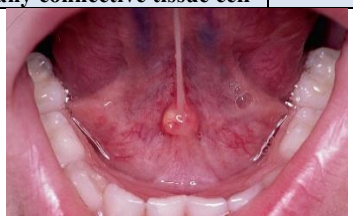

Generalized gingival hyperplasia

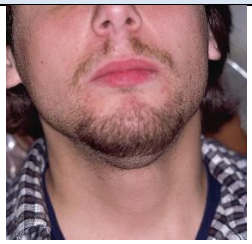
❷Clinical overview➔Floor-of-mouth swellings

Disease	Clinical Features	Cause	Significance
Mucus retention cyst (ranula)	❶elevated, fluctuant, bluish white mass in lateral floor of mouth ❷cyclic swelling often ❸usually painful ❹uncommon	❶sialolith blockage of duct or traumatic severance of duct	❶most are due to sialoliths, some are due to severance of duct with extravasation of mucin into soft tissues ❷recurrence not uncommon

Lymphoepithelial cyst	❶asymptomatic nodules covered by intact epithelium <1 cm in diameter ❷any age ❸on faucial pillars, mouth floor, ventral and posterior-lateral tongue ❸yellowish pink ❹uncommon within oral cavity, common in major salivary glands	❶developmental defect	❶ectopic lymphoid tissue of no significance ❷recurrence not expected
Dermoid cyst	❶asymptomatic mass in floor of mouth (usually midline) covered by intact epithelium of normal color ❷young adult ❸feels doughy on palpation ❹rare	❶proliferation of multipotential cells ❷stimulus unknown	❶recurrence not expected ❷called teratoma with tissues from all 3 germ layers ❸dermoid when secondary skin adnexa are present
Intraoral (minor) salivary gland tumor	❶solitary, firm, asymptomatic mass usually covered by epithelium ❷malignant tumors may cause pain, paresthesia, or ulceration ❸young adults and adults ❸most common➔palate, followed by tongue, upper lip, and buccal mucosa ❹uncommon	❶unknown	❶about half of minor salivary gland tumors➔malignant ❷malignancy may metastasize to bones and lungs, as well as to regional lymph nodes ❸pleomorphic adenoma➔ most common benign tumor
Mesenchymal neoplasm	❶firm, asymptomatic tumescence covered by intact epithelium ❷arise from any connective tissue cell	❶unknown	❶benign tumors not expected to recur ❷malignancies rare

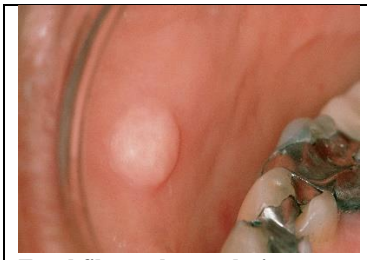
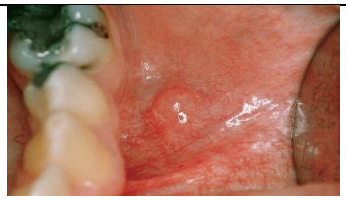
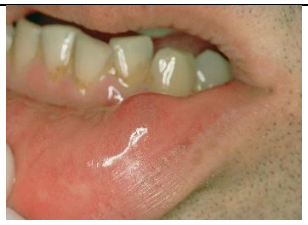

Mucus retention cyst (ranula)


Lymphoepithelial cyst, lingual frenum


Dermoid cyst, midline of neck

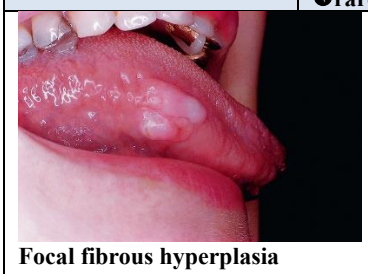
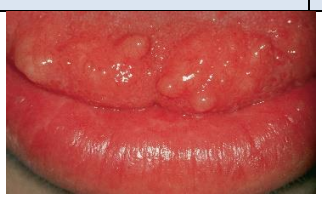
❸Clinical overview➔Lips and buccal mucosal swellings

Disease	Clinical Features	Cause	Significance
Focal fibrous hyperplasia (oral fibroma)	❶firm, asymptomatic nodule covered by epithelium unless secondarily traumatized ❷along line of occlusion in buccal mucosa and lower lip ❸common	❶reaction to trauma or chronic irritation	❶ hyperplastic scar ❷limited growth potential, and no malignant transformation
Salivary gland tumor	❶solitary, firm, asymptomatic mass usually covered by epithelium ❷malignant tumors may cause pain, paresthesia, or ulceration ❸young adults and adults ❹most common in palate, followed by tongue, upper lip, and buccal mucosa ❺uncommon	❶unknown	❶about half of minor salivary gland tumors are malignant ❷malignancies may metastasize to bones and lungs, as well as to regional lymph nodes ❷pleomorphic adenoma➔most common benign neoplasm
Mucus retention cyst	❶solitary, usually asymptomatic, mobile, nontender ❷covered by intact epithelium ❸color same as surrounding tissue ❹adults over 50 years of age ❺common in palate, cheek, mouth floor ❻uncommon in upper lip ❼rare in lower lip	❶blockage of salivary gland excretory duct by sialolith	❶recurrence not anticipated if associated gland removed ❷clinically indistinguishable from more significant salivary gland neoplasms
Mucus extravasation phenomenon (mucocele)	❶bluish nodule (normal color if deep) usually covered by epithelium ❷may slightly painful & associated acute inflammatory reaction ❸most frequently in lower lip and buccal mucosa ❹rare in upper lip ❺adolescents and children❻common	❶traumatic severance of salivary gland excretory duct	❶recurrence expected if contributing salivary gland not removed, or if adjacent ducts severed ❷not a true cyst
Mesenchymal neoplasm	❶firm, asymptomatic tumescence covered by intact epithelium ❷may arise from any connective tissue cell	❶unknown	❶benign tumors not expected to recur ❷malignancies rare

 Focal fibrous hyperplasia	 Mucus extravasation phenomenon, mandibular vestibule	 Mucus extravasation phenomenon	

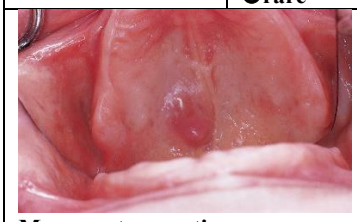
❹Clinical overview➔Tongue swellings

Disease	Clinical Features	Cause	Significance
Focal fibrous hyperplasia (traumatic fibroma)	❶firm, asymptomatic nodule covered by epithelium unless secondarily traumatized ❷usually found along line of occlusion in buccal mucosa and lower lip ❸common	❶reaction to trauma or chronic irritation	❶ hyperplastic scar ❷limited growth potential, & no malignant transformation
Pyogenic granuloma	❶asymptomatic red mass➔ primarily on gingiva but may be anywhere on skin or mucous membrane where trauma has occurred ❷common	❶reaction to trauma or chronic irritation	❶may recur if incompletely excised ❷usually not cause bone resorption
Granular cell tumor	❶painless elevated tumescence covered by intact epithelium ❷color same as or lighter than surrounding tissue ❸strong predilection for dorsum of tongue but may be anywhere ❹any age ❺uncommon	❶unknown➔cell of origin probably Schwann cell	❶not recur ❷of significance➔must be differentiated from other lesions ❸no malignant potential
Neurofibroma/palisaded encapsulated neuroma	❶soft, single or multiple, asymptomatic nodules covered by epithelium ❷same as or lighter than surrounding mucosa ❸most frequent on tongue, buccal mucosa, and vestibule but may be anywhere ❹any age ❺uncommon	❶unknown➔cell of origin probably Schwann cell ❷*NF-1* gene mutation if part of neurofibromatosis syndrome	❶recurrence not expected ❷multiple neurofibromas➔ neurofibromatosis-1 (von Recklinghausen's disease of nerve➔neurofibromas and >6 café-au-lait macules) ❸palisaded encapsulated neuromas➔not syndrome associated
Mucosal neuroma	❶multiple ❷lips, tongue, buccal mucosa ❸may associate with MEN III syndrome	❶unknown ❷MEN III syndrome➔autosomal dominant	❶MEN III syndrome (pheochromocytoma, medullary carcinoma of thyroid, and mucosal neuromas)
Salivary gland tumor	❶solitary, firm, asymptomatic mass covered by epithelium ❷malignant tumors➔ pain, paresthesia, or ulceration young adults and adults ❸most common in palate, followed by tongue, upper lip, and buccal mucosa ❹uncommon	❶unknown	❶about half of minor salivary gland tumors➔malignant malignancies may metastasize to bones and lungs, as well as to regional lymph nodes ❸pleomorphic adenoma➔ most common benign tumor
Lingual thyroid	❶nodular mass in base of tongue ❷may cause dysphagia ❸young adults ❹rare	❶incomplete descent of thyroid anlage to neck	❶lingual thyroid may be only thyroid tissue

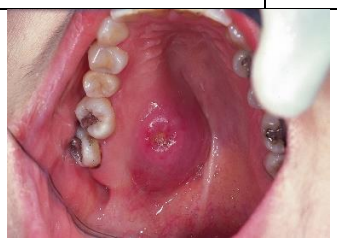
 Focal fibrous hyperplasia	 Granular cell tumor, lateral tongue	 Mucosal neuromas of multiple endocrine neoplasia syndrome III	

❺Clinical overview➔Palatal swellings

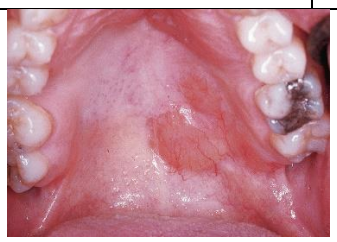
Disease	Clinical Features	Cause	Significance
Mucus extravasation phenomenon (mucocele)	❶bluish nodule (normal color if deep) covered by epithelium ❷may be slightly painful & associate acute inflammatory reaction ❸most frequently in lower lip and buccal mucosa, rare in upper lip and palate ❹adolescents and children ❺common	❶traumatic severance of salivary gland excretory duct	❶recurrence expected if contributing salivary gland not removed or if adjacent ducts severed
Salivary gland tumor	❶solitary, firm, asymptomatic mass covered by epithelium ❷malignant tumors➔pain, paresthesia, or ulceration ❸young adults and adults most common in palate, followed by tongue, upper lip, and buccal mucosa ❹uncommon	❶unknown	❶about half of minor salivary gland tumors➔ malignant ❷malignancies➔metastasize to bones and lungs, as well as to regional lymph nodes ❸pleomorphic adenoma➔ most common benign neoplasm
Palatal abscess from periapical lesion	❶painful, pus-filled, fluctuant tumescence of hard palate ❷color same or redder than surrounding tissue ❸associated with nonvital tooth	❶extension of periapical abscess through palatal bone	❶pus may spread to other areas, seeking path of least resistance
Lymphoma	❶asymptomatic, spongy to firm tumescence of hard palate ❷rare in adults ❸increased frequency in immunosuppressed patients	❶unknown	❶primary non-Hodgkin lymphoma ❷lymphoma workup indicated ❸high grade lesions more frequent in immunosuppressed patients
Torus	❶asymptomatic, bony, hard swelling of hard palate (torus palatinus) ❷bony, exophytic growths along lingual aspect of mandible (torus mandibularis) ❸very slow growth ❹young adults and adults ❺affects up to 25% of population	❶unknown	❶no significance ❷should not be confused with other palatal lesions
Neoplasm of maxilla or maxillary sinus	❶palatal swelling with/without ulcer ❷pain or paresthesia ❸may cause loosening of teeth or malocclusion ❹denture may not fit ❺any age ❻rare	❶unknown	❶ benign or malignant jaw neoplasm or carcinoma of maxillary sinus ❷poor prognosis for malignant lesions



Mucus extravasation phenomenon



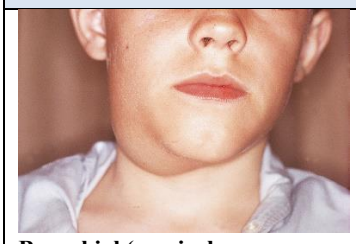
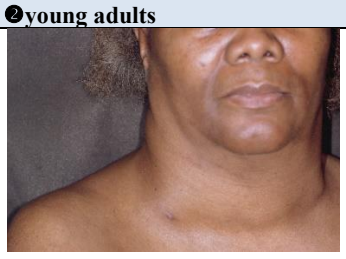
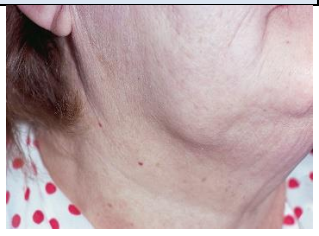
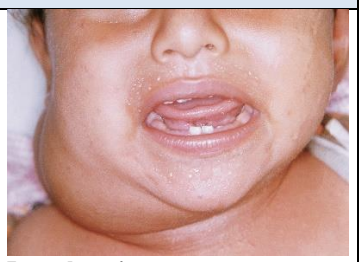
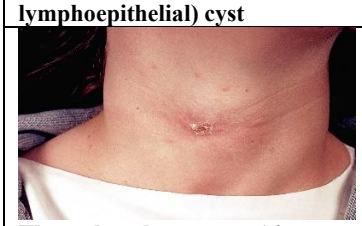
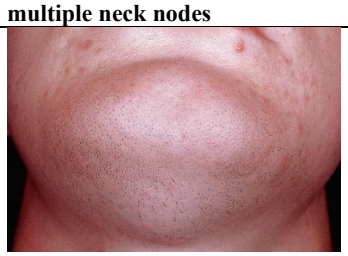
Mixed tumor



Lymphoma

❻Clinical overview➔Neck swellings

Disease	Clinical Features	Cause	Significance
Branchial cyst	❶asymptomatic uninflamed swelling in lateral neck ❷soft or fluctuant ❸children and young adults ❹rare	❶developmental proliferation of epithelial remnants within lymph nodes	❶clinical diagnostic problem
Lymphadenitis➔nonspecific, bacterial, fungal	❶single or multiple painful nodules (lymph nodes) in neck, especially submandibular and jugulodigastric areas ❷usually soft when acute and not fixed to surrounding tissue ❸nonspecific type common	❶any oral inflammatory condition, especially dental abscess ❷oral tuberculosis, syphilis, or deep fungus may affect neck nodes	❶neck disease often reflects oral disease
Metastatic carcinoma to lymph nodes	❶single but may be multiple (rarely bilateral), indurated masses ❷fixed and nonpainful ❸most frequently➔	❶metastatic carcinoma of oral cavity, tongue base, and oropharynx, and less frequent, from distant sites	❶signifies advanced disease with poorer prognosis

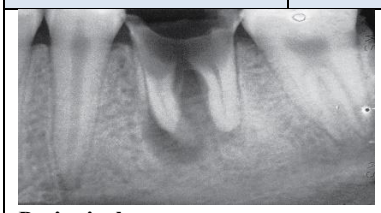
	submandibular & jugulodigastric nodes ❹adults		
Lymphoma	❶single or bilateral swellings in lateral neck ❷indurated, asymptomatic, and often fixed ❸weight loss, night sweats, and fever ❹young adults and adults ❺uncommon	❶unknown	❶after diagnostic biopsy, staging procedures are done ❷prognosis poor to excellent, depending on stage and specific type ❸increased frequency in immunosuppressed patients
Parotid lesion	❶tail of parotid➔neck mass ❷neoplasm➔indurated, asymptomatic, single mass (Warthin's tumor➔may be bilateral) Sjögren's syndrome➔bilateral, diffuse, soft swelling plus sicca complex, affects 1^0 older women infection➔unilateral, diffuse, soft, painful mass	❶neoplasm➔unknown ❷Sjögren's syndrome: autoimmune ❸infection➔viral, bacterial, or fungal ❹metabolic disease➔ diabetes, alcoholism	❶requires diagnosis and treatment
Carotid body tumor	❶firm, movable mass in neck at carotid bifurcation ❷bruit & thrill may apparent ❸adults ❹rarely hereditary	❶neoplastic transformation of carotid body cells ❷SDHD gene mutation	❶morbidity from surgery may be profound because of tumor attachment to carotid sheath
Epidermal cyst	❶elevated nodule in skin of neck (or face) ❷uninflamed & asymptomatic ❸up to several cm in size ❹covered by epidermis and near skin surface ❺common	❶epithelial rest proliferation	❶recurrence not expected ❷more superficially located
Lymphangioma	❶spongy, diffuse, painless mass in dermis ❸may become large ❸lighter than surrounding tissue to red-blue ❹crepitance(劈啪聲) ❺children ❻rare	❶developmental	❶may be disfiguring or cause respiratory distress
Thyroglossal tract cyst	❶midline neck swelling above level of thyroid gland ❷moves when swallowing ❸may develop sinus tract ❹most common developmental cyst of neck	❶failure of complete descent of thyroid tissue from foramen caecum *in utero* with subsequent cyst formation	❶recurrence not uncommon because of tortuous course of cystic lesion
Thyroid gland tumor	❶paramedian swelling in area of thyroid gland ❷firm, asymptomatic ❸uncommon	❶unknown	❶prognosis poor to excellent, depending on stage and histologic type of tumor
Dermoid cyst	❶swelling in mouth floor or midline of neck ❷young adults	❶unknown	❶recurrence not expected
 Branchial (cervical lymphoepithelial) cyst	 Metastatic carcinoma to multiple neck nodes	 Lymphoma, submandibular node	 Lymphangioma
 Thyroglossal tract cyst (sinus tract opening)	 Dermoid cyst		

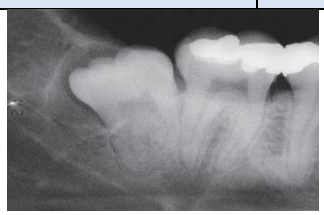
Appendix 2➔jaw lesions

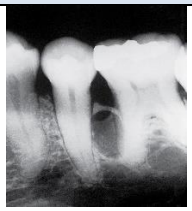
❶Clinical overview➔Cysts of jaws and neck

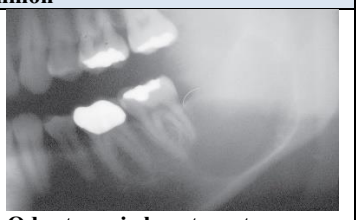
Disease	Clinical Features	Cause	Significance
Periapical (radicular) cyst	❶any age ❷peaks in 3rd-6th decades ❸common ❹apex of any nonvital erupted tooth, especially anterior maxilla	❶well-defined radiolucency at apex of nonvital tooth	❶cannot distinguish radiographically from periapical granuloma ❷develops from inflammatory stimulation of rests of Malassez ❸incomplete enucleation➔ residual cyst ❹chronic process & usually asymptomatic ❺common
Dentigerous cyst	❶young adults ❷associated most commonly with impacted mandibular third molars & maxillary third molars & cuspids	❶well-defined radiolucency around crown of impacted teeth	❶some very large, with rare possibility of pathologic fracture ❷neoplastic transformation of cystic epithelium➔ ameloblastoma & rarely➔ squamous cell or MEC ❸common ❹eruption cyst➔gingival tumescence(腫脹) developing as a dilation of follicular space over crown of erupting tooth
Lateral periodontal cyst	❶adults ❷lateral periodontal membrane, especially mandibular cuspid & premolar area	❶well-defined radiolucency ❷usually unilocular but may be multilocular ❸usually interproximally within the alveolar segment	❶usually asymptomatic ❷associated tooth is vital ❸origin from rests of dental lamina ❹some keratocysts found in a lateral root position ❺gingival cyst of adult is soft tissue counterpart
Gingival cyst of newborn	❶newborn ❷gingival soft tissues	❶usually not apparent on radiograph	❶newborn➔common, multiple, no treatment ❷adult gingival cyst is rare, solitary, & treated by local excision
Odontogenic keratocyst/keratocystic odontogenic tumor	❶any age, especially adults ❷mandibular molar-ramus area favored ❸may be found in position of dentigerous, lateral root, periapical cyst	❶well-defined radiolucency ❷unilocular or multilocular	❶recurrence rate of 5-62% ❷focally infiltrative behavior➔may be ❸may be part of nevoid basal cell carcinoma syndrome (keratocysts, skeletal anomalies, basal cell carcinomas) ❹PTCH gene mutations
Calcifying odontogenic cyst (calcifying cystic odontogenic tumor)	❶any age ❷maxilla favored ❸gingiva➔2nd most common	❶well-defined radiolucency ❷may have opaque foci	❶origin & behavior➔in dispute ❷ghost cell keratinization ❸rare
Glandular odontogenic cyst	❶any age ❷mandible favored	❶well-defined radiolucency	❶recurrence potential
Globulomaxillary lesion	❶any age ❷between roots of maxillary cuspid and lateral incisor	❶well-defined unilocular or multilocular radiolucency	❶teeth are vital ❷asymptomatic ❸anatomic designation ❹not a specific entity➔1 of several different odontogenic cysts/tumors
Nasolabial cyst	❶adults ❷soft tissue of upper lip, lateral to midline	❶no change	❶origin likely from remnants of nasolacrimal duct ❷rare
Nasopalatine canal cyst	❶any age ❷nasopalatine canal or papilla	❶well-defined midline maxillary radiolucency ❷may be oval or heart shaped	❶teeth are vital ❷may be symptomatic if 2^0 infected ❸may be difficult to differentiate from normal canal ❹common
Median mandibular lesion	❶any age ❷midline of mandible	❶well-defined radiolucency	❶teeth are vital ❷asymptomatic ❸represents 1 of several different odontogenic cysts/tumors
Aneurysmal bone cyst	❶2nd decade favored ❷either jaw ❷also long bones and vertebrae	❶radiolucency ❷may be poorly defined ❸may be honeycomb or soap bubble appearance	❶vascular lesion in bone consists of blood-filled sinusoids ❷blood wells up as lesion is entered ❸cause & pathogenesis unknown ❹rare ❺follow-up important
Traumatic (simple) bone cyst	❶second decade favored; mandible favored	❶well-defined radiolucency often extending between roots of teeth	❶dead space in bone without epithelial lining ❷cause & pathogenesis unknown ❸uncommon in oral region ❹can be part of florid osseous dysplasia
Static (Stafne) bone cyst	❶developmental defect ❷mandibular molar area below alveolar canal	❶well-defined oval radiolucency ❷not change with time	❶lingual depression of mandible ❷filled with salivary gland or other soft tissue from mouth floor

