The ABCs of Oral Diagnosis in the Pediatric Patient

Juan F. Yepes DDS, MD, MPH, MS, DrPH
Associate Professor – Indiana University
Clinical Associate Professor – University at Buffalo
Riley Hospital for Children, Indianapolis, Indiana
Diplomate ABOM, ABDPH, ABPD
jfyepes@iupui.edu

Disclaimers
I do not have any affiliation with any commercial company. My only interest is exclusively academic and for the benefit of patients, residents, RDH, dental assistants, managers, dentists, dental therapist, and physicians.

All clinical pictures were authored by myself unless otherwise listed on the slide.

Patients and/or parent consent was received for all photos and radiographs.
Learning Objectives

1. To review the most common oral lesions in children
2. To learn how to develop a correct differential diagnosis.
3. To understand the rationale behind the current treatments.

Best method to learn oral diagnosis in the pediatric patient?

Oral Diagnosis
Ulcers in the oral cavity in children are all the SAME?

Yepes's approach

**AGE !!!**

- Pre-K child
- Kindergarten child?
- Teenager
- Baby?

**MEDICAL HISTORY !!!**

- Chronic GI issues
- Lesions in other places (skin – genitals)
- Periodicity (every 90 days?)
- Other systemic symptoms
- Joint pain

Not assuming the role of the PCP

Ulcers in the oral cavity in children are all the SAME?

Yepes's approach

**Ulc er history !!!**

- First time
- Often
- Almost daily
- For a long time (more than 2 weeks)
Ulcers in the oral cavity in children are all the SAME?

**Clinical appearance !!!**
- Round?
- Irregular?
- Location → Gum line?, NK mucosa?
- Keratinized mucosa?
- Cluster?

Yeses's approach

Ulcers in the oral cavity in children are all the SAME?

NO!

- RAS
- Herpes virus
- Herpangina
- Hand foot mouth disease
- Crohn's disease
- Cycle neutropenia
- SLE
- Trauma

- Erythema multiforme
- Mononucleosis
- Behcet's disease
- MAGIC syndrome
- PFAPA syndrome

**Behcet's disease**

- BD is an idiopathic condition, chronic, relapsing, multi-systemic, characterized by recurrent oral and genital ulcers, ocular disease, and skin lesions.
- The prevalence is higher in countries around the Mediterranean sea.
- The prevalence in the US varies between 0.2 – 5.2 per 100,000.
- BD is more common in females (in North America).
- The diagnosis is based on clinical criteria.
Behcet’s disease
• There are NOT pathognomonic laboratory test for BD
• Diagnosis requires the observation of recurrent oral ulcerations (three episodes within any 12 month period) plus ANY two of the following: recurrent genital ulcers, eye lesions, skin lesions or a positive pathergy test.
• Management of BD is challenging → use of anti-TNF-α, colchicine steroids, immunomodulators and immunosuppressants.

Francisco, 9 year-old

This seems to have all started with a virus that most of his family got.

“He started with small white bumps on his tongue (early April) very painful. Parents took him to the pediatrician who prescribed Chlorhexidine. Then, parents took him to the pediatric dentist; his pediatric dentist said that his tongue was inflamed and prescribed a steroid rinse (Dexamethasone). Within the next 2 days (May 12) the lesion(s) were got worse. His dentist then sent him to an oral surgeon. He couldn’t give the parents any idea what it was and said sometimes things like this just happen and if you get rid of the opening then it would heal. Parents called his pediatrician again who refer him to the ENT. The ENT physician referred again to pediatric dentistry.”

9 years old, boy, Caucasian
9 year old, boy, Caucasian
Never before. First time of something like this

Past Medical History
No chronic or recent issues
Medications: None
Past surgical history: Unremarkable
Allergies: NEPA
Social history: Excellent family support

Review of systems
Neurologic: No symptoms
GI: Occasional GI “disturbances” [not well explained by the mom]
Immun: No symptoms
Cardiovascular: No symptoms
PE: Within normal limits, except for below ideal percentile weight and height

Inflammatory Bowel Disease: Crohn’s Disease
• IBS is a chronic relapsing disorder of unknown etiology (probably immune related) that encompasses two different conditions: Crohn disease (CD) and ulcerative colitis (UC)
• In CD the inflammation occur anywhere in the GI tract (including the mouth)
• CD causes abdominal pain, diarrhea, weight loss and in some cases anemia
• The annual incidence of pediatric CD in the US is between 0.2-8.5 cases per 100,000
• Approximately 10% of patients with CD have oral mucosa ulcers, and the oral manifestations occasionally precede GI symptoms
• Oral ulcers in CD often have indurated borders and are histologically different from RAS

Ulcers in the oral cavity? are all the SAME (caused by a virus!)
Recurrent Aphthous Stomatitis

- RAS is the most common ulcerative disease of the oral mucosa.
- AGE = AGE - AGE
- Healthy individuals.
- Involvement of the heavily keratinized mucosa of the palate and gingiva is uncommon.
- Often complex differential diagnosis: neutropenia, Crohn's, SLE, etc.
- Several factors have been proposed as a possible etiology.
- Extensive research has focused on immunological factors, but a definitive etiology of RAS has not been conclusively established.

