

# ORAL INFECTIONS

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## **Viral infections**

- Herpes
- Human Papilloma Viruses
- Coxsackie
- Paramyxoviruses
- Retroviruses: HIV

## **Bacterial Infections**

- Dental caries
- Periodontal disease
- Pharyngitis and tonsillitis
- Scarlet fever
- Tuberculosis - *Mycobacterium*
- Syphilis - *Treponema pallidum*
- Actinomycosis – *Actinomyces*
- Gonorrhea – *Neisseria gonorrhoeae*
- Osteomyelitis - *Staphylococcus*

## **Fungal infections (Mycoses)**

- *Candida albicans*
  - *Histoplasma capsulatum*
  - *Coccidioides*
  - *Blastomyces dermatitidis*
  - *Aspergillus*
  - *Zygomycetes*
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# VIRAL INFECTIONS

- Viruses consist of:
  - Single or double strand DNA or RNA
  - Protein coat (capsid)
  - Often with an Envelope.
- Obligate intracellular parasites – enters host cell in order to replicate.
- 3 most commonly encountered virus families in the oral cavity:
  - Herpes virus
  - Papovavirus (HPV)
  - Coxsackie virus (an Enterovirus).

## **DNA Viruses:**

### **A. HUMAN HERPES VIRUS (HHV) GROUP:**

#### **1. HERPES SIMPLEX VIRUS**

- Double stranded DNA virus.
- 2 types: HSV-1 and HSV-2.
- Lytic to human epithelial cells and latent in neural tissue.

#### **Clinical features:**

- May penetrate intact mucous membrane, but requires breaks in skin.
- Infects peripheral nerve, migrates to regional ganglion.
- Primary infection, latency and recurrence occur.
- 99% of cases are sub-clinical in childhood.
- **Primary herpes: Acute herpetic gingivostomatitis.**
  - 1% of cases; severe symptoms.
  - Children 1 - 3 years; may occur in adults.
  - Incubation period 3 – 8 days.
  - Numerous small vesicles in various sites in mouth; vesicles rupture to form multiple small shallow punctate ulcers with red halo.
  - Child is ill with fever, general malaise, myalgia, headache, regional lymphadenopathy, excessive salivation, halitosis.
  - Self limiting; heals in 2 weeks.
  - Immunocompromised patients may develop a prolonged form.
- **Secondary herpes: Recurrent oral herpes simplex.**
  - Presents as: a) herpes labialis (cold sores) or  
b) recurrent intra-oral herpes – palate or gingiva.
  - Seen in adults (approx 30%).
  - Predisposing factors: sunlight, fever, allergy, trauma, menstruation, immunosuppression.
  - Herpes labialis:
    - Prodrome of burning and tenderness.
    - Intraepithelial blisters which burst, crust and heal in 10 -12 days.
  - Recurrent intra-oral herpes (uncommon):
    - Vesicles rupture early, form ulcers with red or white bases.
    - Heal in 10 to 12 days.

- **Herpetic whitlow.**
  - Primary or secondary infection localized to hands or fingers, acquired by direct contact with active lesion.

**Histopathology:**

- Keratinocytes show “ballooning degeneration”.
  - Nucleus: margination of chromatin, eosinophilic nuclear inclusions.
  - Multinucleate giant cells (syncytial epithelial cells).
  - Vesicles, which rupture and become erosions.
- **Diagnosis:** Mostly on clinical presentation, but occasionally by Biopsy; Smear; Culture; Fluorescent antibody or Immunohistochemistry; Serology.

**Treatment:**

- Acyclovir, valacyclovir or penciclovir.
- Topical (localised or recurrent lesions) or systemic.

## 2. VARICELLA-ZOSTER VIRUS (HHV3)

- Similar to HSV.
- Primary infection: Chicken pox.
- Recurrent infection: herpes zoster or shingles.

**Clinical features:**

- **Chickenpox (Varicella):**
  - 90% of the adult population will contact the virus and harbour it in its latent form.
  - Generalized, usually itchy, maculo-papular rash of the skin.
  - Vesicles and pustules occur.
  - Malaise, fever, minor oral cavity lesions (vesicles/ulcers).
- **Herpes zoster (shingles):**
  - Recurrent lesion. Affects 10 – 20% of the population
  - Common in elderly and immunocompromised.
  - Skin: unilateral linear vesicular rash outlining the cutaneous distribution of affected peripheral nerves.
  - Trigeminal nerve: unilateral facial and oral lesions may develop.
  - Pain, paresthesia.
  - Potential for post-herpetic neuralgia.

