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

Content

➲References➔Figures

❶Oral & Maxillofacial Pathology, Elsevier, 5th edition ❷oralpathol.dlearn.kmu.edu.tw ❸www.slideserve.com/latika/approach-to-hemolytic-anemia
❹researchgate.net/figure/The-antegonial-notch-depth-and-the-region-of-interest-10-10-mm-2-in-the-human_fig1_51426212
❺researchgate.net/figure/Neural-crest-specification-and-delamination-Neuroectodermal-patterning-is-a-very-dynamic_ fig1_331500570

Taiwan Oral Pathology Association Scholarship

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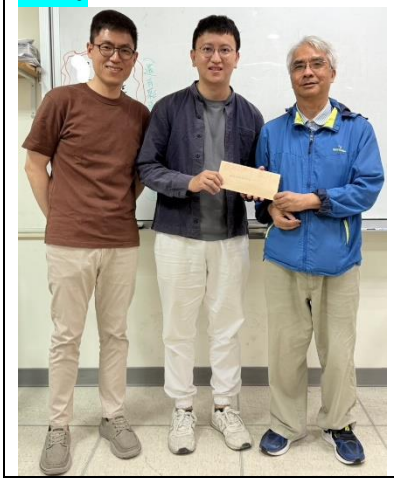

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學 習 目 標

樹老易空，人老易鬆

科學之道

戒之以空，戒之以鬆

願一輩子，從實以終

華羅庚 中國著名數學家

(美國伊利諾大學終身教授)

樹貧易空，人惰易鬆

求學(國考)之道

戒之以空，戒之以鬆

願從此時，從實以終

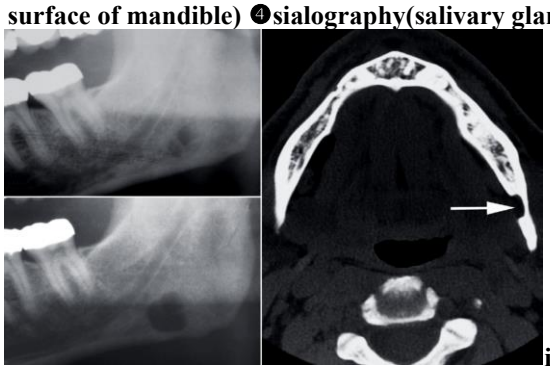
Chapter 1 Developmental defects of oral & maxillofacial region

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

➲developmental in nature➔BUT not present from birth | ➲most➔middle-aged & older adults (children rare)

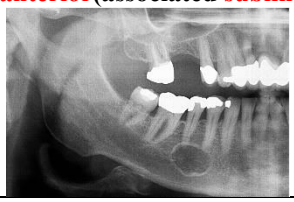
➲defect content➔❶devoid of tissue ❷contain muscle, blood vessel, fat, connective tissue, lymphoid tissue

➲male predilection(80-90%)
➲asymptomatic RL below mandibular canal➔posterior mandible (between molar & mandibular angle)
➲confirm➔❶CT ❷CBCT ❸MRI (well-defined concavity on lingual surface of mandible) ❹sialography(salivary gland tissue in defect)

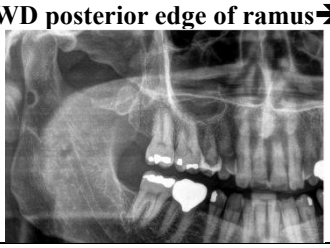


ill-defined

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

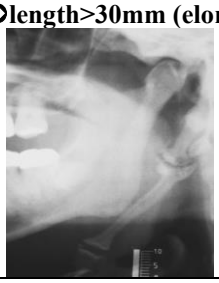


➲WD posterior edge of ramus➔parotid gland



Eagle syndrome

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



➲symptoms
❶swallowing➔tissue in throat rub on SP➔pain along glossopharyngeal nerve
❷pain upon turning head/extending tongue

Developmental cysts(non-odontogenic)

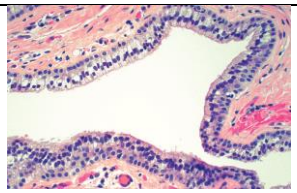
Palatal cysts of new born(Epstein's pearl, Bohn's nodule)

➔also describe gingival cyst of newborn)

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

Nasolabial cyst

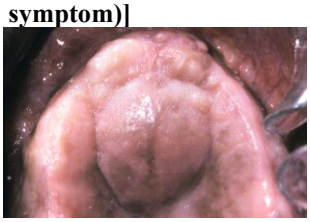
➲pseudostratified columnar epithelium with goblet cell & cilia

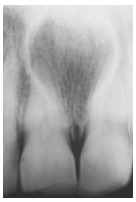


Nasopalatine duct cyst(incisive canal cyst)

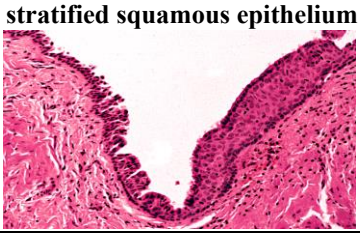
➲most common nonodontogenic cyst(1%) | ➲arise from remnant of nasopalatine duct

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

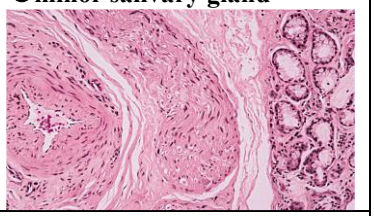




➲cystic lining➔transition from pseudostratified columnar to stratified squamous epithelium



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

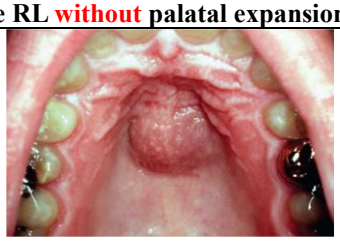
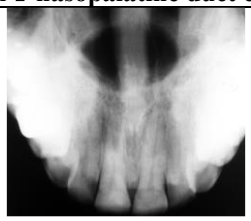


➲develop➔soft tissue of incisive papilla➔cyst of incisive papilla

Median palatal cst

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

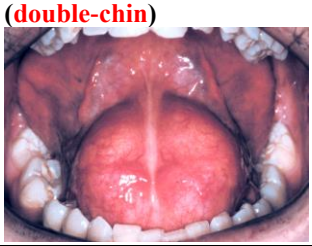
➲❶occlusal radiograph➔hard palate➔WD oval-shaped midline RL
❷posterior to palatine(incisive) papilla
❸not related to non-vital tooth
❹not communicate with incisive canal
❺cystic wall➔no neurovascular bundle, hyaline cartilage, minor salivary gland

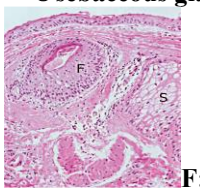
1. Which cyst is *not* an odontogenic cyst?
   (A) dentigerous cyst
   (B) primordial cyst
   (C) median palatal cyst
   (D) lateral periodontal cyst

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

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



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

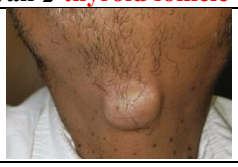
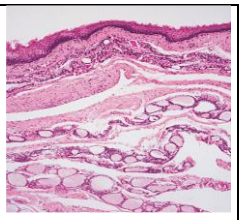


F: hair follicle; S: sebaceous gland

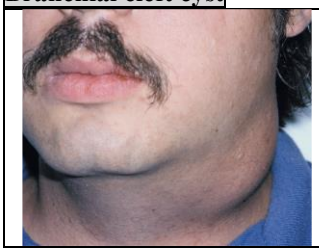
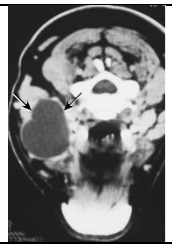
2. With which cyst may the patient complain of **dysphagia**?
   (A) thyroglossal tract cyst (dermoid cyst)
   (B) median palatal cyst
   (C) static bone cyst
   (D) traumatic bone cyst

Thyroglossal duct cyst

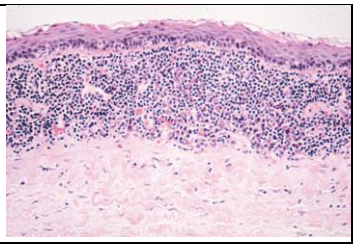
➲swelling➔neck anterior midline(anywhere➔foramen cecum of tongue to suprasternal notch)
➲tongue base➔laryngeal obstruction | ➲75% below hyoid bone | ➲cyst wall➔thyroid follicle
➲attach hyoid bone/tongue➔swallow➔cyst 移動 vertical/tongue protrude
➲suprahyoid➔submental➔dysphagia?
➲arise thyroglossal carcinoma(papillary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

Branchial cleft cyst

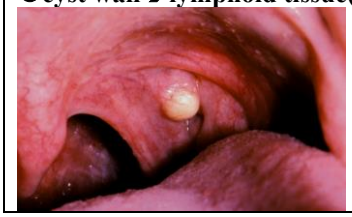



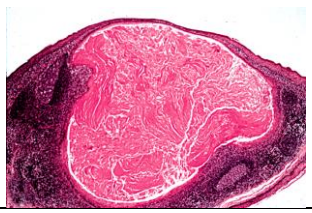
➲2nd arch➔upper lateral neck (anterior/deep to sternocleidomastoid muscle)
➲cyst wall➔lymphoid tissue
➲most➔children & young adult(10-40 y/o)



Oral lymphoepithelial cyst

➲micro➔like branchial cleft cyst(BUT much smaller size) | ➲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)

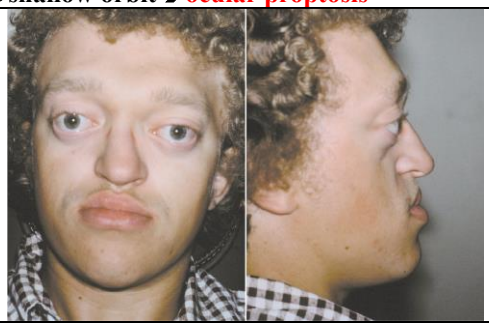
➲rare marked mental deficiency ➲❶visual impairment ❷total blindness ❸hearing deficit

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

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

➲underdeveloped maxilla➔❶midface hypoplasia ❷crowded upper teeth ❸occlusal disharmony

➲shallow orbit➔ocular proptosis



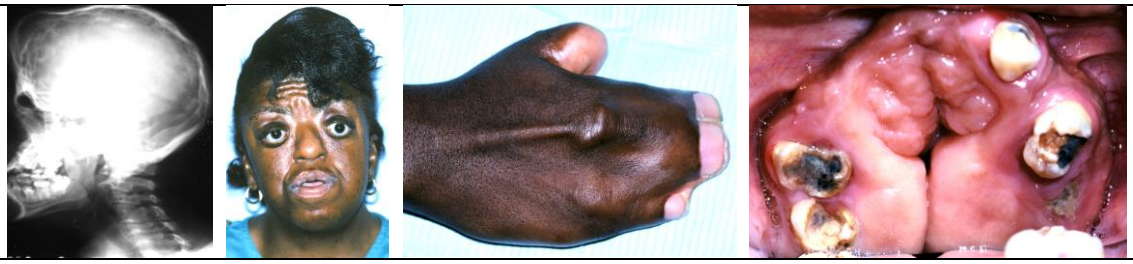
Apert syndrome

➲*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

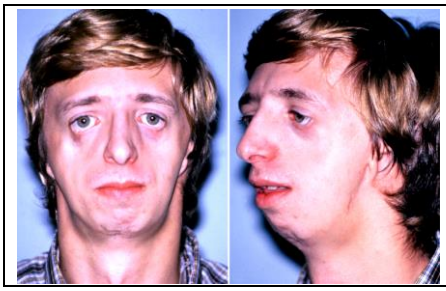


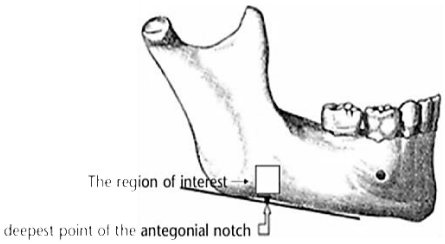
Treacher Collins syndrome(Mandibulofacial dysostosis)

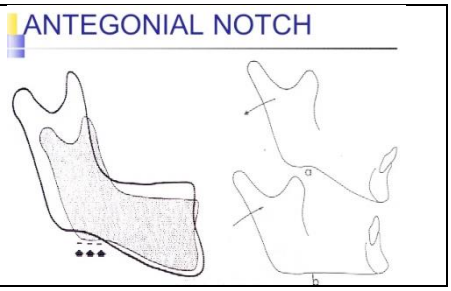
➲parotid gland➔hypoplastic/total absent

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

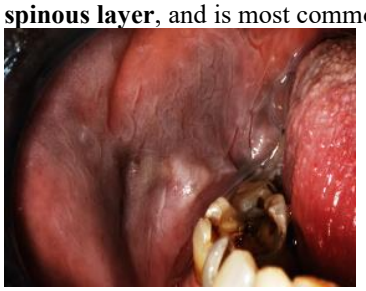
➲hypoplastic mandible, downward-slanting palpebral fissures, ear deformities

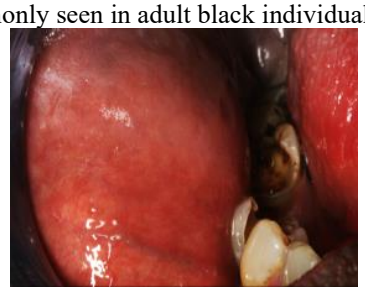


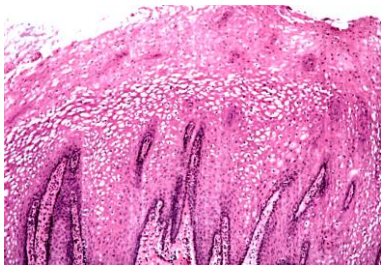




3. Which of the following conditions is a benign anomaly, has a **diffuse gray-to-white opaque** appearance on the **buccal mucosa** (**less opaque on stretching of mucosa**) and histopathological showing parakeratosis & **intracellular edema of spinous layer**, and is most commonly seen in adult black individuals?

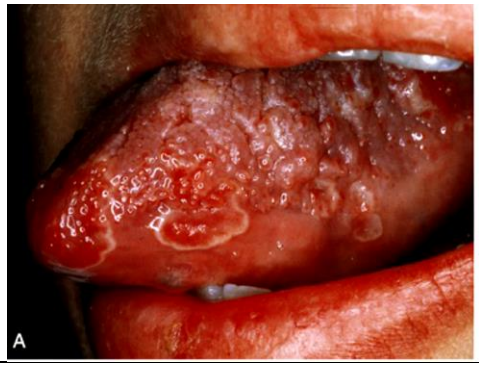


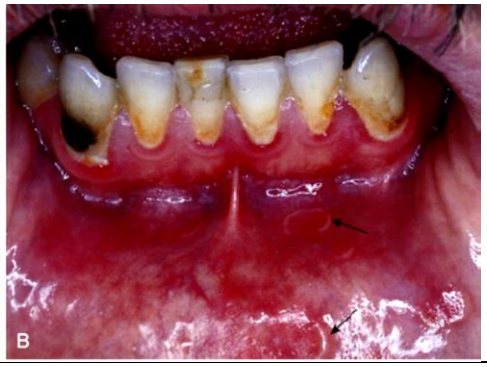




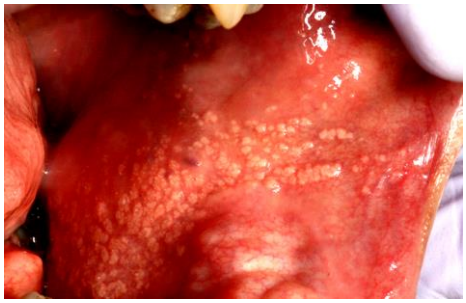
(A) leukoedema
(B) linea alba
(C) lichen planus
(D) ectopic geographic tongue

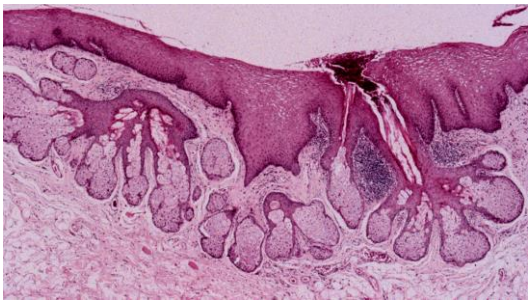
➲**(Fig. A) geographic tongue➔erythema migrans ➲(Fig. B) ectopic geographic tongue(非舌之 erythema migrans)**





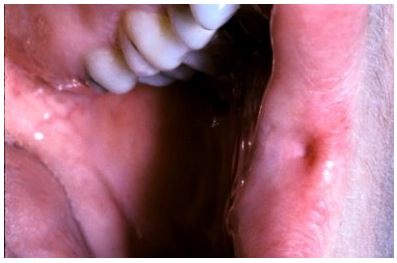
4. Which condition is most often seen on the buccal mucosa?





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

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

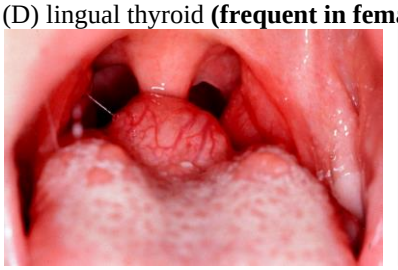
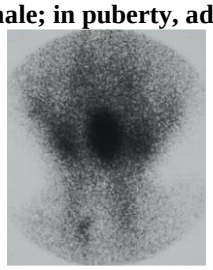


6. The **paramedian lip pit (congenital lip pits)** occurs:
(A) in the commissure
(B) either side of the midline of vermilion of lower lip
(C) in the center of the upper lip
(D) on the mucosa of the upper lip

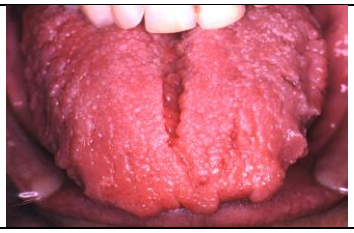
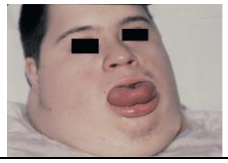
Paramedian lip pit(Congenital lip pits)

➲**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** ❺**joint laxity** ❻**skeletal abnormalities** ❼**intellectual disability**

7. Which term refers to an **ectopic mass of thyroid tissue** on **posterior dorsal tongue between foramen cecum & epiglottis with scan showing central dark zone of iodine/technetium-99m isotope in tongue mass & minimal uptake in neck with risk of malignant transformation and 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%)**

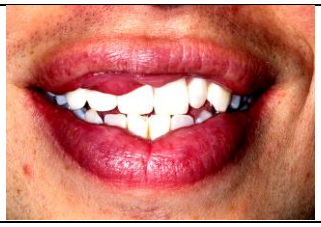
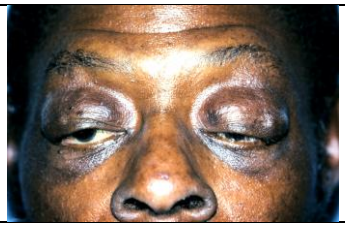



Macroglossia

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

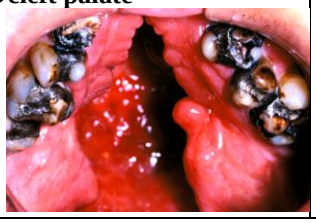
Ascher syndrome

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

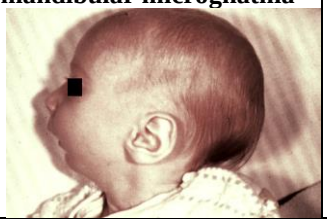



Pierre Robin sequence

➲cleft palate



➲mandibular micrognathia



➲glossoptosis(lower, posterior tongue displacement➔ airway obstruction)

➲isolated or associated with syndromes/other anomalies(❶Stickler syndrome ❷velocardiofacial syndrome)

Caliber-persistent artery

➲arterial branch➔superficial submucosal tissue without reduction in diameter

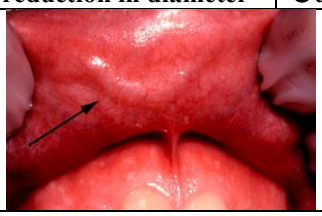
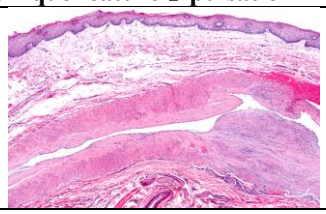
➲unique feature➔pulsation

➲almost exclusively➔lip(either or both lips/ bilateral)

➲pale to normal to bluish color

➲linear, arcuate or papular elevation

➲stretch lip➔artery become inconspicuous

Fissured tongue(Scrotal tongue)

➲strong associate➔geographic tongue

➲depth➔2-6mm

➲dorsolateral tongue

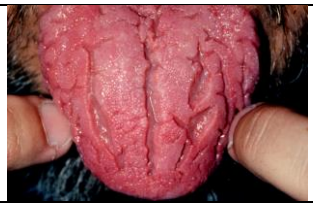
➲component of Melkersson-Rosenthal syndrome

➲asymptomatic(most); mild burning or soreness(some)

➲male predilection

➲2-5% overall population

➲prevalence & severity appear to increase with age



Hairy tongue(Coated tongue)

➲marked keratin accumulated on filiform papillae of dorsal tongue

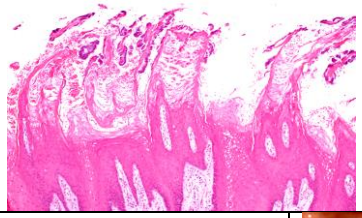
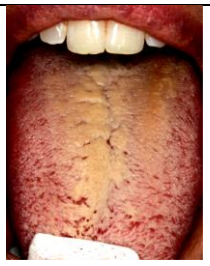
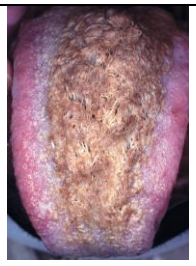
➲0.5% of adult

➲many➔heavy smoker

➲associate factor➔❶debilitation ❷poor oral hygiene ❸drug➔xerostomia ❹HN RT history

➲affect midline just anterior to circumvallate papillae(no lateral & anterior)

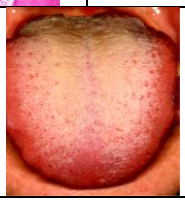
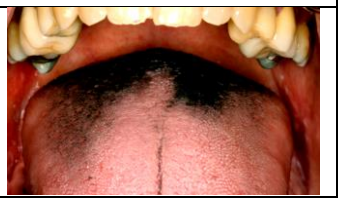
➲elongated papillae➔brown, yellow or black(due to pigment-produce bacteria/tobacco & food stain)

➲coated tongue➔without hairlike filiform projection

➲misdiagnosed➔candidiasis➔treated with antifungal medications

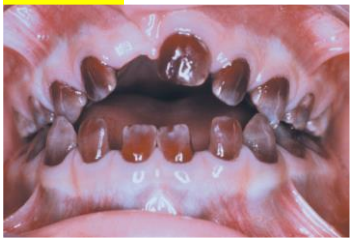
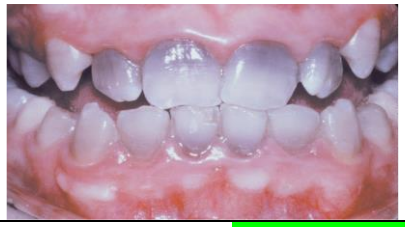
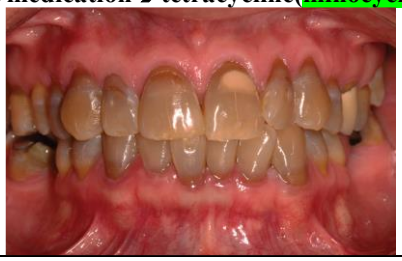
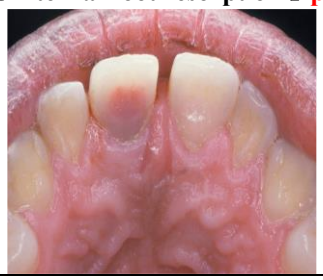
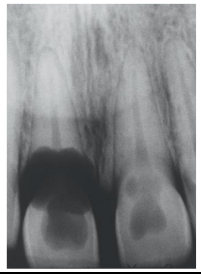
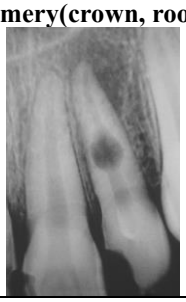
➲transitory staining of posterior dorsal tongue using bismuth subsalicylate➔react with sulfur in saliva➔bismuth sulfide

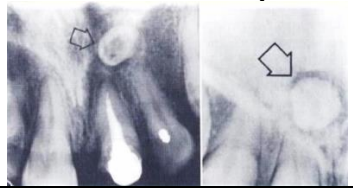
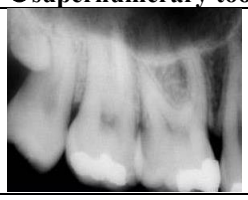
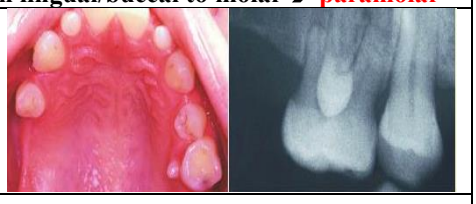
8. **Torus mandibularis** and **torus palatinus** are:
   (A) inherited as an autosomal-recessive trait
   (B) more prevalent in males
   (C) inherited as an autosomal-dominant trait
   (D) sporadic traits

Chapter 2 Abnormalities of teeth

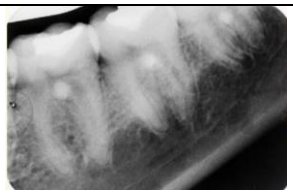
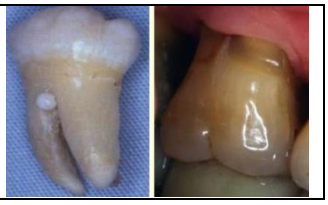
Environmental discoloration of teeth

extrinsic	intrinsic
➲bacterial stains	➲amelogenesis imperfect(AI)
➲iron	➲dentinogenesis imperfecta(DI)
➲tobacco	➲dental fluorosis
➲foods & beverages	➲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 
➲gingiva hemorrhage	➲ochronosis(黃褐斑病)(alkaptonuria)➔blue color(in conjunction with Parkinson disease)
➲restorative materials	➲trauma➔blood accumulated in head➔Hb break down in necrotic pulp
➲medications	➲localized red blood cell breakdown
	➲medication➔tetracycline(minocycline)➔brown/gray(N.B. 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	➲terms of supernumerary tooth depend on location ❶maxillary anterior incisor region➔mesiodens ❷accessory 4th molar➔distomolar/distodens ❸supernumerary tooth lingual/buccal to molar➔ paramolar
➲non-syndromic multiple supernumerary tooth➔most➔ lower premolar area 	 

Developmental alterations in shape of teeth

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

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)➔牙釉質沉積量不夠，導致厚度不足，但硬度正常

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

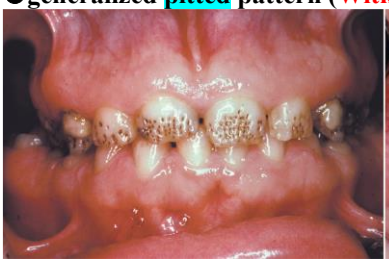
❸牙釉質鈣化不足型(hypocalcification)(autosomal dominant)➔牙釉質厚度正常，但質地很軟，是鈣離子運輸出現問題，發生在牙齒萌發後

(N.B.)有學者統稱❷與❸為hypomineralization

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

❶hypoplastic AI

➲generalized pitted pattern (Witkop phenotypic classification: autosomal dominant smooth pattern, rough pattern)

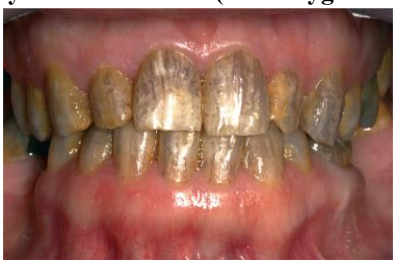



➲localized pattern➔hypoplastic enamel➔❶horizontal row of pits ❷linear depression ❸large area(middle of buccal surface)

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)

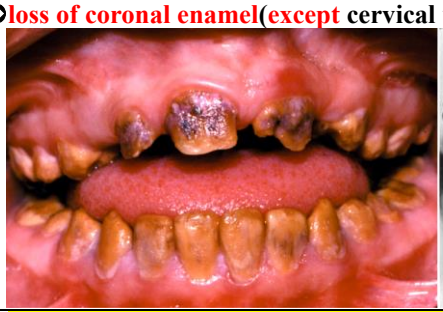
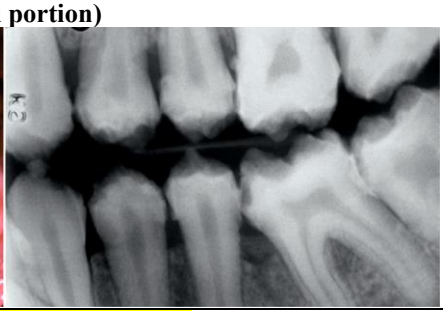



➲snow-capped hypomaturation AI➔white opaque enamel zone(1/4-1/3 incisal & occlusal of crown)

❸hypocalcified AI

➲diffuse yellow-brown discoloration

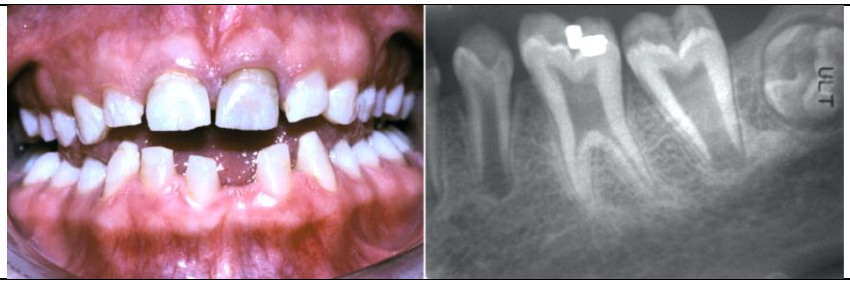
➲loss of coronal enamel(except cervical portion)

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 (shortened ramus & obtuse angle)



Dentinogenesis imperfecta(DI)

➲**half of patient➔together 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 DGI(shell teeth)**

❶**pulp enlarge with normal-thickness enamel➔extreme thin dentin➔entire tooth/isolated to root**

❷**most in deciduous teeth➔DI➔pulp expose**

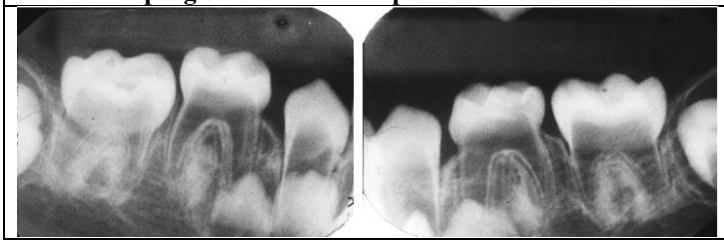
❸**unassociated with DI(isolated type)**

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➔①correlate with *DSPP* mutation ②$2^0$ to 1^0 gnathic change|jaw position➔affect inner ear; 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) 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

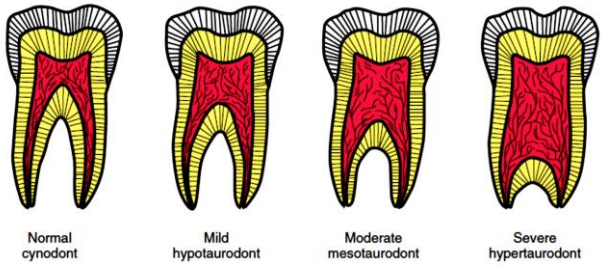
9. The cause of **supernumerary teeth** is most likely:
   (A) genetic
   (B) traumatic
   (C) cystic
   (D) systemic

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

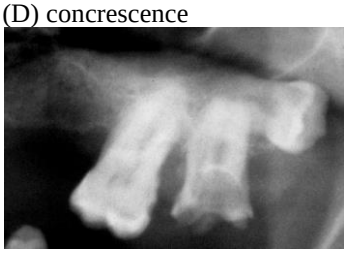
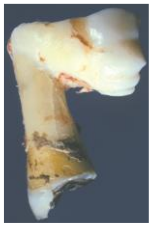
Taurodontism

syndromes associated 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**		



➲❶**rectangular** ❷**pulp chamber➔↑apico-occlusal height** ❸**bifurcation close to apex**
➲**un(bi)ilateral➔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** *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

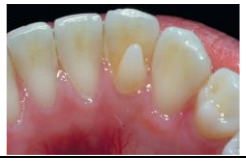
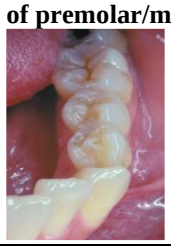
23. When a patient is **missing six teeth** without including third molars, the condition is specifically termed:
(A) hyperdontia
(B) oligodontia
(C) hypodontia
(D) microdontia

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

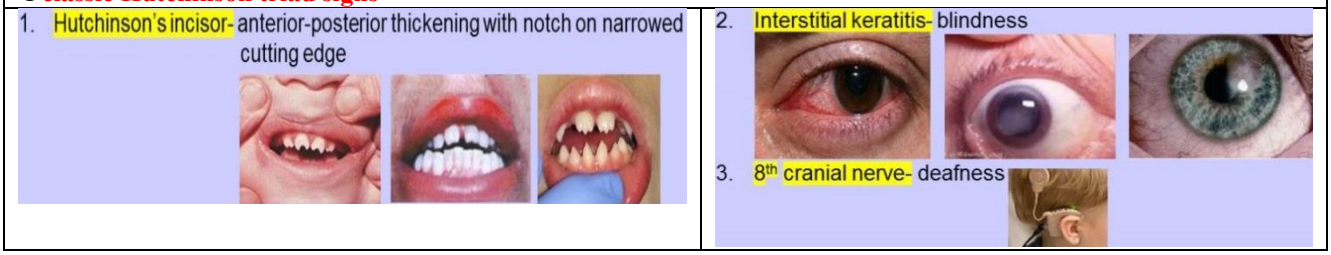
30. Which one of the following describes the appearance of **enamel hypoplasia** resulting from a febrile illness or **vitamin deficiency**?
(A) pitting defects
(B) yellowish-brown discoloration
(C) blackish-brown staining
(D) chalky white spots

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 syphili**s?
(A) turner tooth
(B) Hutchinson incisors
(C) taurodont
(D) dens evaginatus

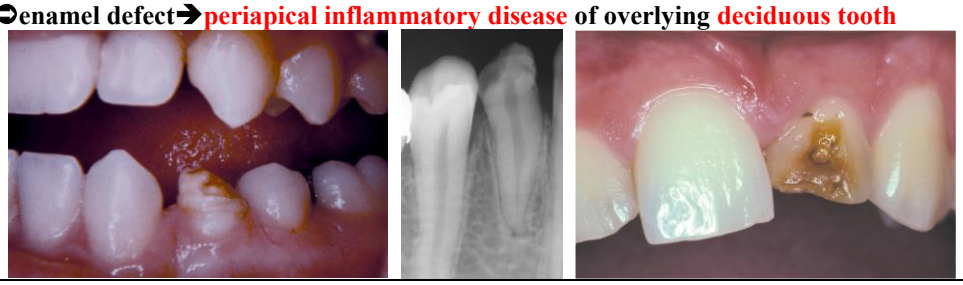
33. Which of the followings are associated with **enamel hypoplasia**?
(1) Ricket (2) Hutchinson incisors (3) congenital syphilis (mulberry molar) (4) Turner tooth
(A) only 1,2,4
(B) only 1,2,3
(C) only 2,3,4
(D) 1,2,3,4

➲**classic Hutchinson triad signs**



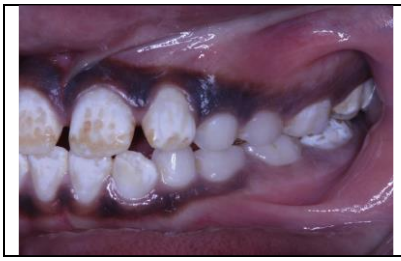
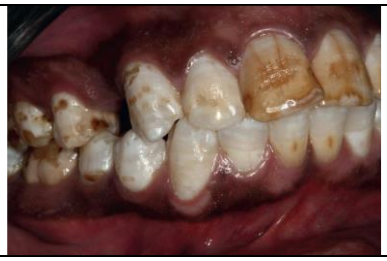
Turner tooth

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



Dental fluorosis

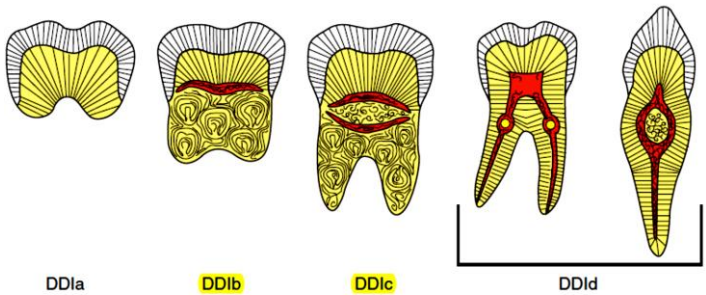
➲**water fluoridation➔recommended concentration 0.7-1.2ppm**
➲**crown of 11, 21➔cosmetic & complete development by age 3➔monitor of fluoride intake during 1st 3s**
➲**enamel defect➔lusterless, white, opaque; brown enamel mottling**

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

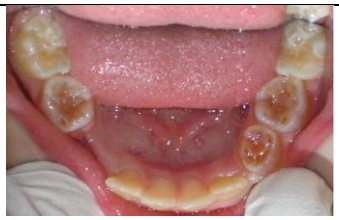
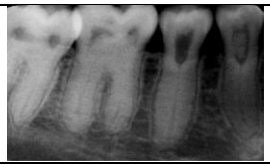


• **Fig. 2-109 Dentin Dysplasia Type I (DD-I).** Illustration demonstrating the variability of the radiographic appearance according to the degree of dentin disorganization within the root.

