Benign? Not So Fast: Challenging Oral Diseases presented with DDX
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COURSE OUTLINE:
Five Topics:
1. Oral squamous cell carcinoma (SCC)-Variability in Etiology
2. Oral Ulcers: Spectrum of Diseases
3. Oral Swellings: Single & Multiple
4. Radiolucent Jaw Lesions: From Benign to Metastatic
5. Radiopaque Jaw Lesions: Benign & Other

Oral SCC: Tobacco-Associated
White lesions
1. Frictional white patches
   a. Tongue chewing
   b. Others
2. Contact white patches
3. Smoker's white patches
   a. Smokeless tobacco
   b. Cigarette smoking
4. Idiopathic white patches

Red, Speckled lesions
5. Erythroplakia
6. Geographic tongue
7. Median rhomboid glossitis

Deep Single ulcers
8. Traumatic ulcer
    - TUGSE
9. Infectious Disease
10. Necrotizing sialometaplasia

Oral Squamous Cell Carcinoma: Tobacco-associated

If you suspect that a lesion is malignant, refer to an oral surgeon for a biopsy. It is the most common type of oral SCC, which accounts for over 75% of all malignant neoplasms of the oral cavity. Clinically, it is more common in men over 55 years of age, heavy smokers and heavy drinkers, more in males especially black males. However, it has been described in young white males, under the age of fifty non-smokers and non-drinkers. The latter group constitutes less than 5% of the patients and their SCCs tend to be in the posterior mouth (oropharynx and tonsillar area) associated with HPV infection especially HPV type 16. The most common sites for the tobacco-associated are the lateral and ventral tongue, followed by the floor of mouth and soft palate area. Tobacco-associated oral SCC varies in presentation from deceptively innocent-looking to obviously malignant. It may present as a non-healing ulcer, or as red or red-and-white lesions. Characteristic signs are non-healing ulcers, red, white, speckled red and white lesions, ulcers with rolled borders, fungation, fixation and induration. Etiology: tobacco, more so smoked and more so cigarettes combined with excessive alcohol use. There is very little evidence indicating that alcohol alone can cause oral SCC but the data is ample with that of the smoked (cigarettes especially) alone can cause oral SCC. Smokeless tobacco has low potential for transformation. Treatment, surgery alone or combined with radiation and/or chemotherapy.
**White patches (leukoplakia)**

White lesions are of varied etiologies and thus each has to be treated according to its etiology or lack of it; see below. White patch “leukoplakia” is defined by WHO as a lesion that cannot be rubbed off and cannot be characterized clinically as any other disease. **Clinical Features:** It affects any age and both genders equally. It progresses slowly. It ranges from thin, grayish and translucent to rough, white to yellow and leathery in consistency. White patches are of varied etiologies including trauma, tobacco, alcohol, vitamin A deficiency and idiopathic. **White patches are particularly important to attend to when they are in heavy smokers, high-risk locations and when they are idiopathic (no known etiology).** The idiopathic white patches are usually in high-risk locations especially in the floor of mouth and ventral/base of tongue and are usually of unknown duration. “High Risk” sites include the Floor of mouth, ventrolateral tongue & soft palate area. Lower lip is high-risk ‘usually’ for sun-exposure related SCC and has a different prognosis.

**When to Biopsy:** It is important to identify the etiology first before you refer the patient for a biopsy.

1. Tobacco induced white lesions—biopsy all except the hard palate in nicotinic stomatitis.
2. Idiopathic white lesions—biopsy all.
3. Friction, mouthwash and alcohol-induced white lesions—remove the stimulus; if it does not regress in six weeks—biopsy.

**Treatment:** Depends on the histologic diagnosis. For example if the histology says epithelial dysplasia, moderate and up remove lesion with clean margins. Mild or mild to moderate epithelial dysplasias can be watched every 4-6 months. **RE-BIOPSY** if the lesions recur, get larger, change color to red or mixed or ulcerate. If you do not see changes, you may do a random biopsy every two to three years. Remove all idiopathic white lesions in high-risk locations especially in floor of mouth and ventral tongue especially in females over the age of 60.

**Frictional white patches (Frictional Keratosis)**

It is very important to identify the etiology of white patches before you decide on a biopsy. Frictional white patches are common. Eliminate the source of friction and watch for 2-6 weeks. The white lesions usually disappear in that period of time, if the white patch persists beyond the six week period, refer for a biopsy. Frictional keratosis represents the epithelial response to chronic trauma such as a sharp tooth, an ill-fitting denture or chronic cheek, tongue or lip chewing. **Clinically,** it can affect any age with no gender predilection. It is commonly found in younger patients involving the lips, cheeks, and lateral tongue. On palpation, it ranges from smooth to rough, irregular and leathery in consistency. **Histopathology:** Hyperkeratosis and/or acanthosis. **Treatment:** remove irritating factor, biopsy if lesion persists beyond six weeks, keep the patient on regular follow-up visits. Rebiopsy if it recurs, gets larger, changes from white to red/mixed color and if it ulcerates.

**Smoker’s white patches: Smokeless tobacco(Snuff Dipper’s) Keratosis**

Biopsy the wrinkled white patches. Also, counsel the patient to stop tobacco use. If the biopsy reading is mild epithelial dysplasia, watch the patient every 4-6 months. Not always, but at times, we recommend treatment of mild epithelial dysplasia (complete removal with clean margins) especially if the patient is A) young, B) continues to smoke C) the lesion is in a “high risk” site. All moderate and higher grade epithelial dysplasias should be removed with clean margins. Smokeless tobacco keratosis is more common in white blue-collar males with an average age of 18 ranging from 10-30 years of age. It occurs in the area where tobacco is held which is mucobuccal fold and gingiva. Color and texture ranges from white well-demarcated translucent grayish to rough and wrinkled or folded with deep furrows that are white or yellow in color. Also present is gingival recession. Severity depends on the time of exposure. **Histopathology:** At early stages, hyperkeratosis and acanthosis. With more
frequent and longer use, epithelial dysplasia and/or invasive carcinoma may occur. **Treatment:**
Prohibition of tobacco use of any type. Lesion may disappear with discontinuation of smoking within two weeks to six weeks, sometimes may take three months or a year. Excise with clean margins if histology shows evidence of dysplasia especially moderate epithelial dysplasia and up.

**Smoker's white patches: Pipe and Cigar smoking (nicotinic stomatitis)**

There is no need to biopsy the palate unless the patient is a reverse smoker. However, examine the lower lip and the oro-naso-pharynx for SCC. Counsel the patient to stop tobacco use. Heavy and long-term pipe smoking is associated with nicotinic stomatitis in the palate and is associated with lip cancer in the area where the pipe is held. Nicotinic stomatitis is also described in heavy cigarette users and is sometimes seen in individuals who are in the habits of drinking very hot tea/coffee. *Nicotinic stomatitis* (palatal lesions) represents a benign epithelial change of both the surface and the minor salivary gland ducts. Clinically, it presents as a diffuse white surface uniformly interspersed by small red dots representing the dilated salivary gland ducts. *Nicotinic stomatitis* of reverse smoking is frequently associated with premalignant and malignant epithelial changes. **Treatment:** Prohibition of smoking. Careful examination of the lower lip and the oro-naso pharyngeal area for squamous cell carcinoma is recommended. Regular follow-up visits are indicated. **Prognosis:** It depends on the histological diagnosis.

**Contact white patches: Mouthwash (alcohol) induced leukoplakia**

Stop the use of the mouthwash and watch for 2-6 weeks. The white lesions usually disappear in that period of time, if not, refer for a biopsy. Alcohol containing mouthwashes especially those with high-alcohol content such as Listerine have been reported to cause white patches, some with dysplasia and rarely with squamous cell carcinoma. Other mouthwashes i.e. Viadent mouthwash & toothpaste have been reported to cause white patches especially in the maxillary vestibule and some in the mandibular vestibule. The old Viadent formula had 10% alcohol and Sanguinaria. Several years ago, Colgate removed Sanguinaria from Viadent mouthwash and toothpaste (called it modified viadent mouthwash) upon the reports that it may cause epithelial dysplasia. Histologically, mouthwashes with 10% alcohol and up have been occasionally reported to be associated with epithelial dysplasia but rarely with SCC. Treatment includes replacing alcohol containing mouthwash with warm water and salt rinses or nothing until the white lesions disappear which may take 6-8 weeks.

**Contact white patches: Direct contact leukoplakia**

Stop holding anything against the oral mucosa, especially in the area where the white lesion is present and watch for 2-6 weeks. The white lesions usually disappear in that period of time, if not, refer for a biopsy. White patches are reported in patients who habitually hold mouthwash, alcohol, cinnamon candy, lozenges, Nicorette gum, sunflower seeds, etc against the oral mucosa. Most of these lesions are reversible and benign

**Idiopathic white patches**

All idiopathic white patches should be biopsied.
White patches of no known etiology are occasionally reported especially in elderly females with no history of any risk factors. The floor of mouth and ventral tongue seem to be a more common location.