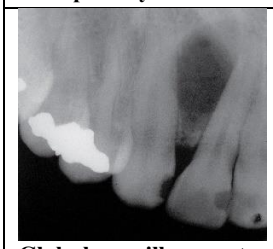
			❸asymptomatic ❹incidental finding➔no biopsy or treatment ❺uncommon
focal osteoporotic bone marrow defect	❶adults ❷mandible favored	❶radiolucency ❷often in edentulous areas	❶hematopoietic marrow ❷probably unusual bone healing ❸must differentiate from other ❹more significant lesions ❺uncommon

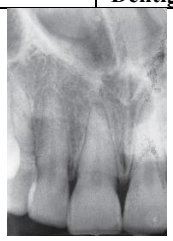

Periapical cyst

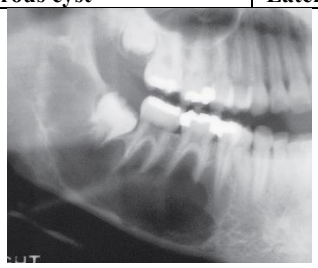

Dentigerous cyst

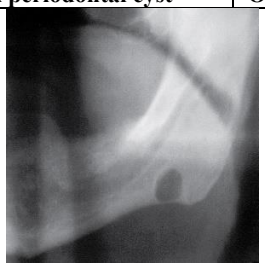

Lateral periodontal cyst

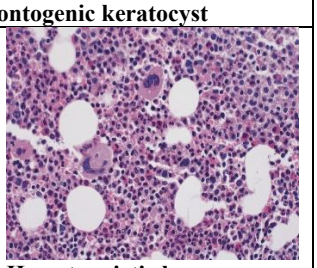

Odontogenic keratocyst


Globulomaxillary cyst


Nasopalatine canal cyst


Traumatic bone cyst

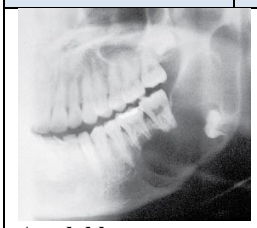

Static bone cyst

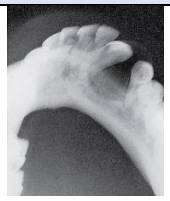

Hematopoietic bone marrow defect

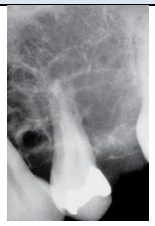
❷Clinical overview➔Odontogenic tumors

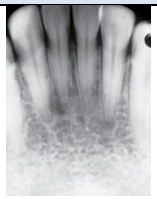
Disease	Clinical Features	Cause	Significance
Ameloblastoma	❶4th and 5th decades ❷mandibular molar-ramus area most common site	❶radiolucent ❷usually well circumscribed ❸unilocular or multilocular	❶locally infiltrative behavior ❷rarely metastasizes (usually to lung) ❸asymptomatic ❹uncommon ❺mandible associated with BRAF V600E mutations & maxilla associated with SMO mutations
Squamous odontogenic tumor	❶mean age of 40 years ❷2nd-7th decades alveolar process ❸anterior more than posterior	❶radiolucency ❷well defined	❶conservative therapy ❷few recurrences ❸rare
Calcifying epithelial odontogenic tumor (Pindborg tumor)	❶mean age around 40 years ❷2nd through 10th decade ❸mandibular molar-ramus area favored	❶radiolucent with/without opaque foci ❷usually well circumscribed ❸unilocular or multilocular	❶behavior and prognosis➔similar to ameloblastoma ❷rare
Clear cell odontogenic tumor	❶7th decade ❷mandible, maxilla	❶radiolucency ❷well defined	❶rare
Adenomatoid odontogenic tumor	❶2nd decade; anterior jaws ❷female preference	❶well-defined radiolucency ❷may have opaque foci	❶usually associated with crown of impacted tooth ❷no symptoms
Dentinogenic ghost cell tumor	❶any age ❷maxilla favored	❶well-defined radiolucency ❷may have opaque foci	❶origin and behavior are in dispute ❷ghost cell keratinization ❸rare
Odontogenic myxoma	❶mean age of about 30 years; ❷ages 10-50 years ❸any area of jaws	❶multilocular or honeycomb radiolucent lesion ❷may be poorly defined peripherally	❶may exhibit aggressive behavior ❷no symptoms ❸uncommon ❹recurrence not uncommon
Central odontogenic fibroma	❶any age ❷any area of jaws	❶radiolucency ❷usually multilocular	❶2 microscopic subtypes➔same benign clinical behavior ❷differentiate desmoplastic fibroma
Cementifying fibroma	❶4th and 5th decades ❷posterior mandible	❶well-defined radiolucency ❷may have radiopaque foci	❶asymptomatic ❷grows by local expansion ❸recurrence unlikely ❹rare
Cementoblastoma	❶2nd and 3rd decades ❷root of posterior tooth ❸mandible more than maxilla	❶radiopaque lesion ❷attached to and replaces root ❸opaque spicules radiate from central area	❶may cause cortical expansion ❷tooth and lesion removed together ❸no symptoms ❹rare
Periapical cemento-osseous dysplasia	❶5th decade ❷mandible, especially apices of anterior teeth ❸usually > 1 tooth affected	❶starts as periapical radiolucencies➔become opaque in months to years	❶may be a reactive process ❷always associated with vital teeth ❸requires no treatment ❹asymptomatic

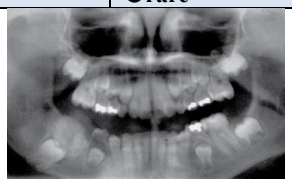
			❺common ❻rare variant➔florid cemento-osseous dysplasia severe form➔affect 1-4 quadrants & may have chronic osteomyelitis & traumatic bone cysts
Odontoma	❶2nd decade ❷any location, especially anterior mandible and maxilla	❶radiopaque ❷compound type➔tooth shapes apparent ❸complex type➔uniform radiopaque mass	❶may block permanent tooth eruption ❷complex type rarely causes cortical expansion, no recurrence ❸compound type➔many miniatures teeth ❹complex type➔conglomeration of enamel and dentin ❺hamartoma rather than neoplasm ❻common
Ameloblastic fibroma and ameloblastic fibro-odontoma	❶1st and 2nd decades ❷mandibular molar-ramus area ❸often in a dentigerous relationship with tooth	❶well-defined radiolucency ❷may be multilocular & large ❸fibro-odontoma may have associated opaque mass representing an odontoma	❶well encapsulated ❷recurrence not expected ❸no symptoms ❹if odontoma present➔called ameloblastic fibro-odontoma ❺rare

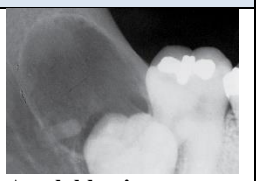

Ameloblastoma


Adenomatoid odontogenic tumor


Odontogenic myxoma


Periapical cemento-osseous dysplasia

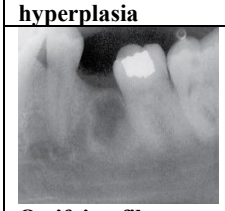

Odontoma

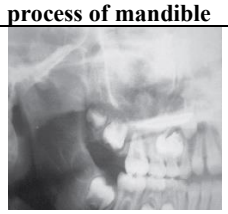

Ameloblastic fibroodontoma

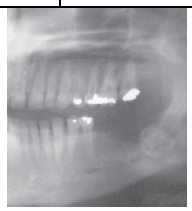
❸Clinical overview➔Benign nonodontogenic tumors

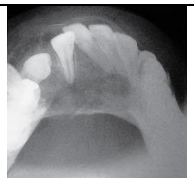
Disease	Clinical Features	Cause	Significance
Ossifying fibroma	❶3rd and fourth decades ❷body of mandible favored	❶well-defined radiolucency ❷may have radiopaque foci	❶slow growing and asymptomatic ❷may be indistinguishable from cementifying fibroma ❸does not recur ❹microscopy similar to that of fibrous dysplasia ❺uncommon
Fibrous dysplasia	❶1st and 2nd decades ❷maxilla favored	❶poorly defined radiographic mass ❷diffuse opacification➔ "ground glass"	❶slow growing and asymptomatic ❷causes cortical expansion ❸may cease growing after puberty ❹cosmetic problem treated by recontouring ❺variants➔monostotic(one bone affected) ❻polyostotic➔>1 bone affected ❼Albright's syndrome➔fibrous dysplasia plus café-au-lait skin macules and endocrine abnormalities (precocious puberty in females) ❽Jaffe-Lichtenstein syndrome➔multiple bone lesions of fibrous dysplasia & skin pigmentations
Osteoblastoma	❶2nd decade ❷either jaw	❶well-defined, lucent to opaque lesion	❶diagnostic feature of pain ❷determination by microscopy often difficult ❸may confuse with osteosarcoma ❹recurrence not expected ❺rare
Chondroma	❶any age ❷any location, especially anterior maxilla and posterior mandible	❶relative radiolucency ❷may have opacities	❶may be difficult to separate microscopically from well-differentiated chondrosarcoma ❷rare
Osteoma	❶any age ❷either jaw	❶well defined	❶asymptomatic ❷may be part of Gardner's syndrome (osteomas, intestinal polyps, cysts and fibrous lesions of skin, supernumerary teeth) ❸rare
Central giant cell granuloma	❶children & young adults ❷either jaw	❶usually well-defined radiolucency ❷may be multilocular or, less frequently, unilocular	❶may exhibit aggressive behavior ❷low recurrence rate ❸asymptomatic ❹uncommon ❺rule out hyperparathyroidism
Hemangioma of bone	❶young adults ❷either jaw	❶radiolucent lesion ❷may have a honeycomb pattern or may be multilocular	❶hemorrhage is significant complication with treatment ❷asymptomatic ❸rare

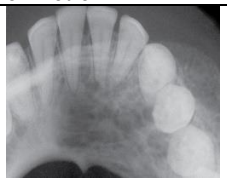
Langerhans cell histiocytosis	❶children & young adults ❷any bone	❶single/multiple radiolucent lesions ❷some➔punch out ❸lesions around root apices ➔resembling floating teeth	❶3 variants➔①Letterer-Siwe syndrome (acute disseminated)➔organs & bone affected, infants, usually fatal ②Hand-Schüller-Christian syndrome (chronic disseminated)➔bone lesions, exophthalmos, diabetes insipidus, & organ lesions; children, fair prognosis ③eosinophilic granuloma (chronic localized)➔bone lesions only, children & adults, good prognosis; surgery, radiation, or chemotherapy ❷cause unknown
Tori and exostoses	❶adults; palate, lingual mandible, and buccal aspect of alveolar bone	❶may appear as radiopacities when large	❶torus palatinus➔25% of population, torus mandibularis➔10% ❷cause unknown ❸little significance
Coronoid hyperplasia	Young adults; coronoid process of mandible	Radiopaque enlargement	Cause unknown; may affect jaw function/range of motion

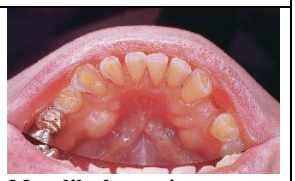

Ossifying fibroma


Fibrous dysplasia


Osteoblastoma

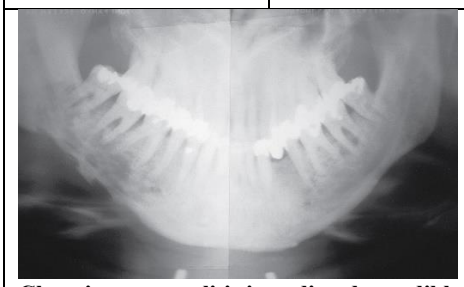

Central giant cell granuloma

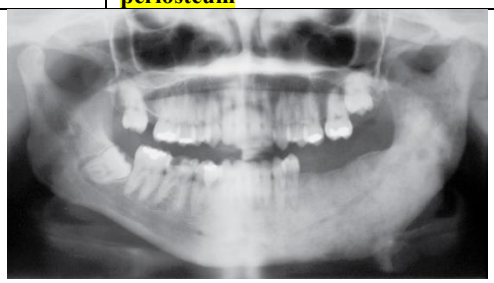

Hemangioma

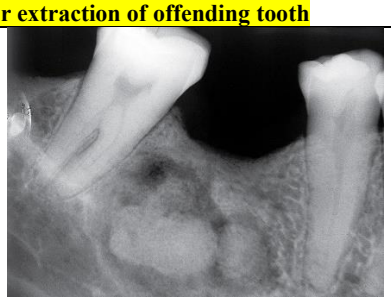

Mandibular tori (exostoses)

❹Clinical overview➔Inflammatory jaw lesions

Disease	Clinical Features	Cause	Significance
Acute osteomyelitis	❶any age ❷mandible favored	❶little radiographic change early ❷after 1-2 weeks➔diffuse radiolucency	❶pain or paresthesia may be present ❷pus if due to *Staphylococcus* infection ❸uncommon in severe form ❹most frequently caused by extension of periapical infection
Chronic osteomyelitis	❶any age ❷mandible favored	❶focal or diffuse ❷lucent with sclerotic foci➔moth-eaten pattern ❸focal sclerotic type➔well-defined opacification ❹diffuse sclerotic type➔diffuse opacification ❺Garré's type➔onion-skin periosteum	❶asymptomatic (may be painful) ❷most cases related to chronic inflammation in bone of dental origin ❸many cases not treated ❹nonvital teeth➔extracted or root canals filled ❺common ❻Garré's type treated by endodontics or extraction of offending tooth


Chronic osteomyelitis in radiated mandible

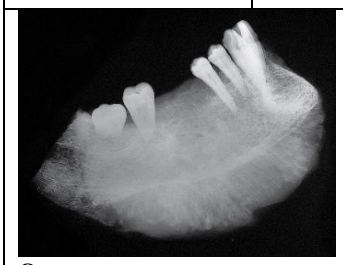

Diffuse sclerosing osteomyelitis

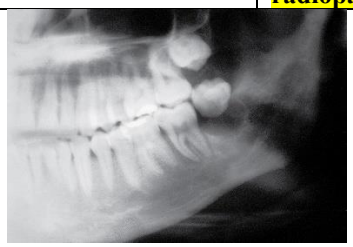

Focal sclerosing osteitis

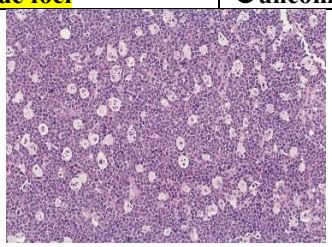
❺Clinical overview➔Malignancies of the jaws

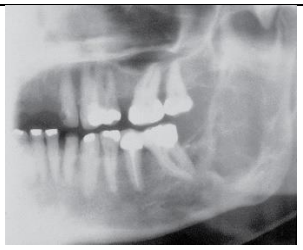
Disease	Clinical Features	Cause	Significance
Osteosarcoma	❶3rd and 4th decades ❷mandible or maxilla juxtacortical subtype arises from periosteum	❶poorly defined radiolucency, often with spicules of opaque material ❷sunburst pattern➔may be ❸juxtacortical lesion➔ radiodense mass on periosteum	❶swelling, pain, and paresthesia➔ diagnostic features ❷may have vertical teeth mobility and uniformly widened periodontal ligament space ❸prognosis fair to poor ❹ juxtacortical lesion➔good prognosis
Chondrosarcoma	❶adulthood and old age maxilla favored slightly	❶poorly defined, lucent to moderately opaque	❶swelling, pain, or paresthesia➔may be ❷prognosis fair to poor (mandible better) ❸misdiagnosed➔benign cartilage lesion ❹rare
Burkitt's lymphoma	❶children ❷mandible or maxilla	❶diffuse radiolucency	❶malignancy of B lymphocytes linked to specific chromosome translocation ❷frequent but not universal EBV infection ❸pain, mobile tooth, paresthesia➔may be ❹prognosis fair ❺rare in United States

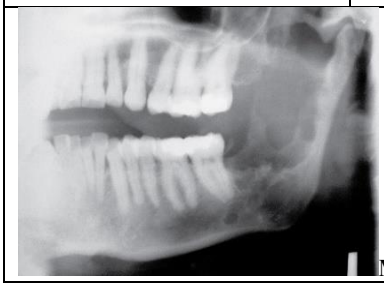
Ewing's sarcoma	❶children and young adults ❷mandible favored	❶diffuse radiolucency ❷poorly defined ❸periosteal onion-skin reaction➔may be ❹ multilocular➔may be	❶swelling, pain, or paresthesia➔may be ❷prognosis is poor ❸unknown cellular origin ❹ EWS-FLI1 genes translocation t(11;22) ❺rare
Multiple myeloma	❶adults ❷mandible favored	❶well-defined radiolucencies ➔"punched-out" lesions ❷some lesions diffuse	❶swelling, pain, or numbness➔may be ❷Bence Jones protein in urine➔majority ❸jaw lesion➔rare ❹prognosis poor ❺solitary lesion eventually➔disseminated
Metastatic carcinoma	❶adults ❷mandible favored ❸soft tissue mass➔occasion	❶ill-defined, destructive radiolucency ❷multilocular➔may be ❸prostate, breast, lung➔ radiopaque foci	❶pain or paresthesia➔common ❷origin is most likely from malignancy of breast, kidney, lung, colon, prostate, or thyroid ❸uncommon

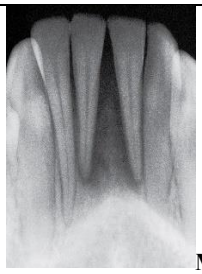

Osteosarcoma


Postradiation chondrosarcoma, third molar area


Burkitt's lymphoma ("starry sky" microscopy)


Multiple myeloma, mandibular ramus

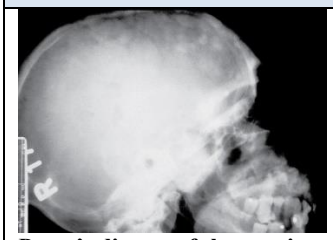

Metastatic breast cancer, ramus


Metastatic osteosarcoma to anterior mandible

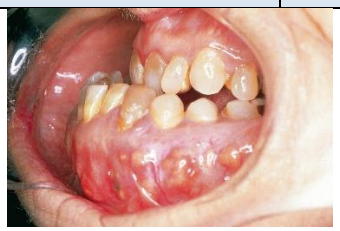
❻Clinical overview➔Metabolic and genetic diseases

Disease	Clinical Features	Cause	Significance
Paget's disease	❶age over 40 years ❷maxilla favored ❸bilateral and symmetric ❹affects entire bone	❶diffuse radiolucent to radiopaque bone change ❷opaque lesion➔cotton wool ❸hypercementosis, loss of lamina dura, obliteration of periodontal ligament space, & root resorption➔ common	❶pain, deafness, blindness, and headache caused by bone changes ❷initial complaint may be ill-fitting denture ❸diastemas may develop ❹complications of hemorrhage early, infection and fracture late ❺serum alkaline phosphatase elevated ❻cause unknown but affects bone metabolism
Hyperparathyroidism	❶any age ❷mandible favored	❶usually well-defined radiolucency(ies) ❷may be multilocular ❸minority➔loss of lamina dura	❶usually asymptomatic ❷micro. identical to central giant cell granuloma ❸serum calcium level elevated ❹most caused by parathyroid adenoma ❺rare
Acromegaly	❶adults (after closure of epiphyses) ❷mandible ❸uniform, bilateral ❹coarse facial features	❶large jaw ❷splayed teeth	❶excess production of growth hormone after closure of epiphyses (condylar growth becomes active) ❷prognathism, diastemas may appear ❸rare
Infantile cortical hyperostosis	❶infants ❷mandible & other bones of skeleton	❶cortical thickening/ sclerosis	❶cause unknown ❷self-limited ❸treatment is supportive
Phantom bone disease	❶young adults ❷mandible > maxilla	❶gradual development of radiolucency of entire bone	❶cause unknown ❷no treatment
Cherubism	❶children ❷mandible favored ❸uniform, bilateral	❷bilateral multilocular radiolucencies	❶autosomal-dominant inheritance ❷ SH3BP2 gene mutation ❸cherub-ke face ❹micro➔similar to central giant cell granuloma ❺process stabilizes after puberty ❻rare

