Lumps and Bumps

-For the Oral Pathology Final Exam-

Constructed by your classmate, Andrew Vorona

Remember: “The hardest part about dental school is getting in…”

For Starters…

I did my best to limit the information presented in this Powerpoint to what I find important for the final exam. This being said, you will not find all of the information from the lecture handouts. In addition, you will find information that was mentioned in class and seemed important, but was not mentioned on the lecture handouts. My recommendation: Go over the two together. Hopefully you will find mine helpful. If not, please address all complaints/ questions/ revisions to Eric Turner (ericturnerjr@gmail.com).

Some comments about my color choices: I change the colors up frequently. For the most part, the differentiations are obvious, but just to clarify…

WHITE = Conventional text that may not stand out as crucial, but nevertheless is still extremely important.

GREEN = I use this to clearly identify the topic of each slide, which for the most part, is the name of the lump/bump being discussed.

RED = This is the color I use to highlight the text on slides that at least to me, appears slightly more important than that which is in **WHITE**.

BLUE = I use this to highlight the proper words/ descriptions/ diseases/ histological findings that are specific to a single disease. Basically, something that is blue is only identifiable to that specific pathology, meaning that it could quite possibly be a test question.

LESION COLORS: Just to help everyone out, the colors of specific lesions will be in their respected colors. They vary, but for the most part are somewhat consistent for what you would expect to fall in the realm of oral pathology.

And remember: Repetition is crucial for the comprehension/retention of this material. Regardless of how clearly it is presented, it will take a few times through to not only understand each pathology, but more importantly to differentiate them from one another. Along the way, do your best to clearly understand what makes each lump/bump different from ones similar, but not quite the same.

The Agenda For This Powerpoint Presentation:

While I do enjoy presenting the information we are responsible for in a clear and coherent manner, I recognize that some things are better left for class capture and the original lecture notes. The general purpose of this Powerpoint is to clear up many of the pathologies that on the lecture handouts, appear as multiple pieces of assorted information with no conceptual foundation. Because of this, I'll break down what exactly it is that I cover, and the things that still need to be covered in addition to what I present.

Things I WILL go over in this Powerpoint:

- The elements of a complete description for a lesion [from 10/13]
- Soft Tissue Tumors [from 10/13, 10/18, and 10/20]
- The differentiation between color changes, ulcers, and lumps/bumps [from the beginning of class on 10/25]
- A somewhat thorough review of the article [from 10/25]
- Salivary Gland Pathology [from 11/8 and 11/10]
- Hematologic Disorders [from 11/15]

Things that are your responsibility to learn/read/watch:

- Dr. Fornatora's presentation on Oral Cancer [from 10/25]
- Dr. Fornatora's presentation on HPV [from 11/1]
- Dr. Sciote's oral cancer prevention lectures [from 10/27 and 11/3]
- The Case Studies and Differential Diagnosis of Soft Tissue Masses [from 11/17, 11/22, 11/29, and 12/1]

To start off, lets begin with…Lesion Descriptions:

- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution

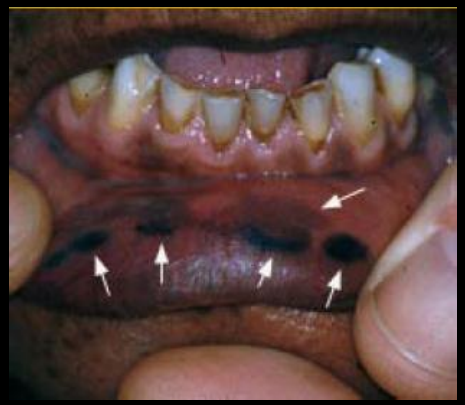
These are the descriptors for skin/soft tissue pathology presented to us in class. I will cover each one, beginning with an obvious emphasis on the different types of lesions.

So, beginning with… Types of Lesions:

I will go over each one in order, so be prepared to compare/contrast the information presented on the first couple of slides. Each one has a solid definition or size parameter which unfortunately simply needs to understood. I will make the descriptions as clear and concise as possible.

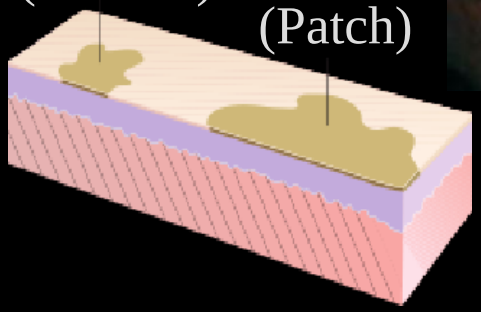
- Macule/macular
- Telangiectasia
- Petechiae
- Ecchymosis
- Papule
- Nodule
- Mass
- Plaque
- Vesicle, Bulla
- Pustule
- Fistula/parulis
- Cyst
- Ulcer
- Erosion
- Fissure

So, to start off…Macule/macular:

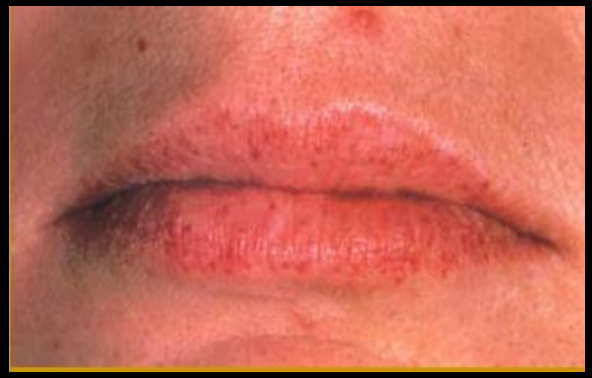


A **macule** is a change in surface color, <u>without</u> elevation or depression. They are: Non-palpable, either well or ill-defined, and variously sized, but usually not exceeding **5-10cm at its widest point.**

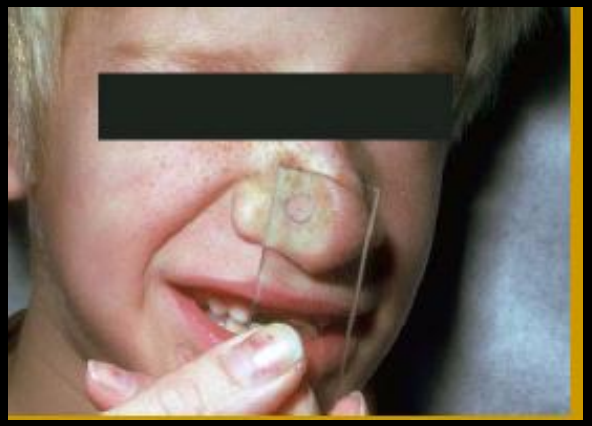
[Anything larger than this would be considered a **patch**.]



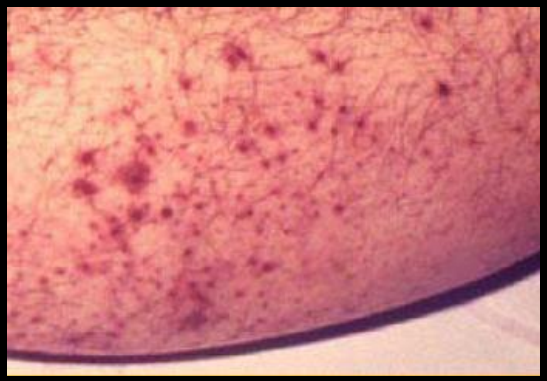
Telangiectasia:



A **telangiectasia** represents an enlargement of superficial blood vessels to the point of being visible. For diagnosis, you need to apply pressure with a glass slide to see if it blanches. Being enlargements of superficial blood vessels, telangiectasia do blanch, and are therefore Diascopy (+).



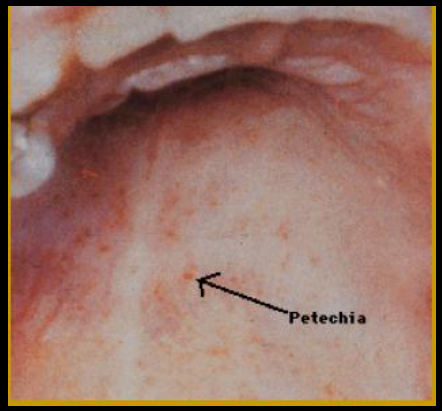
Petechiae:



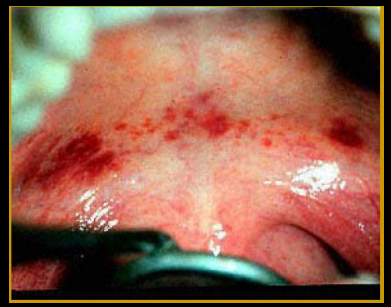
A **petechiae** is a small (1 - 5mm) **red** or purple spot on the body, caused by a minor hemorrhage (broken capillary blood vessels). They will not blanch because they are a pathology caused by bleeding into tissue, and are not directly related to discoloration caused by blood vessels. Therefore, they are Diascopy (-).

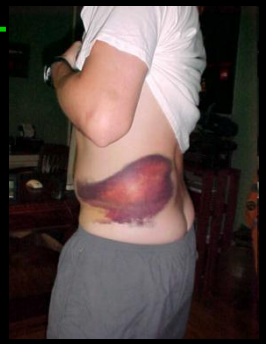
REMEMBER: 1 - 5 MM!

Greater than 5mm is referred to as an Ecchymosis (read on)



Ecchymosis:



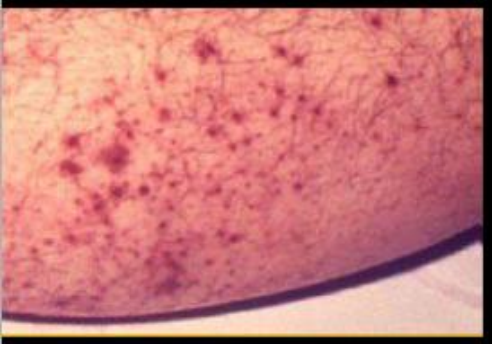


An **Ecchymosis** is the escape of blood into the tissues from ruptured blood vessels. To be considered an ecchymosis and not a petechiae, the diameter at the largest point **must be greater than 5mm**. Expect the same result for blanching [Diascopy (-)].

Of note, a **hematoma** is a localized collection of blood outside the blood vessels, usually in liquid form within the tissue. This distinguishes it from an ecchymosis, which is the spread of blood under the skin in a thin layer, commonly called a bruise.

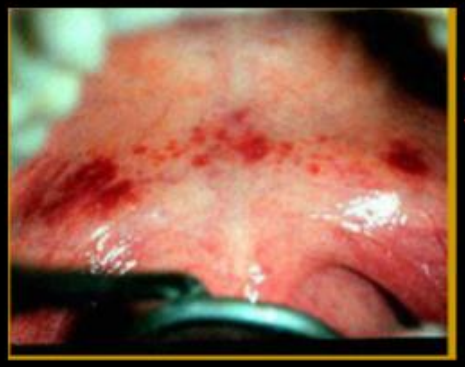
[Simply put, with a hematoma, expect to see inflammation.]

So lets quickly review/compare the 3…



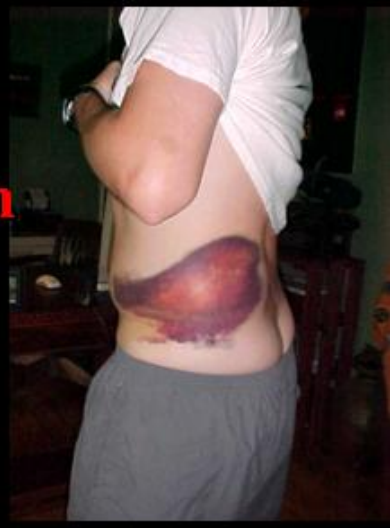
Petechiae

5mm <



Ecchymosis

Inflammation <

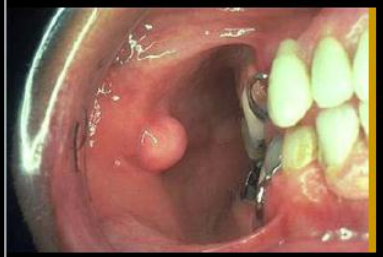


Hematoma

Now onto… Papules, Nodules, and Masses:

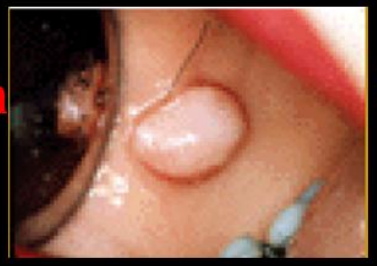
All three are elevated lesions, but of different sizes respectably.

Papule: <5mm
Nodule: 5mm – 2cm
Mass: >2cm



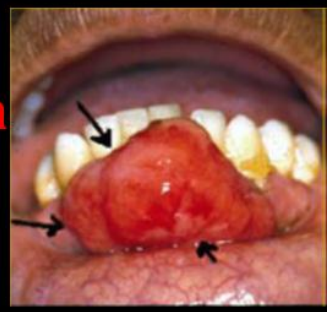
Papule

5mm <



Nodule

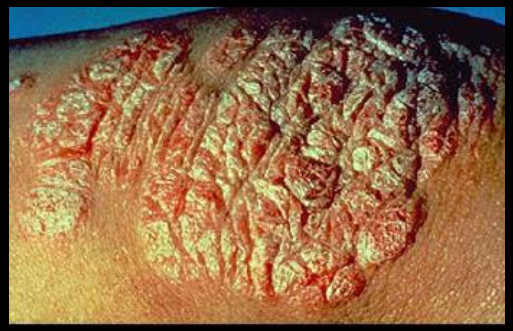
2cm <



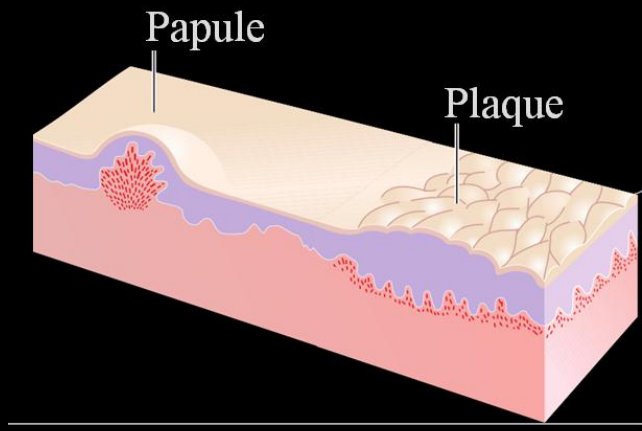
Mass

Onto…

Plaque:

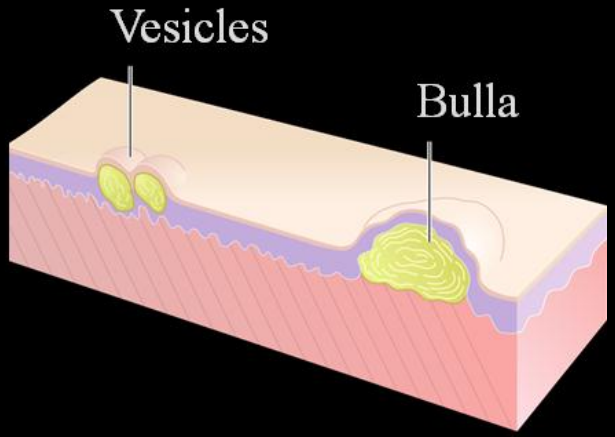


A **plaque** has been described as:
a broad papule, as an elevated, plateau-like lesion that is greater in its diameter than in it's depth.



Vesicle/Bulla:

- A **vesicle** is a circumscribed, fluid-containing, epidermal elevation generally considered less than 5mm in diameter at the widest point.
- A **bulla** is a large vesicle described as a rounded or irregularly shaped blister containing serous or seropurulent fluid, equal to or greater than 5mm.

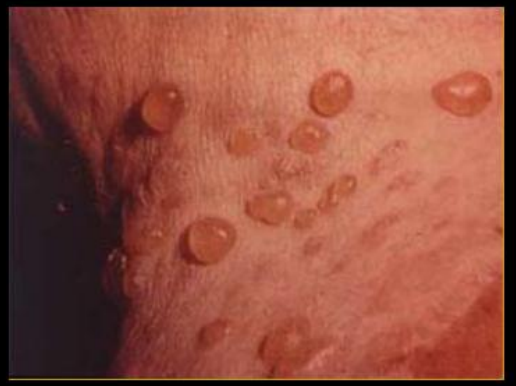


So…

Vessicle

5mm

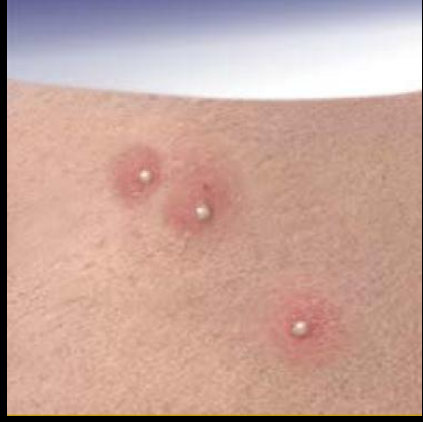
<



Bulla

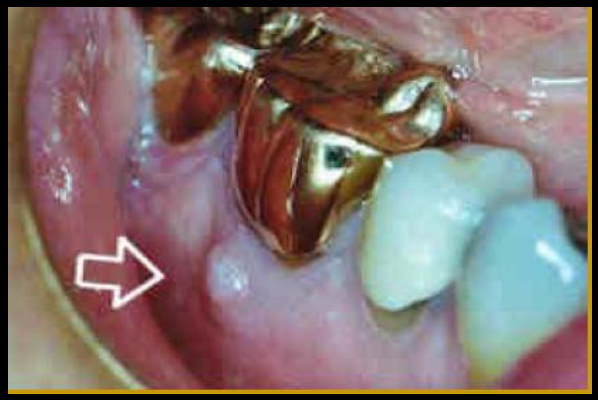
Pustule:

A **pustule** is a small elevation of the skin containing cloudy or purulent material usually consisting of necrotic inflammatory cells. These can be either **white** or **red**.



Fistula/Parulis:

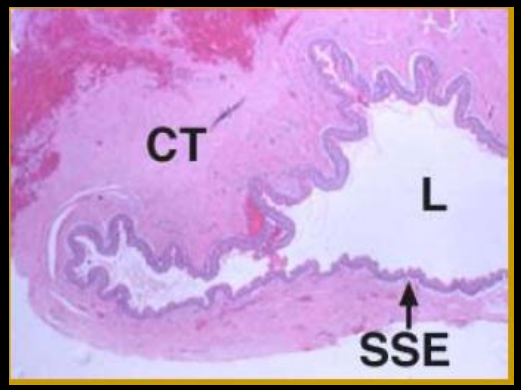
- A **fistula** is an abnormal connection or passageway between two epithelium-lined organs or vessels that normally do not connect.
- A **parulis** is a dental abscess, converted into a cyst with chronic drainage through a fistulous tract.



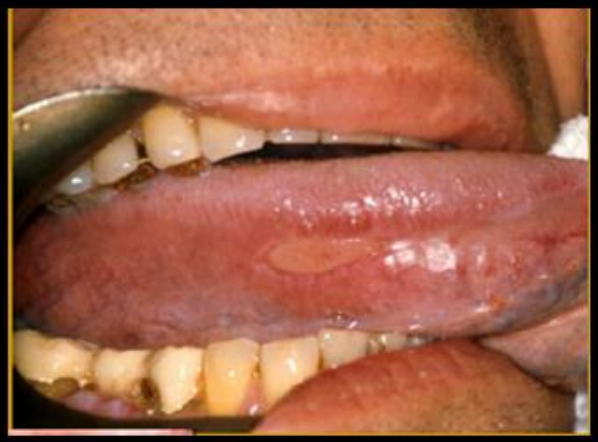
(They are essentially the same thing, but a **parulis** is a **fistula** that arises strictly from dental anatomy.)

Cyst:

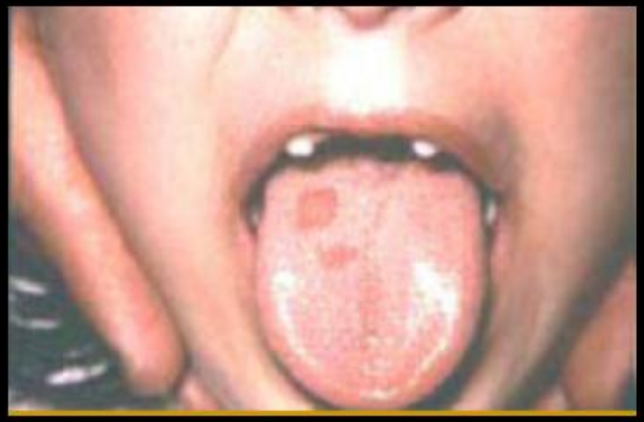
A **cyst** is an epithelial-lined cavity surrounded by a connective tissue wall containing liquid, semi-solid, or solid material.



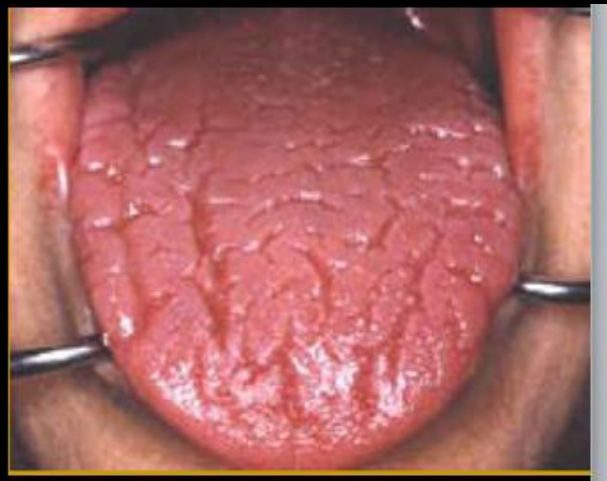
Ulcers/Erosions/Fissures:



Ulcer

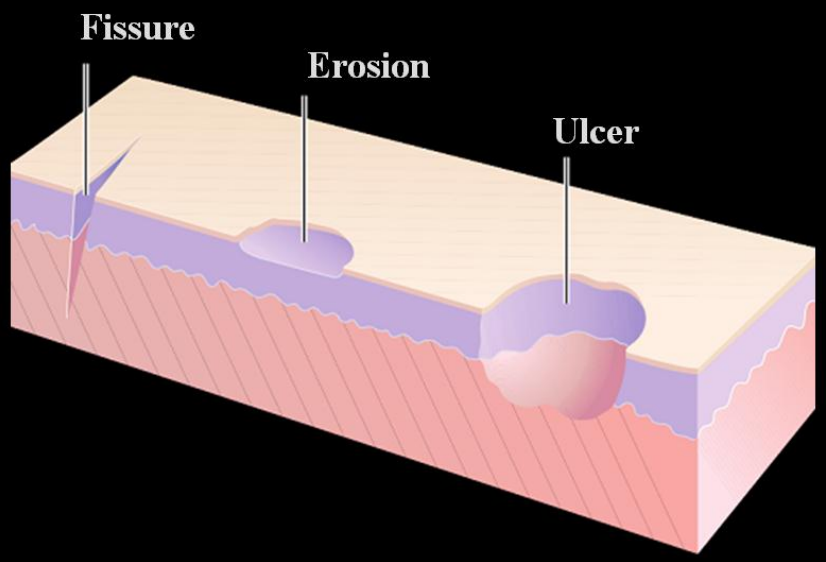


Erosion



Fissure

- An **ulcer** is a discontinuity of the skin exhibiting complete loss of the epidermis and often portions of the dermis and subcutaneous fat. It often appears yellow/granular in appearance.
- An **erosion** is a discontinuity of the skin exhibiting incomplete loss of the epidermis. It is moist, circumscribed, and usually depressed.
- A **fissure** is a crack in the skin that is usually narrow but deep.

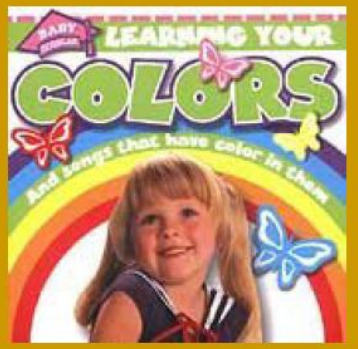


Now lets continue on with the other types of descriptions that can be used for oral lesions… Color:

- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution

Any questions or further clarification on the usage of the color palate can be directed towards certified colorologist, Eric Turner (ericturnerjr@gmail.com).

- Brown
- Yellow
- Blue-gray
- White
- Red

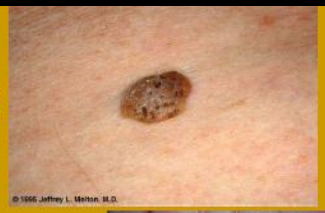


Border:

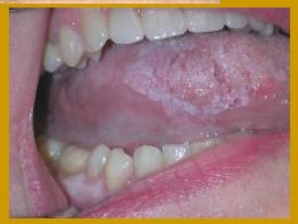
- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution

(The term '**umbilicated**' refers to any wound on the skin that has a depression in the center and resembles the navel or the umbilicus to a certain extent.)

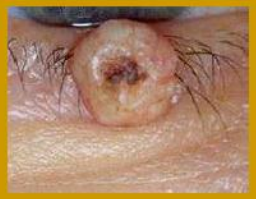
- Well defined



- Poorly defined



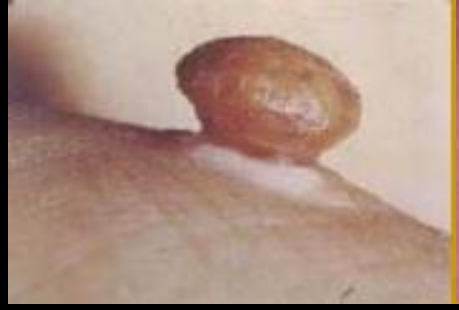
- Umbilicated



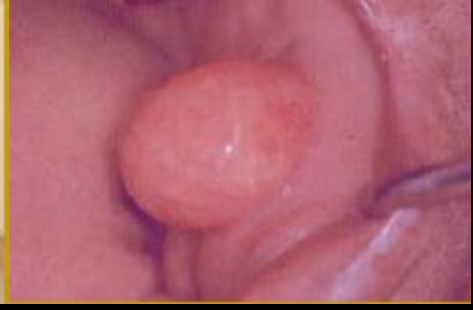
Shape:

- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution

- Round
- Oval
- Pedunculated *(on a stalk)*
- Sessile *(broad base, attaching at the broadest point)*



Pedunculated

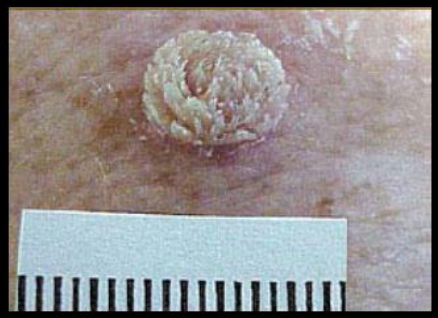


Sessile

Surface Changes:

- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution

- Smooth
- Ulcerated
- Papillary/Verrucous
- Crusted



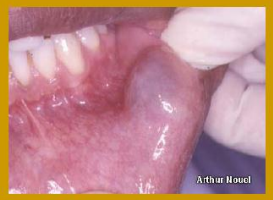
Papillary/Verrucous

Crusted

Palpation:

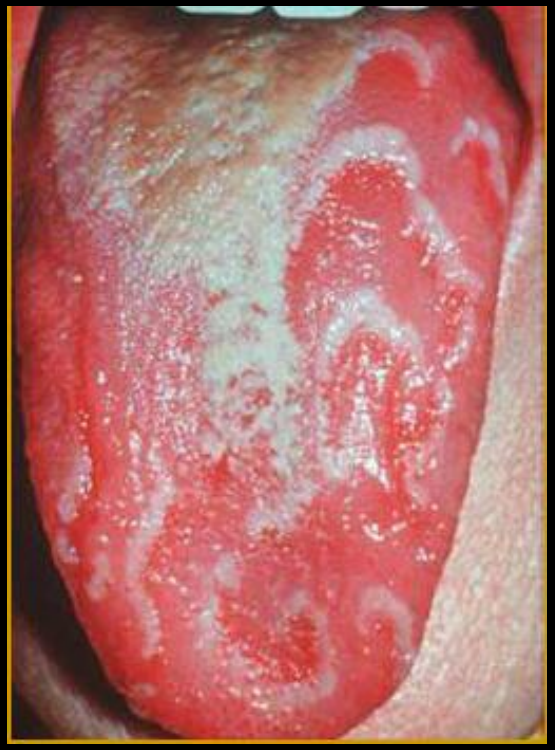
- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution

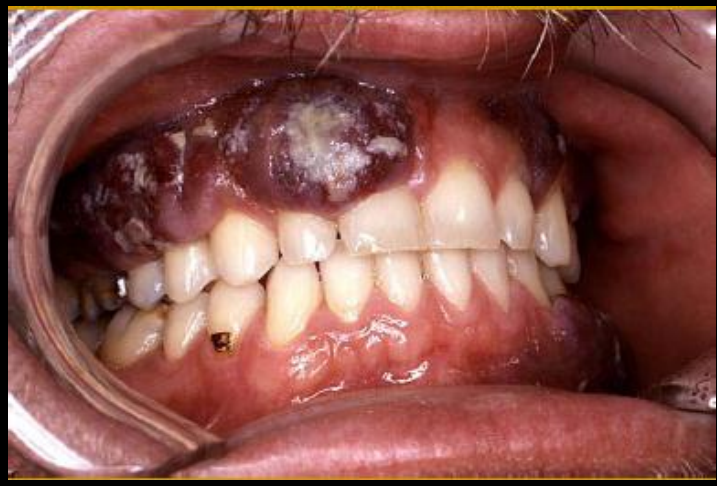
- Consistency
  - Soft
  - Firm
  - Hard – bony
  - Fluctuant
    - containing fluid
- Mobility
- Sx (tenderness,etc.)

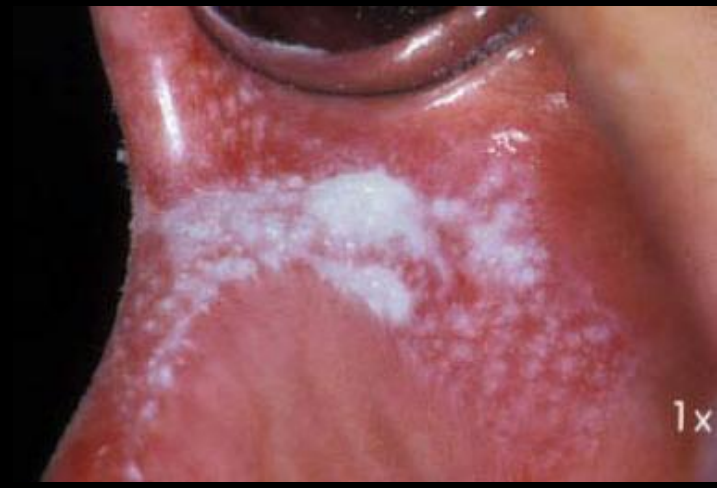


Class Exercise:

- Type of lesion
- Color
- Border
- Shape
- Surface
- Palpation
- Location
- Size
- Distribution







So we spent a decent amount of class time practicing applying these nine descriptions to three different lesions of the mouth. Definitely take the time to at least do it in your head. Further clarification would best come from Dr. Fornatora via class capture (10/13).

Now that we have covered how to completely describe oral lesions, lets transition over to-

Soft Tissue Tumors:

(Chapter 12 from the book)

CHARACTERISTICS OF NEOPLASMS

	Benign neoplasms	Malignant neoplasms
Growth rate	Slow growth	Fast growth
Demarcation	Encapsulated	Non-encapsulated
Mobility	Movable	Fixed
Growth pattern	Expansive	Invasive, tissue destruction
Histology	Well differentiated cells	Poorly differentiated cells
Spread	Local spread only	Metastasis (distant spread)

Notice that **benign** neoplasms are movable while **malignant** neoplasms are fixed in place. **Benign** tumors tend to grow slowly, are encapsulated, and tend to grow like a cyst. **Malignant** tumor cells invade, and the lesion tends to therefore be poorly differentiated.

NOMENCLATURE OF TUMORS

Tissue or cell of origin	Benign tumor	Malignant tumor
Fibroblast	Fibroma	Fibrosarcoma
Fat cell	Lipoma	Liposarcoma
Smooth muscle cell	Leiomyoma	Leiomyosarcoma
Striated muscle cell	Rhabdomyoma	Rhabdomyosarcoma
Blood vessels	Hemangioma	Angiosarcoma
Lymphoid tissue	Lymphangioma	Lymphangiosarcoma

- Recognize that if the tumor has "-sarcoma" as a suffix, it is malignant.

The likelihood of seeing these as oral pathology varies. **Fibromas** are incredibly common in the oral cavity, while **Rhabdomyomas** are hardly ever seen. (After all, fibroblasts are more commonly seen in the oral cavity as opposed to striated muscle cells.)

Lets stop with the learning for a second to better clarify…

The Clinical Norms Of The Pathologies We Are Going to Discuss:

At least for me, one of the hardest things to conceptually remember about the many pathologies that we have covered thus far is the group of people that are most commonly affected by them clinically (age, sex, gender, etc.). Because of this, I will incorporate visual pictures on the slides for each of the pathologies that we cover representing the stereotypical group in our society that disease is most likely to affect. The following slide contains a list of images that I use with their respected descriptions. I provide descriptions for ten of them, but throw a few more in later. They're fairly evident, so even for the ones I don't take the time to explain, any intelligent person should be able to deduce the populations that they represent.

To keep things consistent, for each pathology, this picture will be located in the upper right hand corner, bordered by an orange outline. No picture for a specific pathology implies that no specific group was mentioned in lecture or the lecture notes. I give an example on this slide. (This picture would illustrate a pathology that affects middle-aged African Americans with no prevalence for either gender.) My intention in doing this is to take advantage of the cognitive fact that it is much easier to remember pictures rather than factual information that changes with each disease that we cover.

This methodology may seem confusing at first, so take a minute on the next slide (not to memorize), but rather understand what each picture roughly represents. Also, using only roughly 15 pictures as stereotypes, the picture that I provide for a specific pathology may not be the ideal socio-group. However, it should prove adequate for an understanding of the respected etiologies.