**Red patches (Erythroplakia)**

If you suspect that a lesion is malignant, refer for a biopsy without any delays. All high-grade epithelial dysplasias (moderate and up) should be removed with clean margins. All SCCs are treated according to the stage of the disease. Erythroplakia is defined as a red patch that does not clinically represent any other specific disease. Like leukoplakia, this entity has no histological connotation and should not be used as such. The histological and clinical significance of erythroplakia far exceed leukoplakia. Erythroplakia is 49% premalignant, 51% malignant, while leukoplakia is 80% benign; 17% premalignant and 3% invasive squamous cell carcinoma. **Etiology:** Tobacco, alcohol in over 75% of patients. “High Risk” sites for Erythroplakia include floor of mouth, ventrolateral tongue and soft palate complex. **Clinically,** it presents as red, velvety, and well-demarcated in areas. It can be rough or smooth, sometimes red and white (speckled), and ulcerated. It usually affects males over 45 years. It has also been described in younger patients with a history of smoking and/or tobacco use. The main etiology is tobacco and alcohol use. **Histopathology:** Ranges from mild, moderate dysplasia to CIS and invasive SCC. **Treatment:** red lesions, especially in “high risk” sites, should be biopsied without any delay. Epithelial dysplasia/carcinoma in situ: complete surgical removal with margins. Follow-up is essential.

**Traumatic ulcer**

Eliminate the source of trauma then watch for 2-3 weeks, if the ulcer does not heal biopsy the area. The oral cavity is frequently afflicted with surface ulcerations: single and multiple, superficial and deep, acute and chronic, of local and of systemic origin. It is very important that clinicians view oral ulceration with some attention to etiology. It is important to state that most single oral ulcers are trauma induced and can occur at any age. The source of trauma can be a sharp tooth, an ill-fitting denture or a sharp denture edge, a broken filling, a bite, or any other similar irritant. Chronic single ulcers, especially those associated with dentures, may have rolled borders because of scarring occurring during the healing process. The rolled border-type ulcers are frequently mistaken for SCC. Elimination of the source of trauma will help healing of the ulcer within two to three weeks. Sometimes, however, the source of trauma is difficult to identify, and even when identified and removed, the ulcers do not heal and may remain persistent for months. A biopsy of a non-healing ulcer is warranted for two reasons: to rule out malignancy, such as squamous cell carcinoma, and to initiate healing. This is especially true with ulcers on the lateral border of the tongue, which happens to be a common location for traumatic ulcers. It is good practice to refer patients for a biopsy when they fail to heal within 2-3 weeks.

**Traumatic Ulcerative Granuloma with Stromal Eosinophilia (TUGSE)**

Eliminate the source of trauma and watch for 2-3 weeks, if the ulcer does not heal biopsy the area. These ulcers are also known by other names, including traumatic granuloma, eosinophilic ulcer and eosinophilic granuloma of the tongue (which is not related to eosinophilic granuloma of the bone as in Langerhans cell histiocytosis). TUGSE commonly occurs on the dorsal and lateral tongue in patients with a history of trauma. It rarely occurs on the lip but has been described. It may affect patients of all ages, including infants (Riga-Fede disease occurs during the first year of life as a result of chronic
trauma in the sublingual area to the baby lower incisors during breastfeeding). Traumatic granuloma tends to occur more in males than females. Histologically, these ulcers are deep lesions involving the underlying muscle, which may explain the process of slow healing and the tissue eosinophilia. Healing may take up to eight weeks. Eosinophils are found in areas of muscle damage. Clinically, traumatic granulomas tend to be deep ulcers with rolled borders mistaken for SCC.

**Single deep ulcers: Infectious Diseases**
Many infectious diseases including bacterial and fungal organisms are associated with oral ulcers; single or multiple. Cahncre of primary syphilis can mimic and SCC, so would deep fungal or mycobacterial diseases.

**Necrotizing Sialometaplasia (NSM)**
This lesion is usually biopsied. If you are comfortable with your judgment that this is anesthesia induced deep ulcer, then watch for two weeks. If it does not heal, biopsy. Necrotizing sialometaplasia is a benign inflammatory reaction which both histologically and clinically mimicking a malignant neoplasm. It was first reported by Abrams et al. in 1973. It is caused by local ischemia. **Clinically:** It is more common in men (2:1 male: female ratio) in the fourth or fifth decade of age. It occurs in the palate in about 75% of cases and can occur in the buccal mucosa and lip. About two-thirds of cases are on the bilateral palate. Patients present with an ulcerated and usually painless swelling. The ulcer is typically well circumscribed and deep. **Histopathology:** Ulceration, acinar ischemic necrosis, pseudoepitheliomatous hyperplasia mistaken for SCC. **Treatment:** Debridement and saline rinses. It is a self-healing process. It usually heals spontaneously over 6-10-week period. Healing is accelerated with biopsy.

**Oral Squamous cell Carcinoma: HPV-Associated**

**HPV-associated Oral SCC**

Human Papilloma Virus (HPV)-associated oral squamous cell carcinoma is on the increase and has a different clinical profile than tobacco-induced oral SCC. Human Papilloma Virus is a double-stranded DNA virus that infects skin and mucosa, including oral mucosa. There are over 200 types of HPV. They are divided into low-risk and high-risk categories. Low-risk types of HPV are associated with venereal and common warts and focal epithelial hyperplasia (Heck’s disease). High-risk types of HPV are also known as oncogenic (cancer forming) HPV and are associated with cervical, oral and oropharyngeal, anal, vaginal, vulvar and penile cancers. The clinical presentation, patient profile, and prognosis for HPV-associated oral squamous cell carcinoma is different from that of tobacco-associated oral SCC. HPV-associated oral SCC is believed to be a sexually transmitted disease caused by the same viruses that cause cervical cancer, especially types 16 and 18; more so type 16. The main modes of transmission are oral-genital sex and, to a lesser extent, deep kissing. HPV-oral SCC patients tend to be young adults, especially white young males; the number of young females diagnosed with this condition is on the rise. These patients tend to be under the age of fifty and do not smoke or drink heavily. The posterior mouth oropharynx and tonsillar area is the most common location. The clinical presentation is also different; HPV-associated oral SCC is usually small in size, often presents at a more advanced stage of the disease with an unexplained, non-tender lymphadenopathy in the neck. The lymph nodes are usually very large and cystic. It can also present with dysphagia, odynophagia, weight loss, otalgia, tonsillar mass and less frequently with sore throat. Patients respond better to treatment; have a better prognosis & a better survival rate.

**Oral Squamous cell Carcinoma: Idiopathic**
**Proliferative Verrucous Leukoplakia (PVL)**

In 1985, Hanson et al coined the term proliferative verrucous leukoplakia (PVL) to describe a type of oral leukoplakia that was relentless in its persistence, recurrences and potential transformation to verrucous carcinoma and squamous cell carcinoma (SCC). Most of the 30 cases reported in Hanson’s study presented as flat white patches and progressed to warty leukoplakia. Twenty four of the 30 patients were females, mostly over 60 years of age, with a few patients in their thirties. Eighteen out of 30 patients had used tobacco in their lifetime, though ten had never used tobacco; twelve had superficial candidiasis. This disease was not caused by a specific etiology, which made treatment, control of the progression, and prediction of behavior difficult. Since then, many more reports have emerged, some suggesting new etiology such as human papilloma virus types 16 and 18. The clinical profile, however, did not change: this lesion is far more common in females, especially older females. PVL is a progressive disease, usually presenting as benign hyperkeratosis and progressing to squamous cell carcinoma within five to a ten-year period. Gingiva and palate are the most common locations for PVL-related SCC, where 80% of cases occur, followed by the buccal mucosa, tongue and floor of mouth. Treatment includes scalpel surgery, laser surgery, radiation, chemotherapy, Vit A derivatives therapy, surgery combined with antiviral systemic medications and other combination therapies have been tried, some with success. Most commonly used therapies include scalpel and laser surgery. Verrucous carcinomas and SCC arising in PVL are treated more aggressively and according to the stage of the disease. PVL can be a very aggressive and persistent disease, some lasting for 20 years and others dying of the disease. The original study by Hanson demonstrated 13 out of 30 patients died of the disease and 14 out of 30 alive with the disease—rendering it very aggressive in behavior. Other reports however present a less aggressive picture for example Bagan et al had a much lower mortality rate in their multiple oral SCC patients—where one of seven died of the disease over an average of about six years with a TNM stage two. The current less aggressive behavior may be interpreted to be the result of more awareness of the disease. Given the persistent nature of this disease, close follow-up visits of at least six month duration and even closer in the more aggressive behaving lesions are recommended. Surgical removal of all white lesions is recommended.