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** **❷shortened 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)

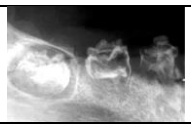
deciduous teeth **❶blue-to-amber-to-brown translucence(like DI)** **❷radiographic dental changes** **①bulbous crown** **②cervical constriction** **③thin roots** **④early pulp obliteration**	
permanent teeth **❶normal color** **❷radiograph** **①pulp chambers enlargement** **②thistle(flame) tube-shaped 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 and dentin** ➲**upper anterior teeth predominance**	

Synopsis➔pathology of teeth

hyperdontia	
idiopathic supernumerary teeth	**mesiodens, paramolar, distomolar**
cleft lip & palate	**extra lateral incisor or canine**
Gardner syndrome	**osteomas and gastrointestinal polyps**
cleidocranial dysplasia	**hypoplastic or missing clavicles; failure of tooth eruption**
hypodontia	
idiopathic hypodontia	**missing third molar, lateral incisor**
cleft lip & palate	**missing lateral incisor or canine**
hereditary hypohidrotic ectodermal dysplasia	**cone-shaped teeth**
incontinentia pigmenti	**cone-shaped teeth**
radiotherapy 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; fourth 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**
radiotherapy 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 associated primary 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
radiotherapy during childhood	stunted 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	—

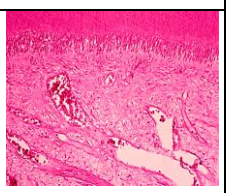
systemic sclerosis(scleroderma)	generalized widening
sarcoma or carcinoma infiltration	esp. osteosarcoma; localized to teeth in area of tumor
generalized loss of lamina dura	
hyperparathyroidism	calcium removed from bones; bone may have ground glass appearance
osteomalacia	vitamin D deficiency in adults
Paget disease of bone	cotton wool change hides lamina dura
fibrous dysplasia	ground glass change hides lamina dura
premature exfoliation of teeth	
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 3 Pulpal & periapical dsease

Pulpitis

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

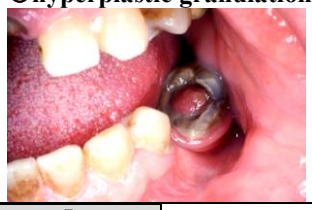
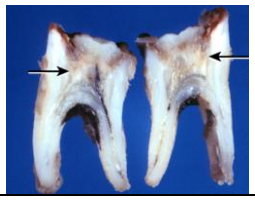
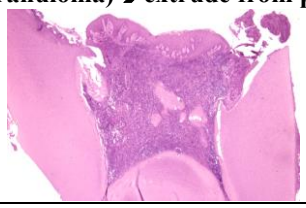
➲classification
❶reversible pulpitis➔EPT➔lower current
①cold/sweet food, heat(sometimes)➔acute pain➔stimulus remove➔discomfort resolve in a few sec
②percussion(-), tooth mobility(-), sensitivity(-)
③cracked tooth upon biting
④pulp➔hyperemia & edema



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

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

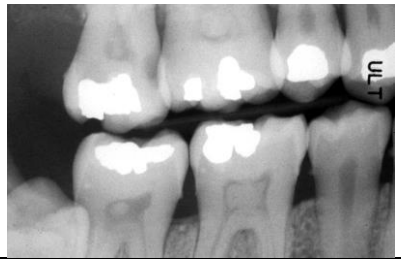
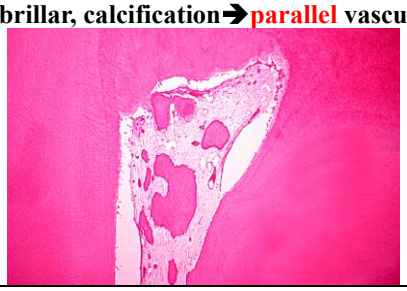
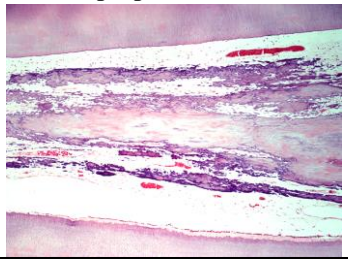
Synopsis➔pulpitis

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 ❺referred from arch to arch	cold➔pain relief	

Pulp calcification➔pulp stone>200μm➔detected by X- ray

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

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

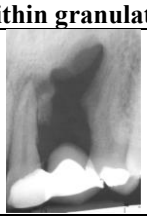
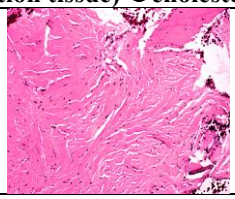
➲associate➔①CVD ②renal stone ③aging ④fluoride supplementation ⑤hypervitaminosis D
➲prominent pulpal calcification associate
❶radicular dentin dysplasia(dentin dysplasia type Id) ❷mild form DI ❸pulpal dysplasia
❹tumoral calcinosis ❺calcinosis universalis ❻Ehlers-Danlos syndrome ❼end-stage renal disease

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

➲affected teeth➔loss of apical lamina dura➔WD/PD➔RO rim(with/withnot)
➲lesion>200mm^2➔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

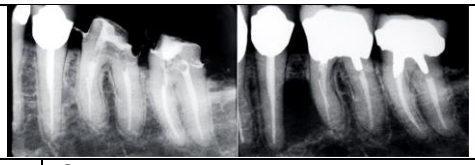
➲periapical scar
❶defect➔dense collagenous tissue➔facial & lingual cortical plate loss➔inform patient➔may form scar➔not indicate future surgery
❷dense fibrotic connective tissue with vital bone without significant inflammatory infiltrate

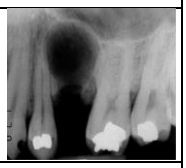
Radicular cyst(odontogenic, inflammatory, most common odontogenic cyst)

➲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 & associated soft tissue➔removed *in tot*

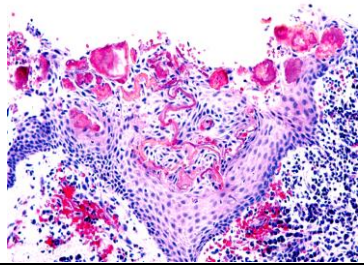
➲ lateral radicular cyst➔ spread through lateral foramen➔X-ray like lateral periodontal cyst



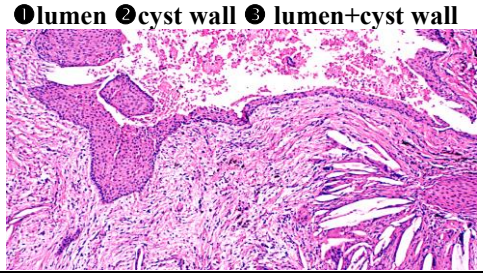
➲periapical inflammatory tissue➔not curetted of tooth removal➔ inflammatory residual cyst



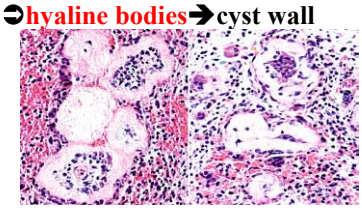
➲Rushton bodies➔cyst lining



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



➲hyaline bodies➔cyst wall

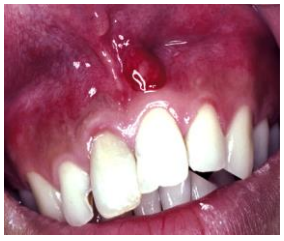
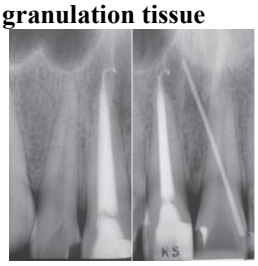


➔corrugated collagenous ring➔ lymphocyte, plasma cell, multinucleated giant cell

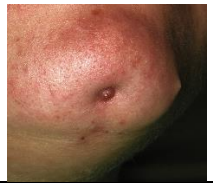
Periapical abscess

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

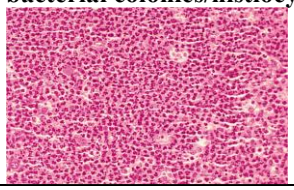
➲parulis(gum boil)➔intraoral opening of sinus tract➔mass of subacute granulation tissue

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



➲micro➔sea of PMN intermixed 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

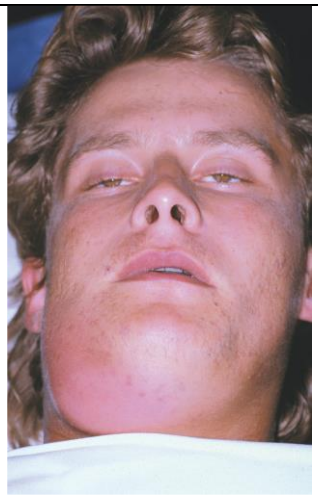
4. A **pink protruding mass** in the occlusal surface of a severely carious **mandibular first or second molar** is most likely a(n):
   (A) irritation fibroma
   (B) pyogenic granuloma
   (C) pulp polyp
   (D) pulpal granuloma

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

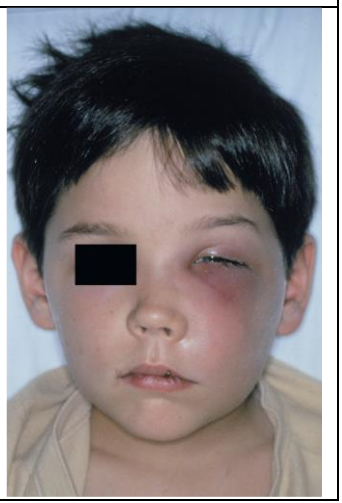
Cellulitis

➲**2 dangerous forms**

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

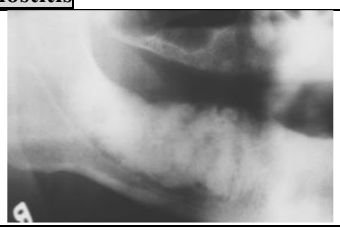


❷**cavernous sinus thrombosis** ①**edematous periorbital enlargement+ involve eyelid(眼瞼) & conjunctiva(結膜)** ②**canine space➔swelling➔lateral border of nose➔medial aspect of eye & periorbital**



❶**Diffuse sclerosing osteomyelitis➔**❷**1^0 chronic osteomyelitis➔**❸**Chronic tendoperiostitis**

❶**diffuse sclerosing osteomyelitis**
①**exclusive in adult** ②**no sex predominance**
③**mandible** ④**develop site of chronic infection**
⑤**sclerosis➔center of crestal(alveolar) bone(alveolar crest) of tooth bearing alveolar ridge**
⑥**not in area of attachment of masseter/digastric muscle**
⑦**not from radiolucent fibro-osseous lesion** ⑧**not predilection for black female**



❷**1^0 chronic osteomyelitis**
①**d.d. chronic suppurative osteomyelitis[2^0 chronic osteomyelitis➔bacteria(streptococcus) infection]➔ no obvious bacterial infection; suppuration & no sequestrum; unable culture organism; no response to long-term antibiotics**
②**SAPHO➔Synovitis, Acne, Pustulosis, Hyperostosis, [Osteitis➔1^0 chronic osteomyelitis & CRMO(chronic recurrent multifocal osteomyelitis)]➔develop an autoimmune disturbance 2^0 exposure to acne bacteria(Propionibacterium acnes)**

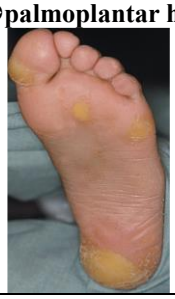
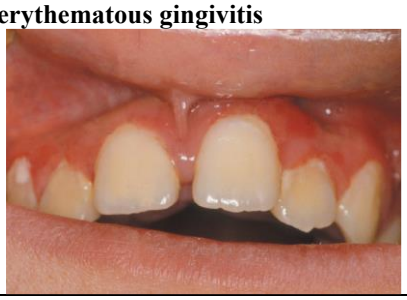
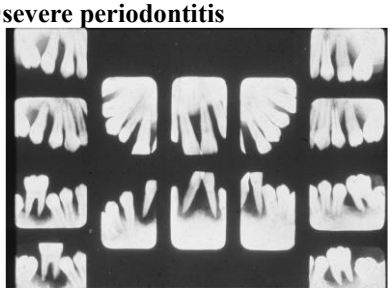
❸**chronic tendoperiostitis**
①**reactive bone change➔chronic overuse of masticatory muscle(masseter & digastric)➔parafunctional muscle habit(bruxism, clenching, nail biting, co-contraction(共同收縮), inability to relax jaw musculature)**
②**limit in➔single quadrant & center on anterior mandibular angle & posterior mandibular body(attachment of masseter muscle)**
③**occasion➔cuspid-premolar & anterior mandible(attachment of digastric muscle)**
④**micro➔dense bone, reactive bone, few signs of inflammation**
⑤**inferior border(anterior to angle) of mandibular body➔erosion**

Chapter 4 Periodontal diseases

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

Papillion-Lefevre syndrome

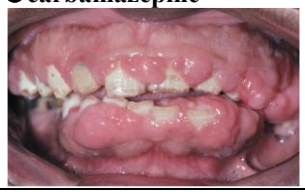
➲palmoplantar hyperkeratosis	➲erythematous gingivitis	➲severe periodontitis
		

Synopsis➔dermal disease associate periodontitis➔Chapter 16

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

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

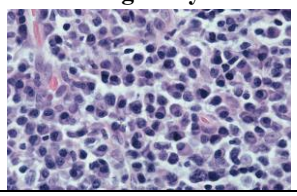
➲superficial peeling of epithelium➔rupture of mucosal vesicles➔mucous membrane pemphigoid

➲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

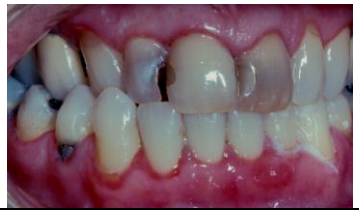
➲**hypersensitivity**➔❶chewing gum ❷herbal toothpaste ❸mint candy ❹pepper

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

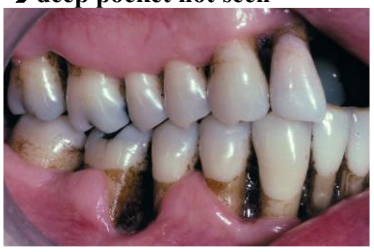
3 atypical of periodontal diseases associated with HIV infection

❶**linear gingival erythema**➔
a linear band of erythema➔
free gingival margin往下2-3mm



❷**necrotizing ulcerative gingivitis**➔
ulcer & necrosis of interdental papillae without attachment loss

❸**necrotizing ulcerative periodontitis**
➔deep pocket not seen



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

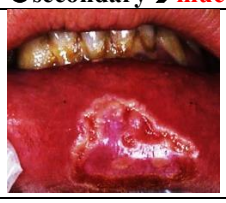
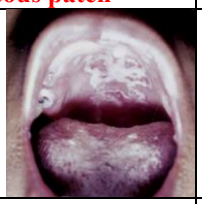
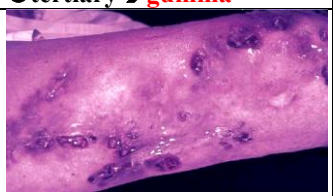
➲vesicle(小水泡)➔superficial blister<5mm in diameter, usu. filled with clear fluid
➲bulla(水皰)➔large blister➔>5mm in diameter
➲pustule(膿包)➔blister filled with purulent exudate

➲fissure(裂縫)➔narrow, slitlike ulceration/groove

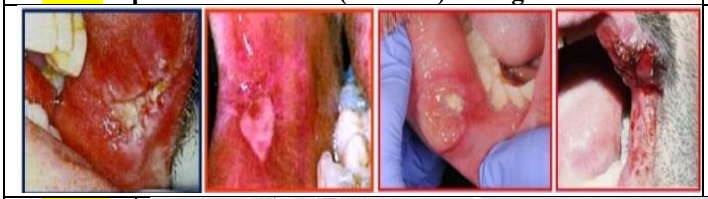
➲petechia(紫癜)➔round, pinpoint area of hemorrhage
➲ecchymosis(瘀斑)➔nonelevated area of hemorrhage>petechia
➲telangiectasia(毛細血管擴張)➔vascular lesion caused by small, superficial blood vessel dilatation

Syphilis(Lues)

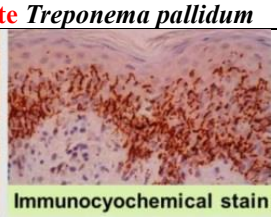
➲stages oral syphilis

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

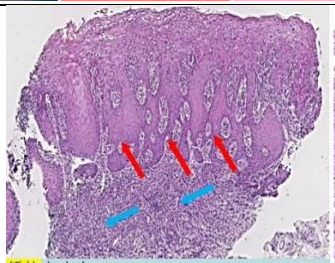
➲clinic➔painless oral ulcer(chancer)➔diagnostic criteria

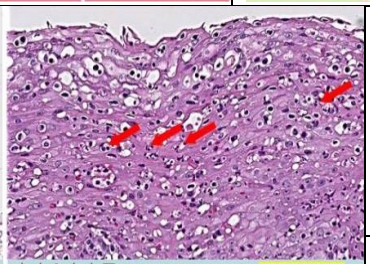


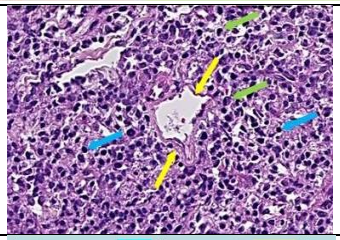
➲detection of spirochete *Treponema pallidum*



➲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

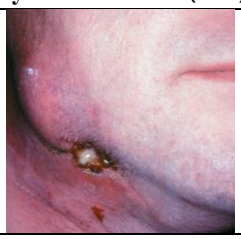
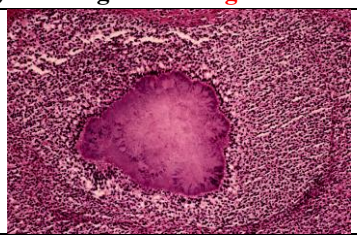
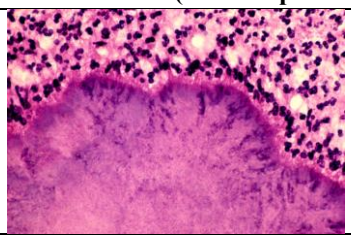
3. Which of the following stages of **syphilis** is *not* infectious?
   (A) primary
   (B) secondary
   (C) tertiary
   (D) all stages are equally infectious

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

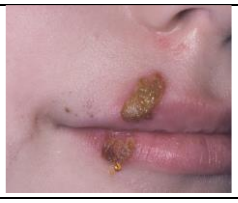
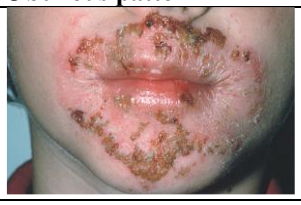
6. A specific clinical characteristic found in **actinomycosis** is:
   (A) periapical radiolucency
   (B) filamentous bacteria
   (C) fungal infection
   (D) sulfur granules present in exudate

Actinomycosis(放線菌病)

➲**infection of filamentous, branching, gram(+) anaerobic bacteria**
➲**yellowish flecks(斑點) discharge➔sulfur granule➔bacteria colonies(club-shaped filament➔radiating rosette)**
  

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)

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

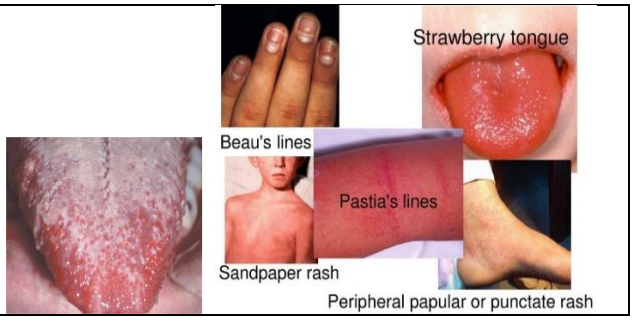
8. Which type of infection is involved when **normal components of the oral microflora** can cause disease?
   (A) chronic inflammatory
   (B) opportunistic
   (C) hyperplastic
   (D) granulomatous

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

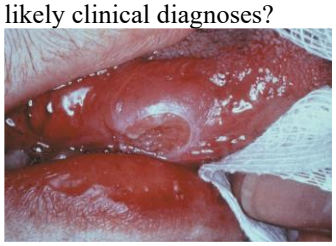
Scarlet fever(猩紅熱)➔group A, streptococci(A型鏈球菌)

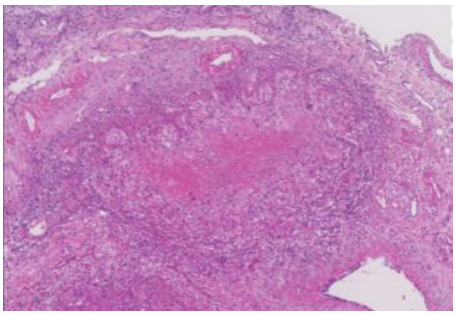
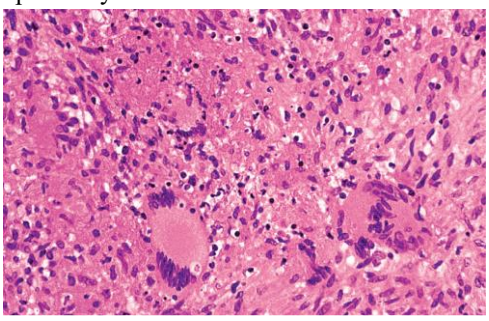
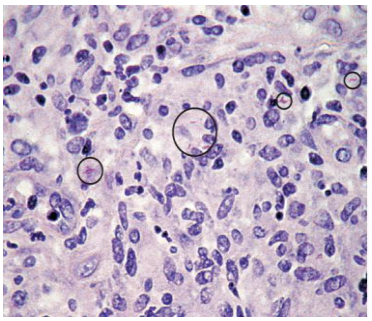
➲**group A, β-hemolytic streptococci➔tonsillitis (pharyngitis)➔erythrogenic toxin➔attack blood vessel➔skin rash**

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

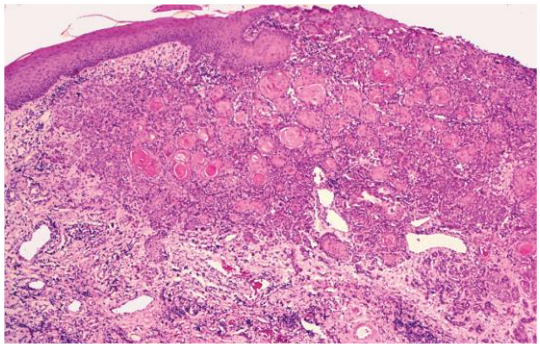
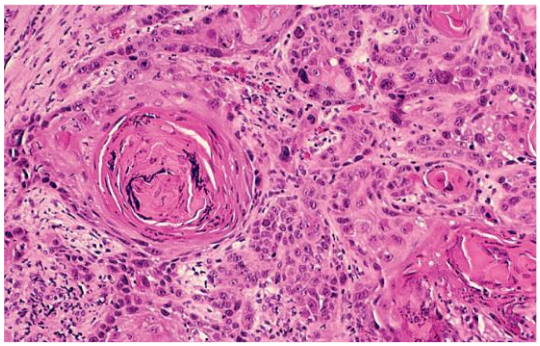
11. A positive skin reaction to **PPD** indicates:
    (A) active tuberculosis
    (B) contagious tuberculosis
    (C) if a person has ever been infected with the tuberculosis bacteria
    (D) need for antibiotic therapy

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?

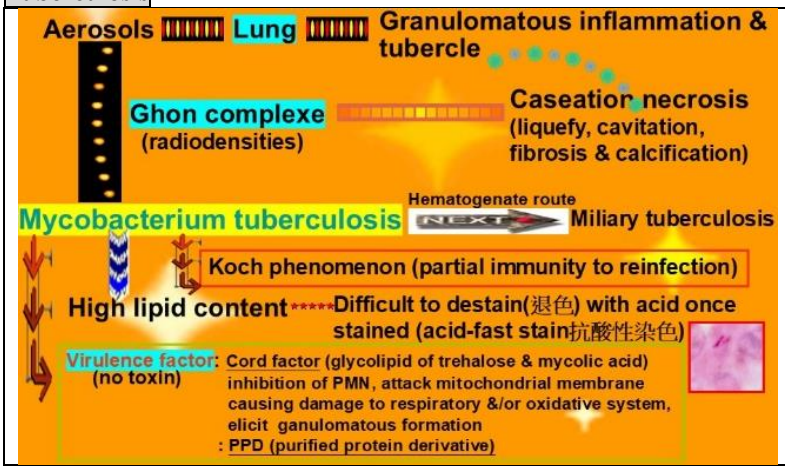



(1) primary oral squamous cell carcinoma (2) metastatic oral squamous cell carcinoma to lung (3) grade 1 (4) grade 3 (5) stage I (6) stage IV

(A) only 1,2,3,5
(B) only 1,2,4,6
(C) only 1,2,4,5
(D) only 1,2,3,6

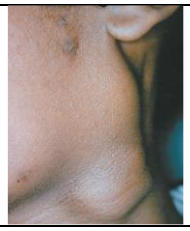
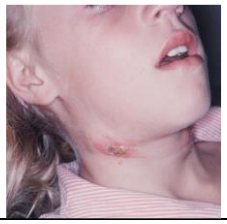
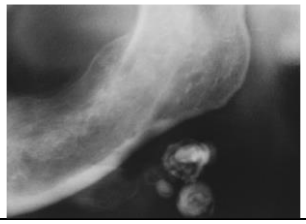
oral ulcer	chest X-ray	biopsy for oral ulcer	diagnosis of oral ulcer
+	+	not done	1^0 SCC, 1^0 TB, meta lung SCC, 2^0 TB
+	-	not done	1^0 SCC, 1^0 TB
+	-	+(OSCC)	1^0 SCC
+	+	+(TB)	2^0 TB
+	-	+(TB)	1^0 TB

Tuberculosis



Scrofula(頸部淋巴腺結核)

➲scrofula➔contaminated milk➔nontuberculous mycobacterial infection➔oropharyngeal lymphoid tissue, cervical LN enlargement (calcified➔like sialolith radiograph)➔caseous necrosis➔skin sinus tract

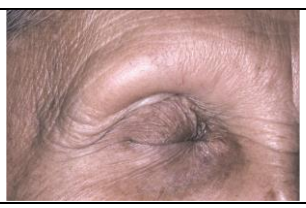




Leprosy(Hansen disease)

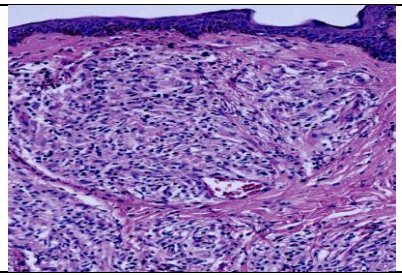
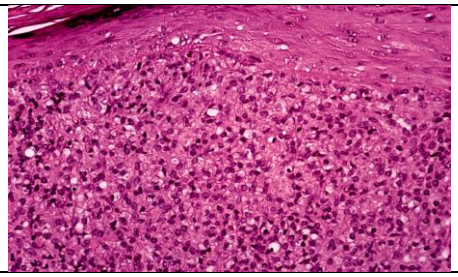
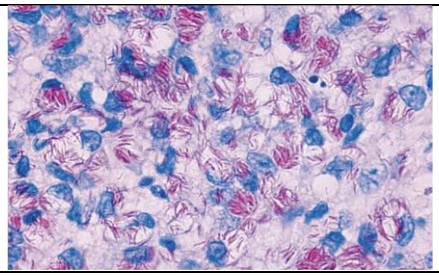
➲*mycobacterium leprae*➔temperature-dependent(?)➔lesion in cooler parts of body(skin, nasal cavity, palate)

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

➲lepromatous(multibacillary) leprosy➔❶numerous thickened facial nodule ❷distorted facial appearance(leonine facies) ❸hair, eyebrow, lashes loss ❹facial, trigeminal n involve(loss of sweat & decreased 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

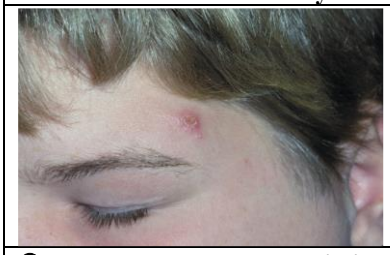
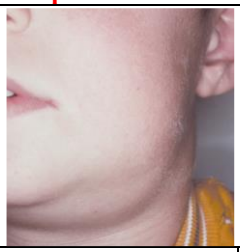
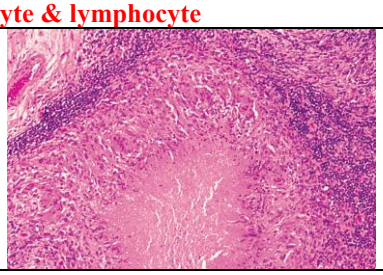


➲granulomatous inflammation ➔lymphocyte & histiocyte	➲sheet of lymphocyte & histiocyte➔ scattered vacuolated lepra cells	➲acid-fast stain➔small mycobacterial organism

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

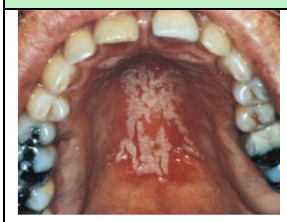
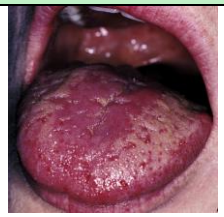
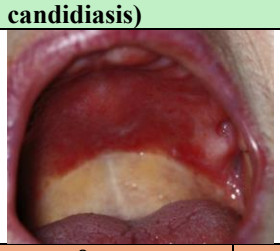
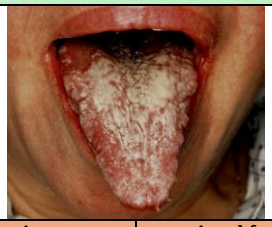
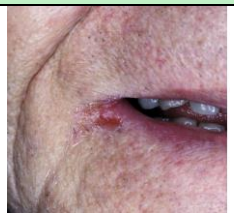
➲dog, monkey, porcupine quill & thorn(豪猪刺)(rare)

Chapter 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

peudomembranous	erythematous	denture stomatitis (chronic atrophic candidiasis)	chronic hyperplastic (candida leukoplakia)	angular cheilitis
				

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	antibiotic therapy, immunosuppression
❷erythematous	red macule, burning sensation	posterior hard palate, buccal mucosa, dorsal tongue	antibiotic 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, loss of vertical dimension
❻denture stomatitis(chronic atrophic candidiasis, denture sore mouth)	red, asymptomatic	confined to 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; care must be taken not to confuse this with other keratotic lesions with superimposed candidiasis
❽mucocutaneous	white plaque, some of which may be removable; red area	tongue, buccal mucosa, palate	rare; inherited or sporadic idiopathic immune dysfunction
❾endocrine-candidiasis syndromes	white plaque➔most not removable	tongue, buccal mucosa, palate	rare; endocrine disorder develops after candidiasis

Mucocutaneous candidiasis

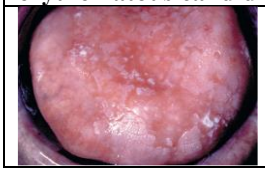
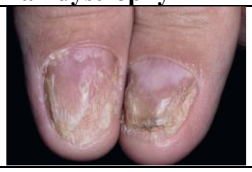
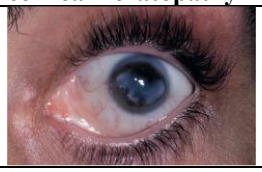
➲severe type➔component of a relatively rare group of immunologic disorders

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

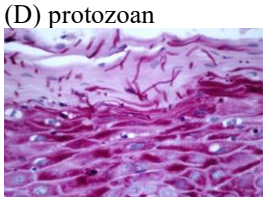
➲oral lesion(chronic hyperplastic candidiasis)➔thick, white plaque(not rub off)

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

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

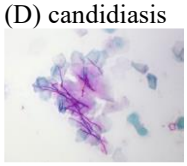
erythematous candidiasis	nail dystrophy	corneal keratopathy
		

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**?

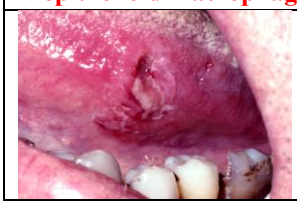
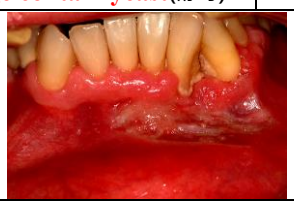
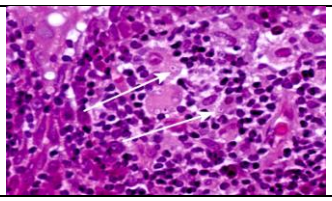
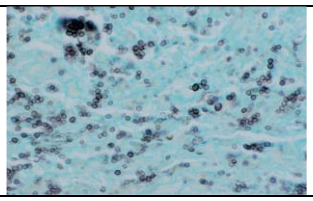
   (A) median rhomboid glossitis
   (B) geographic tongue
   (C) fissured tongue
   (D) lingual thyroid

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➔like TB clinical➔chest X-ray➔upper lob infiltrates & cavitation**	
➲**disseminated histoplasmosis➔AIDS**	➲**oral➔ulcer➔tongue, palate, buccal mucosa➔mistaken as 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

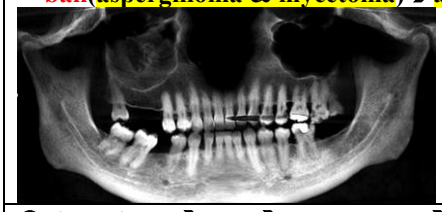
❸extensive invasive➔immunocompromise(chemotherapy, AIDS, solid-organ & bone marrow transplant)

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

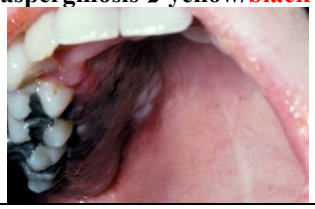
➲resistant spore(孢子)➔air➔ human inhale➔opportunistic fungal infection(2nd in frequency to candidiasis)

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

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



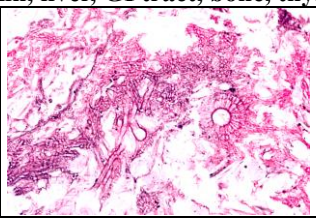
➲immunocompromise➔tooth extraction/endo➔oral aspergillosis➔yellow/black ulcer

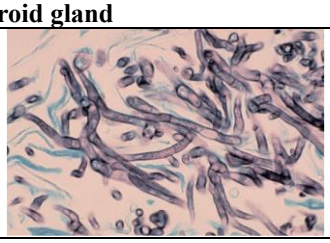


➲disseminate➔lung➔bloodstream➔CNS, eye, skin, liver, GI tract, bone, thyroid gland

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

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





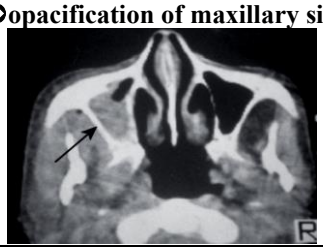
Mucormycosis(毛霉菌病)(Zgomycosis, Phycomycosis)

➲rhinocerebal form➔oral health care provider

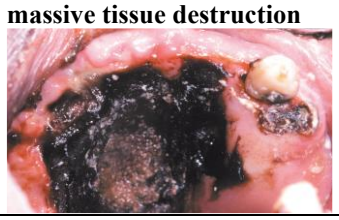
➲Fe(Fe-chelating agent for thalassemia)➔growth of fungi

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

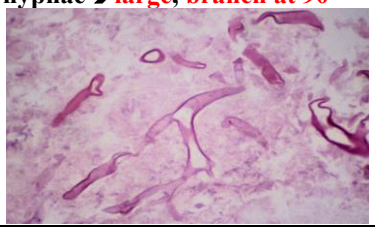
➲opacification of maxillary sinus



➲invasion small blood vessel➔ massive tissue destruction



➲hyphae➔large, branch at 90^0

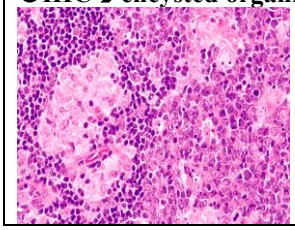


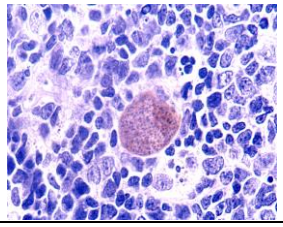
Toxoplasmosis(弓形蟲)➔protozoal organism Toxoplasma gondii infection

➲micro➔LN

❶germinal center➔eosinophilic macrophage

❷IHC➔encysted organism





➲congenital toxoplasmosis➔non-immune mother

❶cross placenta barrier

❷1st trimester of pregnancy➔①blindness ②intellectual impairment ③delayed psychomotor development

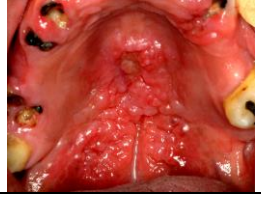
➲immunosuppress➔1^0infection/reactivation➔encysted organism

➲normal➔❶asymptomatic

❷like infectious mononucleosis(low- grade fever, cervical lymphadenopathy, fatigue & muscle/joint pain)

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

➲ulceration & 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 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
	❶herpes 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	❶ rubella(German measles)
human immunodeficiency viurus(HIV)	❶AIDS
covid-19	coronavirus disease 2019

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

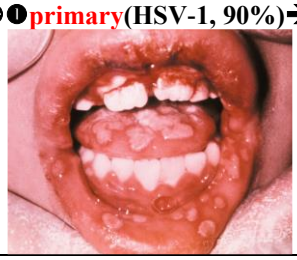
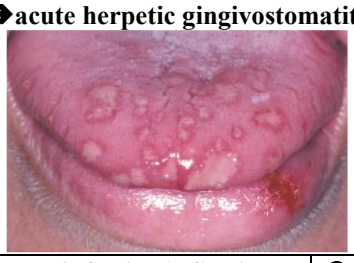
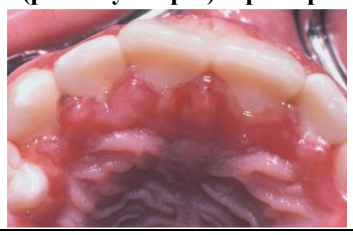
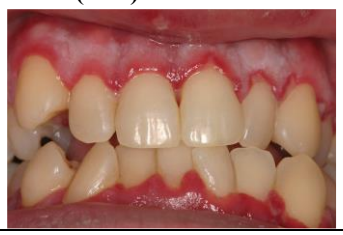
❶herpes simplex virus(HSV) type 1(HSV-1/HHV-1) ❷HSV type 2(HSV-2/HHV-2) ❸varicella-zoster virus(VZV/HHV-3) ❹Epstein-Barr virus(EBV/HHV-4) ❺cytomegalovirus(CMV/HHV-5)	❻human herpesvirus 6(HHV-6) ❼human herpesvirus 7(HHV-7) ❽human herpesvirus 8(HHV-8)➔ ①Kaposi sarcoma-associated herpesvirus(KSHV) ②lymphoma(certain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

Herpes simplex virus(HSV)

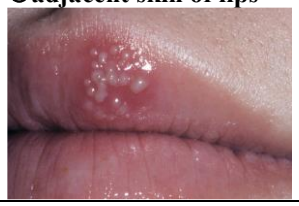
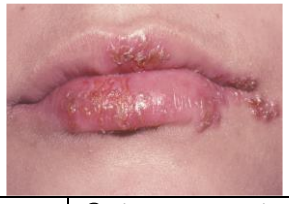
➲HSV-1➔spread via saliva, perioral lesion➔oral, facial, ocular➔pharynx, oral mucosa, lip, eye, skin above waist(腰)

➲HSV-2➔sexual contact➔genitalia & skin below waist

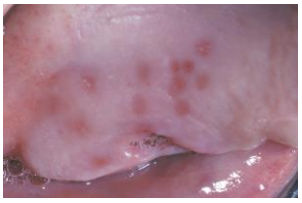
➲❶primary(HSV-1, 90%)➔acute herpetic gingivostomatitis(primary herpes)➔peak prevalence(2-3s)

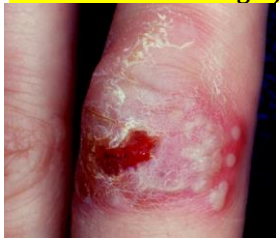
➲❷recurrent secondary simplex infection(HSV-1, most)➔herpes labialis(cold sore)➔①vermilion ②adjacent skin of lips

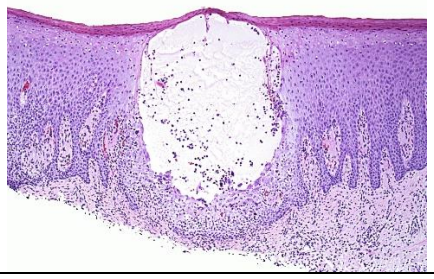
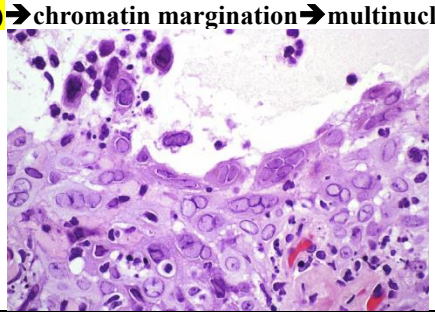
➲❸recurrent intraoral herpes(recurrent herpetic stomatitis)➔keratinized mucosa bound to bone(attached gingiva, hard palate)




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



➲histopathologic features➔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 occur 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

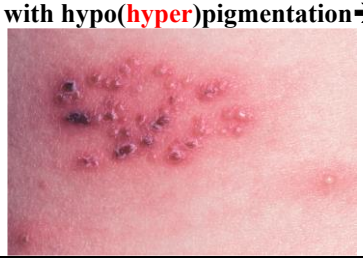
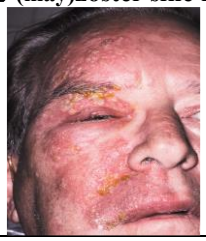
features	recurrent minor aphthous ulcer	recurrent herpes simplex ulceration
➲location	nonkeratinized mucosa	keratinized mucosa
➲number	one to several	multiple (crops)
➲vesicle precedes ulcer	no	yes
➲pain	yes	yes
➲size	<1cm	1-2mm
➲borders	round to oval	cluster of ulcer coalesce➔large irregular ulcer
➲recurrent	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
➲prodrome➔pain➔epithelium innervated by affected sensory nerve(dermatome) with fever, malaise, headache	
➲acute➔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]   	
➲chronic➔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會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, hearing deficit(不足), vertigo(眩暈) ❷loss of taste➔anterior 2/3 tongue	

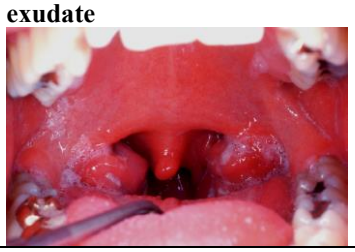
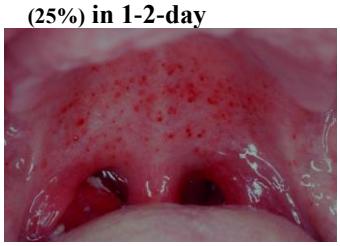
9. 下列那個臨床表現與相關病毒或疾病的配對組合是錯誤的？(114)
   (A) 感染性單核白血球增多症(infectious mononucleosis)和巨細胞病毒(cytomegalovirus)
   (B) 手足口病(hand-foot-and-mouth disease)和腸病毒(enterovirus)
   (C) 柯普里克氏斑(Koplik's spots)和麻疹病毒(Morbillivirus)
   (D) 佛斯克海默爾斑(Forchheimer sign)和德國麻疹病毒(Rubivirus)

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

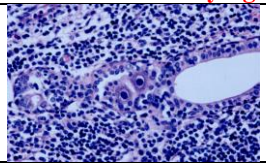
EBV implicated in 4 diseases occurred in oral region