The Clinical Stereotypes of Oral Pathology:

- Represents older adults equally of both genders and all races

- Represents older female adults equally of all races

- Represents older obese adults equally of both genders

- Represents middle-aged female adults equally of all races

- Represents female young adults of all races

- Represents young/middle-aged adults equally of all races and both genders

- Represents female babies equally of all races

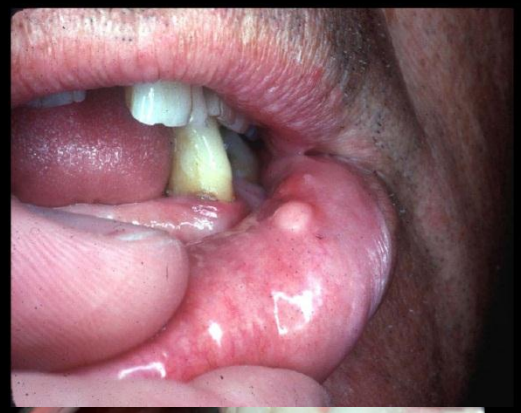
- Represents children equally of all races and both genders

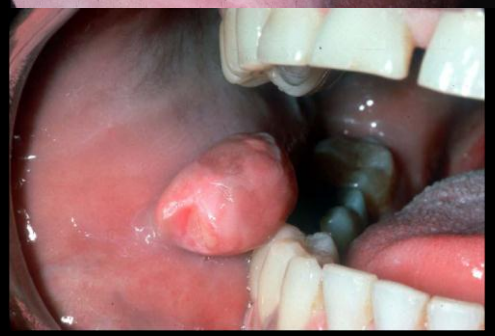
- Represents male children equally of all races

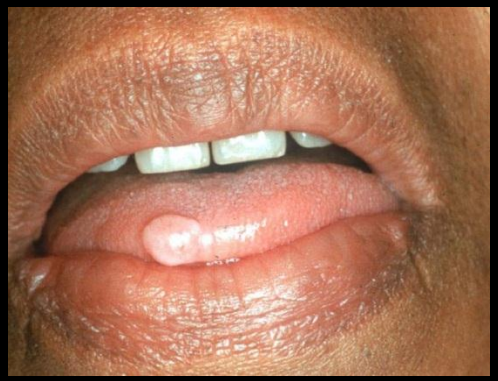
- Represents female children equally of all races

Lets being with a Fibroma:

Caused by chronic "low-grade" trauma. More intense trauma would more likely cause an **ulceration**. Because of this, fibromas are considered to be more of a hyperplasia than a neoplasia.



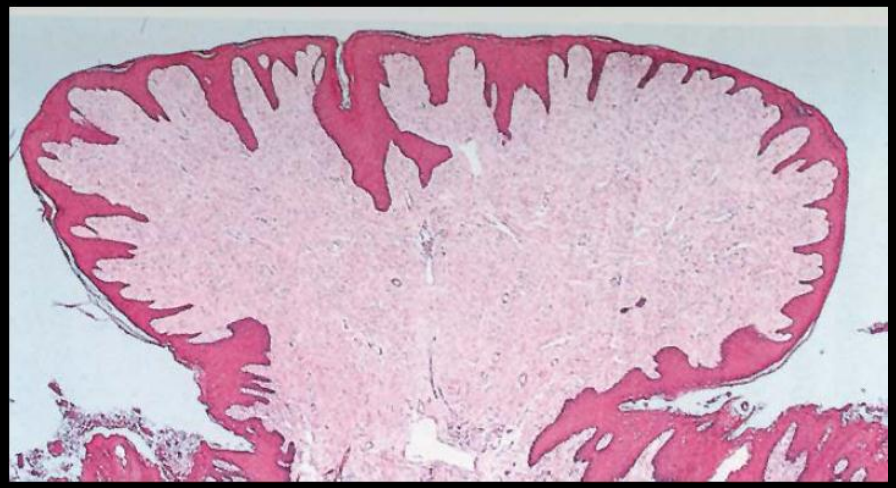




- The most common tumor (common in adults)
- Composed of fibrous connective tissue
- Most common places to get them are places of chronic irritation (the buccal mucosa for example)
- Feels smooth like the adjacent tissue. (Can be considered a papule that does not move with the fingers).

Treatment: Excise/remove surgically and it typically does not return.

Histologically: a modular mass composed of fibrous connective tissue

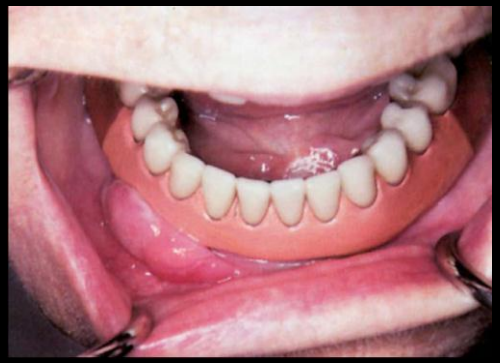


*(In this slide, notice that the fibroma is **pedunculated**. Squamous stratified epithelium on the outside (dark pink) and fibrous connective tissue on the inside (light pink).)*

Epulis Fissuratum:

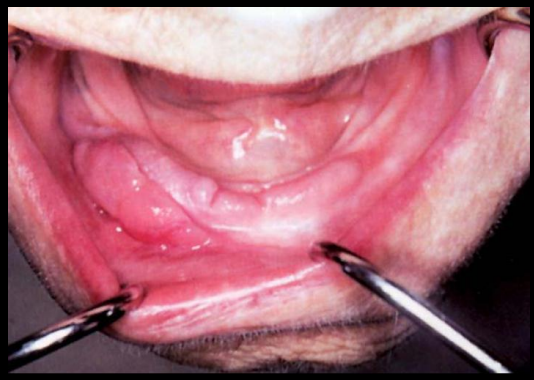
Epulis-any tumor of the gingiva or alveolar mucosa

Another example of fibroblast proliferation. In this case, it is at the flange of an ill-fitting denture.

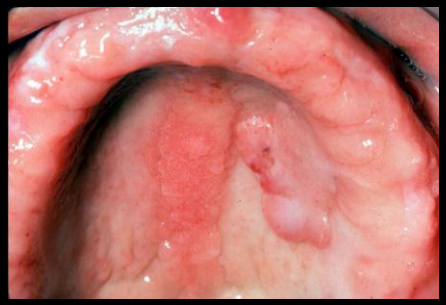


- Happens in conjunction with removable dentures
- Most common in anterior portions of the jaw/alveolar ridge (dentures tend to tip forward)
- Depending on the trauma involved, patients can present with secondary ulcerations

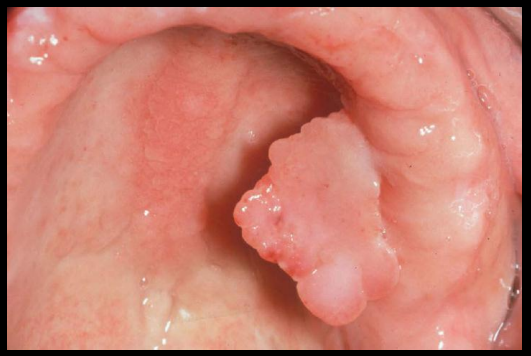
Treatment: Remove the denture to allow tissue to heal (for example at night), or if severe enough, remove surgically.



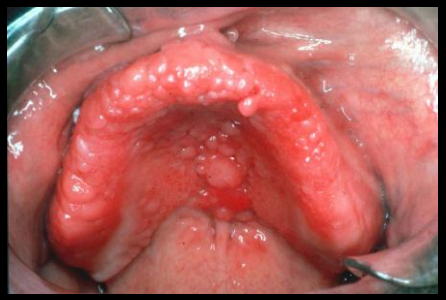
Leaf-Like Denture Fibroma:



- Occurs underneath the hard palate or any surface of a denture
- Much less common than **Epulis Fissuratum**
- Presents as a flat, **pedunculated** lesion of pink color



Inflammatory Papillary Hyperplasia:



Reactive tissue growth underneath a denture secondary to:

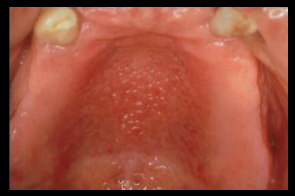
A: Ill-fitting denture

B: Poor denture hygiene

C: Wearing denture 24hrs

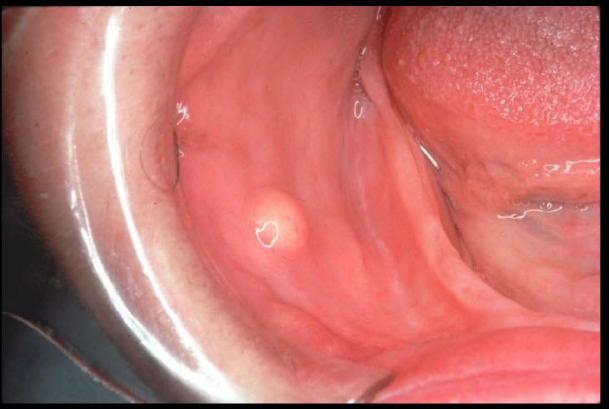
- Usually found on hard palate/ palatal vault.

Treatment: Remove dentures long enough for erythema to clear. Fungal infection may have to be treated (Nystatin). Even after medicine, patient may still present with papillary projections, which may be surgically removed if necessary

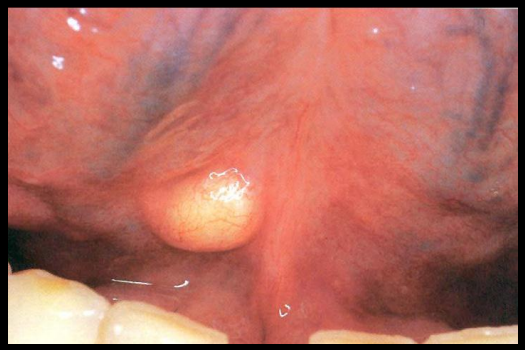


Lipoma:

A benign fatty tumor which is common to see outside the oral cavity (trunk/extremities) in obese adults



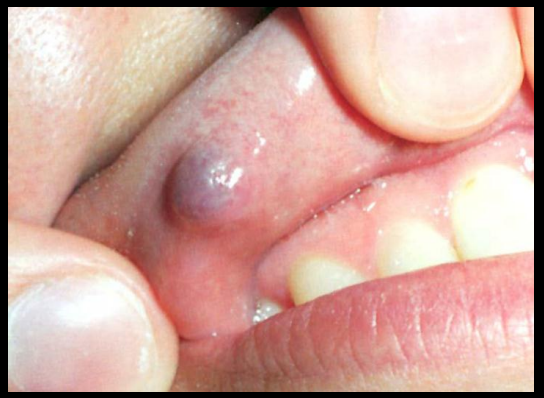
- **Most common soft tissue tumor**
- Present very similar to fibromas (sometimes hard to tell apart)
- Common in fatty areas of the mouth (buccal fat pad/mucosa), which is also a common place for fibromas
- Usually has a yellowish hue

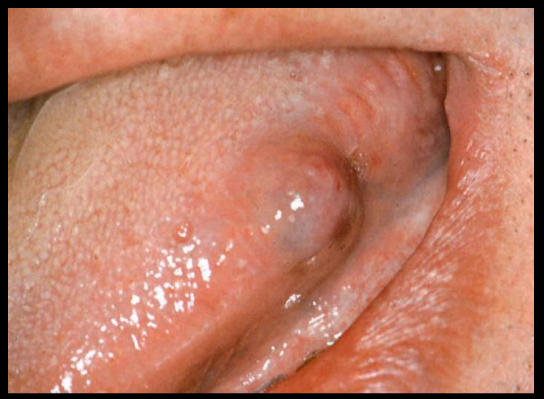


Vascular Leiomyoma:

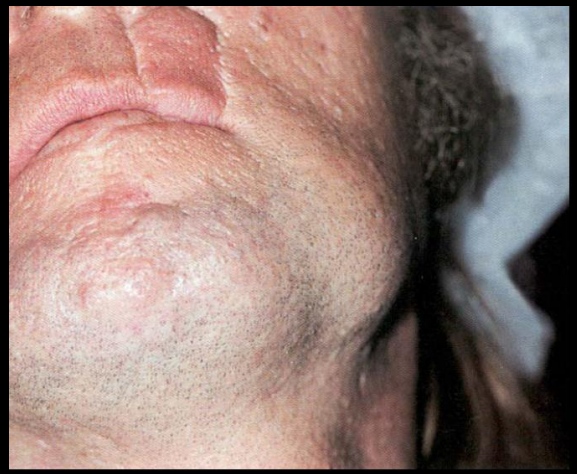
A benign tumor of smooth muscle (in the oral cavity, this would be the area surrounding blood vessels). Therefore, you see a proliferation of blood vessels as well

- Nodule or mass that is either pink or blue in color
- Often slow growing, but can be painful
- Can be located in many different areas of the mouth (common in uterus since it is large collection of smooth muscle)





Rhabdomyoma:



- Benign tumor of striated muscle
- Uncommon (However, **Rhabdomyosarcoma** is not uncommon)
- Associated with the disease **Tuberous Sclerosis**
- Also used to describe hamartomas located in the heart
- Treatment: surgical excision with reoccurrence being uncommon

Usually present as extra-cardiac tumors located in the head/neck. There are two different types of **Rhabdomyomas**:

-**ADULT TYPE**: slow growing nodule located on floor of mouth, soft palate and tongue, in middle aged male patients.
-**FETAL TYPE**: Slow growing nodule on face and preauricular area in male children

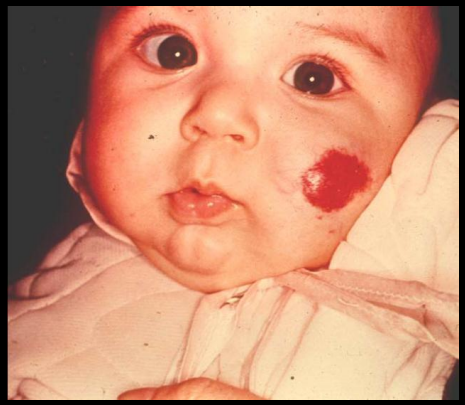
Hemangioma:

Begin (around 6 months of age) as small **pink** macules, and over time grow to become larger **red** raised tumors. Later, most will stabilize, darken, and resolve.

- Benign tumors of blood vessels
- **Most common tumor of infancy** (present in 10% of 1 year olds, 20% of patients have multiple lesions)
- Head and neck the most common location
- Most resolve on their own (50% by 5 y/o, 90% by 9 y/o)

Given it's early onset, there are three possible ways to describe a Hemangioma:

1. **Early lesions:** Endothelial cell proliferation ("**juvenile**" or "**cellular**" hemangiomas)
2. **Mature lesions:** Vascular lumens begin to form capillary spaces ("**capillary**" hemangiomas)
3. **Involuting lesions:** Vessels dilate ("**cavernous**" hemangiomas)



Vascular Malformations:

(Present at birth but do not involute over time)

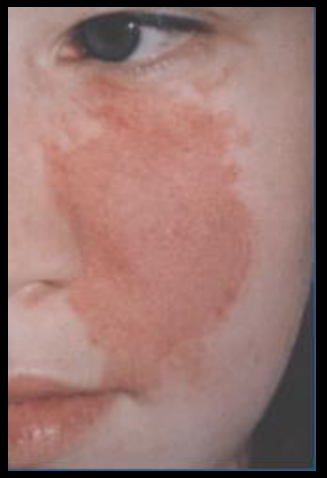
The different types (4) are classified by both the size and the flow of the associated vessels (capillary/arterial/venous)…

1. **Capillary Malformations:** "Port Wine Stains/birthmarks"
2. **Low Flow/Venous Malformations:** thin walled veins having a low blood flow rate
3. **Arteriovenous Malformations (AVM):** arterial/venous systems connected directly without any capillary distribution (can be serious given the high flow rate)
4. **Intrabony malformations:** varying flow rate, but often high flow (from arteries). This type of vascular malformation can consist of arterial, venous, and capillary vessels.

[Vascular Malformations]

Capillary Vascular Malformations "Port Wine Stains":

- Pink-purple large macular lesions that arise at birth, do not go away, and become darker/more elevated over time
- Mostly macular, but can sometimes have slightly elevated areas
- Most commonly seen on the face (associated with **Sturge Weber Syndrome**)



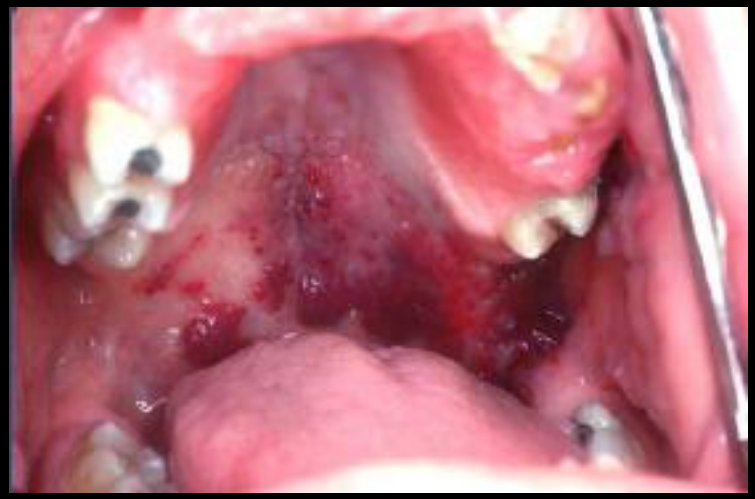
[Vascular Malformations] Low-Flow Venous Malformations:

•The appearance varies depending on the size of the vessels and how big the overall vascular malformation is.

•Often appears **deep red** or **blue**, elevated, and compressible

•Present at birth, becomes darker over time, and eventually develops thromboses and phleboliths (calcium deposits)

(The first question that should be asked to the patient is if they have had it since birth.)



•Will be Diascopy (+), unless there are thromboses or phleboliths constricting blood flow

[Vascular Malformations]

Arteriovenous Malformations (AVM):

- Caused by developmental problem occurring during embryogenesis resulting in a misconnection between arteries and veins
- Can remain unknown until later in life when the patient receives an AV Malformation (in the brain for example)
- They are all present since birth
- They often persist and are first recognized with pain, bleeding, and warm overlying skin which may ulcerate
- Often recognized with a stethoscope (thrill/bruit)

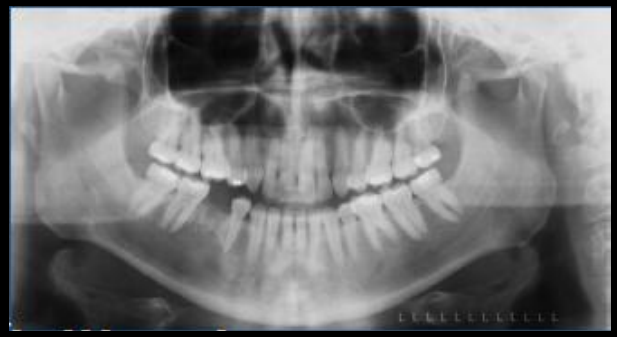
[Vascular Malformations]

Intrabony Vascular Malformations:

Things that indicate an intrabony vascular malformation:

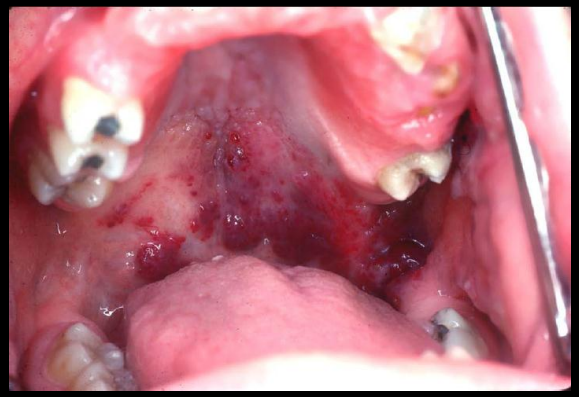
1. Spontaneous/uncontrollable bleeding occurring through the socket of an extracted tooth
2. A tooth becomes spontaneously mobile from resorbing bone underneath

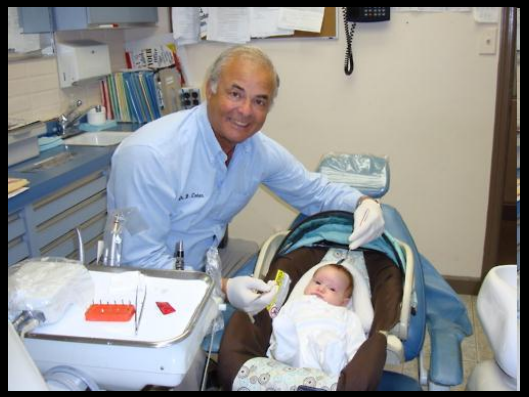
- Usually appear as a **multilocular radiolucency**
- More commonly seen in the mandible (2:1)
- Clinically: jaw expansion (cortical) with or w/o pain
- **Can cause a sunburst periosteal reaction**

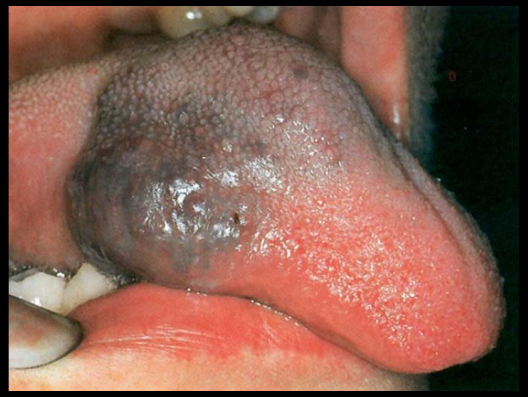


[Vascular Malformations] Diagnosis:

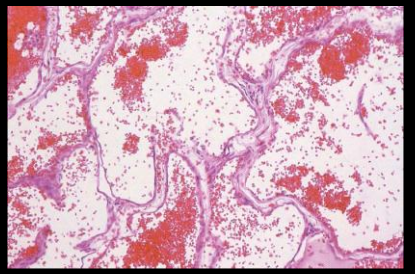
Diagnosis needs to first be based on clinical appearance and patient history (vascular malformations should be present since birth and continue to grow). Move onto biopsy only after ruling out the lesion being of high-flow origin to minimize unforeseen bleeding problems.







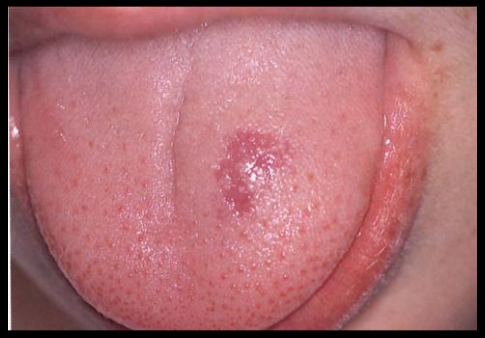
[Vascular Malformations] Treatment:

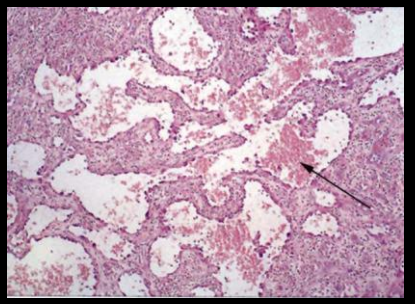


Vascular malformations don't always need to be treated. If treatment is necessary, **angiography** is needed at first, regardless of the lesions size, to identify if the feeder vessels are of high-flow origin. If they are, you may need to sclerose (induce fibrosis) or embolize (occlude) the vessels.

Capillary Vascular Malformations:

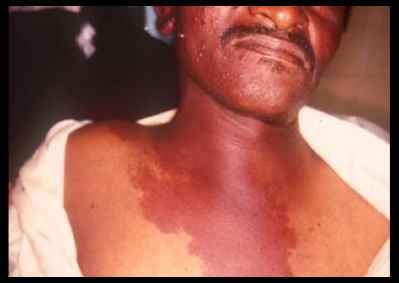
Laser Removal preformed most commonly due to being cosmetically unpleasing (especially on the face, hands, and arms).

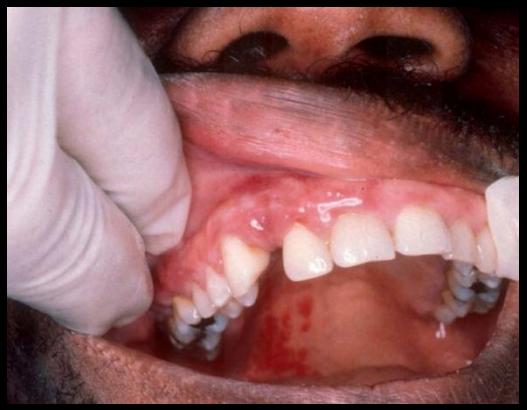




Sturge-Weber Angiomatosis (Sydrome):

There are many syndromes associated with vascular malformations. We only cover **Sturge-Weber** since it presents with lesions in the oral cavity.





•Vascular malformations in the face and brain

•Completely developmental (no genetic factor)

•Port Wine Stains (Nevus): Usually unilateral (close to the midline), with distribution following the distributions of the **Trigeminal Nerve**.

•Associated with **Leptomeningeal Angiomas** that usually present with calcifications within the brain following major vessels linearly (**tram line calcifications**)

•Patients present with mental retardation, motor problems, ocular problems (glaucoma), convulsions, etc.

Oral Lesions: same side hypervascular change and possible gingival hyperplasia

Lymphangioma:

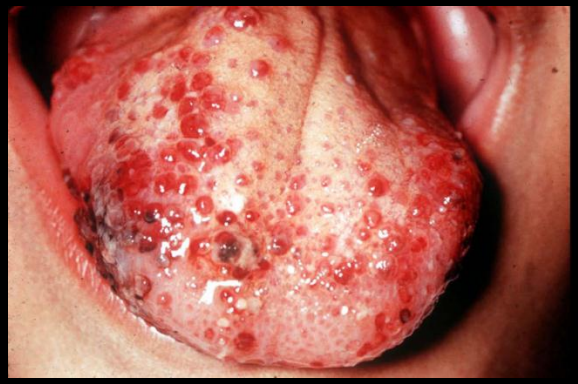
(The lymphatic equivalent of a hemangioma and are also present since birth.)

- Most likely **hamartomas** (sequestration of lymphatic tissue in the correct location)
- Very common to head/neck (75% of those reported)

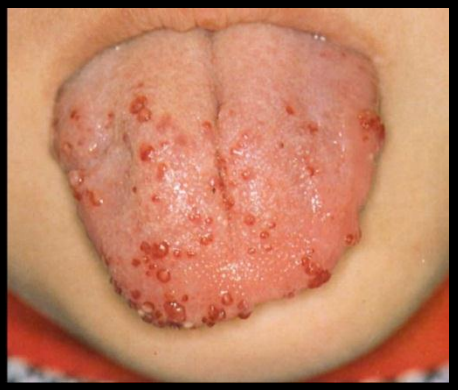
Proper nomenclature based on size:

1. **Lymphangioma simplex (capillary lymphangioma):** small vessels
2. **Cavernous lymphangioma:** larger vessels
3. **Cystic lymphangioma (cystic hygroma):** very large cystic spaces

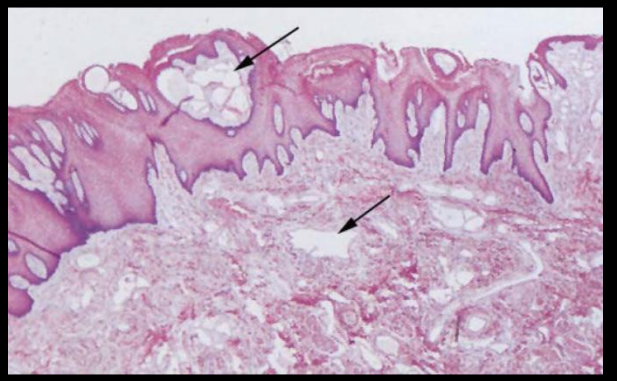
The size of lymphatic vessels is much smaller than blood vessels, and depending upon availability of surrounding space, **lymphangiomas** can proliferate much more easily. Even though **lymphangiomas** are less severe than **hemangiomas**, treatment usually is more difficult due to the smaller size of the malformation.



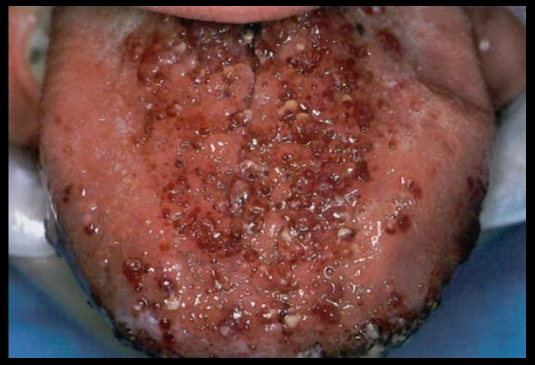
Lymphangiomas are unique in appearance when compared to the other disorders that we discuss. It is often a combination of intensely **red** and **white** tiny vessels that are evident superficially on the tongue, but also have subcutaneous involvement that causes the appearance of swelling/inflammation.



Lymphangioma (cont'd):



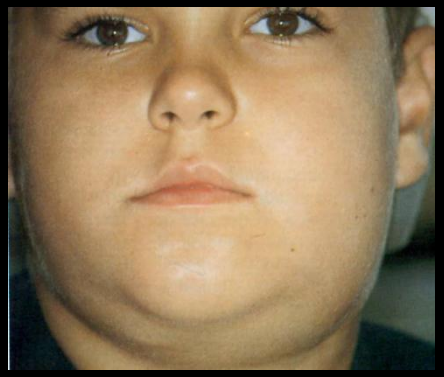
Histology: Lymphatic abnormality that extends to the superficial connective tissue, but originates deep within the tissue.



Remember: White vesicles on the tongue are not an immune reaction, but rather the collection of lymphatic fluid as a result of the underlying **hamartoma**. During differential diagnosis, **Lymphangiomas** will be extremely evident superficially.

Cervical Lymphangiomas:

- Located specifically in the posterior triangle of the neck as a soft fluctuant mass that may or may not extend into the oral cavity, or it may even downward into the mediastinum and cause airway obstruction.



Treatment: Often they are not removed (total removal is difficult), but sometimes they can be surgically excised. They are poorly-defined and commonly reoccur. Some doctors recommend no treatment for **Lymphangiomas** of the tongue unless they are enlarging. (Large neck **Lymphangiomas** may cause airway obstruction and have a mortality rate of roughly 5%.)

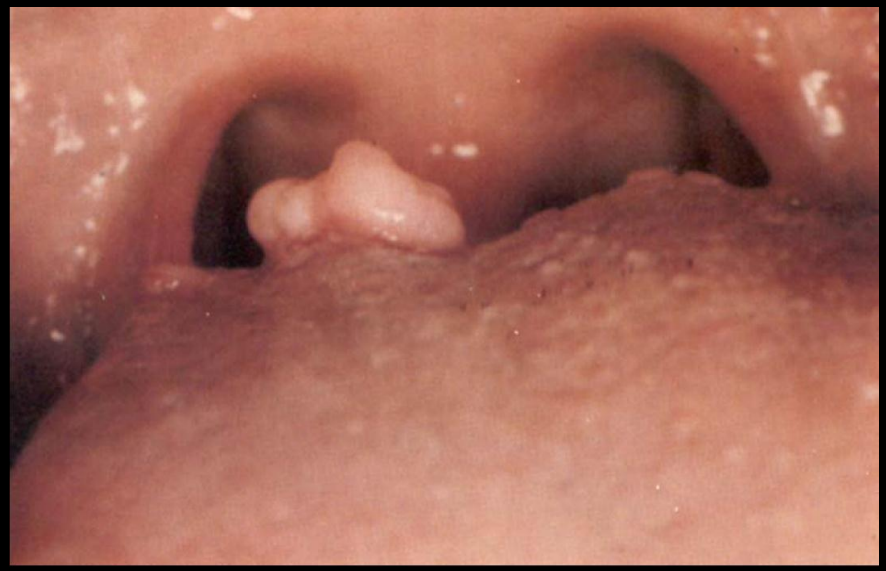
Choristoma:

(a proliferation of "normal" tissue in an abnormal location)

- We first learned about **choristomas** last semester when discussing **Fordyce Granules** as developmental abnormalities. **Fordyce Granules** are **sebaceous glands** found in abnormal locations within the oral cavity (Hence being a **choristoma**.) Just like sebaceous glands, soft tissue can present as **choristomas** as well.
- **Soft Tissue Choristomas** usually appear in the oral cavity as **bone** and **cartilage**:
  1. Bone Choristoma = **Osseous Choristoma**
  2. Cartilage Choristoma = **Cartilaginous Choristoma**
- The most common location for a **choristoma** of the oral cavity is the Posterior Dorsal Tongue (85%) as a firm nodule with a smooth surface.

When doing differential diagnosis, observe the location of the lesion:

- Areas of the tongue that are prone to frequent irritation (ventral, etc.) will most likely produce a **fibroma**
- The **dorsal tongue** is an infrequent location for irritation, so (as seen in this picture) assume that it is a **choristoma**.



Treatment: Local surgical excision.

Nerve Tissue Tumors:

(The tongue is a very common place to receive tumors of nerve origin. We will discuss four different tumors that fall into this category.)

The tumors that we will discuss originate from one of three different types of neuronal cells:

1. Neurons
2. Perineural Fibroblasts
3. Schwann Cells

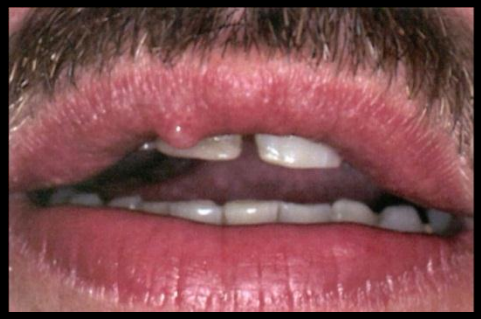
The four different types of nerve tissue tumors that we will discuss are:

- **Traumatic Neuromas:** are not considered a neoplasm, but rather a proliferation of a damaged nerve bundle. It is a result of trauma.
- **Neurilemoma (Schwannoma):** a true neoplasm of the **Schwann Cells** that produce the myelin sheath around nerves.
- **Neurofibroma:** ***The most common type of peripheral nerve neoplasm.*** It is composed of a combination of **Schwann Cells** and **Perineural Fibroblasts**. It is associated with **Neurofibromatosis (von Recklinghausen's disease of the skin)**, where multiple **neurofibromas** are seen.
- **Multiple Endocrine Neoplasia (Type 3):** There are multiple types, but **Type 3** is the only form associated with an oral component. Here, **Neuromas** of the oral mucosa are evident.