<table>
<thead>
<tr>
<th>Type</th>
<th>Size</th>
<th>Duration</th>
<th>Healing Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td>Larger than 1cm</td>
<td>Persists for weeks and months</td>
<td>Heal with scar</td>
</tr>
<tr>
<td>Minor</td>
<td>Less than 1cm</td>
<td></td>
<td>Heal without scars</td>
</tr>
<tr>
<td>Herpetiform</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Recurrent Aphthous Stomatitis

Epidemiology

- Approximately 20% of the general population is affected by RAS.
- The epidemiology of RAS is influenced by the population studied, diagnostic criteria and environmental factors.
- In children, prevalence of RAS may be as high as 39% and is influenced by the presence of RAS in one or both parents.
- The onset of RAS seems to peak between the ages of 10 and 19 years before becoming less frequent in advanced age, gender, or race.

Etiology

Local factors:
- Trauma
- Negative association with smoking
- Changes of saliva pH

Microbial factors:
- Helicobacter pylori → No strong association
- S. sanguis → Antigen stimulant

Underlying Medical Conditions:
- Behçet’s syndrome
- MADD syndrome: mouth and genital ulcers with inflammation of the cartilage
- Cystic fibrosis
- Cyclosporine
- FMF syndrome: periodic fever, RAS, pharyngitis, and cervical adenitis

Hereditary and Genetic Factors

The role of heredity is the BEST defined underlying cause of RAS.

Children with RAS + parents have a 50% chance of developing RAS
- HLA-A2, HLA-B5, HLA-B12
Recurrent Aphthous Stomatitis

**Etiology**

- **Allergic Factors**
  - Hypersensitivity to food
  - Miconazole
  - Sodium Sulfate to toothpaste **

- **Immune Factors**
  - Abnormal proportion of CD4 and CD8
  - Elevated levels of IL-2
  - Elevated levels of IFN alpha
  - Local dysregulated cell-mediated immune response -> accumulation of T cells (CD8)

- **Nutritional Factors**
  - Small number association with low levels of iron, folate, zinc, vitamins B

**Clinical Manifestations**

- RAS patients usually experience a short prodromal burning sensation that last from 2 to 48 hours before an ulcer appears.

- **NO GINGIVITIS**
  - Ulcers are round, well defined with erythematous margins and shallow ulcerated center covered by a yellow pseudomembrane.
  - Usually develop on non-keratinized mucosa.
  - They last approximately 7 to 10 days.
  - Histological characteristics are no specific.

**Treatment**

- **TOPICAL**
  - The treatment depends on the frequency, size, and number of ulcers.
  - Patients with occasional episodes of minor aphthous ulcers experience relief with topical therapy:
    - Zilactin ®, Orabase ®, CankerMelts ®, Amlexanox ®
  - Patients with more frequent or more severe disease -> Topical steroids (Fluocinonide 0.05%)
  - Topical antibiotics: Tetracycline mouth rinses have been reported to decrease both the healing time and pain of the lesions in several trials.
  - More recently -> Penicillin G troches
Recurrent Aphthous Stomatitis

Treatment — SYSTEMIC

- Short course of systemic steroids (prednisone).
- Pentoxifylline (PTX) a methylxanthine related to caffeine, has been used for many years to treat intermittent leg cramps in patients with peripheral vascular disease. PTX improves circulation increasing the flexibility of RBC. PTX has also shown to decrease inflammation by itself.
- Several reports of the use of PTX, 400mg three times a day.
- Other medications: colchicine, thalidomide and Dapsone.

Ulcers in the oral cavity are all the SAME?

Most Common ulcers caused by virus in the oral cavity of children
Most Common Viral Infections of The Oral Cavity

RNA → Coxsackievirus group A
DNA → Herpes Simplex Virus
Human Papilloma Virus

- Herpangina
- Acute lymphonodular pharyngitis
- Hand-foot-and-mouth disease
Most Common Viral Infections of The Oral Cavity

**RNA → Coxsackievirus group A**

- Herpangina: Oral ulcerations limited to the soft palate, uvula, tonsils, and fauces.
- Incidence of the disease peaks during the initial months of summer and fall.
- Sudden fever, sore throat, headache, dysphagia, and malaise followed in 24 to 48 hours by erythema and vesicular eruption.

**HFMD**

- Frequently seen in epidemics outbreaks in day care or school aged children.
- Mild headache and malaise followed by skin and oral lesions.
- Presence of limb lesions.

