A Roundup of New Oral Diseases, New Findings and New Drugs for Tots and Teens

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Objectives
- Identify common oral soft tissue lesions that are pertinent to the pediatric age group.
- Become familiar with new lesions and diseases.
- Describe the new findings of common oral lesions.
- Learn about new treatment approaches for common oral diseases.

U.S. Mortality Drops for Infants
- 6.87 deaths/100,000 live births in 2005
- 6.05 deaths/100,000 live births in 2012
- Deaths declined for congenital defects, premature birth, SIDS (20% drop), maternal complications
- Rates for fatal accidental injuries rose slightly
- Reference: CDC NCHS, 4-2013.

New Problem due to Prevention
- Positional plagiocephaly: occipital flattening, craniofacial asymmetry in infants >6 weeks
- Increase in prevalence since “Back to Sleep Campaign”
- Point prevalence: 22.1% in early infancy
- Cause: Prolonged supine position, torticollis, DD, bottle feeding only?

New Name – Old Disease
- Odontogenic keratocyst is now keratocystic odontogenic tumor
- Uni- or multi-locular radioluclency
- Aggressive jaw lesion with high recurrence rate of 30%
- May be associated with nevoid basal cell carcinoma syndrome

New Causes – Old Diseases
- Rare Pediatric Cancers Tied to Car Emissions
- 3 cancers increased: ALL - 4%, Retinoblastoma - 14%, Germ cell tumors - 17%
- Pregnant women who lived within 1 mile of heavy traffic were at greatest risk
- Heck J et al. AACR 2013
New Infection: Chikungunya

- New viral infection
- Transmission: Mosquitoes, blood-borne; rare in utero
- Incubation: 1-12 days
- Acute symptoms: 7-10 days → Chronic: weeks - years
- S/S: Fever, polyarthralgia, headache, myalgia, arthritis, conjunctivitis, rash, lymphopenia, thrombocytopenia
- Orofacial: Palsy, TMD, facial rash, aphthous, bleeding, photohyperpigmentation, vesiculobullous disease (child)
- TX: Rest, fluids, NSAID, steroids

Chikungunya Disease

Children more prone to vesiculobullous disease and meningoencephalitis

New Disease in East Texas

- Factor V causes east Texas bleeding disorder
- Moderately severe autosomal dominant bleeding disorder that inhibits coagulation
- S/S: Bruising, bleeding gingivae, nosebleeds, surgical bleeding, miscarriages
- Lab studies: Normal conc of coagulation factors; prolonged prothrombin time (PT), activated partial thromboplastin time (APTT)
- UTHealth identified the cause (FVA2440G)


Atypical Gingivitis & Epistaxis

Prolonged bleeding with tooth exfoliation

Age Matters for Oral Lesions
New Study – Common Lesions
Fehmida, Kong, Flaitz AAPD 2014

Purpose: to determine the prevalence of oral mucosal lesions in healthy children (0-20 yr-old)
31 publications met the search criteria
International scope: US, Sweden, Taiwan, Mexico, Brazil, Italy, Spain, Turkey, South Africa, Argentina, India, Iran, Iraq, Israel, Nigeria, Saudi Arabia, South Africa, Hungary
Sample size: Infants: 420 - 2182; Children: 541 - 70,359
Point prevalence of oral lesions and anomalies for infants and children/adolescents, excluding gingivitis.
Lesions documented in 4 studies for inclusion.

Neonatal Oral Lesions & Anomalies:
7 studies with N = 420 – 2182

- Palatal cysts: 65% (54-86%)
- Gingival cysts: 24% (13-97%)
  - Oral cysts: 56-99%
  - Alveolar lymphangioma: 0-4%
- Leukoedema: 0-34%
- Median alveolar notch: 0-23%
- Ankyloglossia: 2.1% (.1-11%)
- Commissural lip pits: 5% (2-8%)
- Fordyce granules: .8% (.09-1%)--

Oral Lesions with Cleft Lip/Palate:
1 study with N = 141

- Overall prevalence: 90%
- Sucking calluses: 69.7%
- Candidiasis: 22.5%
- Ulcers, NOS: 21.1%
- Gingival cysts: 28.2%
- Palatal keratosis: 28.9%
- Neonatal teeth: 5.6%
- Eruption cysts: 1.4%
- Sucking ulcer: 5.6%
- Pyogenic granuloma: .7%
- Alveolar lymphangioma: .7%