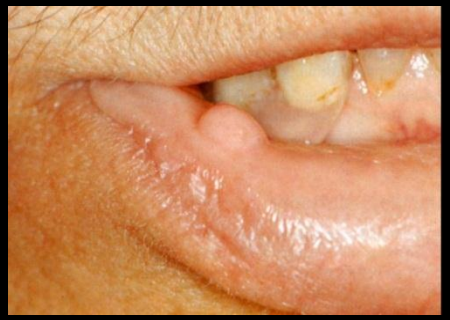
Traumatic Neuroma:

Through trauma, or secondary to surgery, any form of laceration can lead to the severing of nerves. In most cases, the nerves repair themselves. Sometimes though, instead of repair, a traumatic induced proliferation of nerve tissue results in a **Traumatic Neuroma.**

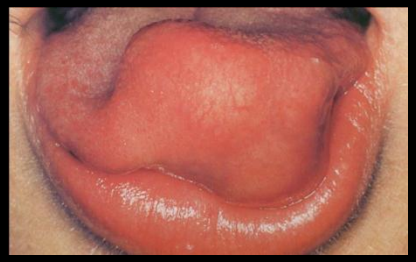
- Presents as a non-ulcerated nodule with a smooth surface
- Contrary to being a result of nerve damage, only a quarter to a third (25%-33%) of **Traumatic Neuromas** present with pain.
- More common in areas with larger nerves (mental nerve area, tongue, and lower labial mucosa)
- Can present intraosseously, but that is less common than a soft tissue appearance.



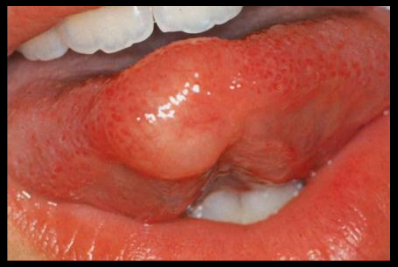
Treatment: Surgical excision of the affected nerve bundle. There is a rare recurrence, but pain can persist.



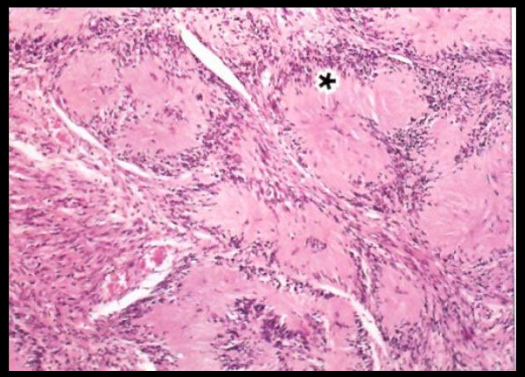
Neurilemoma (Schwannoma):



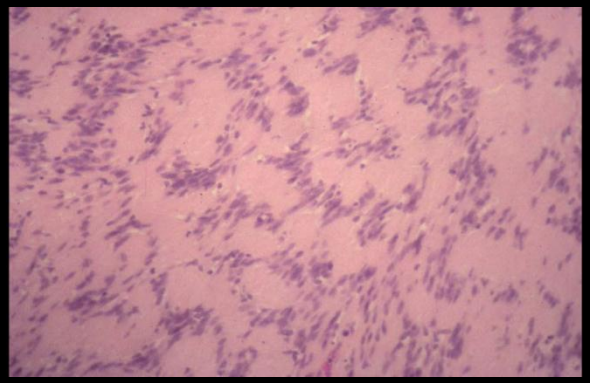
An uncommon neoplasm of the body, but almost half (48%) occur in the head and neck. It is a slow growing nodule or mass that (just like other nerve tissue tumors) is typically seen on the tongue.



- Can also occur in bone however (presents as a **unilocular radiolucency**)
- If found in bone, can produce pain/paresthesia. (Soft tissue **Schwannomas** are usually asymptomatic.)



("*" represents a Verocay Body)



Treatment: Surgical excision with hardly any recurrence. Malignant transformation is rare, and when seen, is usually associated with an underlying syndrome.

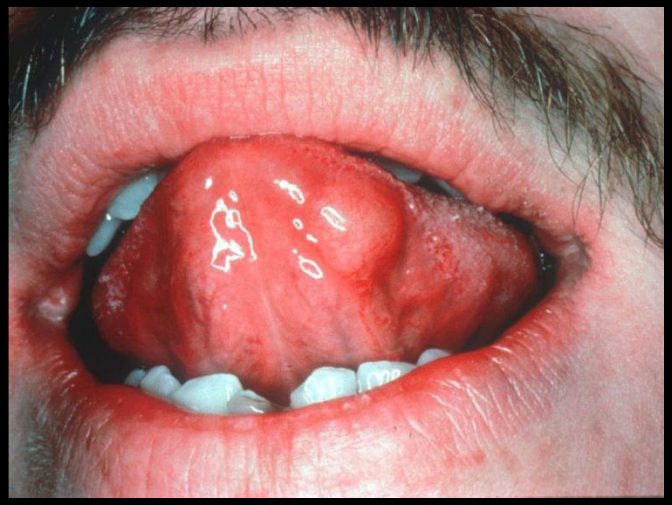
Histology: There are two different types of histological patterns seen with Schwannomas…

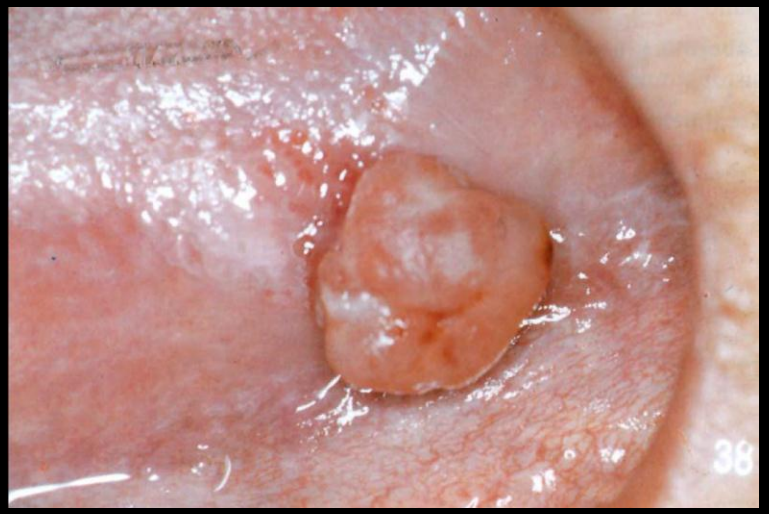
1. **Antoni-A Tissue:** Very well organized spindle cells (Schwann Cells) that often produce a pattern of peripheral cell bodies lined up around acellular eosinophilic (pink) areas called **VEROCAY BODIES**
2. **Antoni-B Tissue:** Less cellular and less organized spindle-shaped cells located in a less dense connective tissue stroma

Neurofibroma:

A benign, asymptomatic, solitary, slow-growing nodule or mass that is most commonly seen on the skin.

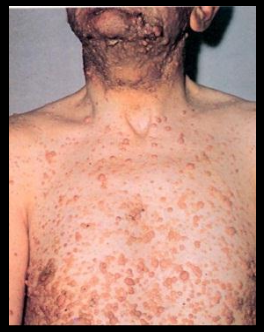
- Within the oral cavity, the most common places for Neurofibromas to occur are the **tongue and buccal mucosa**
- If seen intraosseously, rule out **Neurofibromatosis**

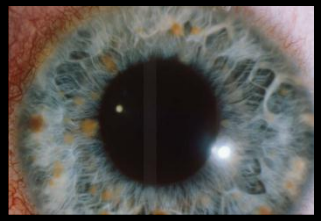




Treatment: Local surgical excision with a rare chance of recurrence. If it recurs or a malignant transformation occurs, rule out **Neurofibromatosis**.

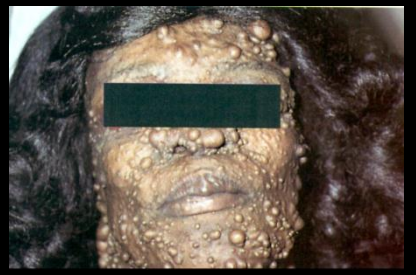
Neurofibromatosis:





There are actually eight different types of Neurofibromatosis, with **Type I** being the most common.

- It is an inherited autosomal dominant disease, so as a clinician, you need to see if either parent has **Neurofibromatosis**. 50% of cases are spontaneous mutations though, so it is not a definitive answer.



Presents as multiple **Neurofibromas** of the skin, appearing as either papules, nodules, or masses. They can get to be rather large. Once malignant transformation occurs, it can be very hard to treat.

- First present at birth, or appear during puberty
- Can be associated with **Café au lait** pigmentation (smooth edged brown macules), which are usually present earlier, before **Neurofibromas** are present
- Can also be associated with
  1. ***Crowe's Sign:*** axillary freckling on peripheries of body
  2. ***Lisch Nodules:*** brown spots located on the iris
- Other possible features include-
  1. CNS Tumors
  2. Macrocephaly: (abnormally large head)
  3. Seizures
  4. Mental Deficiency
  5. Short Stature/Scoliosis

Oral Manifestations: enlargement of the **fungiform papillae** with intraoral Neurofibromas.

Treatment: Removal of the **Neurofibromas** on the skin for cosmetic purposes and genetic counseling.

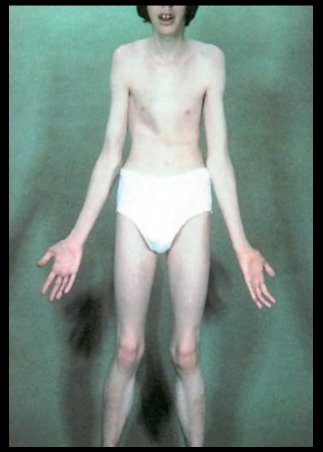
NEUROFIBROSARCOMA: develops in 5% of patients in their trunk/extremities and has a poor prognosis.

Radiographically: can present with an enlarged mandibular foramen or with enlargement/branching of the mandibular canal.

Multiple Endocrine Neoplasia (MEN) Type III:

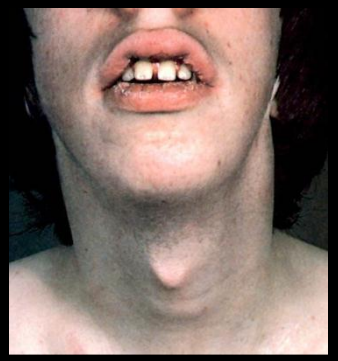
(Another inherited autosomal dominant disease that presents 50% of the time as a spontaneous mutation.)

- Patients present with a **"Marfanoid"** (referring to **Marfan's Syndrome**) body build: abnormally tall/skinny with long extremities.
- Also receive multiple mucosal neuromas (specific to Type 3): papules/nodules that are soft to palpation most commonly on the **LIPS** and **TONGUE**, but can be seen in multiple other areas of the oral cavity **(BILATERAL on the commisures is typical sign)**



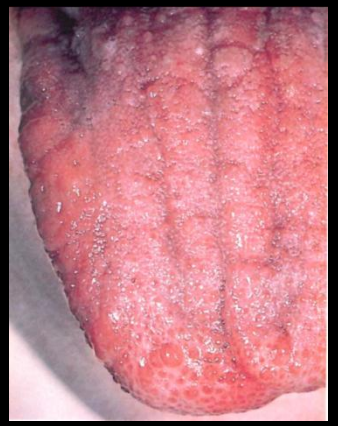
MEN Type III is also associated with **two** other types of benign tumors:

1. ***Pheocromocytoma*** (50%): tumor of the adrenal glands that over-secretes **catecholamines** (epinephrine/norepinephrine). Even though it is a benign tumor, it alone can be life threatening.
2. ***Medullary Carcinoma of the Thyroid*** (90%): usually presents between the ages of 18-25, and is extremely prone to metastasis. With the likelihood and possible severity of the associated Thyroid Carcinoma, the **Thyroid Gland** is often removed.



Lab Findings: markers used to recognize the associated benign tumors, and therefore MEN Type III Syndrome-

1. ***Elevated Calcitonin:*** (in serum or urine) affiliated with Medullary Carcinomas of the Thyroid.
2. ***Elevated VMA (vanillylmandelic acid):*** result of a Pheocromocytoma.
3. ***Altered epinephrine/norepinephrine ratios:*** result of a Pheocromocytoma.



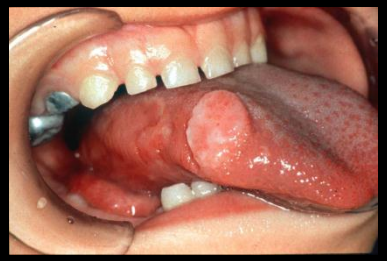
Treatment: early recognition of the syndrome is most important.

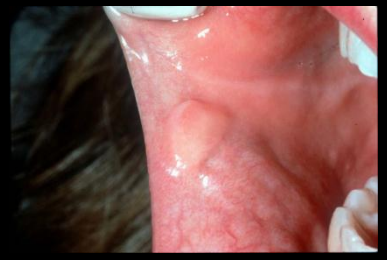
- As mentioned, prophylactic removal of the thyroid. The **Medullary Carcinomas** do have a poor prognosis.
- Associated **Pheocromocytomas** can result in life-threatening hypertensive crisis.

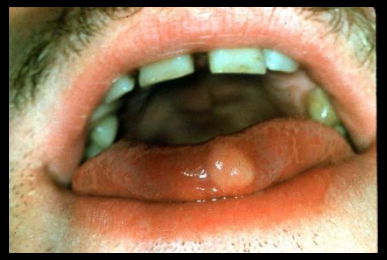
Granular Cell Tumor:

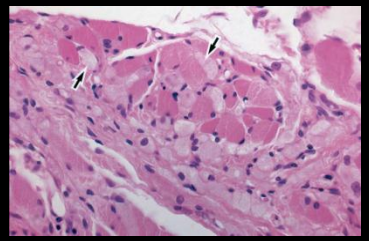
Somewhat uncommon tumor composed of **granular cells** *(cells with granular cytoplasm)*. They were first considered to be associated with muscle cells, so older pathology textbooks have **granular cell tumors** termed **"Granular Cell Myoblastomas"** (Myoblasts are progenitor cells for muscle cells.) This belief has changed however.

- We now know (histologically) that **Granular Cell Tumors** are more closely associated with **Schwann Cells/Mesenchymal Cells (**multi-potent stem cells). Therefore, they are reclassified as **neurogenic tumors**.



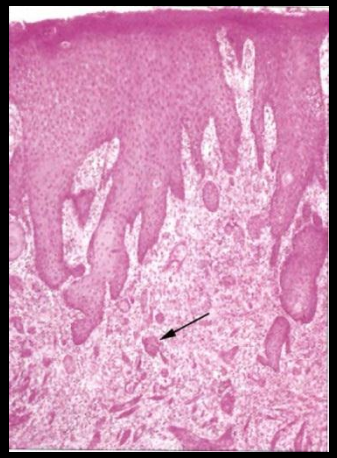






Clinical Features: Granular Cell Tumors commonly occur on the skin and oral cavity, with the **TONGUE (towards dorsal surface)** and **buccal mucosa** being most common locations intra-orally.

- Usually seen as solitary, slow-growing, sessile nodules that are pink or slightly yellow.



Histology: large cells with a granular cytoplasm.

- **Pseudo-hyperplasia (or "Pseudoepitheliomatous Hyperplasia")** in the overlying epithelium (see slide to left). Applying general concepts, the overlying epithelium should appear normal since this is a tumor of connective tissue origin. However, this is not the case, and **Granular Cell Tumors** are considered an exception. The overlying epithelium reacts by growing it's **Rete Ridges** downward and sideways. (This is seen in cross-section histologically by separate/isolated epithelium patches underneath the superficial layer.) This is histologically similar to something more invasive (**Squamous-Cell Carcinoma** for example). For **Granular Cell Tumors** however, the epithelial pockets are not actually completely isolated, and need to be recognized as being a histologic cross-sectional view of **underlying Rete Ridges** (they are benign).
- The bottom left slide shows close proximity to skeletal muscle cells (Hence the original mis-classification of a **Myoblastoma**.)

Treatment: conservative surgical excision with a rare chance of recurrence.

Congenital Epulis:

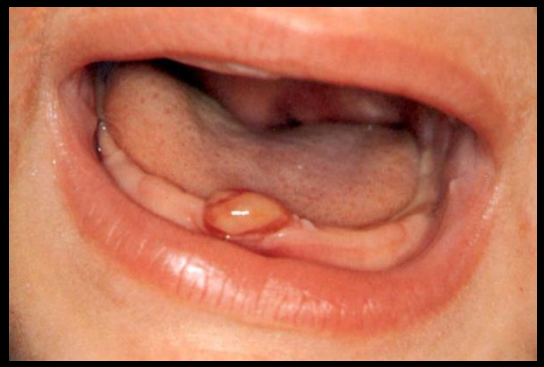
Congenital = "present since birth"

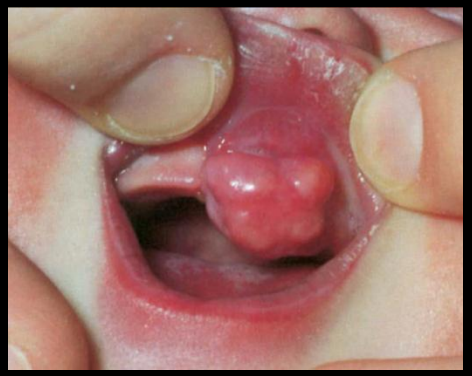
Epulis = "a benign lesion situated on the gingiva"

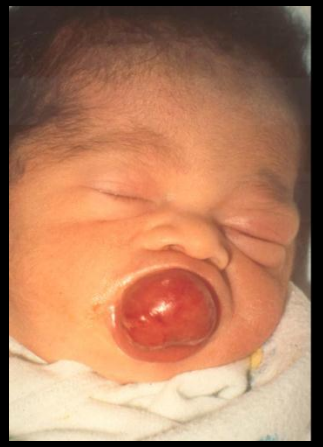
(A related "granular cell" tumor that only differentiates from a conventional Granular Cell Tumor histologically.)

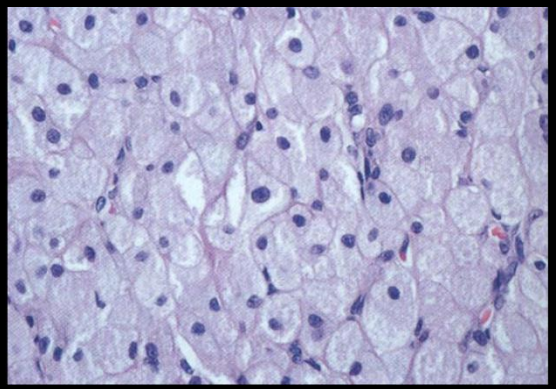
- Under the microscope, **Congenital Epulis** has a different **histogenesis** (the formation of different tissues from undifferentiated cells) than a typical **Granular Cell tumor**.
- Presents as a pedunculated mass on the **ALVEOLAR RIDGE** lateral to the midline (more common on the maxilla and rarely multiple)

Treatment: some may regress without treatment. Surgical excision if needed, and does not typically recur.

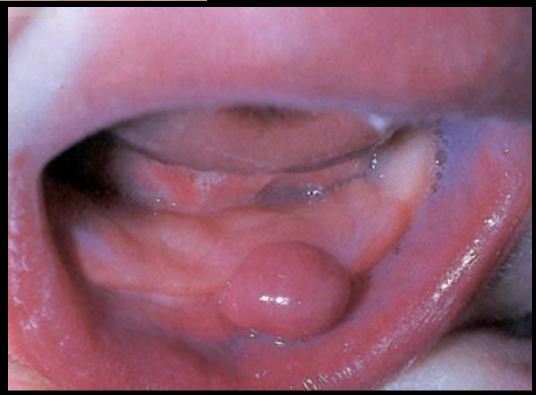








Histologically: (slide to left) resemble Granular Cell Tumors. However, being undifferentiated stem cells, they hardly retain staining methods.



Gingival "Bumps":

(We will discuss three, and their names are easy to remember for their similarity of all starting with the letter "P".)

The three "P's" of the Gingival Bumps category include:

1. Pyogenic Granuloma
2. Peripheral Giant Cell Granuloma (PGCG)
3. Peripheral Ossifying Fibroma (POF)

Remember: Subjectively, it is difficult to differentiate any of these three from eachother. All arise most commonly from the inter-dental papilla/free gingival margin.

- They all have slightly different clinical appearances and age predilections

Therefore, proper differential diagnosis is crucial!

[Gingival "Bumps"] Pyogenic Granuloma:

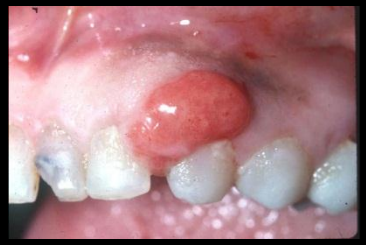
A **Pyogenic Granuloma** is **not** actually a proper pyogenic granuloma.

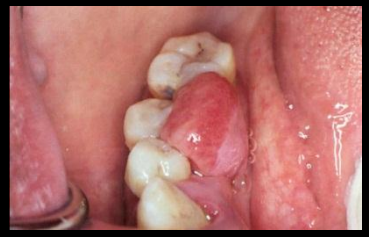
Pyogenic: "involving or related to the production of pus"

Granuloma: "a mass of granulation tissue, typically produced in response to an infection"

Despite the proper definitions of the individual words, a **Pyogenic Granuloma** can be considered an exuberant reaction to irritation or trauma. Histologically however, it is an excess of granulation tissue (but still not properly considered a granuloma) with inflammatory cells, capillaries, and occasionally fibrosis.

- Under the right situation (an example would be the removal of excessive plaque with a continuation of local irritation), a lesion that begins as a granuloma can **fibrose** over time (a **Pyogenic Granuloma** is a connective tissue response to local irritation/trauma.)
- The driving force could also be hormonal. If a Pyogenic Granuloma occurs in a pregnant woman, it is termed a **PREGNANCY TUMOR**. In this situation, it is related to increased levels of progesterone and estrogen. The incidence for Pregnancy Tumors increases as pregnancy progresses, and may resolve on it's own after labor.
- Despite being termed "**pyogenic**", Pyogenic Granulomas are not infectious.



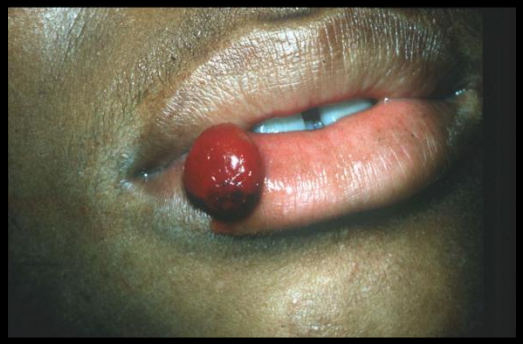


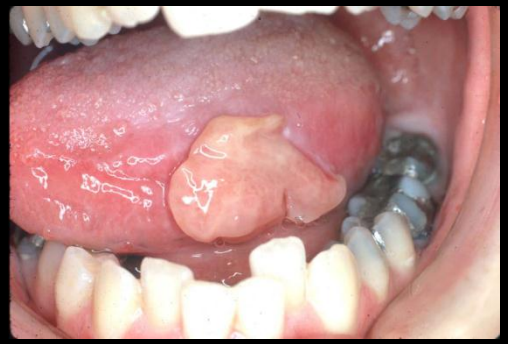
Clinical Features: Often, but not always presents as a **pedunculated**, lobulated, nodule or mass with an ulcerated surface appearing **red** to purple in color.

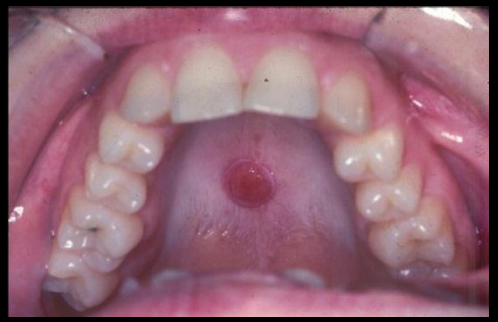
- Often emanate from the inner-dental papilla and attach to the inter-dental papilla.
- Because they are composed of granulation tissue and inflammatory cells, they are often considered **FRIABLE** (they bleed upon touching them). Despite this however, they are often painless.
- Can grow quite rapidly because they are reactive lesions
- Can see them anywhere (not just the oral cavity). Very common on GINGIVA (75%), **especially anterior maxillary area**. Can be seen on lips, tongue, and buccal mucosa as well though.

[Gingival "Bumps"] Pyogenic Granuloma (cont'd):

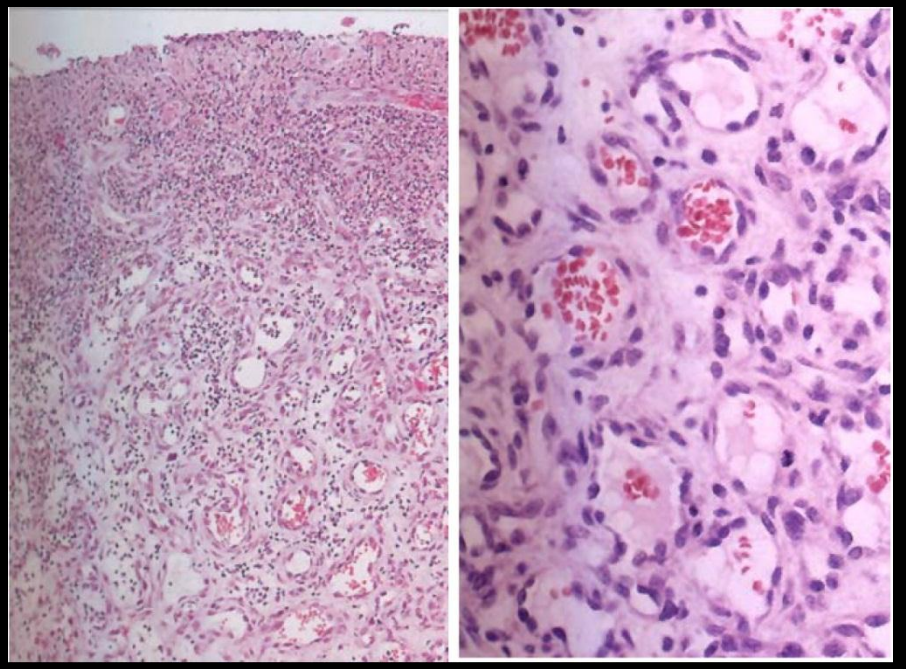
Treatment: Usually surgical excision (down to the periostium for gingival lesions). This can sometimes be difficult, resulting in bleeding and from taking time to make sure that the **Pyogenic Granuloma** was removed entirely. They may sometimes recur, especially if the predisposing factors are still present (pregnancy, poor oral hygiene, etc.).







Histologically: Granulation tissue with no overlying epithelium (because it is ulcerated). The entire lesion is composed of capillary-sized vessels, myofibroblasts (cells that are in-between a fibroblast and a smooth muscle cell in differentiation), and inflammatory cells.



[Gingival "Bumps"]

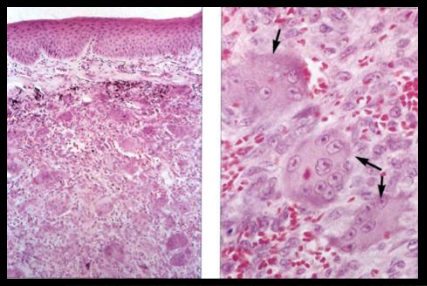
Peripheral Giant Cell Granuloma (PGCG):

We have already went over **Central Giant Cell Granulomas (CGCGs)** for the last exam, which by definition (central), are located within bone. **Peripheral Giant Cell Granulomas** are either located on bone or in soft tissue.

- It is a common reactive lesion secondary to local trauma or irritation

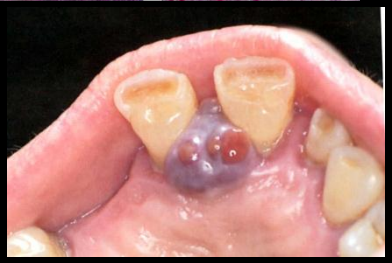
Histologically: **Peripheral Giant Cell Granulomas** present with the same histology as Central Giant Cell Granulomas, being comprised of **multinucleated giant cells and fibrous connective tissue**. Under the microscope, they look identical.

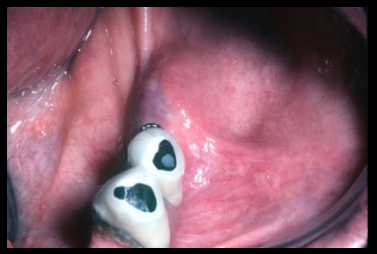
- There is no true granulation formation, but rather a collection of giant cells.

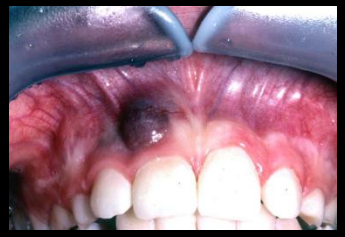


Clinical Features: Peripheral Giant Cell Granulomas **ONLY** occur on the GINGIVA (100%), and more commonly in the mandible.

- Can be either sessile or pedunculated, and sometimes but not always present with an ulcerated surface. They are **red** – blue in color (usually slightly more blue than **Pyogenic Granulomas**)
- Because **Peripheral Giant Cell Granulomas** contain **multinucleated giant cells**, bone reabsorption may be visible on radiograph. (This is referred to "**CUPPING**" of the surrounding bone.)
- Before a biopsy is taken to differentiate, it looks very similar and is hard to differentiate from a **Pyogenic Granuloma**.







Treatment: Treatment is similar to that of a **Pyogenic Granuloma** (When doing the initial biopsy, it is not possible to clinically determine the difference between the two.)

- Has roughly a 10% recurrence rate, which is higher than a **Pyogenic Granuloma**.

[Gingival "Bumps"]

Peripheral Ossifying Fibroma:

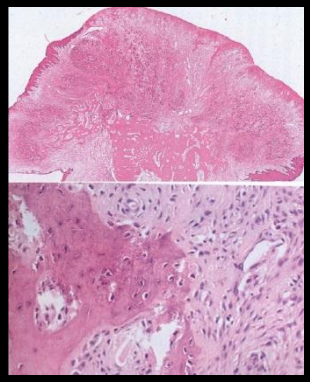
Peripheral: "comprised of soft tissue"

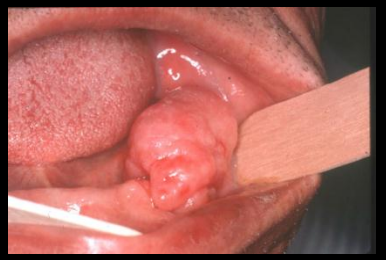
Ossifying: "containing at least a small amount of bony structure"

Fibroma: "composed of fibroblasts"

Like the other gingival "bumps", it can be considered a common reactive lesion. A portion of the fibroblasts associated with a **Peripheral Ossifying Fibroma** will initiate bone formation. Therefore, if you were to section open a **Peripheral Ossifying Fibroma**, you should expect to see a small amount of newly developed bone.

- It should be considered a fibroma that ossifies.
- It is **NOT** considered the soft tissue counterpart of a **Central Ossifying Fibroma**.
- The pathogenesis is still unknown. The most recent theory explains that the mineralized component of a Peripheral Ossifying Fibroma originates in the PDL.

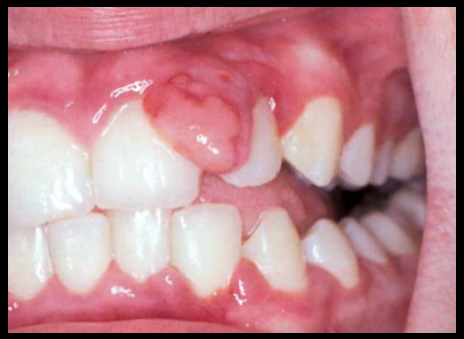


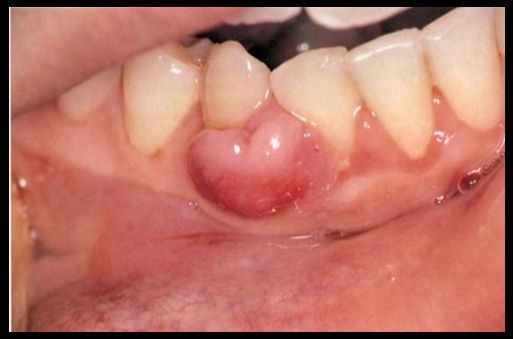


Histologically: **(Bone formation is evident.)**

Clinical Features: Similar to a **Peripheral Giant Cell Granuloma**, a **Peripheral Ossifying Fibroma** is a nodule or mass that **occurs only on the GINGIVA (100%).**

- Upon palpation, you can sometimes actually feel a bony hardness in the center of the nodule/mass.
- They are more common on the **maxillary** arch, usually around the **incisor/canine** area.
- Usually originating from the free gingival margin, **Peripheral Ossifying Fibromas** are **red** to pink in color, and at times can appear ulcerated.