**DNA → Herpes virus**

- Human Papilloma Virus
Oral Herpetic Infections

- Herpes virus cause a primary infection when the patient initially contacts the virus and then remain latent within the nuclei of specific cells for the life of the individual.
- HSV 1 and VZV remain latent in sensory nerve ganglia.

Primary herpes virus infections

- The incidence of primary infections with HSV-1 increases after 6 months.
- The incidence reaches a peak between 2 and 3 years of age.
- A significant percentage of primary herpes infections are subclinical or cause pharyngitis difficult to distinguish from URI.
- Significant prodromal with generalized marginal gingivitis.
- Primary HSV in healthy children is usually a self-limiting disease.
- Treatment: palliative

After reactivation, HV can cause localized symptomatic or asymptomatic recurrent infections.

- They are transmitted from host to host by direct contact with saliva or genital secretions.
Oral Herpetic Infections

Recurrent herpes simplex infections

- Following resolution of a primary HSV infection, the virus migrates to the trigeminal nerve ganglion - latent state
- Reactivation of virus may follow exposure to cold, sunlight, stress, trauma, or immunosuppression
- “cold sore” or “fever blister”

Recurrent herpes simplex infections

- Several studies have been published comparing topical antiviral medications for treating RHV
  - Topical penciclovir (Denavir®) reduces the duration and pain of RHV by 1 or 2 days
  - Topical acyclovir has been reported to decrease duration of RHL lesions by 12 hours and found to be more effective than N-docosanol (abreva®)
- Other topical products
- Systemic treatment

Differential diagnosis:
- RAS (NO prodromal symptoms and NO gingivitis)
- Coxsackie viral infections (hand-foot-and-mouth – herpangina)
- Erythema multiforme

Laboratory testing: It may be necessary to diagnose atypical presentations.
- Gold standard → tissue culture
- Cytology smears → Tzanck smear
- Immunology test → (DNA)
Edward, 10 year-old

Erythema Multiforme

Erythema Multiforme
Erythema Multiforme

- Erythema multiforme (EM) is a typically mild, self-limiting, and recurring mucocutaneous reaction characterized by target lesions of the skin and mucous membranes.
- Great variability between episodes
- Typical age is between 7 and 21 years. More females than males.
- EM is characterized by symmetrically distributed skin lesions.

**Etiology**

- Herpes simplex virus (HSV) is the infectious agent in 60% to 70% of the cases.
- HSV antigens are expressed in the endothelial cells of the blood vessels and keratinocytes of EM lesions → target for the immune attack.
- EM: drugs precipitate some cases of EM (sulfonamides: trimethoprim-sulfamethoxazole, NSAIDs, PNC, etc.)

**Clinical Presentation**

- The lesions are in a fixed position with a symmetric distribution.
- A central blister or area of necrosis may be present.
- Prodromal symptoms are rare, and few systemic symptoms are present during the EM episode.
- Oral mucosal lesions occur in more than 70% of cases of EM although less well recognized. EM does present as oral mucosal ulcerations with few or no skin lesions.
- Preferred sites of involvement include the lips, alveolar mucosa, and palate.
- Oral lesions are painful and may compromise speech and eating → heal without scarring.
Clinical Presentation

- Mild symptoms associated with EM are typically treated symptomatically.
- Topical corticosteroid suspensions provide symptomatic relief of painful oral ulcers
- Systemic antiviral agents (valacyclovir 500 mg bid to abortive or Valacyclovir 500 mg bid x 1 year suppressive)
- Systemic steroids: 48 to 72 hours

Erythema Multiforme

What we learned from Patricia Francisco, and Edward?

1. Not all the ulcers in the oral cavity in children are the SAME!!!
2. “Tips” for the differential diagnosis (not always work ⇒ use glasses!)
3. Different treatments

Josephine.... from 4 y.o. until 12 y.o.
Long History

- 4 years 4 months old
  - Past Medical History: Unremarkable. No medications. No allergies.
  - Oral exam within normal limits. No caries lesions were noted. Follow-up: 6 months. Excellent oral hygiene.

- 5 years 2 months old
  - Past Medical History: Unremarkable. No medications. No allergies.
  - Oral exam within normal limits. No caries lesions were noted. Follow-up: 6 months. Excellent oral hygiene.

- 6 years 2 months old
  - Past Medical History: Unremarkable. No medications. No allergies.
  - Oral exam within normal limits except for marginal gingivitis. No caries lesions were noted. Excellent oral hygiene.

- 5 years 2 months old
  - Past Medical History: Unremarkable. No medications. No allergies.
  - Oral exam within normal limits. No caries lesions were noted. Follow-up: 6 months. Excellent oral hygiene.

7 years old

- Past Medical History: Unremarkable. No medications. No allergies.
- Oral exam within normal limits except for marginal gingivitis. No caries lesions were noted.
- Excellent oral hygiene.