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

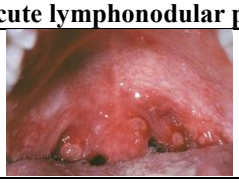
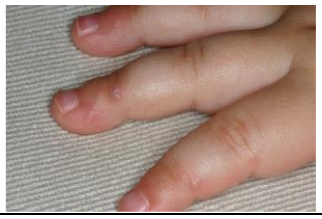
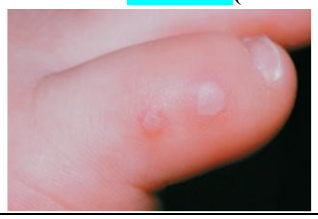
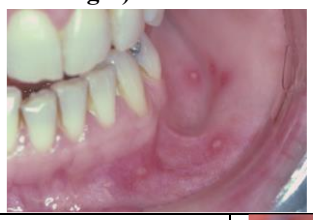
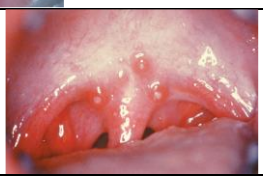
Cytomegalovirus(巨細胞病毒)➔coinfect➔HIV, HSV, EBV

➲latent➔salivary gland cell, endothelium, macrophage, lymphocyte	
➲found➔body fluid➔saliva, blood, urine, tears, respiratory secretion, genital secretion, breast milk	
➲most➔neonate(via placenta, delivery, breast-feeding), immunosuppressed adult(輸血、器官移植), sexual contact	
➲neonatal infection➔teeth➔enamel hypoplasia(hypomaturation), attrition, yellow coloration from underlying 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

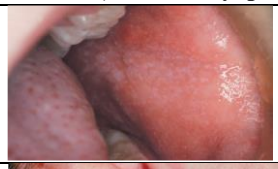
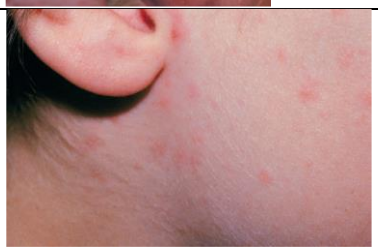
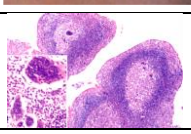
12. All of the following are characteristic features of **hand-foot-and-mouth disease** except one. Which **one is the exception**?
(A) occurs in epidemics in children younger than 5 years
(B) is caused by Epstein-Barr virus
(C) is characterized by painful oral vesicles
(D) is characterized by multiple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

Enterovirus(腸病毒)

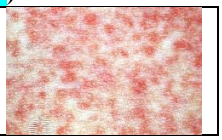
➲❶echovirus ❷coxsackievirus A & B ❸poliovirus	➲acute➔saliva, air droplet	➲chronic➔fecal-oral
➲clinical pattern➔❶herpangina ❷hand-foot-and-mouth disease ❸acute lymphonodular pharyngitis		
➲herpangia(皰疹性咽峽炎)❶echoviruses ❷coxsackieviruses A & B ①ulcer(2-4mm)➔resolve in a few days ②ulcer heal need 7-10-day		
➲hand-foot-and-mouth disease(手足口病)❶echovirus ❷coxsackievirus A ①ulcer(2-7mm; >1cm); heal within a week ②Beau line(nail loss or ridges)   		
➲acute lymphonodular pharyngitis ①coxsackieviruses A ②1-5 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

➲ 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 3-day(1st stage)➔3 Cs➔❶coryza(鼻炎) ❷cough ❸conjunctivitis(red, watery, photophobic eye)	
➲1st stage(fever)➔Koplik's spots➔epithelial necrosis [foci, blue-white macule(grain of salt) encircled by erythema]➔hyperparakeratotic epithelium, spongiosis, dyskeratosis & epithelial syncytial giant cell(often in buccal, labial mucosa)	
➲2nd stage(fever continue) ➔Koplik spot fade ➔skin rash(face先出現,往下至trunk & extremities)	
➲3rd stage(fever end)➔rash fade➔brown pigment (desquamation of skin affected by rash)➔complication腦炎➔subacute sclerosing panencephalitis(SSPE)➔甚至11年initial infection後	
➲Warthin-Finkeldey giant cell➔also in lymphoma, Kimura disease, AIDS-related lymphoproliferative disease, LE	

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

➲ developing fetus➔induce birth defect➔late winter & early spring	
➲transmission(~100%)➔respiratory droplet➔close living condition➔incubate time(12-23-day)	
➲contagious➔1 wk before-1 wk after exanthem(acute rash)➔pink macule➔papule➔fade	
➲infant➔congenital infection➔release virus up to 1 yr➔intraocular virus for decades	

➲**triad of CRS**➔❶**deafness(bilateral)(80%)**➔**evident till 2s** ❷**heart disease** ❸**cataract**	
➲**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)**➔❶**arthritis(most)**➔↑**frequency with age** ❷**encephalitis, thrombocytopenia(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 lesion**➔❶**Forchheimer sign(~20%)**➔**small, discrete, dark-red papule**➔**soft palate**➔**hard palate**➔**evident 6h after 1st symptom**➔**not last longer than 12-14h** ❷**palatal petechiae**	

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

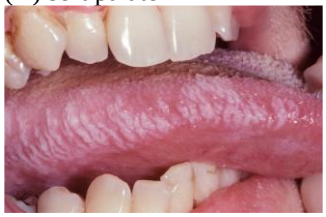
➲**involved site**➔**salivary gland(parotid gland) pancreas, choroid plexus, mature ovary & teste(also frequent)**	
➲**transmit**➔**respiratory droplet, saliva, and urine**➔**incubation time**➔**16-18-d(2–4 wk)**	
➲**contagious**➔**1-day before clinic appear-14-day after clinic resolution**➔**most in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

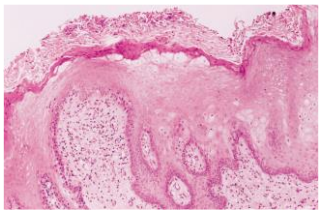
14. All of the following statements are correct statements concerning **HIV infection** *except one*. Which one is the exception?
(A) two positive Elisa tests followed by a positive Western blot test confirms HIV infection
(B) initial infection with HIV can be asymptomatic
(C) antibodies to HIV are usually 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

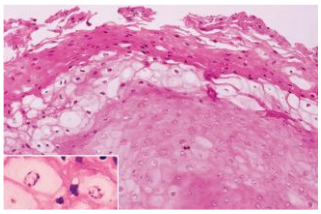
16. Which one of the following oral conditions is an **early sign** of a deficiency in the immune system and is commonly found in patients with **HIV infection**?
(A) erythema migrans
(B) advanced periodontitis
(C) candidiasis
(D) histoplasmosis

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

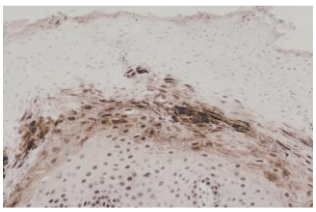




hyperparakeratosis



balloon cell

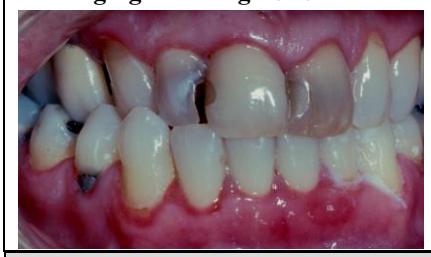
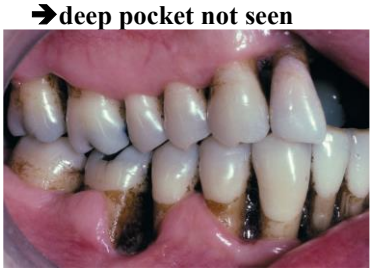


EBV within epithelial cell

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 of periodontal diseases associated with HIV infection

❶linear gingival erythema➔ a 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)	➲histoplasmosis
	➲hyperpigmentation(focal melanosis) ➔skin, nail, mucosa(melanin in basal cell layer)	➲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	

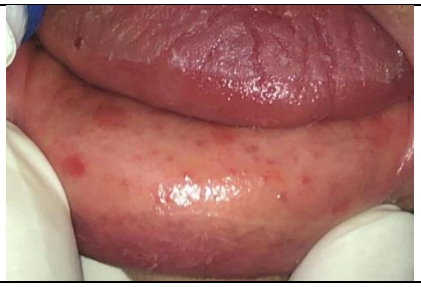
20. Which of the following statements is *false* concerning **oral human papilloma virus (HPV) infection**?
(A) HPV may be present in the oral mucosa without any signs or symptoms
(B) HPV causes papillary oral mucosal lesions
(C) HPV is transmitted by droplet infection
(D) microscopically, HPV-infected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

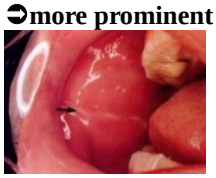
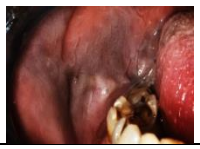
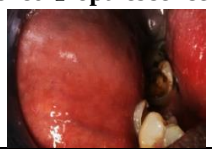
Coronavirus disease 2019➔severe acute respiratory syndrome coronavirus 2(SARS-CoV-2)➔incubate➔2-14-day

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

Chapter 8 Physical & chemical injuries

Linea alba➔white line

➲extend anteroposterior on buccal mucosa ➲bilateral occlusal planes ➲more prominent in clenching/bruxing patient 	➲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:

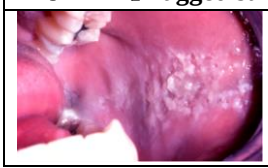
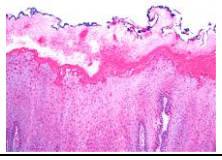
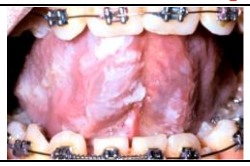
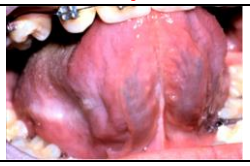
(A) frictional keratosis
(B) leukoplakia
(C) linea alba
(D) a traumatic ulcer

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(zone of erythema, erosion, ulcer)➔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(下左圖)

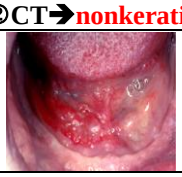
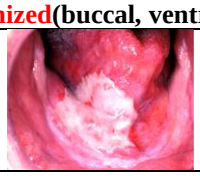
➲micro➔❶like➔①oral hairy leukoplakia(下中圖) ②uremic stomatitis(下 2 右圖) ③betel chewer mucosa ④linea alba ⑤leukoedema
❷HPK➔ragged surface with keratin projection➔bacterial colony➔[vacuolated cell➔prickle cell layer(下中圖)]

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

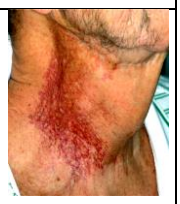
➲hemorrhage➔minor trauma➔petechiae & ecchymosis(any mucosa)➔①labial ②tongue ③gingiva(①②③most)
❶bone marrow suppression➔thrombocytopenia(血小板減少症)
❷intestinal/hepatic damage➔↓vitamin K-dependent clotting factor➔↑coagulation time
❸therapy➔tissue damage➔↑tissue thromboplastin➔disseminated intravascular coagulation(DIC)

➲mucositis[clinic(ulcer)➔RT & CT the same]➔①HN RT(almost all) ②high-dose CT(80%) ③systemic CT(20-40%)
❶①RT➔begin during 2nd wk of Tx ②CT➔Tx 開始後的 a few-day ③RT & CT resolve 2-3-wk after Tx cessation
❷①RT➔mucosa within direct portal ②CT➔nonkeratinized(buccal, ventrolateral tongue, soft palate, mouth floor)

CT-related ulcer | CT-related ulcer | SCC before RT | RT-related mucositis | resolution of SCC, mucositis

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

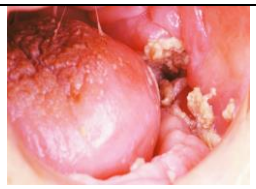
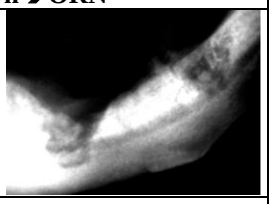


➲xerostomia➔radiation caries(cervical)
❶RT 1-wk begin➔RT 6-wk dramatic ↓saliva flow➔further↓up to 3s
❷radiosensitivity➔serous gland>mucous gland
❸parotid gland➔affect dramatic & irreversible
❹mucous gland➔partial recover(over several months)➔flow approach 50% preradiation level
❺teeth➔①↓microhardness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

➲taste➔①dysgeusia(altered sense of taste) ②hypogeusia(abnormal low sense of taste)
❶RT➔①loss of all 4 tastes in several wk➔return in 4-month(most) ②permanent hypogeusia, dysgeusia(some)

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

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

➲**trismus➔tonic muscle spasm with(out) fibrosis of masticatory muscle & TMJ capsule**

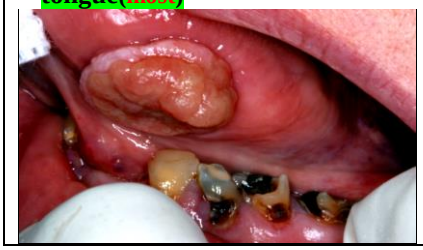
➲**developmental abnormalities(childhood)➔alter facial bone➔①micrognathia ②retrognathia ③malocclusion**
❶**developing teeth➔①root[root dwarfism, blunt root, root dilaceration]**
②pulp canal[premature pulp canal closure(deciduous teeth), enlarged canal(permanent teeth)]
③whole teeth[microdontia, hypodontia,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

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

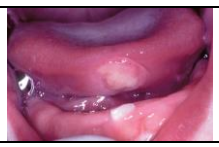
3. 口腔癌病人在接受**放射線治療後的副作用**，下列何者正確？(114)
①味覺喪失且無法恢復 ②味覺喪失但 會逐漸恢復 ③刺激唾液腺分泌，導致唾液變黏稠 ④唾液腺萎縮，且不易完全恢復
(A) ②③
(B) ①④
(C) ①③
(D) ②④

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



❸**similar presentation➔neurologic conditions 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 ulceration, necrosis, self-regression(occasion)➔eosinophilic ulceration**

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

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

➲**stages**
stage 0➔no exposed necrotic bone➔但有associated clinical/radiographic 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)**
❶**tyrosine 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 for antineoplastic
❸aminobisphosphonates for osteoporosis
❹denosumab for osteoporosis
❺romosozumab for osteoporosis

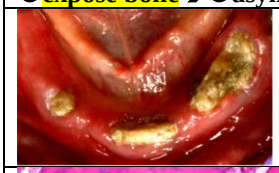
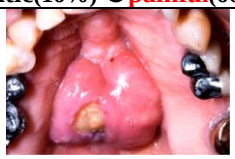
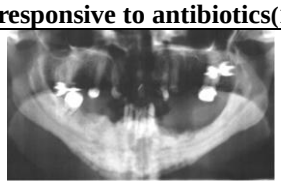
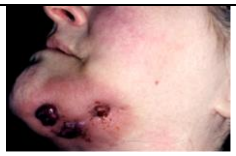
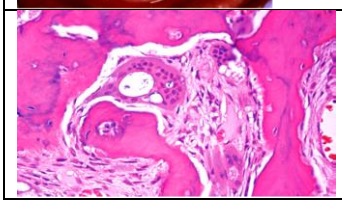
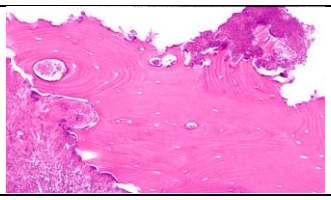
✶正常➲trauma➔clot➔granulation tissue➔woven(immature) bone➔remodel to lamellar bone➔4-mon(2-8-mon)

✶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%)

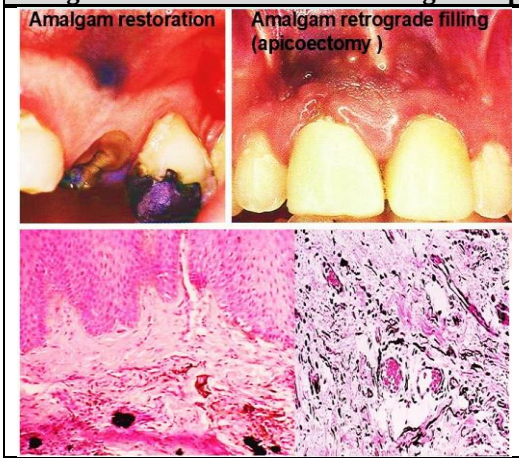
➲expose bone➔❶asymptomatic(16%) ❷painful(66%)➔not responsive to antibiotics(18%)

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

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➔type of material of foreign body

➲large particle➔surround by chronic inflamed fibrous tissue
➲smaller particle➔surrounded 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
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➔first sign in oral cavity ➲grayish discoloration➔face 

bismuth	➲diffuse blue-gray discoloration of skin, conjunctivae, oral cavity ➲blue-gray line along gingival margin
gold	➲metallic taste precedes oral mucositis(buccal mucosa, tongue border, palate, pharynx)
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 area of hyperpigmentation

➲peginterferon alfa➔ethnically pigmented hepatitis C patient➔pigmented filiform papillae(dorsal tongue)

➲minocycline

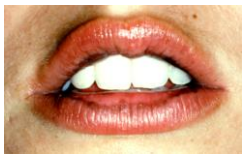
❶linear band➔facial attached gingiva near mucogingival junction

❷hard palate➔broad zone of discoloration

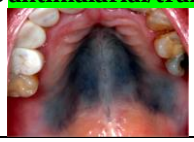
❸dental pulp➔dark stained➔ darkened teeth

❹alveolar bone➔blue-gray discoloration(原為 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

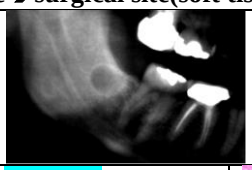
6. Which one of the following **drugs** may stain bone & result in **blue-gray discoloration of alveolar mucosa** adjacent to teeth?
   (A) clotrimazole
   (B) fluconazole
   (C) fluocinonide
   (D) minocycline

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

➲antibiotic placed➔extraction site➔prevent alveolar osteitis

❶asymptomatic WD-RL➔exploration➔black, greasy, tarlike material

❷painful swelling & purulent drainage



➲micro

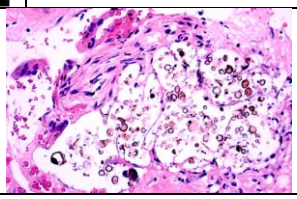
❶dense collagenous tissue mixed with granulomatous inflammation➔ macrophage & multinucleated giant cell

❷c.t.➔cystlike space➔numerous brown-black-stain spherule(小球)➔ surrounded by an outer membrane(parent body)➔bag of marbles

❸spherule➔RBC➔altered by medication

❹dark coloration➔degradation of hemoglobin

❺paranasal sinus➔zygomycetes/aspergillus



➲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
[Plummer-Vinson syndrome(Fe deficiency anemia)➔oral/esophageal SCC)]
②with plasma cell gingivitis

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⇆inflammatory condition of minor salivary gland➔lower lip vermilion

Chapter 9 Allergies & immunologic diseases

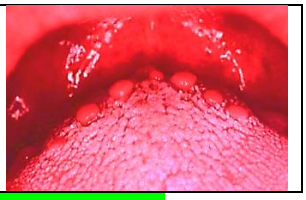
➲4 types of tongue papillae(乳頭)

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

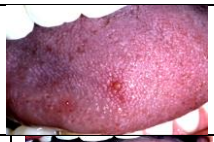
❹foliate(葉狀) papillae➔舌側緣後



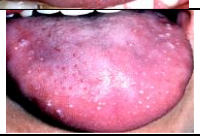
Transient lingual papillitis➔involve fungiform papillae(FP)

➲3 patterns

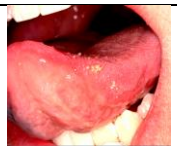
❶first pattern➔female predominance
①localized➔1-several FP➔enlarged & papule➔red with yellow, ulcerated cap
②anterior dorsal(most)➔mild to moderate pain➔resolve spontaneous(hrs-several days)
③transient lingual papillitis(56%)➔single affected papilla(vast majority)➔associate food allergy



❷second pattern➔FP more generalized affect➔tip & lateral dorsal
①FP➔sensitive, enlarged, erythematous, focal erosion
②fever & cervical lymphadenopathy➔spread among family members➔possible correlate to virus
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 vessels & 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 basilar 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

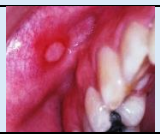
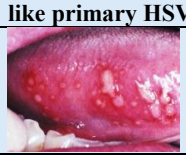
➲mucosa destruction➔T cell-mediated➔TNF(tumor necrosis factor)α(inflammatory cytokine)➔assist cytotoxic T cell(CD8+)➔destruct epithelium

➲systemic disorders associate RAS
①Behcet syndrome ②celiac(腹腔) disease ③cyclic neutropenia
④nutritional deficiencies(Fe, folate, Zn, B1, B2, B6, B12) ⑤IgA deficiency ⑥immunocompromised 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 factors➔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 influences➔↑mucosal barrier(nomal)
❹immunologic factors➔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 20s 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 primary HSV infection
	 		

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

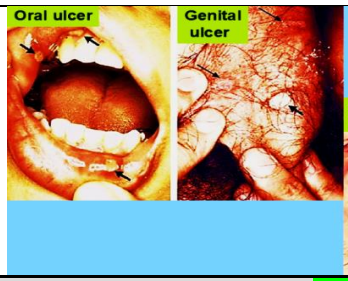
4. Which of the following is the main diagnostic criteria of **Behçet disease**?
   (A) blood routine test
   (B) history and clinical features
   (C) histopathological examination
   (D) titer of autoantibodies

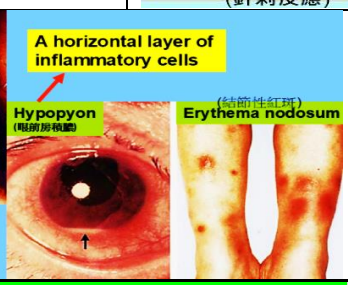
5. **Aphthous ulcers** are seen in each all of the following systemic diseases except
   (A) Behcet syndrome
   (B) Langerhans cell histiocytosis
   (C) ulcerative colitis
   (D) cyclic neutropenia

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

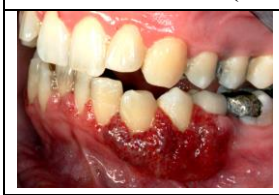
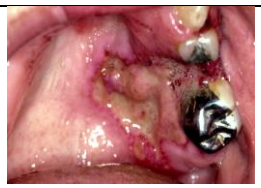
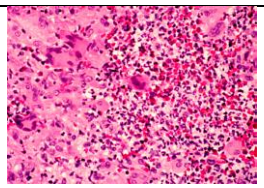
Grade of test	Clinical characteristic of the test at 48 h
Negative (-)	Only erythema < 2 mm
Suspect (+/-)	Only erythema > 3 mm or papule 1-2 mm + erythema < 2 mm
Positive (+)	1+ Papule 2-3 mm + erythema > 3 mm
	2+ Papule > 3 mm + erythema > 3 mm
	3+ Pustule 1-2 mm + erythema > 3 mm
	4+ Pustule > 2 mm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

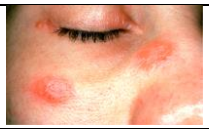
➲acute➔fever, fatigue, anorexia, weight loss + (respiratory symptom, polyarthritis, visual problem & skin lesion)

➲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)

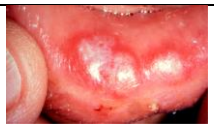
➲skin(nose, ear, lip, face, lower leg)➔violaceous, indurated lesion (lupus pernio)➔erythema nodosum



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

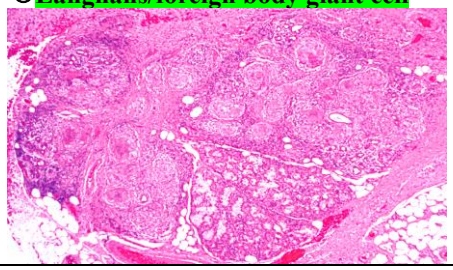
➲intraosseous➔phalange, metacarpal & metatarsal (less frequent➔skull, nasal bone, ribs & vertebrae)

➲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)



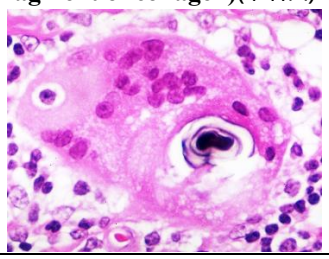
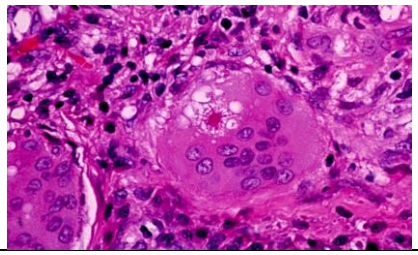
➲micro

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 fragment of collagen)(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]

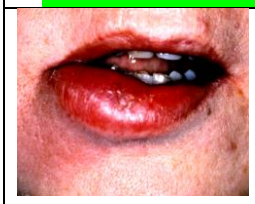
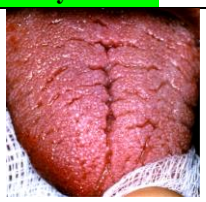
➲R/O local causes

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

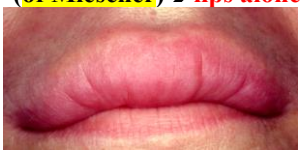
allergy	①cosmetic, food & food additive(aspartate, benzoate, carbone piperitone, carmoisine, carvone, chocolate, cinnamon, cocoa, dairy product, egg, monosodium glutamate, peanut, sun yellow dye, tartrazine, wheat) ②flavor ③OH product(toothpaste & mouth rinse) ④dental restorative metal ⑤patch test(contact 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)

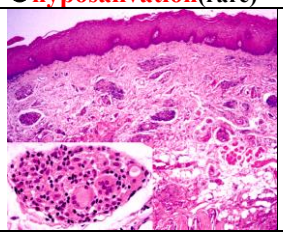
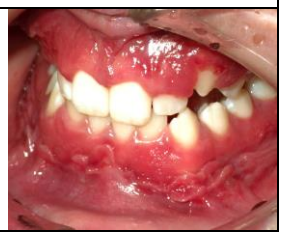



❷cheilitis granulomatosa (of Miescher)➔lips alone



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

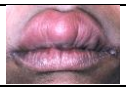
6. All of the following are examples of **hypersensitivity reactions** except
   (A) systemic lupus erythematosus
   (B) urticaria(蕁麻疹)
   (C) angioedema
   (D) contact dermatitis and mucositis

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

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

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

➲diffuse edematous subcutaneous(mucosa) swelling



❶allergen(drug, food, plant, dust, inhalant)➔contact allergic reaction(cosmetic, topical medication, rubber dam)

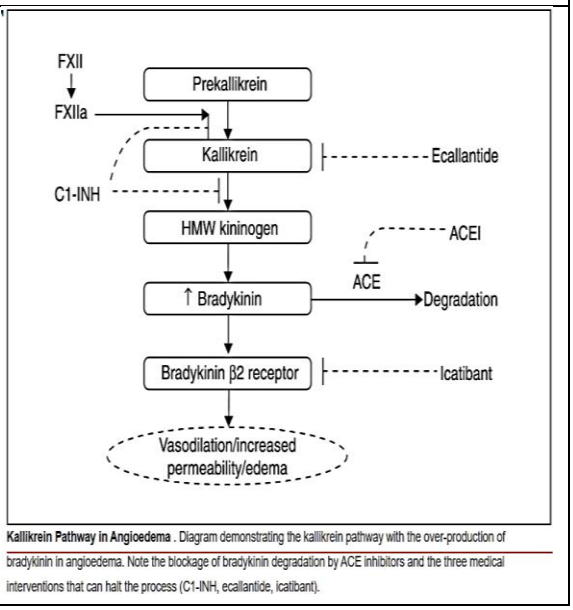
❷physical stimuli(heat, cold, exercise, emotion stress, solar exposure, significant vibration)

❸antihypertensive➔angiotensin converting enzyme (ACE) inhibitor(not mediated by IgE)

➲3 types
①type I hereditary angioedema(HAE I)
②HAE II
③hereditary angioedema with normal C1 esterase inhibitor (C1-INH)(右圖)

➲blockage of bradykinin degradation by ACE inhibitor➔ accelerate the process(右圖)

➲3 medical interventions
①C1-INH ②ecallantide
③icatibant➔❶+❷halt the process(右圖)



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).

Chapter 10 Epithelial pathology

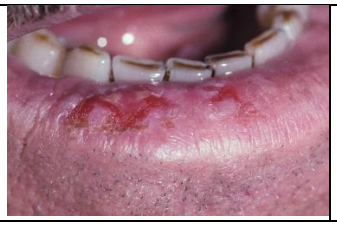
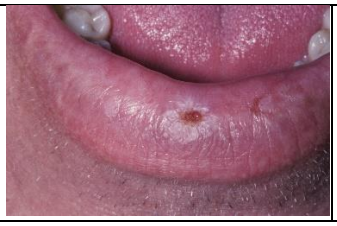
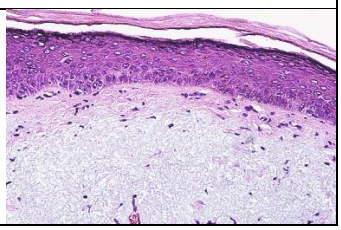
1. All of the following neoplasms arise from **squamous epithelium** *except* one. Which one is the exception?
   (A) squamous cell carcinoma
   (B) verrucous carcinoma
   (C) adenoid cystic carcinoma
   (D) papilloma

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

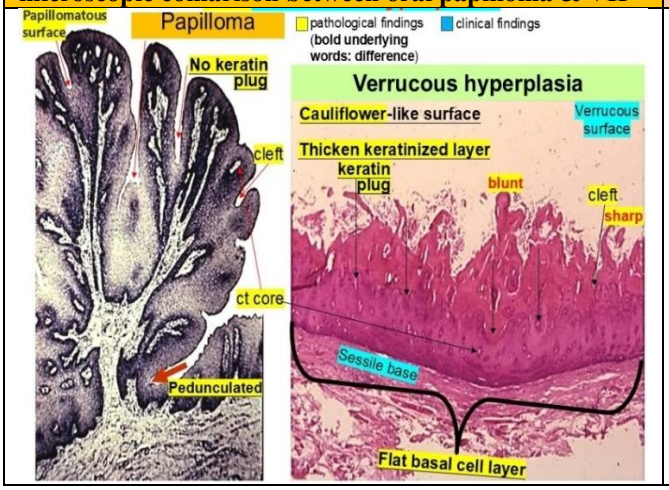





4. Which of the following types of human papilloma virus (HPV) are mostly associated with oral squamous papilloma?
   (A) type 6, 11
   (B) type 3, 32
   (C) type 16, 18
   (D) type 3, 10

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**

5. 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



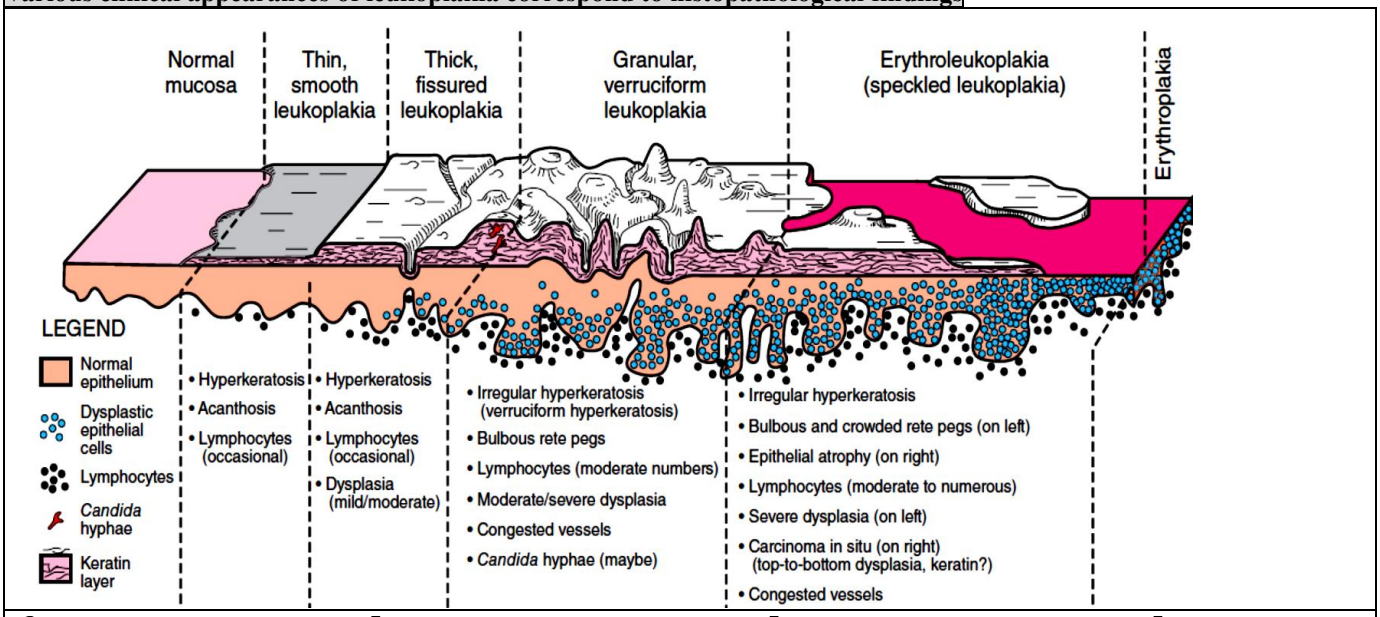
comparison of oral papilloma & verrucous hyperplasia

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

6. Which of the following **precancer** lesion has the **highest malignant transformation rate**
   (A) tongue of Plummer-Vinson syndrome (iron deficiency)
   (B) thin leukoplakia
   (C) thick leukoplakia
   (D) proliferative verrucous leukoplakia (PVL)

7. A white plaquelike 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(M:F=1:4; multiple, slow spread plaques, rough surface)➔VCa➔SCC**

➲**erythroleukoplakia(specked leukoplakia)➔erythroplakia**

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

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

10. 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

11. 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
➲increased 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

12. 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

13. **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]			
TX	primary tumor cannot be assessed	Tis	carcinoma in situ(CIS)
T1	tumor≤2cm with DOI≤5mm	T2	tumor≤2 with DOI >5mm but ≤10mm *or* tumor>2cm but≤4cm with DOI≤10mm
T3	tumor >2cm but ≤4cm with DOI >10mm *or* tumor >4cm with DOI≤10mm		
T4a	(a)tumor>4cm with DOI>10mm (a)tumor invade adjacent structure only(through cortical bone of mandible/maxilla (a)involve maxillary sinus/skin of face) (NB)superficial erosion of bone/tooth socket alone by gingiva primary➔not as T4		
T4b	(b)tumor invade masticator space, pterygoid plate (b)skull 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 metastasis
N1	metastasis in a single ipsilateral LN≤3cm & extranodal extension(ENE)(-)		
N2a	metastasis in a ipsilateral LN >3cm but ≤6cm & ENE(-)		
N2b	metastases in multiple ipsilateral LN≤6cm & ENE(-)		
N2c	metastases in bilateral/contralateral LN≤6cm & ENE(-)		
N3a	metastasis in a LN>6cm & ENE(-)		
N3b	metastasis in any LN & ENE(+)		
distant metastasis(M)			
M0	no distant metastasis	M1	distant metastasis

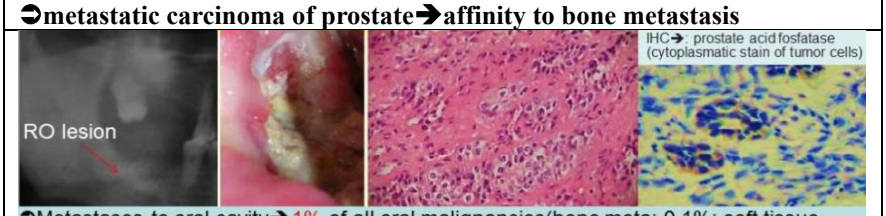
Stage for oral cavity carcinoma

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**

14. 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

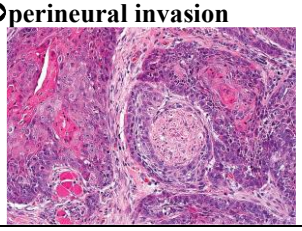
➲Most common sites for bone metastasis➔breast, lung, thyroid, prostate & kidney
➲Most metastatic bone➔vertebrae, rib, pelvis & skull
➲Jaw metastasis➔mandible(molar)
➲Numb-chin syndrome➔mental nerve involve; lower lip paresthesia
➲Bone metastasis➔stage IV
➲PDL widening➔metastatic to jaws
➲Bone scintigraphy➔sensitive to detect bone metastasis

15. 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 patterns➔tumor islands break through basement membrane into subepithelial connective tissues

➲superficial/microinvasive(early)

➲perineural invasion



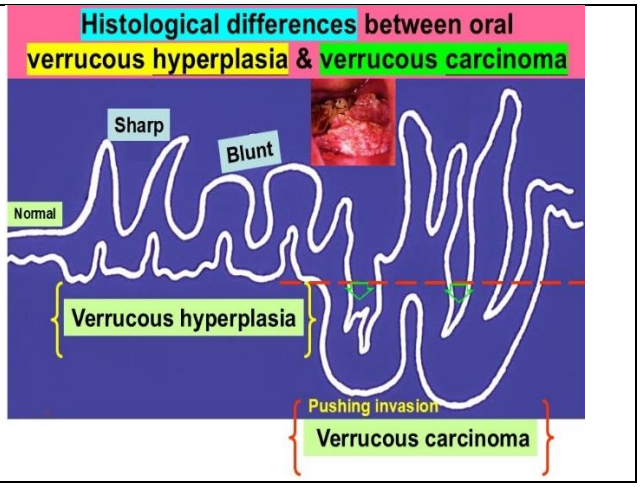
➲vascular invasion

➲desmoplasia(scirrhous change)
➲angiogenesis

16. **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



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

18. 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

19. 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 ❺ Langerhans cell ❻ dendritic cell ❼nevus cell

20. 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	**> 6 mm (diameter of a pencil eraser)**
Evolving	**size, shape, color, surface, or symptoms➔changed over time**

21. 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

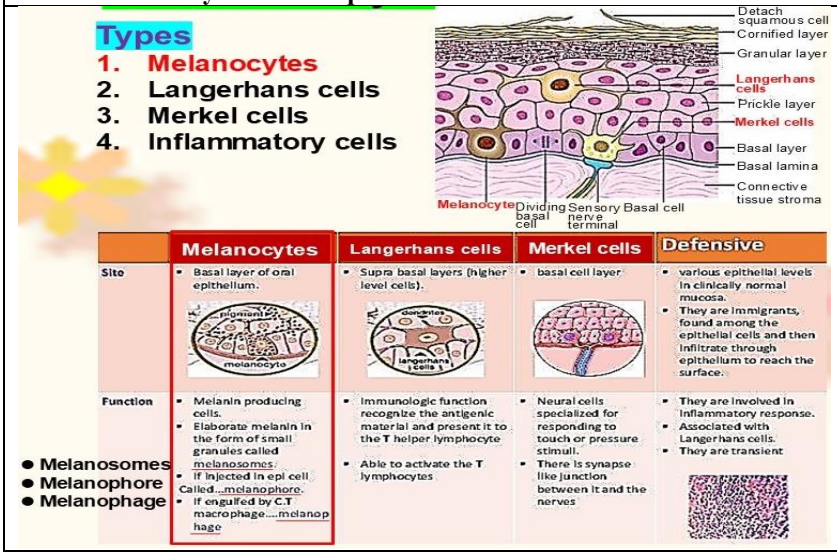
tumor cells	**confined to epithelium**	**Level I**
	penetrating papillary dermis	**Level II**
	filling papillary dermis	**Level III**
	extend into reticular dermis	**Level IV**
	invade subcutaneous fat	**Level V**

22.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

23. 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

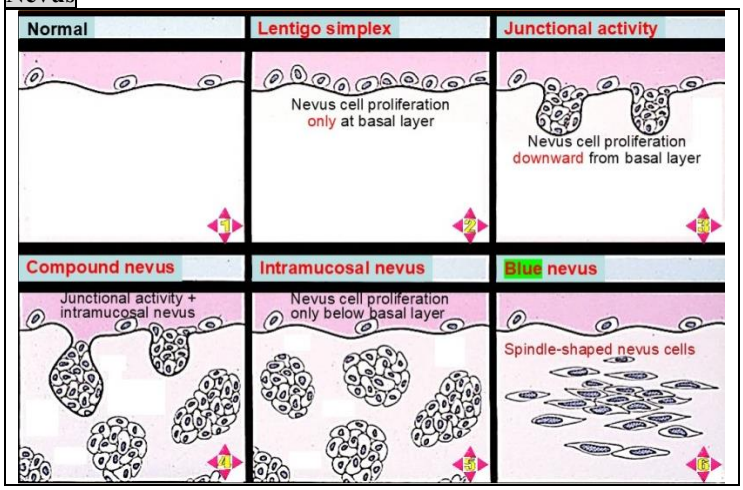
Merkel cell carcinoma➔a neuroendocrine carcinoma