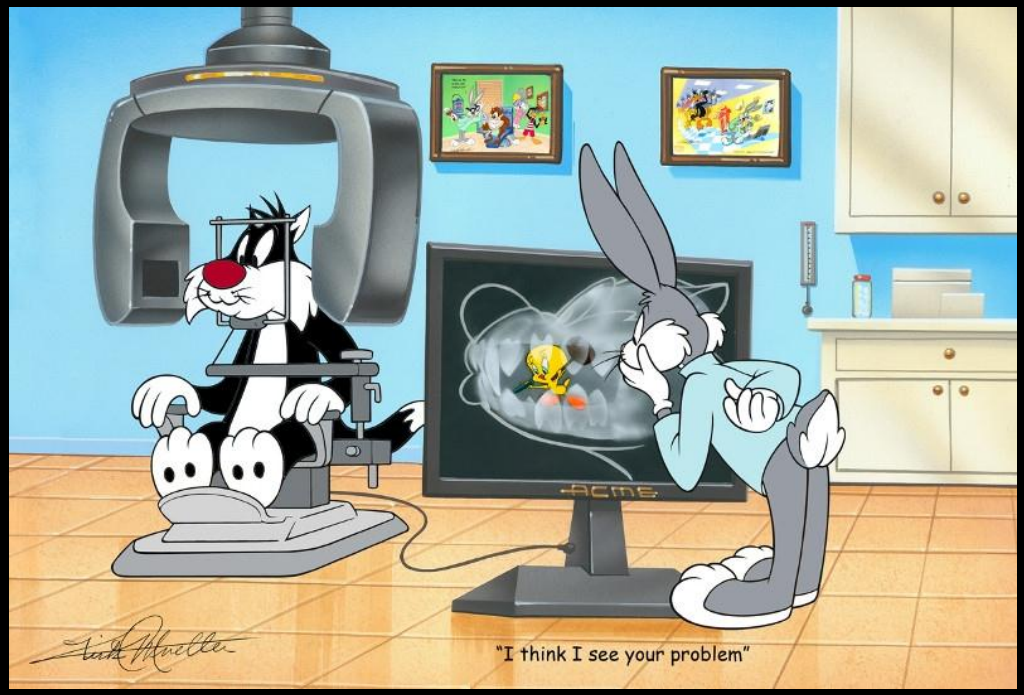
Treatment: Like the other gingival "bumps", local surgical excision is needed down to the periostium. Out of the three, Peripheral Ossifying Fibromas have the highest recurrence rate (16%).

Now, having covered the benign soft tissue tumors, we will proceed to…

Malignant Soft Tissue Tumors:

These include:

- **Fibrosarcoma**
- **Kaposi's Sarcoma**
- **Rhabdomyosarcoma**
- **Liposarcoma**
- **Neurofibrosarcoma**
- **Leiomyosarcoma**



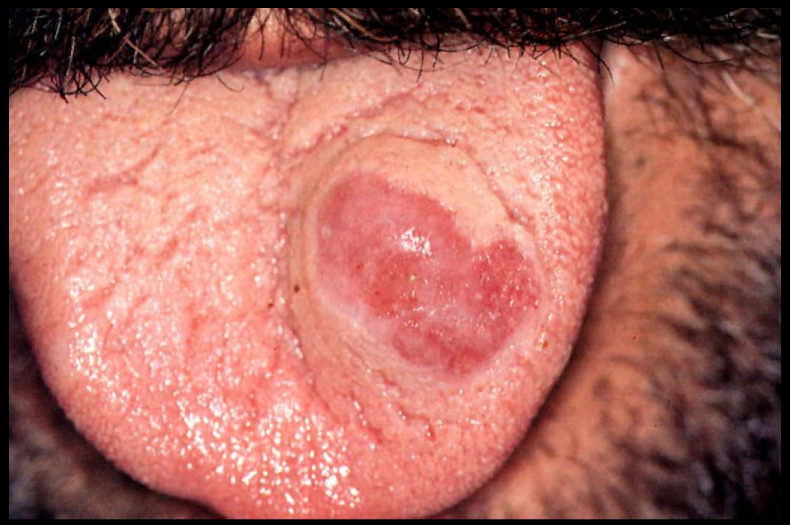
And then finally we'll discuss…

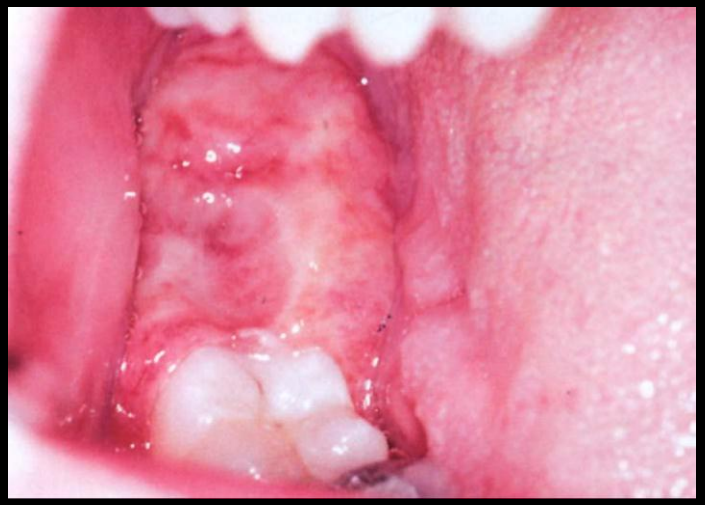
- **Metastasis to oral soft tissue**

Fibrosarcoma:

A malignant tumor of **fibroblasts** is termed a **Fibrosarcoma**. These malignant tumors tend to be slow growing (which is usually a characteristic of benign tumors).

- Only (10%) occur in the head/neck, but when they do, they commonly arise in the **nose and paranasal sinuses**. Because of this, **airway obstruction** is usually the first sign of a head/neck **Fibrosarcoma**.





Treatment: Commonly surgical excision with a wide margin (because it is metastatic).

- There is a (20-60%) recurrence rate, with a 5-year survival of (40-70%)

Kaposi's Sarcoma:

We have already covered **Kaposi's Sarcoma** last semester, when we discussed oral manifestations of systemic diseases. These are tumors of **endothelial cells**. The etiology is actually viral (**Human Herpes Virus Type 8**).

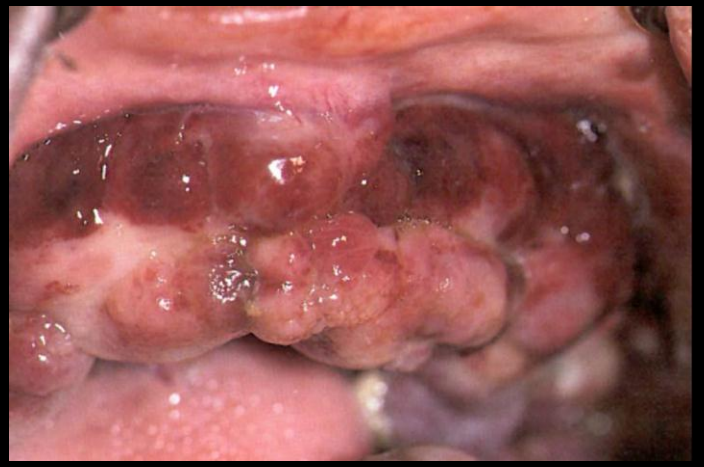
There are four different types:

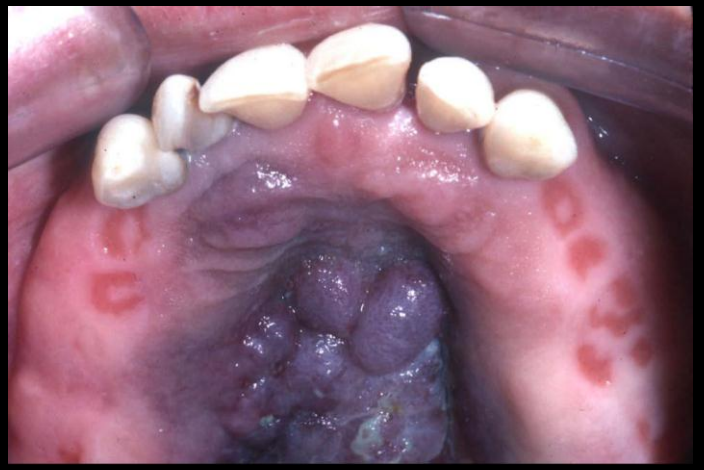
1. **CLASSIC:** (The typical form seen prior to the AIDS epidemic) Commonly seen in older men of Italian/Jewish/Slavic ancestry.
   - Presents as blue/purple macules on the skin of **extremities**, and is rarely seen within the oral cavity.
   - Roughly (33%) of people diagnosed also have **Lymphoma**, which originally supported the belief that **Kaposi's Sarcoma** is more common in immunosuppressed patients.
2. **ENDEMIC:** Common in Africa (even prior to the AIDS epidemic).
3. **IATROGENIC/IMMUNOSUPRESSION ASSOCIATED (Transplant Patients):** Contracted because of the immunosuppression drugs that are affiliated with transplant procedures.
4. **AIDS RELATED:** The most typical from seen since the AIDS epidemic.

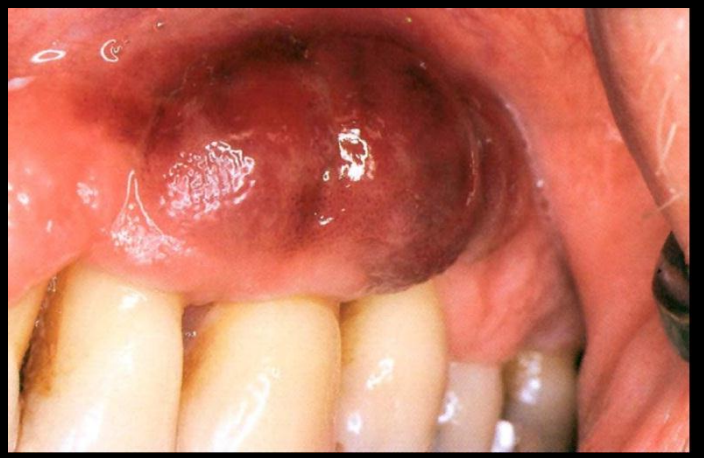
Oral Lesions: More recently (due to advancements in prevention/care), oral lesions have become less common in the United States. And again, most cases are associated with an HIV infection.

- Unlike most soft lesions within the oral cavity, it typically presents as multifocal.
- Most typically located on the HARD PALATE and MAXILLARY GINGIVA **(much less common on mandible)**
- Early oral lesions present as brown/red/purple macules (with pain/bleeding) that progress into plaques or nodules.

Treatment: Because of its malignancy, chemotherapy/radiation therapy is most typical.





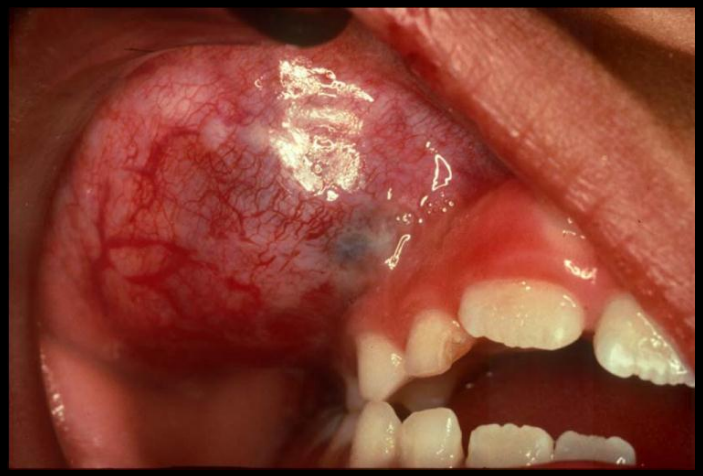


Rhabdomyosarcoma:

This is the most common soft tissue tumor in children (where 40% of cases are reported in the head/neck). It is a malignant tumor that originates in **skeletal muscle**.

- Presents as a rapidly growing painless mass.
- Normally originates in the orbit/nasal cavity/nasopharynx. Intraorally however, it is seen on the **PALATE** (metastasis from orbit/nasal structures).

[Importantly, tooth-borne pathology needs to be eliminated from differential diagnosis. If present in the oral cavity, vitality test teeth to rule out other possibilities.]

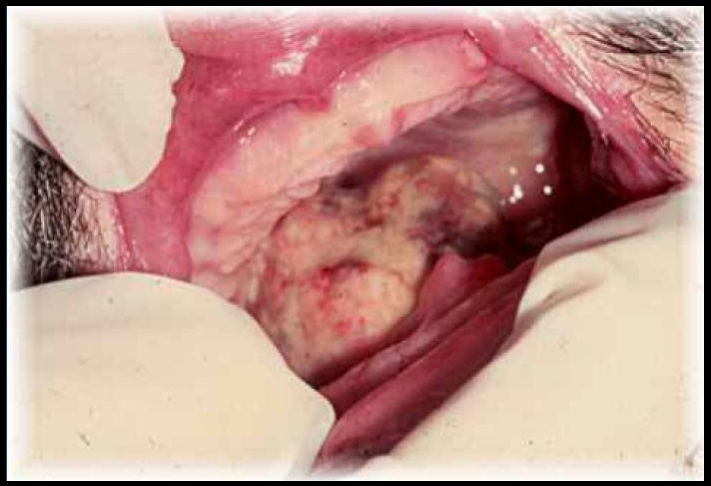


Treatment: Local excision followed by chemotherapy/radiation therapy

- 63% 5-year survival rate

Liposarcoma:

While a **Liposarcoma** (malignant tumor of fat tissue origin) is the second most common soft tissue sarcoma, it is **NOT** commonly seen in the head/neck. They can grow very slowly, and are hard to differentiate from **Lipomas** (benign) clinically without biopsy.



Clinical Features: An ill-defined, slow growing mass that is soft to palpation. It can present as either the color of **mucosa** or slightly yellow.

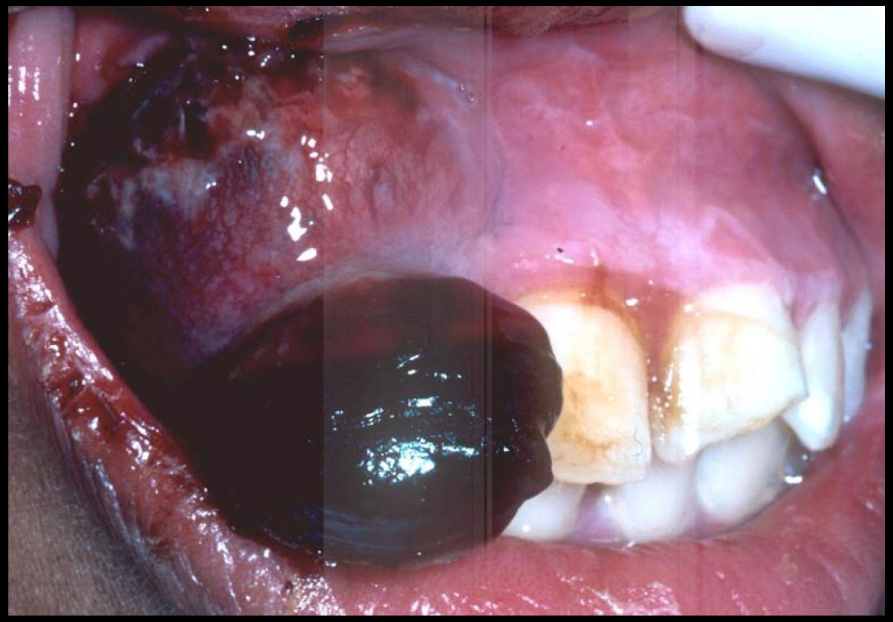
- When seen in the head/neck, the most common locations are the buccal mucosa (which of course is a fatty area), or the neck proper.

Treatment: Radical excision because of its malignant capabilities.

- There is a 50% recurrence with a 10-year survival of around 50%
- Overall prognosis depends on the histopathologic subtype (Histologically, there are different forms, some being more aggressive than others.) We did **not** go into any more detail about this during class.

Neurofibrosarcoma:

A malignant tumor of peripheral nerve tissue that is not common in the head/neck. More than 50% of reported cases occur in patients with **Neurofibromatosis**.



Clinical Features: An enlarging mass that is associated with pain/nerve deficit. It has been known to be fast-growing.

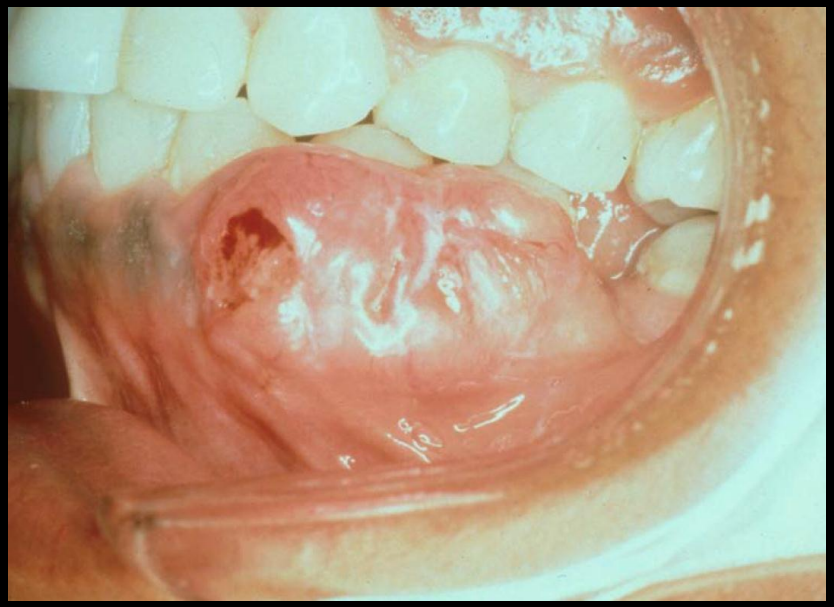
- Oral lesions most commonly seen on the lips/buccal mucosa, and is overall more common on the **mandible**.

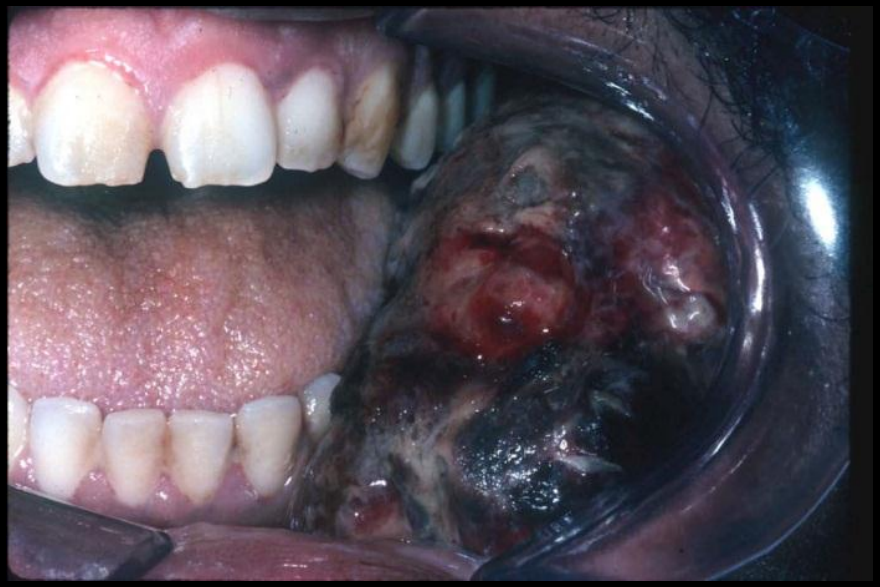
Treatment: Because of it's malignancy, radical surgical excision followed by chemotherapy/radiation therapy.

- A poor prognosis (especially when affiliated with **Neurofibromatosis**)

Leiomyosarcoma:

A malignant tumor originating from smooth muscle. The most common location would be the uterine wall and GI tract (since these places have a large amount of smooth muscle).





Clinical Features: An enlarging mass that may be painful and may present with an ulcerated surface.

Treatment: Because of it's malignancy, radical surgical excision with chemotherapy/radiation therapy

- **Leiomyosarcomas** have a poor prognosis, and tend to recur/metastasize.

Metastasis To Oral Soft Tissue:

Recollecting what we learned for the second exam, the most common malignancy of bone was **Metastatic Carcinoma**. It is much more common to have metastasis to bone rather than soft tissue. However, when metastasis to soft tissue within the oral cavity does occur, the most common places it presents is either on the **GINGIVA** or **TONGUE**.

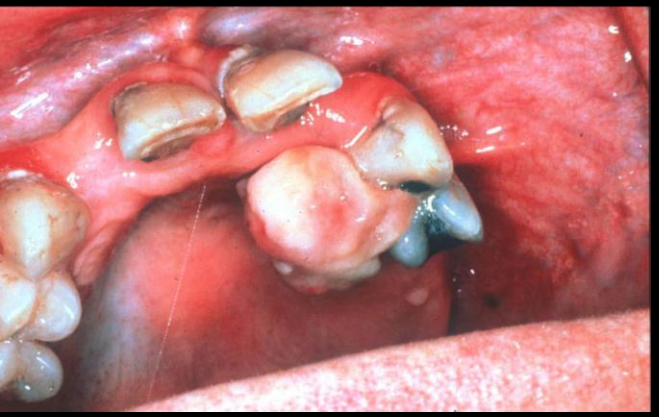
- When a metastasis is seen on the gingiva, the first question that you should ask yourself as a clinician is whether or not it is confined to the gingiva or does it travel down to the underlying bone? Again, metastasis to the gingiva is much less common than that of bone.
- When present, the nodules can be ulcerated. (You might include the 3 P's of Gingival "Bumps" in your differential diagnosis.)
- If it is a direct metastasis to bone or if the gingival metastasis travels into bone, expect to see loose teeth in the area.

Men and Women have different metastatic types of cancer that are most likely to travel to the oral cavity:

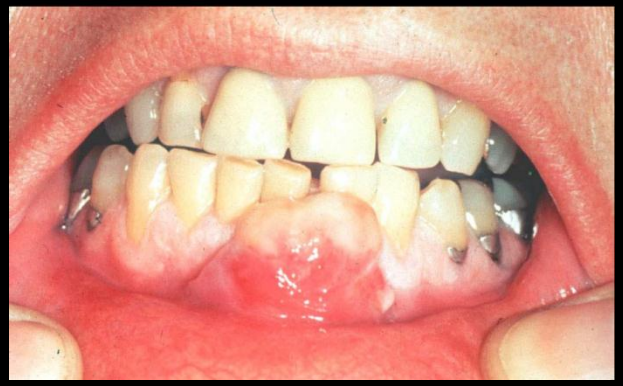
Men: Lung/Kidney/Melanomas (Prostate cancers tend to metastasize to bone)
Women: Lung/Kidney/Breast/Genitals/Bone

Some Examples of Metastasis To The Oral Cavity:

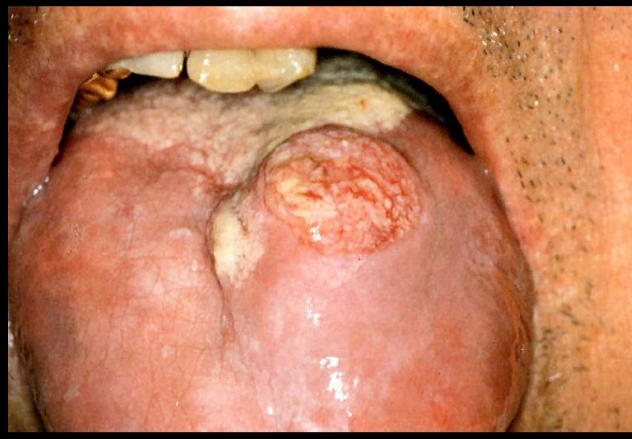
Metastatic renal cell carcinoma to the gingiva



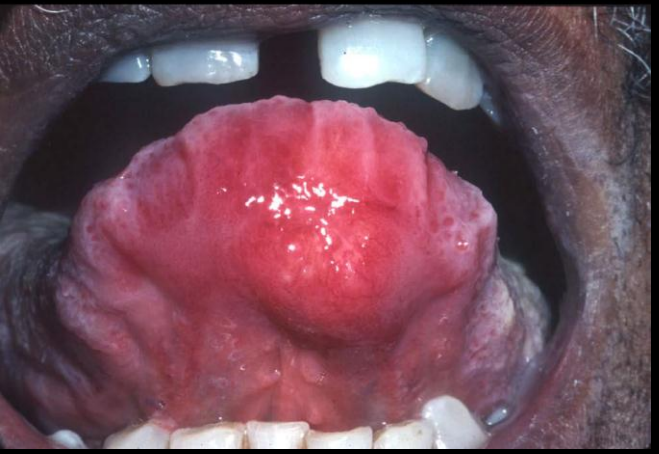
Metastatic squamous cell ca from genital area to the gingiva



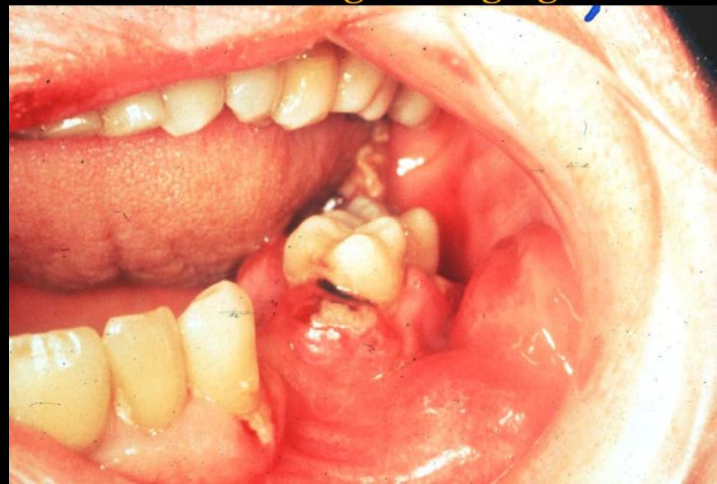
Metastatic Lung Ca to the tongue



Metastatic Lung Ca to the tongue



Metastatic Lung Ca to gingiva



Now that we have completely discussed soft tissue tumors, both benign and malignant,

Lets take a step back for a minute…

Thus far, during both semesters of this course, we have been preforming differential diagnoses for three categories of oral pathology:

1. Last semester we covered ulcers and their respected color changes.
2. For the last exam we covered bone pathologies, and their respected differences both clinically and radiographically.
3. And currently, lumps/bumps.

This should provide a solid framework for us as clinicians to properly begin our diagnosis in the correct category of pathology.

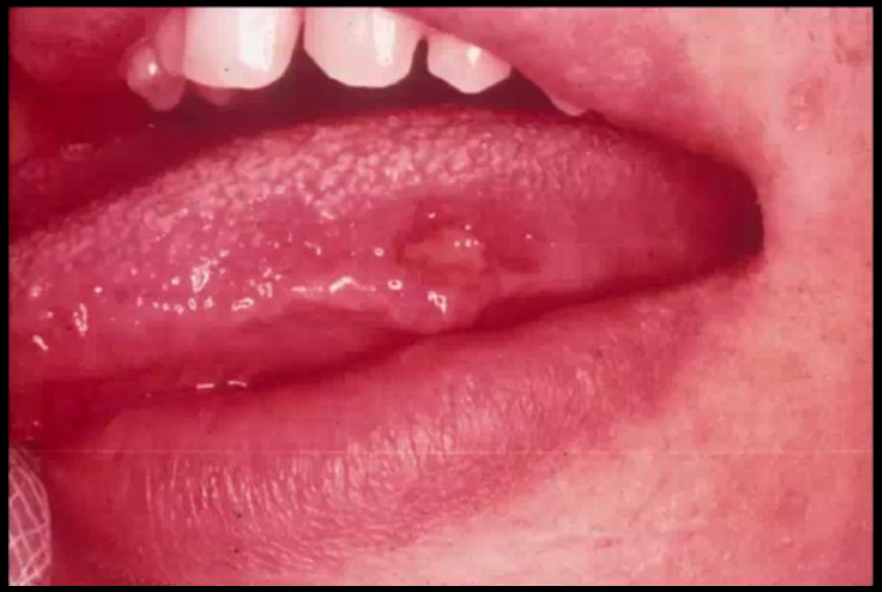
At the beginning of class on (10/25), Dr. Fornatora took some time to show us a few pictures, asking us to place them in one of the three categories above for proper differential diagnosis. It is not something specifically that we should expect to be directly tested on, but nevertheless is a decent review of practically applying the information/knowledge we have already covered/learned. I'll display the pictures, and provide a brief description of which category they belong in.

For each picture, categorize the pathology as either:

1. **A color change**
2. **An ulcer**
3. **A lump/bump**

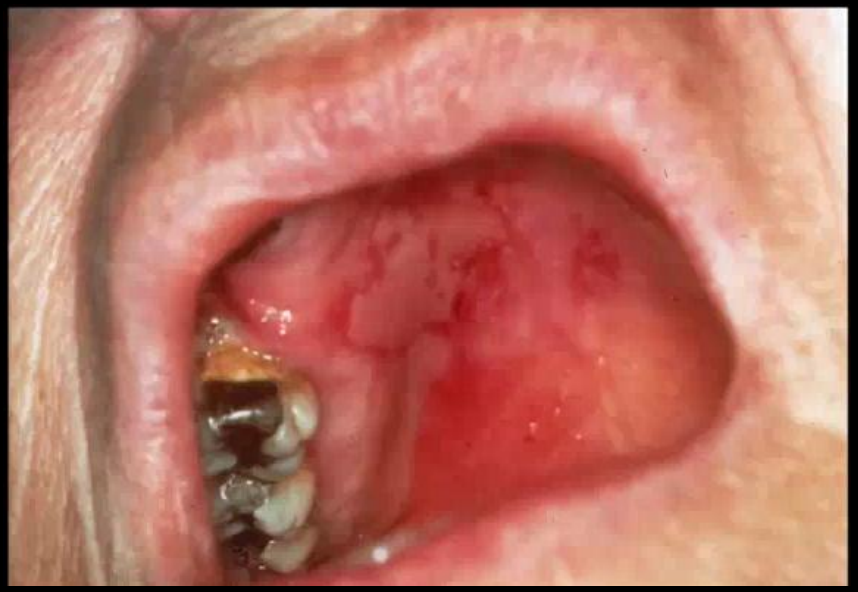
The correct answers will be directly below each picture.

[Differential Diagnosis Review]:



An Ulcer.

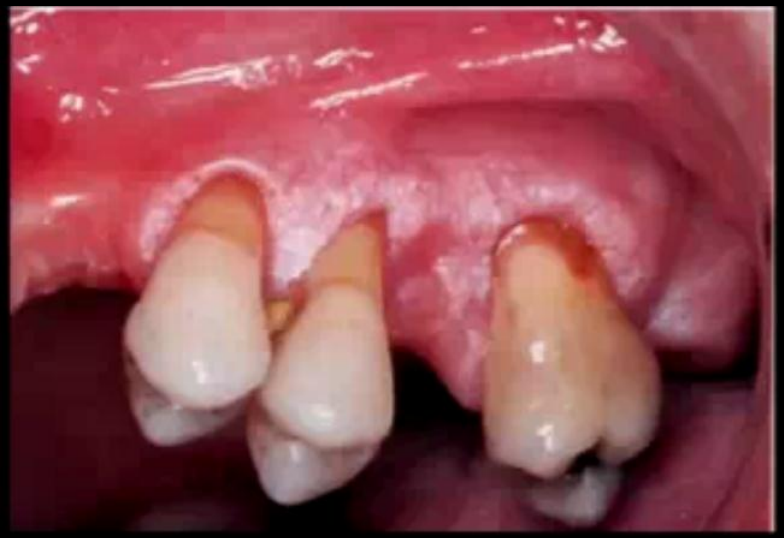
- **Ulcers** are moist with a granular appearance (must dry with an air syringe to notice this)
- Most **ulcers** are **white**/slightly yellowish in appearance. Generally, ulcers appear slightly more yellowish than a **white** color change.
- Also, **ulcers** tend to be **PAINFUL**, so definitely include that in your list of questions to ask the patient.



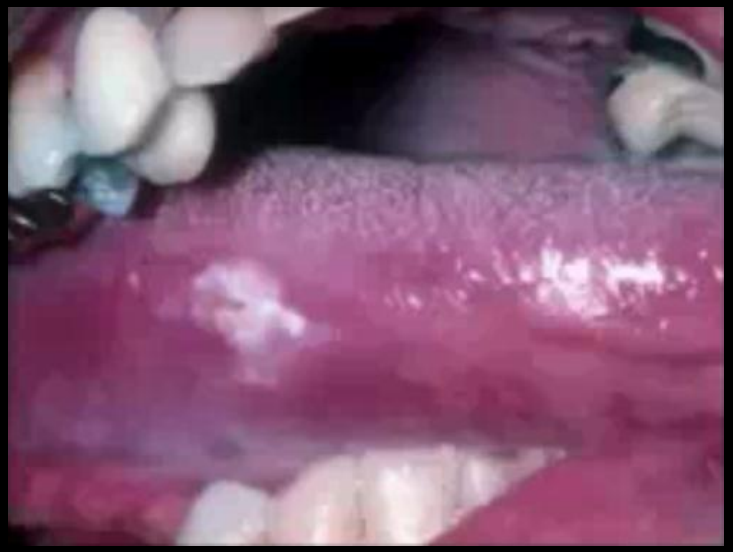
An Ulcer.

- This specific pathology is **white**/red (**white** center with a red periphery) While it may appear as a color change, recognize that **ulcers** usually demonstrate ***edema*** along the periphery
- This pathology appears as multiple **ulcers** that have coalesced to form one single abnormal appearance.
- **White** color changes are partially diagnosed through wiping the surface with gauze. While different **white** lesions produce different results with this test, with ulcerations, the **white** periphery of the lesion will detach, so expect to see slight bleeding.

[Differential Diagnosis Review]:



A Color Change.

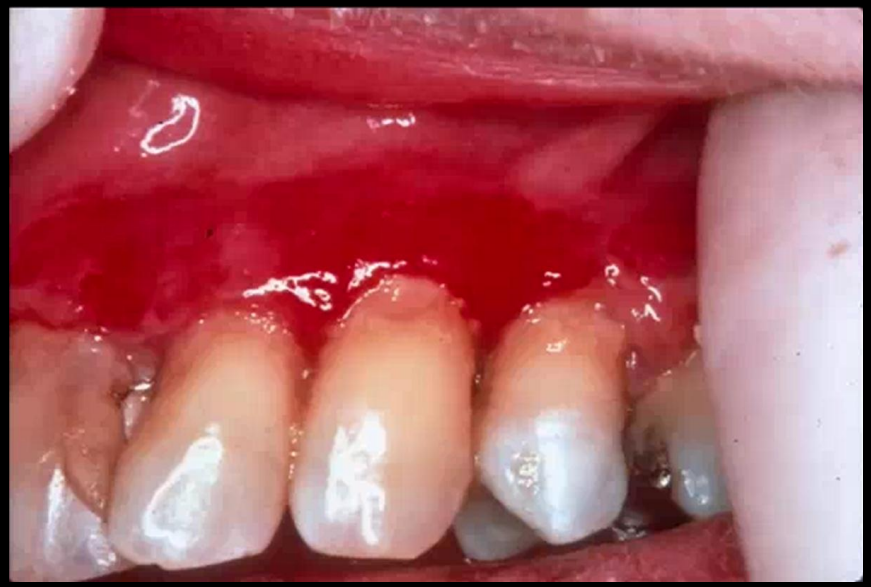


A Color Change.