- 7 years 8 months old
  - Past Medical History: Unremarkable. No medications. No allergies.
  - Oral exam within normal limits except for marginal gingivitis. No caries lesions were noted. Moderate plaque. Treatment: Reinforce OH.

- 8 years 6 months old
  - Past Medical History: Unremarkable. No medications. No allergies.
  - Oral exam within normal limits except for marginal gingivitis. No caries lesions were noted on tooth #12(6) and tooth #30(5). Excellent oral hygiene.

12 years old

- Past Medical History: Unremarkable. No medications. No allergies.
- Oral exam revealed inflammation and erythema on facial gingiva (mandible and maxilla) with NO plaque accumulation. Diagnosis: Puberty gingivitis.

12 years old

- Emergency Appointment
- Chief Complain: "Tissue sloughing from the back of the mouth"
- PE: Noted generalized gingivitis. Gingiva appears to be sloughing (but good OH). Large ulcerations noted lingual to #20 and #21.
- The clinical exam revealed no precipitating factors for gingivitis.
12 year old 5 months

PMH: Unremarkable. No medications. No allergies.

Erythema associated with “peeling off” was noted over the gingiva around the anterior maxillary and mandibular teeth.

Impression: Desquamative gingivitis

• Desquamative gingivitis
• Erosive lichen planus (ELP)
• Mucous membrane pemphigoid (MMP)
• Pemphigus vulgaris (PV)

Plan: Stop all OH products and excisional (“punch”) biopsy

---

Desquamative Gingivitis (pediatric patients)

• Clinical term to describe red, painful, “peeling off” gingiva.
• At least three different mucocutaneous conditions present as desquamative gingivitis in children.
• Desquamative gingivitis can be mistaken for plaque-induced gingivitis and this can lead to delayed diagnosis and inappropriate treatment.
• There is loss of stippling and the gingiva may desquamate easily with minimal trauma.


Desquamative/Gingivitis (pediatric patients)

• Gingival erosive lichen planus (ELP)
• Mucous Membrane Pemphigoid (MMP)
• Pemphigus Vulgaris (PV)
• Crohn’s disease, Linear IgA, plasma cell gingivitis
Pemphigus is characterized by acantholysis within the epithelium owing to the binding of IgG auto-antibodies to desmogleins. (1)
Pemphigus affects between 0.1 and 0.5 patients per 100,000 depending on the population studied. (2)

**Etiology**

- **Diet**: Garlic
- **Drugs**: sulfhydryl radical, penicillamine, captopril, nonthiol, rifampicin, diclofenac
- **Viruses**: HVS
- **Other factors**: Smoking, pesticides

**Suppressed**

- Azathioprine
- Cyclophosphamide
- Methotrexate
- Gold
- Cyclosporine
- Prednisone

**Removal**

- Opportunistic infections
- Bone marrow suppression
- Renal failure
- Skin problems
- Bladder problems

**Pemphigus Vulgaris I**
Pemphigus and pemphigoid are two of a group of bullous diseases affecting the oral mucosa and skin. They are both autoantibody-mediated diseases, although the target antigens are quite different in type and location.

Mucous membrane pemphigoid (MMP) comprises a heterogeneous group of disorders characterized by sub-epithelial separation and the deposition of Ig and complement along the basement membrane (BMZ).

Pemphigus is characterized by acantholysis within the epithelium owing to the binding of IgG auto-antibodies to desmogleins. (1)
Pemphigus affects between 0.1 and 0.5 patients per 100,000 depending on the population studied. (2)
What we learned from Josephine?
The importance of medical and dental history!!!!

Theresa, 10 y.o.

10 year old, girl, Caucasian

A 10-year-old girl presented to the pediatric dentist for a regular 6 months recall. The extra-oral exam was within normal limits. The intraoral exam was within normal limits, except for a well localized erythema at the gingiva of tooth #8. The periodontal exam did not show increase in the gingival pocket of tooth #8 and no bleeding was observed. Fair oral hygiene.
Localized Juvenile Spongiotic Gingival Hyperplasia

This lesion is considered a unique and distinctive form of inflammatory gingival hyperplasia seen in young patients (average age 11.8 years), predominantly female and generally found in the maxillary anterior region.

This type of lesion was first described by Darling et al. as juvenile spongiotic gingivitis.

After the investigation of a larger sample size by Chang et al. the more accurate term LJSGH had been suggested.

It appears as a bright red raised overgrowth with a papillary or finely granular surface, however, it does not seem to be a plaque related lesion.

Localized Juvenile Spongiotic Gingival Hyperplasia

The lesion presents as a small (average size was 6 mm), localized and easily bleeding overgrowth on the gingiva of a child.

It is usually given the clinical diagnosis of pyogenic granuloma and frequently seen in conjunction with orthodontic brackets, which may be purely coincident with the patient population.

The lesion is not painful, but bled easily.