➲histopathologic feature➔small blue round cells(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		



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

Nevus



Chapter 11 Salivary gland pathology

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

Frequency by sites(major, minor gland)

➲**1st common salivary gland tumor➔parotid gland(61-80%;2/3-3/4)➔其中2/3-3/4(benign)➔least common malignant**
➲**2nd common salivary gland tumor➔minor gland(9-28%)➔其中(38-49%)malignant(2nd most common)➔其中1st common➔retromolar(up to 95% mucoepidermoid carcinoma)**
➲**least common salivary gland tumor➔sublingual gland (<1%)➔其中(70-95%)malignant(1st most common)**
➲**1st common of minor gland➔palate (42-54%; posterior lateral hard or soft palate)**

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

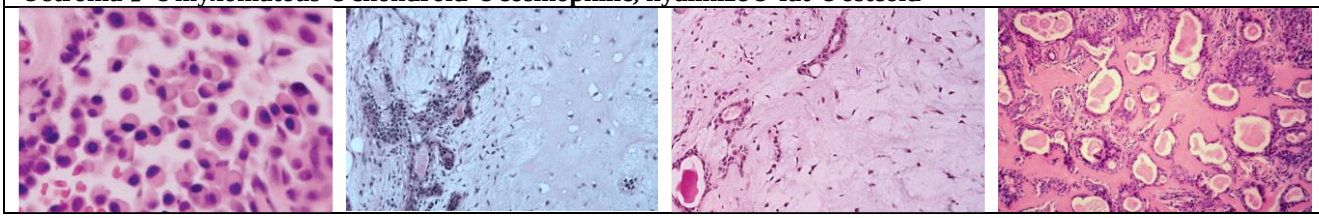
Frequency by types of salivary gland tumors

➲**1st common(benign, all)➔pleomorphic adenoma➔[(parotid 50-77%) submandibular 53-72%) minor(~40%)]**	
➲**1st common malignant salivary gland tumor**	◆**all salivary glands➔mucoepidermoid carcinoma** ◆**parotid gland➔mucoepidermoid carcinoma** ◆**submandibular gland➔adenoid cystic carcinoma** ◆**minor gland➔mucoepidermoid carcinoma**

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

Pleomorphic adenoma(PA)

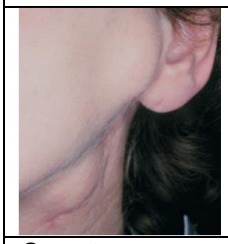
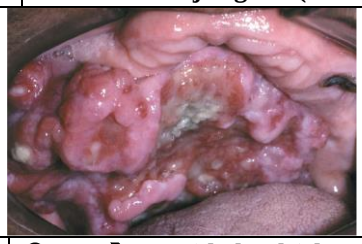
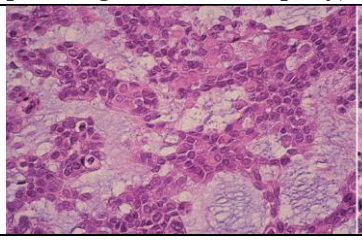
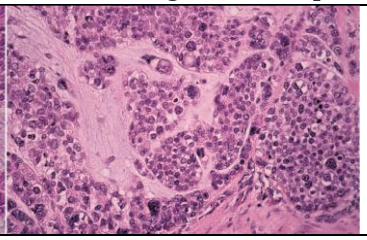
➲**derived from a mixture of ductal & myoepithelial cells**	➲ **slight female predilection**
➲**cytogenetic analysis➔translocation pleomorphic adenoma gene 1(PLAG1) at chromosome 8q12(~70%)**	
➲**most common salivary gland tumor in childhood**	➲**bilateral(synchronous/metachronous)**
➲**superficial lobe(most)➔swelling over ramus before ear**	➲ **deep lobe(beneath facial n)➔~10%**
➲ **most common➔minor gland➔(posterior lateral)palate(50-60%)➔bound palate mucosa➔not movable**	
➲**2nd common➔minor gland➔upper lip(movable)**	➲**3rd common➔minor gland➔ buccal mucosa(movable)**
➲**micro**	
❶**encapsulated➔①incomplete(more in minor gland tumor➔palatal PA beneath epithelial surface) ②infiltrate by tumor cell** ❷**glandular epithelium+myoepithelial cell within stroma➔幾乎全是stroma/highly cellular幾乎無stroma(cellular PA)** ❸**glandular epithelium➔①duct+cystic structure ② island/sheet of cell ③keratinize squamous cell & mucus cell** ❹**myoepithelial cell➔morphology➔①angular/spindle ②plasmacytoid➔more prominent in minor gland PA ③almost entire myoepithelial cell(no ductal cells)➔myoepithelioma** ❺**stroma➔①myxomatous ②chondroid ③eosinophilic, hyalinize④ fat ⑤osteoid**	



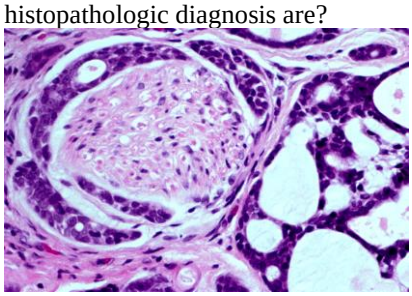
4. Which of the following lesion may undergo **malignant transformation**?
   (A) granular cell tumor
   (B) pleomorphic adenoma
   (C) torus
   (D) hemangioma

Malignant mixed tumors(❶Carcinoma *ex* pleomorphic adenoma(mixed tumor) ❷Carcinosarcoma ❸Metastasizing mixed tumor)

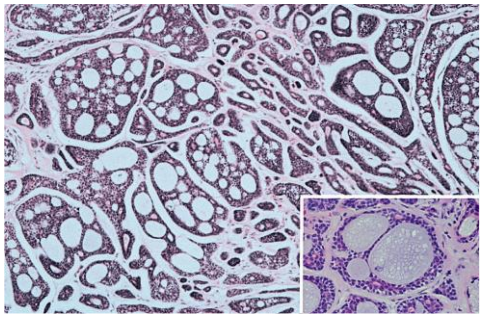
➲**2-4% of all salivary tumors**

❶**carcinoma *ex* PA(3-4%)➔malignant change of epithelial component of benign PA➔evidences** **①mean age 15 years>benign PA** **②a mass for many years➔recent rapid growth with pain or ulceration** **③area of benign PA➔malignant changes (cellular pleomorphic & abnormal mitoses) of epithelial component**	
❷**carcinosarcoma➔carcinoma & sarcoma components**	
❸**metastasizing PA➔histopathologic benign➔metastasis (metastatic tumor➔microscopic benign like 1^0 PA)**	
➲**clinic**	
❶**carcinoma *ex* PA**	**①>80%➔major gland(主要在parotid gland➔facial n palsy) ②近2/3 minor gland case➔palate**
   	
❷**carcinosarcoma**	**①most➔parotid gland (also submandibular gland & minor glands)** **②history of PA or arise *de novo***
❸**metastasizing PA**	**①most➔parotid gland (also submandibular gland/minor gland)** **②most meta➔bone/lung (also regional lymph node, skin, liver)** **③most➔PA excised many years earlier** **④$1^0$ tumor➔multiple recurrences before meta**
➲**micro**	
❶**carcinoma *ex* PA**	**①most➔poor differentiated adenocarcinoma (salivary duct carcinoma)➔also myoepithelial carcinoma, polymorphous adenocarcinoma, mucoepidermoid ca, adenoid cystic carcinoma** **②growth pattern** **◆invasive (extracapsular invasion >1.5mm)** **◆minimal invasive (extracapsular invasion≤1.5mm)** **◆noninvasive[small malignant focus without extracapsular invasion)]➔carcinoma in situ *ex* PA or intracapsular carcinoma *ex* PA**
❷**carcinosarcoma (biphasic①+②)**	**①carcinoma (poor differentiated adenocarcinoma/undifferentiated carcinoma)** **②sarcoma [chondro(osteo)sarcoma, fibrosarcoma, liposarcoma, rhabdomyosarcoma, malignant fibrous histiocytoma]** **③arise from PA(some)**
❸**metastasizing PA**	**①primary & metastatic sites➔microscopic benign PA** **②no malignant histopathologic changes**

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

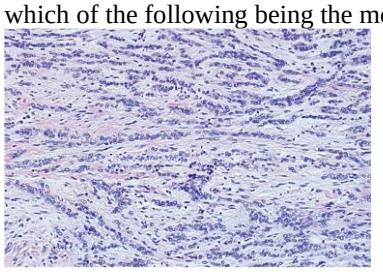
7. Figure below shows **cribriform pattern** of the salivary gland tumor, please identify which of the followings are the most likely histopathological diagnosis?



(1) adenoid cystic carcinoma (2) mucoepidermoid carcinoma (3) polymorphous adenocarcinoma (4) acinic cell carcinoma

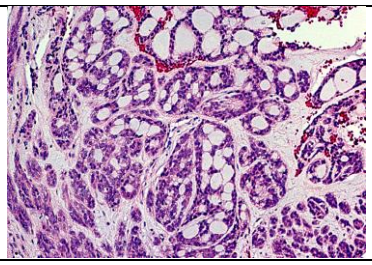
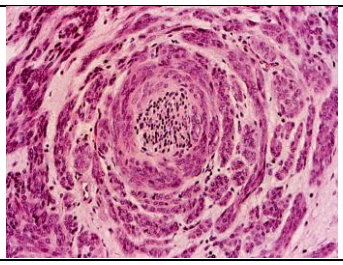
(A) only 1,2
(B) only 1,3
(C) only 2,3
(D) only 1,4

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	
➲rare➔major gland➔❶arising *de novo* ❷malignant component of carcinoma *ex* PA	➲2/3 case➔female	
➲most➔old adult (peak prevalence 6-8th decades)	➲*PRKD1* hotspot mutation(>70%)	➲slow painless growth
➲palatal lesion➔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➔papillary thyroid carcinoma		
➲d.d. with adenoid cystic carcinoma(ACC)➔weaker CD43 & c-kit (CD117) BUT ACC (strong +)		
➲d.d. with PA➔glial fibrillary acidic protein (GFAP) (-) BUT PA (strong +)		
➲micro		
❶different growth pattern(polymorphous) ①solid pattern ②cord, duct, cystic spaces ③cribriform(mimic adenoid cystic carcinoma) ❷mitotic figure➔uncommon ❸tumor cell➔invade adjacent tissue➔ single-file fashion(LP) ❹perineural invasion(mimic adenoid cystic carcinoma)		

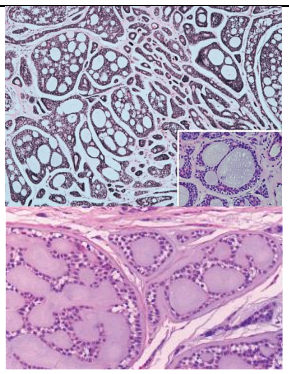
9. Which of the following carcinoma is mostly related to **HPV-related multiphenotypic sinonasal carcinoma** upon histopathological findings?
(A) squamous cell carcinoma
(B) Burkitt lymphoma
(C) adenoid cystic carcinoma
(D) Langerhans cell histiocytosis

Adenoid cystic carcinoma(ACC)

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

➲**micro**

❶**3 patterns**
①**cribriform(Swiss cheese)➔space➔basophilic mucoid material, hyalinized eosinophilic product**
②**tubular➔ductal & myoepithelial cell**
③**solid➔cellular pleomorphism, mitotic activity, central necrosis➔worse prognosis**
❷**perineural invasion(also polymorphous adenocarcinoma)**
❸**CD43 & c-kit (CD117) (+)**
❹**p63+p40➔d.d. ACC & polymorphous adenocarcinoma**
◆**ACC➔myoepitheial cell➔p63&p40(+)**
◆**polymorphous adenocarcinoma➔myoepitheial cell➔p63(+); p40(-)**
❺**K-67(proliferation index)➔ACC(21.4%)>>polymorphous adenocarcinoma(2.4%)**

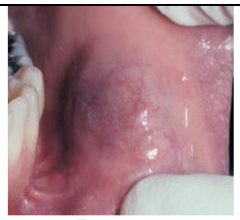


10. **Mammary analogue secretory carcinoma**, a newly recognized salivary gland malignancy, has overlapping microscopic features with which of the following salivary gland tumor?
(A) pleomorphic adenoma
(B) mucoepidermoid carcinoma
(C) acinic cell carcinoma
(D) adenoid cystic carcinoma

Mammary analogue secretory carcinoma

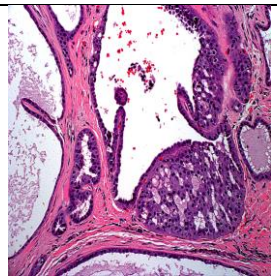
➲**FISH/RT-PCR➔chromosome translocation t(12;15)(p13;q25)➔*ETV6-NTRK3* fusion gene➔like secretory carcinoma of breast**

➲**clinic**
❶**most➔parotid gland (58%); minor gland (31%➔lips, soft palate, buccal mucosa); submandibular gland (9%)**
❸**mean age➔47s**
❹**male➔slightly>female**
❺**slow grow, painless mass**



bluish➔like mucocele

➲**micro**
❶**solid, tubular, micro(macro) cystic structure**
❷**cystic space➔papillary infolding tumor cell➔hobnail appearance**
❸**mitoses➔rare**
❹**tumor cell➔S-100(+), vimentin(+), mammaglobin(+)**

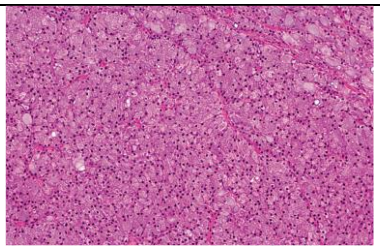


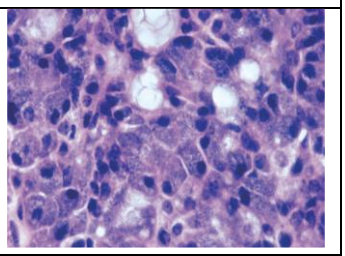
11. **Acinic cell carcinoma** may likely be mistaken as which of the following salivary gland tumor?
(A) mucoepidermoid carcinoma
(B) mammary analogue secretory carcinoma
(C) pleomorphic adenoma
(D) adenoid cystic carcinoma

Acinic cell carcinoma

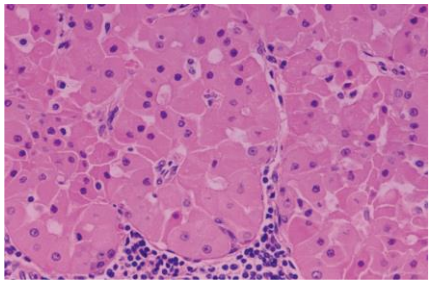
➲**malignant cell➔serous acinar differentiation**
➲**poor in zymogen(inactive precursor of enzyme; proenzyme) granule➔ reclassified➔ mammary analogue secretory carcinoma**
➲**most(85-90%)➔parotid gland**
➲**(2.7- 5%)submandibular gland**
➲**(9%)minor glands➔most common➔buccal, lips, palate**

➲**micro**
❶**solid➔well-differentiated acinar cell➔ resemble normal parotid gland**
❷**microcystic➔small cystic space➔mucinous or eosinophilic material**
❸**papillary cystic➔papillary projection(lined by epithelium)➔into cystic space**
❹**follicular➔like thyroid tissue**
❺**IHC➔DOG1(+), NR4A3(+)**





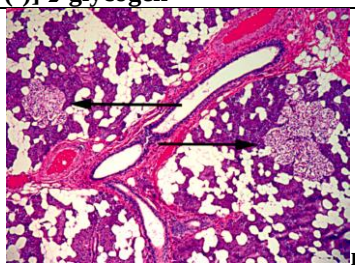
12. Figure below is a case of **oncocytoma** showing sheet of large, eosinophilic oncocytes that can be demonstrated by electron microscopy as an abundance of which of the following?



(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

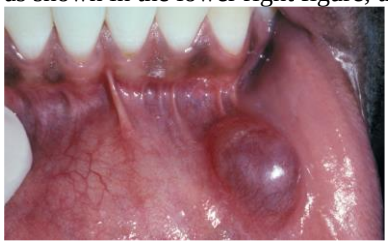
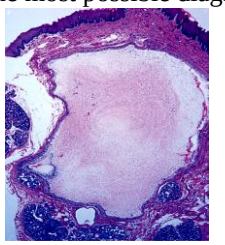
Oncocytoma(oxyphilic adenoma)

➲**~1% of all salivary gland tumor**	➲**most➔major gland(minor gland exceedingly rare)➔most in parotid(85-90%)**	
➲**old adult (6-8th decade)**	➲**painless➔rare>4cm**	➲**oncocytic carcinoma➔reported(rare)➔poor prognosis**
➲**clear cell variant➔d.d. with 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)➔[PAS (+); PAS + diastase (-)]➔glycogen**		
➲**d.d. with oncocytois➔most in parotid➔old adult➔(may)swelling(nodular)➔multifocal➔entire(diffuse hyperplastic oncocytosis)➔benign(metaplastic)** ➲**focal oncocytic metaplasia of ductal & acinar cell➔common➔related to age(uncommon<50s; almost all by 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

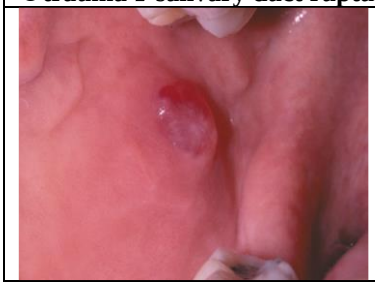
16. A 12 years old boy complained **blue-pigmented nodule on the lower lip** (lower left figure) and received excisional biopsy as shown in the lower right figure, the most possible diagnosis has been which of the following disease?

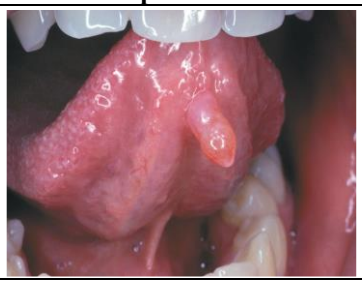



(A) hemangioma
(B) mucocele
(C) fibroma
(D) lipoma

Mucocele(Mucus extravasation phenomenon)

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

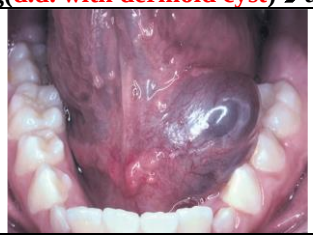
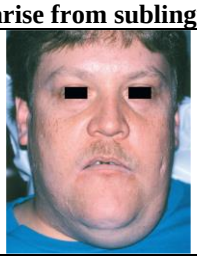




Location	Number of Cases	Percentage of All Cases
Lower lip	1405	81.9
Floor of mouth	99	5.8
Ventral tongue	86	5.0
Buccal mucosa	82	4.8
Palate	23	1.3
Retromolar	9	0.5
Unknown	11	0.6
Upper lip	0	0.0

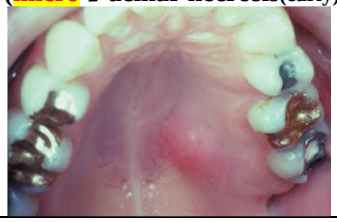
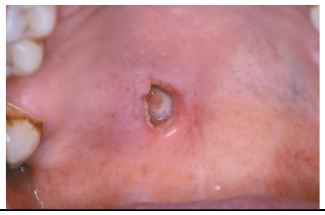
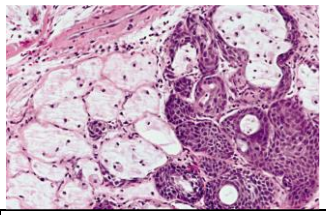
17. A **ranula** is located on the:
(A) lower lip
(B) buccal mucosa
(C) retromolar area
(D) floor of the mouth

Ranula

➲mouth floor(blue, dome-shape, fluctuant lateral swelling(d.d. with dermoid cyst)➔arise from sublingual gland	
➲lesser sublingual gland➔15-30 smaller glands➔ secrete via short duct of Rivinus to sublingual plica	 
➲ greater sublingual gland➔Bartholin duc➔❶join Wharton duct ❷open next at sublingual caruncle	
➲clinical 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

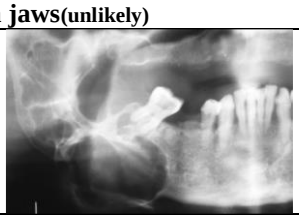
Necrotizing sialometaplasia

➲ salivary tissue ischemia➔infarction➔mimic malignancy[(clinic➔nonulcerated swelling➔pain/paresthesia➔ (2-3-wk)necrotic tissue slough out➔craterlike ulcer(<1->5 cm)➔pain subside➔palatal bone destruction(rare)) & (micro➔acinar necrosis(early)➔ductal squamous metaplasia)➔misdiagnosed➔SCC/MEC]➔self-heal(5-6-wk)		
  		
➲>75%➔post. palate(palate>soft)(others➔minor gland)		➲parotid(reported); submandibular & sublingual(rare)
➲support➔❶low p53 & Ki-67 ❷overall lobular architecture still preserved		
➲most➔adult(mean age 46 yrs)	➲male : female=近2:1	➲palatal lesion➔2/3 unilateral; 1/3 bilateral/midline
➲predisposing factor➔❶traumatic injuries ❷dental injection ❸ill-fitting denture ❹upper respiratory infection ❺adjacent tumor ❻previous surgery ❼eating disorders with binge-purging(暴食症)		
➲many➔without known predisposing factors		

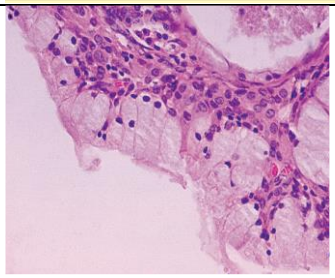
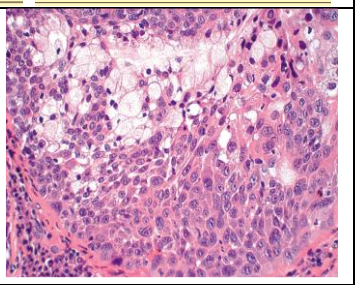
19. **Central** involvement of the jaws may occur with a:
(A) granular cell tumor
(B) peripheral ossifying fibroma
(D) melanocytic nevus
(D) mucoepidermoid carcinoma

Intraosseous(central) mucoepidermoid carcinoma(MEC)

➲most common intrabony salivary tumor	
➲other intrabony salivary tumor ❶adenoid cystic carcinoma ❷benign & malignant PA ❸adenocarcinoma ❹acinic cell carcinoma❺epithelial myoepithelial carcinoma ❻monomorphic adenoma	
➲hypotheses	❶mucus-producing cell➔common in odontogenic cyst lining(esp., dentigerous cyst)➔associate with impacted teeth or odontogenic cyst

	❷ectopic salivary gland tissue entrapped within jaws(unlikely)		
➲clinic	❶most➔middle-aged adult ❷slight female predilection ❸more➔mandible(molar-ramus) ❹most frequent symptom➔cortical swelling ❺WD UL/ML RL➔odontogenic cyst/tumor(usually) irregular & ill-defined bone destruction(some)		➲micro ❶low-grade(most) ❷high-grade(also report)

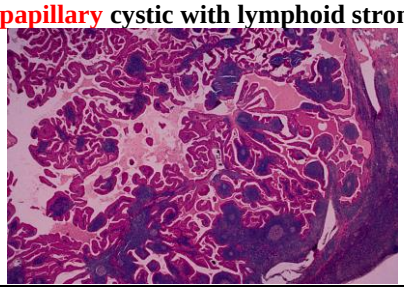
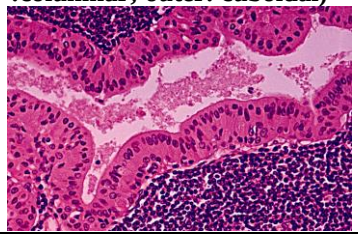
Mucoepidermoid carcinoma(MEC)

➲most common salivary gland malignancy➔4-10% of major gland tumor(parotid gland);13-23% of minor gland tumor(palate)	➲most common malignant salivary gland tumor in children
➲t(11;19) reciprocal translocation➔*CRTC1-MAML2* fusion oncogene➔more in low- & intermediate- grade MEC	
➲3 histopathologic grades ❶amount of cyst formation ❷degree of cytologic atypia ❸no. of ①mucous[(+)mucicarmine stain)] ②epidermoid ③intermediate cells(progenitor of mucous & epidermoid cell)➔vary from small, basaloid cell to 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➔prominent cyst formation, minimal cellular atypia, high proportion of mucous cell ➲high-grade➔solid island of squamous & intermediate cell➔pleomorphism & mitotic activity➔infrequent mucus cell➔difficult to distinguish from SCC ➲intermediate-grade(between low-& high-grade) ➔ cyst less prominent than low-grade➔intermediate cell predominates	 

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 common benign parotid tumor)		➲bilateral (5-17%)➔metachronous(occur at different times)(most)
➲older adults➔6-7th decades		➲male:female=10:1(more equal ratio recently)
➲associated with smoking➔❶more equal sex ratio ❷ more 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(inner luminal :columnar; outer: cuboidal) 

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)

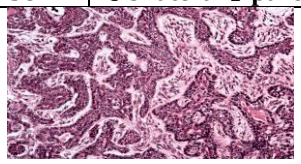
(A) 70%以上的病例發生在舌下腺

(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

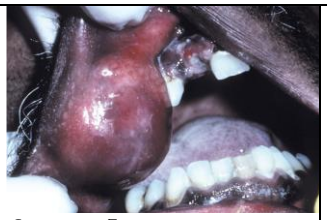
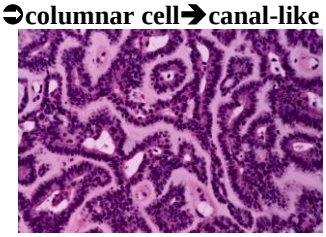
(C) 基底細胞腺癌多由基底細胞腺瘤惡性轉變而成

(D) 病理組織學亞型中的腺管型(tubular variant)具有高度再發率

Basal cell adenoma

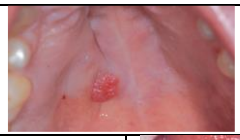
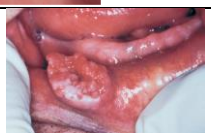
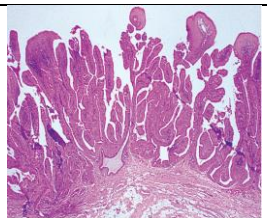
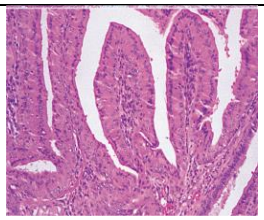
➲(1-4%)all salivary gland tumor	➲1st common➔parotid(75%); 2nd common➔minor gland(upper lip, buccal)		
➲most common➔middle-age; older adult(61~70 y/o)	female : male = 2:1	most< 3cm	➲bilateral➔parotid
➲histopathologic features	❶solid type(like basal cell carcinoma) ❷trabecular type ❸cribriform pattern(some)➔mimic adenoid cystic carcinoma ❹peripheral cell➔hyperchromatic ❺central cell➔eddies(漩渦)/keratin pearl		
➲membranous basal cell adenoma	❶hereditary ❷combined with skin appendage tumor (dermal cylindroma & trichoepithelioma) ❸malignant counterpart➔basal cell adenocarcinoma(good prognosis) ❹ multifocal(jigsaw puzzle)➔recurrence(25-37%) ❺hyaline material between tumor islands ❻hyaline droplets➔among epithelial cells		

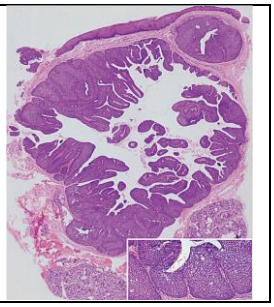
Canalicular adenoma

➲almost exclusive➔minor gland[1st most➔upper lip(近75%)] ➲2nd most➔buccal mucosa ➲other sites of minor gland➔rare (N.B.) canalicular adenoma & pleomorphic adenoma➔1st or 2nd most tumor in upper lip		➲columnar cell➔canal-like ductal structure 
➲most➔幾mm to 2cm	➲bluish➔like mucocele	

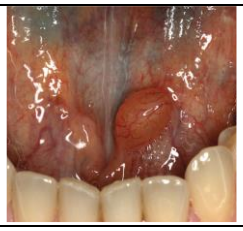
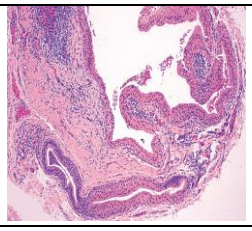
➲salivary gland tumor➔micro➔papillomatous	①papillary cystadenoma lymphomatosum(Warthin tumor)(most) ②sialadenoma papilliferrum(rare) ③intraductal papilloma(rare) ④inverted ductal papilloma(rare)

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

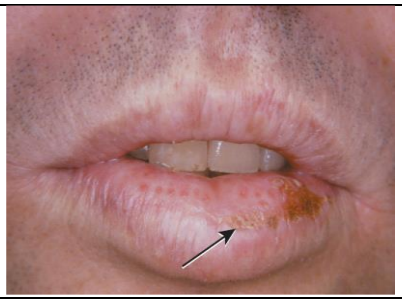
➲clinic		
❶sialadenoma papilliferrum	①most➔minor gland(esp., palate)➔also parotid gland ②older adult ③ male:female ratio=1.5:1.0. ④exophytic papillary surface➔clinic➔like squamous papilloma	
❷intraductal papilloma ①adult ②minor salivary gland ③as submucosal swelling	❸inverted ductal papilloma ①only➔minor gland of adult ②most➔lower lip & mandibular vestibule ③asymptomatic nodule➔a pit/indentation in overlying mucosa	
➲micro		
❶sialadenoma papilliferrum (N.B.) micro➔like cutaneous syringocystadenoma papilliferum	①exophytic papillary stratified squamous epithelium ②與相鄰papillomatous ductal epithelium ③double-row➔◆luminal columnar ◆basal cuboidal cell ④ductal cell➔oncocytic change(variant) ⑤*BRAF*V600E mutation➔classic type & cutaneous syringocystadenoma papilliferum (52%) ⑥NO *BRAF*V600E 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	①proliferation of squamoid epithelium➔thick, bulbous papillary projection➔fill ductal lumen ②contiguous with overlying mucosal epithelium➔communicate with surface via a small pore-like opening ③luminal lining cell➔cuboidal/columnar with scattered mucus cell ④in situ hybridization(ISH)➔HPV type 6 & 11(surface & inverted epithelium)	

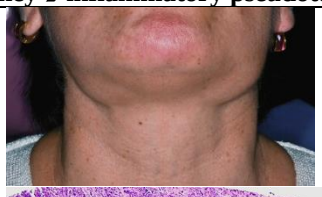
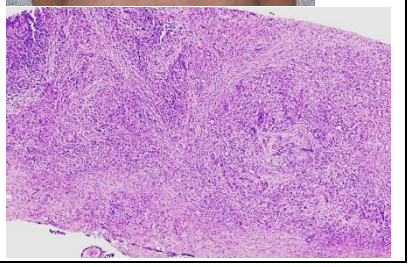
Salivary duct cyst

➲true developmental cyst➔lined by epithelium separate from adjacent normal salivary duct	 
➲major gland➔most➔parotid gland➔slow growth, asymptomatic swelling	
➲intraoral➔most➔mouth floor, buccal, lips	
➲ 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➔actinic damage, tobacco, poor hygiene, heredity	
➲occur➔lower lip vermilion➔hypertrophic & inflamed swelling➔ lower lip eversion(外翻)[albino(白化) patient➔2nd to sun sensitivity]	
➲most➔middle-aged & older men; also women & children(exfoliative cheilitis)	
➲micro➔chronic sialadenitis, ductal dilatation with mucin accumulation, oncocytic ductal metaplasia; dysplastic change➔surface epithelium	
➲3 types➔severity➔❶simple ❷superficial suppurative (Baelz disease) ❸deep suppurative (cheilitis glandularis apostematosa)	

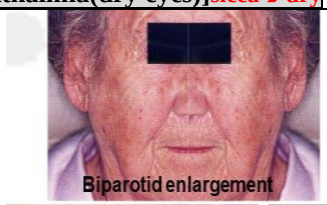
IgG4-related disease

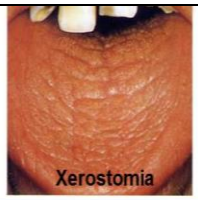
➲1st recognized➔sclerosing inflammation of pancreas(autoimmune pancreatitis)➔↑ serum IgG4➔IgG4(+) plasma cell➔salivary & lacrimal gland		
➲IgG4➔ involved type 2 helper T cell & B cell➔anti-inflammatory(allergic)➔bystander rather than causative		
➲serum IgG4 level➔25× normal level [(N.B.)20-40% patient➔within normal limit(5% of total IgG)]		
➲allergic disorders(asthma, allergic rhinitis, atopic dermatitis)➔common		
➲middle-aged, older adult(mean age➔~60s)	➲men➔affected equally/slight >women(Japan➔female predilection)	
➲1st most➔pancreas➔obstructive jaundice, weight loss, abdominal discomfort	➲ocular➔swollen eyelid, lacrimal inflammation, proptosis(眼球突出), pain, diplopia, optic nerve involved➔visual loss	
➲2nd most➔H&N		
➲ IgG4-related sialadenitis ①submandibular gland(most)➔unilateral /bilateral swelling(1.5-5cm)➔mimic neoplasm ②parotid gland & minor gland(rare)		➲Riedel thyroiditis ➲lymphadenopathy
➲sclerosing cholangitis➔hepatic failure	➲abdominal aoritis➔aneurysm	➲kidney➔inflammatory pseudotumor
➲micro ❶sclerosing sialadenitis➔heavy lymphoplasmacytic infiltrate, hyperplastic lymphoid follicles, acinar atrophy ❷IHC➔↑ IgG4(+) plasma cell(①>30-50/HP) ②(IgG4 (+) plasma cell/total)>40% ❸interlobular fibrosis➔storiform pattern(LP) ❹obliterative phlebitis➔elastic stain➔Kuttner tumor ❺labial biopsy➔minimal invasive➔low sensitivity		 
➲Tx ❶systemic corticosteroid➔prevent significant organ damage & failure ❷glucocorticoid-sparing agent(azathioprine, myophenolate mofetil, methotrexate) ❸immunosuppressive therapy➔rapid response with good prognosis ❹recurrent➔B-cell depletion with rituximab ❺submandibular gland lesion/highly fibrotic orbital pseudotumor➔resection		

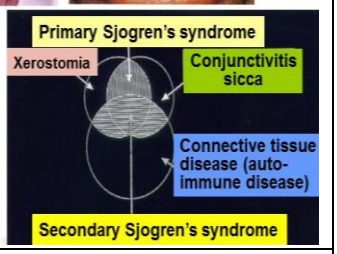
23. The most characteristic oral manifestation of **Sjogren syndrome** is:
(A) xerostoma
(B) geographic tongue
(C) erythema multiforme
(D) acute disseminated reticulosis

Sjogren syndrome[Sicca syndrome➔xerostomia(dry mouth)+xerophthalmia(dry eyes)]sicca➔dry

➲chronic, systemic autoimmune disorder(2nd most; 1st➔ rheumatoid arthritis, RA)➔salivary & lacrimal gland➔ xerostomia & xerophthalmia
➲not hereditary disease *per se*
➲gene➔certain histocompatibility antigen(HLA), interferon response, B-lymphocyte function
➲population prevalence➔1%(0.1-4.8%)
➲ female:male=9:1
➲middle-aged adult➔predominant
➲children➔rare
➲↑severity➔↑salivary enlargement
➲↓ salivary flow➔↑bacterial sialadenitis
➲~15% RA➔Sjögren syndrome
➲30% SLE➔2nd Sjögren syndrome

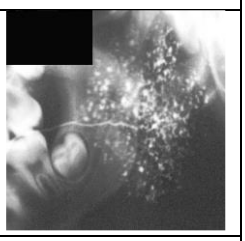






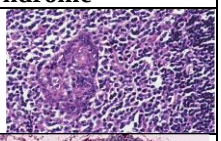
➲ lifetime risk of lymphoma(5-10%)(within salivary gland/lymph node)➔~15–20 ×>general population➔❶low-grade non-Hodgkin B-cell lymphoma of mucosa-associated lymphoid tissue(MALT lymphoma) ❷extranodal marginal zone B-cell lymphoma)

➲sialography➔punctate sialectasia(lack of normal arborization of ductal system)➔fruit-laden, branchless tree(snow storm) pattern
➲scintigraphy➔radioactive technetium-99m pertechnetate➔↓uptake & delayed isotope empty
➲US➔multiple hypoechoic/anechoic area➔parotid & submandibular glands
➲Schirmer test➔無菌濾紙➔lower eyelid margin➔ assess tear➔< 5mm(5min)➔abnormal
➲keratoconjunctivitis sicca➔↓tear+pathologic effect on ocular surface epithelial cell➔blurred vision(aching pain)➔least severe on wakening➔pronounce as daytime

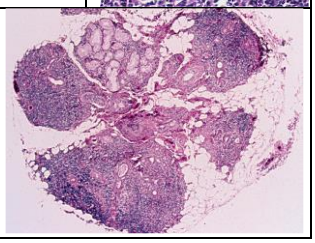


➲lab
❶erythrocyte sedimentation rate➔high ❷serum Ig level(IgG)↑➔high ❸RF factor (+)➔~60%
❹ ANAs➔75-85%[①anti-SS-A(anti-Ro)➔50-76% ②anti-SS-B(anti-La)➔30-60%]➔1^0 Sjögren syndrome

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



➲labial biopsy(minor salivary gland)
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
❺labial biopsy➔也可檢查IgG gene rearrangement➔lymphoma development marker



Sialadenosis(Sialosis)

➲noninflammatory salivary gland enlargement➔parotid gland(particular)

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

➲clinic
❶slow (non)painful bilateral/unilateral parotid swelling
❷submandibular gland(may)
❸minor gland(rare)

➲sialography features
❶ hypertrophic acinar cells compressed finer duct➔leafless tree pattern

➲associate with
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

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

24. 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 ❷heavy-metal poisoning
❸antipsychotic agent➔clozapine, cholinergic agonist(treat Alzheimer dementia & myasthenia gravis)

➲Tx
❶anticholinergic medication➔↓saliva production➔side effect
❷ botulinum toxin➔intraglandular injection➔↓saliva secretions(維持6wk-6m)

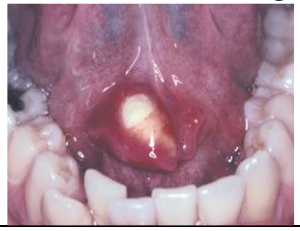
Salivary gland aplasia/hypoplasia

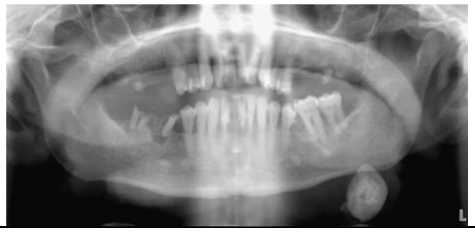
➲M:F ratio=2:1	➲❶pilocarpine ❷sugarless gum/sour candy chewing刺激➔residual salivary gland tissue➔saliva

➲associated with
❶mandibulofacial dysostosis(Treacher Collins syndrome)
❷ectodermal dysplasia
❸oculo-auriculo-dento-digital(LADD) syndrome➔autosomal dominant➔*FGF10* mutation
①lacrimal & salivary gland aplasia/hypoplasia
②cup-shaped ears
③hearing loss
④ hypodontia, microdontia & enamel hypoplasia ④digital anomalies
❹Down syndrome

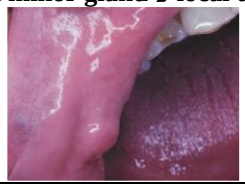
Sialolithiasis

➲most➔submandibular gland➔thicker, mucoid secretion➔Wharton duct



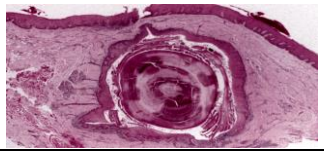


➲minor gland➔local tender swelling



➲micro

❶intraductal concentric calcified mass❷ductal metaplasia



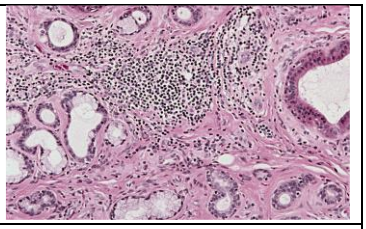
Sialadenitis

➲causes

❶abdominal surgery➔without food/fluids (NPO)+atropine➔acute parotitis (surgical mump)

❷infection➔①bacteria ②virus ③sialolithiasis ④↓saliva flow(xerostomia)

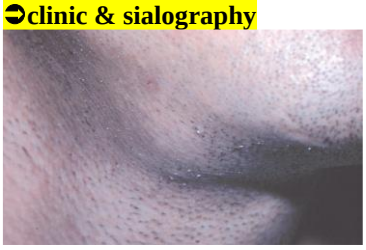
❸noninfectious➔① Sjögren syndrome ②sarcoidosis ③RT ④allergy



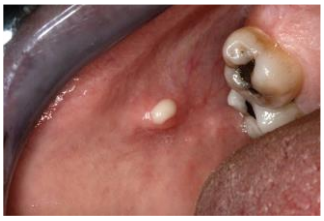
➲micro

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

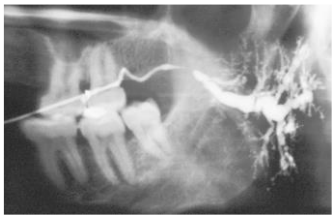
➲clinic & sialography



tender swelling



pus from Stensen duct



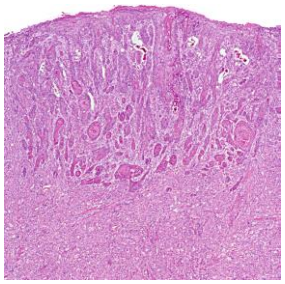
ductal dilatation proximal to obstruction

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

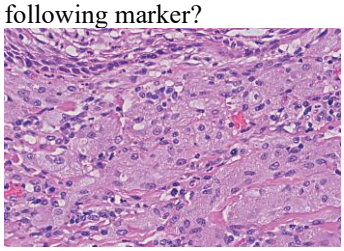
2. Which of the following neoplasms often occurs in the buccal mucosa or vestibule?
   (A) lipoma
   (B) congenital epulis
   (C) lymphangioma
   (D) rhabdomyoma

3. Figure below showing marked **pseudoepitheliomatous hyperplasia** overlying a **granular cell tumor** that may easily be mistaken for which of the following disease?