**Oral Squamous cell Carcinoma: Lichen planus-Associated**

**Lichen Planus (LP)**

If your patient has reticular lichen planus, you do not need to take a base line biopsy but you do need to biopsy when it is erosive. If it is erosive LP, rule our lichenoid drug reaction and treat. Monitor reticular LP every six months, if it changes to erosive, biopsy & treat. Rule out and treat for fungal infection especially if lichen planus is not responding to the conventional topical steroid treatment. If you suspect lichenoid drug reaction, talk to the physician to consider changing the medication(s), otherwise treat as you would erosive LP. Lichen planus is a common skin and mucosal disease, affecting up to 3% of the population. It is a chronic disease that comes and goes over the years. It is believed to be an immune-mediated reaction by T-lymphocytes to epithelial cells, especially those of the basal cell layer. It can occur in the mouth alone, on the skin alone, or on both. 25% of the time it presents in the mouth alone and 35% on the skin alone. LP occurs in adults between 30 & 70 years of age with a strong female predilection. It is often associated with stressful life styles. 40% of patients have both oral and skin lesions. The skin lesions present as purplish papules with a white keratotic surface. Skin lesions are usually itchy and are most commonly present on the flexor surfaces. Oral LP is classified into reticular (most common), erosive (thin and ulcerated mucosa) and hyperplastic (plaque). The plaque type is very hard to distinguish from any other white patch. **Reticular LP** is the most common type in the mouth and is easy to identify since it presents with thin lines interlacing against an erythematous bluish background symmetrically on the bilateral buccal mucosa and vestibule. The lines are known as the striae of Wickham. This type is usually asymptomatic; it may become symptomatic if it progresses to erosive LP. Bilateral buccal mucosa is the most common (80% of cases) location followed by the tongue and gingiva. **Erosive LP** is the second most common type in the mouth. Patients usually complain of sensitivity to hot and cold food and beverages, spicy food and alcohol. Clinically, it is hard to distinguish
it from candidiasis and other mucocutaneous diseases such as MMP and PV. The mucosa appears red, thin and ulcerated. At times, radiating white striae are present at the periphery of the lesions. *Hyperplastic (plaque) LP* is uncommon, presents as confluent white patches simulating Leukoplakia. Dorsal surface of tongue is the most common location for this type.

**Lichenoid Mucositis**

It is clinically similar to erosive LP but can be reticular in type. It is usually due to contact with restorative material, cinnamon aldehyde containing products or to medication (prescribed or over the counter). It is more common in elderly patients but can affect any age. It is rare in children. It is clinically similar to erosive LP as well as histologically and by immunofloresence. Subtle histologic and DIF changes are used to differentiate between the two i.e. the presence of eosinophils, intense lymphocytes infiltrtaes, too many apoptotic cells and others. It is usually generalized as conventional oral LP usually presents but lichenoid mucositis can be localized; affect only half of the mouth; only gingiva or just surrounded the restorative dental material causing it. Drug-induced tends to be more generalized. Consider changing the restoration, stop cinnamon-aldehyde containing products (if this is the cause of the lichenoid mucositis) or ask the physician to use alternate prescription, again if that is the cause of the lichenoid mucositis. The medications known to be associated with this condition include certain antihypertensive drugs, allopurinol (gout), diuretics, antidiabetics, gold, and antihistamines. Steroids treatment may help but is usually a temporary solution. The causing agent should be identified and eliminated to successfully treat the condition.

**Malignant Transformation:**

It is well documented that LP of the mouth, especially the erosive type, has a tendency to transform to SCC in chronic lesions, especially those present for more than five years. There is a mean of 2.5% rate of transformation. Several factors play a role in the transformation of LP; one is the location, and another is the possibility of misdiagnosis of epithelial dysplasia for LP. **Treatment:** Topical steroids, e.g. betamethasone 0.1% cream, and rarely intralesional steroids. Systemic steroid therapy can be used if severe, such as in erosive LP. For lichenoid drug reaction, the best treatment is removal of the causing medication by replacing it with another.

**TOPIC #2: Oral Ulcers: Spectrum of Diseases**

**Multiple Oral Ulcers/Sloughing Epithelium**

1. Chronic immune mediated oral ulcers
   a. Lichen planus
      i. Lichenoid mucositis
   b. Mucous membrane pemphigoid
   c. Pemphigus vulgaris
2. Drug-induced oral ulcers
3. Hypersensitivity and oral ulcers
   a. To gold and other dental restorations
4. Infectious diseases-induced oral ulcers
   a. Herpes Viruses
5. Nutritional conditions and oral ulcers
   a. Anemia
   b. Vitamin B deficiency
6. Oral Manifestation of systemic diseases and oral ulcers
   a. Crohn’s disease
Differential diagnosis for multiple oral ulcers/sloughing epithelium:
1. Immune mediated diseases: LP, lichenoid, MMP, PV, Aphthous ulcers
2. Hypersensitivity: to gold and other restorative material
3. Drug induced
4. Infectious-viral especially primary herpes simplex
5. Iron and Vitamin B deficiency
6. Oral manifestation of systemic diseases

Lichen Planus/Lichenoid Mucositis: Discussed under SCC

Mucous membrane pemphigoid (MMP, BMMP)

Take a baseline biopsy (both H & E and direct immunofluorescence) to establish a definitive diagnosis. Once the diagnosis is established, refer to a dermatologist who treats MMP patients. This condition rarely responds to topical steroids. This is a chronic autoimmune disease affecting predominantly the oral mucous membrane. The immune system recognizes proteins BP and collagen in the basement membrane as foreign forming a complex attracting neutrophils and other inflammatory cells leading to sloughing of the epithelium via the clean separation of the surface epithelium from the connective tissue. The oral MMP is believed to be different from that of other mucosa such as the eyes and nose. Patients with MMP have circulating antibodies but the antibody titer is not related to the severity of the disease, as is the case with PV. It occurs twice as often on the gingiva than anywhere else. If the gingival lesions are untreated, they will slowly involve other areas. It may even extend into the larynx and the esophagus and nasopharynx. It presents as red gingival patches with loss of stippling. There may be sloughing and desquamation of the epithelium, especially to mechanical pressure such as from brushing and denture irritation. The most common age is over 40 years. However, it is also described in children, especially females. It shows a positive Nikolsky sign. Up to 25% of the MMP cases may involve the eyes, sometimes cause blindness through scarring. Local and systemic steroids and immune suppressants are the treatment of choice dependent on severity. Antibiotics for secondary infections.

Pemphigus vulgaris (PV)

Take a baseline biopsy (both H & E and direct immunofluorescence) to establish a definitive diagnosis. Once the diagnosis is established, refer to a dermatologist who treats PV patients. Pemphigus vulgaris is the most common lesion of the pemphigus family. There are various other pemphigus subtypes, including vegetans, foliaceus erythematous, and paraneoplastic. This condition is less common in the mouth than in the lichen planus or mucous membrane pemphigoid. It is an autoimmune disease that causes desquamation of the oral mucosa and skin. The antibody targets intercellular desmosomal adhesion molecules called desmogleins, which results in the breakdown of the middle part of the spinous layer, leaving the basement membrane intact. This is histologically referred to as acantholysis and suprabasilar separation. Pemphigus vulgaris is a serious and life-threatening disease and can kill the patient if not treated. It has a mortality rate of 60-90% in non-treated patients, compared to 5% in treated patients. Complications from steroid treatment and infection can be fatal. Patients with pemphigus vulgaris also develop circulating antibodies; the antibody titer in this disease may be related to the severity of the local disease. Drugs such as penicillin can induce PV, while neoplasms such as leukemia, Hodgkin’s lymphoma, and Castleman’s disease can induce paraneoplastic pemphigus. Several proteins are targeted in paraneoplastic pemphigus. This disease has a high prevalence in patients of Jewish descent, as well as patients of Mediterranean descent (such as Greeks and Italians), with females being affected more commonly than males (2:1 F:M ratio). It occurs more often in patients of ages 40 to 60, and rarely occurs in children, though this has been described. Oral
lesions are usually the first to occur, as is the case in this patient. In the mouth, the soft palate and buccal mucosa are common sites for PV, though it can also affect the gingiva and lateral tongue, mainly because of trauma from brushing and chewing on the lateral tongue. The erosions and sloughing epithelium can be painful, especially with hot drinks, alcoholic beverages, and spicy or acidic food. These patients have difficulty brushing their teeth. PV affects other mucosae including the nasopharynx, anogenital, and esophagus. Skin lesions frequently present with vesicles and bullae that easily rupture, forming ulcers. The Nikolsky sign is positive in patients with PV. This condition presents with supra-basilar clefting, leading to splitting of the epithelium above the basal cell layer, as well as blister formation. This is the result of acantholysis in the middle spinous layer epithelial cells, releasing cells within the cleft known as Tzanck cells. Immunoflorescent (IMF) studies, both direct and indirect, can be useful in reaching a specific diagnosis. By direct IMF, the spinous layer cells are positive with IgG and C3 forming a fishnet pattern around the epithelial cells. Treatment includes systemic and local steroids, as well as immune suppressant-type medications, dependent on the severity of the disease.