**Histopathology:**

- Virtually identical to HSV.
  - Acantholysis, Tzanck cells, with nuclear margination of chromatin and occasional multi-nucleation.
- **Diagnosis:**
    - History, clinical appearance (rash), (Smear, Culture, Serology).

**Treatment:**

- Usually heals spontaneously within about 2 weeks for Chickenpox or 6 weeks for Shingles.
- Herpes zoster: Acyclovir or Valacyclovir. IV in severe cases.

## **B. HUMAN PAPILLOMA VIRUS**

### **1. SQUAMOUS PAPILLOMA**

#### **Definition:**

- benign proliferation of stratified squamous epithelium resulting in a papillary or verruciform mass

#### **Etiology**

- Human papilloma virus (HPV) types 6 and 11?

#### **Clinical features:**

- M=F; 30 – 50 years.
- Site: Tongue; Lips; Soft palate (common); any oral surface.
- Soft, painless, pedunculated, exophytic nodule with surface finger-like projections (cauliflower-like).
- Normal colour.
- Solitary, 0.5mm; occasionally multiple lesions occur.

#### **Histological features:**

- Non-Keratinised stratified (not acanthotic) squamous epithelium.
  - Finger-like projections with Fibrous connective tissue cores.
- Sometimes inflammation in connective tissue.

#### **Treatment:**

- Conservative surgical excision.

### **2. VERRUCA VULGARIS**

#### **Definition:**

- a benign virus-induced, focal hyperplasia of stratified squamous epithelium.

#### **Etiology**

- HPV types 2, 4,.

#### **Clinical features:**

- Frequent in children, but also in older people.
- Site: skin of hands most common.
- Painless papule, papillary projections, rough surface.
- Usually sessile, 5mm diameter.
- Oral lesions almost always white.

#### **Histological features:**

- Hyperkeratotic stratified squamous epithelium, arranged in chevron-like projections.
- Connective tissue cores, chronic inflammatory cells.
- Rete ridges converge to centre of lesion, creating a “cupping” effect.
- Prominent granular cell layer.
- Koilocytes in superficial spinous layer.

#### **Treatment:**

- Conservative surgical excision.
- Cryotherapy on skin and topical medication.
- 2/3 will disappear spontaneously, especially in children.

### 3. CONDYLOMA ACUMINATUM

#### Definition:

- A virus-induced proliferation of stratified squamous epithelium of the genitalia, peri-anal region, mouth and larynx.

#### Etiology

- HPV types 6, 11.
- High risk types 16, 18 also found, especially in anogenital lesions.

#### Clinical features:

- Lesions usually develop at site of sexual contact.
- More frequent in teenagers and young adults, but may affect any age group.
- Oral lesions:
  - Labial mucosa, soft palate, lingual frenum, dorsum of tongue.
- Sessile, pink, well-demarcated non-tender mass, with short, blunted surface projections.
- Usually clustered.
- 1 – 3cm (sometimes larger).

#### Histological features:

- Acanthotic stratified squamous epithelium, mildly keratotic with blunt broad surface papillary projections, and thin connective tissue cores.
- Keratin filled crypts between prominences.
- Koilocytes in prickle cell zone (spinous layer).

#### Treatment:

- Conservative surgical excision.
- In the anogenital area, condylomata caused by HPV types 16 and 18 have been associated with malignant transformation.

### 4. FOCAL EPITHELIAL HYPERPLASIA

#### Definition:

- Virus-induced localized proliferation of squamous epithelium.

#### Etiology

- HPV type 13, possibly 32.

#### Clinical features:

- Usually seen in childhood; no gender bias.
- Sites: Labial, buccal and lingual mucosa.
- Multiple soft non-tender, smooth surfaced, flattened or rounded papules, small (3 – 10 mm) clustered, color of normal mucosa.
- Cobblestone appearance.

#### Histological features:

- Abrupt acanthosis of oral epithelium.

- Thickened mucosa extends upward, above normal surface, so that lesional rete ridges are at same level as normal rete ridges.
- Rete ridges wide, club-shaped or “battle-axe” shaped.
- Koilocytes, and “mitosoid” cells.

**Treatment:**

- Spontaneous regression.

## 5. ORAL SQUAMOUS CELL CARCINOMA

Evidence suggests that there is a role for one or more of HPV16, 18, and possibly 31, 33 in the pathogenesis of some oral squamous cell carcinomas.

## RNA Viruses:

### A. PICORNA VIRUS: COXSACKIE

- Picornavirus.
- Coxsackie A viruses cause herpangina, hand foot and mouth disease, and acute lymphonodular pharyngitis.
- Most cases arise summer/early fall.
- Spread: fecal-oral route.