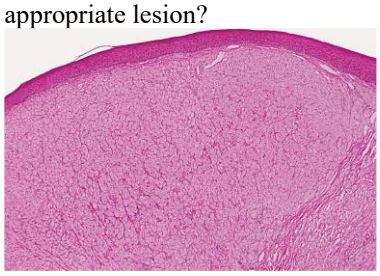
   (A) epithelial hyperplasia
   (B) keratoacanthoma
   (C) congential epulis
   (D) squamous cell carcinoma, grade 1

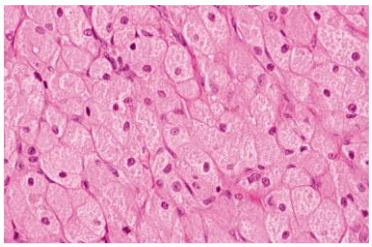
4. Following the question 10 above, the **granular cells** as shown in below figure showing positive staining for which of the following marker?



   (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?



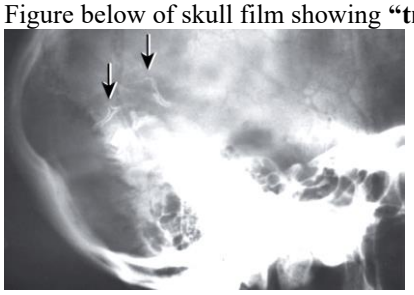


   (A) granular cell tumor
   (B) congential epulis
   (C) hemangilma
   (D) fibroma

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

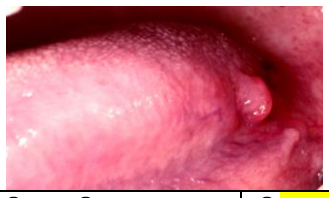
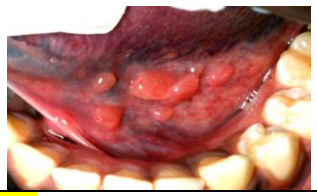
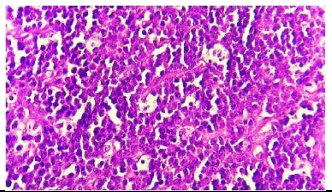
lesion/condition	characteristics
white lesions➔can be scraped off	
white-coated tongue	may be scraped off slightly, with difficulty
pseudomembranous candidiasis	milk curd/cottage cheese appearance; may leave red base when rubbed off
morsicatio	surface may appear to be peeling off
toothpaste or mouthwash 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 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

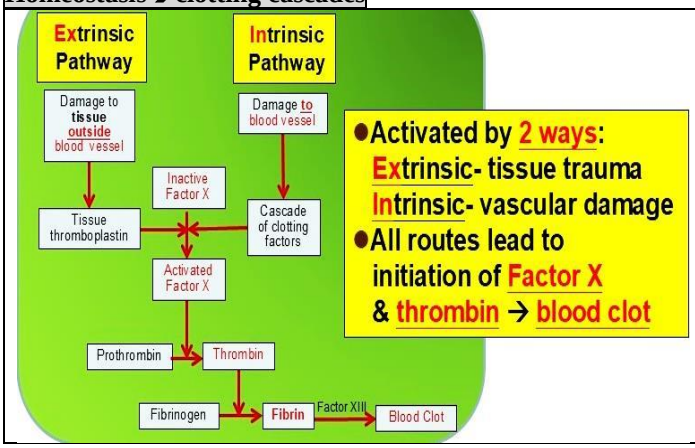
❶acute enlarge LN➔①tender ②soft ③movable	❷chronic enlarge LN➔①nontender ②rubbery firm ③movable

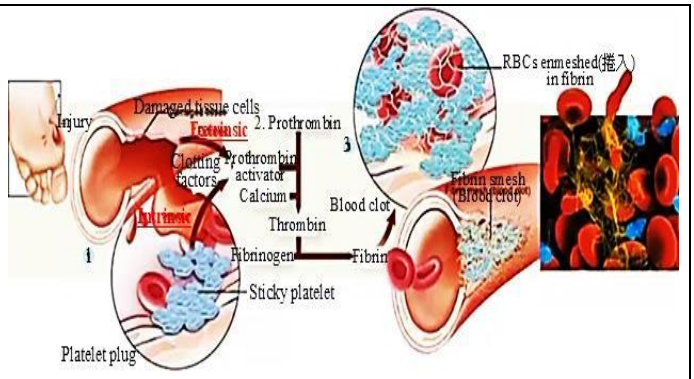
❸LN➔[①multiple ②persistent enlarge ③nontender]➔suspect HIV infection

➲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
❶≥25% normal factor VIII➔function normally
❷<5%➔minor trauma➔bruise

➲Tx guide lines
❶mild(5-40% normal factor VIII)➔no need special Tx for normal activities(IF surgery➔clotting factor replacement therapy)
❷severe(<1% normal level)➔clotting factor injection➔prevent crappie(蹩腳) joint deformities of knee

➲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)

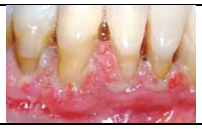
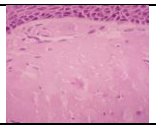
➲autosomal recessive

➲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

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➔①macrocystic 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

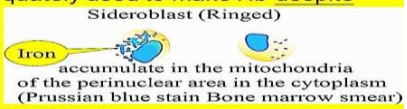
❺mean corpuscular Hb(平均血紅素)(MCH)
MCH=❸Hb含量/❶RBC百萬數=28-34pg➔Hb content

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

❶ANEMIA 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

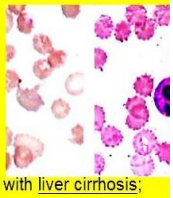


❷MEGALOBLASTIC ANEMIA
①cobalamin(B_{12}) deficiency(pernicious anemia)
②folic acid deficiency

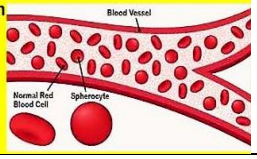
❸HEMOGLOBIN DISORDER
①sickle cell anemia
②thalassemia

❹ANEMIAS 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

❺HEMOLYTIC ANEMIAS
①extrinsic causes
-splenomegaly
-red cell antibodies
-trauma in circulation
-direct toxic effects (microorganisms, Cu salt, snake venom(毒液))



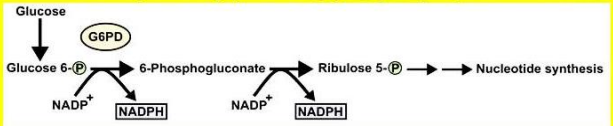
②membrane abnormalities
-spur cell anemia: acquired hemolytic anemia associated with liver cirrhosis; increased large RBC➔covered with spike-like projection
-hereditary spherocytosis
(1)caused by mutations in genes relating to membrane proteins that allow RBC to become sphere-shaped rather than normal 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

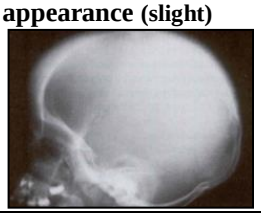
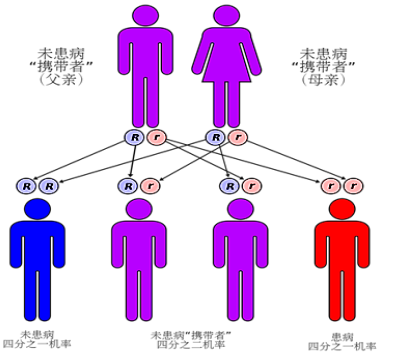
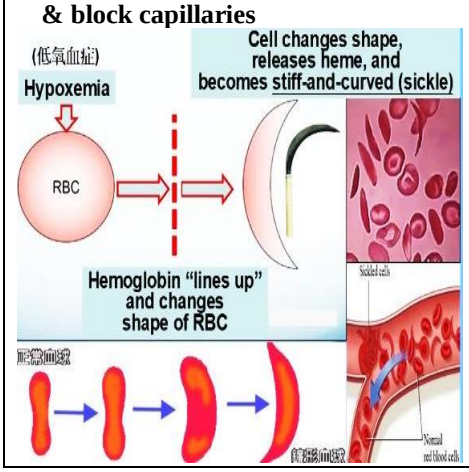
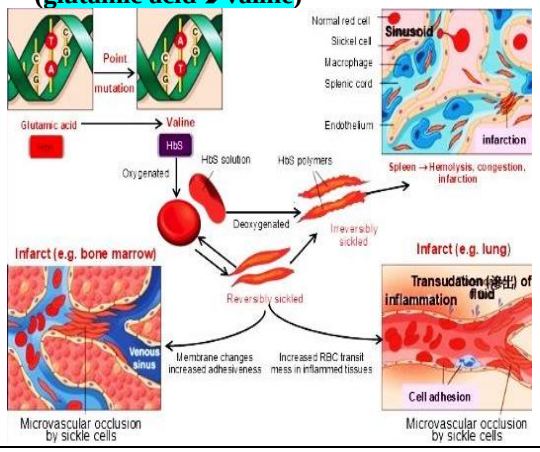


2. Which of the followings are characteristics of **sickle cell anemia**?
(1) large maxilla (2) osteopetrosis (3) thin cortical plate (4) red blood cells are circular
(A) only 1,2
(B) only 1,3
(C) only 2,3
(D) only 1,4

3. 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

4. **Hair-on-end bone pattern of skull** 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 ❷mediterranean South America ❸India➔natural protectve adaptation vs malaria ❹skull X-ray➔hair-on-end appearance (slight) 	➲2 major forms 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)	
➲sickled RBC➔stiff-curved➔fragile & block capillaries 	➲RBC➔point mutation(T:A➔A:T)➔(glutamic acid➔valine) 	➲clinic ❶sickle cell crisis ①dehydration ②stress/strenuous(費勁) exercise ③infection ④fever ⑤bleeding ⑥acidosis ⑦hypoxia(smoking) ❷bone crisis ❸ vaso- 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**

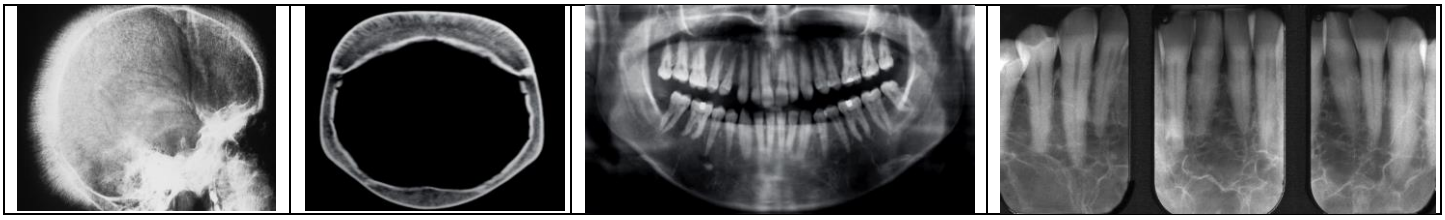
➲Hb➔tetramer(2α+2β chains)➔[❶2 genes encode➔β chain ❷4 genes encode➔α chain]➔one chain with inadequate quantity➔abnormal Hb amount➔excess globin chain in RBC➔abnormal RBC structure & function➔destruction (hemolysis) by spleen➔❶microcytic ❷hypochromic anemia

➲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

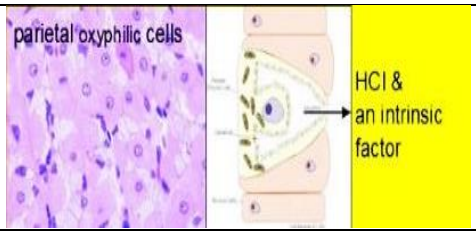
➲radiograph

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 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]



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)

❶/❷➔immune-mediate➔cytotoxic T lymphocyte➔hematopoietic stem cell➔no normal maturation
❶①environment toxin(benzene)
②drug(抗生素chloramphenicol)
③virus感染(non-A, non-B, non-C, non-G hepatitis)
❷associate➔①Fanconi anemia ②dyskeratosis congenita

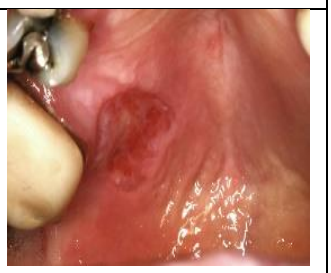
➲oral(右圖)
❶gingiva➔[①hemorrhage ②ulcer ③hyperplasia]
❷oral mucosa➔①petechiae ②purpura[(紫斑)0.3-1cm] ③ecchymoses ④pale

Neutropenia(嗜中性白血球低下)➔↓neutrophil no.➔❶<1.5×10^9/l(adult) ❷[0.5×10^9/l➔pulmonary infection]

➲oral finding➔ulcer(gingiva)(右圖)

➲benign ethnic neutropenia➔低neutrophil no.(1.2×10^9/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➔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(粒性白細胞缺乏症)➔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)

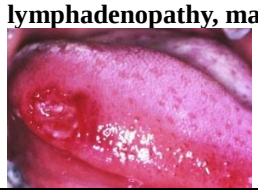
➲clinic
❶bacterial infection(malaise, sore throat, swelling, fever, chill, bone pain, pneumonia, shock)
❷RBC & platelet➔normal/↓slightly
❸oral➔①necrotizing, deep, punched-out ulcer(buccal, tongue, palate)
②necrotizing ulcerative gingivitis(NUG)

Cyclic neutropenia➔regular periodic ↓neutrophil no.

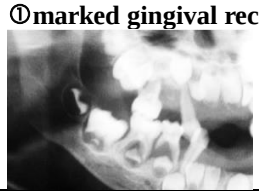
➲cause➔neutrophil elastase(ELA-2/ELANE) gene mutation➔arrested neutrophil develop(promyelocyte stage in marrow)

➲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

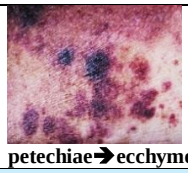
➲thrombocytopenia(血小板減少症)➔platelet no.<150,000/mm^3
❶<50,000➔minor trauma
❷<10,000➔severe bleeding

➲causes➔hypersplenism, autoimmune, hypothermia, viral/bacterial infection➔DIC(disseminated intravascular coagulation), drug-induced, idiopathic

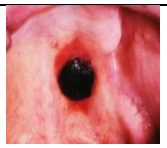
➲↓platelet no.
❶↓production
❷↑destruction➔thrombotic thrombocytopenic purpura(TTP)
➔↓von Willebrand factor-cleaving metalloprotease (ADAMTS13)➔thrombi➔gingiva➔fibrin in small blood vessel

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]

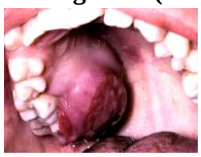
➲myeloid leukemia(differentiate different pathways)➔malignant cell with features
❶granulocyte/monocyte
❷erythrocyte/megakaryocyte(less frequent)

➲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 cells)
②onset rapid & abrupt
③↓survival time

❷classification
①acute lymphoblastic leukemia(ALL)➔least common overall
-children(common)(78%)➔~90% cured if Tx
-adult(much lower 5-yr survival rate)➔remission(80%)
②acute myelogenous leukemia(AML)
-adult(more common)(broader age range, include children)
-5-yr survival rate(40%)
-5-yr survival rate(>60s)➔<10%

➲myelomonocytic type➔oral➔❶diffuse gingival enlargement ❷tumor like growth(ulcer/non-ulcer)



➲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)
-most common type
-survival rate(73%)
-av. survival>10s; advance(2s)
② chronic myeloid leukemia(CML)
-most adult(peak➔3th-4th decades)
-5-year survival(80%)

5. The most common **leukemia of childhood** is:
(A) acute lymphoblastic leukemia
(B) acute myeloid leukemia
(C) chronic lymphocytic leukemia
(D) chronic myeloid 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

7. 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

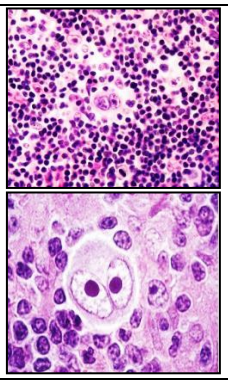
Hodgkin lymphoma(霍奇金氏淋巴癌)

➲neoplastic cell➔Reed-Sternberg(RS) giant cell➔~0.1-2% of cells in enlarged LN | ➲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➔from B-lymphocyte series(85%) | ❷less common➔T-lymphocyte | ❸even rarer➔histiocyte

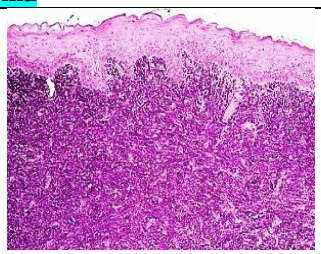
➲EBV-associated lymphoproliferative disorder➔from benign, reactive process through overt malignancies

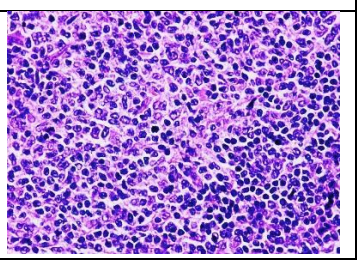
➲HHV-8➔❶Kaposi sarcoma ❷body cavity lymphoma ❸plasmablastic lymphoma

➲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





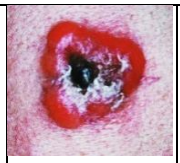
➲micro
❶nodular/follicular
①B-lymphocyte origin ②vague germinal center
❷diffuse
①most➔diffuse large B-cell lymphoma(high grade)(60%)
②destroy normal node architecture
③extranodal➔destroy normal adjacent host tissue

Mycosis fungoides(蕈樣肉芽腫)(Cutaneous T-cell lymphoma) [Dx➔CD4(+)(surface marker of T-helper cell)]

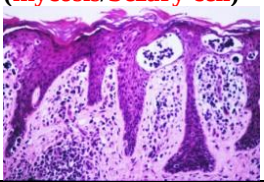
➲derived from T lymphocyte➔T-helper(CD4) cell | ➲most➔cutaneous lymphoma | ➲mean age➔55-60s

➲epidermotropism➔傾向skin epidermis | ➲oral➔infrequent | ➲ M:F=2:1 | ➲middle-aged adult men

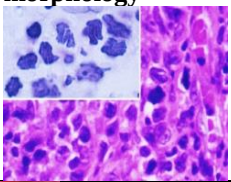
➲clinic➔3-stage
❶eczematous(erythematous)➔well-demarcated, scaly, erythematous patch➔mistaken as psoriasis
❷plaque➔①light elevate ②red
❸tumor➔papule(nodule)(右圖)➔visceral



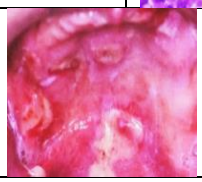
➲micro(plaque stage)➔❶Pautrier microabscess➔atypical lymphocyte (mycosis/Sézary cell)



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

8. 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

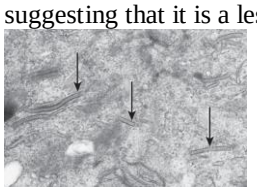
9. Which of the following genetic inhibitor can be used to detect **Langerhans cell histiocytosis**?
(A) *b-raf*
(B) *n-ras*
(C) *k-ras*
(D) *k-raf*

10. 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

11. 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

12. 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

13. 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

14. 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

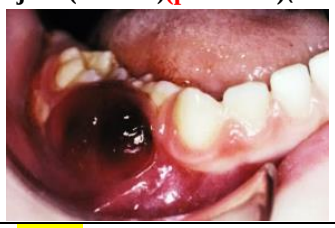
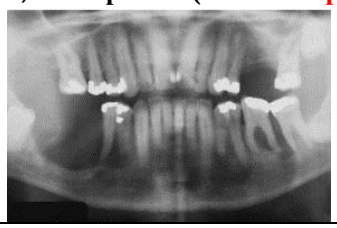
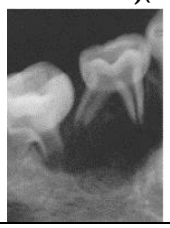
Langerhans cell histiocytosis蘭格罕細胞組織球增生症(LCH)(Histiocytosis X)

LC(histiocyte-like cell)+(eosinophil, lymphocyte, plasma cell, multinucleated giant cell)

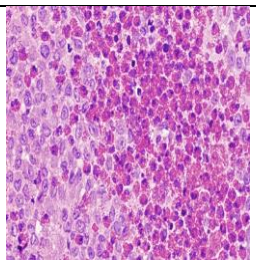
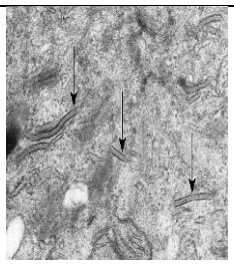
➲<15s(>50%)➔5/million annually	➲adult➔1/million	➲monoclonal proliferation➔neoplastic process
➲LC➔dendritic mononuclear cell➔[❶epidermis ❷mucosa ❸LN ❹bone marrow]➔present antigen to T lymphocyte		
➲BRAF/MAP2K1突變(40-60%)➔[❶early突變➔①more aggressive ②disseminate] [❷later➔①more localize ②benign]		
➲clinic ❶clinicopathologic spectrum ①eosinophilic granuloma of bone➔solitary/multiple bone lesions 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
❶jaws(10-20%)(posterior)(左下圖)➔scooped out(like severe periodontitis)(下中圖)➔teeth float in air(右下圖)

➲micro
❶diffuse infiltration of large, pale-stain mononuclear cell(histiocyte)➔ indistinct cytoplasmic border & rounded/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)(+)

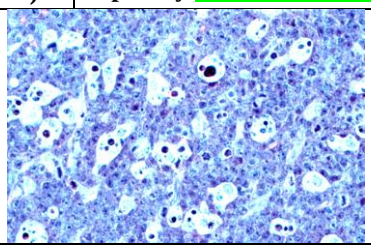
➲Tx
❶accessible bone lesion(maxilla & mandible)➔curettage
❷less accessible bone lesion➔low dose radiation
❸intralesion injection➔corticosteroid agent➔effective in localized bone lesion
❹spontaneous regression of localized lesion(infrequent)
❺bone lesion without visceral involve➔good prognosis
❻≥3 bones➔dissemination 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 develops at very young age ②better➔older at time of onset

15. 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

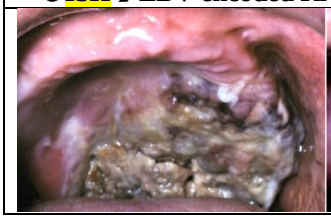
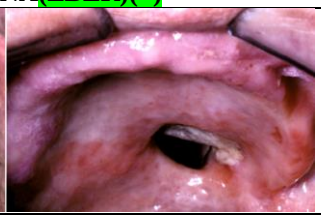
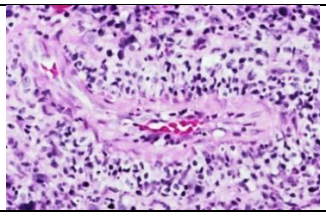
➲micro
❶ Ki-67➔almost 100% labelling index
❷starry[macrophage(histiocyte)➔abundant cytoplasm)]-sky(hyperchromatic neoplastic lymphoid cells)(右圖)
❸similar➔diffuse large B-cell lymphoma
❹t(8;14)(q24;q32) translocation➔oncogene c-myc



Extranodal NK/T-cell lymphoma, nasal-type(angiocentric T-cell lymphoma; midline lethal granuloma

➲mid-palate & nasal fossa destruction➔oronasal fistula(左下圖)	➲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)(+)

16. The cell type involved in **multiple myeloma** is:
(A) lymphocyte
(B) neutrophil
(C) eosinophil
(D) plasma cell

17. Which of the following malignancies is characterized by a **monoclonal spike** on immunoelectrophoresis?
(A) osteosarcoma
(B) squamous cell carcinoma
(C) multiple myeloma
(D) leukemia

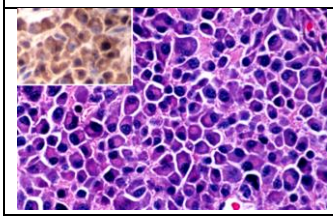
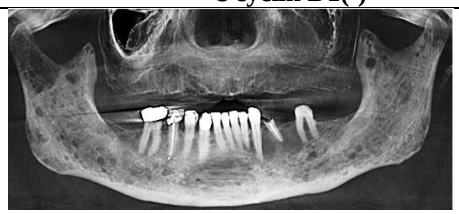
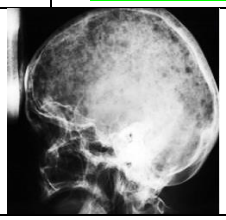
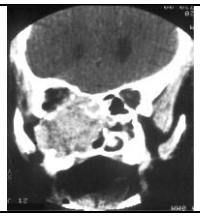
Multiple myeloma多發性骨髓瘤(MM)/Plasmacytoma漿細胞瘤

➲plasma cell malignancy➔derived from B lymphocyte➔monoclonal κ/λ light chains Ig(immunoglobulin)(最左下圖)

➲plasmacytoma➔solitary lesion
- ❶monoclonal(25-50%)➔amount≤MM
- ❷bone marrow biopsy➔no plasma cell infiltration
- ❸no signs of [①anemia ②hypercalcemia ③renal failure]

➲soft tissue➔extramedullary plasmacytoma➔①plasma cell(marked↓)
②CD56(-)
③cyclin D1(-)

➲multiple➔punch out RL(skull)(下圖)
➲50% of all bony malignancy(exclude metastasis)
➲bone pain
➲renal failure➔excess light chain protein of tumor cell
➲Bence-Jones protein(urine, 30-50%)
➲amyloid in soft tissue(tongue, 10-15%)
➲metastatic calcification(soft tissue)

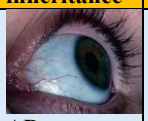





Chapter 14 Bone pathology

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%)

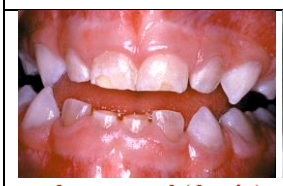
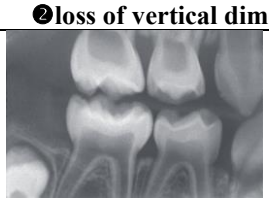
❸sporadic➔可能 | ➲type I collagen(triple helix)➔bone, dentin, sclerae, ligament, skin的主成分

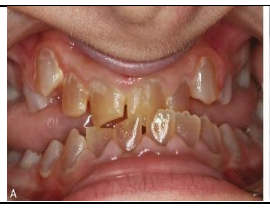
classification	phenotype	inheritance	gene mutated	disease type
OI type 1 (mildest & most common)	mild, nondeforming disease with persistent blue sclerae	 AD	[COL1A1, A2]➔clinic ❶bone fractures(occur when begins to walk➔↓frequency after puberty) ❷no significant bone deformity ❺essentially normal growth	I
OI type 2 (most severe)	severe, perinatal 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	moderate disease, normal 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)

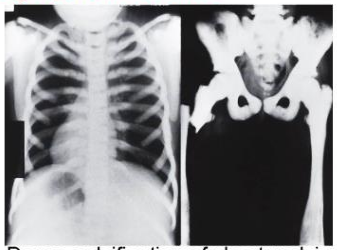
❶autosomal recessive infantile(malignant)(die≤20s)➔at birth/early infancy➔severe & debilitating(虛弱)➔neurologic/hematologic disorders & pathologic fracture

❷autosomal recessive intermediate①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

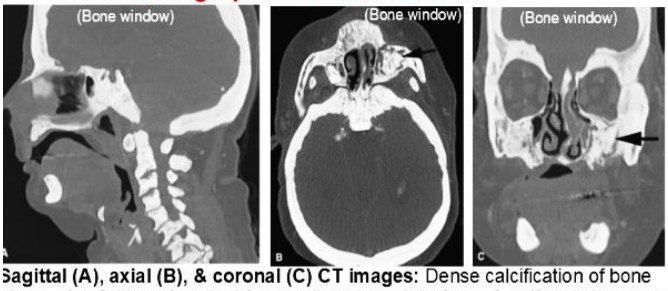
❸autosomal dominant adult(benign)(less severe)➔later in life➔minor trauma➔fracture

General Radiographic Features


Dense calcification of skull & facial bones (jaws enlargement)
類似HYPERPITUITARISM
類似RENAL OSTEODYSTROPHY

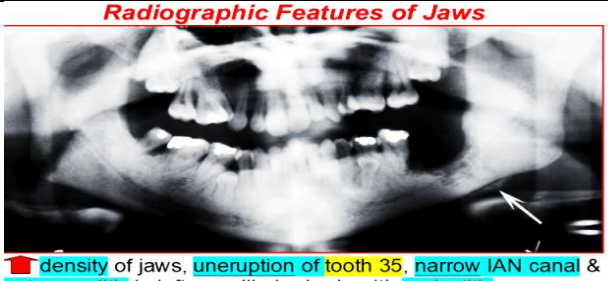

Dense calcification of chest, pelvis & femurs (fracture of proximal right femur)

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)

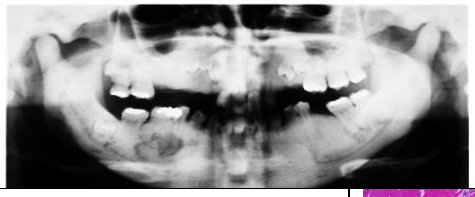
Radiographic Features of Jaws



density of jaws, uneruption of tooth 35, narrow IAN canal & osteomyelitis in left mandibular body with periostitis(arrow)

Radiographic Changes Associated with Teeth

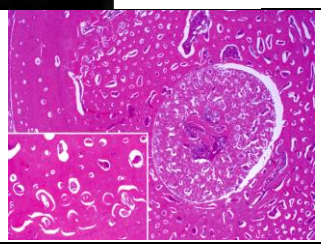
A, Delayed eruption, early tooth loss, missing teeth, malformed root & crown, & teeth that are poorly calcified & prone to caries
B, Bone density ankylosis ➡ delayed eruption of 1° & 2° teeth
C, Lamina dura & cortical border: Thicker than normal



➲**micro**

❶**tortuous lamellar trabeculae replace cancellous bone**
❷**globular amorphous bone deposit➔marrow space(右圖)**
❸**osteophytic bone formation**

❹**osteoclast no.➔[①↑ ②↓ ③正常]➔non-function➔Howship lacuna➔absent/minimal**
❺**osteoclast-rich form➔scant residual hematopoetic marrow➔fibrosis➔↑osteoblast no.**
❻**osteoclast-poor form➔scant residual hematopoetic marrow➔non fibrosis**



1. Which one of the following is *not* a feature of **Paget disease**?
   (A) deposition of amorphous material
   (B) resorption & osteoblastic repair
   (C) chronic metabolic bone disease
   (D) hypercementosis

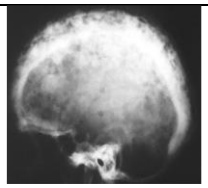
2. Which of the following is helpful in the diagnosis of **Paget disease**?
   (A) immunoelectrophoresis
   (B) serum alkaline phosphatase
   (C) serum calcium
   (D) urinalysis

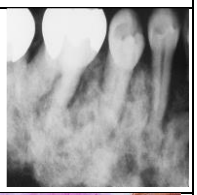
Paget disease of bone(Osteitis deformans)

➲<40s(rare) | ➲**male predilection** | ➲**slow virus infection➔inclusion body➔paramyxovirus(controversial)**

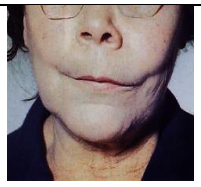
➲**oral complication➔❶unfit假牙 ❷bleeding ❸拔除hypercementosed牙齒➔bone infection**

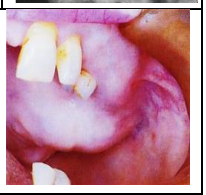
➲**radiograph**
❶**early➔①WD RL(osteoporosis circumscripta)**
②loss of lamina dura
③periapical bone resorption➔like infection
❷**late➔①cotton wool RO**
②hypercementosis





➲**cause**
❶**genetic(40% familial)➔sequestosome 1 gene(SQSTM1; p62) mutation**
❷**environmental factor(8% sporadic)**
➲**jaw(17%)➔maxilla:mandible=2:1**
➲**malignant transformation(1%)➔osteosarcoma**
➲**benign & malignant giant cell tumor➔craniofacial skeleton**

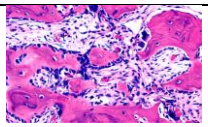




➲**lab➔❶high serum alkaline phosphatase level(700 iu/l) ❷normal blood Ca & P**

➲**limited disease(normal total serum alkaline phosphatase)**
❶**specialized bone formation marker(serum N-terminal propeptide of type 1 collagen)**
❷**resorption marker(urinary N-terminal telopeptide of type 1 collagen)**

➲**micro**
❶**prominent osteoblastic & osteoclastic activity surround bone trabeculae**
❷**resting & reversal line**
❸**benign/malignant giant cell tumor➔facial skeleton**



➲**start➔single bone➔polyostotic(~90%)(common at most 5/6 bones)**

➲**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)**

3. 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

4. The genetic change of **fibrous dysplasia** is associated with the mutation of:
   (A) *G-nas*
   (B) *N-ras*
   (C) *K-ras*
   (D) *B-raf*

5. Which of the following diseases is associated with **café au lait spots**?
   (A) polyostotic fibrous dysplasia
   (B) Paget disease
   (C) monostotic fibrous dysplasia
   (D) periapical cemento-osseous dysplasia

6. 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

7. 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

8. 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

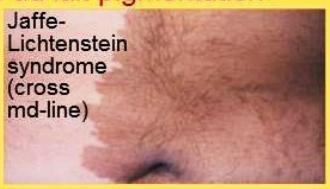
9. Which of the following is characterized by **precocious puberty** in females?
   (A) monostotic fibrous dysplasia
   (B) Jaffe-Lichtenstein-type fibrous dysplasia
   (C) Albright-McCune-type fibrous dysplasia
   (D) focal cemento-osseous dysplasia

Fibro-osseous lesions of jaws

Fibro-osseous lesions of the jaws (NOT include cementoblastoma)
- Fibrous dysplasia
- Cemento-osseous dysplasia
  - Focal cemento-osseous dysplasia, osteosclerosis(idiopathic or periapical)
  - Periapical cemento-osseous dysplasia
  - Florid cemento-osseous dysplasia
- Ossifying fibroma

Fibrous dysplasia (FD)
- *GNAS* mutation (encode α subunit of G protein)
  - → NOT detected in ossifying fibroma or cemento-osseous dysplasia
  - → Occur during early embryonic development (mutation of pluripotent stem cell) → affect osteoblast, melanocytes & endocrine cells
  - → Occur in late stage (mutation of skeletal progenitor) → affect ONLY osteoblast
- Monostotic FD (70-85%; limited to a single bone)
  - → Craniofacial bones, ribs, femur & tibia
  - → Maxilla > mandible (predilection for posterior region)
  - → Maxilla FD → adjacent zygoma, sphenoid, ethmoid, frontal bone, temporal bone occiput → craniofacial FD
  - → Radiographic finding → ground-glass with ill defined borders
  - → Most common clinical finding → painless, unilateral swelling
  - → Mandibular FD → ❶bucco-lingual expansion ❷bulging of inferior border ❸superior IAC displacement; periapical radiograph → ❶PDL narrowing ❷ill-defined lamina dura
  - → Maxillary FD → ❶superior displacement of sinus floor ❷obliteration of antrum ❸extensive skull involvement

➲**Polyostotic FD** (involve 2 or more bones)
➔❶<10-year-old ❷female predilection ❸no. of involved bones: A few to 75% of entire skeleton
➔Affected bones➔fibroblast growth factor 23 (FGF23)➔renal phosphate wasting➔ hypophosphatemia
➔Associate with SYNDROMES
❶**Jaffe-Lichtenstein syndrome**➔①polyostotic FD ②café au lait pigmentation
❷**McCune-Albright syndrome**➔
①polyostotic FD ②café au lait pigmentation;
③multiple endocrinopathies(sexual precocity)
④dental anomalies (tooth displacement, oligodontia, enamel hypoplasia, enamel hypomineralization, **taurodontism** & retained 1^0 teeth)


Jaffe-Lichtenstein syndrome (cross md-line)

❸**Mazabraud syndrome**➔①polyostotic FD ②intramuscular myxomas
➲**Café au lait pigmentation of McCune-Albright syndrome**
➔①Congenital(may) ②well-defined ③tan macule ④unilateral(never cross midline)
⑤affect skin(most common), oral mucosa(possible)

McCune Albright syndrome	Neurofibromatosis (Type 1)
Never cross midline	Cross midline
Irregular borders	Smooth borders
Coast of Maine	Coast of California

➲**Histopathologic features**
➔Curvilinear (Chinese characters) shaped trabeculae of immature (woven) bone in a cellular fibrous stroma
➔Without capsule➔lesion bone fuses with normal bone
➔Osteoblastic rimming absent or minimal
➔ 2^0 aneurysmal bone cyst formation(reported)

10. Which of the following tumors is associated with **von Recklinghausen disease (neurofibromatosis, type 1)**?
(A) neurilemoma
(B) neuroma
(C) fibroma
(D) neurofibroma

11. **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

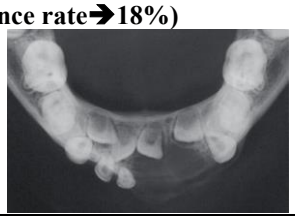
Central giant cell granuloma(CGCG)

➲➔❶[TRPV4 ❷KRAS ❸FGFR1]➔somatic mutation(~70%)➔activate Ras-MAPK路徑

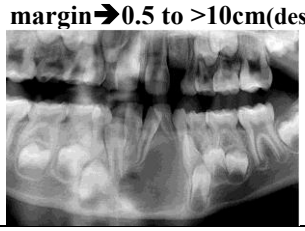
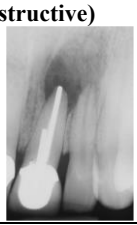
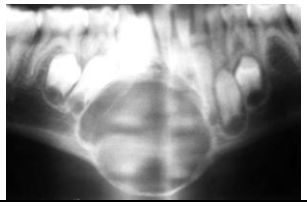
➲long bone nonossifying fibroma & jaw CGCG➔Ras-MAPK路徑➔variant of same entity

➲age(0-86s)➔~70%<30s ｜ ➲女性偏高 ｜ ➲mandible(~70%)➔常過中線➔anterior jaws

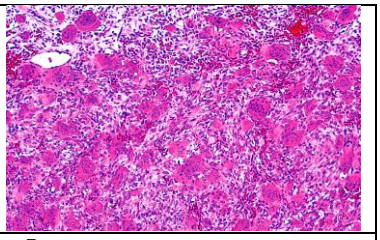
➲2 categories
❶nonaggressive(most)➔①relatively small ②few/no symptoms ③slow growth ④no cortical perforation/root resorption ⑤routine radiograph discover ⑥painless jaw expansion
❷aggressive(下圖)➔①pain ②rapid growth(larger at diagnosis) ③cortical perforation/root resorption ④tooth displacement ⑤paresthesia ⑥extend into soft tissue ⑦overlying mucosa ulcer ⑧younger patient ⑨↑recurrence(recurrence rate➔18%)

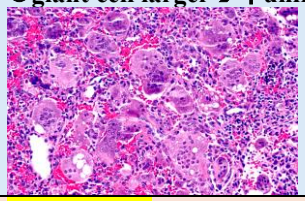
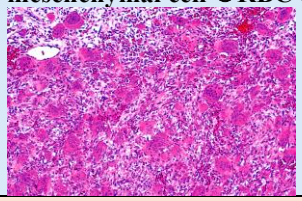
➲radiograph➔WD-UL(small➔like apical granuloma/cyst)/ML-RL(like ameloblastoma)➔without corticated margin➔0.5 to >10cm(destructive)

➲CBCT➔❶bone at periphery➔subtle(細微), granular ❷ML➔wispy(細微) & coarse septa

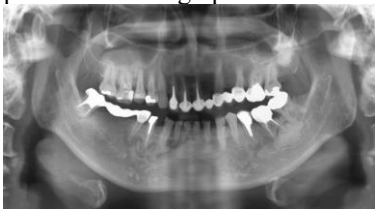
➲micro ❶multinucleated giant cell(few to many)➔[ovoid to spindle-shaped mononuclear stromal cell➔活化RANK/RANKL路徑➔monocyte-macrophage precursor➔分化為osteoclastic giant cell] ❷stroma➔①loose & edematous/cellular ②older lesion➔fibrosis ❸RBC extravasation, hemosiderin ❹focal bone/osteoid	
❺[①↑vascular density ②↑angiogenesis ③↑matrix metalloproteinase(MMP)]➔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)	
➲multi 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
❶不同somatic mutation	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➔較多，較大)	①↑cellular stroma ②↑nuclei no. ③giant cell larger➔↑uniform distributed 	①multinucleated giant cell ②proliferating mesenchymal cell ③RBC extravasation 
❹ biologic behavior	extragnathic(較嚴重)➔①↑aggressive ②↑recurrence rate ③pulmonary meta(benign) ④malignant transformation(~2%)	

12. **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

13. 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

14. 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

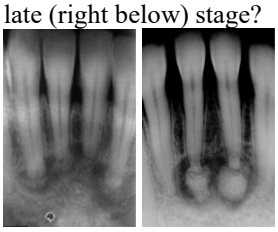
15. Following question 14, what is the most likely clinical diagnosis if the **patient with breast carcinoma having long-term medication of bisphosphonate** having **bilateral ulcerated, painful swellings with pus discharge**?
(A) florid cemento-osseous dysplasia
(B) cemento-ossifying fibroma
(C) medication-related osteonecrosis of jaw
(D) central squamous cell carcinoma

Florid cemento-osseous dysplasia

❶restricted to jaws	❷majority>30s	❸female & black predilection	❹mandible>maxilla
❺early/mild➔symptomless(routine X-ray)		❻advanced➔painless expansion(need consistent prosthesis adjust)	

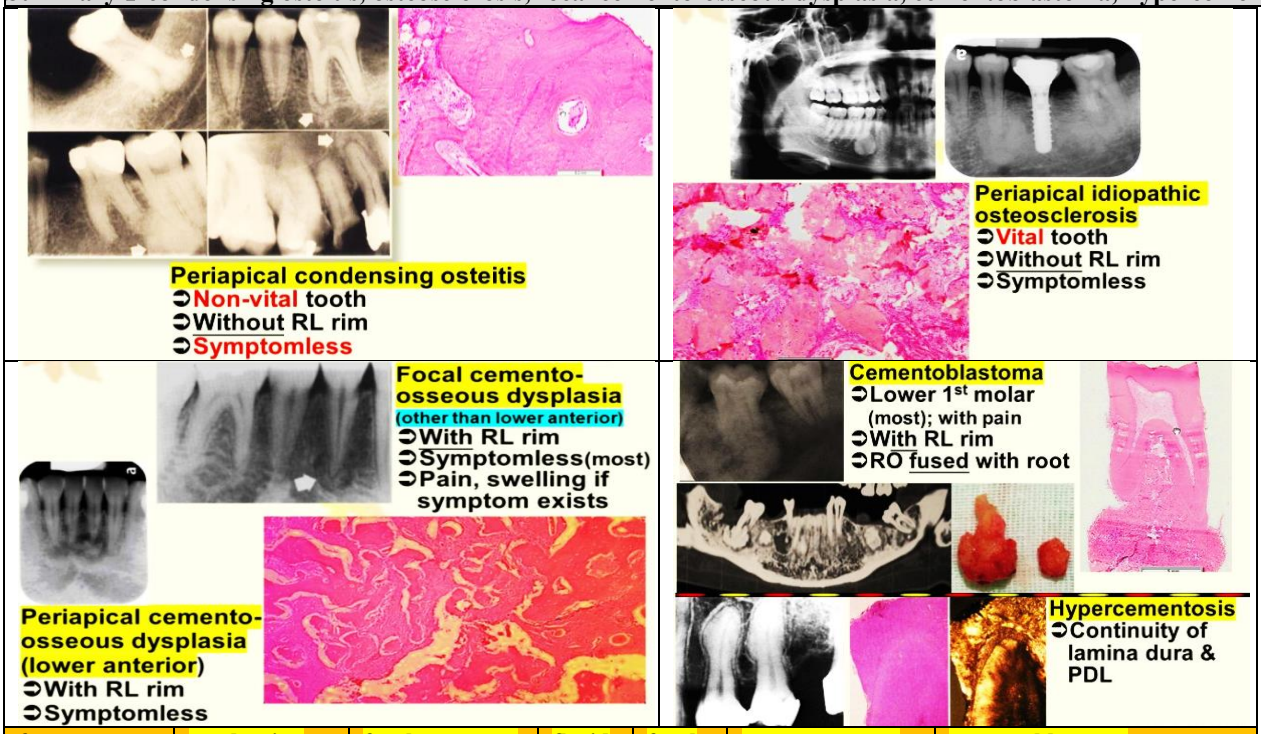
16. **Periapical cemento-osseous dysplasia** is in:
(A) posterior mandible
(B) posterior maxilla
(C) craniofacial bones
(D) anterior mandible

17. What is the disease of the **asymptomatic** patient of the periapical radiographs below suffering from early (left below) and late (right below) stage?