**Erythema Multiforme (EM)**

Erythema multiforme (EM) is an acute, immune-mediated condition divided into major and minor representing a wide range of erythematous mucocutaneous lesions progressing to vesicles/bullae and ulcers. It affects both the skin and mucosa. EM minor tends to be cutaneous lesions without mucosal lesions. Currently EM major is separated from Stevens Johnson Syndrome (SJS) mainly where etiology applies. EM major can appear subsequent to a viral infection especially herpes virus. It can be associated with mycoplasma pneumonia infection or be drug induced similar to SJS. This is a self-limited condition lasting 2-6 weeks and occurs more in males around 20-40 years of age and more on the lips and anterior tongue. EM can occasionally recur and last for a year.

**Stevens Johnson syndrome (SJS)/Toxic epidermal necrolysis (TEN)**

Both Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are considered to be a spectrum of the same disease representing severe mucocutaneous lesions ranging from blisters to severe surface ulceration and sloughing. The main etiology in both conditions is the ingestion of certain medications such as sulfa drugs and others like nonsteroidal anti-inflammatory drugs (NSAID). This disease occurs more commonly in females and at any age ranging from childhood to old age. It is also known to affect the skin and mucosa including the oral cavity, eyes and genitals. In the mouth, it can affect all areas but is more common on the lips and tongue. This condition tends to usually self-limit.

**Delayed Hypersensitivity**

Eliminate the causative agent. You may or may not need to treat with anti-histamine. Delayed-type hypersensitivity is a mucosal reaction that occurs at least 24-48 hours after the exposure to the allergen. Contact stomatitis or Contact dermatitis results from repeated or continuous contact with the allergen. On the skin it is reported with soap, fabric (especially wool), nickel in jewelry, and with flavorings, most commonly with cinnamon oil. Several dental related allergens are known to cause delayed hypersensitivity in the oral cavity such as denture soft lining material, toothpaste, mouthwash, lipstick, candy, and chewing gum, especially those with cinnamon flavoring, gold, resin, acrylic, chrome cobalt and amalgam are among many. Oral manifestations of contact stomatitis include burning sensation, erythema, vesicle formation, epithelial desquamation, ulcerations, erosions, swelling, secondary infection, gingival erythema and swelling similar to that seen in plasma cell gingivitis. Treatment: Eliminate the causative agent. You may or may not need to treat with anti-histamine.
Infectious Diseases
Herpes Simplex 1 (HSV1, HHV1)

Primary: Herpes simplex virus1 (HSV1) is the most common acute viral infection of the oral mucosa. Incubation period is 3 to 9 days. HSV1 usually affect children between the ages of six months to 3 years and especially between 2-3 years of age. It does however affect young adults especially those at late high school or early college age. The children primary manifestation is with no apparent symptoms in more than 80% of the cases and vesicular gingivostomatitis in about 12% of the cases. In adults, the lesions would present more posteriorly in the pharyngeal area (pharyngotonsilitis). Once an individual is infected, the virus will remain in the body for life. The body however develops antibodies to the virus within the first to two days to three weeks of exposure and it is usually IgM and IgG. Medications such as acyclovir treat the symptoms of the disease and may weaken the virus and delay recurrence but acyclovir and other drugs in this family, will not eradicate the virus. HSV1 usually affects children and this is true in congested developing countries. HSV1 affects more than 90% of the population in developing countries and usually children while up to 60% of the population in high socioeconomic countries such as the USA and it affects the adolescent and young adults than children shifting the profile. HSV1 presents in form of small painful vesicles that rupture within a short period of time. The fluid released by the ruptured vesicles releases virions which are live viruses that can infect another person via contact i.e. kissing or sharing food or drink. A person can infect him/herself by touching the open vesicle and touching other areas before washing their hands. It is very important to wash the hands after touching a viral sore. It is best to wear gloves if helping family members with such sores and is expected of the clinicians to handle no patient without gloves. The small percentage of the patients that manifest the disease present with small painful blisters, fever up to 103, drooling, headache, pain upon swallowing, cervical lymphadenopathy and extremely inflamed mucosa, including intra and extra-oral skin. The numerous small vesicles are more common on the palate and dorsal tongue but can be present anywhere. They rupture within hours to one or two days to form shallow, ragged painful small ulcers with uniform size but some coalesce to form irregular larger ulcers. They heal in 10-14 days after which the virus travels along the nerve to remain latent in the ganglion supplying the area. HSV-1 usually travels along the trigeminal nerve and harbors the trigeminal ganglion. Patients can also develop complications such as pneumonia and meningitis. The vesicles break releasing yellow fluid which is replete with live viruses that can be cultured or smeared on a glass slide for cytological evaluation. The cytology would typically show epithelial cells with ballooning degeneration, intranuclear inclusion bodies (Lipschutz bodies) and epithelial cells with multiple nuclei. These changes can also be observed if a biopsy is taken. In mild cases, supportive treatment such as rest, fluids and soft diets along with either topical tetracycline rinses multiple times a day or systemic antibiotics if secondarily infected to expedite healing. In severe cases, systemic Acyclovir can be very helpful especially if used early in the stage of the disease. For immune compromised patients, IV acyclovir is recommended.

Recurrent Intraoral Herpes and Herpes Labialis (cold sore, fever blister)

Fever blister is self explanatory which indicates that these lesions occur during or after a fever of some sort. Cold sore has two meanings; one is a sore that occurs during a “cold” as in a viral cold illness especially if associated with fever. The second meaning indicates a sore that occurs in cold weather. Recurrence can be frequent, rare or never, depending on the person’s immune system. It can recur mildly or aggressively again depending on the individual’s immune system. If it recurs, it is more common on the lips especially the vermilion border and vermilion border and skin known as recurrent herpes labialis. It can also recur intra-orally but less commonly. It usually recurs on bone bound
mucosa such as the hard palate and gingiva and is known as recurrent intraoral herpes. In the immune compromised population, the clinical presentation of recurrence can be aggressive and can get secondarily infected. In the immune compromised population, the infection simulates the primary form in that the vesicles affect both the soft and glandular mucosa and the bone bound mucosa. This virus can become activated and cause new lesions for a variety of reasons including trauma such as dental treatments including routine dental cleaning, sun exposure, cold or other physical illness, hormonal changes including menstrual cycle and pregnancy, emotional or physical stress, sleep deprivation, or over exercise or general fatigue. **Prodromal stage:** This stage of the disease will show no apparent lesion. It precedes the vesicles by a few hours to one or two days. Prodromal period is characterized by burning sensation, itching, tingling or some other type of sensation followed by small vesicles.

Recurrent HSV1 is more common in females than males. It usually presents with clusters of small vesicles that may be intact for a few hours to a few days depending on the location and the toughness of the overlying skin/mucosa. The vesicles enlarge and rupture releasing yellowish fluid forming yellow crusts. The ulcers are usually uniform in size and are superficial but frequently coalesce to form irregular superficial ulcers. Sometimes, only superficial and irregular ulcers are seen; this is especially true of the hard palate area where vesicles break very quickly because of the trauma from eating. Recurrent herpes heals within 7-10 days. Treatment ranges from supportive to systemic anti-viral medications depending on the frequency of recurrence, on the aggressiveness of the disease and on the immune status of the patient. For the mild and occasional breaks, supportive is the treatment of choice. For the more aggressive and frequently recurring, systemic acyclovir or any other medication in this family is recommended. Some patients are placed on maintenance dose of systemic acyclovir but that will not prevent the shedding of the virus and its infectivity. The maintenance dose is used more with genital herpes since it tends to be more aggressive and more frequently recurring than oral herpes. For mild cases, prescription or over the counter topical antiviral creams can also be used effectively but have to be used at the prodromal stage. It is important to know that repeated use of the creams is contra-indicated since resistant strains of the virus may develop. Systemic acyclovir or ganciclovir vary in daily doses depending on the severity of the disease. For immune compromised, such as AIDS and transplant patients, IV acyclovir may be required to control the disease. Antibiotics (mouth rinses or systemic), may be needed in HSV cases that are superimposed with bacterial infection.

**Iron-Deficiency Anemia**

It is best not to treat patients, especially extraction patients if they are severely anemic as in showing the signs and symptoms described below. Refer to their PCP for blood workup. It is the most common form of anemia. It is a result of chronic blood loss (most common etiology); inadequate dietary intake; faulty iron absorption i.e. in Plummer-Vinson syndrome; increased requirement for iron, e.g. pregnancy, growing children. It is most common in females and it can occur at any age. Patients demonstrate clinical changes when hematocrit falls below 30%, which ranges from fatigue and dizziness to pale skin, brittle and spoon-shaped fingernails (koilonychia). Most of the symptoms are related to low-oxygen levels due to decreased hemoglobin concentration. The oral manifestations range from smooth, red and painful tongue with atrophied papillae, generalized atrophy of oral mucosa and angular cheilitis. Pallor of oral mucosa is uncommon and only seen in severe cases. Laboratory testing shows low hemoglobin concentration, low serum iron, and elevated total iron binding capacity (TIBC). It is best to treat the underlying disease and supplement with iron and high protein diet.