- Notice the difference in appearance from the **ulcerative** lesions on the previous slide. There is no yellowish hue and the pathologies are more diffuse in color.

[Differential Diagnosis Review]:

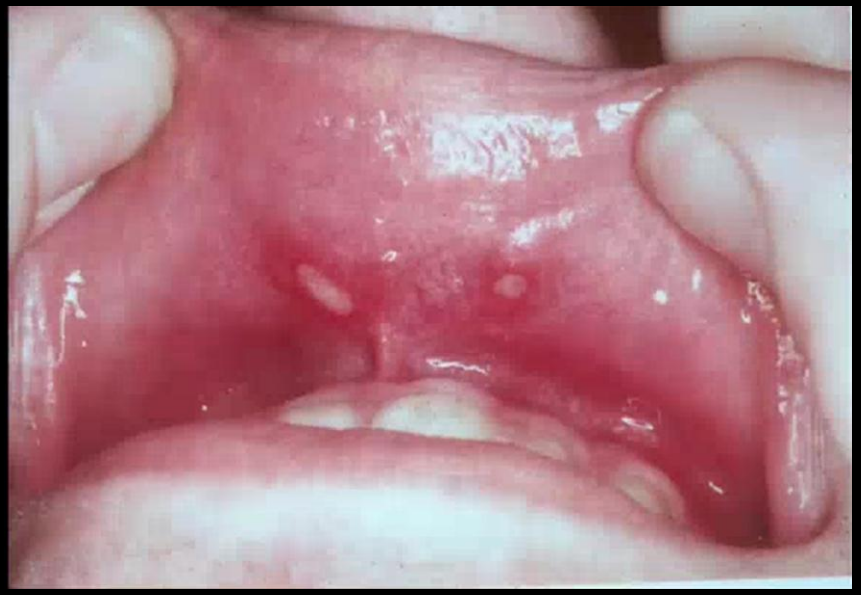
This one is tricky…



An Ulcer.

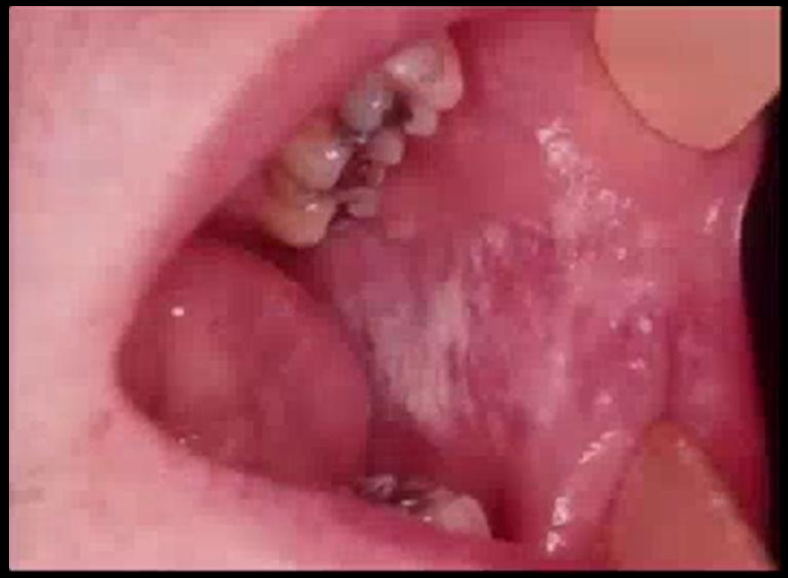
- Remember, the other presentation for **ulcers**, especially those found on the gingiva (such as in **Desquamative Gingivitis**) is **ERYTHEMA**.
- Here, you can see partial stripping of the epithelium (mesial side) with an erythematous base underneath. This example may not be a full **ulcer**, but histologically, you should expect to see a basement-membrane coating (as in **Pemphigoid**) with possibly a single epithelium layer if it is healing.
- Most red pathologies, if they are purely a color change, when blanched **WILL NOT** bleed. However, most red color changes occur in the underlying connective tissue, so when pressed on, they **WILL** blanch. (Red color changes also occur during **Erythematous Candidiasis**, which will not bleed either.)
- So basically… with a red color change, upon **blanching** if you observe bleeding then chances are the pathology is very fragile in-tact mucosa or a very early ulcerative lesion. In this picture, the red color is not actually a true color change, but rather a partially stripped in-tact mucosa.

[Differential Diagnosis Review]:



An Ulcer.

- These are **Apthous Ulcers (canker sores)**
- When deep **ulcers** are present (such as in this picture), there is an actual physical depression within the surrounding tissue with missing mucosa.



A Color Change.

- This is **Morsicatio buccarum**. A decent question to ask this patient would be if they find themselves constantly biting their cheek (not just once).
- Notice the increased **whitish** appearance towards the posterior, and more of a red appearance towards the anterior. The white portion should be wipeable.

Now that we have reviewed the differentiation of pathologies we have already discussed, lets

Move Onto The Article…

Evaluating, documenting and following up oral pathological conditions – A suggested protocol;

Alexander, Wright and Thiebaud, JADA March 2001

Dr. Fornatora has assigned us this article to read for the exam and is considered testable information. In class however (10/25), she took a few minutes to go over some of the important concepts that it presents.

While we spend our time in oral pathology learning about the different diseases/conditions that can affect the oral cavity, the authors do a good job of describing how to actually diagnose them clinically. The next few slides are heavy in text/information that is not specifically pathology related, but nevertheless are things we are expected to know.

[The Article]:

Most textbooks don't adequately discuss how to monitor suspicious lesions. Importantly, the word "suspicious" is very subjective.

Let's define "*suspicious*" as anything not normal.

However, as practicing clinicians, we should be able to define any type of pathology (completely identifiable or not) as more than just suspicious. We have already discussed properly placing lesions in one of the three categories (ulcer, color change, or lump/bump)

Some questions that need to be answered in your head concerning monitoring any "suspicious" lesion seen clinically includes…

1. How frequent should it be monitored?
2. What to include in the record?
3. When to consult with a specialist?
4. When to perform a second biopsy?

[The Article]:

Who should perform the soft tissue exam?

The article discusses how the soft tissue exam is frequently delegated to a dental hygienist by the dentist. However, this task should not be completely delegated to your hygienist. Even if it is preformed by someone other than yourself, the law says (in most states) that it is still the responsibility of the dentist. This means that legally, you are responsible (and not your hygienist) regardless of who performs the complete exam. The initial exam can be done by the hygienist, but should be completed and reviewed by the dentist. It is also important to inform the patient that you are doing a cancer screening/soft tissue exam. Statistically, many patients are not even aware that it occurs.

What if an abnormality is found that requires a biopsy?

You should arrange a referral for the biopsy while your patient is in your office. At our school, it is as simple as an Oral Surgery consultation somewhere in the building. In private practice, it is important to provide the patient with the names and contact information for several Oral Surgeons, and allow them to decide if they have a preference. One study shows that only 50% of patients actually follow through with a biopsy recommendation. It is also your responsibility to send any patient information to that Oral Surgeon, and keep current with the results/lab findings.

[The Article]:

What are the indications for a biopsy?

1. Any persistent pathological condition that cannot be diagnosed clinically, including the following:
   - Lesions with no identifiable etiology that persist for more than 10-14 days, despite local therapy
   - Any intrabony lesions that appear to be enlarging
2. Any lesion that is felt to have malignant or premalignant characteristics, including lesions in the floor of the mouth
3. Confirmation of clinical diagnostic suspicions
4. Any lesion that does not respond to routine clinical management, such as antibiotic therapy or endodontic treatment over a reasonable period
5. Any lesion that is a source of extreme concern to the patient (that is, cancerphobia: the patient's fear about a persistent lesion is greater than the concern about undergoing a minor surgical procedure)

[The Article]:

“It is illogical to continue watching a soft or hard –tissue lesion grow progressively larger while not recommending definitive diagnostic and therapeutic steps to the patient. Even if such a lesion turns out to be benign, the morbidity resulting from the surgery increases proportionately as the lesion grows larger or encroaches on vital structures.”

What are the guidelines for the frequency and length of follow-up if you do not consider to biopsy a lesion?

There are none. You can always decide to monitor ‘pre-biopsy’. Generally speaking, any lesion that appears to be epithelial in nature (ulcers, color changes, etc.), should be monitored for at most 2 WEEKS (7-14 days) prior to determining whether a biopsy is needed or not.

“Generally speaking, a decision to perform a biopsy is superior to a decision not to because a definitive diagnosis can be established”

What are the contraindications for a biopsy?

Basically, any time the risks outweigh the benefits (bleeding, infection, etc.). For example, vascular malformations and fibro-osseous lesions (Periapical Cemento-Osseous Dysplasia, etc.).

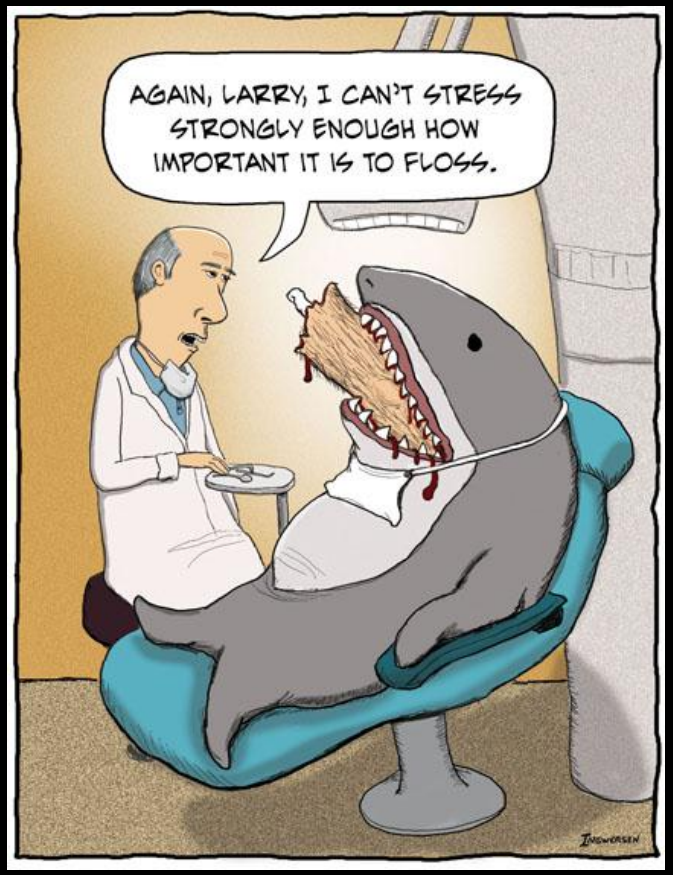
[The Article]:

Remember: Surgical biopsy is the gold standard.

Last semester, we read an article (Lingen) that discussed different (less-invasive) techniques to biopsy suspicious lesions. Remember that in terms of accuracy and reliability, surgical excision is still the most reliable method.

What if you decide to wait and "monitor" the lesion?

1. Enter provisional diagnosis in the record
    - Use phrasing in charting such as consistent with ("c/w") or suggestive of ("s/o")
2. Create plan to follow lesion. Recommendations for following:
    - Re-examined 1month, then 3m, 6m, 12m
    - After 1 year, many lesions remain unchanged and evaluation can be every 6 months and then annually there after.
    - Provide guidelines given in writing to the patient along with instructions that the patient is to contact your office if the lesion changes



[The Article]:

How do you record/document a lesion?

1. Auxiliary staff findings must be reviewed, altered as needed and signed by dentist
   - "If dentist chooses not to follow-up on concerns noted by hygienist, the record should reflect the rationale for the decision".
2. *Record details of lesion:*
   - Your memory will not suffice if you are following a lesion.
   - Photographs are excellent records for chart and referral purposes.
3. Provisional diagnosis or differential diagnosis
   - This should be documented.
4. Record discussions with the patient
   - This includes courses of action, risks, prognosis, tx plans, etc.
   - Informed consent document should be complete if using one.
   - Document if the patient refuses recommended treatment.

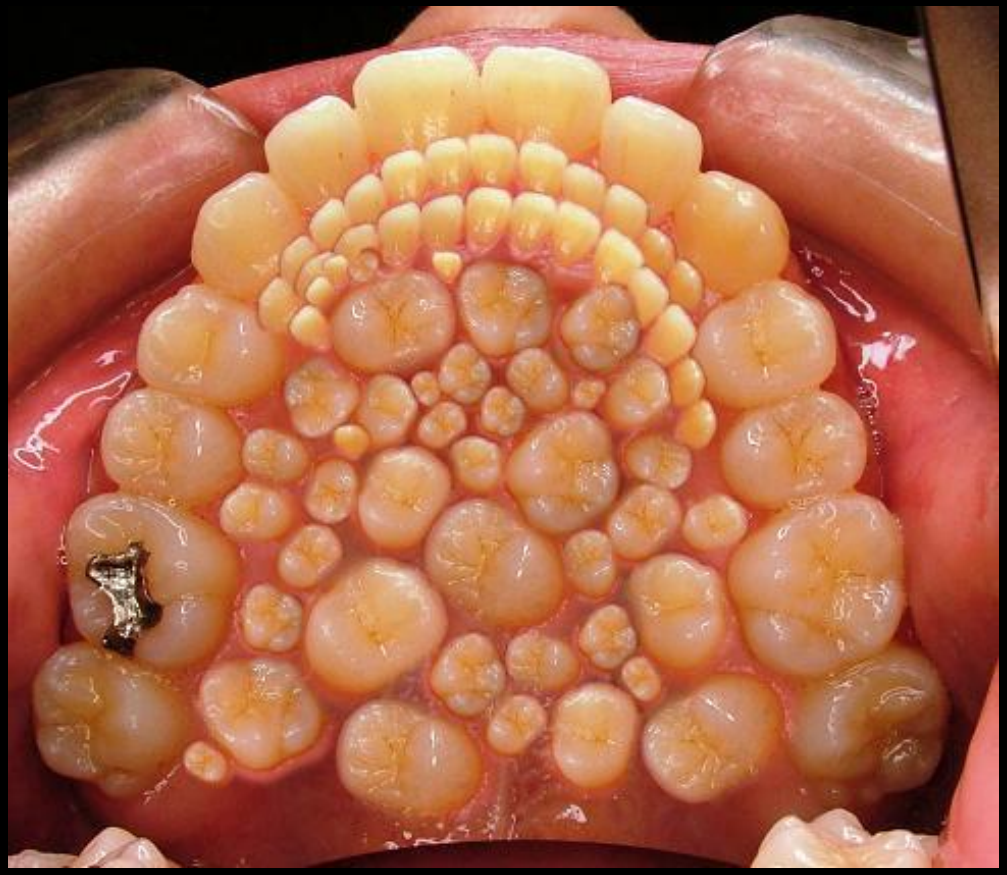
What if the patient fails to return for a follow-up visit?

If a patient fails to return for any follow-up visit, consider sending a letter reminding them of the possible consequences of 'non-compliance'. You may advise the patient that termination of the professional relationship may result, but try to avoid patient abandonment.

Lets move right along to…

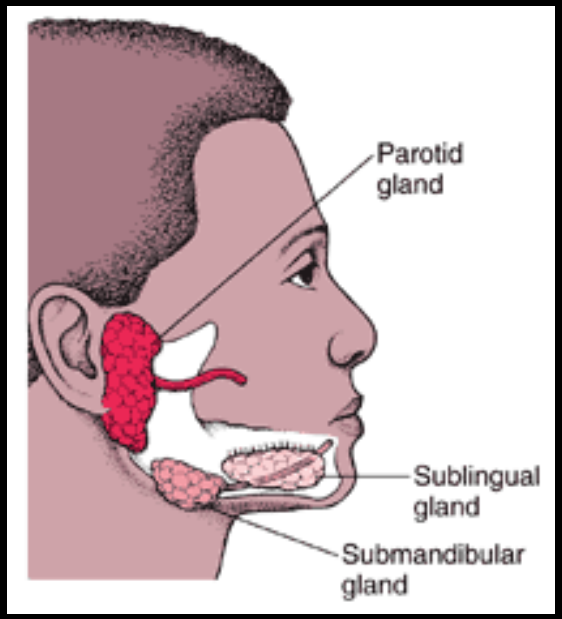
Salivary Gland Pathology:

(Chapter 11 from the textbook)



To begin with, lets discuss

The Salivary Glands:



There are three major salivary glands…

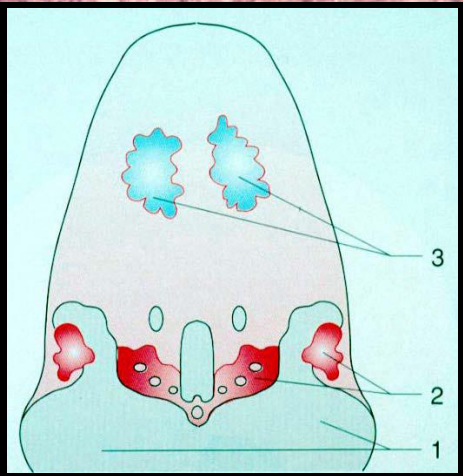
- **Parotid Glands:** serous (watery)
- **Submandibular Glands:** mixed, but more serous
- **Sublingual Glands:** mixed, but more mucous

At rest, most of the watery secretions in the mouth come from the **Submandibular Glands.** The **Parotid Glands** are usually only active when stimulated. Generally speaking however, watery secretions come from the **Parotid Glands**, while mucous secretions come from the **Sublingual Glands**. The **Submandibular Glands** are a combination of both.

There are also minor salivary glands within the oral cavity. Most produce mucous secretions, and the place where there are the **fewest** is on the tongue (particularly towards the dorsal surface).

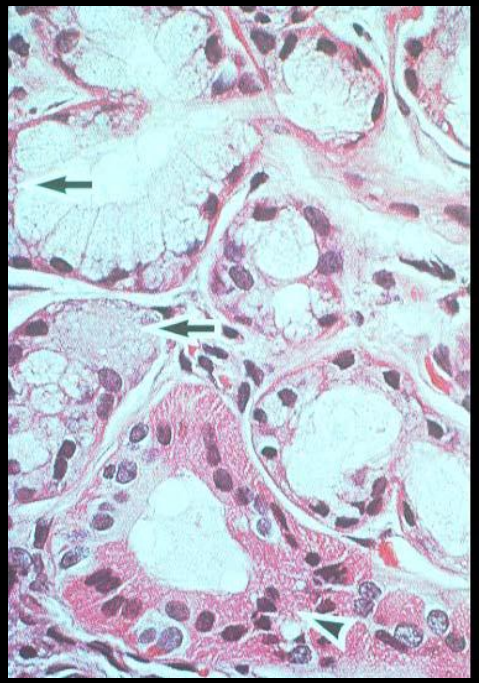
The tongue has three unique minor salivary glands, varying as mucous, serous, or both.

1. **Weber Glands:** mucous glands located far posterior
2. **Von Ebner Glands:** serous glands near located near the circumvalate papillae
3. **Blandin-Nuhn Glands:** mixed glands located on the anterior of the tongue

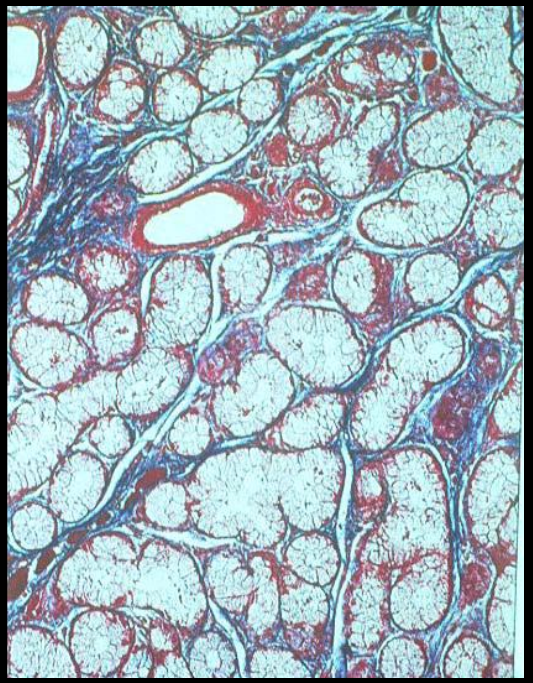


Salivary Gland Histology:

(Mixed with Serous Demilunes)



(Mucous)



Histologically: Exocrine glands (large duct with opening in the middle). **Acinar/Mucous** cells are also present. **Serous cells (Serous Demilunes)** located along the periphery. Saliva is produced in the **Acinar Cells**, and released into the ducts that become progressively larger as they reach the **Terminal Excretory Duct**, which eventually opens into the mouth.

*(As an example, when a clinician milks a salivary gland, they are actually releasing the saliva from the **Terminal Excretory Duct**. After this is preformed once, you must wait for the duct to fill up with saliva once again.)*

Onto the pathologies…

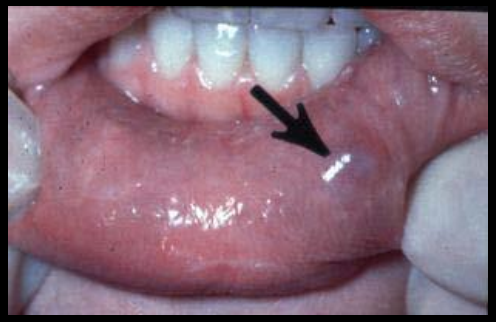
We'll begin with a… Mucocele:

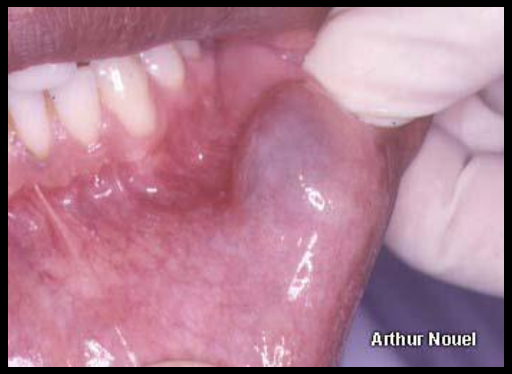
(Erupts from damage/rupture of a **minor salivary gland**. This causes the **mucin** to spill out into the local soft tissue, producing a localized swelling which is actually comprised of **mucin** in the localized connective tissue.)

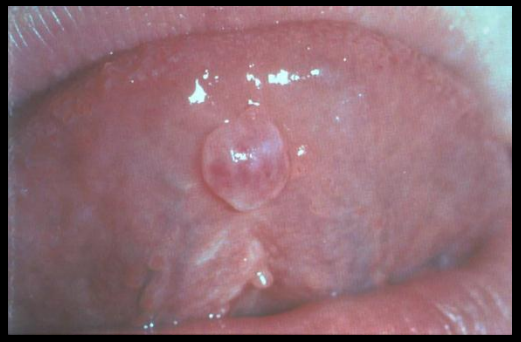
Any locations within the oral cavity that are easily traumatized or have many minor salivary glands are more prone to receive **Mucoceles**. This being said, the lower lip is the most common location for them to arise (upper lip uncommon). Besides for a superficial layer of tiny blood vessels, there are many minor salivary glands in this location. Also, while you can expect to see them on the ventral tongue, they are never found on the dorsal aspect.

Clinical Appearance: commonly seen in kids (because of trauma to the lower lip). Presents as a dome shaped swelling that appears fluctuant/firm, and bluish-normal in color.

- They can be present for years without resolution.
- If present, you should ask if there was trauma to that location. Also, ask if it has been increasing/ decreasing in size. The body will produce an immune reaction to the **mucin** within the connective tissue. Between the immune response and the salivary gland producing more **mucin**, over time, the **Mucocele** could appear to fluctuate in size.
- Over time, the minor salivary glands associated with the Mucocele will fibrose and stop working (so long as there is no new trauma). If large enough however, irritation (trauma) will occur and it will progress.

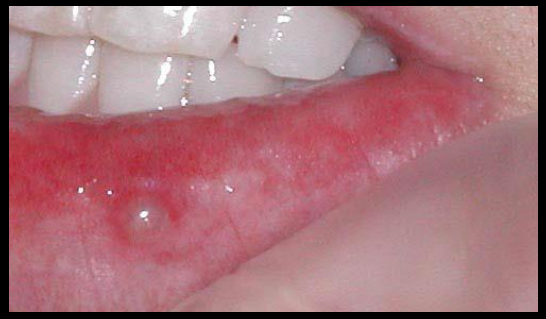




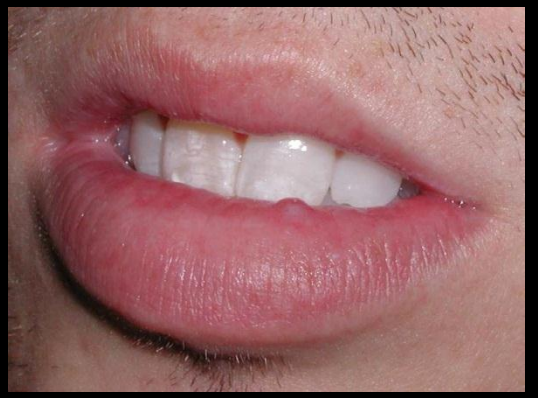


(ventral side of tongue, pedunculated)

Superficial Mucocele:



A variant of the typical **Mucocele**. It is more superficial, so they are easier to rupture (either intentionally or naturally). Patients usually think that they are infections, and try to rupture them. Over time, they will follow the same pattern as a typical **Mucocele** (increase/decrease in size). They will often go away on their own, but they can be surgically excised if needed.

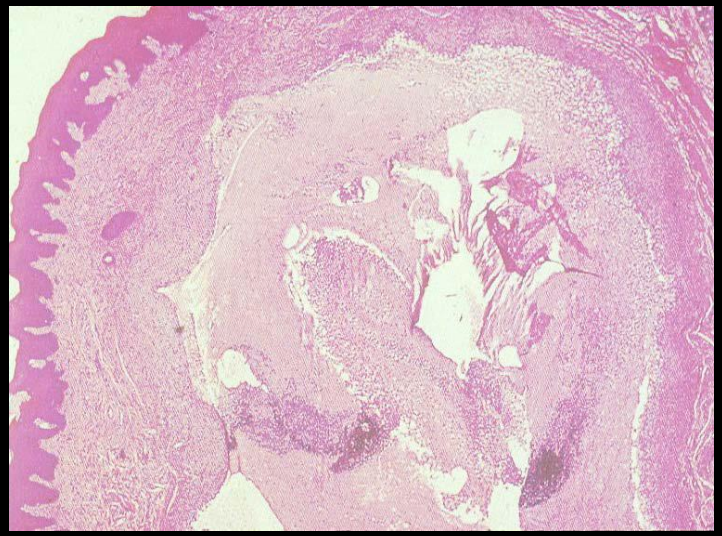


Mucoceles (all of them):

Etiology: most commonly caused by trauma to a salivary duct/gland. In most cases, patients can report the trauma. Other times however, they can arise without trauma (more common for **Superficial Mucoceles**).

Histology: a pool of **Mucin** surrounded by connective tissue (granulation tissue) containing neutrophils and foamy histiocytes, with no epithelial lining (Therefore, it is not a true cyst!).

Treatment: most are self limiting, but can be surgically excised if needed. During excision, affected minor salivary glands need to be removed as well, or else it could recur.



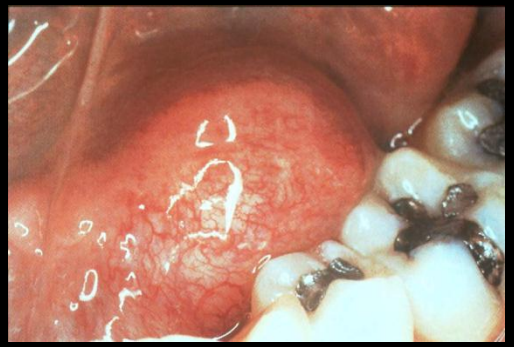
Similar, but not quite the same as a **Mucocele**, lets discuss… # Ranulas:

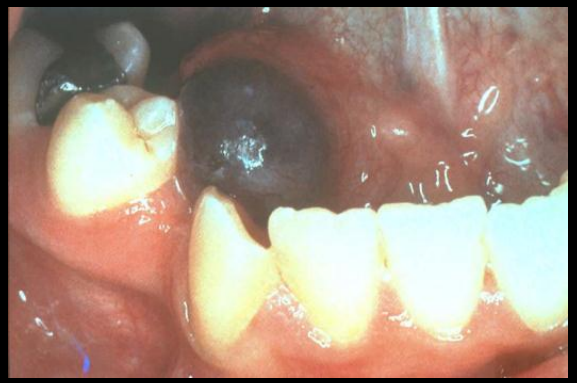
(Simply put, a **Ranula** is a **Mucocele** in the floor of the mouth. However, instead of being a result of spilled mucin from a minor salivary gland, it usually is a result of spilled mucin from the **Sublingual Gland**. Therefore, there is a larger volume of mucin being spilled into the connective tissue.)

Clinical Appearance: larger than a **Mucocele**, and appearing on the floor of the mouth and as dome-shaped fluctuant swelling lateral to the midline (no glands are located on the midline), that can actually elevate the tongue.

Histology: same as a **Mucocele** (no lining, so therefore not a true cyst). It is spilled mucin into the local connective tissue.

Treatment: Unlike a **Mucocele**, it usually needs to be surgically excised along with the feeding gland (Sublingual Gland in most cases).



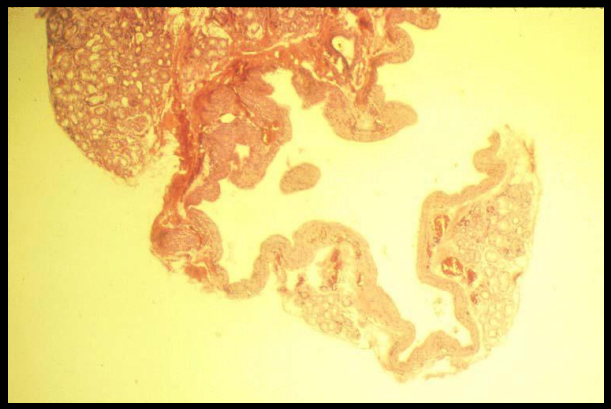


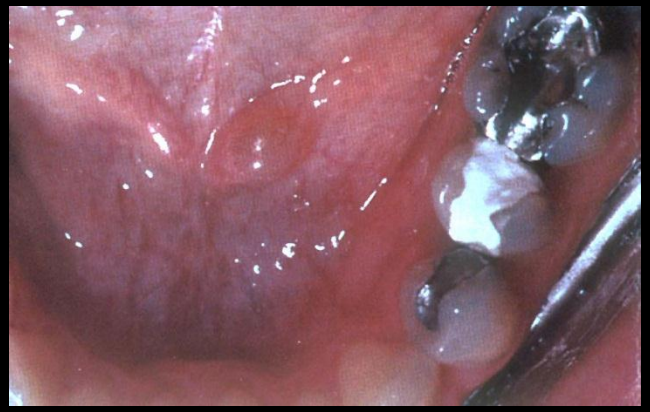
[A variant would be a **PLUNGING-RANULA**, where instead of progressing upward, the **Ranula** descends downwards towards the **Mylohyoid muscle**, eventually producing **a submandibular/neck swelling**.]

Salivary Duct Cyst:

This is a true cyst with a true epithelial lining, containing saliva/mucin in the center. The epithelial lining originates from the epithelium of the duct itself (from either a major or minor salivary gland), which through trauma/irritation produces a cyst.

- **While Mucoceles may be more common in children, Salivary Duct Cysts are more common in adults. However, both share a similar clinical appearance.**
- Most commonly found on the floor of the mouth (expect it to be adjacent to Wharton's Duct), the buccal mucosa, and the upper lip (Remember, **Mucoceles** are uncommon on the upper lip).





Histology: The appearance of an epithelial lining (that may or may not be separated from the salivary duct), with a mucin lumen. Neutrophils and foamy histiocytes may also be present.

Treatment: Excision, along with excision of the associated gland. Even after removal, a **Salivary Duct Cyst** may still recur however.

Sialolithiasis (salivary stones):

Calcified structures that develop in salivary ducts, which will eventually occlude the excretion of **mucin**. Upon formation (when they are small), they typically begin round in appearance. As they progress, they tend to take the shape of the surrounding duct.

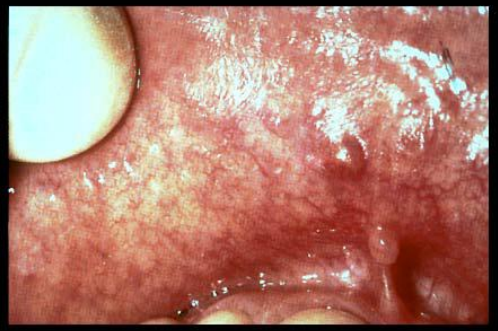
Clinical Appearance: Anyone can get them, but they are most commonly found in young adults (children do not frequently get them). Presents with episodic (comes and goes) pain/swelling that tends to originate from the lower mouth, but can spread to the cheeks and other surrounding areas. The pain is not always typical (can present as a pins/needels sensation). You can also expect the patient to present with intermittent parathesia (tingling, burning, pricking, or numbness).

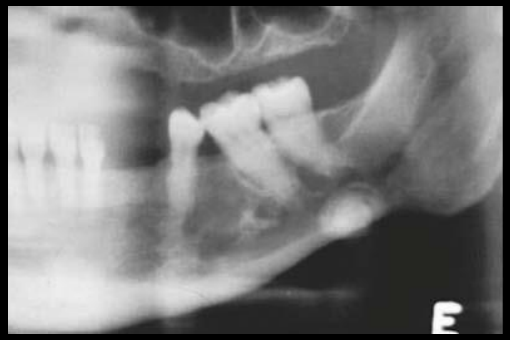
- They can be associated with any major or minor salivary gland. However, the **Submandibular Gland** is the most frequent gland to be affected.
- Symptoms most commonly present during eating (the salivary glands become stimulated).