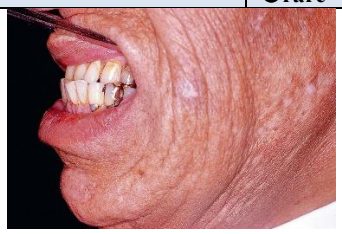
Osteopetrosis	**❶infantile and adult forms** **❷both jaws and skull involved**	**❶diffuse, homogeneous, & symmetric opacification** **❷may cause arrested root development and delayed eruption**	**❶dominant form➔infantile, recessive (severe), and adult** **❷intermediate form also recessive but milder presentation** **❸inhibition of bone resorption** **❹can develop anemia, blindness, and deafness** **❺complication➔osteomyelitis and fracture** **❻rare**



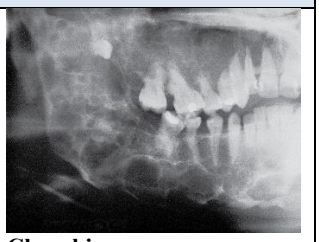
Paget's disease of the cranium



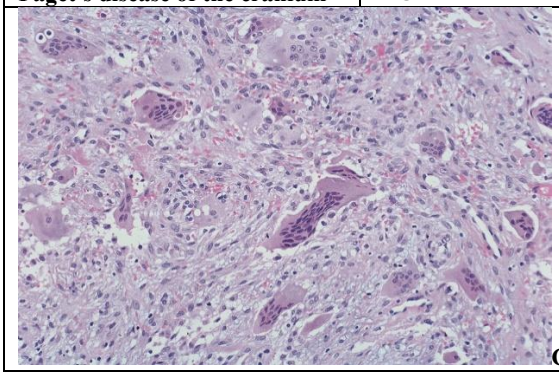
Paget's disease of the mandible



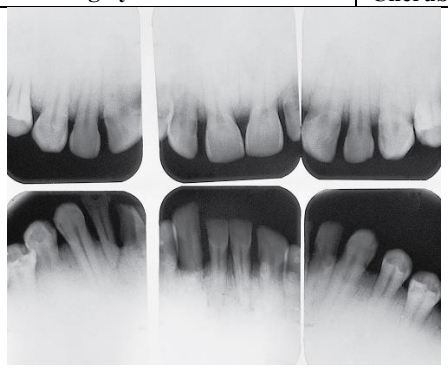
Acromegaly



Cherubism



Cherubism



Osteopetrosis

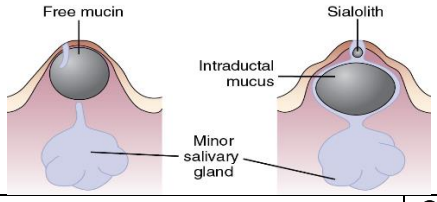
Appendix 3➔Short Handout for Quick Revision

Salivary gland diseases

1➲Mucus Retention Cyst (Obstructive Sialadenitis)

❶Etiology

①Most are caused by obstruction by sialolith
②Stones form by accumulation of calcium salts around a nidus within salivary duct
③Nidus consists of desquamated cells, inspissated mucin, and/or bacteria



(右圖)mucus retention cyst➔sialolith blockage➔mucin retained in excretory duct
(左圖)mucus extravasation phenomenon ➔free mucin in submucosa

❷Clinical features

①Obstruction causes sialadenitis, but not xerostomia
②Adults, male/female = 2: 1, unilateral
③Submandibular gland up to 80%, parotid 20%, sublingual & minor glands 1-15%
④Produce intermittent pain and swelling
⑤Sialoliths in minor glands most commonly found in upper lip
⑥Typically asymptomatic
⑦Stones may be detected by x-ray in major glands

❸Treatment

①Minor glands➔remove retention cyst and associated salivary gland
②Major glands
(1)remove retention cyst and associated salivary gland
(2)remove stone through duct incision
(3)massaging stone through duct orifice

2➲Necrotizing Sialometaplasia

❶Etiology➔Ischemia of minor salivary glands? Trauma? Other?

❷Clinical appearance
①Junction of hard and soft palates
②Unilateral or bilateral
③Swelling, erythema, tenderness, followed by ulceration

❸Clinical differential diagnosis➔Squamous cell carcinoma, salivary gland tumor, chronic infection, traumatic ulcer

❹Treatment
①Incisional biopsy to establish diagnosis
②Observation, because lesion is self-limiting & heals spontaneously in 6-10 weeks

3➲Sarcoidosis

❶Etiology➔Unknown, atypical mycobacteria?

❷Clinical features
①Primary lesion in perihilar lymph nodes; also liver, skin, bone
②Oral lesions in mucosa (nodules) or salivary glands (swelling)
③Ocular and parotid disease known as Heerfordt's syndrome
④May lead to xerostomia

❸Diagnosis➔Biopsy (shows noncaseating granulomas), chest x-ray, serum angiotensin-converting enzyme (ACE) level

❹Treatment
①No specific treatment
②Corticosteroids often prescribed, or occasionally other immunomodulating agents

4➲Causes of Parotid Gland Enlargement

❶Sjögren's syndrome	❽Sarcoidosis (uveoparotid fever or Heerfordt's syndrome)
❷Adenomas and carcinomas	❾Other bacterial infections
❸Lymphoma	❿Metabolic conditions
❹Bacterial infections	⓫Malnutrition, including anorexia and bulimia
❺Mumps	⓬Diabetes mellitus
❻Human immunodeficiency virus (HIV) disease	⓭Chronic alcoholism
❼Tuberculosis	

5➲Sjögren's syndrome

❶Etiology
①Systemic autoimmune disease
②Lymphocyte-mediated destruction of salivary parenchyma

❷Diagnosis➔Requires 2 of the following 3 features (①②③)
①positive serum anti-SSA* and/or anti-SSB or positive rheumatoid factor and antinuclear antibody titer >1:320
②ocular staining score by lissamine green >3
③presence of focal lymphocytic sialadenitis with a focus score >1 focus/4 mm^2 in labial salivary gland biopsy

❸Treatment and prognosis
①Symptomatic treatment
②Artificial saliva and tears
③Scrupulous oral hygiene necessary to prevent xerostomia-associated dental caries
④Chronic disease with risk of lymphoma development (10%)

*SSA➔Sjögren's syndrome-A; SSB➔Sjögren's syndrome-B

6➲Sjögren's Syndrome➔Potential Organopathy

❶Skin➔①Dryness (reduced sweat production) ②Scleroderma ③Lupus erythematosus
❷Salivary and lacrimal glands➔①Enlargement ②Xerostomia, dental caries, candidiasis ③Keratoconjunctivitis sicca
❸Gastrointestinal tract➔①Biliary cirrhosis ②Hepatitis
❹Hematopoietic system➔①Lymphoma ②Anemia ③leukopenia
❺Cardiovascular system➔Vasculitis
❻Musculoskeletal system➔①Rheumatoid arthritis ②Myositis
❼Respiratory tract➔①Rhinitis, pharyngitis ②Obstructive pulmonary disease

7➲Causes of Xerostomia

❶Medications	❷Autoimmune or systemic diseases
①Analgesics	①Sjögren's syndrome
②Opioids	②Primary biliary cirrhosis
③Anticholinergic drugs; Antihistamines; Antidepressants	③Wegener's granulomatosis
④Selective serotonin reuptake inhibitors (SSRIs)	④Sarcoidosis
⑤Tricyclic and heterocyclic antidepressants	⑤Scleroderma
⑥Atypical antidepressants	❸Other conditions

⑦Antihypertensive agents ⑧Diuretics ⑨Muscle relaxants ⑩Sedatives/anxiolytics	①Local radiation therapy ②Type 1 or 2 diabetes ③Radioactive iodine treatment ④Human immunodeficiency virus (HIV)/AIDS ⑤Anxiety/depression

8➲Management of Xerostomia	
❶Palliations	❷Prescription Strategies
①Elimination of alcohol and caffeine consumption ②Elimination of alcohol-containing mouth rinses ③Gustatory salivary stimulation ④Sugarless candies, gum ⑤Moist sugar-free or complex carbohydrate foods ⑥Oral lubricants ⑦Carboxymethylcellulose- or hydroxymethylcellulose-based products ⑧Other polymer-based rinses ⑨Scrupulous oral hygiene	①Cholinergic agonists ②Pilocarpine ③Cevimeline ④Acupuncture

9➲Diseases Associated with Taste Disturbances	
❶Bell's palsy ❷Cancer/oral➔head and neck irradiation ❸Candidiasis (thrush)➔oral ❹Diabetes mellitus with associated peripheral neuropathy ❺Gingivitis, periodontitis ❻Hypothyroidism ❼Multiple sclerosis	❽Parkinsonism ❾Pernicious anemia (vitamin B 12 related) ❿Renal failure/hemodialysis ⓫Sjögren's syndrome ⓬Upper respiratory disturbances and infection/influenza ⓭Zinc deficiency

10➲Drug Classes and Agents Associated with Taste Disturbances	
❶Angiotensin-converting enzyme (ACE) inhibitors ❷Calcium antagonists ❸Diuretics ❹Antiarrhythmics ❺Antithyroid agents ❻Antidiabetics ❼Antihistamines ❽Antiasthmatics	❾Antidepressants ❿Antipsychotics ⓫Antineoplastics ⓬Chelating agents ⓭Neuromuscular/antiseizure drugs ⓮Nitroglycerin ⓯Opioids

11➲Anatomic Origins of Halitosis
❶Oral cavity➔①Poor oral hygiene/prosthesis hygiene ②Posterior dorsal surface of tongue
❷Periodontal pathogens➔①Porphyromonas gingivalis ②Prevotella intermedia ③Fusobacterium nucleatum ④Bacteroides forsythensis ⑤Treponema denticola
❸Oral infection (primary and secondary)➔①Candidiasis ②Pericoronitis ③Postextraction alveolitis
❹Oral ulcerative and erosive diseases
❺Dietary considerations➔①Volatile sulfur-containing foods (onions, garlic, others) ②Hydrogen sulfide ③Dimethyl disulfide ④Methyl mercaptan
❻Xerostomia
❼Nasal cavity➔①Nasal infection ②Sinusitis ③Nasal polyps and nasal foreign bodies
❽Other airflow obstruction➔①Tonsils ②Infection ③Tonsilliths ④Neoplasia
❾Other sites➔①Bronchial and pulmonary infection ②Renal failure

12➲Management of Halitosis of Oral Origin
❶Proper oral and prosthesis hygiene
❷Treatment of existing dental and periodontal disease
❸Daily gentle scraping of the posterior dorsum of the tongue
❹Avoidance of foods containing sulfide compounds
❺Daily use of mouth rinses with antimicrobial properties

13➲Benign Salivary Gland Tumors	
❶pleomorphic adenoma (mixed tumor)	❸Sebaceous adenoma ❹Ductal papilloma ❺Inverted ductal papilloma ❻Sialadenoma papilliferum ❼Intraductal papilloma
❷Monomorphic adenomas ①Basal cell adenomas➔solid, tubular, trabecular, membranous ②Canalicular adenoma ③Myoepithelioma ④Oncocytoma ⑤Warthin's tumor and papillary cystadenoma	

14➲Salivary Gland Tumors		
	Frequency, %	% Malignant
Parotid glands	65	25
Submandibular glands	10	40
Sublingual glands	<1	90
Minor salivary glands	25	50

15➲Pleomorphic Adenoma
❶Clinical features ①Adults; men and women affected equally ②Asymptomatic submucosal mass ③Sites➔palate > upper lip > buccal mucosa > other sites
❷Histopathology➔Encapsulated; variable glandular patterns; epithelial and myoepithelial differentiation; no mitoses
❸Treatment➔Excision; occasional recurrence in major glands

16➲Malignant Salivary Gland Tumors	
❶Mucoepidermoid carcinoma	❽Epimyoepithelial carcinoma
❷Polymorphous (low-grade) adenocarcinoma	❾Salivary duct carcinoma
❸Adenoid cystic carcinoma	❿Basal cell adenocarcinoma
❹Clear cell carcinoma	⓫Oncocytic adenocarcinoma
❺Acinic cell carcinoma	⓬Sebaceous adenocarcinoma
❻Adenocarcinoma NOS (Not otherwise specified)➔Rare, predominantly parotid tumors	⓭Mammary analog secretory carcinoma
❼Carcinoma ex-mixed tumor/malignant mixed tumor	⓮Squamous cell carcinoma

17➲Malignant Salivary Gland Tumors➔Biological Classification	
❶Low-grade malignancies ①Mucoepidermoid carcinoma (low grade) ②Polymorphous low-grade adenocarcinoma ③Acinic cell carcinoma (low to intermediate grade) ④Clear cell carcinoma ⑤Basal cell adenocarcinoma	❸High-grade malignancies ①Mucoepidermoid carcinoma (high grade) ②Adenoid cystic carcinoma ③Carcinoma ex-mixed tumor ④Salivary duct carcinoma ⑤Squamous cell carcinoma ⑥Oncocytic adenocarcinoma
❷Intermediate-grade malignancies ①Mucoepidermoid carcinoma (intermediate grade) ②Epimyoepithelial carcinoma ③Sebaceous adenocarcinoma ④Mammary analog secretory carcinoma	

18➲Malignant Minor Salivary Gland Tumors
❶Clinical features ①Adults; men and women affected equally ②Mass or ulcerated mass ③Asymptomatic in early stages ④Sites➔palate > buccal mucosa > retromolar pad > upper lip > tongue ⑤Low-grade mucoepidermoid carcinoma > polymorphous low-grade adenocarcinoma > adenoid cystic carcinoma
❷Histopathology➔Highly variable but characteristic patterns; infiltrative margins; rare mitoses; little pleomorphism
❸Treatment and prognosis ①Wide excision; radiation added for problematic cases ②Ranges from low- to high-grade behavior (adenoid cystic carcinoma has worst long-term prognosis) >➔More frequently affected than

19➲Comparison of Salivary Gland Tumors		
	Benign	Malignant
Growth rate	Slow	Varied, usually rapid
Ulceration	No	Yes
Fixation	No	Yes
Facial nerve palsy	No	Yes
Encapsulated	Yes	No
Natural history	Slow growth	Slow to rapid growth
Metastasis	No	Yes
Treatment	Local excision	Surgery with or without radiation

20➲Mucoepidermoid Carcinoma
❶Most common malignancy of salivary glands
❷Most common salivary malignancy in children
❸Palate, most common intraoral site; rare primary intrabony (jaws) tumors
❹Low-, intermediate-, and high-grade lesions
❺More ducts and mucous cells in low-grade lesions
❻Most oral lesions of low grade
❼Low-grade lesions➔excellent prognosis (>95% five-year survival)
❽High-grade lesions➔fair prognosis (<40% five-year survival)

21➲Mucoepidermoid Carcinoma➔Histologic		
	Low Grade (Good Prognosis)	High Grade (Fair Prognosis)
Cell type	Numerous mucous cells and intermediate cells; few epidermoid cells	Mainly epidermoid cells and few mucous cells; looks like squamous cell carcinoma
Microcystic spaces	Large and numerous cysts; >20% of area	Few cysts; <20% of area; mainly solid tumor
Cytologic atypia	None to little	Abundant
Necrosis	Absent	Present
Perineural invasion	Absent	Present

22➲Polymorphous (Low-Grade) Adenocarcinoma
❶Malignancy of minor salivary gland; second in frequency to mucoepidermoid carcinoma
❷Presents as asymptomatic submucosal mass
❸Polymorphous microscopic pattern (most cases show small nerve invasion but no effect on prognosis)
❹Low-grade malignancy; good prognosis
❺Treatment by wide excision; recurrence rate,10%
❻Occasional metastasis
❼Regional nodes <10%
❽Rare to lungs

23➲Polymorphous (Low-Grade) Adenocarcinoma➔Location	
❶Minor salivary glands ①45% palate ②20% lips ③23% buccal mucosa ④10% retromolar mucosa ⑤1% floor of mouth ⑥1% tongue	❷Parotid gland➔Arising out of malignant transformation of a pleomorphic adenoma
	❸Submandibular gland➔Rare
	❹Nasal/nasopharynx➔Few cases reported

24➲Adenoid Cystic Carcinoma	
❶High-grade salivary gland malignancy	❹Spread through perineural spaces
❷Adults; palatal mass/ulceration	❺Local recurrence and metastasis; lung > nodes
❸Cribriform microscopic pattern	❻5-year survival 70%; 15-year survival 10%

25➲Salivary Gland Clear Cell Tumors	
❶Clear cell tumors ①Clear cell carcinoma ②Epimyoepithelial carcinoma	❷Clear cell change/artifact in other tumors ①Adenoid cystic carcinoma ②Oncocytoma ③Acinic cell carcinoma ④Mucoepidermoid carcinoma

Appendix 3➔Short Handout for Quick Revision

Odontogenic tumors

1➲Biological Classification of Odontogenic Tumors	
❶Benign, no recurrence potential	❷Benign, some recurrence potential
①Adenomatoid odontogenic tumor ②Squamous odontogenic tumor ③Cementoblastoma ④Odontoma	①Cystic ameloblastoma ②Calcifying epithelial odontogenic tumor ③Central odontogenic fibroma ④Ameloblastic fibroma and fibro-odontoma
❸Benign aggressive	❹Malignant
①Ameloblastoma ②Clear cell odontogenic tumor ③Odontogenic ghost cell tumor ④Odontogenic myxoma ⑤Odontoameloblastoma	①Malignant ameloblastoma ②Ameloblastic carcinoma ③Primary intraosseous carcinoma ④Odontogenic ghost cell carcinoma ⑤Ameloblastic fibrosarcoma

2➲Ameloblastoma➔Pathogenetic Mechanisms	
❶Cell cycle-related factors	❷Interface factors (invasive properties enhanced)
①Low proliferation rate; few cells in cell cycle based on low Ki-67 expression ②Antiapoptotic proteins expressed; overexpression of Bcl-2 & Bcl-x L ③Overexpression of EGFR ④Some positive p53 staining; probably wild-type protein inactivated by MDM2 binding ⑤TNFα expression ⑥Mutations in the BRAF (MAP kinase signaling) and SMO (hedgehog signaling) genes	①Enhanced osteolysis by RANKL ②Altered laminin 5 at interface ③Expression of FGF and interleukins (1 and 6) ④Overexpression of proteinases (MMPs 9 & 20; EMSP1)

EMSP1, Enamel matrix serine proteinase; RANKL, receptor activator of nuclear factor-kB ligand; FGF, fibroblast growth factor; MDM2, murine double minute 2; MMPs, matrix metalloproteinases

3➲Ameloblastoma➔Clinical Features	
❶Benign, aggressive tumor that is invasive and persistent	❻Always radiolucent; radiolucency with radiopacity (some)
❷Sometimes called solid or multicystic ameloblastoma	❼Unilocular or multilocular
❸Adults most commonly affected	❽Slow-growing and typically well defined radiographically
❹Broad age range; mean age, 40 years	❾Treated by surgical excision to resection
❺Mandibular molar-ramus most commonly affected site	❿Recurrence rate higher with conservative treatment

4➲Ameloblastoma➔Biological Subtypes	
❶(Solid) ameloblastoma	❹Malignant ameloblastoma
❷Cystic (unicystic) ameloblastoma	❺Ameloblastic carcinoma
❸Peripheral ameloblastoma	

5➲Peripheral ameloblastoma	
❶Ameloblastoma developing in gingival soft tissue	❺Presents as a painless gingival mass
❷May originate from gingival epithelium	❻Mandibular gingiva > maxillary gingival
❸Typically does not invade underlying bone	❼Treated with local excision; rarely recurs
❹Older adults most commonly affected	>➔More frequently affected than

6➲Cystic (Unicystic) ameloblastoma	
❶Clinical features➔Multilocularity and cortical perforation (25% of cases)	❸Microscopic patterns ①luminal growth ②intraluminal growth ③mural invasion
❷Histopathology ①Thin, nonkeratinized epithelium ②Basal palisading ③Spongiosis ④Epithelial invaginations(內陷) ⑤Subepithelial hyalinization	❹Treatment ①Excision ②Curettage; recurrence rate as high as 40% (seen as late as 9 years after surgery)

7➲Ameloblastoma➔Histologic Subtypes/Patterns	
❶All subtypes mimic enamel organ	❹No clinical significance to subtypes
❷Peripheral palisades and budding	❺Microscopic➔desmoplastic, follicular, plexiform, granular cell, basaloid
❸No hard tissue formation	

8➲Calcifying Epithelial Odontogenic Tumor (Pindborg Tumor)	
❶Histogenesis➔Unknown; may be dental lamina or stratum intermedium	❹Histopathology ①Epithelioid strands/nests/sheets ②Amyloid and calcification ③Rare clear cell variant ④Rare Langerhans cell rich variant
❷Clinical features ①Adults 30 to 50 years old ②Posterior mandible favored	
❸Behavior➔Benign; recurrence potential (<20%)	