Oral Lesions & Anomalies in Children:
24 studies with N = 541-70,359

- Aphthous ulcers: 2.5% (.1-11%)
- Herpes labialis: 1.4% (.4-5%)
- Cheek biting/ linea alba: 2.5% (1.5-29%)
- Traumatic injury: 2.4% (.4-12%)
- Candidiasis: .15% (.01-8%)
- Angular cheilitis: 2.5% (0-15%)
- Commissural lip pits: 0-8.4%
- Fordyce granules: 2.5% (.1-11%)
- Mucocele: .3% (.03-1.5%)
- Oral warts: 2% (.02-6%)
- Melanotic macule: 1.1% (.1-14%)
- Hemangioma: .2% (.2-3.8%)
- Primary HSV: .3% (.02-1.3%)
- Overall prevalence: 27.5% (2.3-40.7%)

Tongue Lesions & Anomalies in Children

- Benign migratory glossitis: 1.9% (.2-27%)
- Fissured tongue: 1.7% (.1-29%)
- Median rhomboid glossitis: .2% (0-1.75%)
- Ankyloglossia: .8% (0-8.4%)
- Coated tongue: 3.3% (3-24%)
- Macroglossia: .3% (0-1.8%)
- Hairy tongue: .3% (0-1.7%)
- Overall prevalence: 29.6 % (5-40%)

Benign migratory glossitis and Fissured tongue

New Oral Lesions and Anomalies

Herniated Dental Follicle
- Eruption of part of the dental follicle
- Usually primary teeth
- S/S: Nontender, red, white or amber in color
- Bleeds with manipulation
- TX: None needed; most resolve as tooth erupts
- Mimics: Pyogenic granuloma, abscess, tooth

Residual Operculum
1 week followup

FDA: Teething Gel Warning
- Methemoglobinemia
  - Rapid onset
  - Gray, blue skin, lips, nails
  - Shortness of breath
  - Headache
  - Confusion
  - Rapid heart rate
  - Fatigue
- Cause: Benzocaine (>7.5%)

No Anesthetic Pain Control for Teething
- FDA Black Box Warning for use of viscous lidocaine in children for teething
- Problem: Easy to overdose
- S/S: Confusion, vision problems, vomiting, sleepiness, shaking, seizures, choking, aspiration, cardiac and nervous system toxicity, death
- TX: Coolness to the tissues; rub and clean the gum pads

Licorice Poisoning
- Licorice extract for medicinal use
- Active agent: Glycyrrhizic acid
- Found in foods, candies, soft drinks, herbal tea, cigs, snuff, mouthrinses, topical oral anesthetics, laxatives, cough syrups
- US consume up to 3.6 mg/kg/d
- Problem: Hypermineralocorticoidism: edema, hypokalemia, hypertension
- Side effects reversible
Localized Juvenile Spongiotic Gingival Hyperplasia (LJSGH)

- Distinct, new subtype of gingival hyperplasia
- Other names: Juvenile spongiotic gingivitis or juvenile gingival papillomas
- Origin: Sulcular/junctional epithelium
- Cause: Unknown – not strong bacterial plaque association; viral cause, especially HPV?
- Factors: Orthodontics (15%), tooth eruption, lip incompetence/mouthbreathing, puberty
- Age/Gender/Race: Ave = 12 YO (range 5-39)/ F>M = 2.3:1 / White

Juvenile Spongiotic Gingivitis

- Site: Anterior facial gingiva, esp. maxillary (84%); may be multifocal
- S/S: Papillary, pedunculated, red nodule or velvety - granular patch; bleeds easily; nontender
- Characteristic feature: Does not respond to traditional periodontal treatment or oral hygiene
- TX & Prog: Excisional biopsy; 6-16% recur within 1 year; may spontaneously resolve


Vascular Variant of Incisive Fossa

- Anatomy: Incisive fossa is oval bony depression that contains the descending branch of greater palatine vessels & nasopalatine n
- Location: Midline anterior hard palate distal to incisive papilla
- S/S: Blue macule that blanches, asymptomatic
- Mimics: Blue nevus, tattoo ecchymosis, hemangioma.
**Infantile Hemangioma**
- **Type:** Vascular hamartoma
- **Age/Gender:** 4-10% of age 1 YO; F:M::3:1-5:1
- **Site:** Head & neck = 60%; lips, tongue
- **Growth period:** 6-10 months
- **S/S:** Red or blue, flat or nodular lesion; blanches; 20% are multiple
- **TX:** Involution starts at 18 mos; 50% by 5 – 90% by 9 yrs; propranolol, steroids, laser, excision
- **Complication:** Ulcer, bleeding, infection, scar (40%)

**Involuting Hemangioma**

**New Treatment: Hemangioma**
- Hemangeol (Propranolol) Beta blocker – FDA-approved
- Regranex gel for ulcerated hemangiomas