Localized Juvenile Spongiotic Gingival Hyperplasia

The histologic presentation is an exophytic lesion with a subtle papillary architecture composed of interconnecting bands of epithelial hyperplasia.

The histology is unique and characterized by prominent intercellular edema (spongiosis) and neutrophilic exocytosis.

The presence of highly vascular connective tissue cores is seen containing mostly acute, but with some chronic inflammatory cells. LJSGH displays as a gingival overgrowth rather than a pure inflammatory process with minimal to no tissue swelling.
Localized Juvenile Spongiotic Gingival Hyperplasia

The etiology is unknown and the lesion does not respond to periodontal treatment showing a lack of association with plaque or calculus.

Darling et al. compared juvenile spongiotic gingivitis (LSGH) with puberty gingivitis and found several distinguishing features including a lack of immunoreactivity for estrogen and progesterone receptors in LSGH.

Treatment for LSGH is conservative surgical excision and the carbon dioxide laser is ideal for treating this lesion. The young age of the patient makes laser ablation a preferred and very efficient procedure, well tolerated by this population of patients. Recurrence is rare and when it does occur, may be due to incomplete removal of the lesion.

What we learned from Theresa?

Alex.. 3 year-old
3 year old, girl, Caucasian

Patient is a 3 year old healthy girl who presented to the pediatric dental office with “white stuff” in her mouth for the last week. No complain of pain.
PMH: Non contributory  Allergies: NKDA
Medications: None
Review of systems: Essentially negative except for a recent episode of otitis media

Based on the clinical pictures and history, which of the following diagnosis at this point you will place higher in the differential?

1. Candidiasis
2. Candidiasis
3. Candidiasis
4. Other (idiopathic candidiasis)

Patient laboratory results:

- RBC: 4.5 mm³
- Platelet: 250,000
- Hg: 14 gr/dl
- WBC: 6,300
- Lymphocytes: 10%
Clinical features which may indicate immunodeficiency

- Three or more episodes of otitis media in 6 months
- Persistent purulent ear discharge
- Two or more serious sinus infection within one year
- Two or more episodes of pneumonia within one year
- Failure to thrive
- Recurrent deep skin infections
- Persistent candidiasis
- Family history

Primary Immunodeficiency Disorders

- B cell (antibody) deficiencies
- T cell deficiencies
- Combination B and T cell deficiencies
- Defective phagocytes
- Complement deficiencies
- Unknown (idiopathic)
Immunity to infection

The areas of the immune system to consider are:

- Humoral immunity (B cells and Immunoglobulins production)
- Cell-mediated immunity (T cells), neutrophils
- Complement cascade
Selective IgA deficiency

- Selective IgA deficiency is one of the most common types of primary immunodeficiency
- Many patients go undiagnosed because they are never sick enough to be seen by a doctor
- Patients with selective IgA deficiency do produce all the other Ig
- The cause is unknown
- Children with selective IgA deficiency are at risk of infection; about half have repeated infections of the ears, sinus, and airway
- Children with IgA deficiency are at increased risk for anaphylactic reactions

What we learned from Alex?

Sophia
Hillary
Bobby
Kawne
• Age: 13 y.o, girl.
• Chief Complaint: “There is something in my gums”
• HPI: Asymptomatic lesion between 10 and 11. Unknown duration. Pedunculated.
• Past Medical History (PMH):
  - Hypothyroidism
  - Anemia
  - Vision problems
• Past Dental History (PDH): Last visit to the dentist: 18 months ago

The microscopic sections reveal a papillary nodule of mucosa that is surface by parakeratotic stratified squamous epithelium which forms several short projections of mucosa with connective tissue cores.

The underlying lamina propria consists of fibrous connective tissue with scattered small vascular channels and neural bundles.

**Diagnosis: Papilloma**

• Age: 4 y.o, girl.
• Chief Complaint: “There is something in the back of my mouth”
• HPI: Asymptomatic lesion at the junction between hard and soft palate at the right side. Unknown duration. Well pedunculated.
• Past Medical History (PMH):
  - Unremarkable
• Past Dental History (PDH): Last visit to the dentist: 6 months ago
- **Age:** 17 y.o., boy.
- **Chief Complaint:** “There is something in the front of my mouth”
- **HPI:** Asymptomatic lesion between maxillary central incisors. Unknown duration. Well pedunculated.
- **Past Medical History (PMH):**
  - Asthma well controlled. Using steroids PRN
- **Past Dental History (PDH):** Last visit to the dentist: 6 months ago

---

- Squamous Papilloma
- Verruca Vulgaris (common wart)
- Condyloma Acuminatum
- Multifocal Epithelial Hyperplasia (Heck Disease)

---

**Squamous papilloma**
- Benign proliferation of stratified squamous epithelium
- The lesion is induced by HPV
- Exact mode of transmission is unknown
- Equal frequency in boys and girls
- More common places: tongue, lips, and soft palate.
- The papilloma is usually solitary
- Histopathology: proliferation of keratinized stratified squamous epithelium in “finger like projections” with fibro-vascular connective tissue cores.
Condyloma Acuminatum

Condyloma acuminatum is a STD appearing most frequently as a soft, pink cauliflower like growth.