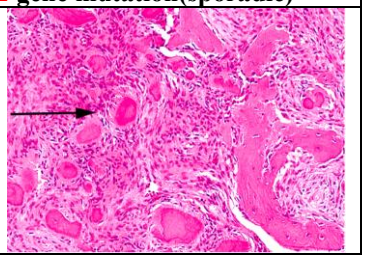
(A) florid cemento-osseous dysplasia
(B) periapical cemento-osseous dysplasia
(C) focal cemento-osseous dysplasia
(D) fibrous dysplasia

Summary➔condensing osteitis, osteosclerosis, focal cemento-osseous dysplasia, cementoblastoma, hypercementosis

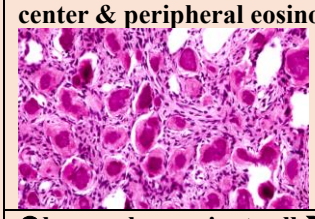
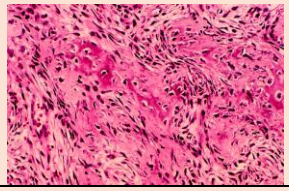


features	condensing osteitis	focal(periapical) osteosclerosis	florid	focal	periapical(單/多)	cementoblastoma	
			COD				
disease type	inflammatory	idiopathic	fibro-osseous lesions			odontogenic tumor	
tooth vitality	non-vital	vital	vital			vital	
RL rim	without	without	with			with (thin)RL rim	
tooth position	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	av 40s	30-50s	20s(1/2)	30s(3/4)

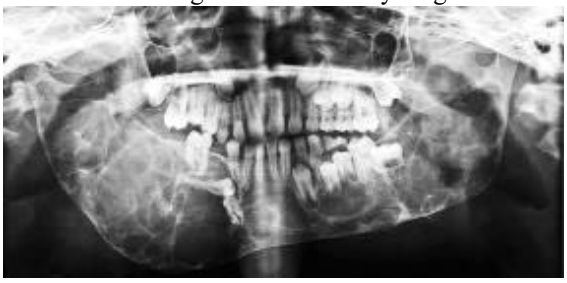
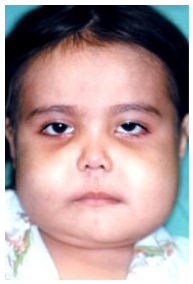
Cemento-ossifying fibroma(true tumor➔osteogenic)

➲clinic➔solitary(most) ❶mandible>maxilla ❷like focal cemento-osseous dysplasia(radiograph & micro) ❸multiple synchronous(rare)➔①isolated ②hyperparathyroidism-jaw tumor syndrome➔[parathyroid adenoma/ carcinoma, jaw ossifying fibroma, renal cyst, Wilms tumor]	➲radiograph ❶UL-RL(small) ❷mixed RL+RO ❸RO ❹ML-RL➔with ABC ➲HRPT2 gene mutation(sporadic)
➲micro ❶most➔①WD(unencapsulated) ②capsule(some) ❷osteoid(woven bone), bone(trabeculae/lamellar), acellular(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 vs COF & craniofacial FD		
➲no GNAS/HRPT2 mutation➔distinct from FD & COF	➲often➔children, adolescents, young adult	
➲comparison between psammomatoid & trabecular		
	psammomatoid	trabecular
age range	broader(3 mon-72s)	narrower(1-33s)
mean age	younger(~12s)	older(~19s)
gender	both slight male/no gender predilection	
favor site	paranasal sinus & orbital	jaws
gnathic involvement	both slight favor maxilla	
craniofacial	more frequent	less frequent
radiography	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	

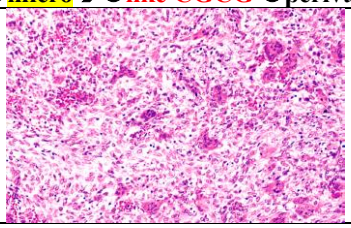
18. A **10–12-year-old** girl is seen in consultation because of **bilateral symmetric painless mandibular expansions (angles, ascending rami & coronoid processes)**. A panoramic radiography is shown as the figure below. The mother of the patient has similar findings. The most likely diagnosis is:

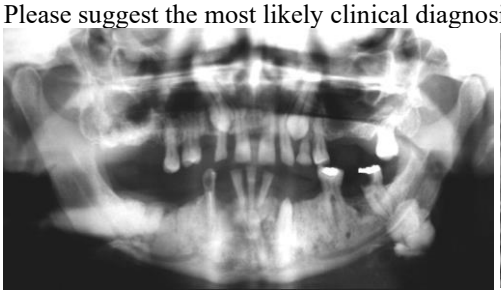
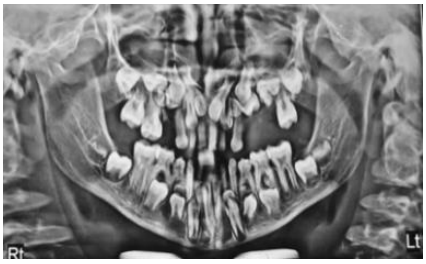
(A) cherubism
(B) cleidocranial dysplasia
(C) nevoid basal cell carcinoma syndrome
(D) Ellis-van Creveld syndrome

Cherubism

➲SH3BP2 gene(chromosome 4p16) mutation➔↑3BP2 adaptor protein stability➔↑signal transduction pathway ➔↑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		
➲maxillary tuberosities/entire maxilla(possible)➔V-shaped palatal arch		
➲rib involvement(reported)	➲bilateral ML-RL(most)	➲UL-RL(less common; may be)
➲serum Ca^{2+} & P^{3-}➔normal	➲↑serum alkaline phosophatase➔active disease	
➲children(bilateral giant cell jaw lesions)➔lab data➔not suggest hyperparathyroidism➔cherubism(most likely)➔others(Ramon syndrome, Jaffe-Campanacci syndrome, RASopathies(Noonan syndrome, neurofibromatosis type 1)		
➲most➔regress spontaneous after puberty➔4th decade➔normal facial feature		
➲micro➔❶like CGCG ❷perivascular eosinophilic cuffing(28%)		
		

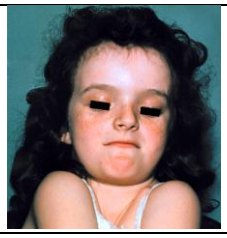
19. Please suggest the most likely clinical diagnosis for the patient of the **right and left panoramic radiography** respectively.

(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

20. 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	
❶extraoral signs➔①frontal bossing ②hypoplastic midface ③prognathic mandible ④quatermoon-physiognomy	
❷intraoral sign➔①erupted 2nd molars ②spacing of lower incisors	
❸panoramic sign➔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 region	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)

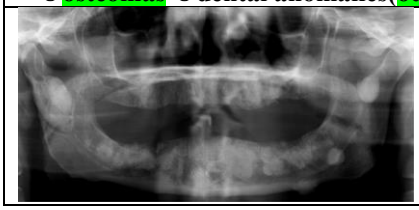
21. Which of the following is the most **serious component** of **Gardner syndrome**?
(A) mandibular odontomas
(B) multiple osteomas
(C) teeth hypercementosis
(D) intestinal polyposis

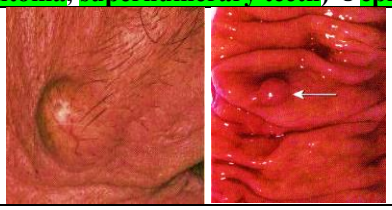
22. Which of the following diseases are most likely having **intestinal polyposis**?
(1) Gardner syndrome (2) cleidocranial dysplasia (3) Addison disease (4) Peutz-Jeghers syndrome
(A) only 1,2
(B) only 2,3
(C) only 2,4
(D) only 1,4

Gardner syndrome

➲frequency➔~1:1,000,000 | ➲autosomal dominant | ➲osteoma precede intestinal polyposis➔10s➔early Dx

➲extracolonic manifestations
❶osteomas ❷dental anomalies(odontoma, supernumerary teeth) ❸epidermoid cysts



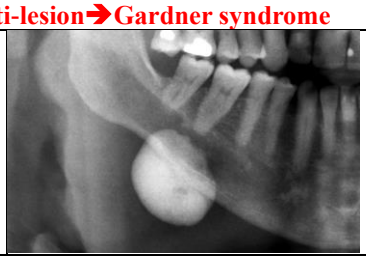


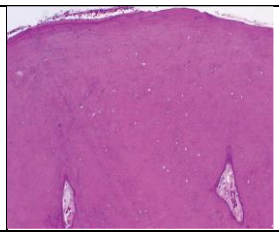
➲familial adenomatous polyposis➔ intestinal adenomatous polyp(hundreds-thousands)➔premalignacy➔~100% colorectal cancer(untreated)

Osteoma➔mature compact/cancellous bone➔1^0 involve craniofacial skeleton

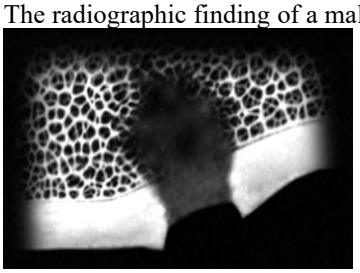
➲paranasal sinus osteoma➔>gnathic lesion | ➲multi-lesion➔Gardner syndrome

➲types
❶bone surface(periosteal, peripheral, exophytic)
❷within medullary bone(endosteal/central)
❸extraskeletal[within muscle/dermis(osteoma cutis)]





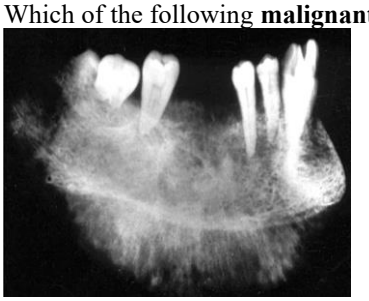
23. The radiographic finding of a malignant neoplasm shown in the **figure below** is so called:



(1) sunray (2) periosteal reaction (3) bony spicules (4) Codman triangle
(A) 1,2
(B) 2,4
(C) 1,3
(D) 1,4

24. 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

25. 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

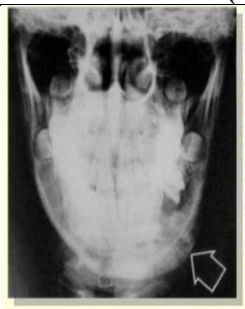
Ewing sarcoma(EW)➔❶2nd most[after osteosarcoma(1st most)] ❷$1^0$ malignant pediatric bone tumor

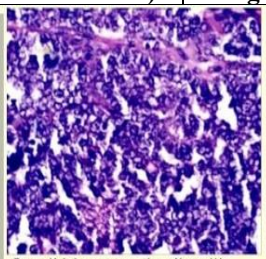
➲EW➔❶classical EW of bone
❷extraosseous EW
❸primitive neuroectodermal tumor(EW with neuronal differentiation)
❹Askin tumor(small round cell tumor of chest wall)➔same tumor type

➲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)]

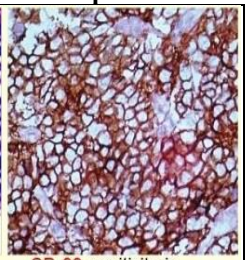
➲Ewing-like sarcoma➔distinct entities
❶undifferentiated small round cell sarcomas of bone & soft tissue➔EWSR1-non-ETS fusion
❷CIC-rearranged sarcoma sarcoma➔BCOR genetic alteration]

➲most➔adolescent(median➔15s) | ➲slight male predominance | ➲majority➔white





Small blue round cells with large nuclei, peripheral ring of cytoplasm & scanty stroma



CD-99 positivity in cytoplasm of tumor cells

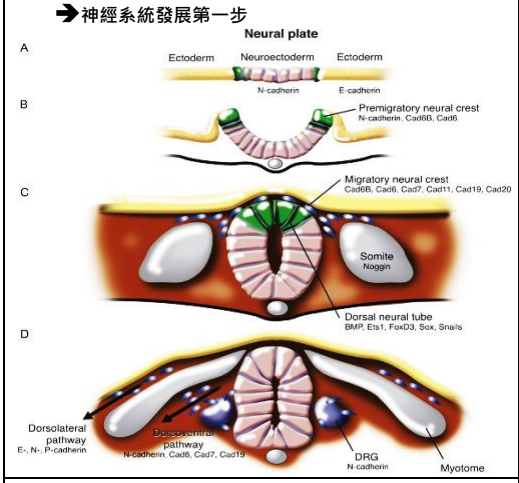
➲radiograph➔onionskin periosteal reaction(❶long bone EW常見 ❷jaw EW少)

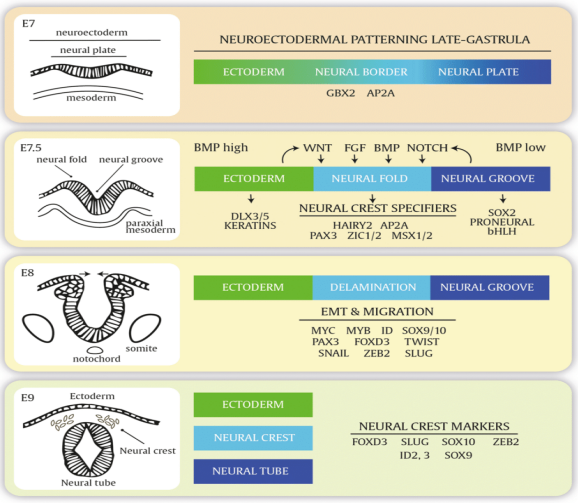
➲micro➔small blue round cell
❶IHC
①CD99(MIC2)➔membrane stain
②NKX2.2➔nuclear stain
❷PAS➔intra-cytoplasmic glycogen

➲most meta➔①lung ②bone

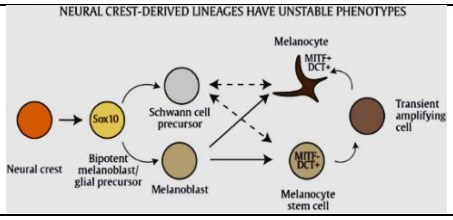
➲extrapulmonary meta➔prognosis worse

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➔central(most)➔medullar cavity[(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 syndrome ④Bloom syndrome ⑤Werner syndrome ⑥Diamond-Blackfan anemia)

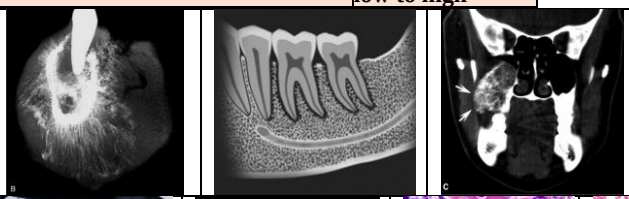
➲genetic profile➔TP53, RB1, MDM2, CDKN2A, ATRX, DLG2

➲extragnathic➔bimodal age distribution ❶major peak(adolescence) ❷lesser peak(adult>60s➔Paget disease of bone/irradiation)

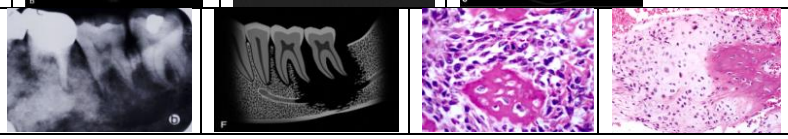
➲gnathic(~6%)➔❶no gender predilection ❷broad age range ❸peak(3rd-5th decade) ❹mean age(~35-41s) [~2 decade>mean age of long bone lesion]

type		grade
central(intramedullary)	conventional ❶osteoblastic ❷chondroblastic ❸fibroblastic	high
	other rare variants (telangiectatic, small cell, epithelioid, giant cell-rich, osteoblastoma-like, chondroblastoma-like)	high
	low-grade central	low
surface(juxtacortical)	parosteal	low
	periosteal	intermediate
	high-grade surface	high
extraskeletal		low to high

➲radiograph➔mixed RL+RO/PD-RL
❶cortical destruction(expansion)
❷periosteal reaction
①sunburst/sunray(~25%➔jaw)
②Codman▲(▲periosteum elevation)
③spiculated new bone



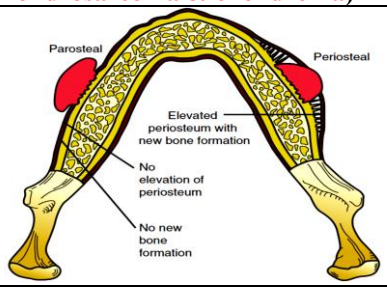
❸spiking root/floating tooth
❹Garrington sign(symmetric PDL widening)➔clue for early diagnosis



➲micro
❶conventional type(>90%)➔①osteoid(右上圖)(osteoblastic) ②chondroid(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➔almost malignant cartilage(foci of osteoid)➔osteosarcoma rather than chondrosarcoma

❻chondroblastic➔lack isocitrate dehydrogenase 1,2(IDH1,2) gene mutation(such mutation➔frequent in chondrosarcoma & chondroma)

➲surface(juxtacortical osteosarcoma)
❶parosteal
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➔sessile mass➔↑periosteal reaction
❸high-grade surface osteosarcoma



26. 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

➲產生3-55s after radiation➔mean latency period➔~4-17s➔post-irradiation bone/soft tissue sarcoma(0.03-0.2%)

➲日本atomic bomb survivor➔↑bone sarcoma➔dose as low as 0.85Gy

➲❶most➔osteosarcoma(49-85%)
❷other➔undifferentiated pleomorphic sarcoma(malignant fibrous histiocytoma), fibrosarcoma, chondrosarcoma

27. 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

28. 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 lesion(20-30%)]

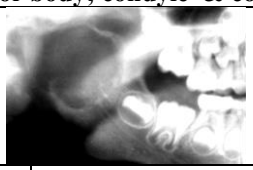
➲pathogenesis➔❶reactive ❷traumatic ❸vascular malformation
❹neoplasm➔disrupt osseous hemodynamic➔ hemorrhage & osteolysis

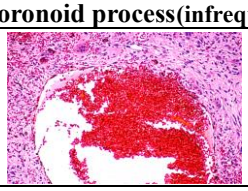
➲cytogenetic➔1^0 ABC➔neoplastic
❶translocation of USP6(ubiquitin-specific protease 6; Tre-2/TRE17)(chromosome 17p13)➔[t(16;17)(q22;p13)]➔ fusion with➔[①cadherin 11(CDH11) ②zinc-finger 9(ZNF9) ③collagen 1A1(COL1A1) ④thyroid receptor-associated protein(TRAP150) ⑤osteomodulin gene(OMD)](few craniofacial lesion)
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 of jaws[(mandible➔ramus & posterior body; condyle & coronoid process(infrequent)]

➲radiograph
❶WD/PD-UL/ML-RL
❷marked cortical expansion & thinning
❸ballooning/blow-out distention
❹small RO foci➔reactive bone trabeculae➔within RL



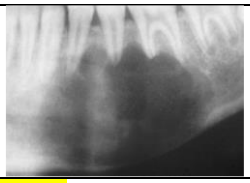
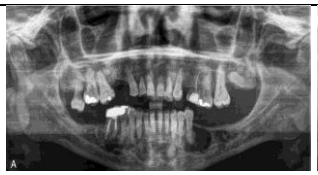
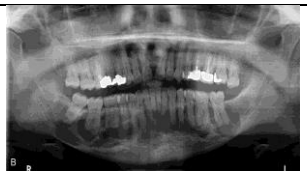


➲micro➔blood-filled space➔no endothelial-epithelial lining
❶fibroblastic/myofibroblastic spindle cell
❷multinucleated giant cell, osteoid, woven bone
❸associate➔COF, FD, CGCG

Simple bone cyst(Traumatic bone cyst)➔no epithelial lining➔pseudocyst

➲empty/fluid-containing bone | ➲subset of extragnathic cases➔FUS::NFATC2/EWSR1::NFATC2 fusion

➲radiograph➔1-10cm
❶scallop between roots of teeth➔ suggestive➔not diagnostic
❷most➔WD-UL RL, PD & ML-RL(possible)
❸most➔solitary(multifocal reported) ❹associate➔cemento-osseous dysplasia (older female)(下圖)

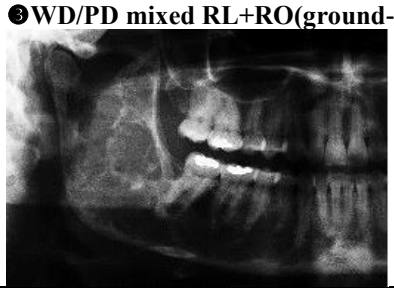




➲clinic
❶mandible predominant➔(pre)molar, symphysis
❷maxilla➔anterior region
❸most➔young patient➔peak➔2nd decade
❹jaw➔no gender bias (extragnathic➔male predilection)

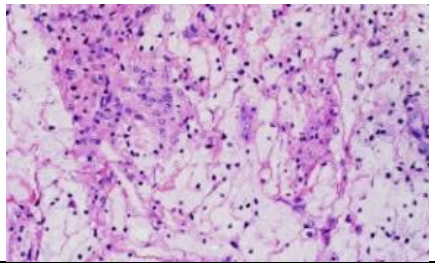
Central xanthoma of jaws➔reactive process/benign neoplasm➔lipid-laden macrophages[xanthoma(foamy)cell]

➲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)

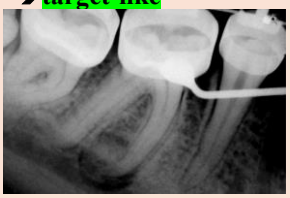
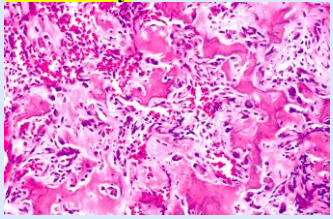


➲micro➔abundant foamy cell
❶IHC➔CD68(+)
❷CD1a(-), CD207(-)➔not Langerhans cell histiocytosis
❸d.d➔①Erdheim-Chester disease ②lipid reticuloendothelioses



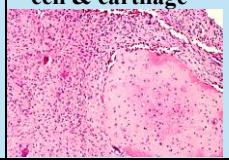
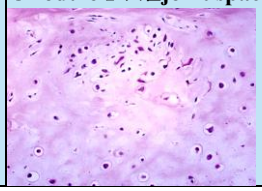
Osteoblastoma(Giant osteoid ostoma) & Osteoid osteoma

➲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

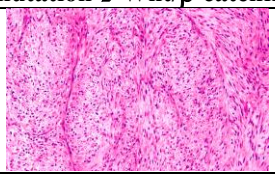
	osteoblastoma	osteoid osteoma
clinic	❶mandible predilection➔posterior ❷ 85%<30s ❸slight female predominance ❹2-4cm➔10cm ❺夜間dull疼痛➔NSAID no舒緩 ❻tender swelling	❶slight mandible➔posterior ❷peak➔2nd-3rd decade ❸no gender predilection(顎外➔male較多) ❹<1.5/2cm ❺夜間dull疼痛➔NSAID舒緩 ❻more limited growth potential
radiograph	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. with 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) ❸CDKN2A 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 ①(osteo)cartilaginous nodule➔synovial lining ②nodule➔①detach➔在joint space ②other➔synovial membrane ③nodule➔只在joint space(loose bodies) 

Desmoplastic fibroma➔jaws➔associate tuberous sclerosis

➲local aggressive ➲<30s ➲ most➔[mandible, femur, pelvis, tibia, radius]
➲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 +)


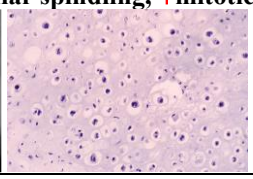
Synopsis➔radiographic pathology

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 RO/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
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 RO	
osteosarcoma	often painful; usu. young adult
intraosseous hemangioma(教課書 5th p. 549)	esp. younger patient
onion-skin RO	
proliferative periostitis	younger patient; often associate with nonvital tooth; best seen with occlusal radiograph
Ewing sarcoma	young children
Langerhans cell histiocytosis	histiocytosis X; usu. Children/young adults

Chondrosarcoma

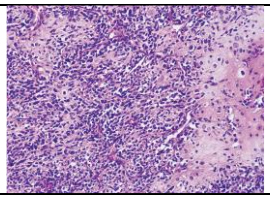
➲frequency➔❶half as osteosarcoma ❷2× as Ewing sarcoma
➲11%➔all 1^0 malignant bone tumor➔jaws rare[(~1-12%)H&N; (0.1%)all H&N malignancies]
➲↑risk➔[❶Ollier disease ❷Maffucci syndrome]➔associate IDH1,2(isocitrate dehydrogenase 1,2) gene mutation (such mutation also frequent in chondroma & chondrosarcoma)
➲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)

❶1ow-grade➔like normal cartilage➔difficult d.d. chondroma
❷↑grade➔↓cartilaginous matrix; [↑cellularity, ↑nuclear size, ↑nuclear pleomorphism, ↑bi/multinucleate chondrocyte, ↑cellular spindling, ↑mitotic activity, ↑necrosis]

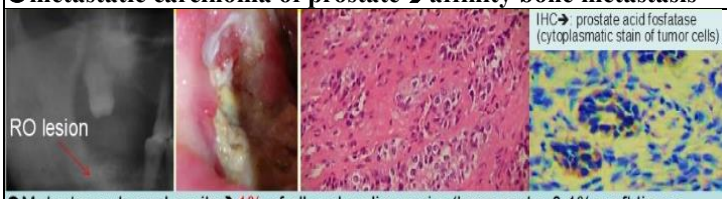
➲variants
❶clear cell➔low-grade➔difficult d.d. metastatic clear cell carcinoma
❷dedifferentiated➔high-grade➔mixture of well-differentiated & high-grade sarcoma
❸myxoid➔soft tissue tumor(intraosseous possible)➔proliferation of clear vacuolated cell/cell with eosinophilic cytoplasm within mucoid material

❹mesenchymal(1-9%)➔high-grade(aggressive)➔2nd-3rd decade➔jaw often(22-27%)
①PD-RL with(out) calcification(maxilla➔predominant RO)
②2 distinct micro elements➔①well-differentiated cartilaginous nodule(chondroma to low-grade) ②undifferentiated small spindle/round cell(like hemangiopericytoma; rhabdomyosarcoma, Ewing sarcoma, lymphoma, metastatic small cell carcinoma)



Metastatic tumors

➲metastatic carcinoma of prostate➔affinity 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
➲25% oral metastases➔first sign of malignance

➲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

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

	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
	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*

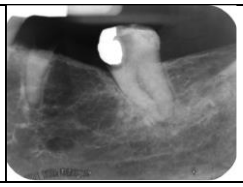
IHC: Immunochemistry
FISH: Fluorescence in situ hybridization

Focal osteoporotic marrow defect➔hematopoietic marrow➔RL➔not pathologic➔confuse with intraosseous neoplasm

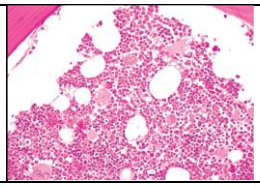
➲pathogenesis
❶aberrant bone regeneration after tooth extraction
❷persistence of fetal marrow
❸marrow hyperplasia due to ↑RBC demand

➲clinic
❶adult female(~75%)
❷posterior mandible(~70%) ❸most➔edentulous area
❹asymptomatic ❺nonexpansile

➲WD-RL with fine central trabeculation



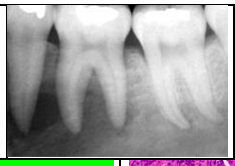
➲cellular hematopoietic &/or fatty marrow



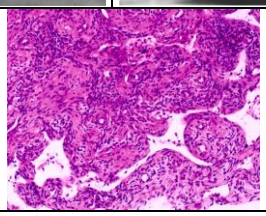
Massive osteolysis(Gorham disease)➔destroyed bone➔replaced by vascular proliferation➔dense fibrous tissue

➲proposed mechanism(no underlying metabolic/endocrine imbalance)
❶trauma-induced➔①proliferation of vascular granulation tissue ②activation of previous silent hamartoma
❷↑osteoclastic activity mediated by IL-6
❸lymphangiogenesis mediated by VEGF & PDGF(platelet-derived GF)
❹agenesis/dysfunction of thyroid C cell
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➔loss of lamina dura & thinning of cortex ➔bone loss



➲micro➔early➔vascular proliferation{❶blood vessel &/or ❷ [lymphatic vessel D2-40(+)] predominate} intermixed with fibrous tissue & chronic inflammatory cell



Chapter 15 Odontogenic tumors

Calcifying odontogenic tumor(Pindborg tumor)➔PTCH1 gene➔mutation

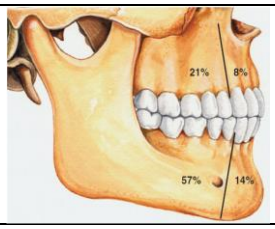
➲arises from dental lamina ➲most➔posterior mandible

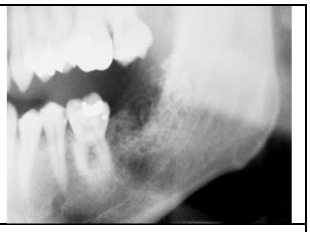
➲most common sign➔painless, slow-growing swelling

➲UL(maxilla more)/MLRL➔calcification(driven-snow pattern)(some)

➲peripheral(extraosseous) counterpart(sessile gingival mass, anterior)

➲(rare)malignant with metastasis to regional lymph nodes & lung





➲micro

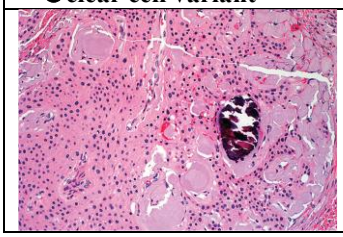
❶amorphous, eosinophilic, hyalinized(amyloid-like) extracellular material

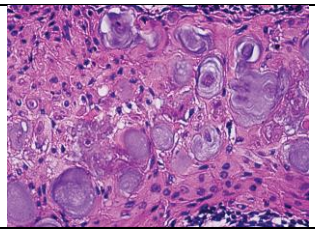
❷calcification(develop within amyloid)

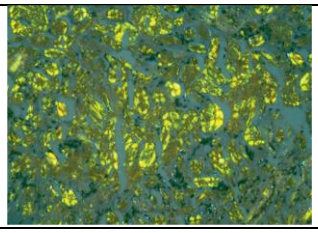
❸concentric Liesegang ring calcifications

❹Congo red staining➔amyloid➔apple-green birefringence with polarized light

❺clear cell variant



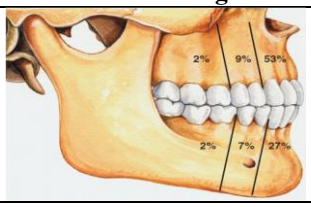




1. The odontogenic tumor that characteristically appears as a well-circumscribed radiolucency located in anterior maxilla of an adolescent girl is:
   (A) ameloblastic fibro-odontoma
   (B) adenomatoid odontogenic tumor
   (C) peripheral ossifying fibroma
   (D) odontogenic myxoma

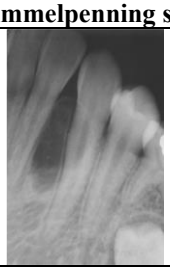
Adenomatoid odontogenic tumor➔2-7% of all odontogenic tumors

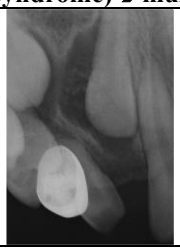
➲histogenesis
❶enamel organ epithelium
❷reduced enamel epithelium
❸rests of Malassez
❹remnant of dental lamina associates gubernacular cord



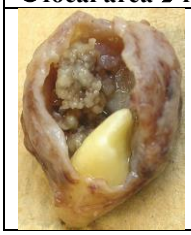
➲clinic➔2/3 patient➔10-19s
❶>30s➔uncommon
❷common➔anterior jaws
❸maxilla:mandible=2:1 ❹female:male=2:1
❺seldom>3cm
❻extraosseous(rare)➔maxilla(facial gingiva

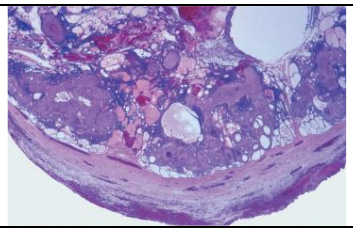
➲radiograph
❶UL-RL➔unerupted tooth crown(canine)
❷follicular type(like dentigerous cyst)➔d.d. as RL extends apical along root past CE junction
❸extrafollicular type(less common)➔not relate to unerupted tooth➔between roots of erupted teeth
❹nevus sebaceus syndrome(Schimmelpenning syndrome)➔multiple AOTs associate impacted teeth

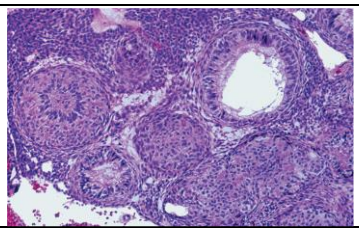




➲micro➔spindle-shaped epithelial cell➔sheet, strand, whorled➔scant stroma
❶epithelial cell➔rosette about a central space➔empty/small amount eosinophilic material➔stain for amyloid
❷tubular/ductlike structure(not true duct➔no glandular element)➔central space surrounded by layer of columnar/cuboidal epithelial cell
❸small foci of calcification➔abortive enamel formation
❹larger calcification➔dentinoid/cementum
❺focal area➔resemble COET/COT







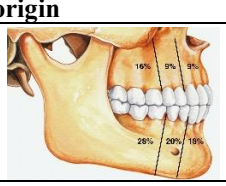
2. Which odontogenic tumor most closely resembles the **mesenchyme of dental follicle**?
(A) cementoblastoma
(B) odontogenic myxoma
(C) compound odontoma
(D) ameloblastoma

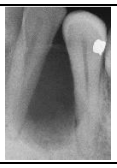
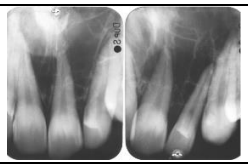
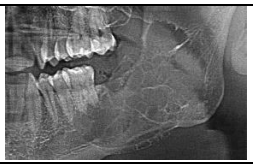
Odontogenic myxoma

➲**arise from odontogenic ectomesenchyme➔like mesenchymal portion of developing tooth**

➲**myxoma of jaws➔odontogenic origin**

➲**clinic**
❶**young adult predominant**
❷**average age➔25-30s**
❸**slight female sex predilection**
❹**mandible>maxilla**

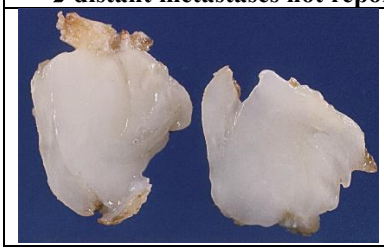
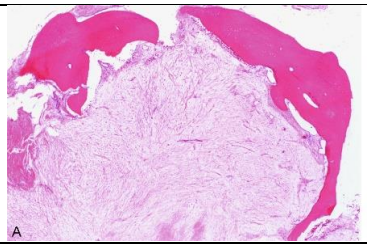


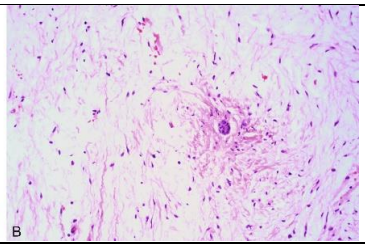




➲**radiograph➔UL/ML RL(displace/teeth resorption)➔wispy trabeculae➔at right angle to one another**
❶**large lesion➔soap bubble RL➔indistinguish from ameloblastoma➔sun-burst(ray)➔like osteosarcoma**

➲**micro(gross➔gelatinous, loose structure)**
❶**haphazard arranged stellate, spindle-shaped, round cell➔abundant, loose myxoid stroma➔a few collagen fibril**
❷**histochemical➔ground substance➔glycosaminoglycan➔hyaluronic acid & chondroitin sulfate**
❸**IHC➔①vimentin(+) ②muscle-specific actin(+)**
❹**inactive odontogenic epithelial rest➔scattered in myxoid ground substance**
❺**cementum-like calcification(rare)**

➲**fibromyxoma/myxofibroma/chondromyxoid fibroma/myxoid neurofibroma**
➲**myxoid change in an 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)➔marked cellularity & cellular atypia➔death(vital structure)**
➔distant metastases not reported

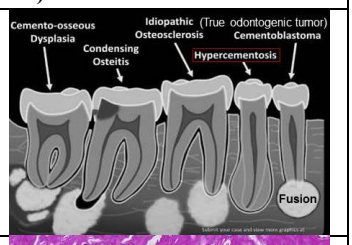


3. Which one of the following best describes **cementoblastoma**? It is a:
(A) well-circumscribed radiopaque lesion with a radiolucent halo fused to root of a vital tooth
(B) radiolucent multilocular lesion
(C) radiolucent lesion surrounding the crown of an impacted tooth
(D) lesion composed of numerous toothlike structures

Cementoblastoma(True cementoma)

➲**下顎(近80%)➔(小)大臼齒➔下顎恆牙第一大臼齒(近半)➔阻生, unerupt,乳牙(rare)➔EPT(+)/(-, 20%)**

➲ **pain & swelling(~70%)** | ➲ **no sex predilection** | ➲**mean size➔~2cm(0.5-8cm)**



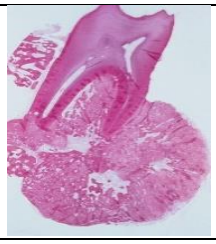
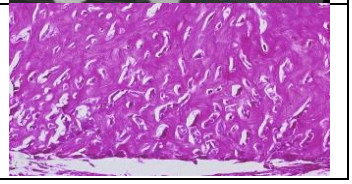
➲**主要在年輕人➔average 24s➔peak➔2nd-3rd decade**

➲**fused to tooth root➔distinguish osteoblastoma**

➲**bony expansion/cortical perforation➔↑recurrent(~12%)**

➲**infiltrate pulp chamber & root canal(may)**

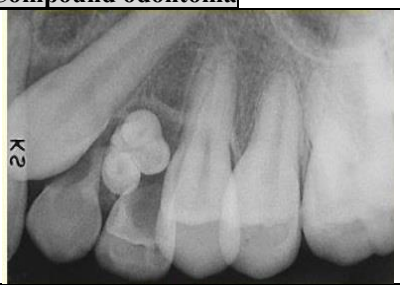
➲**micro➔resemblance osteoblastoma**
❶**mineralized trabeculae**
①**lacunae & basophilic reversal line**
②**multinucleated giant cell & prominent blast-like cell(周邊)**
③**stroma➔cellular fibrovascular tissue**
❷**radiating uncalcified matrix(周邊)➔RL rim**

4. **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

5. **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 located in the posterior mandible

Compound odontoma



- Odontomas➔Most common odontogenic tumors (prevalence >all other odontogenic tumors combined)
- Odontomas➔Frequency in maxilla > mandible
- **Compound type➔**More in anterior maxilla
- **Complex type➔**More in molar regions of either jaw
- Odontoma➔develop within gingival soft tissues(may)
- Radiographic findings Diagnostic
- **Compound type➔**Seldom confused with other lesion(toothlike structures of varying size & shape surrounded by a radiolucent zone)
- **Complex type➔**A calcified mass

Ameloblastoma➔BRAF p.V600E mutation(80%)➔MAP K kinase pathway

➲frequency=frequency of all other odontogenic tumors(exclude odontoma)➔most common odontogenic tumor
❶conventional solid/multicystic(~75-86%)
❷unicystic(~13-21%)➔ameloblastic-like cells➔①luminal ②intraluminal ③mural(tumor cell infiltrate cyst wall)
❸peripheral (extraosseous)(~1-4%)

➲whether unicystic ameloblastoma can have a truly ML➔arguable(值得商榷)

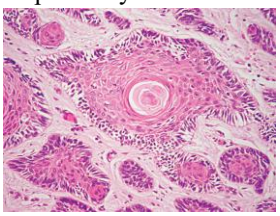
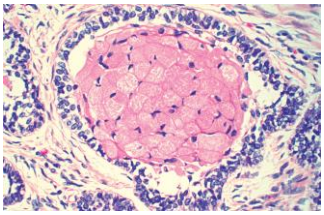
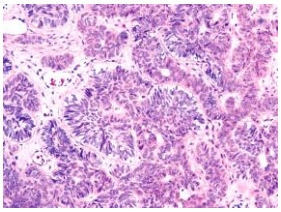
➲micro➔conventional solid(multicystic intraosseous)
❶ameloblastic-like cell(nuclei➔reverse polarity)➔①follicular(cyst formation) ②plexiform(stroma degeneration) ➔①,②most common
❷satellate reticulum like cell➔①acanthomatous(squamous metaplasia) ②granular cell ③basal cell
❸stroma➔desmoplasia
❹cystic degeneration➔central zone(satellate-like reticulum like cell area)

6. 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

7. 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

8. 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

9. What is the most possible histopathological diagnosis of the patient with intrabony biopsy as shown in the figures below respectively?