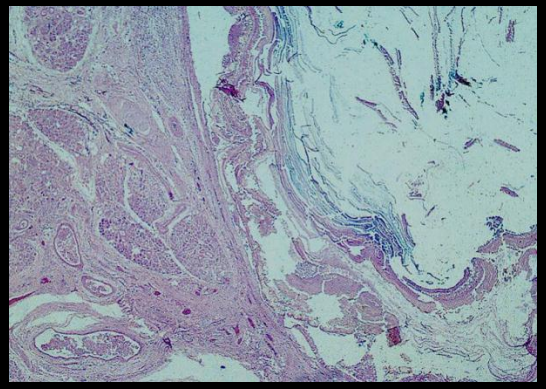
Radiographically: **does not** always present as radioopaque (if **Sialolithiasis** is not calcified enough). Typically beginning as a mucin plug, before calcification, a radioopacity will hardly be noticeable on radiograph.

- If there is a radioopacity, it needs to be determined that it is of soft tissue origin, and not bone pathology.

Histologically: layers of calcification on the periphery of the salivary stone, making it progressively thicker. There will also be localized inflammation in the surrounding duct tissue (becoming fibrotic/necrotic).







Treatment: If the salivary stone is close to the duct opening, patient can use moist heat (warm rag) to try to clear the obstruction. You can also attempt to "milk" the stone from the duct, but this is not always effective (salivary stone must be in the right position, close to the duct opening). If this does not work, surgical excision needs to be preformed. At times, the affected gland also needs to be removed with the **Sialolithiasis**.

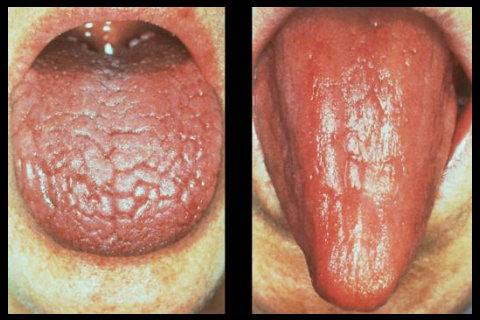
Xerostomia (dry mouth):

Dry mouth (**Xerostomia**) can be caused by any one of a number of reasons. The first question that needs to be answered is if it is a glandular problem, or a signaling/dehydration problem (Basically, is there intrinsic salivary gland destruction?).

- Direct glandular pathology can be caused by any one of a number of reasons (radiation therapy, glandular aplasia, **Sjogren's Syndrome**). In these circumstances, medications (example: **pilocarpine**) would not be effective, because the salivary gland is not functioning properly.
- If the **Xerostomia** is caused indirectly by a secondary pathology, medications would work however (and are therefore easier to treat).

Examples of a few pathologies that secondarily cause Xerostomia include:

- Systemic diseases (diabetes, dehydration)
- Medications taken for systemic diseases that cause autonomic mis-signaling of the glands (antihistamines, decongestants, antidepressants, antipsychotics, antihypertensives, etc.)
- Habits (smoking, mouth breathing, etc.)



Clinical Appearance: Clinically, **Xerostomia** is a rather subjective diagnosis (asking the patient if their mouth feels dry). It is a patient reported pathology. Even if mucosa appears dry/sticky and saliva seems more viscous, if patient reports not having a dry mouth, they do not have **Xerostomia**.

- **Xerostomia** will eventually cause clinically evident secondary pathology of the oral cavity (examples: balding of the tongue, candidiasis with the associated burning sensation, caries, etc.).

Treatment: To consider treatment options, patient must either report having dry mouth or secondary pathology to dry mouth (caries, etc.) must be present.

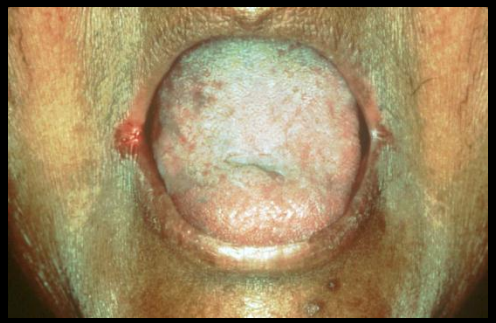
- If the salivary gland is the direct source of the pathology causing the **Xerostomia**, **sialogogues** (drugs that increase saliva flow) may not be effective. Instead, use hydration, saliva substitutes, and topical floride.
- If the dry mouth is being caused by a secondary pathology (so long as there is functioning glands to stimulate) , you can promote gland secretion through hydration/sugar-free candy, and speak with the patient's physician about adjusting the medications they are on if needed. **Sialogogues** such as pilocarpine may also be used.

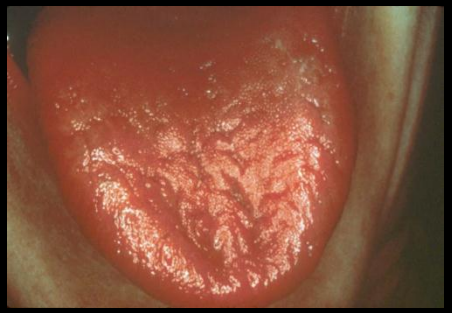
While on the topic of salivary gland pathology and **Xerostomia**, lets discuss…

Sjogren's Syndrome:

Even though it is an acquired systemic autoimmune disease, **Sjogren's Syndrome** has a direct effect on the oral cavity, and is therefore extremely relevant to our profession. Like most other autoimmune diseases, it is more common in women. While it predominately affects lacrimal and salivary glands (producing **xerostomia** and **xerophthalmia**), it can be considered a multi-system disease. There are two forms:

- **Primary Sjogren's Syndrome (Sicca Syndrome):** Sicca is a fancy way of saying "dry". In this form, no other autoimmune conditions are present.
- **Secondary Sjogren's Syndrome:** Another autoimmune condition is present (most often **Rheumatoid Arthritis**)





Clinical Appearance: Being a systemic disease, patients often present with **SYMPTOMS** of both dry mouth (**xerostomia**) and dry eyes (**xerophthalmia**). The **SIGNS** that are present with the disease are often the secondary effects of the symptoms.

- ***ORAL SIGNS:*** dysphagia (difficulty swallowing), candidiasis, caries, papillary atrophy of the dorsal tongue, and diffuse/painless bilateral major salivary gland enlargement
- ***OCULAR SIGNS:*** xerophthalmia that is due to decreased tear production by lacrimal glands and **Keratoconjunctivitis Sicca** (gritty dry eyes that are a result of the pathologic effect on the epithelial cells of the ocular surface)
- ***SYSTEMICALLY:*** skin, other mucosa, lungs, kidneys, nervous system, etc.

Sjogren's Syndrome (Diagnosis):

The proper diagnosis of **Sjogren's Syndrome** often varies depending on the institution that patient is seen at and what criteria are used. The diagnosis of **Sjogren's Syndrome** is preformed through the following blood tests (which are common tests generally preformed for any **rheumatological** disorder, and are not specific for Sjogren's Syndrome):

- **ANA (Anti-Nuclear Antibody) Blood Test:** ANA's are a group of antibodies that react against normal components of a cell nucleus (70% of Sjogren's patients have a positive ANA test result).
- **RF (Rheumatoid Factor) Blood Test:** An antibody test that is indicative of rheumatic disease (70% of Sjogren's patients have a positive RF test result).

There are also certain antibodies that are used specifically in the identification of **Sjogren's Syndrome**…

- **SSA and SSB (Sjogren's Syndrome Antibody A and Antibody B) Test:** 70% of patients test positive for SSA and 40% of patients test positive for SSB. SSA also goes by the name "**RO**", and SSB also goes by the name "**LA**"; don't ask why this is.

Since no single test is completely conclusive, a combination of these blood tests are used when diagnosing **Sjogren's Syndrome**.

Other blood tests for **Sjogren's Syndrome** include:

- **ESR (Erythrocyte Sedimentation Rate) Test:** this is a non-specific test that measures inflammation within the body. A positive ESR Test would indicate an inflammatory disorder (not just **Sjogren's Syndrome** though, so it can be considered non-specific).
- **IGs (Immunoglobins) Test:** Immunoglobins are considered normal blood proteins. While they are elevated in a Sjogren's patient, this test is also considered non-specific.

Sjogren's Syndrome (Examination):

Once blood tests are preformed and **Sjogren's Syndrome** is diagnosed via lab findings, patients need to have clinical tests preformed on their eyes and salivary glands. For an eye exam, the patient will typically see an opthamologist, who will preform a series of clinical tests including:

- **The Schirmer Test:** used to measure tear production (a positive test for **Sjogren's Syndrome** would be less than 5mm of tear production in 5 minutes time).
- **Rose Bengal and Lissamine Green Dye Test:** dyes that are used to observe abnormal cells on the surface of the eyes.
- **A Slit-Lamp Exam:** indicates the volume of tears by magnifying the eye and viewing it in it's resting state.

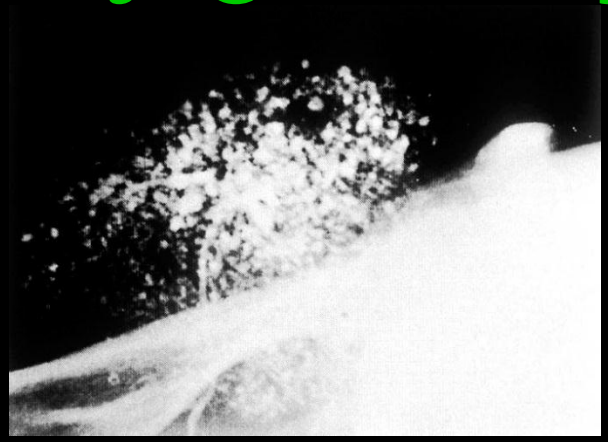
After these ocular tests are preformed, the patient can then move onto an examination of their salivary glands (there are actually not too many dentists who are properly trained in preforming these diagnostic tests). They include:

- **Parotid Gland Flow:** measures the amount of saliva produced over a certain period of time. Actually, this can be from a specific gland like the **Parotid**, or a simple measure of total salivary flow. Total flow is easier to measure than that from a specific gland because stimulation/unstimulation is much easier and the patient simply spits into a cup. Stimulated salivary flow (usually observed by having the patient chew on paraffin wax) is compared to unstimulated salivary flow. The flow rate from a specific gland (such as the **Parotid Gland**) must be measured directly from that specific duct. There are devices that can be inserted into a specific duct to measure it's flow rate.
- **A Lip Biopsy:** an easy biopsy that can be preformed by most surgeons to confirm lymphocyte infiltration into the minor salivary glands. Histologically, the individual glands are observed, and the number of lymphocytes located in the peri-ductal areas are counted. [50+ lymphocytes or plasma cells located in an area less than $4mm^2$ would indicate **Sjogren's Syndrome**].

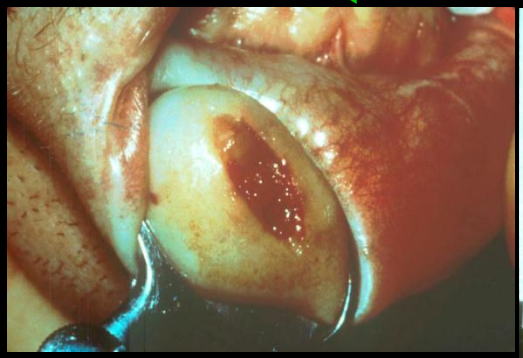
There are also two other tests that can be preformed by an interventional radiologist, and are not commonly done because limited clinicians actually know how to properly preform them:

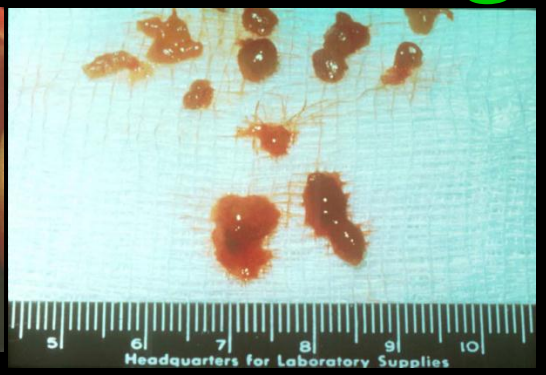
- **Salivary Scintigraphy:** measures salivary gland function. The injection of radioactive dye measures the uptake and delayed emptying of major salivary glands.
- **Sialography:** an x-ray of the salivary duct system is taken after radioactive dye is injected. Someone with **Sjogren's Syndrome** would present with **Punctate Sialectasia** (resembling a fruit-laden, branchless tree). This pattern presents as a result of Sjogren's-like changes to the ductal system and associated glands.

Sjogren's Syndrome (Exam Findings):



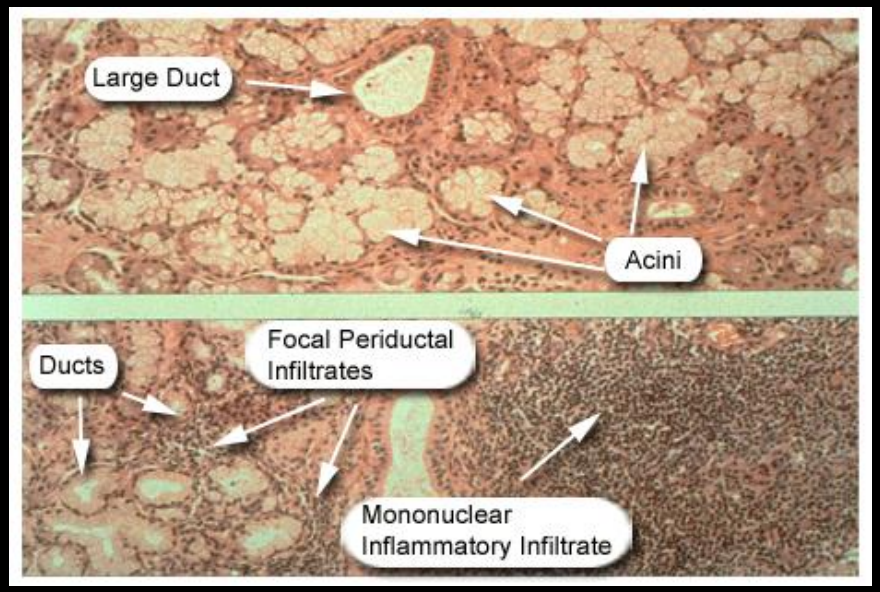
(*Punctate Sialectasia finding during Sialography*)



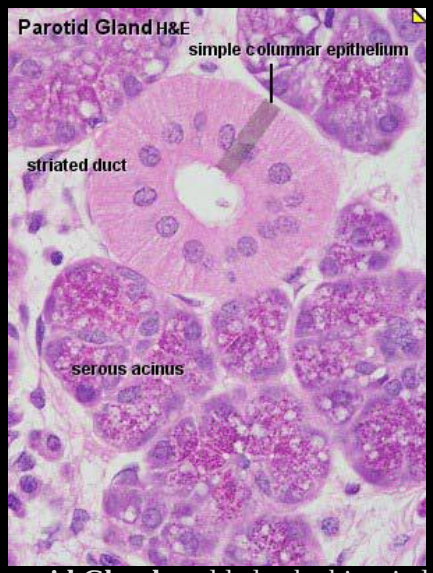


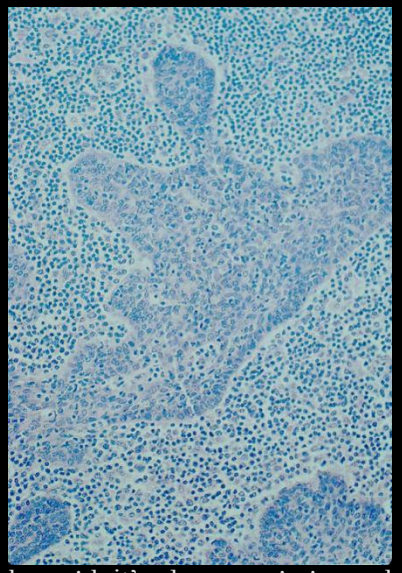
(Minor salivary glands biopsied from the lip)

The difficulty in diagnosing **Sjogren's Syndrome** is the multiple findings from multiple lab/clinical tests preformed from multiple clinicians that need to be comprised and evaluated.



(Histologic findings of a minor salivary gland in Sjogren's Syndrome [bottom] compared to that of a healthy person [top])





(The **Parotid Gland** could also be biopsied, but with it's close proximity to the facial nerve, it is not often done. A healthy **Parotid Gland** [left] can be compared to one affected by **Sjogren's Syndrome** [right]. Notice the **benign lymphoepithelial lesion**.)

Sjogren's Syndrome (Penn Center):

Because of the difficulty of having multiple health professionals working alongside each other with the proper collaboration, The University of Pennsylvania (Penn) has created a **Sjogren's Syndrome** Center, where all of the professionals/diagnostic capabilities are located in one place.

- PENN uses something called the **European-American Diagnostic Criteria** to diagnose **Sjogren's Syndrome**. It consists of six (6) criteria that can be used for a diagnosis.
  - **Diagnosis of Primary Sjogren's Syndrome (1º) requires four of the six criteria for diagnosis (including number five or six).**
  - **Diagosis of Secondary Sjogren's Syndrome (2º) requires the patient to have an already established connective tissue disease, either the first or second criteria, and two of the remaining criteria.**

(WE ARE **NOT** ACTUALLY RESPONSIBLE FOR KNOWING THE CRITERIA)

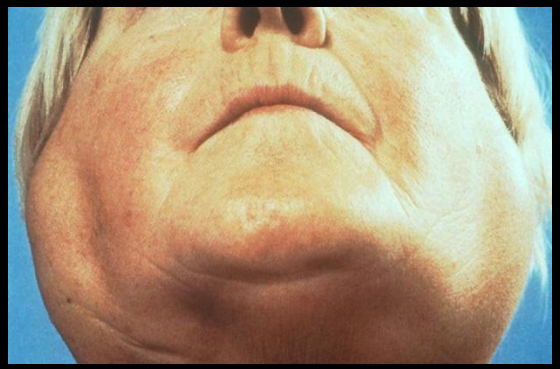
The Criteria are:

1. **Oral Symptoms (any one of the three)**
   - Dry mouth for more than 3 weeks
   - Salivary gland swelling
   - The need for liquids to swallow foods
2. **Ocular Symptoms (any one of the three)**
   - Dry eyes for more than three months
   - Foreign body sensation in the eyes
   - The use of artificial tears more than three times per day
3. **Oral Signs of Sjogren's (at least one)**
   - Abnormal salivary scintigraphy
   - Abnormal parotid sialography
   - Whole mouth unstimulated flow rate (a 15 minute collection less than 0.1 cc per minute.
4. **Ocular Signs of Sjogren's (at least one)**
   - Positive vital dye staining
   - Unanesthetized Schimer's Test: less than 5mm every 5 minutes
5. **Salivary Gland Biopsy**
   - Positive lip biopsy showing focal lymphocytic sialadenitis with a focus score of more than 50+ lymphocytes or plasma cells located in an area less than $4mm^2$
6. **Autoantibodies**
   - Positive Anti-SSA and/or Anti-SSB

Sjogren's Syndrome (Treatment):

Because the glands are damaged, you can expect to see a variable effect from sialogogues (pilocarpine, etc.). If the glands are completely destroyed, you can expect to see no effect. If the disease has only partially destroyed them, sialogogues may work so they are definitely worth trying.

- While there is no equivalent replacement for saliva, hydration and saliva substitutes can also be attempted.
- Because of the increased risk for caries, topical fluoride should be administered on a regular basis.
- There is also an increased risk for candidiasis, which should be treated immediately if it arises.
- Just like other autoimmune diseases, there is an increased risk for lymphoma (40x more than the general population). When lymphoma occurs, it usually begins in the affected glands.



(A unilateral/bilateral swelling would be indicative of secondary ***lymphoma*** *from* ***Sjogren's Syndrome****)*

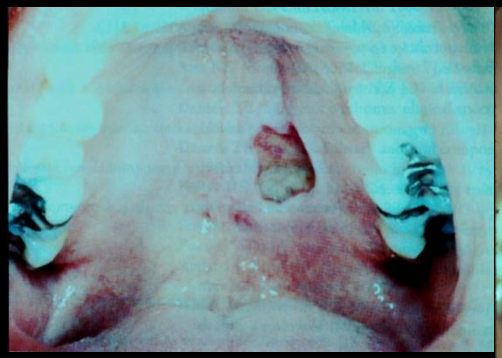
Before we begin our discussion on salivary gland neoplasms, lets quickly discuss…

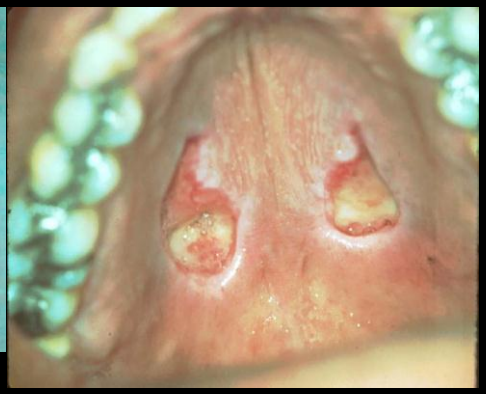
Necrotizing Sialometaplasia:

An inflammatory condition of salivary glands that most commonly affects minor glands of the hard and soft palate unilaterally. Histologically, it mimics a malignant process. It can be considered uncommon, but is usually seen in adult males.

- It begins as a painful swelling (with or without paresthesia). Within 2-3 weeks, the center sloughs out, leaving a crater which is less painful. Through this process, the underlying bone may be destroyed.
- At first it looks like an infection (not to be confused with a tooth abscess), and transforms over time into a crater, where the underlying bone may actually be visible.

Diagnosis: A typical dentist will send this to an oral surgeon for a biopsy. During that time, the lesion may actually progress and change appearance. Histologically, it may resemble Squamous Cell Carcinoma. The granular cells appearance resemble a malignancy. Because of this, it was originally referred to as "Self-Healing Carcinoma", since unlike malignant cancer, it usually resolves on its own.





Treatment: usually resolves on its own within 1-2 months. Can consider excision, but if bone is visible, this is not an intelligent option.

Now, lets shift the discussion to…Salivary Gland Neoplasms:

Before we go into much detail about anything specific, here are some general considerations about their clinical features:

- **BENIGN** salivary tumors tend be very similar to other benign tumors (slow growing, painless swellings, with no surface ulcerations).
- **MALIGNANT** salivary tumors tend to present with a more rapid growth with **pain**. Muscular and sensory changes may also be present (Bell's Palsy/paresthesia are associated with malignancies of the **Parotid Gland** since the facial nerve is located very close by).
- The hard/soft palate is a common site for neoplasms, but an uncommon site for mucoceles *(Superficial Mucoceles are relatively common on the palate however)*. The palate is similar to the tongue in terms of differential diagnosis. Depending upon where the lesion occurs, you can rule out/include certain pathologies.
- If you exclude tumors of the **Sublingual Gland** (which exhibits rare, yet often malignant tumors), **"the smaller the gland, the greater the likelihood of malignancy for a salivary gland tumor"**. So basically, from the **Parotid Gland**, to the **Submandibular Gland**, to the minor salivary glands, the greater the likelihood for a neoplasm to be malignant (Therefore, most Parotid Gland tumors are benign.)
- The most common site for salivary gland tumors is the **Parotid Gland**. [66%-75% of all salivary gland tumors occur in the Parotid Gland, and of those, 66%-75% of the are benign]. In fact, most of them are **Pleomorphic Adenomas (PAs)**. We will discuss them in a little bit.
- In terms of minor salivary gland tumors, the most common site for the to arise is the **posterior lateral palate**. The likelihood of a minor salivary gland tumor being either benign or malignant depends on the site which it is located. The breakdown goes as follows (**I would have an understanding of this for this exam**):
    - **Palate** – 50% are malignant
    - **Upper Lip** – 20% are malignant
    - **Lower Lip** – 75% are malignant (and are often Mucoepidermoid Carcinomas)
    - **Floor of Mouth/Tongue/Retromolar Pad** – 90%+ are malignant

Since we now understand the general considerations for salivary gland neoplasms, let's move onto…

Benign Salivary Gland Tumors:

There are more than a dozen different types of benign salivary gland tumors. However, we will simply take a look at the four which are most common. These include:

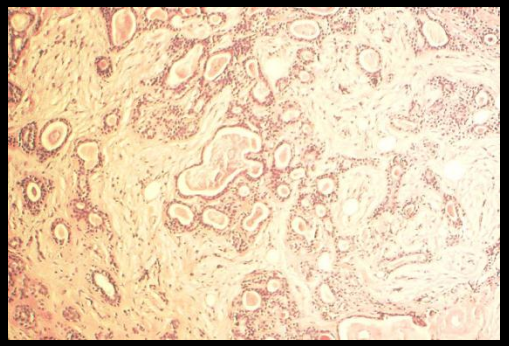
- Pleomorphic Adenoma
- Monomorphic Adenoma
- Wharthin's Tumor
- Oncocytoma

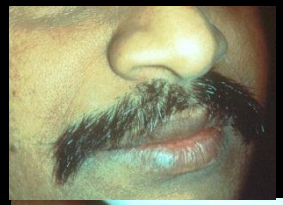
Also, the order in which we discuss them relates to the prevalence in which they are expected to arise. [**Pleomorphic Adenoma** being the most common on the list, and **Oncocytoma** being the least common on the list]

Pleomorphic Adenoma (PA) (Mixed Tumor):

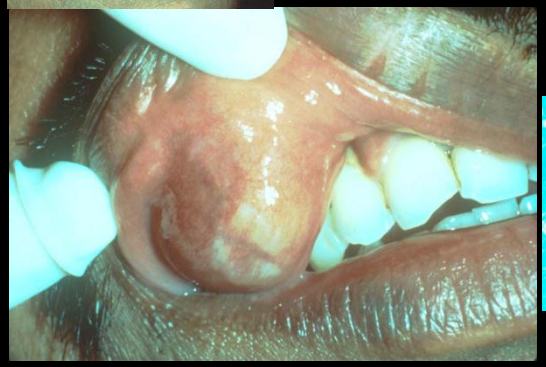
Pleomorphic = comprised of different histologic patterns
Adenoma = a benign glandular tumor

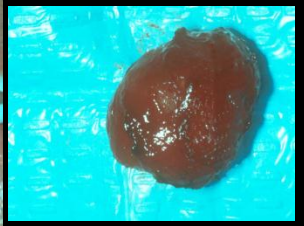
The most common salivary gland tumor. [As a refresher, the most common odontogenic tumor is an **Odontoma**, or an **Ameloblastoma** if you consider an **Odontoma** to be a hamartoma instead of a tumor] It presents like other bengin tumors as a slow-growing painless mass most commonly seen in young adults.





- **Pleomorphic Adenomas** arising from the **Parotid Gland** often appear as a superficial lobe which causes **a 'preauricular' swelling, or swelling over the angle of the mandible.**
- If present in a minor salivary gland, the most common location to see one is the **lateral palate or upper lip**.
- Typically, the mucosa is intact, and you will be able to palpate the tumor underneath. Most benign tumors have fibrous connective tissue on the periphery. Clinically, this is evident by being able to determine the borders of the tumor with your fingers.





Histologically: described as a pleomorphic adenoma because when observed histologically in different areas, the cell pattern changes (pleomorphic). For example, in one area you could expect to find myoepithelial cells producing cartilage, and in other areas fewer myoepithelial cells incorporated into a ductal-cell network (you will not find cartilage in these areas). Also, varying with each tumor, you should expect to see different combinations of the cell types mentioned. Basically, the term 'pleomorphic' describes the histology as being variable.

Diagnosis: All **Pleomorphic Adenomas** are diagnosed via biopsy. (The only thing that can be determined clinically is a differential.)

Treatment: Surgical excision. While **Pleomorphic Adenomas** are benign, they are extremely aggressive (highest recurrence rate of the benign tumors). Also, 5% of them have a malignant transformation.

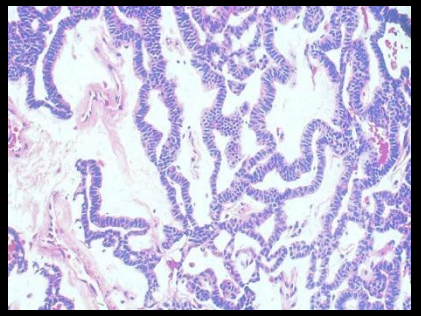
Monomorphic Adenomas:

Monomorphic = presenting in only one form
Adenoma = a benign glandular tumor
There are actually two different types of Monomorphic Adenomas:

- **Canalicular Adenoma** – only seen in minor glands (most often on the upper lip)
- **Basal Cell Adenoma** – only seen in major glands (most often in the Parotid Gland) and is associated with syndromes

Canalicular Adenoma:

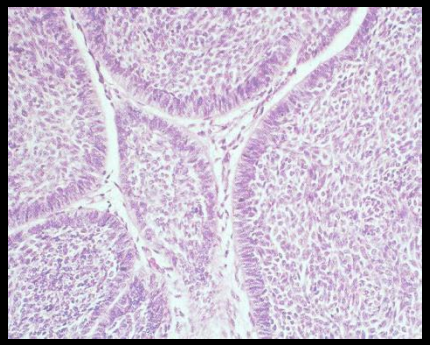
Benign minor salivary gland tumors typically seen on the upper lip of adults. It presents as a painless, slow growing mass that can be multifocal with several separate masses adjacent to each other. This can be considered atypical since multiple tumors (localized) could be considered of the same pathology. They are highly vascular, so **Canalicular Adenomas** often present with a bluish color (blood).



Histologically: very vascular single layered ducts with 'long' canals (hence the name **Canalicular Adenoma**).
Diagnosis: Preformed through biopsy. Based on the location (upper lip), some may be evident as **Canalicular Adenomas**, but you do need a biopsy to make the diagnosis definitive.
Treatment: Excision with a rare recurrence rate (you might use the phrase 'ideal tumor')

Basal Cell Adenoma:

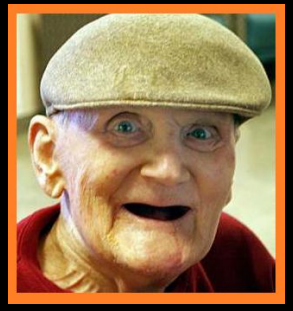
Benign major salivary gland tumor, that presents as a slow-growing painless mass, most often occurring in the superficial lobe (expect to see extra-oral swelling) of the **Parotid Gland** of adults. **Basal Cell Adenomas** are sometimes associated with a syndrome. When the syndrome is present, the patient will also have skin tumors that resemble **Basal Cell Carcinomas**, but are actually **Basal Cell Adenomas**.



Histologically: solid 'islands' inter-digitating with peripheral palisading (common with basal cells)
Diagnosis: Preformed through biopsy.
Treatment: Surgical excision with a rare recurrence rate if it is not affiliated with the syndrome.

Wharthin's Tumor

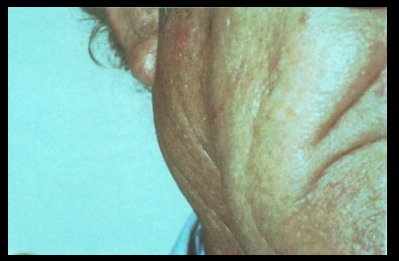
(Papillary Cystadenoma Lymphomatosum):



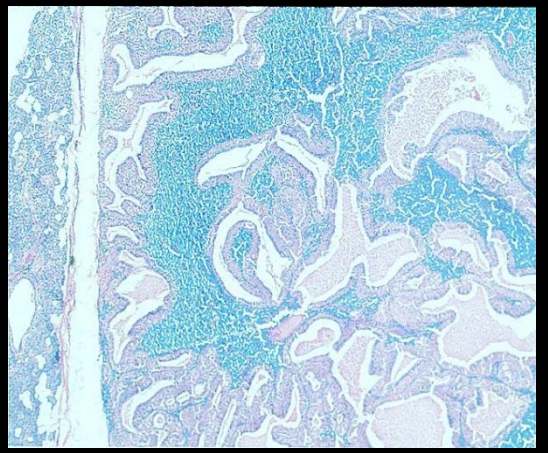
Papillary = papillaries are present
Cyst = cysts are present
Adenoma = a benign glandular tumor
Lymphomatosum = many lymphocytes will be present

Considered a major salivary gland tumor (almost exclusively in the tail of the **Parotid Gland**), and is the second-most common **Parotid Gland** tumor (second to **Pleomorphic Adenoma**). Presents as slow-growing painless masses, most commonly in older men (especially smokers), that can be either unilateral or bilateral. If bilateral, they can occur at either the same time (synchronous) or at different times (metachronous).

- They are believed to be tumors that develop within intra-Parotid Gland lymph nodes, which has trapped salivary epithelium (embryologically/developmentally) that undergoes neoplasia.



Histologically: lymphocytes (blue) and salivary gland cells (pink), with ductal spaces in the center (which eventually are what turn into cysts). Sometimes, papillary projections ascend into the ductal spaces.



Diagnosis: Biopsy the hell out of it.

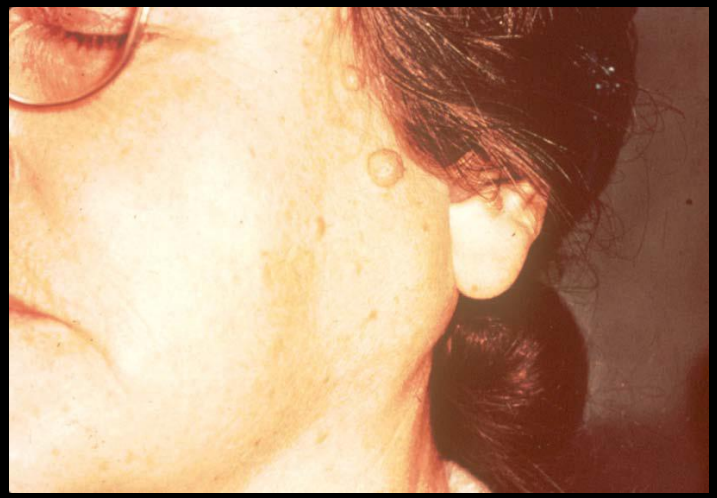
Treatment: Surgical excision. It does sometime recur. When it does, it is hard to differentiate from a true recurrences and a second primary tumor. There is a rare possibility of a malignant transformation (either the epithelial or lymphocytic component can become malignant). Therefore, the malignancy can either turn into a carcinoma or a lymphoma.