9➲Adenomatoid Odontogenic Tumor

❶Epithelial odontogenic hamartoma containing pseudoducts and enameloid
❷Tumor of "two-thirds"➔maxilla, females, anterior jaws, crown of impacted tooth
❸Teenagers most commonly affected; rarely seen over the age of 30 years
❹Lucent and lucent-opaque patterns
❺Treatment by enucleation; no recurrences

10➲Odontogenic Lesions that may have Opaque FOCI	
❶Calcifying epithelial odontogenic tumor	❺Ameloblastic fibro-odontoma
❷Adenomatoid odontogenic tumor	❻Odontoma
❸Dentinogenic ghost cell tumor (calcifying odontogenic tumor)	❼Odontoameloblastoma
❹Cementifying fibroma	

11➲Clear Cell Odontogenic Tumor	
❶Histogenesis➔Unknown; probably odontogenic	❹Behavior➔Recurrence and metastasis (neck nodes/lung)
❷Clinical features ①Age over 60 years; women affected more often than men ②Either jaw ③Occasionally painful	❺Microscopic differential diagnosis ①Calcifying epithelial odontogenic tumor ②Mucoepidermoid carcinoma ③Renal cell carcinoma
❸Histopathology ①Nests/cords of clear cells, some palisades ②Some glycogen; mucin negative	

12➲Odontogenic Myxoma	
❶Histogenesis➔Periodontal ligament or dental pulp	❹Microscopic differential diagnosis ①Hyperplastic follicular sac and dental pulp ②Odontogenic fibroma ③Desmoplastic fibroma
❷Clinical features ①Adults (median age, about 30 years) ②Either jaw	
❸Histopathology ①Bland myxoid ②Rare epithelial rests ③Variable amounts of collagen	❺Behavior ①Recurrences ②No capsule and loose tumor consistency

13➲Central Odontogenic Fibroma	
❶Histogenesis➔Origin unknown; may be from periodontal ligament or dental pulp	❹Behavior➔Few recurrences
❷Clinical features ①Adults ②Well-defined lucency	❺Microscopic differential diagnosis ①Desmoplastic fibroma ②Fibromyxoma ③Hyperplastic follicular sac
❸Histopathology➔Collagenous with epithelial strands	

14➲Cementoblastoma	
❶Young adults, mandible > maxilla	❺Histologic features of osteoblastoma
❷Attached to and replaces tooth root	❻Attached to tooth; tooth removed with lesion
❸Periodontal ligament space surrounds lesion	❼No recurrence
❹Opaque mass; may rarely cause cortical expansion	>➔More frequently affected than

15➲Ameloblastic Fibroma/Fibro-odontoma	
❶Occurs in children and teenagers	❹Treatment by curettage or excision
❷Often associated with an impacted tooth	❺Excellent prognosis; rarely recurs
❸Composed of neoplastic epithelium and neoplastic myxomatous connective tissue	❻Malignant counterpart is rare

16➲Odontoma	
❶Most common odontogenic tumor	❼Compound type ①Composed of multiple miniature teeth ②Most commonly found in anterior maxilla
❷Regarded as a hamartoma rather than a neoplasm	
❸Children	
❹Asymptomatic	❽Complex type ①Conglomerate mass of enamel and dentin ②Most commonly found in the posterior jaws
❺Treated by enucleation; does not recur	
❻Discovered on routing radiographic examination or when it blocks tooth eruption	

Appendix 3➔Short Handout for Quick Revision

Benign odontogenic tumors

1➲Fibro-Osseous Lesions of Jaws	
❶Generic(通用) microscopic term ❷Benign fibrous stroma with immature bone ❸Includes reactive, dysplastic, neoplastic lesions	❹Histologic overlap ❺Diagnosis based on clinical pathologic correlation

2➲Fibro-Osseous Lesions of Jaws➔Entities Most Commonly Included	
❶Ossifying fibroma ❷Fibrous dysplasia	❸Periapical/focal cemento-osseous dysplasia ❹Florid cemento-osseous dysplasia

3➲Ossifying Fibroma	
❶Clinical features ①Third and fourth decades ②Mandible > maxilla ③Well circumscribed ④Lucent or lucent/opaque pattern ⑤Continuous growth >➔More frequently affected than	❷Histopathology ①Cellular fibrous matrix ②Islands/trabeculae of new bone ③Osteoblasts; no osteoclasts ④Relatively homogeneous pattern ⑤No inflammatory cells ❸Treatment➔Curettage/excision

4➲Ossifying Fibroma Variants	
❶Juvenile trabecular ossifying fibroma ①Younger patients ②Aggressive clinical course ③Cellular (benign) stroma ④Trabecular or spherical bone	❷Juvenile psammomatoid ossifying fibroma ①Biologically same as ossifying fibroma ②Spherical islands of bone (cementum) ③Bone and cementum microscopically identical

5➲Fibrous Dysplasia	
❶Clinical features ①First and second decades (stabilizes at puberty and very slow growth thereafter) ②Maxilla > mandible (one or more bones) ③Ribs, femur, tibia also affected ④Unilateral diffuse opacity ⑤Asymptomatic; self-limiting ⑥Serum laboratory values normal	❷Histopathology ①New fibrillar bone trabeculae ②Few osteoblasts; no osteoclasts ③Homogeneous pattern ④Vascular matrix ⑤No inflammatory cells >➔More frequently affected than

6➲Fibrous Dysplasia vs. Ossifying Fibroma	
Fibrous Dysplasia	Ossifying Fibroma
First and second decades	Third and fourth decades
Maxilla > mandible	Mandible > maxilla
Diffuse opacity	Circumscribed
Self-limited	Continuous growth
One or more bones	One bone
Vascular matrix	Cellular fibrous matrix
Woven bone trabeculae	Bony islands and trabeculae
Stabilizes at puberty	Not hormone related
Recontour for cosmetics	Excise
Majority with mutations in GNAS gene	No genetic mutations identified

7➲Osteoblastoma	
❶Large counterpart of osteoid osteoma ①Osteoblastoma >1.5 cm ②Osteoid osteoma <1.5 cm ❷50% are painful ❸Second decade is characteristic age	❹Circumscribed ❺Benign cellular (osteoblasts) neoplasm with new bone in scant fibrous stroma ❻Treatment by excision; few recurrences

8➲Desmoplastic Fibroma	
❶Young adults (<30 years of age) ❷Bony counterpart of fibromatosis ❸Recurrence potential	❹Microscopic differential ①Odontogenic fibroma ②Odontogenic fibromyxoma ③Low-grade fibrosarcoma ④Follicular sac

9➲Central Giant Cell Granuloma	
❶Clinical features ①Most patients younger than 30 years of age; females affected more often than males ②Radiolucency; mandible > maxilla; anterior jaw > posterior jaw ③ Recurrences unpredictable (10%-50%) ❷Treatment➔Traditional excision vs medical management➔ calcitonin (osteoclast inhibition)	❸Histopathology ①Benign fibroblast matrix (in cell cycle) ②Giant cells variable (size, number, distribution) ③Few to many mitotic figures ④Cannot separate aggressive from nonaggressive lesions >➔More frequently affected than

10➲Central Giant Cell Granuloma➔Microscopic Differential	
❶Hyperparathyroidism ①Elevated serum parathormone and alkaline phosphatase ②Multiple bone lesions; loss of lamina dura ❷Aneurysmal bone cyst➔Blood-filled sinusoids present	❸Cherubism ①Symmetric lesions ②Family history ③Perivascular collagen cuffing

11➲Langerhans Cell Disease➔Classification
❶Eosinophilic granuloma (chronic localized)➔solitary or multiple bone lesions ❷Hand-Schüller-Christian (chronic disseminated)➔bone lesions, exophthalmos, diabetes insipidus ❸Letterer-Siwe (acute disseminated)➔ bone, skin, internal organs affected

12➲Langerhans Cell Disease
❶Proliferation of dendritic cells with Langerhans cell features ①Cells are CD1a+, CD207 and S-100+ ②Cells contain Birbeck granules (ultrastructure) ❷Few macrophages (histiocytes) are present ❸Cause unknown ❸Any age; three variants ❹Radiograph shows punched-out noncorticated lesions or “floating teeth” ❺Several treatment options ❻Prognosis good to excellent; depends on form

12➲Langerhans Cell Disease➔Treatment
❶Localized disease ①Curettage ②Radiation, low dose ③Intralesional corticosteroid injection ④Rare spontaneous regression ❷Disseminated disease➔Immunosuppressive agents, corticosteroids, cytosine arabinoside

Appendix 3➔Short Handout for Quick Revision

Metabolic and genetic diseases

1➲Paget Disease

❶A progressive metabolic disturbance of many bones; undetermined cause
❷Commonly affects the spine, femurs, cranium, pelvis, and sternum
❸Adults, typically older than 50 years
❹Symptoms➔bone pain, headache, altered vision and hearing, facial paralysis, vertigo
❺Oral signs
❻Bilateral, symmetric jaw enlargement➔15% of all patients with Paget disease; maxilla > mandible
❼Acquired diastemas, ill-fitting denture, patchy opacities, and hypercementosis
❽Oral complications
❾Early phase disease➔bleeding following jaw surgery
❿Late phase disease➔jaw fracture, osteomyelitis >➔Affected more frequently than

2➲Hyperparathyroidism

❶Primary hyperparathyroidism➔parathyroid adenoma, hyperplasia, and adenocarcinoma
❷Secondary hyperparathyroidism➔compensatory hyperplasia for low serum calcium levels caused by renal failure, malabsorption, or vitamin D deficiency
❸Elevated serum parathormone (PTH), calcium, alkaline phosphatase levels, and decreased phosphate levels
❹Kidney stones, metastatic calcification, osteoporosis, fibroblastic/giant cell tumors of bone, neurologic alterations, arrhythmias, and polyuria

3➲Oral Manifestations of Hyperparathyroidism, Hyperthyroidism, and Hypophosphatasia

❶Primary hyperparathyroidism➔multiple jaw lucencies (giant cell lesions); loss of lamina dura; pulp calcifications
❷Hyperthyroidism➔premature exfoliation and eruption of teeth; osteoporosis
❸Hypophosphatasia➔premature loss of teeth; reduced cementum and dentin; short roots; large pulps

4➲Hypothyroidism

❶Delayed skeletal and dental development
❷Sexual immaturity
❸Edema of face, eyes, lips, and tongue
❹Mental lethargy
❺Skin changes➔dry, cold, scaly, discolored (yellowish to hyperpigmented)
❻Hair/Nails➔hair loss common; nails brittle
❼Slow pulse
❽Fatigue, lethargy
❾Anemia➔ microcytic, hypochromic
❿Hyperlipidemia

5➲Cherubism➔Clinical Features

❶Symmetric (bilateral), asymptomatic swelling of jaws
❷Mandible➔lingual surface unchanged, condyles spared
❸Maxilla➔elevation of orbital floor causes upward gaze(凝視)
❹Buccal expansion to 12 years of age, then stabilization
❺Regression after 2 to 4 years and resolution by age 30
❻“Soap bubble” radiolucencies

6➲Osteogenesis Imperfecta➔Clinical Features of Head & Neck

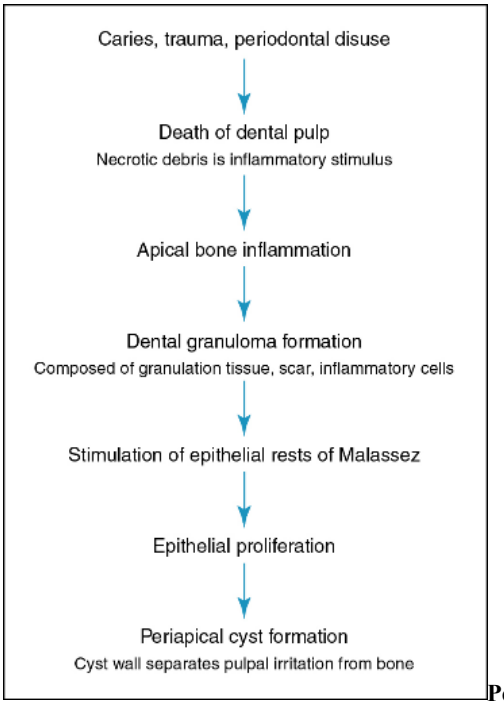
❶Bone fragility
❷Skull base deformities
❸Blue sclera
❹Hearing loss
❺Dentinogenesis imperfecta
❻Wormian bones (skull)
❼Laxity of skin and ligaments (TMJ)

Appendix 3➔Short Handout for Quick Revision

Cysts of jaws and neck

1➲Cysts of the Jaws➔ Epithelial Origin

Type	Source	Origin of Rests	Cyst Examples
Odontogenic rests	Rests of Malassez	Epithelial root sheath	Periapical (radicular) cyst
	Reduced enamel epithelium	Enamel organ	Dentigerous cyst
	Rests of dental lamina (rests of Serres)	Epithelial connection between mucosa and enamel organ	Odontogenic keratocyst Lateral periodontal cyst
			Gingival cyst of adult
			Gingival cyst of newborn
			Glandular odontogenic cyst
Nonodontogenic rests	Remnants of nasopalatine duct	Paired nasopalatine ducts (vestigial)	Nasopalatine duct cyst



Periapical (radicular) cyst developmental sequence

2➲Periapical (Radicular) Cyst

❶Pathogenesis
①Preceded by periapical granuloma (chronic inflammation) associated with nonvital tooth
②Rests of Malassez stimulated by chronic inflammation
③Products of cyst epithelium and inflammation cause bone resorption
④Cyst expands because of increasing osmotic pressure in lumen

❷Clinical appearance
①Most common type of jaw cyst
②Radiographically, cannot distinguish cyst from preexisting granuloma
③Persists if treated by root canal filling only
④Treated by cystectomy (apicoectomy) and retrograde root filling
⑤Incompletely removed cyst lining results in a residual cyst

3➲Lateral Periodontal Cyst

❶Origin from rests of dental lamina in bone
❷Occurs along lateral surface of tooth root
❸Associated with a vital tooth
❹Most found in mandibular canine-premolar area
❺Males affected more than females
❻Treated by cystectomy; multilocular variant has recurrence potential
❼Dental lamina rests in soft tissue give rise to gingival cysts of adult

4➲Dentergous Cyst

❶Clinical
①Second most common odontogenic cyst after periapical cyst
②Third molars and canine teeth most commonly affected
③Stimulus unknown

❷Clinical appearance
①Most common type of jaw cyst
②Radiographically, cannot distinguish cyst from preexisting granuloma
③Persists if treated by root canal filling only
④Treated by cystectomy (apicoectomy) and retrograde root filling
⑤Incompletely removed cyst lining results in a residual cyst

❸Radiographic features➔Lucency associated with crown of impacted tooth

❸Histopathology
①Lined by nonkeratinized stratified squamous epithelium
②Proliferation of reduced enamel epithelium

❹Possible complications
①Extensive bone destruction with growth
②Resorption of adjacent tooth roots
③Displacement of teeth
④Neoplastic transformation of lining (rare)➔ameloblastoma formation; carcinoma very rarely

5➲Glandular Odontogenic Cyst (Sialo-Odontogenic Cyst)➔Rare developmental cyst

❶Clinical features
①Adults
②Either jaw (anterior > posterior) >➔More frequently affected than

❸ Behavior➔Locally aggressive; recurrence potential

❷Histopathology
①Focal mucous cells, pseudoducts
②Resembles low-grade mucoepidermoid carcinoma but no rearrangement of MAML2 gene

6➲Odontogenic Keratocyst/Kertaocystic Odontogenic Tumor➔Pathogenetic Mechanisms

❶High proliferation rate➔Ki-67 staining
❷Overexpression of antiapoptotic protein➔Bcl-2 staining
❸Overexpression of interface proteins➔MMPs 2 and 9, TGF, IL-1α, and IL-6
❹Mutations in PTCH tumor suppressor gene (protein receptor in hedgehog signaling pathway)
❺Found in basal cell carcinomas and medulloblastomas of nevoid basal cell carcinoma syndrome
❻PTCH mutations noted in syndromic and nonsyndromic odontogenic keratocysts/keratocystic odontogenic tumors

IL➔Interleukin; MMP➔matrix metalloproteinase; TGF➔transforming growth factor

7➲Odontogenic Keratocyst➔Clinical Features

❶Aggressive; recurrence risk; association with nevoid basal cell carcinoma syndrome
❷Solitary cysts➔common (5%-15% of odontogenic cysts); recurrence rate 10% to 30%
❸Multiple cysts➔5% of OKC patients; recurrence greater than with solitary cysts
❹Syndrome-associated, multiple cysts➔5% of OKC patients; recurrence greater than with multiple cysts

OKC➔Odontogenic keratocyst

8➲Odontogenic Keratocyst➔Diagnosis

❶Thin epithelium (6-10 cell layers)
❷Refractile, parakeratotic lining
❸Epithelial budding and “daughter cysts”
❹Characteristic microscopic features lost when inflamed

❺Orthokeratinized odontogenic cyst
①Lined by thin orthokeratinized epithelium
②Less common
③Not syndrome associated
④Lower recurrence rate

9➲Nevoid Basal Cell Carcinoma Syndrome

❶Etiology
①Autosomal-dominant inheritance pattern
②Mutations found in the PTCH gene (hedgehog signaling)

❷Clinical Features
①Multiple odontogenic keratocysts/keratocystic odontogenic tumors
②Multiple basal cell carcinomas
③Skeletal anomalies (e.g., bifid rib, kyphoscoliosis 背側彎症)
④Calcified falx cerebri
⑤Facial defects

10➲Calcifying Odontogenic Cyst (Calcifying Cystic Odontogenic Tumor)

❶Clinical features
①No distinctive age, gender, or location
②Lucent to mixed radiographic patterns
❷Histopathology
①Basal palisading
②Ghost cells and dystrophic calcification
③Similar to pilomatrixoma of skin

❸Behavior➔Unpredictable
❹Variants
①Odontogenic ghost cell tumor➔solid
②Odontogenic ghost cell carcinoma➔cytologic atypia, mitoses, pleomorphism, necrosis

11➲Globulomaxillary Lesions

❶Nonspecific designation for any lesion in the globulomaxillary area (between maxillary lateral incisor and canine)
❷Inverted pear-shaped radiolucency
❸Asymptomatic; teeth vital; divergence of roots
❹May represent odontogenic cyst or neoplasm, or nonodontogenic tumor
❺Biopsy necessary to establish definitive diagnosis

12➲Nasopalatine Duct (Incisive Canal)

❶Most common nonodontogenic oral cyst
❷Arises from remnants of the vestigial paired palatine ducts
❸Stimulus for cyst development undetermined

❹Most occur in bone, soft tissue lesion in incisive papilla
❺Asymptomatic unless secondarily inflamed
❻Adults, males more commonly affected

13➲Aneurysmal Bone Cyst

❶Etiology➔Unknown; may be related to altered hemodynamics or abnormal healing of bone hemorrhage
❷Clinical features
①Teenagers and young adults affected
②Multilocular lucency
③No associated thrill or bruit on auscultation
❸Histopathology
①Blood-filled spaces lined by connective tissue and multinucleated giant cells
②Differential diagnosis includes central giant cell granuloma, hyperparathyroidism, cherubism
❹Treatment➔Excision➔no bleeding hazard

14➲Traumatic Bone Cyst

❶Etiology
①Unknown; trauma sometimes suggested
②May be related to bleeding in the jaw with clot resorption
❷Clinical features
①Lucency discovered on routine examination
②Empty “dead” space in medullary bone, especially mandible
③Teenagers most commonly affected

❸Treatment
①Surgical entry to initiate bleeding and stimulate healing
②Some may heal spontaneously

15➲Static (Stafne’s) Bone Cyst

❶Developmental defect
❷Located below mandibular canal in molar region
❸Salivary gland or adipose tissue in defect
❹Discrete corticated margin
❺Diagnostic on panoramic film
❻No symptoms
❼No biopsy or treatment➔radiographic diagnosis

16➲Branchial Cyst

❶Developmental cyst➔arises from epithelium entrapped in lymph node
❷Lateral neck mass➔along anterior border of sternocleidomastoid muscle
❸Fluctuant texture
❹Young adults
❺Lymphoid tissue surrounds a squamous or pseudostratified epithelial lining

17➲Dermoid Cyst

❶Mass in midline of neck or floor of mouth (location depends on relationship to mylohyoid and geniohyoid muscles)
❷Young adults
❸Doughy by palpation because of sebum in lumen
❹Lined by epithelium and secondary skin structures (sebaceous glands, hair)
❺Designated as teratoma if all three germ layers are represented

18➲Thyroglossal Tract Cyst

❶Arises from epithelial remnants of thyroid gland development
❷Occurs in midline of neck➔anywhere between thyroid embryonic origin (foramen caecum of tongue) and thyroid gland
❸Lingual thyroid
❹Mass in tongue base caused by failed descent of thyroid tissue
❺May be only functional thyroid tissue in patient
❻Treatment by excision; may recur because of tortuous configuration
❼Rare cases of thyroid cancer develop along the cyst tract