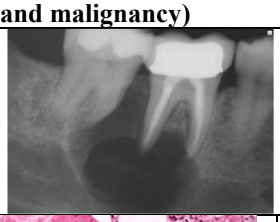
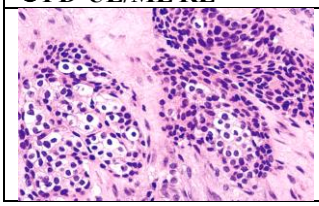
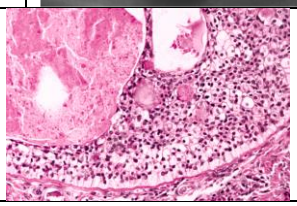
(1) ameloblastoma, plexiform (2) ameloblastoma, follicular (3) acanthomatous (4) granular cell (5) basal cell
(A) right: 1,3; middle: 2,4; left: 1,5
(B) right: 2,5; middle: 1,4; left: 2,3
(C) right: 1,3; middle: 2,4; left: 1,5
(D) right: 2,3; middle: 2,4; left: 1,5

10. 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

11. 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

12. 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

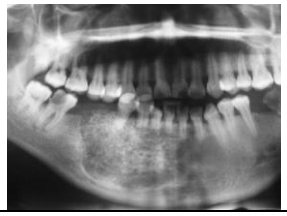
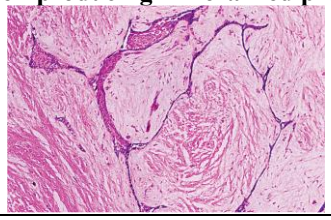
Clear cell odontogenic carcinoma➔EWSR1 gene translocation(fuse with ATF1 gene)➔also often in hyalinizing clear cell carcinoma(a rare salivary gland malignancy)

➲clinic **❶65%➔female** **❷slight>80%➔mandible** **❸pain/lower lip paresthesia** **❹80%➔ bony swelling** **❺PD-UL/ML RL**		**➲micro➔3 patterns** **❶biphasic➔clear/faint eosinophilic cytoplasm + eosinophilic polygonal epithelial cell** **❷ monophasic➔only clear cell➔nest & cord** **❸like ameloblastoma➔palisading clear cell island**
		**❹nuclear/cytologic pleomorphism➔not significant** **❺mitoses➔sparse** **❻necrosis➔not prominent** **❼clear cell➔small amount glycogen➔mucin stain(-)**

13. **Peripheral odontogenic tumors** are located on:
(A) palate
(B) gingiva
(C) lower lip
(D) buccal mucosa

14. 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

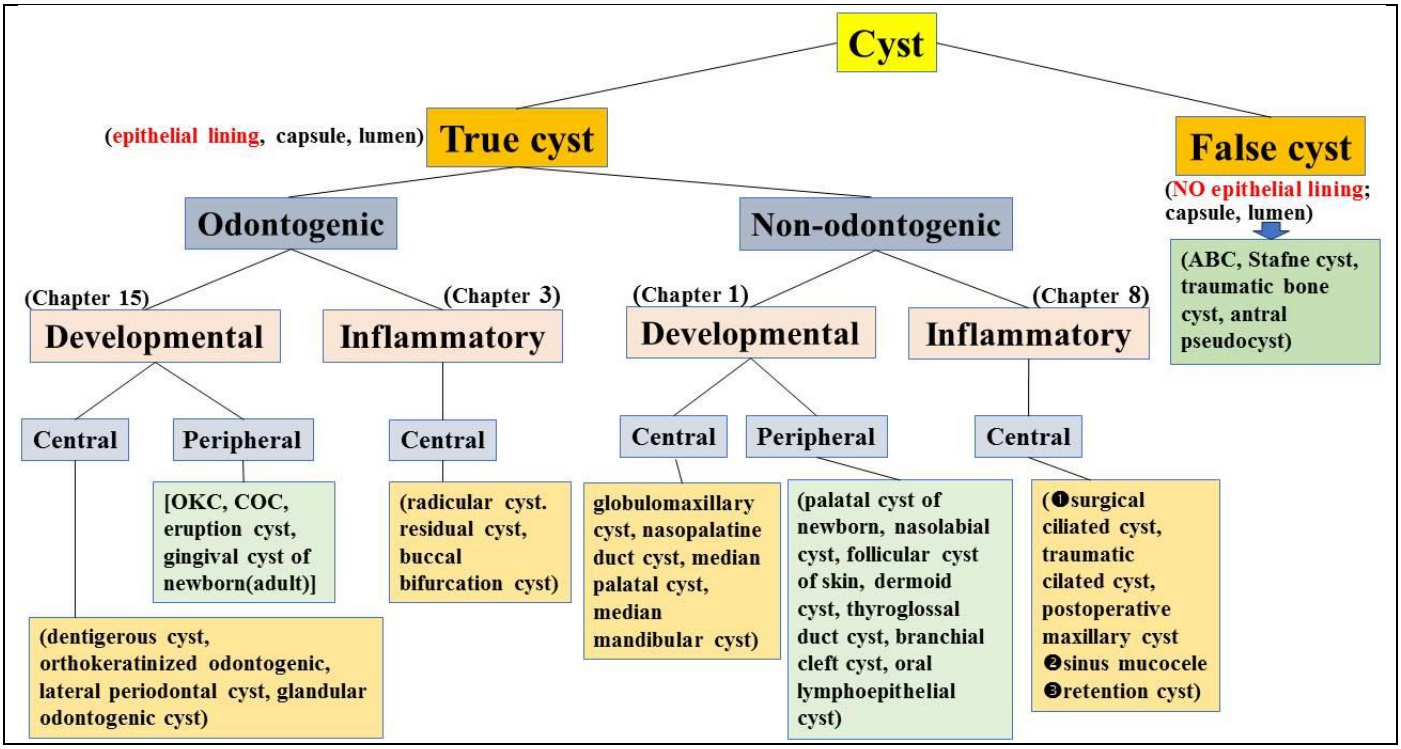
Desmoplastic ameloblastoma

➲predilection in anterior region of the jaws	**➲mandible:maxilla=1:1**
➲IHC➔↑ TGF-β in association with the lesion➔responsible for desmoplasia	
➲radiograph➔resemble fibro-osseous lesion➔mixed RL & RO(osseous metaplasia within dense fibrous septa) ➔NOT because tumor itself producing mineralized product  	

Chapter 15 Odontogenic cysts

➲classification

❶developmental(#➔also with soft tissue counterpart; ✶soft tissue cyst) ①dentigerous cyst ②eruption cyst ③odontogenic keratocyst(OKC)# ④orthokeratinized odontogenic cyst ⑤gingival(alveolar) cyst of newborn* ⑥gingival cyst of the adult(counterpart of ⑦)* ⑦lateral periodontal cyst ⑧calcifying odontogenic cyst(COC)# ⑨glandular odontogenic cyst	❷Inflammatory ①periapical(radicular) cyst ②residual cyst ③buccal bifurcation cyst



15. 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

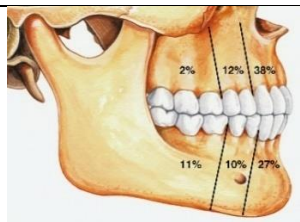
(C) 好發於臼齒區，尤其是阻生齒

(D) 一般需以骨切除手術(resection)治療

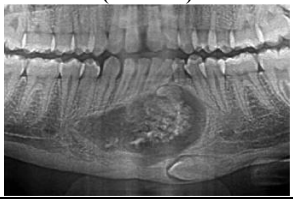
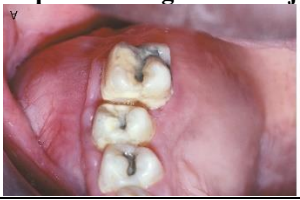
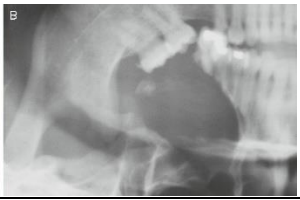
Calcifying odontogenic cyst(Gorlin cyst; Calcifying cystic odontogenic tumor)

➲**2022 WHO classification**➔ghost cell lesion➔3-type➔❶cystic ❷solid ❸malignant nature➔
❶calcifying odontogenic cyst ❷dentinogenic ghost cell tumor ❸ghost cell odontogenic carcinoma

➲COC➔ *CTNNB1*mutation➔encode β-catenin➔similar mutation➔dentinogenic ghost cell tumor & ghost cell odontogenic carcinoma

➲clinic➔frequency(maxilla=mandible) ❶ incisor& 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 as aggressive as intraosseous counterpart

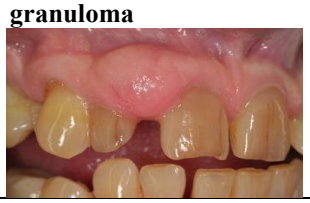
➲radiography(2-4cm➔12cm)➔WD-UL with RO(1/3-1/2 case)➔calcification/toothlike(1/3 case, unerupt canine)/ WD-ML(occasion)➔root resorption/divergence of adjacent teeth

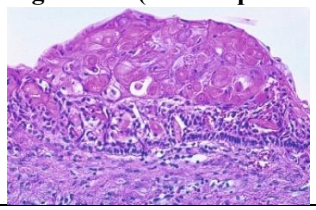
➲**intraosseous dentinogenic ghost cell tumor➔most 3rd-5th decades➔ posterior both jaws➔more aggressive➔root resorption, cortical plate perforation, sinus destruction**

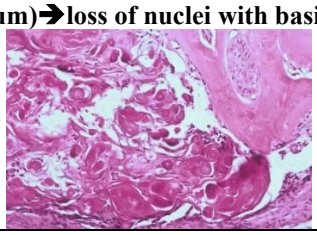
➲**ghost cell odontogenic carcinoma(maxilla>mandible)➔aggressive➔*de novo*/malignant change from COC/ dentinogenic ghost cell tumor**

➲**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 cells in thickness)**
❶**basal cells of epithelial lining(cuboid/columnar)➔like ameloblasts**
❷**epithelium➔stellate reticulum of ameloblastoma**
❸**ghost cell(within epithelium)➔loss of nuclei with basic cell outline**





➲**ghost cell➔❶coagulative necrosis/enamel protein accumulation ❷a form of normal/aberrant keratinization of odontogenic epithelium ❸fuse to form large sheet of amorphous, acellular material ❹calcification➔fine basophilic granules➔extensive mass of calcified material ❺areas of eosinophilic matrix➔dysplastic dentin(dentinoid) adjacent to epithelium➔an 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

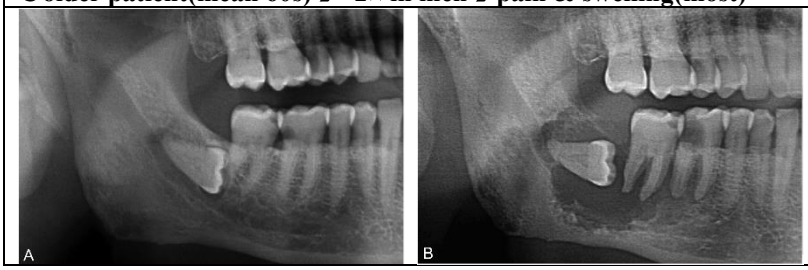
➲**solid dentinogenic ghost cell tumor[intraosseous/extraosseous(more)]➔nests of ghost cells & juxtaepithelial dentinoid➔d.d. from peripheral ameloblastoma**

➲**ghost cell odontogenic carcinoma(solid)➔cellular pleomorphism, ↑mitotic activity, necrosis, invade surround tissue**

Carcinoma arising in odontogenic cysts

➲**odontogenic carcinoma**
❶**de novo(no preexist lesion)➔ameloblastoma(rare from other odontogenic tumors)**
❷**arise from epithelial lining of odontogenic cyst➔(central MEC➔arise from mucous cell lining of dentigerous cyst)**
①from residual periapical cyst(60%)
②from dentigerous cyst(16%)
③from lateral periodontal cyst(one case)
④from orthokeratinized odontogenic cyst
⑤from OKC

➲**older patient(mean 60s)➔>2× in men➔pain & swelling(most)**



Chapter 16 Dermatologic diseases

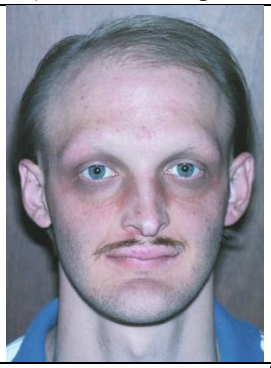
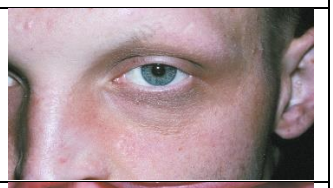
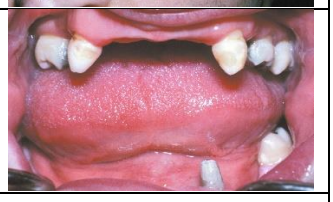
Synopsis➔terminology

➲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

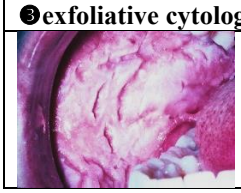
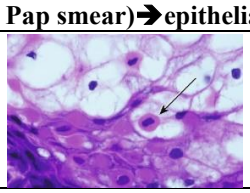
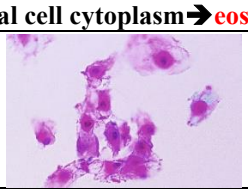
1. Patients with an **X-linked hereditary condition**?
   (A) are always men
   (B) are generally affected more severely if they are men
   (C) are always women
   (D) have cells with many Barr bodies

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[skin, hair, nail, teeth, sweat(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 wrinkling 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)➔thickened, white, corrugated/velvety(天鵝絨般), diffuse plaque ❷other common oral sites➔①ventral tongue ②labial ③soft palate ④alveolar mucosa ⑤mouth floor ❸extraoral➔①nasal ②esophageal ③laryngeal ④anogenital mucosa(less common)	
➲micro➔①prominent hyperparakeratosis ②acanthosis with clear cytoplasm➔spinous layer 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

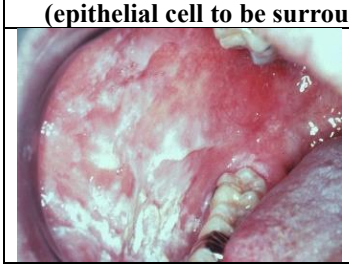
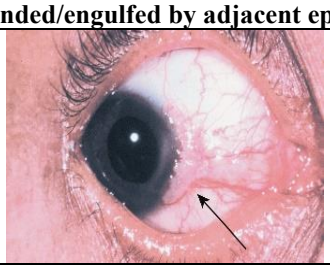
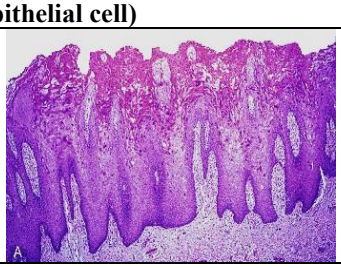
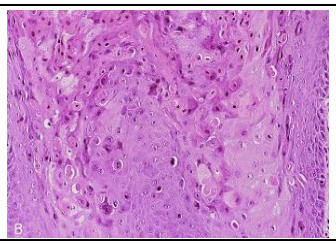
➲clinic➔oral(like white sponge nevus) & conjunctival mucosa of childhood

❶oral➔①buccal & labial[opalescent(乳白色) leukoedema(mild case)]➔superimposed candidiasis
②mouth floor & lateral 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)

➲micro➔①prominent parakeratin ②marked acanthosis

❶dyskeratosis(like Darier disease)➔scattered throughout upper spinous layer➔cell-within-a-cell phenomenon (epithelial cell to be 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

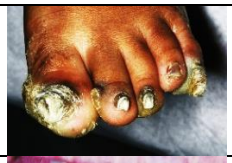
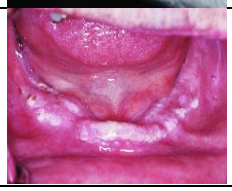
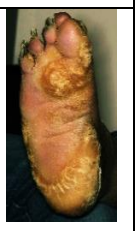
❷skin➔punctate papule➔hair follicle➔abnormal keratin accumulation

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)

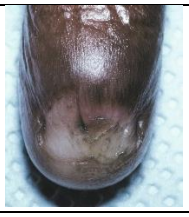
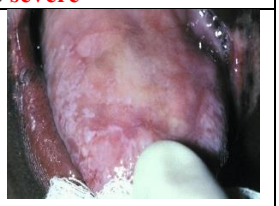
➲❶DKC1 gene mutation➔telomere(端粒) disorder➔X-linked recessive➔male predilection
❷autosomal dominant(recessive)(less common) ❸autosomal recessive+X-linked recessive➔more severe

➲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)

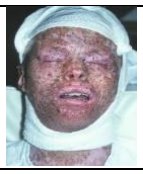
➲autosomal recessive➔DNA repair defect➔epithelial cell unable to repair UV damage➔mutation➔(non)melanoma skin cancer➔❶10,000×>normal ❷<20s

➲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%)➔subnormal智能, ataxia(運動失調), sensorineural deaf, impaired eyesight

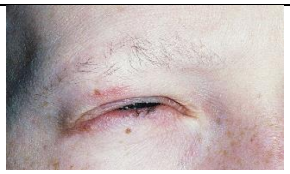
❸oral SCC➔lower lip & tongue tip➔<20s ➲micro➔skin (pre)malignancy

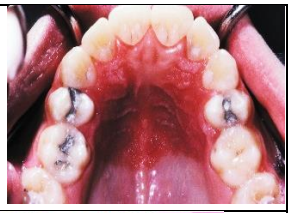


Hereditary mucoepithelial dysplasia➔epithelial cell➔not normal develop➔無↑risk of malignant transformation

➲sporadic/autosomal dominant ➲Pap smear➔epithelial cell➔misinterpret atypical➔hysterectomy(子宮切除術)

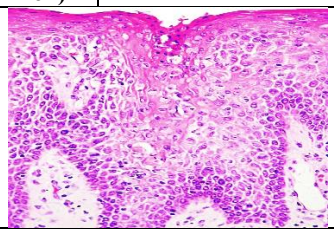
➲clinic➔severe lung complication
❶eyelash睫毛(brow)眼眉➔sparse, coarse hair➔nonscar alopecia
❷severe photophobia(early age)➔cataract➔vision impaired
❸rough dry skin➔follicular keratosis(濾泡性角化病)
❹infancy➔prominent perineal(會陰) rash





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

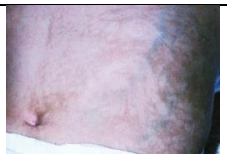
Incontinentia pigmenti(色素失調症)(Bloch-Sulzberger syndrome)➔genodermatosis(genetic skin disorder)

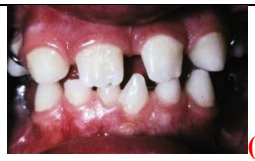
➲Xq28 locus➔IKBKG(inhibitor of kappa B kinase gamma)gene➔X-linked dominant➔F:M ratio=37:1

➲IKBKG gene➔於早期embryogenesis active➔保護embryo from apoptosis➔mutation in female➔less impact(因有 2X chromosome)➔mutated male embryo➔lethal➔if survive➔Klinefelter syndrome(XXY karyotype染色體圖譜)➔affect ❶skin ❷eye ❸CNS ❹oral

➲clinic➔infancy(1st few wks)
4 classic stages➔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





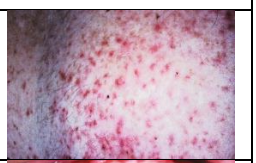
(乳牙及恆牙)

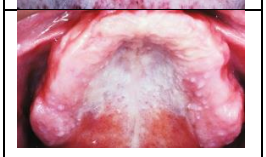
Darier disease(Dyskeratosis follicularis; Darier-White disease)➔genodermatosis(genetic skin disorder)

➲epithelial cell➔lack cohesion➔abnormal desmosomal organization➔↑epithelial cleft

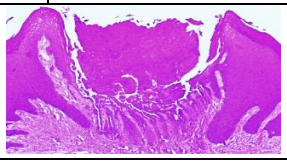
➲autosomal dominant➔ATP*2A2* gene mutation➔intracellular Ca^{2+} pump(SERCA2-sarco/endoplasmic reticulum Ca^{2+}-ATPase isoform 2)

➲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





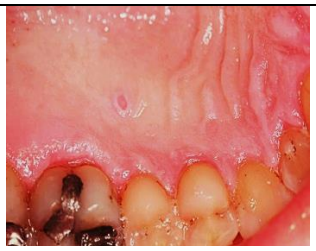
➲micro
❶dyskeratosis➔①central keratin plug ②overlies epithelium➔suprabasilar cleft➔ acantholysis(also in pemphigus vulgaris)
❷rete ridge➔narrow, elongated, test tube-shaped
❸2-type dyskeratotic cell➔①corps ronds(round bodies) ②grain(resemble cereal grain)

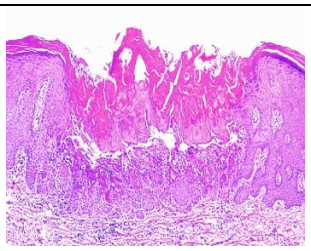


3. 關於**疣狀角化不良(warty dyskeratoma)**的敘述何者錯誤？
(A) 好發於中老年人頭頸區的皮膚
(B) 若發生於口內，則常出現在角質化黏膜區間(keratinized mucosa)
(C) 多數皮膚病灶的直徑大於2cm
(D) 組織學上可見上皮內陷(invagination)中充滿角質栓(keratin plug)

Warty dyskeratoma疣状角化不良(**Isolated Darier disease**)micro➔identical to Darier disease

➲clinic➔solitary skin/oral mucosa
❶ HN skin➔asymptomatic, umbilicated papule➔older adult(multiple reported)
❷oral➔>40s➔slight male predilection➔pink/white umbilicated papule➔①hard palate ②alveolar ridge➔warty surface➔most≤0.5cm
➲micro➔❶like dyskeratosis follicularis ❷dyskeratosis, basilar hyperplasia, suprabasilar cleft(acantholysis)

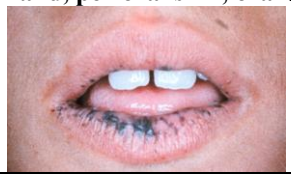


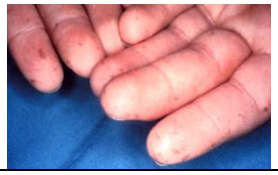


4. Which of the following is a component of **Peutz-Jeghers syndrome**?
(A) multiple jaw cysts
(B) multiple supernumerary teeth
(C) multiple pigmented macules in lower lip
(D) multiple nodules on the tip of tongue

Peutz-Jeghers syndrome

➲hand, perioral skin, oral➔freckle-like lesion





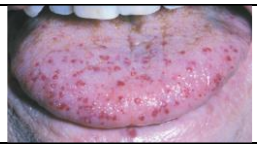
➲intestinal polyposis➔intestinal glandular epithelium overgrowth supported by smooth muscle core➔epithelial atypia NOT prominent(not premalignant)
➲ predisposition to develop GI cancer(not from polyp)
➲oral lesion(>90%)(1-4mm brown to blue-gray macule)➔❶vermilion ❷labial ❸buccal mucosa ❹tongue

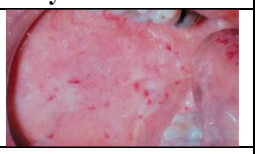
5. The major concern when treating a patient with **Osler -Rendu syndrom**e should be:
(A) gingival hemorrhage
(B) spontaneous ulcerations
(C) severe infections
(D) epithelial desquamation

Hereditary hemorrhagic telangiectasia(**HHT**)(**Osler-Weber-Rendu syndrome**)

➲autosomal dominant➔mutation[❶HHT1➔endoglin(ENG) gene(chromosome 9) ❷HHT2➔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 ❷juvenile polyposis➔上&下GI tract➔↑risk of early colorectal ca.

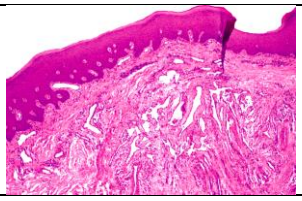
➲epistaxis(鼻出血)➔nasal & oropharyngeal mucosa➔scattered red papule(1-2mm)➔blanch(發白)when diascopy(玻片壓診法)➔red color➔telangiectasia(multiple dilated capillaries)➔close to mucosa➔❶vermilion zone of lips ❷tongue ❸ buccal





➲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➔lung, liver, CNS
❹HHT family history



➲micro➔superficial thin-walled vascular space➔RBCs

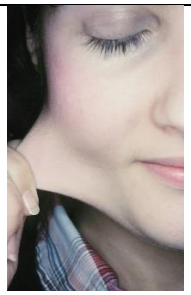
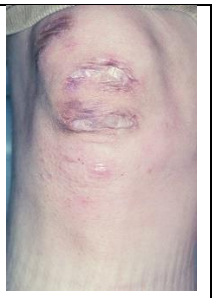
➲d.d. with CREST syndrome(calcinosis cutis, Raynaud phenomenon, esophageal dysfunction, sclerodactyly, telangiectasia)➔anticentromere autoantibodies➔ONLY in CREST syndrome

Ehlers-Danlos syndromes➔abnormal collagen(connective tissue main structural component) production

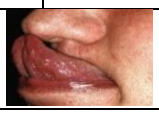
➲common types

type	clinic	genetic	collagen mutation
❶classic(severe)	hyperextensible skin, easy bruising, hypermobile joints, papyraceous scarring of skin, pulp stone	AD	type V
❶classic(mild)➔normal life span	less severe classical manifestation	AD	type V
❷hypermobility	soft skin, no scarring, marked joint hyperextensibility	AD	not known
❸vascular(ecchymo(tic)sis)	severe bruising; risk for arterial, bowel, uterine rupture	AD	type III

➲clinic➔4 types
❶classical(~80%)➔①hyperelasticity of skin & skin fragility ②minor injury➔ papyraceous scar➔resemble crumple(皺巴巴) cigarette paper
❷hypermobility➔①remarkable joint hypermobility➔no scar ②greater degree chronic musculo-skeletal pain
❸vascular➔①extensive bruise➔everyday trauma 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 ②reduced/no attached gingiva ③C1R & C1S mutations

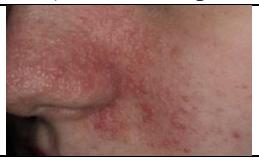
➲oral➔❶nose tip touch with tongue(Gorlin sign)(50% vs<10% general population)(右圖)
❷bruise & bleed ❸mucosa friability ❹TMJ recurrent subluxation
❺teeth➔①malformed ②stunted root ③pulp stone ④enamel hypoplasia



Tuberous sclerosis(結節性硬化症)➔intellectual disability, seizures, skin angiofibroma

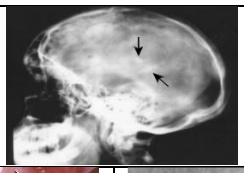
➲❶autosomal dominant ❷sporadic mutation(2/3 cases)➔2 tumor suppressor genes[①TSC1(chromosome 9) ②TSC2 (chromosome 16)(more common➔2/3 cases)]➔target of Rapamycin(mTOR)路徑➔multiple hamartomas

➲clinic
❶facial angiofibroma➔multiple smooth papules➔nasolabial fold
❷(peri)ungual(指(趾)甲 fibromas➔nail margins

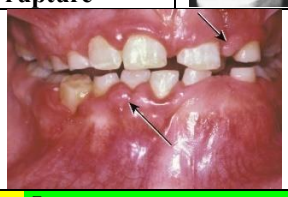
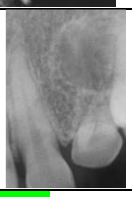



❸ash-leaf spots(90-98%)➔shagreen(鯊革➔表面粗糙又有粒狀的生皮)patch & ovoid hypopigmentation(UV lamp)
❹confetti(五彩纸屑) spots➔1-3mm pale macules➔trunk-extremities(symmetrical distribute)

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(lips, buccal, palate, tongue可能有)
③diffuse fibrous gingiva enlargement(even without phenytoin)
④RL of jaws➔dense fibrous connective tissue proliferations

➲diagnosis➔≥ 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

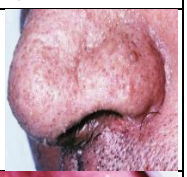
➲diagnosis➔1 major & 2 minor feature
❶multiple, randomly distributed enamel pits
❷gingiva fibromas
❸bone cysts(actually fibrous proliferations)
❹confetti skin lesions
❺multiple renal cysts
❻non-renal hamartomas

Multiple hamartoma syndrome(Cowden syndrome; PTEN hamartoma-tumor syndrome)

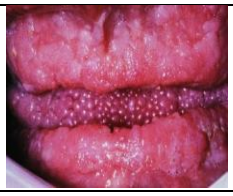
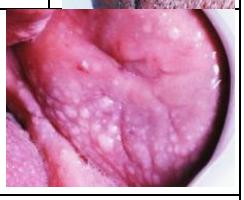
❶autosomal dominant ❷phosphatase & tensin homolog deleted on chromosome 10(PTEN)基因突變(45%)(chromosome 10)

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 hamartomas(trichilemmomas)
②acral keratosis(光化性角化)➔warty➔hand dorsal surface, palmoplantar keratosis(腳底明顯callus)
③hemangiomas, sclerotic fibromas, neuromas, xanthomas, lipomas



❷thyroid➔①goiter/thyroid adenoma ②papillary/follicular adenocarcinoma
❸breast➔①fibrocystic disease ②breast cancer
❹GI tract➔multiple benign hamartomatous polyps
❺oral➔①multiple papules➔gingiva, dorsal tongue, buccal mucosa
②high-arched palate
③periodontitis ④caries

➲diagnosis
❶2 out of ①-③pathognomonic signs➔①facial trichilemmomas ②oral papule ③acral keratoses
❷PTEN gene mutation➔20%(-)➔(-) not preclude multiple hamartoma syndrome

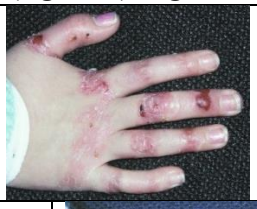
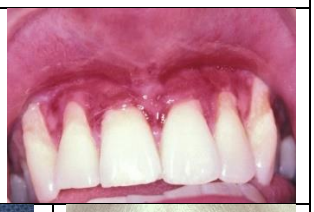
6. What is the **target structure** of **epidermolysis bullosa acquisita**?
(A) desmoglein 3 of desmosome
(B) hemidesmosome
(C) type VII collagen of anchoring fibrils
(D) basement membrane zone

Epidermolysis bullosa(EB)表皮溶解水皰➔inherited blistering mucocutaneous disorders

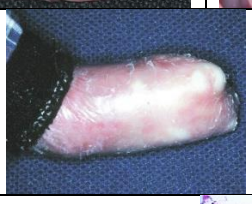
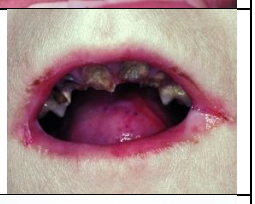
➲**4 categories**
❶**simplex➔①hand & feet blister(mucosa uncommon)➔heal without scar➔癒後good ②keratin 5,14 mutations**
❷**junctional➔①death at birth➔skin sloughing during passage via birth canal ②laminin-332, collagen XVII, α6β4 integrin mutation(hemidesmosome) ③dental abnormalities(anodontia, enamel hypoplasia, enamel pit, neonatal teeth, severe periodontitis, severe caries)➔↑significant**
❸**dystrophic➔①collagen VII mutation ②oral lesion➔most common**
❹**Kindler syndrome➔hemidesmosome attachment protein, kindlin-1 mutation**

✹**EB acquisita➔similar name(unrelated condition)➔autoimmune(非genetic) origin**

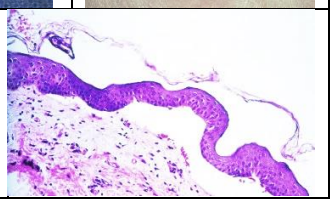
➲**clinic**
❶**dominant dystrophic➔disfiguring➔not life threat**
①vesicles/bullae(early in life)➔low-grade, chronic trauma➔ knuckle(關節)/knee➔rupture➔erosion/ulcer➔heal with scar ➔fingernail loss
②oral➔gingiva erythema(recession), ↓buccal vestibule depth

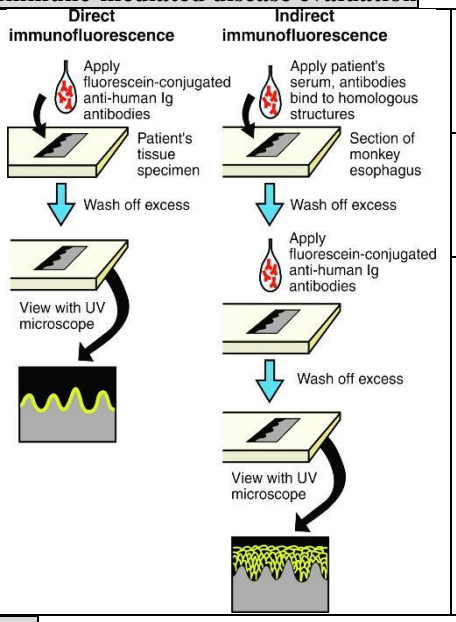
❷**recessive dystrophic**
①generalized recessive EB➔severe mucosa involve; hand & feet mittenlike scar(deformities); die early adulthood
②oral➔food with some degree of texture(even soft diet➔caries) ➔vesicles/bullae➔cycle of scar➔microstomia & ankyloglossia➔ severe esophagus stricture

➲**micro**
①simplex form➔intraepithelial cleft
②junctional, dystrophic, Kindler forms➔subepithelial cleft
EM➔⊙junctional form➔cleft at level of lamina lucida of basement membrane
⊙dystrophic form➔cleft below lamina densa of basement membrane
⊙Kindler form➔cleft just below basal cell layer(interface with lamina lucida)

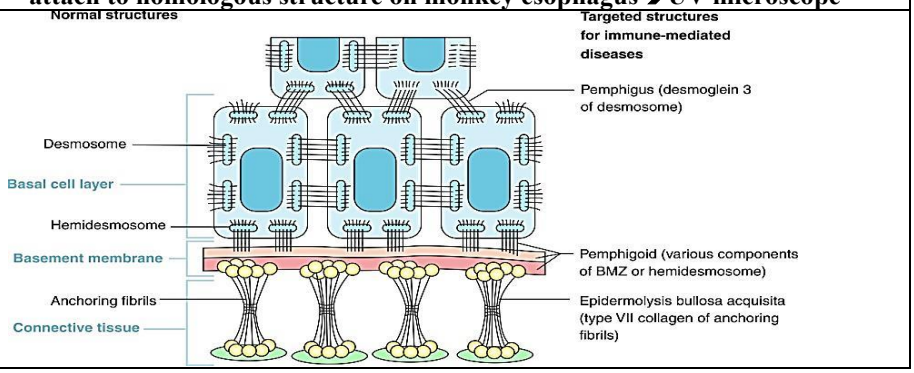


Immune-mediated disease evaluation



➲**direct immunofluorescence(IF)**
❶**detect autoAb bound to patient's tissue**
❷**frozen section➔incubate fluorescein-conjugated goat antihuman Ab➔ bind to human Ig➔UV microscope**

➲**indirect immunofluorescence(IF)**
❶**detect autoAb bound to monkey esophagus(like human oral mucosa)**
❷**frozen section➔incubate patient's serum autoAb *vs* epithelial structure➔ attach to homologous structure on monkey esophagus➔UV microscope**



Synopsis

➲**X-linked recessive➔male predominant**
❶**ectodermal dysplasia(ED)**
❷**dyskeratosis congenita(先天性角化不全)**
➲**X-linked dominant➔female predominant**
❶**incontinentia pigmenti(色素失調症)➔male lethal➔if survive➔ Klinefelter syndrome**

➲**risk of /SCC & epithelial dysplasia/ other malignancy**
❶**dyskeratosis congenita(先天性角化不全)**
①leukoplakia (epithelial dysplasia)➔SCC
②aplastic anemia
❷**xeroderma pigmentosum(著色性乾皮症)**
①SCC ②BCC ③melanoma

➲eyebrow眉毛(lash睫毛) ❶ED➔fine sparse hair ❷hereditary mucoepithelial dysplasia➔coarse sparse hair	❸GVHD➔SCC & epithelial dysplasia ❹hereditary hemorrhagic telangiectasia(HHT) (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➔HPK+atrophy ❶dyskeratosis congenita(先天性角化不全)	➲micro➔keratin plug+suprabasilar cleft(acantholysis ➔Tzanck cell)+basilar hyperplasia ❶Darier disease(dyskeratosis follicularis) ❷warty dyskeratoma(疣状角化不良) ➲micro➔intraepithelial cleft(acantholysis) ❶incontinentia pigmenti(色素失調症)➔vesicular stage ❷(paraneoplastic) pemphigus ❸epidermolysis bullosa(simplex form)
➲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) ❹epidermolysis bullosa acquisita

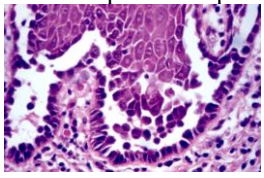
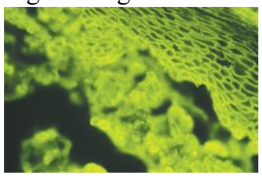
Chronic vesicuoulcerative diseases➔❶Pemphigus vulgaris ❷Paraneoplastic pemphigus ❸Mucous membrane pemphigoid ❹Mucous membrane pemphigoid ❺Erythema multiforme ❻Lichen planus

condition	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)	subepithelial edema & 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) and **direct immunofluorescence** pattern of immunoreactants deposited in intercellular areas between the surface epithelial cells, resulting in a **"chicken wire" pattern** (right); what is the most adequate histopathological diagnosis?