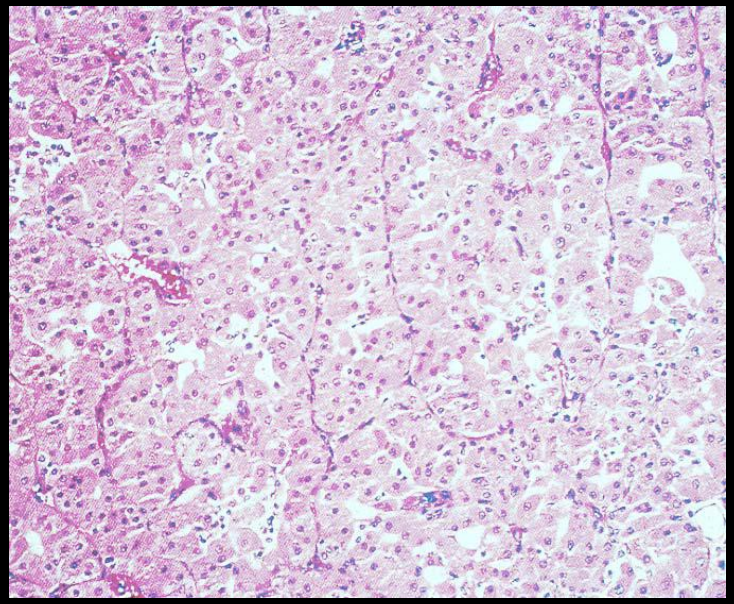
Oncocytoma (oxyphilic adenoma):

So this benign tumor is rather rare. Dr. Fornatora said in class that the only reason she is taking the time to discuss it is because it is one of those pathologies that sometimes arises on the boards.

It can be considered yet another major salivary gland tumor (often the Parotid Gland) that presents as a slow-growing painless mass.

Histologically: called an **Oncocytoma** because of the presence of **Oncocytes** (pale-satining pink cells with a large amount of granules within their cytoplasm) when viewed under the microscope.





(Diagnosed through biopsy, the treatment is surgical excision with an excellent prognosis and a rare recurrence rate.)

With the benign tumors under our belts, lets discuss…

Malignant Salivary Gland Tumors:

There are roughly two dozen known different malignant salivary gland tumors. Fortunately, we will only be discussing the five which are most common and well-documented. They are:

- **Mucoepidermoid Carcinoma**
- **Malignant Mixed Tumor**
- **Adenoid Cystic Carcinoma**
- **Acinic Cell Adenocarcinoma**
- **Polymorphous low-grade Adenocarcinoma**

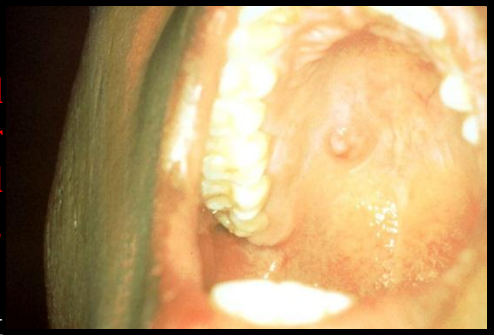
(From the perspective of a pathologist, malignant salivary gland tumors can be hard to differentiate/classify (which is why there are so many). Again, the five that we will discuss are rather clear-cut and relatively easy to understand.)

Mucoepidermoid Carcinoma:

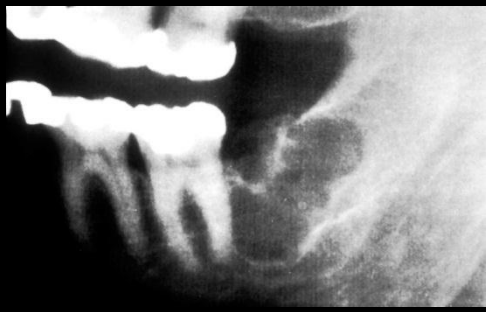
Muco = mucous cells are present
Epidermoid = epithelial cells (squamous) are present
Carcinoma = a malignant glandular tumor

A common malignant salivary gland tumor that most commonly occurs in the **Parotid Gland** (second most common location is minor salivary glands). If it occurs within a minor salivary gland, the most common location within the oral cavity is the **posterior lateral palate**. A **Mucoepidermoid Carcinoma** presents as a posterior lateral palatal swelling. Because these tumors contain mucin, they can clinically appear blueish in color.

- The amount of mucin varies per tumor (those with a lot of mucin might actually present like a **Mucocele**). However, as we have already discussed, normally **Mucoceles** do not present on the lateral palate (which makes the differential diagnosis a little easier).
  - However, a **Mucocele**-like swelling on the **lower lip** may be slightly more difficult to properly diagnose. **If you notice a lesion on the lower lip that looks like a Mucocele, do not rule out Mucoepidermoid Carcinoma. [Children will most likely have a Mucocele, while an adult could present with either.]**
- Larger **Mucoepidermoid Carcinomas** may present with characteristics similar to many malignancies (rapid growth, neurologic problems, etc.). When located in the **Parotid Gland**, there is also the possibility of paresthesia and Facial Nerve palsy.
- **Mucoepidermoid Carcinomas** can also occur within bone (intra-bony). Even though there are no salivary glands within the bone (obviously), just like many of the odontogenic pathologies we have discussed, it could be caused by epithelial rests (Serres/Malassez) remaining within the mandible/maxilla after tooth formation/development, and through a metastatic process, producing **Mucoceles**.
  - This would fall in the differential diagnosis category of a multi-locular radiolucency of the posterior mandible (which would then be called a **Central Mucoepidermoid Carcinoma**).



(posterior lateral palate), [much too close to the midline to be considered an abscess from any of the maxillary teeth]



(intra-bony multi-locular radiolucency of the posterior mandible)

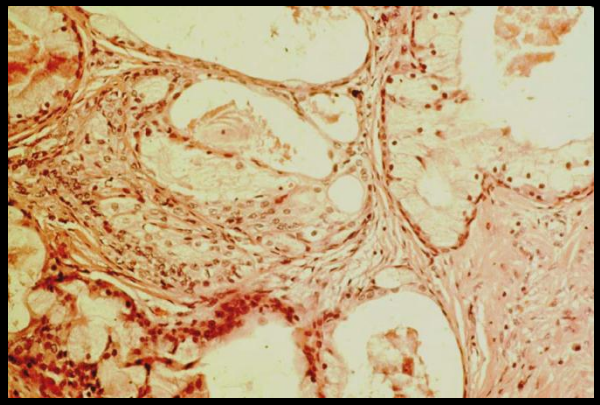
Mucoepidermoid Carcinoma (cont'd):

Histologically: Both **Mucous Cells** and **Epidermoid Cells** are present. Also, **Intermediate Cells** should be seen. Histologists are not really sure what these are, but they do not look like either of the other two cell types (hence, "Intermediate Cells").

- Varying with each tumor, the proportion of these cell-types changes. (For example, a **Mucoepidermoid Carcinoma** with a lot of Mucous Cells will present with much more mucin in the lumen.)

There are three histological 'grades' used to describe **Mucoepidermoid Carcinomas**:

- Low Grade – mostly mucous cells (and mucin) present
- Intermediate Grade – an equal combination of both mucous and epidermal cells
- High Grade – mostly epidermoid cells present



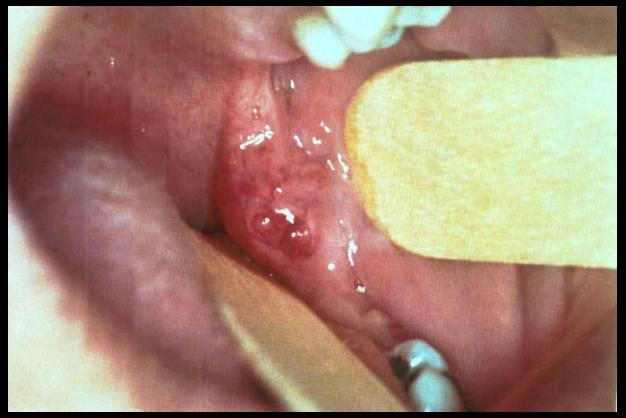
*(notice **Mucous Cells** close to the lumens and **Epidermoid Cells** outside on the periphery)*

Treatment: Surgical excision with a wide margin (due to the malignancy potential). The degree of peripheral excision is determined by the tumor's location and the histological grade (lower grade **Mucoepidermoid Carcinomas** tend to be less aggressively surgically excised, while ones of higher grade need a larger margin).

- If the **Mucoepidermoid Carcinoma** is of a higher grade, or is located within the **Parotid Gland** (and next to the **Facial Nerve**), Radiation Therapy is also used because of the difficulty of completely excising malignant cells from the periphery of a nerve.

Prognosis: depends on the grade/stage of the tumor,

- Low Grade = good prognosis (90% cure rate)
- High Grade = poor prognosis (30% survival rate)



(over retromolar pad)

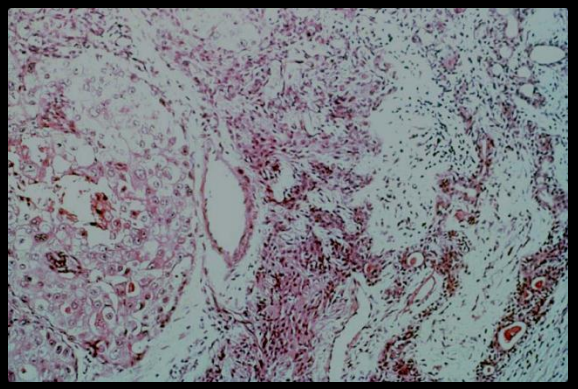
Malignant Mixed Tumor:

Remember that another name for a **Pleomorphic Adenoma** is a "**Mixed Tumor**". Therefore, a **Malignant Mixed Tumor** is the malignant counterpart to a **Pleomorphic Adenoma**. There are three different ways that these can arise…

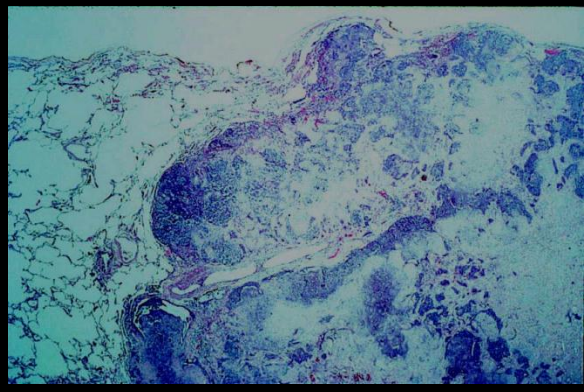
1. **"Carcinoma ex PA"**, where the epithelial component of a long-standing **Pleomorphic Adenoma** becomes malignant. (Clinically, this would present with a long-standing and untreated **Pleomorphic Adenoma** that spontaneously demonstrates rapid growth.) If the tumor is in the **Parotid Gland**, eventually expect facial nerve involvement. Histologically, areas of benign **Pleomorphic Adenoma** are seen along with a malignant epithelial component. (This is the most common of the three types.)
2. **"Metastasizing Mixed Tumor"**, where a **Pleomorphic Adenoma** that has been surgically excised (possibly more than once), spontaneously metastasizes somewhere else within the body (**lungs** and **bone** are the most common places). Histologically, these metastasized tumors would look identical to a **Pleomorphic Adenoma**. It is believed that this process is from repeated surgical intervention.
3. **"Carcinosarcoma"** , where the malignancy occurs from the very beginning (de novo) (both the epithelial and mesenchymal cells appear malignant). Histologically, it would appear as **Squamous Cell Carcinoma** and **Chondrosarcoma** within the same tumor.

Treatment: treat with excision. Knowing that they are malignancies, also preform a lymph node dissection, along with radiation therapy.

Prognosis: unfavorable, especially if the malignant component extends outside of the tumor capsule.



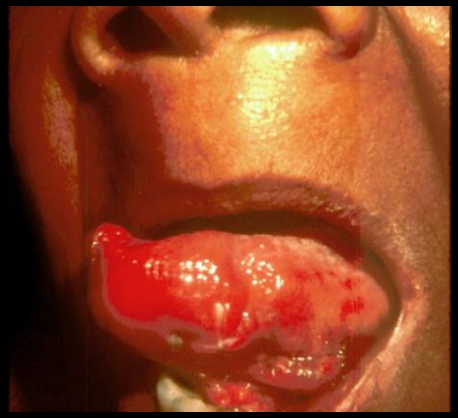
(Carcinoma ex PA, notice both the benign and malignant portions)

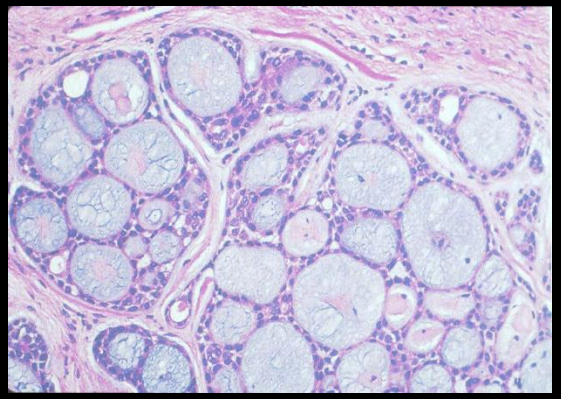


(Metastasizing Mixed Tumor to the lung)

Adenoid Cystic Carcinoma:

These present as a slow growing mass either on the palate or a major salivary gland that typically demonstrate with pain very early on. (The tumor has a tendency to wrap around nerves of varying sizes.) **Adenoid Cystic Carcinomas** of the **Parotid Gland** may actually yield facial paralysis. Ones that appear on the palate they my be ulcerated, and can cause local bone destruction.



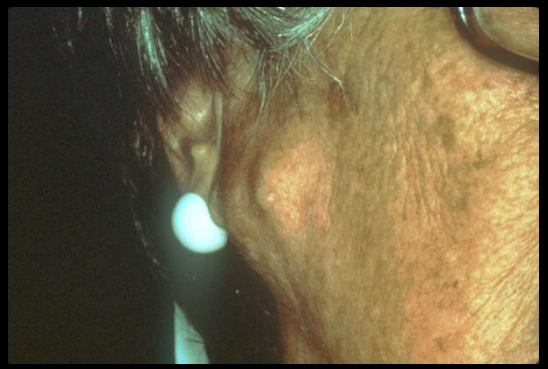


(cribiform "Swiss cheest" histologic pattern)

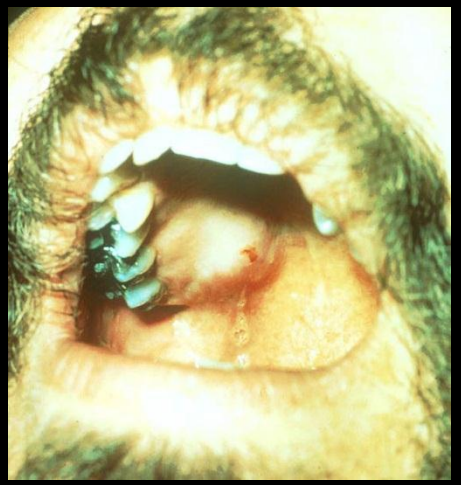
Histologically: demonstrates a **cribiform ("Swiss cheese") pattern** of ductal/ myoepithelial cells. Commonly, peri-neural invasion is evident.

Treatment: surgical excision, but because they tend to travel with nerve, very hard to completely remove without radiation therapy.

- Considered a relentless tumor, which is prone to local recurrence and eventually distant metastases (to lungs and bone)
- 5-year survival is 70%, while 20-year survival is 20%



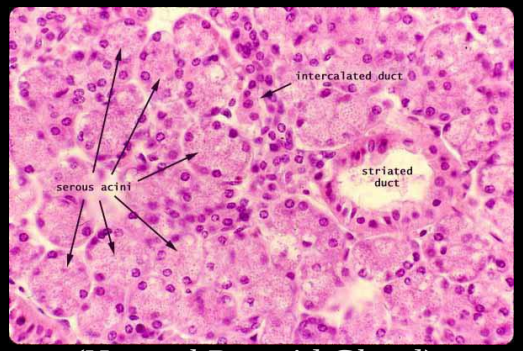
(Facial Nerve involvement)



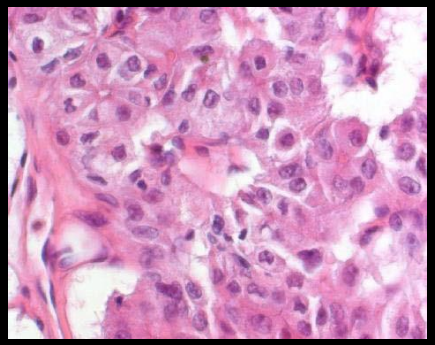
(palatal swelling, so must rule out abscess)

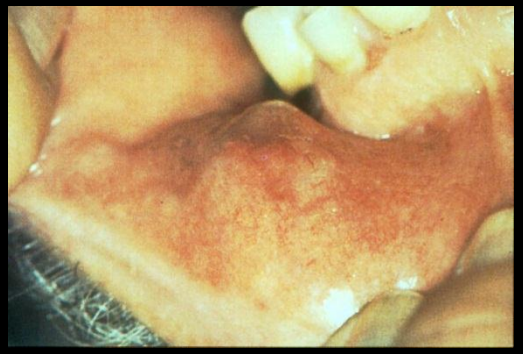
Acinic Cell Adenocarcinoma:

Most often seen in the **Parotid Gland**, **Acinic Cell Adenocarcinomas** are low-grade, slow growing masses that are infrequently associated with pain and facial paralysis.



(Normal Parotid Gland)


(Acinic Cell Adenocarcinoma)

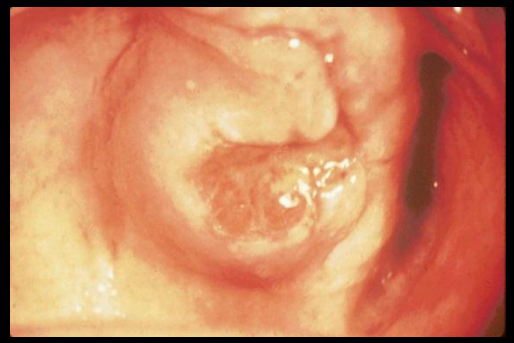


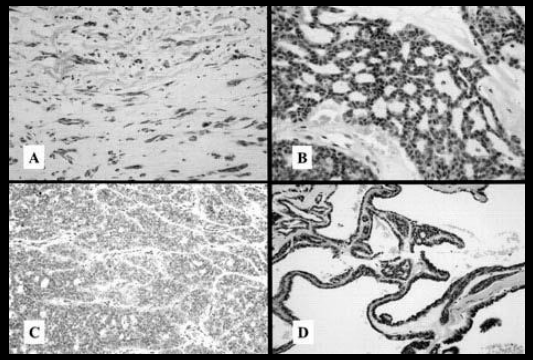
Histologically: appear as normal looking **Acinic Cells** that you would expect to see within normal salivary glands.
Treatment: surgical excision with a good prognosis (80% of patients remain tumor-free after excision).

Polymorphous Low-Grade Adenocarcinoma:

A low-grade tumor that is exclusively a minor salivary gland tumor, that typically presents as a slow-growing painless mass often seen on the **lateral palate**.

Histologically: given from the name "polymorphous", the involved ductal cells demonstrate varied growth patterns.
Treatment: surgical excision with a good prognosis (80% of patients remain tumor-free after excision).


(lateral palatal mass with a central ulceration)



(four slides from the same tumor demonstrating the varied growth patterns)

[Salivary Gland Neoplasms],

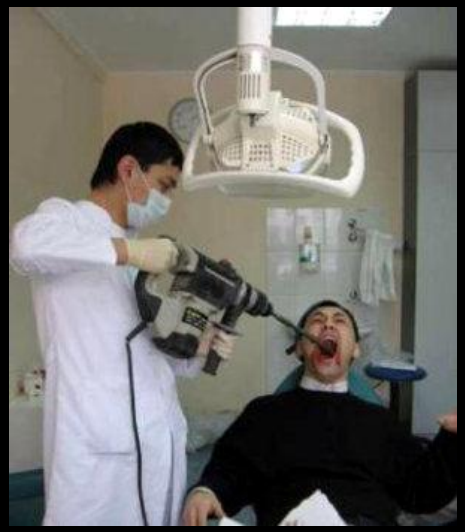
General Considerations:

(Both **Benign** and **Malignant**)

Let's recap some of the general characteristics and trends about salivary gland tumors, both benign and malignant.

- **BENIGN** salivary gland tumors tend to present as **slow growing**, **painless swellings** with **no surface ulceration.**
- **MALIGNANT** salivary gland tumors tend to **grow more rapidly**, with **an associated pain and possibly muscular/sensory changes** (Bell's Palsy, paresthesia, etc.)

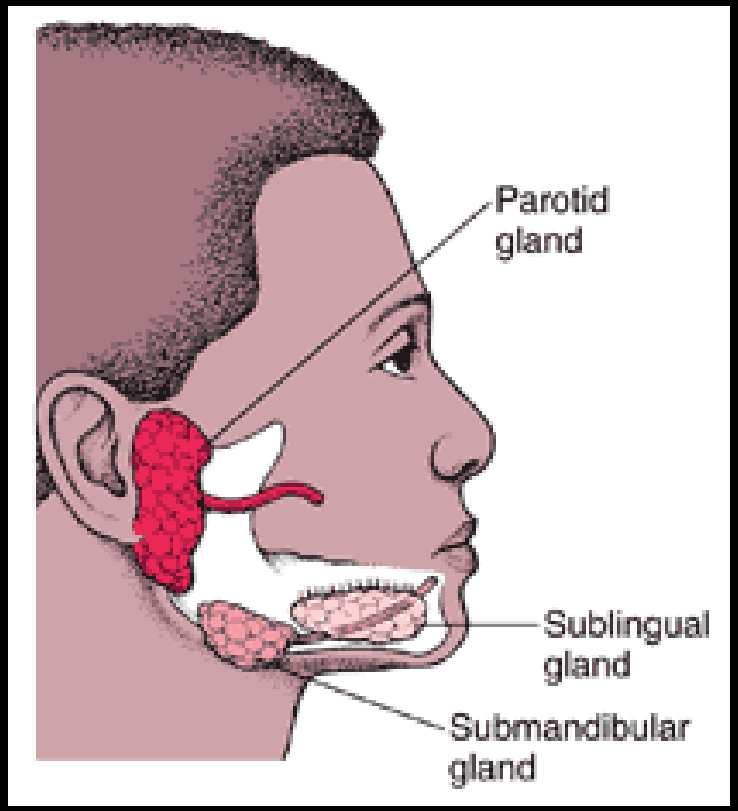
➢ Some of the 'low-grade' malignant salivary gland tumors can be slow growing, so growth rate alone is now an adequate determination between **benign** and **malignant** (a biopsy is always needed).



[Salivary Gland Neoplasms],

General Considerations:

(Both **Benign** and **Malignant**)



- The **palate** is the most common site that **neoplasms** occur (however, this is an uncommon site for **mucoceles**).
- Tumors of the **Sublingual Gland** are **rare** and often **malignant**.
- Excluding the **Sublingual Gland** (where tumors rarely occur, and when they do are often malignant), **"the smaller the gland, the greater the likelihood of malignancy for a salivary gland tumor"**.
- The **most common** site for a salivary gland tumor is the **Parotid Gland** *(66%-75% of all salivary gland tumors occur in the **Parotid Gland**)*.
  - Of the tumors that do arise in the **Parotid Gland**, *66%-75% of them are **benign*** (most often being a **Pleomorphic Adenoma**)

[Salivary Gland Neoplasms],

General Considerations:

(Both **Benign** and **Malignant**)

Having broken down the neoplasm statistics for the major salivary glands, lets quickly review the **minor salivary glands**:

- For minor salivary glands, the most common location within the oral cavity to see a neoplasm is the **lateral palate**.
- However, the likelihood for a minor salivary gland to present a malignancy varies with where the minor salivary gland is located.

- Upper Lip: **20%** malignancy
- Palate: **50%** malignancy
- Floor of Mouth / Retromolar Pad / Tongue: **90%+** malignancy
- Lower Lip: **75%** malignancy (often Mucoepidermoid Carcinomas)

[Salivary Gland Neoplasms],

General Considerations:

(Both **Benign** and **Malignant**)

So lets end our discussion on salivary gland pathology with a review of the **HISTOLOGY** that we have already discussed:

- Most **BENIGN** tumors have a **tumor capsule of fibrous connective tissue** which surrounds the neoplasm.
  - The exception to this would be that **benign minor salivary gland tumors** may not have a capsule (especially those located on the **palate**).
- Most **MALIGNANT** tumors do not have a capsule and show an infiltrative growth pattern.

Cruising right along, the next topic on our list is…

Hematologic Disorders:

(Chapter 13 from the textbook)

(blood, artist's rendition)

Remembering the advice of my high school basketball coach, lets start with the fundamentals. For those of you who don't know,

Hematology: the branch of biology, physiology, internal medicine, pathology, clinical laboratory work, and pediatrics that is concerned with the study of blood, the blood-forming organs, and blood diseases.

The first thing we need to do is review where exactly the lymphoid tissue of the head and neck is located. We'll soon appreciate that Hematologic disorders and lymphoid tissue go hand-in-hand.

So where is the lymphoid tissue of the oral cavity located?

? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ? ?

If you said the **TONSILS**, you are correct! In fact, we have three (3) sets.

1. **The Adenoids (Pharyngeal Tonsils):** don't expect to see these, they're far back
2. **Palatine Tonsils:** these can be seen (especially in children)
3. **Lingual Tonsils:** embedded in the tongue deep to the *Foliate Papillae* (typically cannot be seen unless they are enlarged secondary to pathology

COLLECTIVELY, these three sets of tonsils are called **WALDEYER'S RING**: which is an imaginary circle/ring connecting all three tonsils on each side. Within this 'ring' is a large collection of lymphoid tissue.

But that's not it! (that would be too easy) Does the abbreviation **MALT** sound familiar?

It stands for- **Mucosa-Associated Lymphoid Tissue:** located beneath the mucosa, it can be considered a poorly-differentiated aggregate of lymphoid tissue located underneath the superficial surface of the oral cavity (In a pathology-free person, MALT should not be observable).

- If you biopsied a section of lymphoid tissue, or if MALT underwent hyperplasia, it could be noticeable (creamy yellow swelling beneath the surface).
- In a healthy person, you should not be able to see MALT!

More about oral cavity lymphatics:

The **lymphatics** of the oral cavity can be compared to the salivary glands in terms of distribution.

- The **TONSILS** could be considered the major lymphatics of the oral cavity (located in specific locations), while **MALT** can be considered the minor lymphatics of the oral cavity (aggregates that are dispersed throughout)…

So what about extra-orally?

- Believe it or not, extra-oral examinations are preformed for a reason during DRC duty (identifying the Sternocleidomastoid Muscle and palpating the **Anterior and Posterior Cervical Lymph Nodes**).
- Don't forget about the **Submandibular Lymph Nodes** and **Submental Lymphnodes** either!

So why do we palpate the **Cervical/Submandibular/Submental Lymph Nodes** during DRC duty?

- Most commonly, enlarged lymph nodes represent a reactive hyperplasia that is indicative of an infection/immune response within that area.
- If the lymph nodes are not enlarged because of an infection, consider the possibility of a **MALIGNANCY** (being either Metastatic Carcinoma or Lymphoma).
    - Lymphoma: is a primary malignancy of lymphocytes that predominately occurs in lymphnodes.

So if you see an enlarged lymph node, you need to ask yourself if it is either…

1. A reactive lymphadenopathy

or,

2. A neoplastic lymphadenopathy

…because each one is indicative of two separate types of pathology.

Continuing the discussion in the same direction…

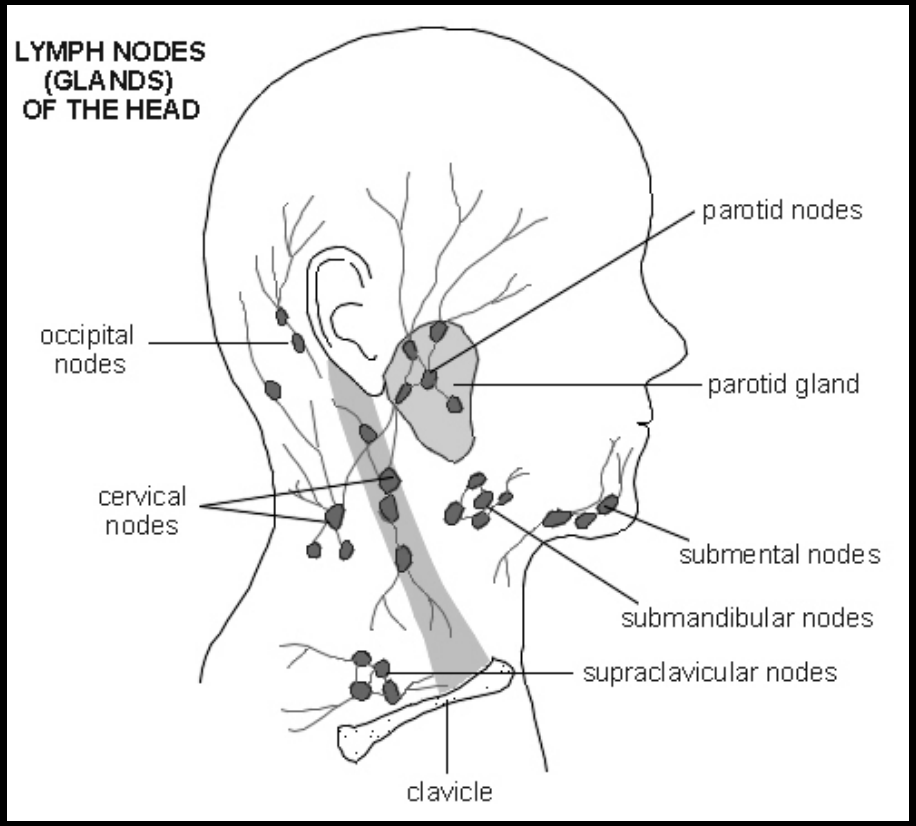
What if you come across enlarged **Submandibular Lymph Nodes**? What does that most commonly mean?

Chances are, this means that there is a tooth borne infection (**odontogenic infection**) somewhere in the oral cavity. (Most of the teeth drain into the **Submandibular Lymph Nodes**.)

What are you hoping to find upon palpating an enlarged lymph node?

You are looking to see if the lymph nodes are **tender** (indicative of an **acute infection**).