**Pernicious Anemia (Vit B_{12} anemia)**

It is best not to treat patients, especially extraction patients if they are severely anemic as in showing the signs and symptoms described below. Refer to their PCP for blood workup. It is relatively uncommon disease resulting from atrophy of gastric mucosa or post gastrectomy. This will lead to failure to secrete
"intrinsic factor" which is needed for the absorption of Vitamin B₁₂. Deficiency of vitamin B₁₂ results in pernicious anemia. It usually occurs in males over the age of 30, usually of Northern European descent. Patients complain of generalized weakness, numbness and tingling sensation of the extremities, pale skin and sclera (sometimes), loss of appetite and weight. These patients have a risk for gastric carcinoma. Laboratory tests reveal decreased hemoglobin concentration. Oral manifestation includes glossitis, painful and burning tongue, ulceration, atrophy of papillae (tongue) and generalized atrophy of the oral mucosa. Monthly injections of the extrinsic factor; oral lesions heal shortly after the injections.

**Crohn’s disease (CD)**

Crohn’s disease (CD) is an immune mediated chronic inflammatory disorder characterized by granulomatous inflammation of the transmural gastrointestinal tract, including the small intestine, large intestine, and the entire tract from the mouth to the perianal area. It affects different areas in different patients. Up to 25% of CD cases are diagnosed in children less than 18 years of age. The main clinical sign and symptoms include abdominal pain in up to 95% of cases and weight loss and diarrhea in almost 80% of cases. Oral manifestation of CD in children occurs in around 40% of cases, and about 30% of CD cases in children occur first in the mouth. The most common clinical presentation in the mouth is mucogingivitis, which occurs in about 25% of cases, followed by oral ulcers simulating aphthous ulcers, which occur in about 8% of cases. A cobblestone appearance of the mucosa and swelling of the lip occur in about 6% of patients. Two age peaks in occurrence are described: one among teenagers and the other in patients over 60 years of age. Treatment includes sulfa-type drugs, i.e. sulfasalazine; systemic steroids; or chemotherapy agents such as azathioprine. Biopsy of the ulcer or the cobblestone plaque may yield histology of a granulomatous inflammation which should be helpful in including Crohn’s disease of the list of exclusion; this is how this patient was diagnosed with CD.

**TOPIC #3: Oral SWELLINGS: Single & Multiple**

**Single swellings**

1. Reactive gingival swellings  
   a. PG; Pregnancy tumor; POF; PGCG
2. Neoplastic gingival swellings  
   a. SCC  
   b. Kaposi Sarcoma  
   c. Metastatic Cancer
3. Palatal Swellings  
   a. Torus palatinus  
   b. Mucoepidermoid carcinoma  
   c. Pleomorphic adenoma
4. Tongue Swellings  
   a. Hemangioma  
   b. Fibroma
5. Lip Swellings  
   a. Mucocele  
   b. Fibroma
6. Buccal Mucosa  
   a. Fibroma

**Pyogenic Granuloma**
Remove any local irritants i.e. calculus, heavy plaque, sharp edged tooth, etc. Give good homecare instructions and refer for conservative surgical removal. This is a common reactive swelling of the gingiva. This lesion represents an exuberant mass of granulation tissue. It can occur at any age and sex. Some suggest a slight predilection to young females. This is certainly true with the “pregnancy tumor” variant. The gingiva is the most common location, followed by tongue and lips. It presents as a rapidly growing, well-demarcated, hemorrhagic, ulcerated nodule. It becomes pinkish as the lesion heals. Size ranges from 2 mm to 2 cm. If the ulcer is covered by pseudomembrane, it will appear white. Treatment: Excision with the removal of the local irritant. Scaling and polishing prior to surgical removal helps shrink the lesion. Prognosis: good, it can recur in about 5%.

**Pregnancy Tumor**

Same as pyogenic granuloma; remove any local irritants i.e. calculus, heavy plaque, sharp edged tooth, etc. Give good homecare instructions and ask the patient to wait until two months after the delivery of the baby to remove the lesion. Sometimes patients insist on surgery before delivery, that is OK, but the patient needs to know that the lesion may recur. This is a variant of pyogenic granuloma that occurs during pregnancy. It usually occurs during the mid- to late stages of pregnancy. In addition, the patient will also have pregnancy gingivitis. All the clinical and histologic criteria of PG can be applied to this lesion with the exception of location—pregnancy tumor occurs usually on the gingiva. It is believed to be hormonally induced. Some regress after delivery. Delay treatment to two months post partum. Significant reduction in size may be noted within three to four months of delivery. Treatment of PG during pregnancy is followed by around 16% recurrence rate.

**Peripheral Ossifying Fibroma (POF)**

Although these lesions are not believed to be local irritant induced, clean the area as if it is PG and give good oral hygiene instructions and refer for conservative surgical removal. Patient should be informed of the tendency of POF to recur and be placed on annual follow-up visits. This tumor occurs exclusively on the gingiva. It has been reported, but rarely, on edentulous alveolar mucosa. It is believed to arise from the periodontal ligament or the periosteum. This lesion is more common in young patients between 10 and 19 years of age and has a predilection for females, in whom almost two thirds of cases occur. They occur exclusively on the gingiva; some report occurrences anterior to molar with a slight predilection for the maxilla. They present as well-demarcated sessile nodules, firm or hard depending on the amount of ossification and calcification. Color is usually pink but can be red focally if ulcerated. Histology shows moderately cellular fibrous connective tissue with calcified bone or osteoid some cementum-like hard tissue. The surface is usually ulcerated. Surgical excision deep to include the periodontal ligament. If it recurs more than twice despite proper treatment, the associated tooth should be extracted. **On the average** 16-20% recurrence rate.

**Peripheral Giant Cell Granuloma**
Remove any local irritants i.e. calculus, heavy plaque, sharp edged tooth, etc. Give good homecare instructions and refer for conservative surgical removal. This is believed a reactive lesion, probably originates from the periodontal ligament or the peristomeum. **Clinically,** it occurs in young patients with an average age of 30 and is more common in females (2:1). It occurs exclusively on the gingiva, edentulous and dentate mainly anterior to molars. It presents as sessile, red or red-blue lesion. Sometimes it resorbs the underlying bone in a uniform manner with a concave “saucer-like” appearance. Radiographically, "Cuffing" effect with slight bone resorption as described. This is not a common occurrence. Treatment: Complete excision including curettage of underlying bone. Remove any local irritants. Recurrence rate around 10%.

**Kaposi Sarcoma (KS)**

This is a malignant neoplasm of vascular origin that can be multifocal. Before HIV, KS was rarely reported, more commonly outside the mouth. The classical KS affects older males of Mediterranean origin and occurs mostly on the extremities. The classic KS is a slow-growing neoplasm that is rarely fatal. It is believed to originate from the endothelial cells of the blood vessels, but can be from the lymphatics as well. Four types are reported: classic, African, immunosupression-associated and AIDS-related. Clinical Features: Classic KS occurs as multiple reddish-purple macules to plaques on the lower extremities. It is slow-growing and asymptomatic. Kaposi sarcoma in AIDS patients takes on a different clinical behavior. It affects mostly young males and can be very aggressive in behavior. Aggressive and florid behaving KS have also been described in African-type KS. KS is seen in 50% of AIDS patients. In 25%, the oral cavity is the primary presentation. It is relatively common in AIDS patients, affecting the oral cavity and the skin of the head and neck, trunk, etc. The most common location in the mouth is the palate. It may present as flat purplish red to nodular lesion(s). It is usually asymptomatic, but may be painful. Human herpes virus #8 is believed to be the etiology of this disease. The African type is divided into four subtypes, three of which are aggressive and fatal, especially the type that occurs in children (lymphadenopathic type). Although the head and neck area is a common location for the AIDS-related type, it is not for the other three types. Histopathology: KS is made up of irregular vascular spaces that fail to complete. Several types are described including patch, plaque and tumorous. The latter is much easier to diagnose that the former two. Histologically it is very difficult to differentiate KS from bacillary angiomatosis, a vascular lesion associated with cat-scratch bacillus. Treatment: ranges from intralesional injections to systemic chemotherapy.

**Metastatic malignancies to the oral cavity-simulating PG**

Cancer metastasis to the oral cavity is cover under unilocular radiolucencies of the jaw. By far the most common location in the mouth for cancer metastasis is the posterior mandible, where 80% of cases present as painful radiolucencies. **Gingiva is the second most common site for metastasis simulating pyogenic granuloma.** Metastasis is mostly described in adults over the age of 30 and rarely in children. Pain and swelling are the most common clinical symptoms. Tumor metastasis to the oral cavity carries a poor prognosis because the oral cavity is usually not an isolated site and tends to project a more disseminated clinical behavior. Patients are typically treated with chemotherapy and the five-year survival rate is poor.