Appendix 3➔Short Handout for Quick Revision

Malignancies of jaws

1➲Malignancy in the Jaws➔Signs and Symptoms	
❶Paresthesia ❷Pain ❸Loose teeth, vertical mobility, premature loss ❹Tooth resorption more likely than displacement ❺Rapid growth	❻Acquired malocclusion ❼Radiographic changes ❽Uniformly widened periodontal membrane space ❾Ill-defined lesion

2➲Osteosarcoma of Jaws	
❶Etiology ①No known risk factors ②Genes that may be altered➔*p53, Rb, met, fos, sas, mdm2, cdk4,* and *c-myc* ❷Clinical features ①Swelling, pain, paresthesia, periodontal ligament invasion, tooth mobility/displacement ②Mean age➔35 years; age range from 8 to 85 years ③Males and females equally affected; mandible > maxilla	❸Histopathology ①Malignant cells producing osteoid ②Well differentiated ③Chondroblastic osteosarcoma most common subtype ❹Treatment➔Resection to multimodality; good prognosis

3➲Multiple Myeloma	
❶Origin➔B-lymphocyte malignancy; monoclonal population; abnormal monoclonal immunoglobulin produced ❷Clinical and laboratory features ①Types➔multiple, solitary, extramedullary ②Patients older than 50 years ③Pain, swelling, numbness ④Weight loss, weakness, anemia, bleeding, infection, amyloidosis (10%) ⑤Punched-out skeletal lesions ⑥Bence Jones protein (light chains) in urine ⑦M protein in serum	❸Treatment➔Chemotherapy; poor prognosis

4➲Amyloidosis
❶Occurs in 10% of myeloma patients ❷May appear secondary to chronic disease (e.g., rheumatoid arthritis, chronic osteomyelitis, chronic renal failure) ❸Kidney, heart, gastrointestinal tract, liver, spleen commonly affected ❹Oral lesions seen in tongue (macroglossia), gingiva

5➲Malignancies Most Likely to Metastasize to the Jaw	
❶Breast carcinoma ❷Lung carcinoma ❸Prostate adenocarcinoma	❹Colorectal carcinoma ❺Renal cell carcinoma

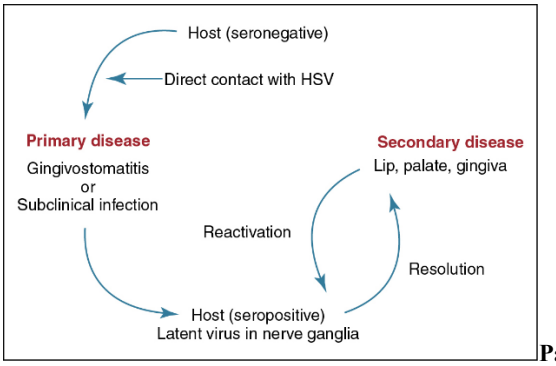
6➲CK 7 & 20 Expression in Various Epithelial Malignancies		
Tumor	**CK7**	**CK20**
Lung (adenocarcinoma)	+	−
Lung (squamous cell carcinoma)	−	−
Colon	−	+
Breast	+	−
Kidney	−	−
Prostate	−	−

Appendix 3➔Short Handout for Quick Revision

Vesiculobullous diseases

1➲Viruses Relevant to Dentistry	
Herpesviruses Family	**Disease**
HSV1	Primary herpes gingivostomatitis
	Secondary herpes infections
HSV2	Genital herpes
Varicella-zoster	Varicella (chickenpox), zoster (shingles)
Epstein-Barr	Mononucleosis
	Burkitt's lymphoma
	Nasopharyngeal carcinoma
	Hairy leukoplakia
Cytomegalovirus	Salivary gland inclusion disease
HHV6	Roseola infantum
HHV8	Kaposi's sarcoma
Papillomaviruses (HPV)	Oral papillomas/warts, condyloma acuminatum, focal epithelial hyperplasia, nasopharyngeal carcinoma, oropharyngeal and base of tongue carcinoma
Coxsackie viruses	Herpangina, hand-foot-and-mouth disease
Measles virus	Measles
Mumps virus	Mumps parotitis

HHV➔Human herpesvirus; HSV➔herpes simplex virus

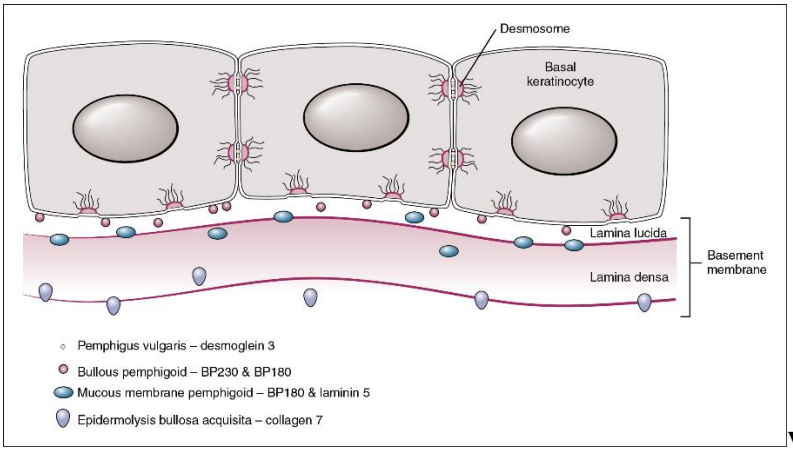


Pathogenesis of herpes simplex infections

2➲Primary Herpes Simplex	
❶Clinical features ①Few primary infections result in clinical disease ②Oral and perioral vesicles rupture, forming ulcers ③Intraoral lesions may be found on any surface ④Systemic signs/symptoms include fever and malaise ⑤Self-limited disorder; symptomatic care is provided ⑥Immunocompromised patients have more severe disease	❷Treatment ①Acyclovir and analogs may control virus ②Treatment must be provided early to be effective

3➲Secondary Herpes Simplex	
❶Etiology ①Reactivation of latent herpes simplex virus type 1 ②Triggers➔sunlight, stress, immunosuppression ③Reactivation common; frequency decreases with aging ④Prodromal symptoms➔tingling and burning ❷Clinical features ①Affects perioral skin, lips, gingiva, palate ②Self-limited ❸Treatment ①Possible control with acyclovir and analogs ②Must be administered early ③Systemic treatment much more effective than topical treatment	❹Differential diagnosis ①Pemphigus vulgaris ②Erosive lichen planus ③Linear immunoglobulin (Ig)A disease ④Contact allergy ⑤Discoid lupus erythematosus ⑥Epidermolysis bullosa acquisita

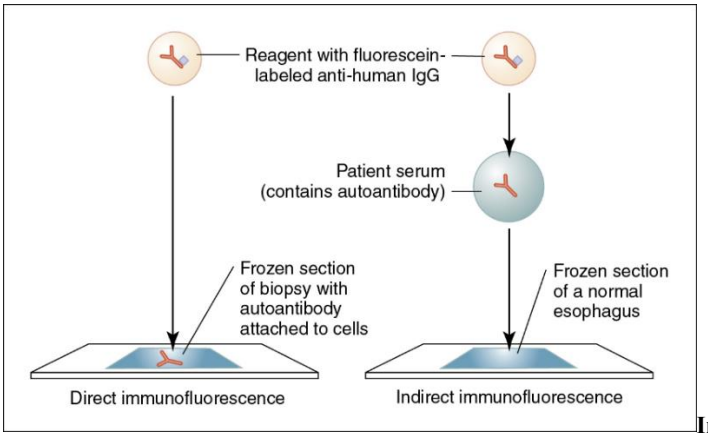
4➲Varicella-Zoster	
❶Primary disease (varicella, chickenpox) ①Self-limiting ②Historically common in children ③Vesicular eruption of trunk & head and neck occurring in crops ④Systemic signs/symptoms➔fever, malaise, other ⑤Symptomatic treatment⑤	❷Secondary disease (zoster, shingles) ①Self-limiting ②Adults ③Rash, painful vesicles & ulcers, unilateral along dermatome ④Possibly severe post-herpetic pain/neuralgia (~15% of cases) ⑥Immunocompromised and lymphoma patients at risk ⑦Treated with acyclovir and analogs



Vesiculobullous diseases➔antigenic targets

5➲Pemphigus Vulgaris

❶Etiology
①Self-limiting
②Autoimmune reaction to intercellular keratinocyte protein (desmoglein 3)
③Intraepithelial blisters caused by antibodies directed at desmosomal components
❷Clinical features
①Affects skin and/or mucosa
②Majority of cases begin in the mouth (“first to show, last to go”)
③Presents as ulcers preceded by short-lived vesicles or bullae
④Persistent and progressive
❸Treatment
① *Treatment*
②Controlled with immunosuppressives (corticosteroids/azathioprine/cyclophosphamide/mycophenolate/IVIg) and biologic agents (rituximab)
③High mortality when untreated (dehydration, electrolyte imbalance, malnutrition, infection-sepsis)
④*IVIg*, Intravenous immunoglobulin G
⑤Plasmapheresis
⑥Immunoadsorption



Immunofluorescence➔laboratory method

6➲Side Effects of Topical Corticosteroids

❶Candidiasis
❷Epithelial atrophy
❸Telangiectasias
❹Additional effects on skin-striae, hypopigmentation, acne, folliculitis

7➲Side Effects of Systemic Corticosteroids

❶Anti-inflammatory➔therapeutic
❷Immunosuppression➔therapeutic
❸Gluconeogenesis➔diabetes, osteoporosis/muscle atrophy
❹Redistribution of fat➔buffalo hump, hyperlipidemia
❺Fluid retention➔moon face, weight gain
❻Vasopressor potentiation➔hypertension worse
❼Gastric mucosa effects➔peptic ulcer worse
❽Adrenal suppression➔adrenal atrophy
❾CNS effects➔psychological changes (e.g., euphoria; psychosis)
❿ Ocular effects➔ cataracts, glaucoma

8➲Mucous Membrane Pemphigoid

❶Etiology➔Autoimmune reaction to basement membrane proteins (laminin subtypes, BP180, integrins and others)
❷Clinical features
①Oral mucosa (gingiva often only site) and conjunctiva; skin rarely affected
②Subepithelial blistering caused by autoantibodies
③Present as ulcers/redness in older adults (over 50 years of age)
④Persistent, uncomfortable to painful

❸Treatment
①Controlled with corticosteroids; sometimes resistant to systemic therapy; topical agents useful (topical steroids); control of dental
②plaque/frequent oral hygiene procedures
③Significant morbidity if untreated, including pain and scarring, especially of conjunctiva

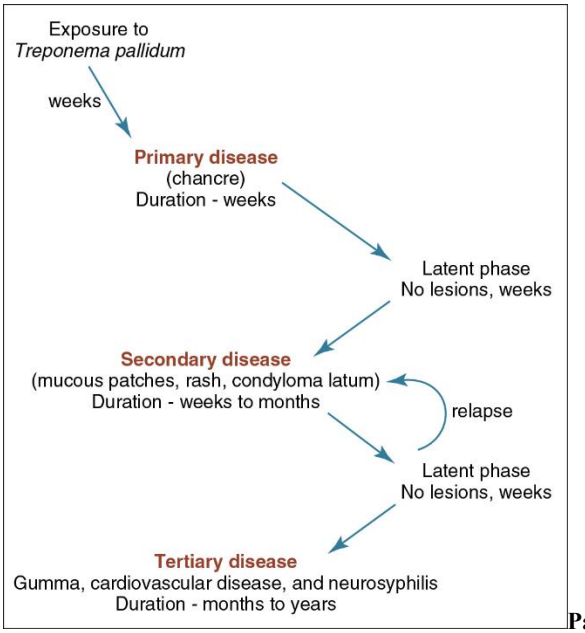
9➲Pemphigus Vulgaris versus Mucous Membrane Pemphigoid		
	Pemphigus	**Pemphigoid**
Tissue antibody	**IgG, C3**	**IgG, IgA, C3**
	Circulating auto-IgG	**No circulating auto-IgG**
Target protein(s)	**Desmoglein 3 (desmosomes)**	**Laminin 5 and BP180 (basement membrane)**
Vesicles	**Intraepithelial**	**Subepithelial**
Sites	**Oral and skin**	**Oral and eyes**
Treatment	**Corticosteroids, steroid sparing agents; rituximab**	**Corticosteroid**
Prognosis	**Fair, significant mortality if untreated**	**Good, significant morbidity**

BP➔Bullous pemphigoid antigen; C➔complement; Ig➔immunoglobulin

Appendix 3➔Short Handout for Quick Revision

Ulcerative conditions

1➲Traumatic Ulcers	
❶Acute ulcer ①Pain ②Yellow base, red halo ③History of trauma ④Heals in 7 to 10 days if cause eliminated	❷Chronic ulcer ①Little or no pain ②Yellow base, elevated margins (scar) ③History of trauma, if remembered ④Delayed healing if irritated, especially tongue lesions ⑤Clinical appearance mimics carcinoma and infectious ulcers



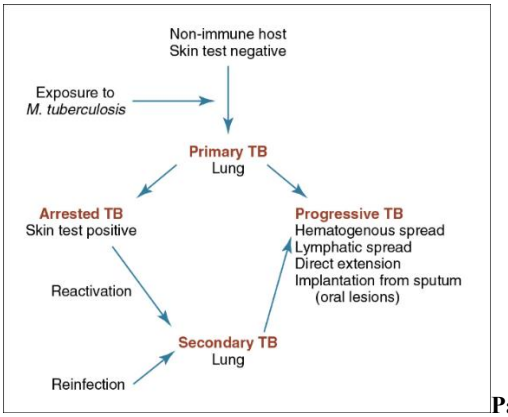
Pathogenesis of syphilis (untreated)

2➲Classification of Syphilis

❶Acquired syphilis
①Early
(1)Primary (chancre)
(2)Secondary (oral mucous patches, skin lesions, other organopathy)
Latency
②Late
(1)Latency
(2)Tertiary (gumma, cardiovascular disease, neurosyphilis)
❷Congenital syphilis
①Early
(1)Secondary disease
(2)Spirochetemia affecting many organ systems
(3)Stigmata include dental defects, eighth-nerve deafness, ocular keratitis, bone and joint lesions, other organopathy
②Late➔Latency

3➲Syphilis

❶Cause➔*Treponema pallidum*, sexually transmitted
❷Clinical features
①Primary phase➔chancre, a chronic ulcer at the site of infection
②Secondary phase➔oral mucous patches, condyloma latum, maculopapular rash
③Tertiary phase➔gummas (destructive ulcers), central nervous system and cardiovascular diseases
④Congenital form➔abnormal shape of molars/incisors, deafness, ocular keratitis, skeletal defects
❸Treatment➔Penicillin, tetracyclines



Pathogenesis of tuberculosis

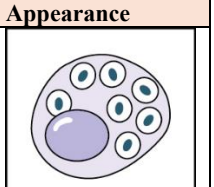
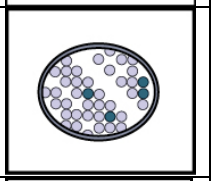
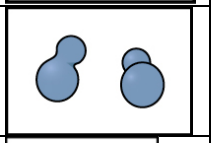
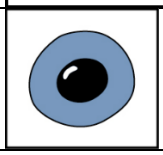
4➲Tuberculosis

❶Etiology
①*Mycobacterium tuberculosis*; oral lesions follow lung infections
②Risk factors➔overcrowding, debilitation, immunosuppression
③Important public health disease
❷Clinical features➔Chronic ulcers, nonhealing and indurated, often multiple
❸Histopathology➔Caseating granulomas (macrophages) with Langerhans giant cells
❹Treatment➔Prolonged, multidrug therapy required (isoniazid, rifampin, ethambutol)

5➲Deep Fungal Infections

❶Pathogenesis➔Inhalation of spores
❷Symptoms➔Cough, fever, weight loss, other
❸Primary site➔Lung; may be asymptomatic
❹Oral lesions➔Chronic, nonhealing ulcers resulting from lung disease
❺Microscopy➔Granulomatous inflammation with organisms
❻Treatment➔Ketoconazole, fluconazole, itraconazole, amphotericin B

6➲Deep Fungal Infections➔Morphologic Features

Organism	Size (m)	Histology	Appearance
Histoplasmosis	2-5	Yeasts in macrophages	
Coccidioidomycosis	30-60	Endospores in spherules	
Blastomycosis	8-15	Budding yeasts	
Cryptococcosis	2-15	Yeasts with thick capsule	

7➲Chronic Infectious Ulcers

❶Types➔Syphilis, tuberculosis, histoplasmosis, other deep fungal infections
❷Clinical features
①Mimic carcinomas and traumatic ulcers
②Nonhealing, persistent, often multiple
❸Diagnosis
①Biopsy necessary
②Culture may be required
❹Treatment➔Appropriate antimicrobial agent

8➲Aphthous Ulcers➔Possible Causes

❶Immunologic disorder➔T-cell mediated
❷Neurogenic inflammation➔Neuropeptide (e.g., substance P) induced
❸Mucosal healing defect➔Inhibition by cytokines
❹Microbiological➔Viral, bacterial
❺Nutritional deficiency➔Vitamin B_{12}, folic acid, iron
❻Chemical➔Preservatives, toothpaste components

9➲Aphthous Ulcers vs. Secondary Herpes Simple Infection

	Aphthous Ulcers	Herpes Infection
Cause	Immune dysfunction	HSV1
Triggers	Stress, trauma, diet, hormones, depressed immunity	Stress, trauma, ultraviolet light, depressed immunity
Prodrome	Little prodrome	Prodromal symptoms
Appearance	Nonspecific microscopy	Viral cytopathic changes
	No vesicles	Vesicles precede ulcers
	Single, oval ulcer	Multiple, confluent ulcers
Sites	Nonkeratinized mucosa	Keratinized mucosa
Treatment	Corticosteroids, tetracycline	Antiviral treatment

HSV1➔Herpes simplex virus type 1

10➲Aphthous Ulcers➔ Clinical Features			
	Minor Aphthae	Major Aphthae	Herpetiform Aphthae
Size	<0.5 cm	>0.5 cm	<0.5 cm
Shape	Oval	Ragged oval, crateriform	Oval
Number	1-5	1-10	10-100
Location	Nonkeratinized mucosa	Nonkeratinized mucosa	Any intraoral site
Treatment	Topical corticosteroids, tetracycline mouth rinse	Topical/systemic/intralesional corticosteroids, immunosuppressives	Topical/systemic corticosteroids, tetracycline mouth rinse

11➲Topical Corticosteroid Preparations

❶Clobetasol propionate (Temovate)
❷Clobetasol propionate plus "oral adhesive" (50% Temovate ointment plus 50% Orabase)
❸Betamethasone dipropionate (Diprosone)
❹Fluocinonide (Lidex)
❺Betamethasone plus clotrimazole (Lotrisone)

12➲Behçet's Syndrome

❶Etiology➔Immunodysfunction, vasculitis
❷Organs affected
①Nonkeratinized oral mucosa (minor aphthae)
②Genitals (ulcers)
③Eyes (conjunctivitis, uveitis, retinitis)
④Joints (arthritis)
⑤Central nervous system (headache, nerve palsies, inflammation)
❸Treatment➔Corticosteroids, other immunosuppressives

13➲Erythema Multiforme

❶Etiology
①Minor (less severe) form usually triggered by herpes simplex virus
②Major form (Stevens-Johnson syndrome) often triggered by drugs
③Hypersensitivity reaction to infectious agents, drugs, or idiopathic
❷Clinical features
①Multiple oral ulcers and/or target skin lesions
②Self-limiting, but may recur
❸Treatment
①Supportive therapy
②Corticosteroids occasionally used for severe form

14➲Erythema Multiforme vs. Primary Herpes Simplex Infection		
	Erythema Multiforme	Herpes Infection
Appearance	Large oral and lip ulcers	Small oral/perioral ulcers
	Skin target lesions	Skin ulcers
Symptoms	Mild to severe	Moderate to severe
Sites	Buccal, tongue, lips, palate, extremities	Gingiva, lips, perioral skin
Age	Young adults	Children
Cause	Hypersensitivity	HSV
Treatment	Symptomatic, steroids	Acyclovir

HSV➔Herpes simplex virus

15➲Ulcerative and Erythematous Drug Reactions➔ Representative Causative Drugs

❶Analgesics
①Aspirin
②Codeine
③Oxicams
④Propionic acid derivatives

❷Antibiotics
①Erythromycin
②Penicillin
③Streptomycin
④Sulfonamides
⑤Tetracycline
❸Anticonvulsants
①Barbiturates
②Phenytoin

❹Antifungals➔Ketoconazole
❺Anti-inflammatory➔Indomethacin
❻Antimalarial➔Hydroxychloroquine
❼Cardiovascular
①Methyldopa
②Oxprenolol

❽Psychotherapeutic
①Meprobamate
②Chlorpromazine
❾Other
①Retinoids
②Cimetidine
③Gold compounds
④Local anesthetics

16➲Drug Reactions➔ Mechanisms

❶Hyperimmune response (allergy)➔Related to drug immunogenicity, frequency, route of delivery, patient's immune system
❷Mediated by
①Mast cells coated with IgE
②Ab reaction to cell-bound drug
③Deposition of circulating Ag-Ab complexes
❸Nonimmunologic *response (not ab dependent)*
①Direct release of inflammatory mediators by mast cells
②Overdose, toxicity, side effects