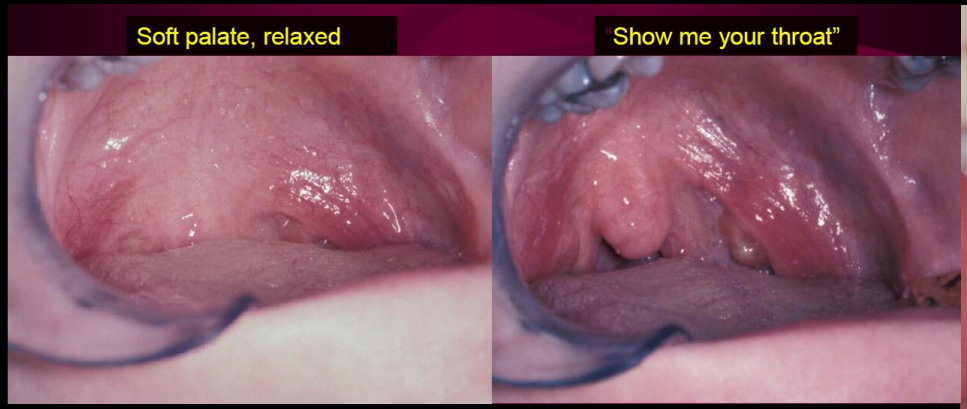
- **Chronic infections** (periodontal disease for example) also produce enlarged lymph nodes. However, enlarged lymph nodes due to chronic infection will present as **non-tender**, and much more difficult to distinguish from a **malignant process**. (The first site of metastasis is typically the **Cervical Lymph Nodes**)



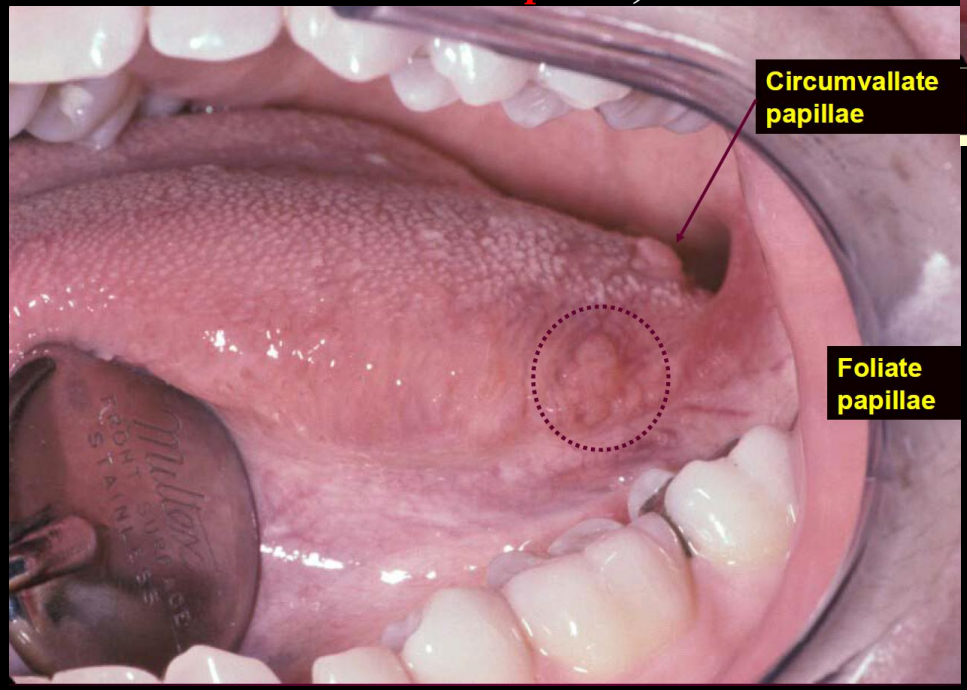
(Remember that the lymph nodes of the head & neck are located underneath muscle, which needs to be moved out of the way for a proper palpation.)
*[Also, notice that there are a few lymph nodes embedded in the **Parotid Gland** (remember: Wharthin's Tumor)]*

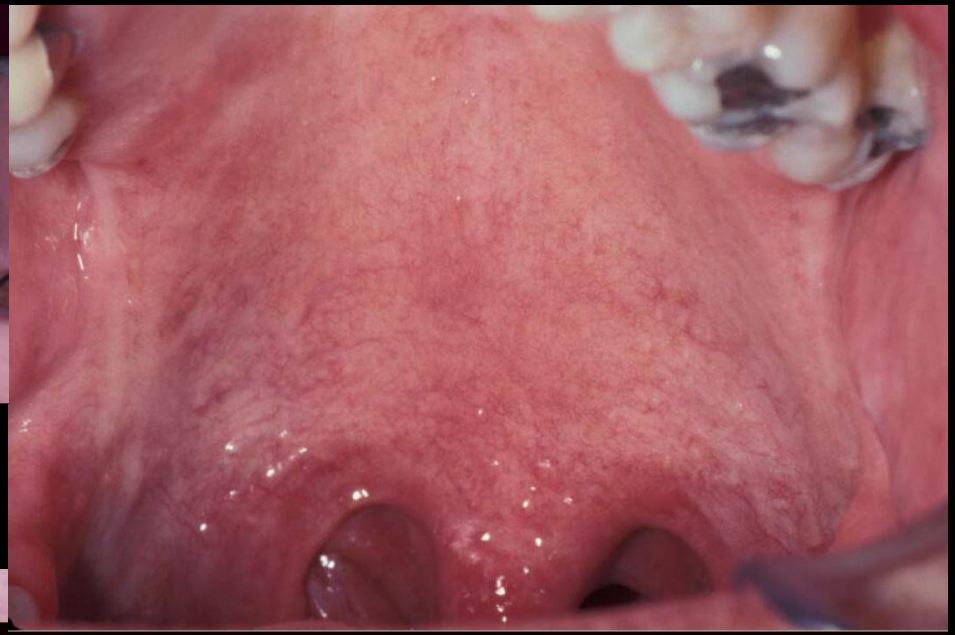
With an understanding of the head & neck lymphatics, lets discuss…

What to look for during an intra-oral lymph node exam:



*(Bottom: While the **Lingual Tonsils** are not evident on a healthy person, recognize that they are deep to the **Foliate Papillae**.)*





Soft palate of same patient as previous hard palate photo - note uvula, tonsillar pillars (anterior - palatal glossal arch, posterior - palatal pharyngeal arch) & tonsil

*(Top Left and Right: Then move onto the **pharynx**. You want the patient to elevate their soft palate, which is typically done by saying "Ahhhhhhh". Here, you can see the **anterior and posterior tonsillar pillars** as well as the **uvula**. The **Palatine Tonsils** sit in-between the anterior and posterior tonsillar pillars.)*

Continuing with the previous slide,

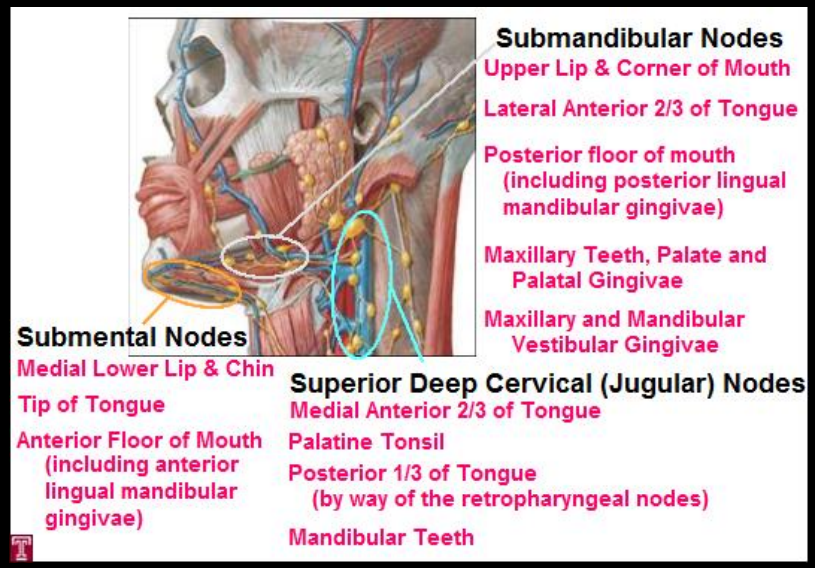
What to look for during an extra-oral lymph node exam:

*(The **Submental Lymph Node** exam is preformed directly posterior to the midline of the mandible. In most adults, they are non-palpable. In children however, they should be rather prominent)*

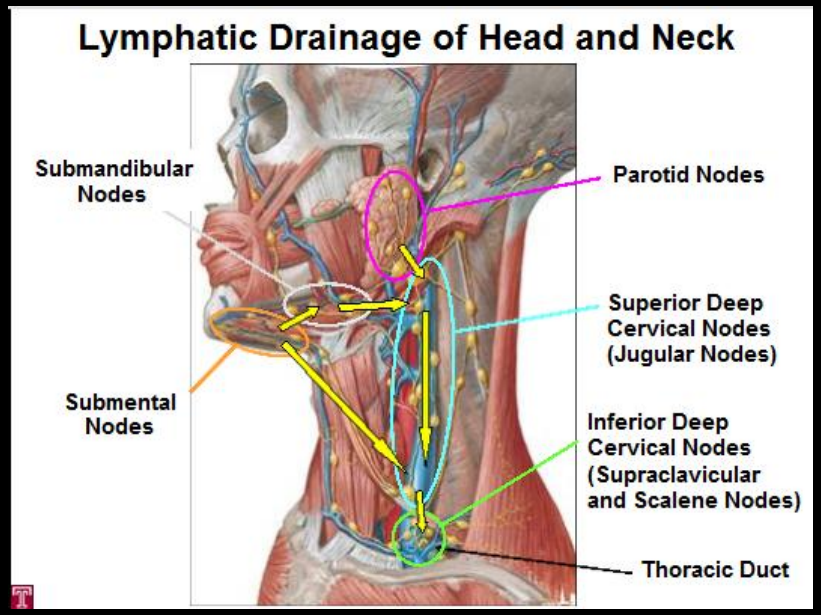
*(The **Submandibular Lymph Nodes** are slightly harder to feel. They are more tucked into the substance of the anatomic area in which they are located. A common technique is to pull laterally towards the inferior border of the mandible. In this area, the **Facial Artery** can sometimes be mistaken for a lymph node. If what you're palpating presents with a pulse, then you know it's the **Facial Artery** and not a lymph node.)*

Before we can adequately say that we understand the lymph nodes of the head & neck, we need to discuss...

Lymphatic Drainage of the Oral Cavity:



(Two throwback slides from Gross Anatomy)



The first question we need to ask is…

Where do the lymphatics of our teeth drain?

- The **mandibular incisors** drain into the Submental Lymph Nodes
- The **maxillary third molars** drain into the Superior Deep Cervical Lymph Nodes
- **All other teeth** drain into the Submandibular Lymph Nodes

Once there, where do those lymph nodes drain?

- The **Submandibular Lymph Nodes** drain into the Superior Deep Cervical Lymph Nodes
- The **Superior Deep Cervical Lymph Nodes** then drain into either the Inferior Deep Cervical Lymph Nodes or directly into the blood stream at the jugular trunk.

Remember: a lymph node that is involved in an infection increases in size and becomes of a firmer consistency. This transformation allows them to be palpable, and is described as **Reactive Lymphadenopathy**.

This brings us to our first Hematologic pathology,

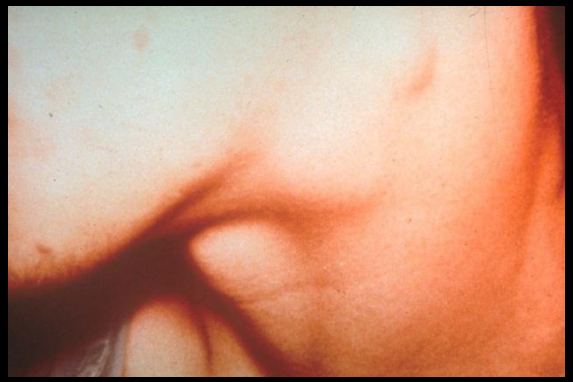
Lymphoid Hyperplasia (Reactive Lymphadenopathy):

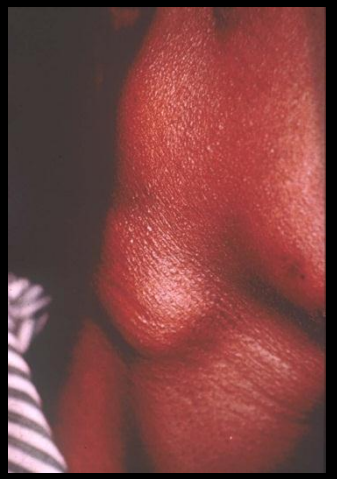
Considered common, as part of the normal immune system response. Any lymph node of the oral cavity can present with hyperplasia (Waldeyer's Ring, MALT, etc.) As we have already discussed, acute and chronic infections will cause the lymph nodes to present in two different ways…

- **Acute Infections:** will present with enlarged **TENDER** lymph nodes that are soft and freely movable.
- **Chronic Infections:** will present with enlarged **RUBBERY/FIRM** lymph nodes that are non-tender and freely movable.
  - And remember, when the lymph nodes present in this manner, **Lymphoma/Carcinoma** needs to be ruled out from the differential diagnosis!

Also, while the MALT aggregates are not typically observable intra-orally, hyperplasia causes them to expand large enough to be seen upon examination.

- Most commonly, they present as discrete and non-tender submucosal swellings (1cm or less in size) that appear **normal** to yellow in color (they resemble **Lipomas**)
- They most often can be observed on the posterior lateral tongue and anterior lateral floor of the mouth.





(Lateral Cervical Lymphadenopathy)

Diagnosis: is made based on appearance, the patients history, and the lack of progression in size (thus ruling out other pathologies).
Treatment: none (considered a secondary pathology)

Lets begin our discussion on…

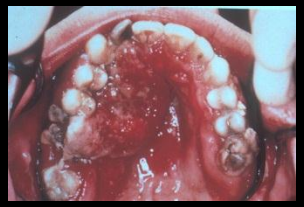
Lymphoma:

Considered a malignancy of lymphocytes, it is generally characterized into two broad categories:

- Non-Hodgkin's Lymphoma: can consist of a variety of different cell types **(B-cells, T-cells, histiocytes)**
- Hodgkin's Lymphoma: consists of **Reed-Sternberg Cells**, which are of B-cell origin but unfortunately not very well understood

It is important to know that patients with **Lymphoma** will present with constitutional symptoms **(fever, night sweats, malaise, weight loss, etc.)**. Remember, this is a systemic disease.

There's just so much to talk about in terms of Lymphoma. We'll being with…



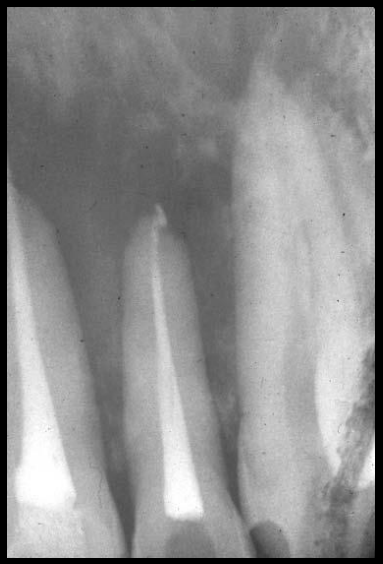
Non-Hodgkin's Lymphoma:

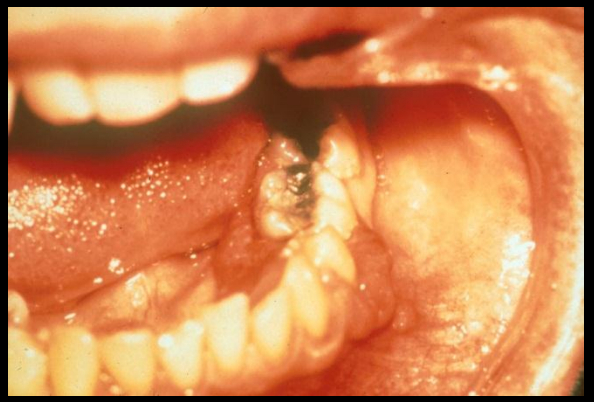
There are many different types with varying histologic grades (there is a low/intermediate/high grade classification system based on the Lymphoma's aggressiveness). It is typically of B-cell origin, usually arising in the lymph nodes.

- Patients with autoimmune diseases or immune suppression due to any sort of therapy are more likely to receive **Non-Hodgkin's Lymphoma**.

Clinically: It usually presents as an enlargement of lymph nodes or chains of lymph nodes with associated constitutional symptoms. The lymph nodes begin as slow-growing non-tender masses, which over time become hard and fixed to the surrounding tissue.

- Lymphomas occurring within the oral cavity usually are "extra-nodal" (meaning: occurring outside of the lymph nodes), within the soft tissue. The most common places to see these are [the vestibules, **the posterior lateral palate**, on the gingiva, or within bone]. They appear as red/purple firm masses.
  - When present, intrabony lymphomas present with pain and paresthesia as an ill-defined radiolucency with bony expansion that eventually causes destruction of the cortical plate. (They may actually mimic a dental abscess.)





(Lymphomas located within the oral cavity are often described as "boggy")

Treatment: The first step for the treatment **Non-Hodgkin's Lymphoma** is determining it's staging within the patient. This includes taking the medical history, preforming a physical, ordering a CBC, chest radiograph, CT of the patient's pelvis and abdomen, lymphangiography, and bone marrow biopsy. This is done to determine which parts of the lymphatic system are involved, and the histologic type of the Lymphoma.

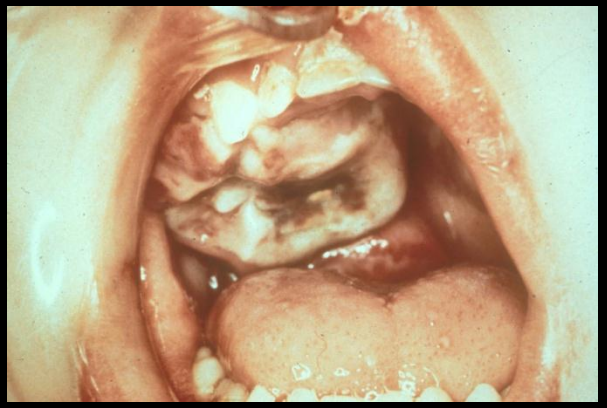
- Treatment depends on the stage and grade of the Lymphoma, and generally consists of chemotherapy & radiation therapy. They **cannot** be treated with surgery!

Prognosis: depends on the stage and grade (but usually carries a successful cure rate of 50% for intermediate and high-grade Lymphomas) The lower-grade Lymphomas are usually indolent, and may be "watched" until treatment is necessary.

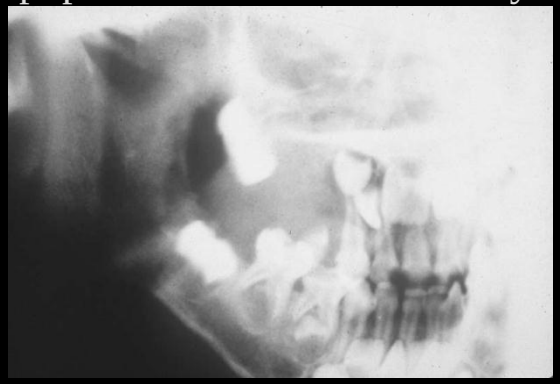
Burkitt's Lymphoma:

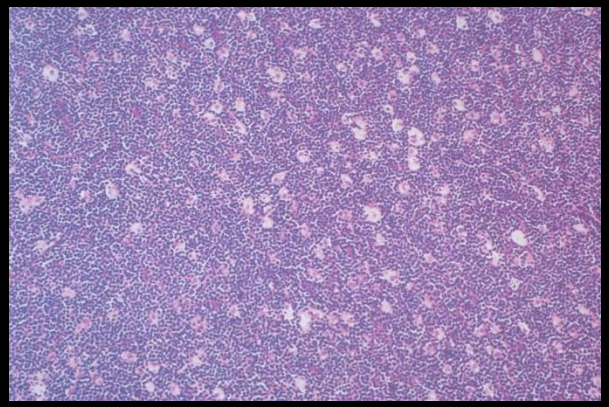
Described as a type of high-grade **Non-Hodgkin's Lymphoma**, the B-cell type associated with the pathology is related to the **Epstein-Barr Virus (EBV)**, so therefore is of oncogenic origin.

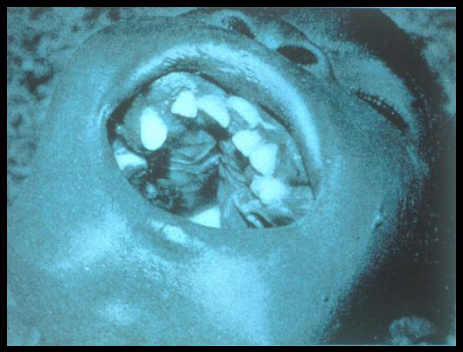
- Endemic Burkitt's Lymphoma (also known as "African Lumpy Jaw") was commonly reported in children as rapidly growing masses (24-hour doubling time) in the posterior quadrants of the oral cavity (especially the maxilla).
- Prior to the HIV epidemic, "American Burkitt's Lymphoma" commonly presented as an abdominal pathology in the older population within our country.



(Often rapidly affects all four quadrants with extra-oral expansion)







Jaw Presentation: **Burkitt's Lymphoma** presents with a minimally painful facial swelling, proptosis (forward displacement and entrapment of the eye from behind by the eyelids), and tooth mobility, which appears as ill-defined radiolucencies with the patchy loss of lamina dura.

Histology: presents as a "**starry-sky**" appearance that is actually clusters of lymphocytes with multiple spaces of apoptosis and phagocytosis. Because the tumor is so rapidly growing, the body does it's best to break down the lymphocytes that are not receiving proper blood supply.

Treatment: using a multi-agent chemotherapy regiment. It does go into remission. However, most patients do relapse.

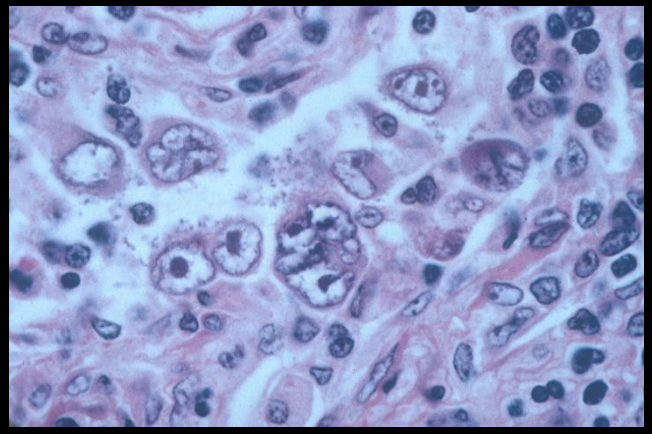
Hodgkin's Lymphoma (Hodgkin's Disease):

"Hodgkin's disease is a type of lymphoma distinguished by the presence of a particular kind of cancer cell called a Reed-Sternberg cell."

While the cause of **Hodgkin's Lymphoma** is unknown, there is strong evidence that (at least for some people) an **Epstein-Barr Virus** infection causes **B-cells** to become cancerous/malignant, and transform into **Reed-Sternberg Cells**.

- **Hodgkin's Lymphoma** is less common than **Non-Hodgkin's Lymphoma**, and most commonly begins in the **Cervical or Supraclavicular Lymph Nodes** and spreads to distant lymph node chains (**down the body**). It almost always presents as an intra-nodal metastasis.
- The enlarged affected lymph nodes become hard and fixed to the surrounding tissue. Commonly, the entire chain of lymph nodes becomes involved. As the disease progresses down the body, the [spleen, liver, bone marrow, and lungs] may become affected as well.
- Because **Hodgkin's Lymphoma** is typically intra-nodal, oral lesions (which are extra-nodal) are very rare. However, neck involvement is quite common.

Histology: There are four (4) different histological subtypes associated with **Hodgkin's Lymphoma** (we do not need to know them), each with their own clinical presentation and prognosis. For each of the subtypes, **Reed-Sternberg Cells** vary in number, but nevertheless are considered the malignant cells for this pathology.



(Reed-Sternberg cells which are said to resemble "owl eyes")

Let's talk for a second about how **Hodgkin's Lymphoma** is staged using the…

Cotswolds Staging System:

Let's first begin by discussing the methodology behind staging **Hodgkin's Lymphoma**. Before staging, certain tests/procedures need to be ordered.

- Start with basic blood tests (especially those that test for liver and kidney function since any type of lymphoma would alter their function).
- CT scans of the chest, abdomen, and pelvis are also standard procedure. CT scans are quite accurate in detecting enlarged lymph nodes or the spread of the lymphoma to the liver and other organs.
- Positron Emission Tomography (PET) scanning is the most sensitive (accurate) technique for determining the stage of the **Hodgkin's Lymphoma**, and for evaluating the patient's response to treatment regiments.
- Sometimes (uncommonly), a patient with **Hodgkin's Lymphoma** needs surgery to determine whether the disease has spread to the abdomen. During a surgery like this, the spleen is often removed (to determine the stage of the disease), and a liver biopsy is preformed to determine if the lymphoma has spread to these organs.

Once these diagnostic tests are preformed, proper staging can be preformed using the protocol below (total of four different stages):

1. **Stage 1:** limited to one lymph node (cure rate of 95%+)
2. **Stage 2:** involves two or more lymph nodes on the same side of the diaphragm [meaning either above or below it] (90% cure rate)
3. **Stage 3:** involvement of lymph nodes on both sides of the diaphragm [both above and below] (80% cure rate)
4. **Stage 4:** involvement of other parts of the body besides lymph nodes [such as bone marrow, lungs, liver, etc.] (60% cure rate)

The four different stages are further subdivided into two categories:

- **(A) Absence**
- **(B) Presence**

Which are based on any of the symptoms listed to the right. (This differentiation does not affect prognosis, staging, or treatment however.)

- Unexplained fever (more than 100° F for 3 consecutive days
- Night Sweats
- Unexplained loss of more than 10% body weight in the preceding six months

Let's finish up with… Hodgkin's Lymphoma: [Treatment]

Quickly, lets clarify the chemotherapy regiments as "little" as we need to:

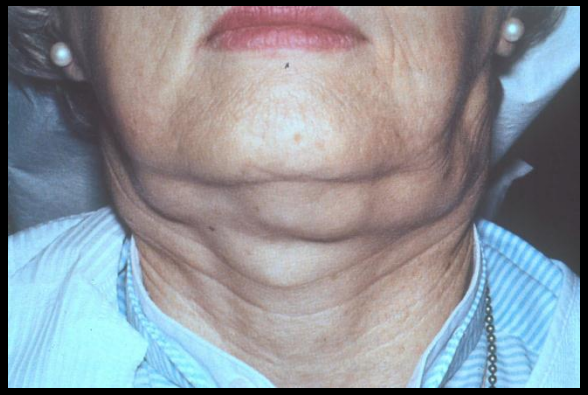
- The old chemotherapy regiment used to be **MOPP** (acronym for the four specific agents used. Unfortunately, MOPP was not that effective. A new regiment, **ABVD** (same acronym system for different chemotherapy agents), was created and had proven to be more effective.
- Of note, there is also a newer chemotherapy regimen (Stanford 5), which has been shown to be at least as good as ABVD.

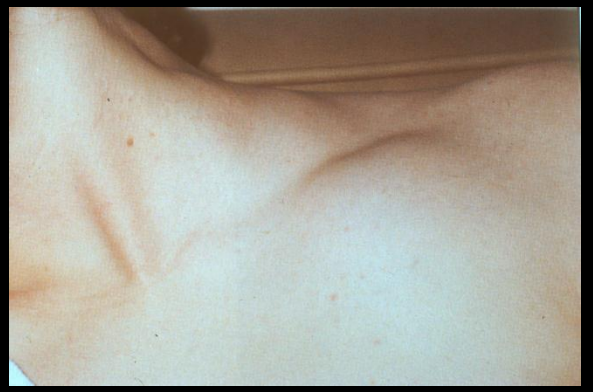
Treatment: is dependent on the stage of the **Hodgkin's Lymphoma** (each chemotherapy cycle lasts one month):

- Early Stages: treated with 2-4 cycles of ABVD and radiation therapy of localized areas.
- Later Stages: treated 6-8 cycles of ABVD, after which the patient's response to the regimen is evaluated. Radiation therapy is only added if there is an incomplete response to the chemotherapy.

Prognosis: is of course dependent on the stage of the **Hodgkin's Lymphoma**

- Early Stages: 90% survival rate (where completely curing the patient is possible)
- Later Stages: 50% - 70% survival rate





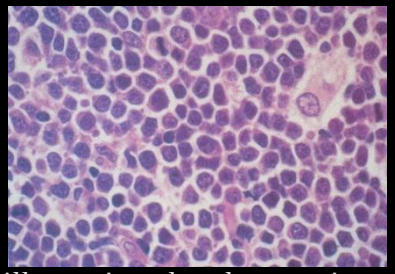
Onto… Multiple Myeloma:

Considered a B-cell proliferation of malignant **plasma cells** (remember that plasma cells arise from B-cells).

- **Multiple Myeloma** is the most common primary malignancy of bone in patients over 40 years of age.
- Presents with bone pain, fatigue, constitutional symptoms, and pancytopenia (reduction in white blood cells / platelets)

Furthermore, because **Multiple Myeloma** is a clonal expansion of **plasma cells** (immunoglobulin producers), there will be an excessive production of immunoglobulins. This entails an overproduction of either Kappa or Lambda chains (since this is a clonal expansion).

- Some of the immunoglobulins are excreted in the urine as **Bence-Jones Proteins**, which eventually leads to renal failure.
- The rest of the immunoglobulins are deposited in soft tissue as amyloids, causing the patient to eventually present with **Amyloidosis**.



(bone biopsy illustrating clonal expansion of plasma cells)

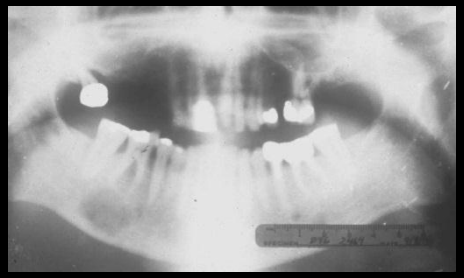
Oral Manifestations:

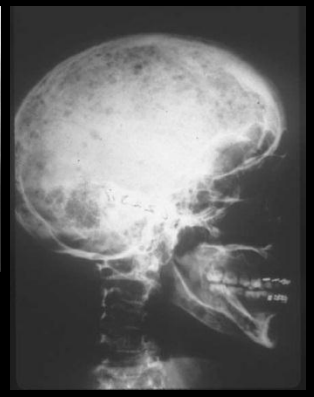
- Pathologic fractures of various bones
- Amyloid deposits (commonly in the tongue) that appear as diffuse firm enlargements that are sometimes nodular. Clinically, this will be observed as either discrete yellowish deposits or diffuse **macroglossia**

Radiographically: punched out radiolucencies (fairly well-defined, but without any corticated edges)

- 30% of patients with **Multiple Myeloma** present with jaw pathology.

Treatment: chemotherapy to a point where a bone marrow transplant is a possibility. Prognosis is poor but improving with more recent therapies.





*(The classic radiographic appearance of **Multiple Myeloma** is diffuse involvement of many of the bones of the body.)*

Neutropenia: Defined as less than **1500 neutrophils per mm^3** in an adult.

This may arise in one of three ways:

1. Congenitally: there are certain syndromes that render you with a low neutrophil count your entire life (an example would be **Dyskeratosis Congenita**)
2. Acquired: through a drug side-effect, including chemotherapy or antibiotics
3. Viral/Bacterial Infections: as a side-effect, some may cause Neutropenia (examples would include **Hepatitis**, **Varicella**, and **HIV**)

Oral Manifestations: Due to a lack of neutrophils, there will be a high rate of oral bacterial infections.

- Also, neutropenic ulcers may arise within the oral cavity (**Agranulocytosis**), which appear as "ANUG-like" punched out gingival ulcerations.

Treatment: It is most important to try and eliminate the underlying cause of the Neutropenia (drug, etc.).

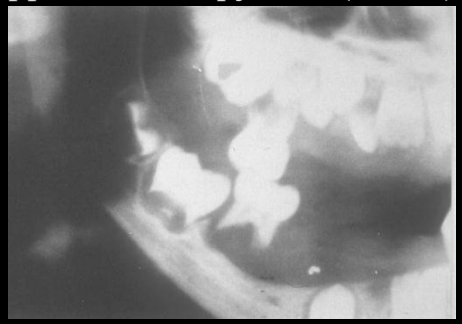
- Granulocyte Colony Stimulating Factors (GCSF) can also be prescribed.

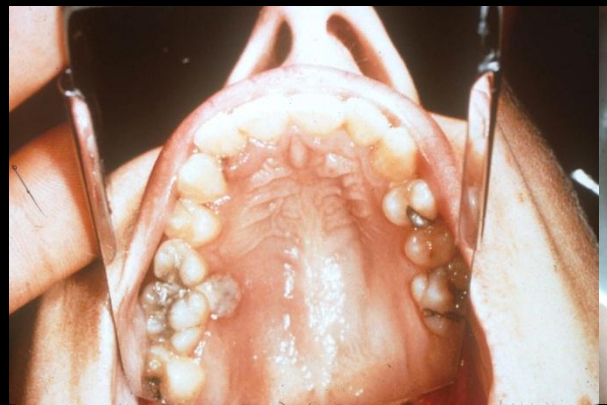
Cyclic Neutropenia: *(Considered a rare condition. However, most of the clinical manifestations are oral.)*

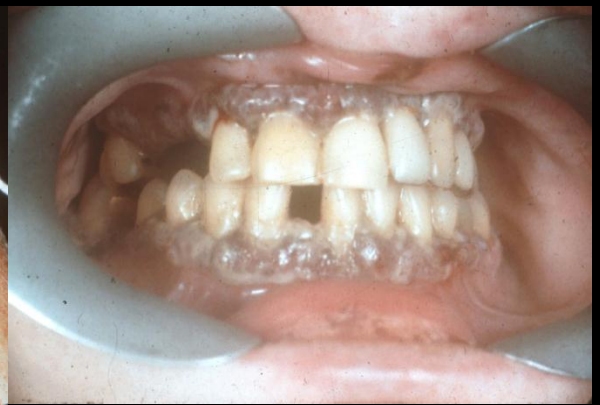
Described as uniformly spaced cycles, beginning in childhood, where the patient presents with low neutrophil counts.

- Each cycle lasts for roughly **21 days**, in which there is a **3-6 day** period where neutrophil counts are at a pathologically low level.
- During periods of **Neutropenia**, patients typically present with **Aphthous-like ulcers** within the oral cavity. These may arise in various mucosal sites (especially the gingiva). Attached mucosa (gingiva) is not typically a location that you would expect to find conventional **Aphthous Ulcers**.
- Because of the long-term depressed neutrophil counts, severe periodontal bone loss, gingival recession, and tooth mobility are often also present.

Treatment: supportive therapy with (GCSF) if needed







Let's finish our discussion on Hematologic Disorders by looking at… # Leukemias:

Described as malignancies of the hematopoietic stem cells that are located within bone marrow. The cells that undergo malignant transformation can differ, depending upon the Leukemia.

- **Myeloid Leukemias:** malignancies of granulocytes, monocytes, erythrocytes, or megakaryocytes
- **Lymphocytic Leukemias:** malignancies of white lymphocytes

Also, depending upon the Leukemia, it can be classified as either…

- Acute: (tends to be more aggressive)
- Chronic: (usually slow growing and indolent)

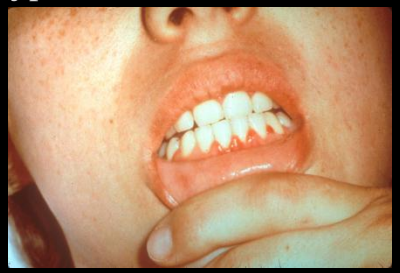
*(This classification system describes the general difference between the different types of Leukemia [**ALL**, **AML**, **CML**, and **CLL**])*

Regardless of how the **Leukemia** is classified, clonal expansion is taking place within the bone marrow (the same concept as **Multiple Myeloma**, where **plasma cell** clonal expansion occurs). This prevents other cell types from replicating, and the patient presents as [thrombocytopenic, etc.].

- The patient will present with constitutional symptoms (including **dyspnea** due to a lack of oxygen carrying capacity from a lack of erythrocytes).

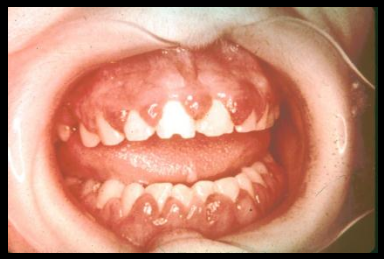
Oral Manifestations: In most cases, oral manifestations of Leukemia arise from the **MYELOID** subtypes.

Secondary oral pathology to Myeloid Leukemias include:



- **Ulceration** of the gingiva due to bacterial load
- Deep "**punched-out**" ulcers with a white necrotic base
- Diffuse swelling of the gingiva (soft tissue infiltration)
- [If the patient is **Thrombocytopenic**]: gingival enlargement/bleeding
- **Periapical Granulomas/Cyst** from periapical infiltration (The teeth will be vital however.)
- **Candidiasis** and **Herpes** infections (In this situation, Herpes infections can occur on unattached gingiva as well)

[In most cases where a dentist diagnosis Leukemia in a patient, it is because of a sudden and rapid onset of periodontal disease. Remember: If the patient presents with bruising/shortness of breath as well, there is a high probability that the oral pathology is secondary to Leukemia.]



Treatment: chemotherapy. Depending on the type of Leukemia, the prognosis varies.

This concludes the Powerpoint-

Just To Recap…

Things that I HAVE gone over in this Powerpoint:

- The elements of a complete description of a lesion [from 10/13]
- Soft Tissue Tumors [from 10/13, 10/18, and 10/20]
- The differentiation between color changes, ulcers, and lumps/bumps [from the beginning of class on 10/25]
- A somewhat thorough review of the article [from 10/25]
- Salivary Gland Pathology [from 11/8 and 11/10]
- Hematologic Disorders [from 11/15]

Things that are still your responsibility to learn/read/watch:

- Dr. Fornatora's presentation on Oral Cancer [from 10/25]
- Dr. Fornatora's presentation on HPV [from 11/1]
- Dr. Sciote's oral cancer prevention lectures [from 10/27 and 11/3]
- The Case Studies and Differential Diagnosis of Soft Tissue Masses [from 11/17, 11/22, 11/29, and 12/1]

Good luck with finals and best wishes for a happy holidays!