**Torus Palatinus**

Explain to the patients the complications of thinning of the overlying mucosa and ulceration. If this is a patient about to be treated with Fosamax, it is a good idea to recommend removal of the large torus to prevent osteonecrosis. It is more commonly seen in East and Southeast Asians and Eskimos. Etiology
is unknown but can be inherited as autosomal dominant. Clenching and bruxism are implicated as etiology factors. One study of Malaysian found an incidence of 22.6% maxillary tori. This is a bony outgrowth at midline of the hard palate covered by normal, sometimes, thin mucosa. It is smooth surfaced but may have a multilobular appearance. Torus palatinus is slow-growing and painless except if traumatized. The lesion occurs by age 30 and affects females twice as often as males. No treatment is necessary unless it interferes with function or is symptomatic. Recurrent ulceration of the overlying mucosa may occur. It should be excised if creating difficulty with prostheses.

**Mucoepidermoid Carcinoma**

With the exception of torus palatinus, all palatal swelling should be removed. Therefor, they should all be referred to an oral surgeon for a biopsy and treatment. It is a malignant neoplasm with both mucous secreting and epidermoid type cells. It is the most common malignant salivary gland neoplasm. This neoplasm accounts for 10% of all salivary gland neoplasms. The majority occur in the parotid. It occurs also in minor salivary glands especially the palate, tongue, buccal mucosa, retromolar pad area. It can occur at any age. It is the most common malignant salivary gland neoplasm in children; where around 40% occur in patients under 20 years of age. Clinically, Low-grade lesions present as slowly enlarging, painless lesions, not encapsulated, sometimes resembling mucoceles (especially those at the retromolar pad area). Therefore, consider what appears clinically as a mucocele in the retromolar pad area as a mucoepidermoid carcinoma until proven otherwise. High-grade lesions present as rapidly growing, painful lesions with facial nerve paralysis and sometimes with regional lymph node metastasis. Treatment: Complete surgical removal with clean margins. Radiotherapy has a place in the management of recurrent or not surgically curable cases.

**Mixed Tumor (Pleomorphic adenoma)**

With the exception of torus palatinus, all palatal swelling should be removed. Patients should be referred to an oral surgeon for a biopsy and treatment. It is the most common benign salivary gland neoplasm of both the major and minor salivary glands. It originates from the myoepithelial cells and the reserve cells of the intercalated duct. It accounts for 80% of all benign salivary gland neoplasms. It occurs in both major and minor salivary glands and accounts for up to 77% of parotid, 68% of submandibular, and 43% of minor salivary gland tumors. It is most common in females 30-50 years of age, but it is also seen in children. It presents as a small, painless, slowly enlarging nodule. If left untreated it can reach large sizes, sometimes several pounds in weight. It also occurs in the oral cavity, especially the palate and lips. The palatal mixed tumor is fixed due to the bone-bound anatomy of the region. The tumor is otherwise movable. Mixed tumor is well-demarcated to an encapsulated neoplasm made up of cords, strands, and islands of cuboidal and spindle cells. The stroma is loose and mucoid to dense. Cartilage, bone and keratin pearls are present. Complete surgical removal with clean margins is the treatment of choice. Parotid: removal of the involved lobe with preservation of the facial nerve. Submandibular: removal of the whole gland including tumor. Minor salivary glands: removal with clean margins. If in palate, excise in one piece with the periosteum and overlying mucosa. Prognosis: Good, but has a tendency for recurrence (as high as 44% in the parotid) if not treated thoroughly. Risk of recurrence is less with minor salivary glands. Risk of malignant transformation is about 5%.
Hemangioma

It is a benign proliferation of blood vessels. Most are probably hamartomas. **Clinical:** It occurs equally in males and females (some suggest female predominance), mainly in children and can even be present at birth. The most common location is the head and neck and the most common sites in the oral cavity are the tongue (macroglossia), buccal mucosa, and lips. These lesions present as flat or elevated and purplish-red in color. They blanch on pressure, unless there is a thrombus. These lesions are also present centrally. For this reason, always aspirate the central lesions before surgery. It is associated with syndromes such as Sturge-Weber syndrome, and Hereditary Hemorrhagic Telangiectasia. Several histologic types are described, i.e. capillary, cavernous. Treatment depends on the size of the lesion, its relationship to other anatomical structures and the rate of blood flow. Treatment varies from injection of sclerosing agents to surgical debulking to complete excision. True hematomas occur most frequently on the upper lip and regress as the child ages. These lesions require no treatment initially but may need revision of the lip scar to improve cosmetics.

Mucocoele

**Superficial mucocoeles should be watched for three weeks; deep mucocoele should be excised.**

Mucous extravasation (mucous retention) phenomenon is the most common type of mucocoeles followed by mucous retention cyst (duct blockage phenomenon). Ranula can be of either type. Clinically and Histologically the term mucocoele is applied to mucous retention or extravasation phenomenon. The most common type of mucocoele is the mucous extravasation type, which develops as a result of trauma to the salivary gland ducts leading to pooling of mucous which in turn stimulates the formation of granulation tissue to wall it off. This type occurs most commonly on the lower lip. It is rare on the upper lip. It may occur anywhere else in the oral cavity. It presents as a swelling with a light-blue color (if superficial) that increases and decreases in size. It is usually associated with a history of trauma such as lip or cheek biting. Histology shows a cyst-like structure lined with fibrous or granulation tissue and filled with mucous and macrophages. Mucous retention cyst is a cavity lined by epithelium and filled with mucous. Surgical removal is the treatment of choice.

Fibroma (traumatic fibroma, irritation fibroma)

Fibroma is the most common soft tissue tumor in the oral cavity. Trauma is usually the etiology; especially chronic cheek chewing is the most common cause. It affects any age, but mostly those around 30-50 years of age with no sex predilection. It occurs anywhere in the oral cavity, most commonly on the buccal mucosa and lip. It presents as a dome shaped, smooth surfaced, pink or whitish sessile nodule. Surgical removal and elimination of the initiating factor is the treatment of choice.

Swellings-Multiple

1. HPV-associated multiple lesions
   a. Verruca vulgaris
   b. Condyloma accuminatum
   c. Focal epithelial hyperplasia
2. Inflammatory papillary hyperplasia
3. MEN 2b
4. Lingual papillitis
**Verruca Vulgaris (common warts)**

Patients or their parents should be informed of the potential for transmission to others and to self (auto inoculation). You can wait for the lesions to regress or remove. Human papilloma virus-induced epithelial lesions tend to present in multiples. Verruca vulgaris, known as common wart, is a benign lesion induced by human papilloma virus (HPV) types 2 and 4. It is transmitted via contact and can be auto-inoculated. HPV types 2 and 4 and low risk type. Verruca vulgaris is very common in the US; about 23% of the children are infected. The lesion however involutes between six months to three years of infection. If it presents like a single lesion, it would be indistinguishable from a papilloma. It is papillary (cauliflower, or finger-like projections) and white, but it usually presents in multiple. It is most common on the fingers and hands but due to its potential for autoinoculation, it can also be present in the mouth, nose, eyes, etc. Treatment ranges from no treatment to treating with liquid nitrogen. The latter is especially true with skin lesions. Laser treatment is effective especially for oral lesions. Most of these warts involute within three years but while present can shed the virus, thus the potential for transmission to self or others.

**Condyloma acuminatum (venereal wart)**

Patients should be informed of the potential for transmission to others and to self (auto inoculation). Genital lesions should be treated before oral and all sexual partners should be treated. Laser works best for the oral condylomas. Condyloma acuminata are benign and papillomatous proliferations of surface epithelium induced by HPV types 6 and 11. It is transmitted via contact. The majorities of Condyloma cases are sexually transmitted and account for 20-30% of all sexually transmitted diseases. If condylomas are reported in a child, before sexual abuse is discussed, other explanations should be ruled out and these include the child borne of a mother with condyloma of the birth canal, the child’s care giver having the anogenital lesions and not washing his/her hands after the use of the bathroom or the child care giver having condlyomas on the hands. Condylomas are more common in the genitalia but occur in the oral cavity. It usually presents as multiple, membranous pink and papillomatous lesions but can also present as a single pinkish or white lesion. It is obviously more common in the genitalia but can be transmitted to the mouth via oral genital contact and therefore when treated all lesions should be treated and sexual partner(s) as well. In the mouth, the commissures and dorsal tongue are more commonly affected but can occur anywhere else including the gingiva, floor of mouth and upper lip. There are a number of treatment modalities ranging from chemical cauterization, laser, to conventional surgery in case of a single lesion. The key to proper treatment is to first treat the genital lesions before treating the oral lesions to prevent autoinoculation. It is also very important that the sexual partner(s) be also treated to break the transmission between them. If this is not followed, the lesions will continue to occur as a result of re-inoculation.