**Clinical features:**

- Mainly children; spread aided by crowding, poor hygiene.
- Self-limiting disease.

**1. Herpangina:**

- Multiple Coxsackie subtypes.
- Sore throat, dysphagia, fever. Occasional cough, rhinorrhea, anorexia, vomiting, headache, myalgia.
- Oral lesions, confined to posterior: sites are soft palate, tonsil; begin as red macules and petechiae, form vesicles and ulcerate (2-4mm).
- Heals within 7 – 10 days.

**2. Hand-foot-and-mouth disease.**

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- Coxsackie subtypes A9 and A16.
- Sore throat, dysphagia, fever. Occasional cough, rhinorrhea, anorexia, vomiting, headache, myalgia. (flu-like symptoms).
- Skin rash on palms and soles. Oral and hand lesions almost always present; other sites variable.
- Oral lesions similar to herpangina but not confined to posterior mouth.

**3. Acute lymphonodular pharyngitis.**

- Sore throat, fever, mild headache.
- Yellow to dark pink nodules develop on soft palate and/or tonsillar pillars.
- Nodules are hyperplastic lymphoid aggregates.
- Resolves within 7 – 10 days.

**Histology:**

- Epithelium shows inter- and intracellular edema; extensive spongiosis and formation of intraepithelial vesicle in Herpangina and Hand Foot and Mouth Disease (not for Acute lymphonodular pharyngitis).
- Epithelial necrosis and ulceration follow.

**Diagnosis:**

- Clinical features; rare culture and serology.

**Treatment:**

- Disease is self-limiting.
- Symptomatic in more severe cases.

**B. RETROVIRUS****ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)****Definition:**

- a human immunodeficiency state caused by the human immunodeficiency virus (HIV) and associated with several life-threatening opportunistic infections and malignant neoplasms.

**Etiology:**

- Human immunodeficiency virus (HIV).

**Susceptible individuals and predisposing factors:**

- Homosexual/bisexual men (sexual intercourse).
- Intravenous drug users (contaminated needles).
- Haemophiliacs (via infected blood transfusions).
- Heterosexual contacts (sexual intercourse).
- Vertical transmission – mother to child (in-utero).

**Clinical features:**

- Fever, generalized malaise, unexplained weight loss, night sweats, lymphadenopathy (persistent cervical, axillary and inguinal), diarrhoea, persistent cough, infections.
- Associated infections:
  - Pneumocystis carinii (pneumocystis pneumonia).
  - Candidiasis (oral and genital).
  - Herpes (oral, genital, ocular, encephalitis).
  - Cytomegalovirus (CMV) in kidney, lung and brain.
  - Mycobacterium avium intracellulare.
- Associated malignant neoplasms:
  - Kaposi's sarcoma (hard palate, gingiva, skin).
  - Lymphoma.
  - Squamous cell carcinoma of the oral cavity.

**Oral findings:**

- Hairy leukoplakia on lateral borders of tongue.
- Candidiasis.
- Recurrent herpes simplex infections.
- Kaposi's sarcoma – association with HHV 8.

- Lymphoma (hard palate; tonsils; intra-bony in mandible and maxilla) – some associated with Epstein Barr virus.
- Salivary gland cystic lymphoepithelial lesion.
- AIDS periodontitis (rapidly progressive); necrotising ulcerative gingivitis.
- Aphthous-like ulcers.

**Treatment:**

- HAART – highly active antiretroviral therapy.
  - Nucleoside reverse transcriptase inhibitors
    - e.g. AZT (azidothymidine) [RETROVIR]
    - Slows replication of HIV – does not kill the virus.
    - Viral cultures remain positive but fewer in number.
    - Acts to inhibit reverse transcriptase which can terminate viral DNA-chain elongation.
    - Slows progress of disease but not a cure.
    - Patients feel better.
  - Non-Nucleoside reverse transcriptase inhibitors e.g. nevirapine
  - Protease inhibitors.
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# BACTERIAL INFECTIONS

- Bacteria are prokaryotes: lack membrane bound nucleus and cell organelles.
- Consist of cell wall:
  - Thick: Gram positive; Thin: Gram negative.
  - Cell membrane.
  - Most synthesize DNA, RNA and proteins.
  - Many have flagellae, and/or pili.
- Healthy people may carry:
  - $10^{12}$  bacteria on skin.
  - $10^{10}$  in mouth.
  - $10^{14}$  in GIT.

## TUBERCULOSIS

### Etiology:

- Mycobacterium tuberculosis, an acid fast bacillus.
- TB is a “granulomatous disease” characterized by “granulomatous inflammation” which includes epithelioid histiocytes + multinucleated giant cells + lymphocytes.
- Primarily a lung disease but can affect any organ.