   (A) pemphigus vulgaris
   (B) mucous membrane pemphigoid
   (C) lichen planus
   (D) epidermolysis bullosa

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➔cell of spinous layer➔fall apart

五型：
(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 hemidemosomes	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

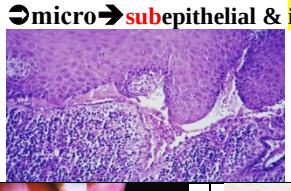
Paraneoplastic pemphigus➔cytotoxic T lymphocyte

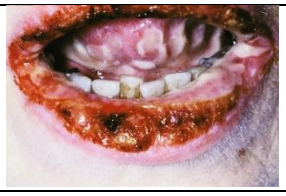
➲伴隨 lymphoma/chronic lymphocytic leukemia(CLL)➔↑(cytokine, IL-6)➔↑Ab attack desmosome & BMZ

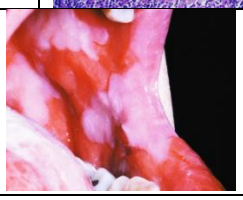
➲伴隨 benign lymphoproliferative disorder➔angiofollicular LN hyperplasia(Castleman disease)

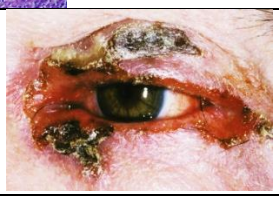
➲clinic
❶multiple vesiculobullous lesions➔skin & oral mucosa
❷palmar/plantar bullae➔a feature uncommon in pemphigus vulgaris
❸skin lesion➔more papular & pruritic➔like skin lichen planus
❹lip➔hemorrhagic crusting ➔like erythema multiforme
❺conjunctiva➔cicatrizing conjunctivitis➔like mucous membrane pemphigoid
❻anogenital, nasopharyngeal, esophageal, respiratory tract mucosa➔involved
❼lung➔bronchiolar mucosa➔slough➔occlude bronchiolar lumina & alveoli➔bronchiolitis obliterans

➲micro➔subepithelial & intraepithelial cleft







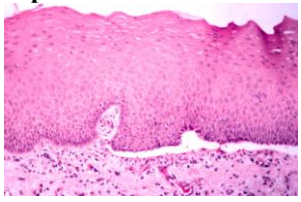


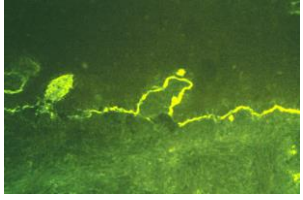
10. **Mucous membrane pemphigoid** not only affecting **oral cavity and skin,** it also likely involves which of the following region?
(A) ocular
(B) brain
(C) intestine
(D) bone

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

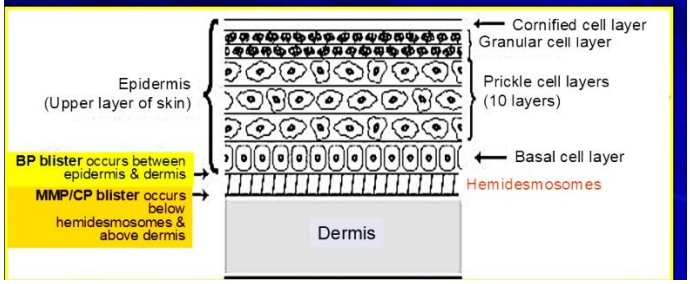
15. Which of the following statements about autoimmune disease with oral manifestations is considered *false*?
(A) the bullae in pemphigus vulgaris are more fragile than those in bullous pemphigoid
(B) acantholysis of the epithelium is seen in pemphigus vulgaris
(C) in pemphigoid the separation of the 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

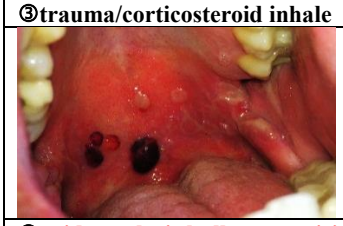
Two major forms of pemphigoid:
1. Mucous Membrane Pemphigoid/Cictricial Pemphigoid (MMP/CP)
2. Bullous Pemphigoid (BP)
Type of pemphigoid depends on which autoantibodies are produced, & in which layer of skin blister occurs



➲MMP➔below hemidesmosome; above dermis(blister roof)
➲BP➔between epidermis & dermis(just below basal cell layer)

➲other conditions(micro like pemphigoid)
❶linear IgA bullous dermatosis
①linear deposition only IgA➔BMZ ②skin predominant

❷angina bullosa hemorrhagica➔middle-aged/older adult
①oral mucosa➔soft palate➔pain blood-filled vesicle/bulla
②blister➔rupture spontaneous➔heal without scar➔subepithelial cleft
③trauma/corticosteroid inhale

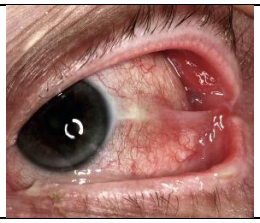


❸epidermolysis bullosa acquisita
①autoAb➔type VII collagen(ancho fibril bind epith. to ct)➔bulla(minimal trauma)➔middle-aged/older adult
②oral(50%)➔uncommon without skin lesion
③perilesional skin➔incubate in concentrated salt solution ➔epithelium separate from c.t.➔artificial bulla➔IHC➔IgG autoAb deposit
✪bulla floor(ct➔type VII collagen ✪blister roof➔MMP

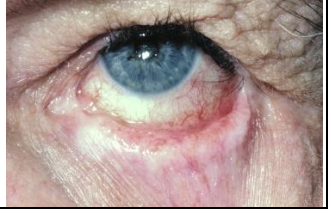
❶Mucous membrane pemphigoid(Cicatricial pemphigoid)

➲ocular➔oral lesion patient(25%)➔ocular lesion➔affect one eye before the other

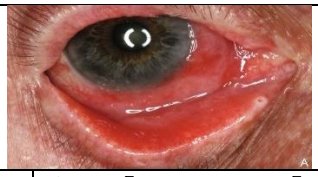
❶earliest➔subconjunctival fibrosis(ophthalmologist➔slit-lamp micro exam)➔inflamed & eroded conjunctiva➔scar between bulbar(lining eye globe) & palpebral (lining eyelid inner surface) conjunctivae➔symblepharons

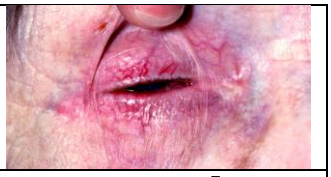


❷severe➔scar➔eyelid (眼瞼)內翻(entropion) ➔eyelash(睫毛)rub cornea(角膜) & globe (trichiasis)(倒睫)

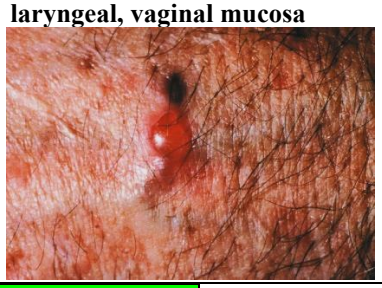


❸scar➔closes off lacrimal gland opening➔loss of tear ➔dry eye➔cornea➔ keratin➔blindness(上下眼瞼 adhesion)

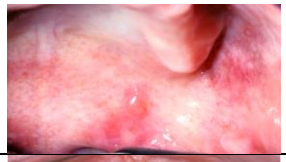
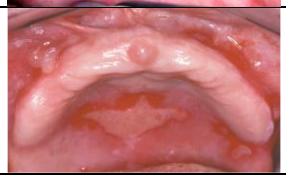




➲skin(20%)➔tense bullae
➲conjunctiva, nasal, esophageal, laryngeal, vaginal mucosa



➲oral➔vesicle/bulla➔ulcer

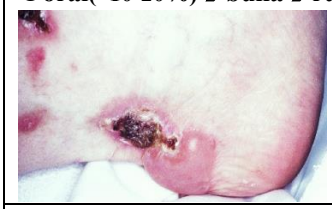
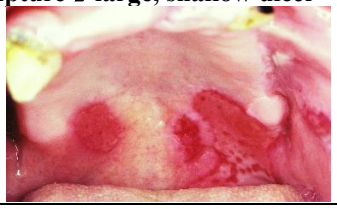



➲gingiva➔desquamative gingivitis ➔also erosive lichen planus & pemphigus vulgaris

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%)➔tilter ➔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

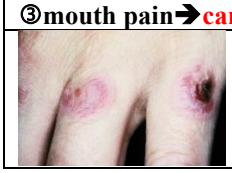
Erythema multiforme(EM)(多形性紅斑)➔electron microscope➔spectrum of severity➔❶EM minor ❷EM major

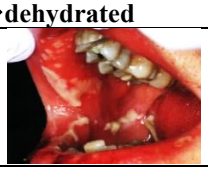
➲cell-mediated(非humoral) immune-attack➔oral mucosa &/or epidermis(mucocutaneous condition)➔blister, ulcer

➲precipitating cause➔❶infection(herpes simplex, Mycoplasma pneumoniae ❷antibiotic/analgesic➔trigger attack

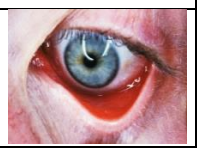
➲clinic➔20s/30s➔prodromal(前驅) symptom(onset前1-wk)➔fever, malaise(身體不適), headache, cough, sore throat

❶EM minor
①slight↑ round dusky(昏暗)-red patch➔skin of extremities➔concentric erythematous ring➔target lesion/(resemble bull eye)➔bullae with necrotic center
②oral➔erythematous patch➔necrosis➔large, shallow erosion & ulceration➔hemorrhagic crust➔lip vermilion (common➔lip, labial mucosa, buccal mucosa, tongue, mouth floor, soft palate; spare➔gingiva & hard palate)
③mouth pain➔cannot ingest liquid➔dehydrated

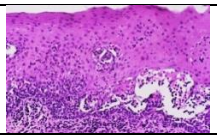
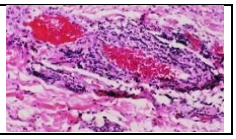




❷EM major
①≥2 mucosa+skin+ocular/genital
②ocular➔scar(symblepharon瞼球粘連)➔ like mucous membrane pemphigoid



➲micro
❶subepithelial/intraepithelial vesicle➔basal keratinocyte(necrotic)
❷perivascular inflammatory infiltrate➔lymphocyte, neutrophil, eosinophil

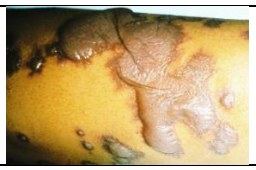
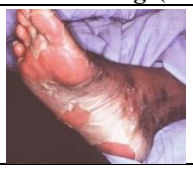



Stevens-Johnson syndrome & toxic epidermal necrolysis➔drug exposure trigger➔↑apoptosis➔epithelium damage

➲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

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)

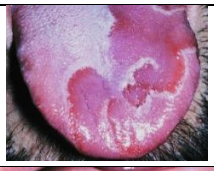
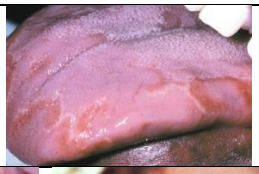
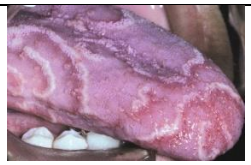




➲micro
❶subepithelial blister➔degenerate, necrotic basal keratinocyte
❷underly connective tissue➔sparse chronic inflammatory cell

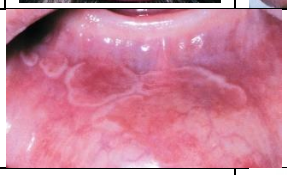
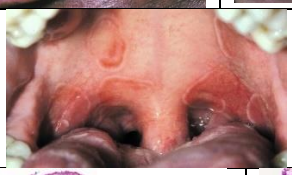
Erythema migrans遊走性紅斑(Geographic tongue; Benign migratory glossitis)➔tongue➔無症狀(燒灼感/熱/辣食物)

➲occur➔❶1-3% of population ❷not frequent➔cigarette smoker ❸not-related➔age, sex, oral contraceptive, allergy, DM, psycho/dermal conditions

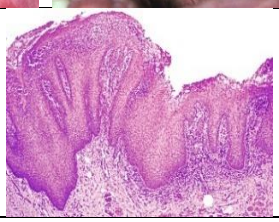
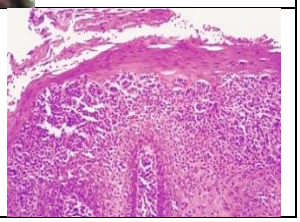
➲clinic➔filiform papillae atrophy➔multiple well-demarcated erythema➔anterior 2/3 dorsal tongue(tip & lateral)(~1/3 with fissured tongue)➔heal(in a few days/wks)➔develop in very different area

➲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
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)

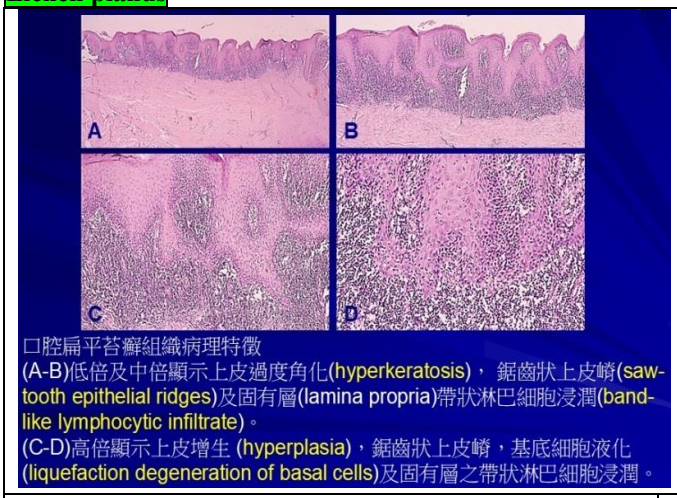
➲clinic

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 circinata

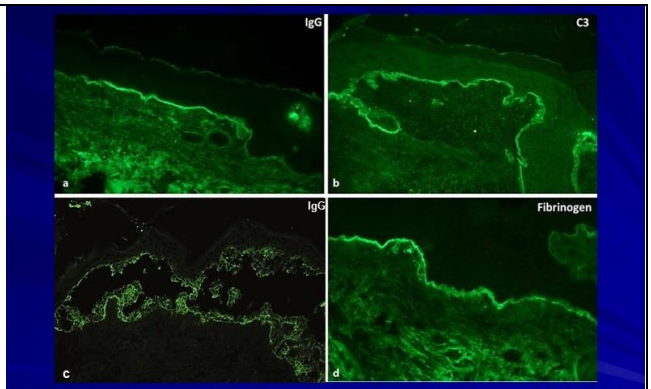
➲micro➔like psoriasis
❶hyperparakeratosis with elongate, thin rete ridge ❷microabscess➔epithelium surface

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

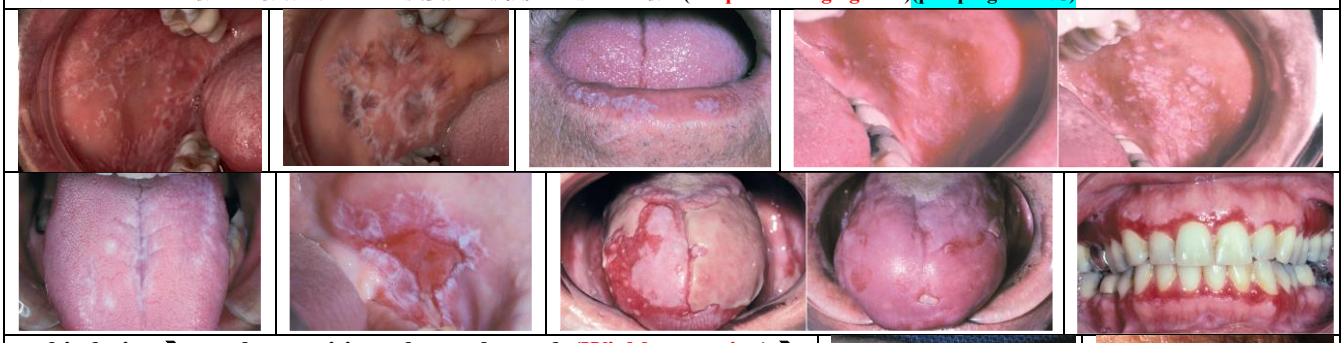


口腔扁平苔癬組織病理特徵
(A-B)低倍及中倍顯示上皮過度角化(hyperkeratosis)， 鋸齒狀上皮嵴(saw-tooth epithelial ridges)及固有層(lamina propria)帶狀淋巴細胞浸潤(band-like lymphocytic infiltrate)。
(C-D)高倍顯示上皮增生 (hyperplasia)，鋸齒狀上皮嵴，基底細胞液化(liquefaction degeneration of basal cells)及固有層之帶狀淋巴細胞浸潤。

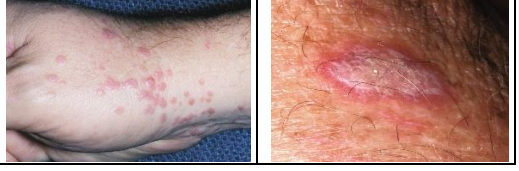


*Linear IgG (**a**) and C3 (**b**) along dermoepidermal junction of pemphigoid
*Fishnet IgG (**c**) within intercellular of pemphigus
*Linear with shaggy deposition of fibrinogen (**d**) along dermoepidermal junction of lichen planus.

➲ 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)



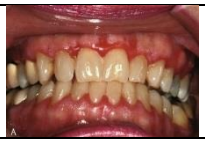
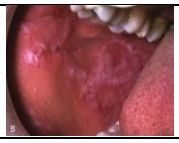
➲skin lesion➔purple, pruritic, polygonal papule(Wickham striae)➔ extremities flexor surface➔no excoriation(表皮脫落)➔itch(癢)
➲other extraoral site➔❶glans penis ❷vulvar



Chronic ulcerative stomatitis慢性潰瘍性口炎(CUS)➔immune-mediated disorder➔oral mucosa

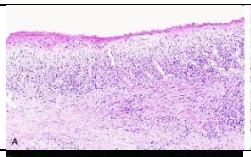
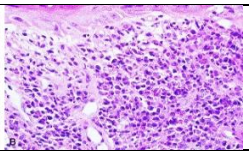
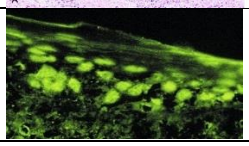
➲autoAb *vs* 70kD nuclear protein(ΔNp63α➔ p63isoform)➔中斷epithelium/connective tissue交接處的正常維護

➲clinic
❶like erosive lichen planus➔d.d. with 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 mucosa 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
❶like lichen planus ❷epithelium more atrophic
❸inflammatory infiltrate➔significant plasma cell, lymphocyte
❹artefactual epithelial separation from underly 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(+)

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

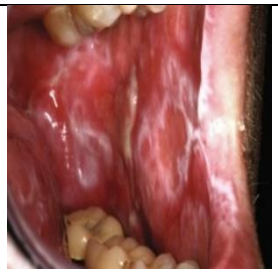
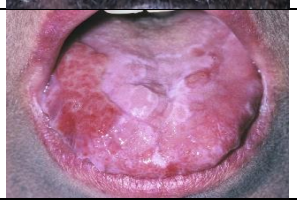
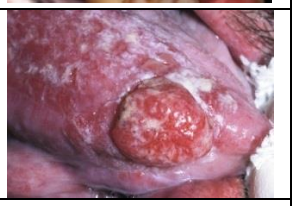
➲❶graft-versus-leukemia effect➔donor cell➔leukemic cell as foreign body ❷mini-allograft(nonmyeloablative allogenic hematopoietic cell transplantation)➔not all WBC destroyed➔donor cell➔attack leukemic cell ❸autologous stem cell transplantation➔cell derived from patient➔no GVHD risk

➲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↑oral & skin epithelial dysplasia & SCC risk

➲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

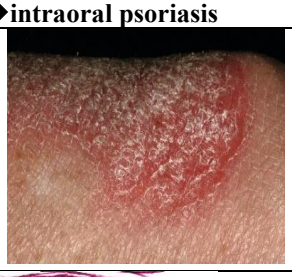
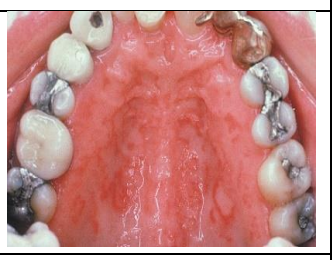
➲oral➔❶white to red plaque to ulcer ❷erythema migrans➔intraoral psoriasis

➲clinic➔well-demarcated, erythematous plaque with silvery scale➔①scalp ②elbow ③knee

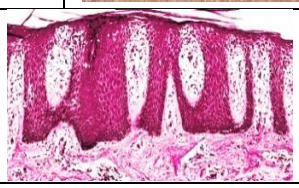
❶2nd/3rd decade➔persist years➔惡化-靜止➔夏季改善-冬季惡化③UV ❷psoriatic arthritis (25-30%)➔TMJ

❸其他➔inflammatory bowel disease, non-alcoholic liver disease, mood disorder(心境障礙), CVD

❹more prevalent periodontitis

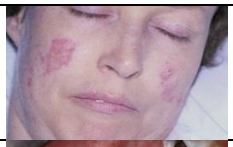
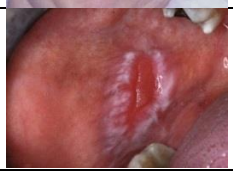



➲micro
❶↑parakeratin(Munro abscess➔neutrophil)
❷elongated rete ridge ❸connective tissue papilla➔dilated capillaries➔close to epithelial surface
❹perivascular chronic inflammatory cell infiltrate



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
(C) 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

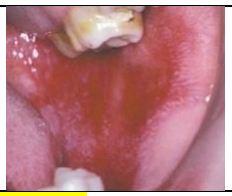
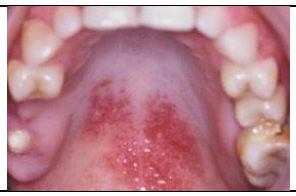
➲systemic LE(SLE)(全身性紅斑狼瘡)➔multisystem with oral/cutaneous manifestation
❶women>men(近8-10×) ❷average age➔31s ❸common finding➔fever, weight loss, arthritis, fatigue, malaise ❹butterfly rash(40-50%)➔malar & nose➔spare nasolabial fold
❺sunlight➔lesion worsen
❻kidney(~40-50%)➔kidney failure
❼cardiac➔pericarditis(Libman-Sacks 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%

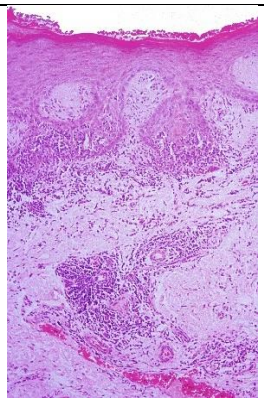
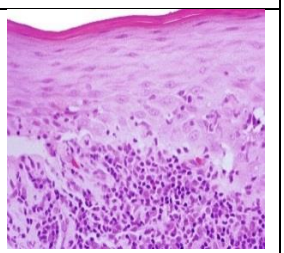
findings	frequency
thrombocytopenia(<100,000/μL)	15%
hemolytic anemia	10%
NEUROLOGIC SIGNS AND SYMPTOMS	60%
cognitive disorder	50%
headache	25%
seizures	20%
CARDIOPULMONARY SIGNS	60%
pleurisy, pericarditis, effusions	30-50%
myocarditis, endocarditis	10%
RENAL SIGNS	30-50%
proteinuria >500mg/24h, cellular 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-exposed HN skin➔heal spontaneous in one area➔appear another area➔healing➔skin atrophy➔scar & hypo(hyper) pigmentation
❷conjunctiva(結膜)➔cicatrizing(瘢痕) conjunctivitis➔mucous membrane pemphigoid
❸oral➔erosive lichen planus

➲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
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

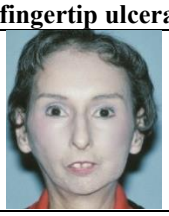
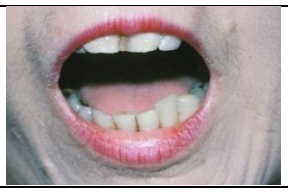
(D) small nuclear RNA的抗體存在，對於全身性紅斑性狼瘡的診有被高的專一性

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

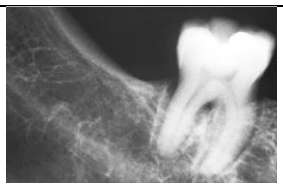
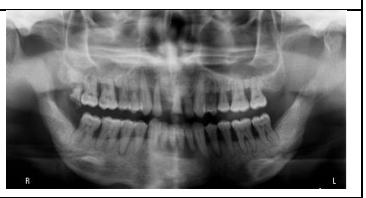


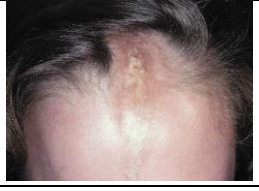
❹skin➔diffuse smooth hard texture
①facial➔subcutaneous collagen deposition➔smooth, taut(繃緊), masklike face
②nasal ala➔atrophy➔pinch nose➔mouse face
③hand, face, feet, limb(lower portion)➔limited cutaneous SSc➔pulmonary hypertension later
④trunk, proximal limbs➔diffuse cutaneous SSc(③④different prognoses)➔lung(hypertension & 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

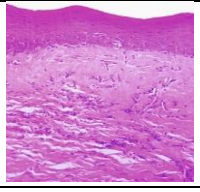
➲radiograph
①diffuse PDL space widening➔throughout dentition
②posterior ramus, coronoid process, chin, condyle resorption(10-20%)➔pano➔↑pressure associated with ↑collagen deposit
③individual tooth resorption➔higher frequency

➲milder➔localized scleroderma/ morphea➔solitary patch➔like scar➔en coup de sabre(strike of sword)➔cosmetic problem➔ rare life threatening➔unrelated to SSc



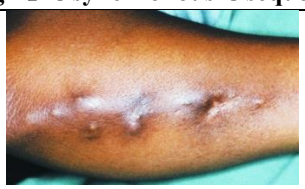
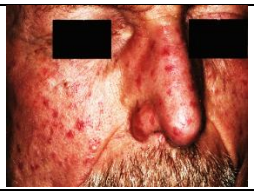
➲micro
❶diffuse deposition of dense collagen➔replace & destroy normal tissue➔loss of normal tissue function



➲diagnosis
①anticentromere Ab➔limited cutaneous SSc(include CREST syndrome)➔late-onset lung hypertension
②anti-topoisomerase I(Scl 70) & anti-RNA polymerase III Ab➔diffuse cutaneous SSc➔lung fibrosis

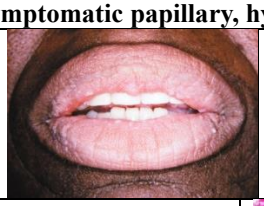
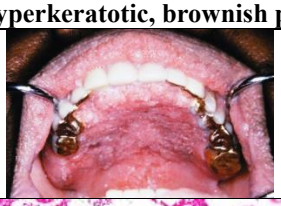
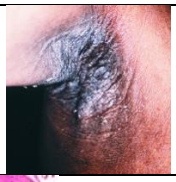
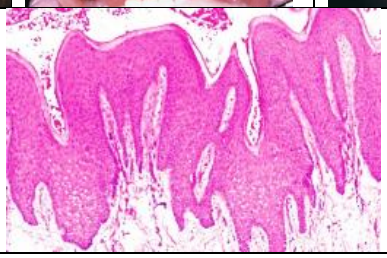
27. Which one of the following is involved in the **Raynaud phenomenon**?
(A) kidney
(B) ocular components
(C) fingers and toes
(D) joints

CREST syndrome(limited scleroderma)➔variant of limited cutaneous SSc

➲CREST➔Calcinosis cutis, Raynaud phenomenon, Esophageal dysfunction, Sclerodactyly, Telangiectasia		
➲clinic➔6-7th decade women	➲sign➔❶synchronous ❷sequential over months to years	
➲calcinosis cutis ❶multiple movable nontender subcutaneous nodules(0.5-2cm) ❷larger more numerous superficial calcification➔removal		➲Raynaud phenomenon hands/feet➔cold expose➔blanch of digits➔dead-white color(severe vasospasm)➔bluish color(venous stasis)(few min later)➔warming (dusky-red hue)➔hyperemic blood flow return➔throbbing pain
➲esophageal dysfunction➔↑collagen deposit ❶not noted in early phase ❷initial sign➔barium swallow radiograph	➲sclerodactyly➔↑collagen deposit➔dermis ❶finger➔stiff(smooth shiny skin)➔permanent flexure➔claw deformity	
➲telangiectasias➔like hereditary hemorrhagic telangiectasia (HHT) ❶superficial dilated capillary(facial skin & vermilion zone of lips)➔↑bleeding ➲micro➔like SSc(milder) ❶superficial dilate capillary➔telangiectatic vessel		➲diagnosis➔d.d. with HHT ❶anticentromere Ab➔specific➔CREST syndrome & limited cutaneous SSc

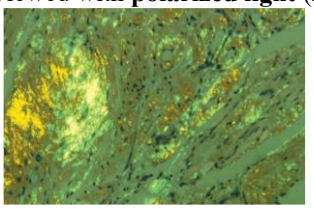
28. **Acanthosis nigricans** is a skin disorder associated with which condition?
(A) anemia
(B) hyperthyroidism
(C) type 2 diabetes
(D) Addison disease

Acanthosis nigricans(黑色棘皮症)➔velvety(絲滑)/像皮革brown skin➔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➔asymptomatic papillary, hyperkeratotic, brownish patch			
➲oral(25-50%)➔malignant form ❶diffuse papillary patch ①tongue ②lips(upper) ③buccal ❷brown pigment➔not seen			
➲micro ❶hyperorthokeratosis & papillomatosis ❷oral lesion➔①↑more acanthosis ②minimal↑melanin(rather mild)			

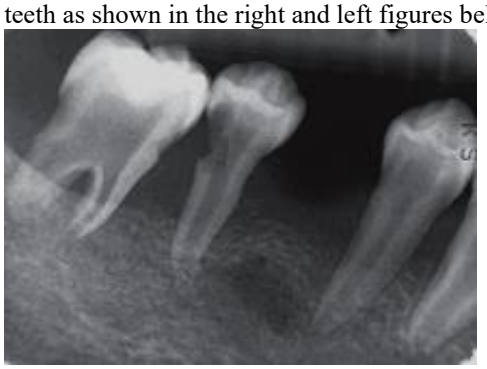
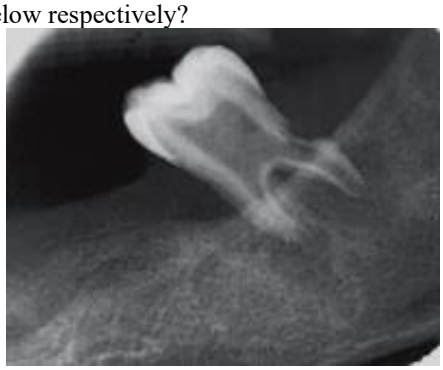
Chapter 17 Oral Manifestations of systemic diseases

1. 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

2. 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

3. **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

4. **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

5. 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

6. 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

7. **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) only 2,3,4,5,6

8. **Osteomalacia** is usually caused by a **nutritional deficiency** of:
(A) vitamin B12
(B) vitamin D
(C) alkaline phosphatase
(D) potassium

9. **Osteomalacia in children** is called:
(A) florid cemento-osseous dysplasia
(B) osteogenesis imperfecta
(C) Albright syndrome
(D) rickets

10. 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

11. 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

12. 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

13. A **multilocular radiolucency** is most likely associated with:
(A) fibrous dysplasia
(B) osteomalacia
(C) Paget's disease
(D) hyperparathyroidism

14. **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

15. 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

16. **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

17. **Hypercalcemia**, **hypophosphatemia**, **elevated serum alkaline phosphatase** & **abnormal bone metabolism** are features of:
    (A) Hyperthyroidism
    (B) hypothyroidism
    (C) hyperparathyroidism
    (D) hyperpituitarism

18. 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

19. **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

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			
Thalassemia	Decrease	Large maxilla	(large bone marrow space)		hair-on-end (skull)

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

Chapter 18 Facial pain & neuromuscular diseases

Frey syndrome(auriculotemporal syndrome)➔facial flushing & sweating along auriculotemporal nerve

➲auriculotemporal nerve ❶sensory fiber to preauricular & temporal region ❷parasympathetic fiber➔parotid gland ❸sympathetic vasomotor & sudomotor(sweat) fiber to preauricular skin	➲parotid abscess, trauma, mandibular surgery, parotidectomy➔parasympathetic n severed➔reestablish innervation➔fiber misdirected➔regenerate along sympathetic n pathway➔communicate with sympathetic n 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	

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(blurred vision with exercise, diplopia, transient vision loss)➔early manifestation ❻systemic S/S➔fever, malaise, fatigue, anorexia, weight loss ❼polymyalgia rheumatic(風濕性多肌痛)(40%)➔pain & morning stiffness➔①neck ②shoulder ③pelvic girdle(骨盆带) ❽ undetected aortic inflammation➔aneurysm(rupture)➔↑risk CV accident, cardiac infarction, limb 跛行, vasculitis		
➲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		
➲lab❶↑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**
❶**clinically observable hyposalivation** ❷**chronic mechanical trauma** ❸**oral fungal, bacterial, or viral infection** ❹**contact stomatitis** ❺**geographic tongue** ❻**local manifestation of immune-mediated/autoimmune disease**	❶**vitamin B deficiency** ❷**vitamin B1/B2 deficiency** ❸**pernicious anemia(B12)** ❹**pellagra(糙皮病)(niacin 維他命 B3 deficiency)** ❺**folic acid deficiency** ❻**Fe deficiency** ❼**DM** ❽**chronic 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**

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**
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**
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**
Chapter 10	**Epithelial pathology** **(1)C (2)C (3)A (4)A (5)D (6)D (7)C (8)A (9)C (10)D (11)B (12)D (13)B (14)C (15)A (16)A (17)A (18)B (19)B (20)C (21)C (22)D (23)B (24)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)A (24)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)B (3)D (4)D (5)A (6)C (7)D (8)D (9)A (10)C (11)B (12)B (13)A (14)C (15)B (16)D (17)C**
Chapter 14	**Bone pathology** **(1)A (2)B (3)C (4)A (5)A (6)C (7)A (8)C (9)C (10)D (11)B (12)D (13)B (14)A (15)C (16)D (17)B (18)A (19)D (20)B (21)D (22)D (23)B (24)A (25)C (26)D (27)D (28)B**
Chapter 15	**Odontogenic tumors & cysts** **(1)B (2)B (3)A (4)A (5)A (6)B (7)D (8)D (9)B (10)B (11)C (12)D (13)B (14)D (15)A (16)B**
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)C (25)D (26)C (27)C (28)C**
Chapter 17	**Oral manifestations of systemic diseases** **(1)D (2)C (3)C (4)A (5)D (6)C (7)A (8)B (9)D (10)B (11)C (12)B (13)D (14)B (15)D (16)C (17)C (18)C (19)D**
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➔S/S or features or tests⇆across different chapters ★radiographic pathology➔P. 91(Chapter 14 Bone disorders)

➲xx sign⇆diseases

❶Forchheimar sign⇆German measles(rubella)(oral small dark-red papule)
❷Gorlin sign⇆Ehler-Danos syndrome
❸Hutchinson sign⇆herpes zoster(nose tip lesion➔severe ocular risk)
❹Nikolsky sign⇆pemphigus
❺Crowe sign(freckle of axilla/intertriginous zone)⇆neurofibromatosis type I (von Recklinghausen disease of skin)
❻string sign⇆parosteal osteosarcoma(RL line➔periosteum between tumor & cortex)

➲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

➲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
❻desquamative gingivitis⇆systemic lupus erythematosus(SLE)
❼desquamative gingivitis⇆chronic ulcerative stomatitis
❽desquamative gingivitis⇆paraneoplastic pemphigus(less frequent)
❾desquamative gingivitis⇆coronavirus disease-2019

➲xx bodies⇆periapical granuloma	**xx body⇆periapical(radicular cyst**
❶Russell bodies(plasma cell product)	❶Rushton bodies(cyst lining)
❷pyronine bodies(plasma cell product)	❷hyaline body(cyst wall)

➲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 near mucogingival junction)⇆ minocycline discoloration

➲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

➲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

➲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

➲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⇆HSV/VZV(varicella; chickenpox) infection
❷Tzanck cell⇆pemphigus

➲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⇆resemble amyloid(fibrin)
★xanthelasma(cutaneous xanthoma)⇆like cutaneous amyloid

➲xx facies⇆diseases

❶leonine facies⇆leprosy
❷leonine facies⇆Paget disease
❸munk(花栗鼠) facies⇆β-Thalassemia major

➲strawberry xx⇆diseases

❶strawberry tongue⇆scarlet fever
❷strawberry gingivitis⇆Wegner granulomatous

➲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

➲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

➲hyaline body⇆diseases

❶hyaline body(pulse granuloma/giant cell hyaline angiopathy) ⇆radicular cyst
❷hyaline body⇆lichen planus

❻Behcet syndrome(disease)➔①oral ②genital ③ocular
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 fibrous dysplasia(Jaffe-Lichtenstein syndrome, Mccune-Albright syndrome)

➲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

➲strawberry xx⇆diseases

❶strawberry tongue⇆scarlet fever
❷strawberry gingivitis⇆Wegener granulomatosis(granulomatosis with polyangitis)

➲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[Plummer-Vinson syndrome➔Fe deficiency anemia, oral/esophageal SCC)]
②with plasma cell gingivitis
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⇆inflammatory condition 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
❷ABC⇆fibrous dysplasia
❸ABC⇆CGCG

➲chondrosarcoama⇆with other diseases

❶chondrosarcoama⇆Ollier disease ❷chondrosarcoama⇆Maffucci syndrome

➲bone diseases⇆genetic changes

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
❾ osteosarcoma⇆①P53 ②RB1 ①MDM2 ④CDKN2A ⑤ATRX ⑥DLG2
❿chondrosarcoma⇆①MDM2 amplification ②IDH1,2 mutation
⓫aneurysmal bone cyst⇆USP6 translocation
✶Ewing-like sarcoma⇆①EWSR1-non-ETS fusion ②BCOR genetic alteration

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

114-1 midterm exam

1. Which of the following statements 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 statements 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 statements 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

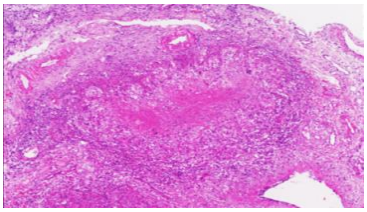
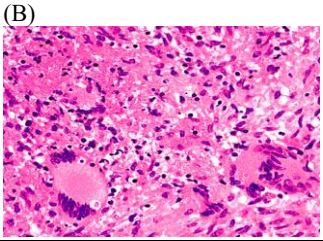
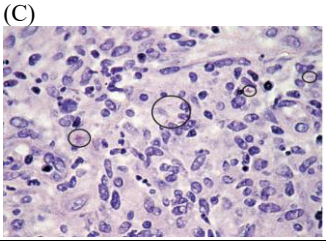
5. Desquamative gingivitis *cannot* be noted in: (Chapter 4)
(A) mucous membrane pemphigoid
(B) erosive lichen planus
(C) coronavirus disease-2019
(D) erythroplakia

6. Which statement 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)


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

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