Ab➔Antibody; Ag➔antigen; IgE➔immunoglobulin E

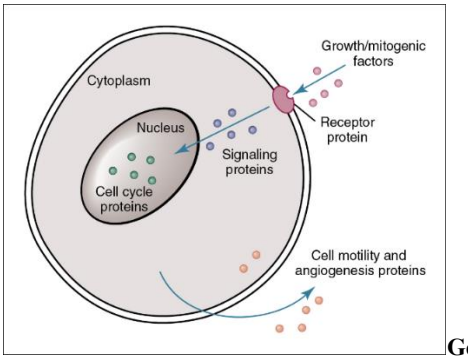
17➲Lichenoid Drug Reactions➔Drugs with Causative Potential

❶NSAIDs
❷Antihypertensives➔ACE inhibitors, beta blockers, nifedipine, methyldopa
❸Diuretics➔hydrochlorothiazide, furosemide, spironolactone
❹Phenothiazine antipsychotics➔chlorpromazine, prochlorpromazine, fluphenazine, trifluoperazine, thioridazine, others
❺Anti-seizure drugs including➔carbamazepine, phenytoin
❻Anti-tuberculosis drugs
❼Antimalarials
❽Chemotherapeutic drugs including➔5-flurouracil, hydroxyurea, tyrosine kinase inhibitors, eg. imatinib
❾Oral hypoglycemic agents including➔biguanides, sulfonylureas, thiazolidinediones
❿Tumor necrosis factor antagonists➔adilumimab, etanercept, infliximab
⓫Phosphodiesterase inhibitors➔sildenafil
⓬Antifungal agents➔ketoconazole, other azoles
⓭Sulfa drugs including➔sulfonylurea hyopglycemics, mesalazine, sulfasalazine, sulfonamides, celecoxib
⓮Others➔gold salts, mercury, penicillamine

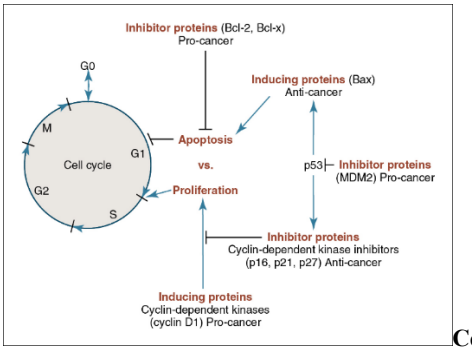
NSAIDs➔Nonsteroidal anti-inflammatory drugs

18➲Wegener's Granulomatosis vs Midline Granuloma (T-Cell Lymphoma)

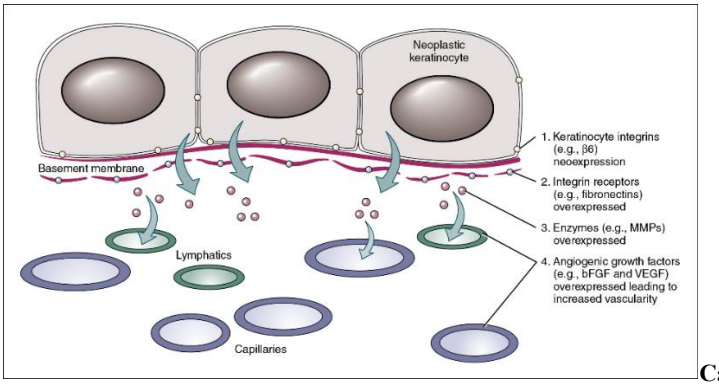
	Wegener's Granulomatosis	Midline Granuloma
Etiology	Unknown? Infectious? Immune dysfunction	Malignancy of natural killer (NK)/T cells
Organs	Upper airways, lungs, kidneys	Upper airways, palate, gingiva
Pathology	Granulomatous and necrotizing vasculitis	NK/T-cell lymphoma (angiocentric)
Diagnosis	Biopsy, positive antineutrophil cytoplasmic antibodies (cANCAs)	Biopsy, immunologic studies
Treatment	Cyclophosphamide, prednisone	Radiation, chemotherapy



Gene expression in oral cancer



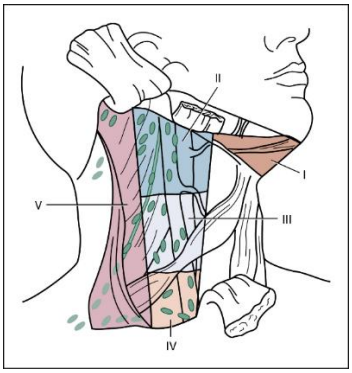
Cell cycle regulation➔controls at G1-S



Cancer cell invasion through enhanced cell motility & angiogenesis

19➲Oral Cancer Pathogenesis

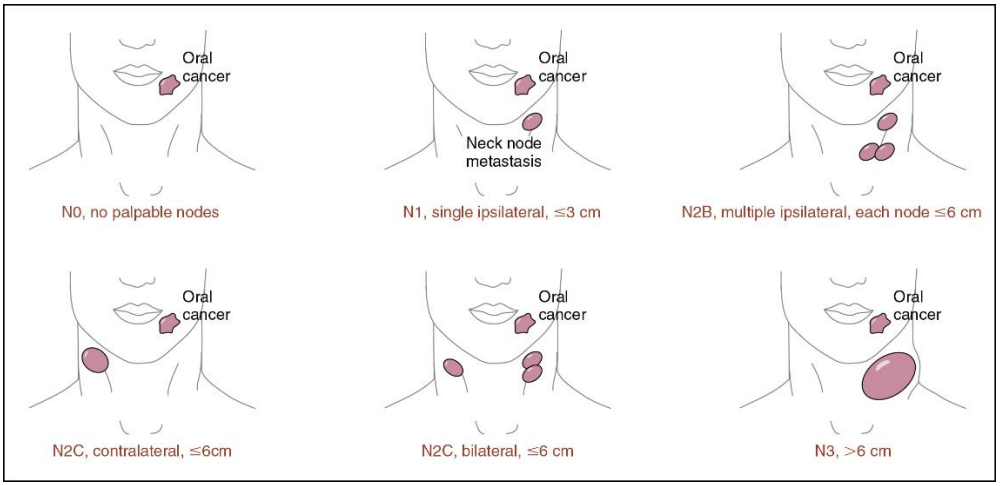
❶Oncogenes and tumor suppressor genes➔Mutation, amplification, or inactivation
❷Loss of control of
①Cell cycle (proliferation vs. inhibition, signaling)
②Cell survival (apoptosis vs antiapoptosis)
③Cell motility



Oncologic lymph node levels of the neck. Level I = submental/submandibular nodes; level II = upper jugular nodes; level III = middle jugular nodes; level IV = lower jugular nodes; level V = posterior triangle nodes

20➲Therapeutic Radiation Side Effects	
❶Temporary side effects	❷Permanent side effects
①Mucosal ulcers/mucositis	①Xerostomia
②Pain	②Cervical caries
③Taste alterations	③Osteoradionecrosis
④Candidiasis	④Telangiectasias
⑤Dermatitis	⑤Epithelial atrophy
⑥Erythema	⑥Focal alopecia
⑦Focal alopecia	⑦Focal hyperpigmentation

21➲TNM Clinical Staging System for Oral Squamous Cell Carcinoma		
❶T➔tumor	❷N➔nodes	❸M➔metastasis
①T1➔tumor <2 cm	①N0➔no palpable nodes	①M0➔no distant metastasis
②T2➔tumor 2-4 cm	②N1➔single ipsilateral node <3 cm	②M1➔distant meta
③T3➔tumor >4 cm	③N2A➔ingle ipsilateral node 3-6 cm	
④T4➔tumor invades deep subjacent structures	④N2B➔multiple ipsilateral nodes ≤6 cm	
	⑤N2C➔contralateral or bilateral nodes ≤6 cm	
	⑥N3➔node >6 cm	



Lymph nodes in tumor, node, metastasis (TNM) staging (N2A, single ipsilateral node 3 to 6 cm)

22➲TNM Clinical Staging of Oral Squamous Cell Carcinoma	
Stage	TNM Designation
I	T1, N0, M0
II	T2, N0, M0
III	T3, N0, M0
T1-3, N1, M0	
IV	T4, N0, M0
	T4, N1, M0
	T any, N2-3, M0
	T any, N any, M1

Appendix 3➔Short Handout for Quick Revision

White lesions

1➲White Sponge Nevus➔Key Feature	
❶Asymptomatic ❷Bilateral folded/shaggy white buccal mucosal change ❸Hereditary; appears early in life	❹Does not disappear when cheek is stretched ❺Intracellular edema with perinuclear condensation of keratin ❻No treatment, no malignant potential

2➲Bilateral Buccal Mucosal White Lesions➔Differential Diagnosis	
Disease	**Features/Action**
White sponge nevus and HBID	Hereditary; does not disappear when stretched; biopsy to confirm; HBID may also involve conjunctiva
Lichen planus	Look for bilateral white reticulations (striae), erosions, atrophy and associated skin lesions; biopsy
Lichenoid drug reaction	Look for white lesions, often asymmetrical, in context of new drug history
Cheek chewing	White shaggy lesions along occlusal plane or trauma sites
Lupus erythematosus	Delicate radiating striae; biopsy
Candidiasis	Look for predisposing factors; can rub off; responds to antifungal therapy

HBID➔Hereditary benign intraepithelial dyskeratosis

3➲Frictional Hyperkeratosis➔Key Feature	
❶Common traumatized site➔ lips, lateral tongue, buccal mucosa ❷Edentulous ridges and vestibules may be affected in denture wearers ❸Hyperkeratosis➔opacification (white lesion) of traumatized area	❹Microscopically, hyperkeratosis➔no dysplastic change ❺If cause is removed, lesion should subside ❻When in doubt, perform a biopsy

4➲Solitary White Lesion➔Differential Diagnosis	
Disease	**Features/Action**
Frictional keratosis	Determine cause (e.g., ill-fitting dentures, trauma); biopsy
Dysplasia, in situ carcinoma, squamous cell carcinoma	Assess risk factors; biopsy
Burn (chemical)	History of aspirin or other agent application at site of lesion—discontinue use
Lupus erythematosus	Delicate radiating striae; usually unilateral; biopsy
Hairy leukoplakia	Lateral borders of tongue; look for irregular surface architecture; often bilateral; immunosuppression biopsy

5➲Smokeless Tobacco–Associated Lesions

❶Etiology
①Direct contact of mucosa with smokeless tobacco and contaminants
②Snuff form of tobacco most likely to induce lesions
❷Clinical features
①Prevalence associated with regional use (e.g., 1% of New York population, 20% of West Virginia population)
②Mostly seen in white males
③Asymptomatic white lesion in mucosa where tobacco is held
④Most commonly seen in the mandibular vestibular mucosa surrounding tobacco (snuff dipper's pouch)
⑤Damage seen in adjacent teeth and periodontium
❸Treatment
①Discontinue use
②Biopsy if ulcerated, indurated, or persistent
③Slight risk of malignant transformation with long-term use (decades)

6➲Nicotine Stomatitis	
❶Etiology ①Caused by pipe, cigar, and cigarette smoking ②Opacification of the palate caused by heat and carcinogens ③Most severe changes seen in patients who "reverse smoke" ❷Clinical features ①Generalized white change (hyperkeratosis) seen in hard palate ②Red dots in the palate represent inflamed salivary duct orifices	❸Treatment ①Discontinue tobacco habit ②Observe and examine all mucosal sites ③Little risk of malignant transformation in palate, except for "reverse smokers"

7➲Oral Manifestations of AIDS	
❶Infections ①Viral➔herpes simplex, herpes zoster, hairy leukoplakia, cytomegalovirus, warts ②Bacterial➔tuberculosis, bacillary angiomatosis ③Fungal➔ candidiasis, histoplasmosis ④Protozoan➔Toxoplasmosis	❷Neoplasms ①Kaposi's sarcoma (HHV8) Lymphomas, high grade ❸Other ① Aphthous ulcers ②Xerostomia ③Gingivitis and periodontal disease

AIDS➔Acquired immunodeficiency syndrome; *HHV8,* human herpesvirus 8

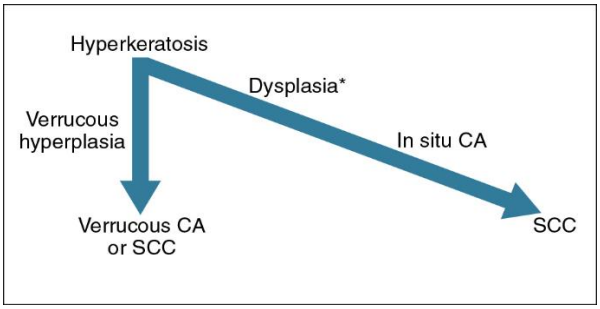
8➲Hairy Leukoplakia

❶Etiology ①Associated with local or systemic immunosuppression (esp. AIDS and organ transplantation) ②An opportunistic infection by Epstein-Barr virus ❷Clinical features ①Most commonly seen on lateral tongue, often bilateral ②Asymptomatic white lesion	③Papillary, filiform, or plaquelike architecture ④May occur before or after the diagnosis of AIDS ⑤May be secondarily infected by *Candida albicans* ❸Treatment ①None, unless cosmetically objectionable ②Antiviral and antiretroviral agents likely to cause lesion to regress

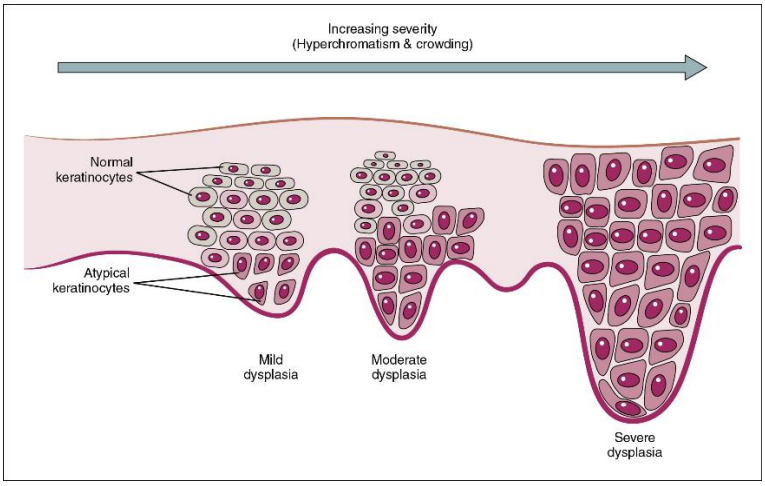
9➲Hairy tongue	
❶Etiology➔Not well understood➔related to oral flora change ❷Initiating factors ①Use of broad-spectrum antibiotics, systemic corticosteroids, hydrogen peroxide ②Intense smoking ③Head and neck therapeutic radiation ❸Clinical features ①Overgrowth of filiform papillae & chromogenic microorganism	②Dense hairlike mat formed by hyperplastic papillae on dorsal tongue surface ③Usually asymptomatic ④Cosmetically objectionable due to color (usually black) Treatment ①Identify and eliminate initiating factor ②Brush/scrape tongue with baking soda ③Little significance other than cosmetic appearance

10➲Actinic Cheilitis	
❶Etiology ①Overexposure to ultraviolet light (esp. UVB [2900-3200 nm]) ②A premalignant lesion ❷Clinical features ①Lower lip affected due to exposure to sun; upper lip➔minimal change ②More severe in light-skinned individuals ③Atrophic, finely wrinkled, and often swollen appearance of lip ④Possible presence of white and/or pigmented foci ⑤Poorly defined vermilion–skin junction ⑥Possible chronic ulceration in more severely damaged lips	❸Treatment ①Avoidance of direct sunlight ②Use of sunscreen/sun-blocking agent ③Biopsy of persistent ulcers and indurated lesions ④Vermilionectomy possibly needed in problematic cases ⑤Wedge excision of suspicious lesion is an alternative

UVB➔Ultraviolet B



Idiopathic leukoplakia pathogenesis➔Malignant transformation 10-15%

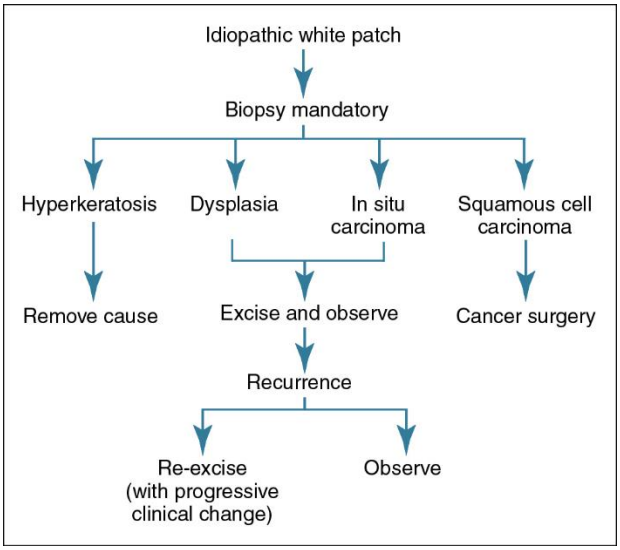


Progression of dysplasia

11➲Idiopathic Leukoplakia	
❶Risk factors➔Tobacco, alcohol, nutrition, unknown ❷Sites of occurrence➔Vestibule > buccal mucosa > palate > alveolar ridge > lip > tongue > floor of mouth ❸High-risk sites for malignant transformation➔Mouth floo > tongue > lip > palate > buccal mucosa > vestibule > retromolar ❸Age➔Usually over 40 years >➔More frequently affected	❹Microscopic diagnoses at first diagnosis ①Hyperkeratosis➔80% ②Dysplasia➔12% ③In situ carcinoma➔3% ④Squamous cell carcinoma➔5% ❺Transformation rates ①All idiopathic leukoplakias➔5% to 10% ②All dysplasias➔10% to 15%

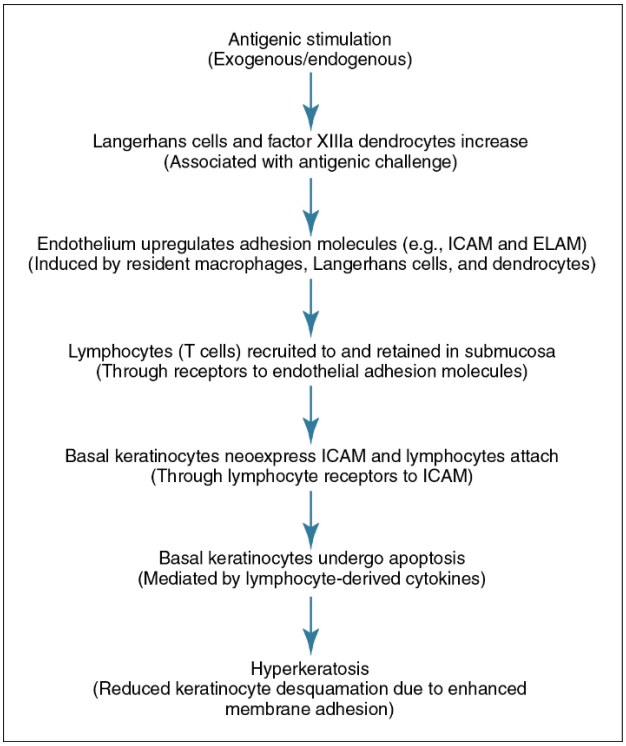
12➲Dysplasia➔Microscopic Features

❶Epithelial architecture ① Drop-shaped epithelial ridges ②Basal cell crowding ③Irregular stratification ④Reduced intercellular adhesion	❷Cytologic atypia ①Pleomorphic nucle➔hyperchromatic, smudgy, angular ②Increased nuclear-cytoplasmic ratios ③Increased and abnormal mitoses



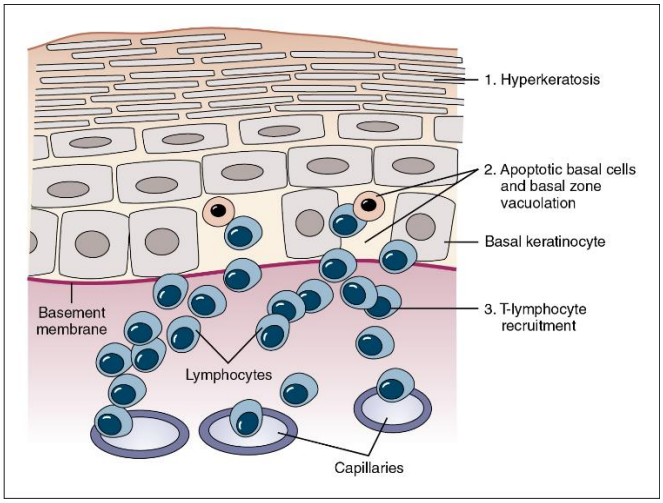
Idiopathic leukoplakia➔diagnosis and management