The condition is highly contagious

Both genders are affected equally

The peak incidence is between 17 to 20

The histology shows \( \rightarrow \) papillary lesions

Multifocal Epithelial Hyperplasia (Heck's Disease)

- Virus induced, localized proliferation of oral squamous epithelium that was first described in Native Americans
- Associated with HPV 11 and 13
- In some populations, as many as 39% of children are affected.
- The condition usually affects multiple members of the same family
- Multiple, flattened, soft, non tender papules, usually clustered with the same color of the oral mucosa.

Human papillomavirus infection of the oral mucosa
1. Human papillomavirus infections of the oral mucosa

Classification

- Papillomaviruses are small, double stranded DNA viruses.
- Human can be infected only by HPV's, not by papillomaviruses found in animals.
- The HPV genome contains eight open reading frames (ORFs) which are potentially coding sites of six early proteins (E) and two late proteins (L). The L1 ORF is used to identify the different types of HPV because it is the most conserved of the eight ORFs within the genome. (1)

1. Rautava J, Syrjanen S. Human papillomaviruses infections in the oral mucosa. JADA 2011; 142(8):905-914

- Investigators have described more than 120 different HPV types on the basis of the isolation and sequencing of complete genomes. (1)
- Most HPV that infect oral mucosa site belong to the alpha papillomaviruses, which consist of 15 species. (2)
- To date, investigators have identified 30 HPV genotypes: 15 high-risk types, 3 types that probably are high risk and 12 low risk types.

1. Rautava J, Syrjanen S. Human papillomaviruses infections in the oral mucosa. JADA 2011; 142(8):905-914

**HPV-16**
- Major capsid protein
- Minor capsid protein
- Membrane signaling protein

**LCR**
- Regulation and virus gene expression and synthesis
Maria Fernanda
14 year-old
(this is my only change
to get invited again)

Idiopathic Bone Sclerosis
vs.
Cemento-osseous dysplasia

Principles of Radiographic Interpretation
There is a radiopacity, not too big, not too small, looks actually funny... located at the apex of tooth #28.

Some definitions
Summary of Interpretation Steps

1. Radiopaque / Radiolucent / mix
2. Well defined / ill defined / mix
3. Corticated / non-corticated / mix
4. Location, size and shape
5. What happen in the “neighborhood”
6. Differential interpretation

let’s practice with some films

Summary of Interpretation Steps

1. Radiopaque / Radiolucent / mix (my mom)
2. Well defined / ill defined / mix (my mom)
3. Corticated / non-corticated / mix (my mom)
4. Location, size and shape
5. What happen in the “neighborhood”
6. Differential interpretation
Most common jaw lesions in children

1. Idiopathic Bone Sclerosis
2. Fibrous Dysplasia
3. Simple Bone Cyst
4. Cemento-osseous dysplasia
Idiopathic Bone Sclerosis

(not condensing osteitis!)

Idiopathic Bone Sclerosis

IBS is a focal solitary sclerotic lesion that arises in the late 1st or early 2nd decade of life.

Its cause is unknown.

It is asymptomatic, is not associated with inflammation, and may remain static or demonstrate slow growth that usually stops when the patient reaches skeletal maturity.

Idiopathic Bone Sclerosis

In 90% of patients it occurs in the mandible, usually near the first molar or second molar or premolar.

At imaging, IBS is radiopaque, well defined, well localized, non-corticated, located at the apex of vital teeth. No root resorption and no teeth displacement.

Some patients may have multiple lesions.
Simple Bone Cyst

- Traumatic bone cyst, hemorrhagic bone cyst, solitary bone cyst
- Simple bone cyst: it is a cavity within bone that is lined with connective tissue. It may be empty or it may contain fluid
- It is not a true cyst
- Etiology unknown, however localized aberration in normal bone remodeling or metabolism
- First two decades of life (mean 17 years)
- Females 2:1
- Expansion is possible but unusual, discovery by chance

- Mandible
- Posterior mandible
- Associated with cemento-osseous dysplasia and fibrous dysplasia
- Margin: Well defined to ill-defined border
- Internal structure: Radiolucent, it may appear multilocular, although the lesion does not contain true septa
- No effect on the surrounding teeth
- Lamina dura intact and vitality positive
Localized change in normal bone metabolism \(\rightarrow\) replacement of all components of normal bone by fibrous tissue containing varying amounts of abnormal appearing bone

- Solitary or multiple (monostotic 70% of all cases)
- McCune-Albright syndrome
- Asymptomatic, rare associated with pain
- The lesion may become active \(\rightarrow\) Pregnant, etc.
- The skull is involved in 10 to 25% of cases
- Patients between 10 and 30 years old