**Focal Epithelial Hyperplasia**

The parents of such patients should be informed of the potential for transmission to others. You can wait for the lesions to regress. They are too many to surgically treat. Focal epithelial hyperplasia also known as Heck’s disease, is a rare disease of the white and the black population but is common in the Native Americans, more in the South American Indian population. It is of an infectious disease caused by HPV types 13 and 32. It was first described by Archard et al in the Eskimo population of the Greenland. It is transmitted via contact and runs in families and schools. Clinically, it has a distinct presentation in that the lesions are multiple and slightly raised by are smooth surfaced and usually same color as the surrounding mucosa. It usually occurs in children younger than teenager years but has also
been described, but rarely in individuals around fifty years of age. It is more common in children living in congested and poor conditions. It presents in multiple small (around 5mm or slightly larger) slightly elevated, smooth-surfaced and sometimes dome-shaped nodules. These lesions can be isolated or coalesced forming more diffuse and ill-defined elevation of the mucosa. Lip and buccal mucosa are the most common locations, but can also occur on the gingiva, palate and other areas. It has been described in adult AIDS patients as multiple papillary lesions. Histologically, blunt dome shaped epithelial hyperplasia with mitosoids (the latter are not always present). No treatment is indicated in otherwise healthy children; some can regress spontaneously and others respond to laser treatment, intralesional injections or topical chemotherapy. They are however infective on contact and the patient and the parents should be alerted to the fact that they may be transmitted via contact i.e. sharing of food and drink. Recurrence in this group of patients is rare once the lesions disappear or are treated. Similar lesions are described to occur in AIDS patients which are resistant to treatment and have high recurrence rate.

**Inflammatory papillary hyperplasia (IPH)**

This is also a localized fungal infection. It should be treated candidiasis. Dentures should also be treated for candidiasis or relined. It is a reactive response to local irritant, usually seen under a denture. Clinical Features: Occurs at any age and with equal gender distribution. It is pink to red, pebbly and asymptomatic. It is usually reported in patients that wear their ill-fitting dentures 24 hours with poor hygiene. 24% of patients that wear their dentures for 24 hours have this condition. Candidal infection has been implemented. The hard palate is the most common location. It is also seen in dentate patients who habitually lick their palate, breathe through their mouth or have a high vaulted palate. Candida with IPH has been reported in immune deficiency patients. Histopathology: Papillary mass of dense and hyperplastic fibrous connective tissue with dilated blood vessels and inflammatory cells, mainly lymphocytes and plasma cells. The surface epithelium is usually proliferative. Candida may or may not be found. Treatment: Ranges from removal of the stimulus to antifungal agents to superficial surgery and denture reconstruction.

**Multiple Endocrine Neoplasia Syndrome Type 2b (MEN 2b)**

Biopsy the small nodules and when the diagnosis of MEN2b is suggested, refer to a pediatrician that works with MEN2b patients in major Children’s Hospitals throughout the states. MEN2b frequently presents with multiple small nodules in the anterior oral cavity of children. Multiple Endocrine Neoplasia Syndrome (MEN) is a rare group of diseases affecting the endocrine system; many are inherited as autosomal dominant, with the genetic defect (RET) mapped on chromosome 10. Some are the result of a mutation. Three types have been described. Type 2b is the one that affects the oral cavity with multiple neuromas, alerting the dentist to identify the more serious elements of the syndrome, such as the medullary carcinoma of the thyroid and pheochromocytoma of the adrenal glands. Dentists can be the first to identify the multiple oral nodules which are present as early as birth or shortly thereafter. Most are present at childhood. The medullary carcinoma affects 90% of the patients and is present between 18 and 25 years of age, but it has been described in patients as young as two years of age. Pheochromocytoma occurs in the second and third decade, as well as later, and causes profuse sweating, diarrhea and severe hypertension. The multiple neuromas present as nodules of the oral cavity, eyes, nose and the gastrointestinal tract. The nodules are frequently present on the tip and the anterior dorsal tongue, and on the lips and bilateral corner of the mouth. The latter is highly characteristic of the disease. Eye and bowel nodules are usually present along with the oral counterpart. In addition, the patients may have marfanoid habitus, a thick lower lip, and an everted upper eyelid. The multiple small
neuromas are histologically composed of multiple discrete hyperplastic peripheral nerve bundles surrounded by fibrotic perineural sheath. High levels of catecholamines and calcitonin are detected if the patients have pheochromocytoma and medullary carcinoma. Preventive removal of the thyroid gland is one life-saving treatment, but other treatments are applied to the various components of the syndrome.

**Transient Lingual Papillitis (TLP)**
Also known as "lie bumps.”
TLP is an inflammation of the fungiform papillae; etiology can be hypersensitivity reaction to certain foods especially sugar and acid; stress and gastrointestinal disorders; typically clears in a few days or even one day. Lesions may or may not be painful.

**Eruptive Lingual Papillitis (ELP)**
ELP is almost identical to TLP but affects children five years of age or younger; known to spread to the child’s family members and lesions tend to be painful; patients may develop fever, lymphadenopathy and therefore infection is suggested as the main etiology

**TOPIC #4: Radiolucent Jaw Lesions: From Benign to Metastatic**

**Radiolucent Jaw Lesions**

**Odontogenic cysts**
1. Dentigerous cyst
2. Odontogenic keratocyst
3. Traumatic bone cavity
4. Salivary gland depression

**Odontogenic Neoplasms**
5. Central odontogenic fibroma
6. Central odontogenic fibroma
7. Odontogenic myxoma

**Malignant Jaw Neoplasms-Primary**
8. Multiple myeloma
9. Osteosarcoma

**Malignant Jaw Neoplasms-Metastatic**
10. Sarcoma
11. Breast
12. Cervix
13. Other

**Dentigerous Cyst (Follicular Cyst)**
This is a very common odontogenic cyst, accounting for 20% of cysts of the jaw, and is almost always associated with the crown of a tooth attached to the cemento-enamel junction. It is believed to originate from the accumulation of fluid between the reduced enamel epithelium and the tooth crown. Therefore, this cyst develops after the formation of the crown and this explains its association with the crown of impacted or un-erupted teeth. This cyst can present as an asymptomatic radiolucency discovered during a routine dental exam or can act aggressively by expanding the jaws, leading to facial asymmetry with extreme displacement of adjacent teeth as well as the involved tooth. It can also lead to root resorption of the adjacent teeth. Sometimes, patients complain of pain, especially if the cyst is infected. It is more common in the third molars and upper canines and can also involve supernumerary teeth and odontomas. Radiographic Features: It presents as a smooth border, usually unilocular or sometimes multilocular radiolucency, located around the tooth circumferentially, laterally or in the form of a "doughnut" ring. The size varies from small to extremely large and extending into the ramus of the mandible. Treatment depends on the size; it ranges from thorough curettage to marsupialization. Recurrence is rare. DC can be associated with ameloblastoma, epithelial dysplasia and/or SCC and mucoepidermoid carcinoma.

**Odontogenic Keratocyst (OKC)**
The OKC is well recognized for its tendency for recurrence and its aggressive behavior. In 2017, WHO reversed its 2005 suggestion that OKC be considered a cystic neoplasm. The WHO classification is
back to classifying OKC as a cyst. OKC occurs at any age, but is most common in males between 10 and 40 years of age. It is most common in the molar-ramus area of the mandible. The patient may complain of pain, swelling, drainage and even paraesthesia if the cyst displaces the nerve bundles. It also displaces and resorbs teeth and expands the jaw. Radiographically, it presents as either a unilocular or multilocular radiolucency with well-defined smooth or scalloped borders. Sometimes, it is associated with impacted teeth, especially third molars. It is also seen in edentulous areas. Treatment depends on the size, but complete. There is often a high rate (5-60%) of recurrence. It is sometimes associated with bifid rib basal cell nevus syndrome. Occasionally the cyst lining may be associated with epithelial dysplasia or carcinoma, extremely rare. It is important to place the patient on an annual follow-up for at least five years. The patient should be made aware of the behavior of this cyst.

**Solitary Bone Cyst (Traumatic bone Cyst, Traumatic bone cavity, Hemorrhagic Cyst)**

The preferred terminology is traumatic bone cavity. This lesion is seen as frequently in the jawbones as in other bones such as the femoral tibia. Trauma has been suggested to be associated with this lesion. It presents in young males around 10 to 20 years of age and more often in the posterior portion of the mandible. It is usually asymptomatic, but expansion is reported. The associated teeth are vital. Radiographically, it has distinct and characteristic features, especially when the cavity involves the roots of the teeth. It presents as a well-circumscribed radiolucency with sclerotic border (sometimes) and a scalloped appearance between the roots of the teeth. This cavity usually lies above the mandibular canal. Treatment includes exploration surgery (most recommended), injection of host blood in the cavity, occasionally follow-up that would lead to spontaneous healing. Regarding follow-up, it is important that the area be explored in some way within six months, even if simple needle exploration to feel the area for any solid tissue. Recurrence is very rare but has been described.