13➲Geographic Tongue	
❶Etiology➔Unknown ❷Clinical features ①Usually discovered as incidental finding on oral examination ②Common; 2% of U.S. population affected ③Appears as red atrophic patches surrounded by hyperkeratotic (white) margins ④Dorsum and lateral surfaces of tongue usually affected; rarely other mucosal sites	⑤Pattern changes with time (migratory glossitis) ⑥Often seen in company with fissured tongue ⑦Spontaneous regression/worsening ⑧Usually asymptomatic, but may be slightly painful ❸Treatment ①Usually none ②When painful, baking soda rinses, antifungals, or topical corticosteroids may help



Lichen planus: hypothetical molecular events

14➲Lichen Panus	
❶Cause➔unknown; basal keratinocyte destruction by T cells ❷Clinical features ①Adults; relatively common (0.2%-2% of population); persistent ②White keratotic striae characteristic ③Types➔reticular, erosive (ulcerative), plaque, papular, atrophic (erythematous) ④Pain➔erosive form (occasionally erythematous form)	❸Possible risk of carcinoma ①Concurrent tobacco use increases risk of carcinoma ②Risk may be slightly increased with erosive form (0.4%-2.5% of cases), especially in smokers ❹Pathology➔Interface mucositis with hyperkeratosis ❺Treatment➔Observation, topical and systemic corticosteroids, or other immunosuppressive agents



Lichen planus➔diagnostic features

15➲Lupus Erythematosus		
	Discoid	**Systemic**
Organs	**Skin and oral only**	**Skin, oral, heart, kidneys, joints**
Symptoms	**No**	**Fever, malaise, weight loss**
Serology	**No detectable antibodies**	**Positive ANA, anti-DNA antibodies**
Histopathology	**Basal cell loss, lymphocytes at interface and perivascular, keratosis**	**Similar to discoid**
DIF	**Granular/linear basement membrane deposits of IgG and C3**	**Similar to discoid**

ANA➔Antinuclear antibody; C➔complement; DIF➔direct immunofluorescence; IgG➔immunoglobulin G

16➲Candidiasis

❶Synonyms➔Thrush, angular cheilitis, median rhomboid glossitis, denture sore mouth, yeast infection, candidal leukoplakia, antibiotic stomatitis, moniliasis
❷Causes
①*Candida albicans* and other *Candida* species in oral flora
②Predisposing factors required
③Opportunistic overgrowth
❸Types➔Acute, chronic, mucocutaneous

17➲Candidiasis➔ Predisposing Factors

❶Immunodeficiency
❷Immunologic immaturity of infancy
❸Acquired immunosuppression
❹Endocrine disturbances
❺Diabetes mellitus
❻Hypoparathyroidism
❼Pregnancy
❽Hypoadrenalism
❾Corticosteroid therapy, topical or systemic
❿Systemic antibiotic therapy
⓫Malignancies and their therapies
⓬Xerostomia
⓭Poor oral hygiene

18➲Candidiasis➔ Classification

❶Acute
①Pseudomembranous (white colonies)
②Erythematous (red mucosa)
❷Chronic
①Erythematous (red mucosa)
②Hyperplastic (white keratotic plaque)
❸Mucocutaneous
①Localized (oral, face, scalp, nails)
②Familial
③Syndrome associated

18➲Candidiasis➔ Treatment

❶Topical
①Nystatin➔oral suspension* & pastille*; powder & ointment for denture; vaginal tablets (dissolved in mouth)
②Clotrimazole➔oral troches*
***Contains sugar; do not use with dentate patients with xerostomia**
❷Systemic
①Fluconazole
②Ketoconazole

Appendix 3➔Short Handout for Quick Revision

Red-blue lesions

1➲Congenital Vascular Lesions		
	Hemangioma	Vascular Malformation
Description	Abnormal endothelial cell proliferation	Abnormal blood vessel development
Elements	Results in increased number of capillaries	A mix of arteries, veins, & capillaries (includes arteriovenous shunt)
Growth	Rapid congenital growth	Grows with patient
Boundaries	Often circumscribed; rarely affects bone	Poorly circumscribed; may affect bone
Thrill and bruit	No associated thrill or bruit	May produce thrill and bruit
Involution	Usually undergoes spontaneous involution	Does not involute
Resection	Persistent lesions resectable	Difficult to resect; surgical hemorrhage
Recurrence	Recurrence uncommon	Recurrence common

2➲Gingival Reactive Hyperplasias		
	Pyogenic Granuloma	Peripheral Giant Cell Granuloma
Etiology	Initiated by trauma or irritation	Probably trauma or irritation
	Modified by hormones, drugs	Not related to hormones or drugs
Location	Predominantly gingiva, but any traumatized soft tissue	Exclusively gingival Usually anterior to first molars
Histopathology	Hyperplastic granulation tissue Misnomer—neither pus producing nor granulomatous	Hyperplasia of fibroblasts with multinucleated giant cells Not granulomatous inflammation
Treatment	Excision to periosteum or periodontal membrane	Excision to periosteum or periodontal membrane
Recurrence	Some recurrence; no malignant potential	Some recurrence; no malignant potential

3➲Erythroplakia	
❶Idiopathic mucosal red patch ①Cause unknown➔ome related to tobacco ②Age➔typically between 50 and 70 years ③High-risk sites➔floor of mouth, tongue, retromolar, soft palate	❷Histopathology ①Squamous cell carcinoma (50%) ②Severe dysplasia or in situ carcinoma (40%) ③Mild to moderate dysplasia (10%) ④Biopsy must be performed

4➲Kaposi Sarcoma			
	Classic Type	Endemic Type	Immunodeficiency Type
Etiology	HHV8	HHV8	HHV8
Geography	Mediterranean basin	Africa	AIDS and transplant patients
Prevalence	Rare	Endemic	Uncommon
Age	Older men	Children and adults	Young adults
Sites	Skin, lower extremities	Skin, extremities	Skin, mucosa, internal organs
Course	Indolent but progressive	Prolonged	Aggressive
Prognosis	Fair prognosis	Fair prognosis	Poor prognosis

AIDS➔Acquired immunodeficiency syndrome; *HHV8*, human herpesvirus 8

5➲Kaposi Sarcoma➔Key Features
❶Initiation by HHV8 (human herpesvirus 8) control of endothelial cell proliferation ❷Perpetuation by cytokines and growth factors released by macrophages, lymphocytes, and other cells ❸Incidence➔immunodeficiency type markedly reduced following use of new drugs to treat AIDS ❹High-risk oral sites➔palate and gingiva ❺Early lesions➔blue macule(s) ❻Differential➔ecchymosis, vascular malformation, erythroplakia, melanoma, blue nevus, amalgam tattoo ❼Advanced lesions➔nodular red-blue mass ❽Treatment➔combination antiretroviral therapy and other types of chemotherapy, intralesional chemotherapy, radiation, and surgery occasionally used for localized lesions

6➲Niacin deficiency
❶4D➔①Dermatitis ②Diarrhea ③Dementia ④Death

7➲Burning Mouth (Tongue) Syndrome	
Potential Causes	Potentially Helpful Regimens
Varied	Empathy
Candida albicans	Antifungals
Xerostomia➔drugs, anxiety, Sjögren's syndrome	Oral lubricants➔Moi-Stir, MouthKote, Salivart, Sialor
Nutritional deficiency➔B vitamins, iron, zinc	Dietary supplement➔vitamins, minerals
Abnormal tongue habit	Topical corticosteroids
Depression, anxiety	Tricyclic antidepressants, other
Pernicious anemia Diabetes mellitus Hormone imbalance	Medical referral➔internist, psychiatrist, gynecologist

8➲Oral-Facial Pain Conditions				
Site	Cause	Character	Initiating Factors	Treatment
Burning Mouth Syndrome				

Mouth	Unknown, psychiatric factors, habits, fungi, blood dyscrasia, neuropathy	Burning: constant to increasing through the day	None	TCA, SSRI, local measures, psychotherapy
Trigeminal Neuralgia				
Face	Unknown, demyelination, aneurysm	Sharp, stabbing, shooting	Light touch	Carbamazepine, phenytoin, baclofen, surgery
Glossopharyngeal Neuralgia				
Throat, tonsil	Space-occupying lesion, unknown, demyelination, aneurysm	Sharp, stabbing, shooting	Swallowing, chewing	Surgery, carbamazepine, phenytoin, baclofen
Postherpetic Neuralgia				
Face	Post varicella-zoster	Burning, constant dull pain	None	Gabapentin, TCA
Atypical Facial Pain				
Face	Unknown, psychiatric factors	Boring, constant ache	None	TCA, SSRI, psychotherapy
Atypical Odontalgia				
Tooth, alveolus	Unknown, psychiatric factors	Boring, constant ache	None	TCA, SSRI, psychotherapy

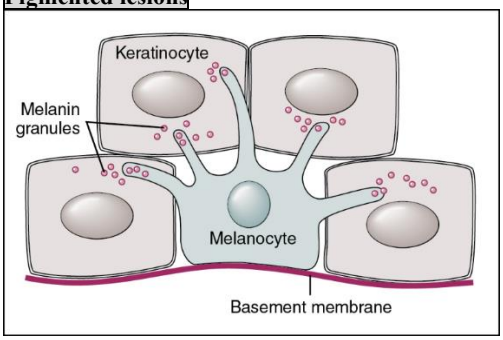
SSRI➔Selective serotonin reuptake inhibitor; TCA➔tricyclic antidepressant

9➲Blood Dyscrasias That May Have Oral Manifestations	
❶Leukemia > monocytic > myelocytic > lymphocytic	❼Macroglobulinemia
❷Agranulocytosis	❽von Willebrand's disease
❸Cyclic neutropenia	❾Multiple myeloma
❹Infectious mononucleosis	❿Polycythemia vera
❺Thrombocytopenic purpura (ITP and TTP)	⓫Sickle cell anemia
❻Hemophilia A and B	⓬Thalassemia

10➲ Blood Dyscrasias➔Oral Manifestations	
❶Mucosal petechiae and ecchymoses➔reduced platelets and/or clotting factors	❻Refractory gingivitis
❷Gingival enlargement	❼Leukemic infiltrates
❸Leukemic infiltrates	❽Loose teeth➔leukemic infiltrates in periodontal ligament
❹Inflammation and hyperplasia (poor oral hygiene)	❾Mucosal ulcers➔cyclic neutropenia; ulcer mechanism undetermined
❺Excessive bleeding with minor trauma, gingivitis➔reduced numbers of platelets and/or clotting factors	

Appendix 3➔Short Handout for Quick Revision

Pigmented lesions



Melanocyte-keratinocyte unit➔dendritic processes of melanocyte and melanin transfer to keratinocytes

1➲Ectodermal Dysplasia

❶Melanotic Macule
❷Characteristic signs and symptoms
①A complex group of inherited conditions
②A combination of defects expressed in 2 or more ectodermal-derived tissues
③Hair, exocrine glands, teeth, and nails may be affected
④Most common form is X-linked recessive
②Anodontia or hypodontia with abnormal tooth morphology (peg-shaped)
③Sparse, lanugo-like hair
④Dystrophic nails
⑤Pyrexia (eccrine hypoplasia and an inability to sweat)
⑥Defective hearing and abnormal pinna morphology
⑦Dysphagia (mucosal gland hypoplasia)
⑧Xerostomia (mucosal gland hypoplasia) and caries
⑨Xerophthalmia (lacrimal hypoplasia) and associated conjunctivitis

1➲Melanotic Macule

❶Common oral pigmentation
❷Idiopathic (ephelis 雀斑)
❸Postinflammatory
❹Syndrome associated (Peutz-Jeghers, Addison's disease, Laugier-Hunziker, Bandler syndrome)
❺Early melanoma may have similar appearance
❻Melanin seen in basal keratinocytes
❼Medication related (e.g., antimalarials [melanin complexed with ferric iron])

2➲Systemic Conditions Associated with Oral Melanotic Macules

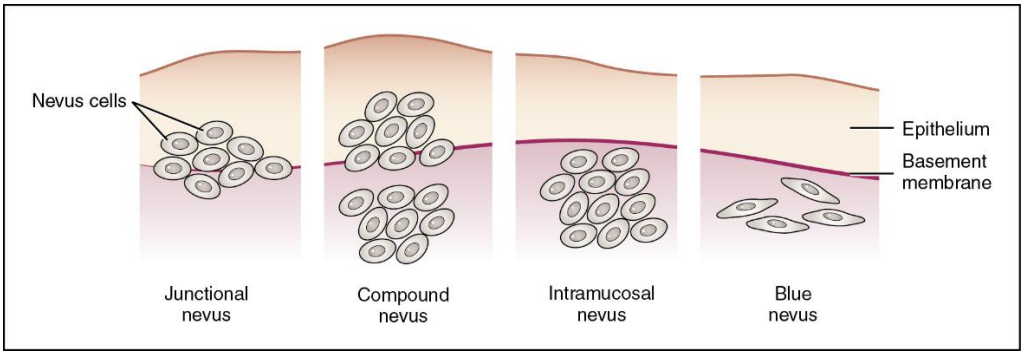
❶Peutz-Jeghers syndrome
①Intestinal polyposis (hamartomas)
②Autosomal-dominant inheritance
③Risk of other cancers
❷Addison's disease
①Macules and diffuse bronzing
②Adrenal cortical insufficiency➔weakness, hypotension, nausea, weight loss
❸Laugier-Hunziker syndrome➔ Oral, subungual, and skin macules
❹Bandler syndrome➔Small intestine hemangiomas and mucocutaneous macules

3➲Differential Diagnosis➔Pigmented Macule

❶Physiologic (ethnic) pigmentation
❷Melanotic macule
❸Smoking-associated melanosis
❹Syndrome-associated pigmentation
❺Peutz-Jeghers syndrome
❻Bandler syndrome
❼Addison's disease
❽Laugier-Hunziker phenomenon
❾Melanocytic nevus
❿Melanoma
⓫Amalgam tattoo
⓬Drug-induced pigmentation

4➲Oral Lesions Associated with Cutaneous Pigmented Macules

❶Neurofibromatosis
❷Neurofibromas of skin, oral mucosa, jaws
❸Café-au-lait macules of skin
❹McCune-Albright syndrome
❺Polyostotic fibrous dysplasia, including jaws
❻Endocrine abnormalities (e.g., precocious puberty)



Melanocytic nevus subtypes

5➲Mucosal Melanocytic Nevus	
❶Palate is most common site ❷Must differentiate from melanoma (biopsy) ❸Probably has no malignant potential	❹Types (in order of frequency) ①Intramucosal nevus ②Blue nevus ③Compound nevus ④Junctional nevus

6➲Oral Melanoma	
❶Palate and gingiva are high-risk sites ❷Early lesion➔pigmented macule ❸Advanced lesion (ABCS)➔*a* symmetry, *b* orders irregular, *c* olor variable, *s* atellite lesions ❹No known risk factors	❺Biological subtypes ①In situ melanoma (1)Prolonged preinvasive junctional phase (2)Poor prognosis due to delayed diagnosis and undertreatment ②Invasive melanoma (1)Connective tissue invasion without junctional phase (2)Poor prognosis

7➲Drugs with Oral Pigment–Producing Potential		
❶Amiodarone ❷Aminoquinolines ❸Clofazimine	❹Cyclophosphamide ❺Heavy metal–containing compounds ❻Quinacrine	❼Minocycline ❽Premarin ❾Zidovudine

Appendix 3➔Short Handout for Quick Revision

Verrucal-papillary lesions

1➲Lesions Caused by Human Papillomavirus Subtypes	
Lesion	**HPV Subtype**
Oral papilloma/wart	2, 6, 11, 57
Focal epithelial hyperplasia	13, 32
Dysplastic wart (HIV)	16, 18, others
Verruca vulgaris, skin	2, 4, 40, others
Flat wart	3, 10
Condyloma acuminatum	6, 11, others
Laryngeal papilloma	11
Conjunctival papilloma	11
Maxillary sinus papilloma	57

HIV➔human immunodeficiency virus; HPV➔human papillomavirus

2➲Papilloma

❶Common oral epithelial proliferation
❷Most caused by HPV
❸Nononcogenic subtypes (HPV subtypes 2, 6, 11, and 57)
❹"Oral wart" (verruca vulgaris)➔synonym for papilloma
❺Very low level of infectivity
❻Little significance
❼Recurrence/multiple lesions in immunosuppressed patients (e.g., HIV-positive patients, transplant recipients)

3➲Dysplastic Oral Warts

❶HIV-positive patients only
❷Multiple HPV subtypes, including 16, 18
❸Oral mucosa only
❹Histopathology➔ranging from dysplasia to in situ carcinoma
❺Invasive/metastatic potential unknown

4➲Verrucous Carcinoma

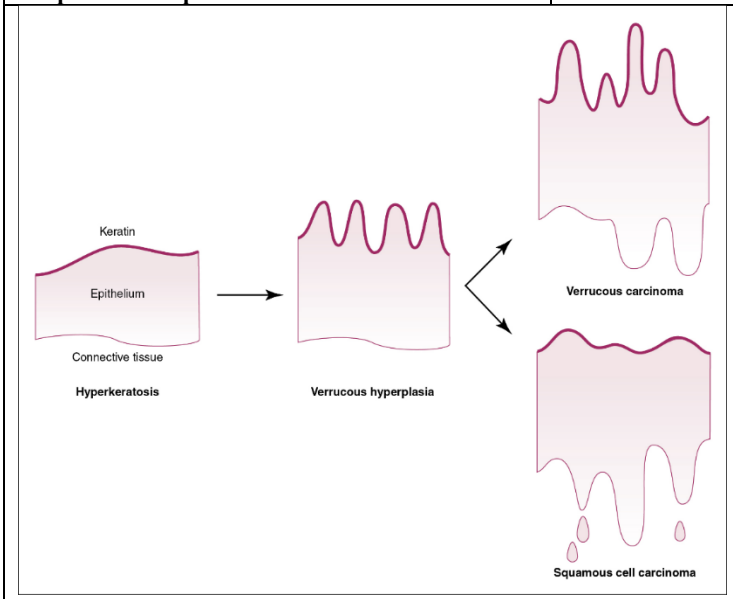
❶Etiology➔Tobacco
❷Clinical features
①Slow-growing verrucous patch
②Locally destructive; rarely metastasizes
③Buccal mucosa > gingiva > tongue > palate > other

❸Microscopy
①Well-differentiated carcinoma
②Little or no dysplasia
❹Treatment
①Excision
②prognosis excellent

5➲Proliferative Verrucous Leukoplakia

❶Etiology
①A subset of idiopathic leukoplakia
②Unproven association with HPV subtypes 16 and 18
③Tobacco not a strong etiologic factor, as with idiopathic leukoplakia

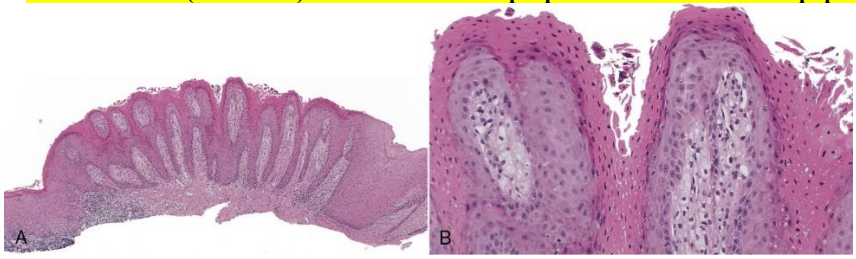
❷Clinical features
①Females more often affected than males
②Recurrent/persistent; multiple sites typical
③Progression from simple keratosis to well-differentiated verruciform lesions
④High risk of malignant transformation to verrucous carcinoma or squamous cell carcinoma



Proliferative verrucous leukoplakia

6➲ Verruciform xanthoma

❶Characteristics➔uncommon➔benign oral mucosa (occasional on skin, typically on genitalia)
❷Etiology
①unknown
②missense mutation in exon 6 of 3 beta-hydroxysteroid dehydrogenase (NSDHL) gene➔solitary verruciform xanthoma
③mutation in NSDHL➔confined within exons 4 & 6➔multiple syndromic verruciform xanthomas
❸Clinical features
①well-circumscribe, with granular to papillary surface
②size➔2 mm_> 2 cm
③level of keratinization of surface influences color (from white to red)
④most white➔no gender predilection
⑤average age➔45 years (some 1st & 2nd decades)
❹Histopathology
①papillomatous/verrucous surface composed of parakeratinized epithelial cells
②elongated epithelial ridges extend into lamina propria at uniform depth
③no dysplasia
④numerous foam(xanthoma) cells within lamina propria or connective tissue papillae



⑤foam cell➔granular to flocculent cytoplasm➔contain PAS(+), diastase-resistant granule or lipid droplet (or both)
⑥IHC➔CD68(+) & CD163(+)➔foam cells➔monocyte/macrophage lineage
❺Differential diagnosis➔squamous papilloma, papillary squamous carcinoma, verrucous carcinoma & condyloma acuminatum
❻Treatment➔excision(no recurrence reported)