Fibrous Dysplasia

- Maxilla almost twice as often as the mandible, unilateral
- Ill-defined, radiopaque
- Gradual blending of normal trabecular bone
- Density and trabecular pattern of fibrous dysplasia vary considerable
- Granular appearance: "ground glass", "orange peel"
Focal Cemento-Osseous Dysplasia

- Localized change in normal bone metabolism ➔ Replacement of the components of normal bone with fibrous tissue and cementum-like material, abnormal bone or a mixture of the two
- Near the apex of a tooth
- Middle age, females 9:1, Afro-American
- Incidental finding
- The involved teeth are vital
- Sometimes quite larger

Focal cemento-osseous dysplasia

- Epicenter usually at the apex of a tooth
- Well defined, irregularly shaped
- Internal structure: Varies ➔ Radiolucent area
  - Mixed stage: Radiopaque and Radiolucent areas
  - Mature stage: Radiopaque
- Lamina dura of the teeth involved with the lesion is lost
- Rare: resorption of the roots

Source: Oral Radiology, Principles and Interpretation. White et al, 2000
let’s come back to Maria Fernanda…..

According to the patient’s mother “she had her wisdom teeth out 2 months ago and she had a knot in the area right after the extraction but eventually went away”. Then 2 months later with swelling and pain over the left mandible.

Mom consulted with the oral surgeon. No concerns over the area of extraction of tooth #17.

Pain partially controlled with ibuprofen and antibiotics (?).

According to the patient, “my whole jaw hurts, those three teeth are aching (18-19-20)”.

Initially referred to the endodontist for root canal of tooth #20.

My differential diagnosis ➔ Neuropathic pain?

Neuropathic pain is chronic pain condition caused by an alteration in the peripheral or central nervous system (trigeminal neuralgia, atypical odontalgia, burning mouth syndrome, traumatic neuropathies, post-herpetic neuralgia, and complex regional pain syndrome).

Often neuropathic pain is misdiagnosed which can lead to unnecessary treatment.

Vascular compression, radiation, inflammation, trauma, infection, etc. can lead to neuropathic pain.
Differential diagnosis

Neuropathic pain?


Extraction of third mandibular molars, dental injections, implant treatments, and endodontic treatments are the most common procedures in dentistry associated with neuropathic pain

Treatment: Amitriptyline, pregabalin, gabapentin

Suggested to see a neurologist

What we learned from Maria Fernanda?

1. Radiographic interpretation (probably the MOST important goal)
2. Common bone lesions in children (just remember one: IBS)
3. Neuropathic pain in children (you can delete that from your brain immediately)
4. Use of CBCT in pediatric dentistry (who cares?)

Mary, 4 year-old
4.5 year-old, girl, Hispanic

6 months ago, parents noticed intraoral swelling of the gingiva (not a lot of pain)...Dad said it was mostly around the back teeth. He took them to their general dentist.

PMH: Unremarkable

Allergies: NKDA

Orofacial Granulomatosis I

Orofacial granulomatosis has become a well accepted and unifying term encompassing a variety of clinical observations (biopsy = non-specific granuloma).

Orofacial granulomatosis ~ Aphthous stomatitis (idiopathic but appears to be an abnormal immune reaction)

Systemic disease that mimics OG: Crohn's disease, sarcoidosis, tuberculosis

Several triggers are involved.

The majority of patients are adults. However, when is in children ~ strong association with asymptomatic inflammatory gastrointestinal process (different from Crohn's disease) an associated with dietary triggers

Clinical presentation is highly variable. Most common site: LIPS

When the signs are combined with facial paralysis and fissure tongue: Melkersson Rosenthal syndrome

Intraoral: Tongue and gingiva (swelling and erythema)

Orofacial Granulomatosis II

The diagnosis of OG ~ Histopathology: presence of granulomas associated with negative stains for organisms and no foreign material

Treatment:

• First goal ~ Identify the possible cause (not easy at all)

• In children ~ Strong consideration to dietary allergens or an association with underlying GI disease

• Topical use of steroids (similar to RAQ), TNF-α antagonist (infliximab), intra-lesional injections of steroids

Prognosis ~ highly variable
What we learned from Mary?

1. The importance of a detailed medical history (Most important goal)
2. Orofacial Granulomatosis (well... not to common)

Soft Tissue Lesions in Children and Adolescents (besides we already reviewed)

Idiopathic Gingival Fibromatosis

Idiopathic gingival fibromatosis (IGF) is an enlargement localized or generalized of the gingival tissue characterized by an expansion and accumulation of the connective tissue, mainly collagen type 1. Gingival fibromatosis is commonly induced as a side effect of systemic drugs (such as phenytoin, nifedipine, and cyclosporine).
Idiopathic Gingival Fibromatosis

However, in some cases the gingival overgrowth is idiopathic. The enlargement is more prominent during the eruption of the primary and permanent teeth. Poor oral hygiene has been also associated with the condition.