**Segmental Odontomaxillary Dysplasia**
- **Developmental disorder**
- **Unknown cause**
- **Age:** Usually diagnosed in first decade
- **Location:** Posterior maxilla
- **Unilateral facial swelling**
- **Affects face, alveolar bone, teeth**

**Facial asymmetry; unilateral enlargement of maxillary bone**
- **Hyperplastic gingiva**
- **Dental:** missing premolar teeth; hypoplastic primary teeth; large, splayed roots; delayed eruption
- **Bone abnormalities:** Vertically oriented, coarse trabeculae
- **Diff DX:** Fibrous dysplasia, Regional odontodysplasia, segmental hemifacial hypoplasia
Segmental Odontomaxillary Dysplasia

- Other reported features
  - Hypertrichosis of ipsilateral facial skin
  - Hypertrichosis and hyperpigmentation of ipsilateral facial skin (Becker’s nevus)
  - Hypopigmentation of lip vermilion

New Disease – New Location

- Segmental Odontomandibular Dysplasia
  - Gingival hyperplasia
  - Alveolar expansion
  - Coarse bone
  - Macrodontic lateral incisor

Transient Lingual Papillitis

- Lesion: Inflamed fungiform papillae
- Cause: Unknown, trauma, allergy/sensitivity, GERD, hormonal, URI, viral infection
- Gender/Age: F>M; Wide age range
- Site: Dorsal tongue; Anterior, lateral
- Duration: 1 to 7 days
- 3 types: Single, diffuse or clustered
- S/S: Painful, red or white papules +/- fever, lymphadenopathy, may recur
- TX: Topical steroids, anesthetics, coating agents

Pain is out of proportion for size of the lesions
Subtle Erythema Migrans

Chronic Lingual Papulosis
- Fibrous hyperplasia of filiform & fungiform papillae
- Cause: Chronic, mild irritation, mouth-breathing, tongue thrusting, appliances; developmental anomaly
- Concurrent lesions: BMG, fissured tongue; possible chronic counterpart of TLP
- Age: Wide age range
- Site: Dorsal tongue; Anterior, lateral
- Distribution: Clustered to diffuse
- S/S: Persistent red, pink papules; 1-5 mm; +/- burning
- TX: None, unless symptomatic

Squamous Papilloma
- HPV 6,11 - Low virulence and infectivity rate
- Sexual, nonsexual transmission
- Comprise 8% of all oral growths in children
- Site: Tongue, lips, palate
- S/S: Solitary, pink, red, or white papillary nodule
- Tx: Excise; not precancerous

Verruca Vulgaris (Common Wart)
- Cause: HPV 2, 4
- Prevalence: 10-50% of children
- Site: Hands, face are common
- Oral Site: Lip, labial mucosa, anterior tongue
- S/S: Nodule with fingerlike projections or rough pebbly surface; pink, brown or white; painless
- TX: Remission – 20% in 6 mos; 65% in 2 yrs; excise, laser, cryotherapy, salicylic acid (skin), zinc, cimetidine, duct tape (skin), imiquimod, other
- Prognosis: Recurs, no malignant potential
Verruca Vulgaris

Verruca Vulgaris on Skin

Angular Cheilitis or Not?

Verruca Plana (Flat Warts)

Orofacial Warts

Fibrosing Parulis May Mimic a Wart

What Else Can It Be?

- Verruca vulgaris
- Squamous papilloma
- Condyloma acuminatum
- Multifocal epithelial hyperplasia
- Giant cell fibroma
- Localized juvenile spongiotic gingival hyperplasia
- Inflammatory papillary hyperplasia
- Molluscum contagiosum

NB: Lesions on the gingiva – take a radiograph

Condyloma acuminatum
Acquisition of Oral HPV in Children

- Overall pediatric prevalence: 2%
- Transmission: Casual, sexual contact, vertical, autoinoculation
- Breast milk – 4.5% (Giovannelli, 2002)
- Placental HPV+ = 4.5%; Cord blood HPV+ = 3.5%
  - Both ↑ risk for oral HPV at birth – 12.2% (Rombaldi, 2008)
- Persistent infection in mother increases risk of HPV infection in infants (OR = 6.7)
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- Persistent infection in mother increases risk of HPV infection in infants (OR = 6.7)
- Contaminated toys – 4% (Roman & Fife, 1986)
- Oral sex transmission is inconclusive
  - Rautava et al. 2011; Pinheiro et al. 2011

Salivary HPV Diagnostics

- OraRisk HPv Salivary DNA test by OralDNA Labs, Quest Diagnostics
- Purpose: Uses PCR DNA to detect HPV types
- Non-invasive, easy to use screening tool
- Provides risk profile for HPV type
- www.OralDNA.com