**Salivary Gland Depression (Static Bone Cyst, Stafne’s defect)**

Salivary Gland Depression (Stafne’s defect, Static Bone Cyst) is a developmental defect believed to be a defect or depression caused by pressure from growing salivary gland tissue. The most common is the submandibular gland depression located in the lingual aspect of the mandible below the second molar tooth; second to this would be the depression caused by the sublingual gland which is usually present in the lingual mandible below or around the canine tooth. The least common type is the parotid gland depression in the upper and lingual ramus. This condition is usually asymptomatic and tends to occur more often in males. They present as small and round to large and ovoid, usually well-defined radiolucencies. The submandibular depression is usually below the mandibular canal. This is not of the sublingual gland defect located in the anterior mandible. Occasionally, they can be bilateral; this is especially true of the posterior mandible (submandibular gland). No treatment is necessary. The submandibular depression is the most radiographically diagnostic and the sublingual is the least diagnostic because of its inconsistent radiographic presentation and for that reason, surgical exploration is indicated to rule out other lesions. The submandibular defect may occasionally enlarge. Under these circumstances, exploration is recommended.

**Unicystic Ameloblastoma**

The unicystic type of ameloblastoma is a less aggressive neoplasm and occurs in younger patients. Clinically, it usually occurs in patients around 18 to 20 years of age with a strong predilection for the posterior mandible. Almost 90% of cases are associated with the crown of impacted third molar teeth with the radiographic presentation of a dentigerous cyst. This type of ameloblastoma can arise from a dentigerous cyst or de novo next to a cyst. About 10% of times, it can present as a unilocular radiolucency simulating a residual cyst, periapical, primordial cyst or Odontogenic keratocyst (OKC). Radiographically, it is unilocular and corticated radiolucency and at times, the margins are scalloped, simulating an OKC. Treatment, the intraluminal and plexiform are treated with curettage. Mural unicystic ameloblastoma is treated with curettage or partial resection depending on the involvement of the full
thickness of the wall. Patients should be placed on follow-up for more than five years. It can recur, but not as commonly as the classical ameloblastoma. It still requires long-term follow-up.

Central Odontogenic Fibroma
This is a rare odontogenic neoplasm. It is classified into 2 types: Simple and WHO types. In the past, some pathologists were diagnosing hyperplastic dental follicles as central odontogenic fibromas and for that reason this lesion was considered to be common at some point. It is of mesenchymal origin. Clinical: It occurs most frequently in children and young females. The female-to-male ratio is 7:1. It occurs most often in the maxilla anterior to first molar tooth. It presents with swelling but is otherwise, asymptomatic. Radiographic: It can present as a unilocular or multilocular expansile radiolucency. Treatment: Simple surgical excision. Prognosis: Good prognosis. This lesion may recur and has been described to transform to odontogenic fibrosarcoma.

Odontogenic Myxoma
This is a rare and unique odontogenic neoplasm. It has only been described in the jaws so far. No other bone in the body demonstrates such a lesion. It is believed to originate from the dental papilla. It presents primarily in patients ages 23-30 years and is slightly more common in the posterior mandible. It is rare in children under 10 or adults over 50 years of age. It is also described in the condyle of the mandible. Pain may occur. Radiographically, it presents in various ways. It can present as an expansile multilocular, or a destructive radiolucency with mottled appearance. Margins can be scalloped. Treatment ranges from resection of the affected segment to curettage with cautery. The gelatinous nature of the neoplasm makes complete removal difficult.

Multiple Myeloma
This is an uncommon malignant neoplasm of plasma cell origin. This can be multicentric (arising in several regions at the same time - multiple myeloma) or localized (myeloma or plasmacytoma) This neoplasm is characterized by widespread osteolytic bone lesions—especially bones with red marrow such as the skull, ribs, pelvis and mandible. This lesion is a disease of patients over 40 years of age, twice as common in black and has a male predominance. Patients usually present with pain, bone fracture, or vertebral collapse. The oral changes include macroglossia due to amyloidosis and destructive bone lesions (although not necessarily the "punched out" radiolucencies seen in the skull). Also, loose teeth, pain, and numbness of the lip or chin may occur. Treatment includes chemotherapy and/or radiation.

Giant cell rich osteosarcoma of the mandible
Giant cell rich osteosarcomas are usually undifferentiated forms of osteosarcoma; thus, the prognosis is much poorer than that of conventional osteosarcoma. The radiological features of giant cell rich osteosarcoma are different from those of conventional osteosarcomas. They mimic non-mineralized benign or malignant bone tumors, especially central giant cell granuloma of the jaw or giant cell tumor of the long bones. They are osteolytic lesions with cortical thinning and ballooning without obvious cortical destruction. Histologically, giant cell rich osteosarcoma is an undifferentiated sarcoma with scanty osteoid formation. The microscopic appearance of giant cell rich osteosarcoma is characterized by numerous osteoclast-like giant cells dominating the field; the presence of osteoid formation by the tumor cells gives a clue regarding the diagnosis. The most important prognostic indicator for all osteosarcomas is the ability to obtain initial complete surgical removal. Osteosarcomas have an aggressive local growth potential and a propensity to spread systemically via hematogenous routes. The lung is the most frequent site of metastasis. Metastases from mandibular lesions are more frequent
than those from maxillary lesions. Today, therapy is typically multi-disciplinary, focusing on both local and systemic manifestations of osteosarcoma and thus incorporating both surgery and chemotherapy.

**Metastatic malignancies to the Jaw**

Cancer metastasis to the oral cavity is neither specific nor common. Although such cases constitute less than 1% of all oral malignant neoplasms, it may have a devastating result to the patient mainly because metastasis to other sites has already developed or is inevitable. Theoretically, any malignant neoplasm can metastasize to the oral cavity, but in actuality few do and of the ones that do, the majority are carcinomas rather than sarcomas. The most common malignant neoplasms that metastasize to the mouth are from the breast, lung, kidney and prostate. Malignant neoplasms from the colon, pancreas, esophagus, thyroid, cervix, and liver have also been described. Breast cancer is the most common neoplasm to metastasize to the oral cavity altogether. Lung and prostate cancers are the most common neoplasms to metastasize to the oral cavity in men. In most cases, the oral presentation is a secondary diagnosis when the primary diagnosis of malignancy in a distant organ has been already made and the patient has had or is undergoing treatment for it. In rare cases, the oral lesion is the first manifestation of the disease. By far the most common location is the posterior mandible, where 80% of cases occur, followed by the gingiva. Metastasis is mostly described in adults over the age of 30 and rarely in children. Pain and swelling are the most common clinical symptoms. Metastatic lesions may also present as asymptomatic, simulating a periapical lesion, or with gingival swelling like a pyogenic granuloma. They can cause anesthesia and parasthesia, especially when they involve the inferior alveolar canal. The latter results in so-called “numb-chin syndrome.” Tooth looseness, displacement and sharp resorption have also been described. The radiographic appearance of the borders can range from moderately well demarcated to diffusely irregular. The majority of neoplasms cause bony destruction with ill-defined borders; the moth-eaten appearance of some bony destruction indicates aggressive behavior. It is also important to mention that at times, well-demarcated lesions with a benign morphology, as well as cystic radiographic morphology, have also been described. Metastatic neoplasms from the prostate are usually bone-forming, resulting in radiopaque or mixed radiolucent and radiopaque lesions misdiagnosed as benign fibro-osseous lesions. Tumor metastasis to the oral cavity carries a poor prognosis since it tends to project a more disseminated clinical behavior. Patients are typically treated with chemotherapy and the five-year survival rate is poor.

**TOPIC #5: Radiopaque Jaw Lesions: Benign & Other**

**Radiopaque Jaw Lesions**

1. Osteosclerosis
2. Gardner’s syndrome

**Benign Osteosclerosis (idiopathic osteosclerosis, condensing osteitis)**

Once you establish that this is idiopathic osteosclerosis, do not treat. Osteosclerosis, or very dense bone, is a benign and reactive process. The etiology ranges from idiopathic to reaction to a mild inflammatory process, developmental, mechanical and orthodontically induced. It may result from any chronic inflammatory condition of bone such as local or diffuse chronic sclerosis osteomyelitis. Late periapical cemental dysplasia may produce a similar clinical and radiographic morphology but with a radiolucent rim at the periphery. Osteosarcoma rarely produces significant amounts of dense bone but should be on the differential diagnosis for the large and irregular one especially those that displace and resorb teeth which, very rarely, can happen. Metastatic prostate carcinoma may induce hyperostosis in the surrounding bone and should be on the differential diagnosis. Hyperostotic bone tends to brittle and poorly vascularized and may predispose to both fracture and infection. No specific treatment indicated.
Once you establish that your patient has multiple radiopaque lesions in his jaws, or multiple odontomas or multiple supernumerary teeth, the patient should be referred to a physician to rule out Gardner’s syndrome. Family doctor would be a good start. This is an autosomal dominant condition with complete penetrance and variable expressivity. The gene is localized to chromosome 5. This condition presents with intestinal polyposis with 100% transformation rate in late age. They may appear before puberty but transformation does not take place until around 30, where 50% of the patients develop cancer of the polyps. Up to 60% of GS patients develop multiple epidermoid cysts. Oral manifestations include multiple osteomas of the jaws, sinuses including frontal sinuses. Almost 46% have multiple osteomas and about 90% may have one or more. GS osteomas are not always expansile, some mimic idiopathic osteosclerosis of the jaw but in multiple. Also described are multiple odontomas, and multiple supernumerary teeth.