The diagnosis is established through history, clinical examination and histopathology.

Surgical treatment including gingivectomy and gingivoplasty are usually the treatment.

Dermoid Cyst

Dermoid cyst are malformations that are common in the oral cavity.

Dermoid cyst are development lesions found inside organs or tissues as a result of the inclusion of tissue from diverse sources (ectoderm, mesoderm or endoderm)

Dermoid cyst of the oral cavity are often relatively soft unfluctuating masses, frequently adhered to the child’s hyoid bone.

The differential diagnosis includes lipoma, ranula, thyroglossal duct cyst, cystic hygroma, and malignant tumors.

Boys are more affected than girls by a ratio of 3:1.

Almost one in five of the dermoid cyst that occur in the head and neck area are located in the floor of the mouth and often they cause tongue elevation.

Usually they are diagnosed at young ages. The treatment is complete surgical excision and they have a good prognosis.
Mucocele

- Common lesion of the oral mucosa that results from rupture of salivary gland duct and spillage of mucin into the surrounding soft tissues
- The most common reason: TRAUMA
- It is not a true cyst (no epithelial lining)
- Typically they are dome shaped swelling that can range from 1 to 2 mm
- Most common lesion in children
- Often translucent
- Fluctuant at palpation: From a few days to few years: History of recurrent swelling

Mucocele

- The lower lip is by far the MOST common site
- Some mucoceles are short-lived lesions that rupture and heal by themselves
- Some mucoceles are chronic in nature and surgical excision is necessary
- Excellent prognosis

Pyogenic Granuloma

It is a common tumor-like growth of the oral cavity that traditionally has been considered to be non-neoplastic.

- Unrelated with infection and granulomas!
- It is an exuberant tissue response to local irritation or trauma.
- It is a smooth, lobulated mass, usually pedunculated.

- Microscopic evaluation shows a highly vascular proliferation.
Pyogenic Granuloma

Etiology:
- Connective tissue reaction to injury or other stimulus
- Hormonal changes/puberty
- Composed of hyperplastic granulation tissue

Treatment:
- Surgical excision
- Frequently recurs

Neville, Damm, Allen, Bouquot. Oral and Maxillofacial Pathology 3 edition

Eruption Cyst

The eruption cyst (or in some textbooks, eruption hematoma) develops from separation of the dental follicle from around the crown of a tooth who is erupting.

The eruption cyst is a soft, swelling in the gingiva overlying the crown of an erupting primary or permanent tooth. The majority of cases of eruption cysts are seen in children under the age of 10.

The lesion is most commonly associated with the central permanent incisors or central primary molars.

Treatment is usually not required because the eruption cyst ruptures spontaneously.

Leiomyomas

Leiomyomas are benign tumors that originate from smooth muscle.

The most common place that leiomyomas are found is the uterine myometrium. However, leiomyomas are also found in the gastrointestinal tract, skin and lower extremities.

Leiomyomas are rare in the oral cavity, the most common place is the lips followed by tongue, cheeks, palate and gingiva.
Leiomyomas

Usually the lesion is asymptomatic, slow-growing. In children is rare. Histopathology has a key role in establishing the diagnosis.

The differential diagnosis when located in the oral cavity is Mucocele and fibromas. Leiomyomas in the oral cavity are characterized by a solitary, usually ovoid and mobile mass covered by normal appearing epithelium.

The consistency is usually firm with a well-defined margins. The treatment of leiomyomas in the oral cavity is the complete resection of the lesion.

Giant Cell Fibroma

The giant cell fibroma is a fibrous tumor that is probably unrelated with chronic trauma (difference with the traumatic fibroma).

Typically the giant cell fibroma is asymptomatic and represents 2% to 5% of all oral fibrous proliferations submitted for biopsy.

A common differential diagnosis is papilloma. Compared with the irritation fibroma, the lesion occurs at a younger age.

There is a slightly female predilection. The mandibular gingiva is affected twice as often as the maxillary. The palate is also a common place. From the histopathology perspective, the hallmark is the presence of fibroblast within the superficial connective tissue. The treatment is conservative surgical excision.

Peripheral Giant Cell Granuloma

Found only in gingiva

Usually distal to incisors

May cause bone resorption

Appear as red or blue broad-based masses

More frequent in females
### Peripheral Giant Cell Granuloma

**Etiology:**
- Hyperplastic connective tissue response to gingival tissue injury
- Histologically see multinucleated giant cells
- Similar in appearance to pyogenic granuloma

**Treatment:**
- Surgical excision
- Recurrence is uncommon

---

**Thank you so much!!!**

Juan F. Yepes DDS, MD, MPH, DrPH  
jfYepes@iupui.edu