OraRisk HPV Salivary Test

- Swish & gargle 3 mL of saline solution for 30 sec
- Expectorate in tube
- Place collection tube in mailer for DNA-PCR analysis
- Complete report
- Results emailed
- ADA CDT code: DO418

HPV Vaccine

- Gardasil® (Merck): Quadrivalent vaccine to prevent cervical cancer and genital warts
  - Protects against HPV types 6,11,16,18; cause 70% of cervical cancer and 90% of genital warts
  - Recommended for females, ages 11-12 with range of 9-26 yrs; recently approved for males
  - Cervarix® (GlaxoSmithKline): Bivalent vaccine
  - Protective role in oropharyngeal cancer?
  - ↓ oral HPV detection in vaccinated women after 4 yrs
  - Herrero R et al 2013

Mucoceles

- Type: Reactive lesion of salivary glands
- Cause: Trauma to ducts and glands
- Age: Children and young adults
- Site: Lower lip (81%), buccal mucosa (5%), ventral tongue (6%), floor of the moth (6%)
- S/S: Translucent blue, fluid-filled swelling; fluctuates in size; may be tender
- TX: Excisional biopsy with adjacent glands; 40% spontaneously resolve; recur – 6%
- Variant: Ranula – floor of the mouth

Pedunculated Mucocele

- Type: Reactive lesion of salivary glands
- Cause: Trauma to ducts and glands
- Age: Children and young adults
- Site: Lower lip (81%), buccal mucosa (5%), ventral tongue (6%), floor of the moth (6%)
- S/S: Translucent blue, fluid-filled swelling; fluctuates in size; may be tender
- TX: Excisional biopsy with adjacent glands; 40% spontaneously resolve; recur – 6%
- Variant: Ranula – floor of the mouth
**Mucocele**

- **Glands of Blandin-Nuhn**

**Superficial Mucocele**

- **Oral Fixed Drug Eruption**
  - FDE is a recurrent site-specific lesions of the skin and/or mucosa when a drug is taken.
  - Age: Wide age range, including <10y.
  - Oral lesions occur alone (14%) or with genital, ocular, nasal or skin lesions.
  - Site: Tongue, palate, labial mucosa.
  - S/S: Ulcers, erythema, bullae +/- pigmentation.
  - Drugs: Naproxen, co-trimoxazole – most common; fluconazole, tetracyclines, ibuprofen, clindamycin.
  - Tx: ID and DC drug; palliative care.

**Oral Fixed Drug Eruptions**

- 3 YOM taking Bactrim for otitis media.
- 8 YOM taking Aleve for sinus headache.

Ozkaya B, 2012
Fixed Drug Reaction
- Focal increase in melanin
- Skin: Ephelis (freckle)
- Age/Sex: All ages; F>M
- Rare congenital lingual lesion
- Site: Lip, buccal mucosa, gingiva, palate
- S/S: Solitary, oval brown, gray macule
- TX: None required; no malignant potential

Melanotic Macule
- Focal increase in melanin
- Skin: Ephelis (freckle)
- Age/Sex: All ages; F>M
- Rare congenital lingual lesion
- Site: Lip, buccal mucosa, gingiva, palate
- S/S: Solitary, oval brown, gray macule
- TX: None required; no malignant potential

Papillary Tip Melanosis
- Pigmented fungiform and some filiform papillae
- Cause: Unknown, normal pigmentation, post-inflammatory pigmentation
- Starts in childhood; may be congenital
- Ethnic: Hispanic, Black, Asian
- Tx: None

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Acanthosis Nigricans
- Type: Acquired or inherited hyperpigmented skin condition
- Associated with diabetes, obesity, other endocrine disorders, genetic conditions, malignancies, drugs
- Onset: Wide age range depending on cause
- Sites: Flexural sites, axilla, neck, groin, fingers, lips
- S/S: Leathery or velvety, thickened to papillary, brownish patches, nontender
- TX: ID the cause, retinoic acid, may fade

Ref: Adibi S et al, 2011
**Oral Candidiasis**
- **Cause:** *Candida species, Candida albicans*
- **Prevalence:** 40 – 60% normal oral inhabitant
- **Predisposing factors:** ↓ immune status, medications, poor oral hygiene, appliances, pacifiers, poor diet, diabetes, dry mouth
- **Site:** Usually multifocal oral involvement
- **Variants:** Pseudomembranous, erythematous, hyperplastic types
- **S/S:** Red or white patches, erosions, burning sensation, taste perversion, sore throat
Pigmented Candidiasis