Appendix 3➔Short Handout for Quick Revision

Connective tissue diseases

1➲Oral Fibrous Hyperplasia➔Synonyms

❶Traumatic fibroma	❹Inflammatory fibrous hyperplasia	❼Denture (-induced fibrous) hyperplasia
❷Irritation fibroma	❺Peripheral fibroma of gingiva	❽Epulis fissuratum (denture-induced)
❸Hyperplastic scar	❻Fibrous epulis of gingiva	

2➲Gingival Hyperplasia➔Causes/Modifiers

❶Local factors➔plaque, calculus, bacteria
❷Hormonal imbalance➔estrogen, testosterone
❸Drugs➔phenytoin (Dilantin); cyclosporine; nifedipine and other calcium channel blockers
❹Leukemia (due to leukemic infiltrates and/or local factors)
❺Genetic factors/syndromes

3➲Oral Fibroblastic Proliferations

❶Fibrous hyperplasia➔very common oral lesion	❻Fibrosarcoma➔rare oral tumor
❷Solitary fibrous tumor➔uncommon to rare tumor	❼Fibrous histiocytoma
❸Nodular fasciitis➔rare oral tumor	❽Benign➔uncommon to rare oral tumor
❹Myofibroma➔uncommon to rare tumor	❾Malignant➔rare oral tumor
❺Fibromatosis➔rare oral tumor	

3➲Oral Solitary Fibrous Tumor

❶Oral counterpart of pleural solitary fibrous tumor	❹Immunochemistry➔positive for STAT6, CD34, CD99, and Bcl-2
❷Benign spindle cell proliferation➔fibroblastic origin	❺Circumscribed
❸Buccal mucosa commonly affected	❻Treatment by excision; no recurrence

4➲Mucosal Myxoid Lesions➔Microscopic Differentiation

	Mast Cells	Reticulin	Pattern	Periphery
Soft tissue myxoma	No	Yes	Diffuse, uniform	Blending, infiltration
Nerve sheath myxoma	Yes	Yes	Lobular	Condensed fibrous tissue
Focal mucinosis	No	No	Uniform	Circumscribed

5➲Nodular Fasciitis, Fibrous Histiocytoma, Fibromatosis

	Nodular Fasciitis	Fibrous Histiocytoma	Fibromatosis
Tumor type	Reactive	Benign	Benign, aggressive
Age	Young adults, adults	Adults	Children, young adults
Symptoms	Often	Infrequently	Infrequently
Sites	Trunk, extremities; head and neck 10%	Skin, mucosa	Shoulder, trunk; head and neck 10%
Growth rate	Rapid	Slow	Moderate
Periphery	Nodular	Circumscribed	Infiltrative
Recurrence	Rarely	Uncommon	Common
Treatment	Excision	Excision	Aggressive surgery

6➲Macroglossia

❶Congenital hyperplasia/hypertrophy
❷Tumor➔lymphangioma, vascular malformation, neurofibroma, granular cell tumor, salivary gland tumor
❸Endocrine abnormality➔acromegaly, cretinism
❹Infections obstructing lymphatics
❺Beckwith-Wiedemann syndrome➔macroglossia, exomphalos, gigantism
❻Amyloidosis
❼Angioedema

7➲Oral Granular Cell Tumor

❶Clinical features	❷Histopathology
①Benign tumor of neural sheath origin	①Large, uniform cells with granular cytoplasm
②Any age; females slightly more than males	②Overlying pseudoepitheliomatous hyperplasia
③Any site; usually tongue	③Cells positive for neural-associated proteins (e.g., S-100) and negative for muscle proteins (actin)
④Asymptomatic submucosal mass (1-2 cm)	❸Treatment➔Excision; no recurrence
⑤Same or lighter than mucosal color	
⑥Intact overlying epithelium	

8➲Congenital l Granular Cell Tumor (Epulis)

❶Clinical features	❷Histopathology
①Benign tumor of disputed origin	① (Large, uniform cells with granular cytoplasm
②Infants only	②No overlying pseudoepitheliomatous hyperplasia
③Gingiva only	③Cells negative for S-100 and actin but positive for NKI-C3
④Usually pedunculated, nonulcerated mass	❸ Treatment➔Excision; no recurrence

9➲Neural Tumors➔Comparative Features

	Schwannoma	Neurofibroma	Mucosal Neuroma	PEN
Cell of origin	Schwann cell	Schwann cell and perineural fibroblast	Nerve tissue, hamartoma	Schwann cell

Age	**Any**	**Any**	**Children, young adults**	**Adults**
Site	**Any, especially tongue**	**Any, especially tongue, buccal mucosa**	**Tongue, lip, buccal mucosa**	**Palate, lip**
Number	**Solitary**	**Solitary to multiple**	**Multiple**	**Solitary**
Bone lesions	**Occasionally**	**Frequently**	**No**	**No**
Syndrome association	**Neurofibromatosis**	**Neurofibromatosis**	**MEN III**	**None**
Malignant potential	**Rarely with syndrome**	**Infrequently with syndrome**	**No**	**No**

MEN III ➔Multiple endocrine neoplasia syndrome type III; PEN ➔palisaded encapsulated neuroma

10➲Soft Tissue Tumors➔Cytogenetic Abnormalities		
Tumor Type	**Cytogenetic Change**	**Gene Abnormality**
Alveolar rhabdomyosarcoma	**t(2;13), t(1;13)**	***PAX3-FKHR*** **PAX7-FKHR**
Synovial sarcoma	**t(X;18)(p11.2;q11.2)**	***SYT* + one of SSX1, SSX2, SSX4 SSX2-SYT**
Lipoma	**Rearranged 12q13-q15**	***HMGA2/LPP, HMGA2/LHFP***
Myxoid liposarcoma	**t(12;16)(q13;p11)**	***DDIT3 (CHOP) + FUS (TLS)***
Mucosal neuroma (MEN III)	**Chromosome 10 mutation**	***RET***

MEN III➔Multiple endocrine neoplasia syndrome type III

11➲Oral Spindle Cell Neoplasms: Differential Immunoprofile							
	S-100	**Neurofilament**	**Muscle Actin**	**Desmin**	**CD34**	**CD99**	**CD31**
Nerve sheath tumors (benign and malignant)	+	+	–	–	–	–	–
Myofibroma	–	–	+	–	–	–	–
Leiomyoma/sarcoma	–	–	+	+	–	–	–
Rhabdomyoma/sarcoma	–	–	+	+	–	–	–
Fibrous histiocytoma and MFH	–	–	–	–	–	–	–
Solitary fibrous tumor	–	–	–	–	+	+	–
Kaposi's sarcoma	–	–	–	–	–	–	+ #

MFH ➔Malignant fibrous histiocytoma

Appendix 3➔Short Handout for Quick Revision

Lymphoid lesions

1➲Modified WHO Classification of Lymphomas

	B-Cell Neoplasms	T-Cell and Postulated NK-Cell Neoplasms
Precursor cell neoplasms	Precursor B-lymphoblastic lymphoma/leukemia	Precursor T-lymphoblastic lymphoma/leukemia
Peripheral (mature) cell neoplasms	B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma (B-CLL/SLL)	T-cell chronic lymphocytic leukemia
	Lymphoplasmacytoid lymphoma	Large granular lymphocytic leukemia (T-cell or NK-cell type)
	Mantle cell lymphoma	Mycosis fungoides
	Marginal zone B-cell lymphoma (extranodal or nodal)	Peripheral T-cell lymphoma, unspecified
	Splenic marginal zone B-cell lymphoma	Angioimmunoblastic lymphoma
	Hairy cell leukemia	Intestinal T-cell lymphoma
	Plasmacytoma	Adult T-cell lymphoma/leukemia
	Diffuse large B-cell lymphoma Burkitt's lymphoma	Anaplastic large cell lymphoma

***NK*➔Natural killer**

2➲Characteristic Cytogenetic Findings in Selected, Specific Lymphomas

Lymphoma Type	Translocation	Oncogene or Tumor Suppressor Genes	Mechanism
Follicular lymphoma	t(14;18)	*Bcl-2*	Juxtaposition of *Bcl-2* with IgH promoter results in overexpressed antiapoptotic protein *Bcl-2*
Extranodal marginal zone	t(11;18) t(1;14)	*AP12, MLT* *Bcl-10*	Chimeric protein that inhibits apoptosis. Juxtaposition of lymphoma *Bcl-10* with IgH promoter results in overexpressed *Bcl-10* protein
Mantle cell lymphoma	t(11;14)	*Bcl-1* (cyclin D1)	Juxtaposition of *Bcl-1* with IgH promoter results in overexpressed cyclin D1 protein
Burkitt's lymphoma	t(8;14) t(8;22) t(2;8)	*c-Myc*	Overexpression of *Myc* is due to juxtaposition of the *c-Myc* gene with IgH, Igκ, or Igλ
Anaplastic large cell lymphoma	t(2;5)	*NPM, ALK*	Production of chimeric *NPM, ALK* protein, which has lymphoma tyrosine kinase activity

Ig➔Immunoglobulin.

3➲Ann Arbor Staging System for Non-Hodgkin's Lymphoma

Stage	Definition
I	Involvement of a single lymph node region or of a single extranodal organ or site (I_E)
II	Involvement of two or more lymph node regions on the same side of the diaphragm, or localized involvement of an extranodal site or organ (II_E) and one or more lymph node regions on the same side of the diaphragm
III	Involvement of lymph node regions on both sides of the diaphragm, which may also be accompanied by localized involvement of an extranodal organ or site (III_E) or spleen (III_S), or both (III_{SE})
IV	Diffuse or disseminated involvement of one or more distant extranodal organs with or without associated lymph node involvement

Subclassification

A. Without systemic symptoms

B. Systemic symptoms: unexplained fever >38° C; unexplained weight loss >10% of body weight in past 6 months; night sweats

4➲Comparison of Clinical Features of Indolent, Aggressive, and Highly Aggressive Lymphomas

	Indolent	Aggressive	Highly Aggressive
Examples of types	Follicular lymphoma B-CLL/SLL Mantle cell lymphoma	Diffuse B-cell lymphoma Peripheral T-cell lymphoma	Burkitt's lymphoma
Age	Adults	Any	Children, young adults
Stage at presentation	High (>80% stages III and IV)	Any	High
Tumor growth rate	Slow; proliferative fraction is low	Fast	Very fast; proliferative fraction >95%
Bone marrow involvement	Yes	Uncommon	Common
Natural history if untreated	Indolent, usually takes years to kill patient	Patient death in 1-2 years	Patient death in weeks to months
Response to treatment	Poor	Responsive	Very responsive

B-CLL/SLL➔B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma

5➲Antibodies to CD Markers Useful in the Diagnosis of Lymphoma

CD Marker	Expression in Normal Tissues	Expression in Malignancy
CD1a	Langerhans cells	Langerhans cell disease
CD3	T cells NK cells	T-cell neoplasms NK neoplasms
CD4	Helper/inducer T cells Monocytes Histiocytes	Some T-cell neoplasms Langerhans cell disease

	Langerhans cells	
CD8	Suppressor/cytotoxic T cells NK cells	Some T-cell neoplasms Some NK-cell neoplasms
CD10(CALLA)	Follicular center B cells Granulocytes	Follicular center cell lymphomas Burkitt's lymphoma
CD15(LeuM1)	Granulocytes Monocytes	Classic Hodgkin's disease
CD20	B cells but not pre-B cells or plasma cells	B-cell neoplasms Weak in B-CLL/SLL Nodular lymphocyte–predominant Hodgkin's disease
CD22	B cells but not plasma cells	B-cell neoplasm
CD23	B cells Follicular dendritic cells	B-CLL/SLL Some follicular center cell lymphomas
CD30	Activated T and B cells	Classic Hodgkin's disease ALCL
CD43	T cells Histiocytes	T-cell neoplasms Some B-cell neoplasms
CD45RB	All leukocytes Not plasma cells	Lymphomas and leukemias
CD45RO (UCHL-1)	T cells Histiocytes Myeloid cells	T-cell neoplasms
CD56	NK cells	NK-cell neoplasms Some peripheral T-cell lymphomas
CD79a	B cells, including plasma cells	B-cell neoplasms including plasma cell tumors Nodular lymphocyte–predominant Hodgkin's disease
CD138	Plasma cells and precursors	Plasma cell tumors
Pax5	All B cells but not plasma cells	B-cell neoplasms
Oct2	Immunoglobulin producing B cells	B-cell neoplasms

ALCL➔Anaplastic large cell lymphoma; B-CLL/SLL➔B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma; NK➔natural killer

6➲Antibody Panel for Immunophenotyping of Lymphomas

Lymphoma Type	CD5	CD20	CD23	CD10	CD30	Cyclin D1	Bcl-2	CD3
B-CLL/SLL	+	+	+	−	−	−	−	−
Mantle cell	+	+	−	−	−	+	−	−
Marginal zone	−	+	−	−	−	−	−	−
Diffuse B-cell	−	+	−	−	−	−	±	−
Follicular	−	+	−	+	−	−	+	−
ALCL	−	−	−	−	+	−	±	+ *

ALCL➔Anaplastic large cell lymphoma; B-CLL/SLL➔B-cell chronic lymphocytic leukemia/small lymphocytic lymphoma➔NK, natural killer

7➲Amyloidosis Classification According to Fibril-Forming Proteins

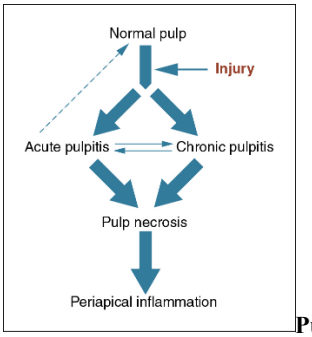
Disease	Amyloid Subtype and Protein	Precursor Protein
Primary amyloidosis (myeloma associated)	AL	Igκ, Igλ
Secondary amyloidosis (chronic inflammatory disease associated)	AA	Serum amyloid A (apoSAA)
Chronic renal failure	$A\beta_2M$	β_2-Microglobulin
Alzheimer's disease	Aβ	Amyloid β-precursor protein
Medullary carcinoma of thyroid	ACa	Calcitonin

Ig➔Immunoglobulin

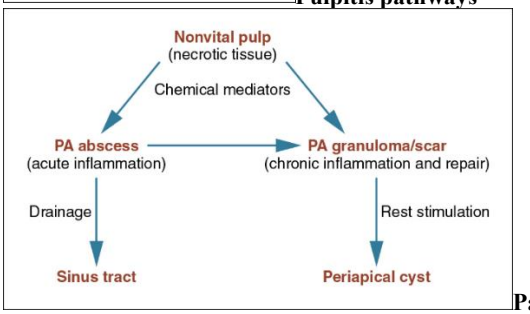
Appendix 3➔Short Handout for Quick Revision

Inflammatory jaw lesions

1➲Pulpitis and Periapical Diseases			
	Pain	Vitality Tests	Radiographs
Reversible pulpitis	Mild	Reversible sensitivity to cold	No change
Acute pulpitis	Severe, constant	Hyperresponse to none	No change
Chronic pulpitis	Mild, intermittent	Reduced response	No change
Acute periapical abscess	Severe; pain on percussion	No response	No change
Periapical granuloma	None to slight	No response	Lucency
Periapical cyst	None to slight	No response	Lucency



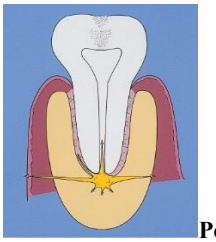
Pulpitis pathways



Pathogenesis of periapical inflammation

2➲Periapical Pathology			
❶Inflammatory ①Periapical granuloma ②Scar ③Cyst ④Chronic abscess ⑤Actinomycosis	❷Benign, aggressive ①Odontogenic keratocyst ②Calcifying odontogenic cyst ③Central giant cell granuloma ④Ameloblastoma ⑤Calcifying epithelial odontogenic tumor ⑥Myxoma	❸Benign ①Traumatic bone cyst ②Nasopalatine canal cyst ③Langerhans cell disease ④Adenomatoid odontogenic tumor ⑤Periapical cemento-osseous dysplasia ⑥Ossifying fibroma	❹Malignant ①Metastasis ②Lymphoma ③Myeloma

3➲Noninflammatory Periapical Disease➔Signs and Symptoms	
❶Paresthesia or atypical pain	❸No relationship to periodontal ligament or lamina dura
❷Large lesions and lesions with ill-defined margins	❹Tooth vitality positive or equivocal



Potential spread of pus from a mandibular periapical abscess

4➲Chronic Osteomyelitis➔Types and Features				
	Etiology	Clinical Features	Radiographs	Treatment
Chronic osteomyelitis	Most infectious (bacteria)	Variable pain, swelling, drainage	Lucent or mottled pattern	Appropriate antibiotic, sequestrectomy
Chronic osteomyelitis with proliferative periostitis	Sequela of tooth abscess, extraction	Usually associated with lower molar; periosteum involved; children	Lucent or mottled pattern with concentric periosteal opacities	Tooth removal, antibiotics
Diffuse sclerosing osteomyelitis	Probably low-grade infection, pulpitis, periodontal disease	Occasional pain, swelling, drainage; mandible	Opacification throughout jaw	Antibiotics; find cause and, if possible, treat
Focal sclerosing osteitis	Low-grade focal bone irritation (e.g., pulpitis)	Asymptomatic; found on routine examination	Opaque mass, usually at root apex	Treat offending tooth

5➲Bisphosphonates Currently Prescribed		
Generic Name	**Brand Name**	**Route of Administration**
Pamidronate	Aredia	Intravenous
Alendronate	Fosamax	Oral
Ibandronate	Boniva	Oral
Risedronate	Actonel	Oral
Zoledronic acid	Zometa, Reclast, Aclasta	Intravenous
Clodronate Etidronate	Bonefos Didronel	Oral/Intravenous Oral

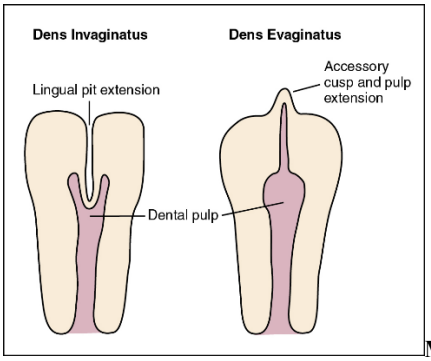
6➲Bisphosphonates➔Risks and Benefits	
❶Benefits ①Inhibition of bone resorption by osteoclasts ②Possible antitumor effect ③Useful for osteoporosis, Paget's disease, medullary bone cancers (prevent fracture)	❷Risks ①Bone fracture due to suppressed remodeling ②Hypocalcemia ③Impaired renal function ④Esophagitis ⑤Osteonecrosis of the jaws

7➲Bisphosphonate-Related Osteonecrosis Risk Factors		
❶Drug associated ①High drug dosage ②Long duration of drug usage ③High drug potency ④Intravenous (as opposed to oral) route of administration	❷Dental or local factors ①Poor oral hygiene ②Ill-fitting dentures ③Periodontal disease ④Dentoalveolar infection	❸Systemic factors ①Patient medications (1)Cancer chemotherapeutic drugs (2)Systemic corticosteroids ②Diabetes mellitus ③Smoking ④Renal dialysis ⑤Obesity ⑥Older age

Appendix 3➔Short Handout for Quick Revision

Tooth abnormalities

1➲Ectodermal Dysplasia	
❶Etiology	❷Characteristic signs and symptoms
①A complex group of inherited conditions ②A combination of defects expressed in 2 or more ectodermal-derived tissues ③Hair, exocrine glands, teeth, and nails may be affected ④Most common form is X-linked recessive (1)Known as Christ-Siemens-Touraine syndrome (2)Also known as hypohidrotic/anhydrotic ectodermal dysplasia (3)Usually due to mutations in the EDA (ectodysplasin) gene	①Dry, scaly skin (eccrine hypoplasia) ②Anodontia or hypodontia with abnormal tooth morphology (peg-shaped) ③Sparse, lanugo-like hair ④Dystrophic nails ⑤Pyrexia (eccrine hypoplasia and an inability to sweat) ⑥Defective hearing and abnormal pinna morphology ⑦Dysphagia (mucosal gland hypoplasia) ⑧Xerostomia (mucosal gland hypoplasia) and caries ⑨Xerophthalmia (lacrimal hypoplasia) and associated conjunctivitis



Morphology of dens invaginatus and dens evaginatus

2➲Hereditary Conditions of Teeth			
	Amelogenesis Imperfecta	Dentinogenesis Imperfecta	Dentin Dysplasia
Heredity	Many patterns	Autosomal dominant	Autosomal dominant
Teeth affected	All teeth, both dentitions	All teeth, both dentitions	All teeth, both dentitions
Tooth color	Yellow	Yellow	Normal
Tooth shape	Smaller, pitted	Extreme occlusal wear	Normal
X-ray findings	Normal pulps/dentin; reduced enamel	Obliterated pulps, short roots, bell crowns	Obliterated pulps, periapical cysts/granulomas
Systemic manifestations	No	Osteogenesis imperfecta occasionally	No
Treatment	Full crowns	Full crowns	None; early tooth loss

3➲Supernumerary roots
❶Accessory roots➔most commonly seen in mandibular canine, premolar, and molar (especially third molars)
❷Upper anterior teeth and mandibular incisor rare
❸Radiographic recognition important when extractions or root canal fillings