Oropharyngeal Candidiasis

Topical Agents:
- Nystatin suspension 100,000 U/mL
- Clotrimazole troches 10 mg
- Oravig (miconazole) buccal tabs 50 mg

Systemic Agents:
- Ketoconazole 200 mg tabs (Not recommended)
- Diflucan, g (fluconazole) 100 mg tabs, 10 mg/mL, 40 mg/mL susp (birth defects rare but ↑ risk for tetralogy of Fallot) Molgaard-Nielsen, NEJM, Aug 2013
- Sporanox (itraconazole) 100mg/10mL

Miconazole (Oravig): Topical
- Form: Adherent, slowly dissolving 50 mg tablet
- Usual dosage:
  - Adolescents >16 yrs: 1 tablet for 14 days. Apply to the upper gum region, just above the upper lateral incisor. Alternate sides of the mouth.

Probiotics and Oral Health
- Probiotics: Living microorganisms (primarily bacteria) that are safe for consumption and when ingested in sufficient quantities have beneficial effects on human health beyond basic nutrition (UN & WHO)
- Purpose: To help prevent diarrhea from antibiotics
- Examples: Culturelle (lactobacillus GG), Dan Active (lactobacillus, strep thermophilus), others
- Duration: Take probiotics during antibiotic treatment and up to a week afterwards
- Sig: Take 2 hours after each antibiotic dose to improve probiotic survival

Secondary HSV Infection
- Cause: Reactivation of HSV-1
- Types: Herpes labialis, facialis, intraoral HSV
- Prevalence: 20-35%; ↑ with lower SES
- Risk factors: UV light, trauma, fever, teething, menses, genetic predisposition
- Site: Perioral skin, vermillion, gingiva, hard palate
- S/S: Recurrent, acute onset, prodromal redness, tender, clustered vesicles & ulcers, referred pain
- Complication: Scars, erythema multiforme, Bell’s palsy, herpetic whitlow, blindness
Herpes Labialis & Facialis

Recurrent Oral HSV Infection
- Who is at risk for recurrence?
- Reduced Interferon-lambda - required for antiviral immunity
- Gene on the long arm of chromosome 21 (21q21.1) – associated with frequency of outbreaks
- Apolipoprotein E4 gene (chromosome 19q13.32) – associated with oral but not genital HSV

Recurrence Herpetic Infection
Systemic Agents:
- Sitavig (acyclovir) 50 mg buccal tablets
- Zovirax, g (acyclovir) 400 mg capsules
  - Take 1 capsule 3 times a day X 5 days
- Valtrex, g (valacyclovir) 1g tablets
  - Take 2 tablets twice daily, 12 hours apart, when symptoms first develop
- Famvir, g (famciclovir) 500 mg tablets
  - Take 3 tablets as a single dose at first sign of infection (not as effective in adolescents)

Topical Antiviral Agents for Lips
- Docosanol (Abreva) cream 10% (OTC)
  - Sig: Apply 5 times/day for up to 10 days
- Penciclovir cream 1%
  - Sig: Apply q2h while awake for 4 days
- Acyclovir cream 5%
  - Apply 5 times/day for 5 days
- Xerese (acyclovir 5%/hydrocortisone 1%) cream
  - Apply 5 times/day for 5 days (new, expensive)

Perioral Impetigo
Topical Antibiotics:
- Bactroban (mupirocin) 2% ointment
- Altabax (retapamulin) 1% ointment
- BID X 5 days

Herpes Zoster (Shingles)
- Reactivation of varicella-zoster virus following varicella infection (chickenpox)
- 5% of cases occur in children <15 YO
- Prodromal pain from ganglionitis and necrosis due to replicating viruses
- S/S: fever, malaise, headache, lymphadenopathy, sensitive teeth, otitis media; unilateral prodromal pain, burning, itching, dysphagia
- Rarely tooth devitalization & osteonecrosis of bone
- May have no vesicles (zoster sine herpete)
HZ Risk Factors in Children
- Leukemia, other malignancies
- Immunocompromised
- In utero varicella exposure
- Primary VZV in first year
- Antitumor necrosis factor agents
- Immune reconstitution inflammatory syndrome

Herpes Zoster (Shingles)
- 1-4 mm vesicles widely scattered along dermatome
- Shallow ulcers that stop at midline
- Duration: 2-4 weeks
- Postherpetic neuralgia: uncommon in children
- Ocular involvement - blindness
- Ramsay Hunt syndrome: facial paralysis, vertigo with involvement of external auditory canal; may have acute onset dysphagia, dysphonia and cranial, cervical, or pharyngeal pain

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