### Clinical features:

- Chills, fever, weight loss, fatigue, malaise, persistent cough with haemoptysis.
- Source of infection: air borne droplet.
- Tests: BCG = Bacille Calmette-Guerin.  
PPD = purified protein derivative (Mantoux test).  
OT = old tuberculin.
- Oral lesions: 20% of patients; usually ulcer of tongue. N.B. dentist is at risk of infection from direct contact or droplet infection. Organisms are seen in 45% of oral washings.

### Histology:

- Granulomatous inflammation with or without caseous (cheese-like) necrosis.
- Ziehl-Neelsen stains AFB's red.

### Treatment:

- INH = isoniazid.
- Rifampin
- Duration: 18 to 24 months.

Mycobacterium leprae: causes leprosy.

Mycobacterium avium intracellulare: seen in AIDS.

## **SYPHILIS**

### **Etiology:**

- *Treponema pallidum* (a spirochete).
- Identified by silver stains (Warthin-Starry, Steiner or Leveditti).

### **Clinical features:**

- Transmission: a. Sexual intercourse with infected partner.  
b. contact with open wound (e.g. dentists).
- 3 clinical stages occur for Acquired syphilis:

#### **A. Primary syphilis** (lesion is the Chancre).

- Ulcer (chancre) appears 1-3 weeks after contact.
- Site: penis, vulva, cervix (95% of cases).
- Oral: lip, tongue, palate, tonsil, buccal mucosa.
- Chancre is indurated, painless, (or painful + regional lymphadenopathy).
- Ulcer exhibits many spirochetes if smeared.
- Histology: ulcer with many plasma cells.
- Heals within a few weeks.

#### **B. Secondary syphilis** (skin rash and mucous patches).

- 1-3 months after primary lesion.
- Skin rash: macules and papules.
- Oral: mucous patch and “snail track” ulcers.
- Mucous patches are highly infectious.
- Heals in a few weeks, but may recur many times.

#### **C. Tertiary Syphilis:**

- 1-3 or more years after secondary lesions.
- Manifestations:
  - Gumma (necrotic tumour-like mass exhibiting granulomatous inflammation).
  - Gummatous perforation of the hard palate.
  - Syphilitic glossitis (previously associated with carcinoma).
  - Cardiovascular lesions: aortic aneurysms.
  - CNS: neuronal loss; dementia.
- Not infectious.

#### **Congenital syphilis:**

- Acquired in-utero from infected mother.
- Rare today because of routine serologic tests.
- Features:
  - frontal bossing of skull.
  - Short maxilla with high palatal vault.
  - Saddle nose.
  - Hypoplastic teeth (Hutchinson’s incisors and Mulberry molars).
  - Rhagades: fissures around mouth.
  - Hutchinson’s triad:
    - A. mulberry molars + Hutchinson’s incisors.
    - Interstitial keratitis (scarred cornea).
    - 8<sup>th</sup> nerve deafness.

#### **Serologic tests for syphilis:**

- VDRL = venereal disease research laboratory test.

- Wasserman, STS = standard test for syphilis,

**Treatment:**

- Antibiotics (penicillin).

## ACTINOMYCOSIS

**Etiology:**

- Actinomyces species (*A. bovis*, *israeli*). N.B. this organism is a bacterium, not a fungus, although it has been called a “ray fungus”.
- The organism attracts calcium, and causes calculus formation – calculus in the pus formed during such an infection has been termed “sulphur granules”.

**Clinical features:**

- Cervicofacial (most common type; 66%).
- Pulmonary.
- Abdominal.

**Histology:**

- Induces abscesses with fistula formation.
- Diagnosis: calcified colonies of organisms in a “sea” of neutrophils (pus).

**Treatment:**

- Penicillin or tetracycline.

## GONORRHEA

**Etiology:**

- *Neisseria gonorrhoeae* – a gram negative paired coccus.

**Clinical features:**

- **Spread:** sexual contact. Organism sensitive to drying and cannot penetrate intact stratified squamous epithelium.
- Acute purulent inflammation and discharge.
- **Males:** anterior urethra affected. Females: cervix, endometrium, fallopian tubes.
- **Complications:** bacteraemia, myalgia, arthralgia, polyarthrits, dermatitis with skin rash.
- **Oropharyngeal involvement** in 20% of patients. Transmission by fellatio, kissing, cunnilingus – therefore majority reported in females or homosexual men.  
Sore throat; diffuse oropharyngeal erythema. Requires a large dose for oral lesions since saliva is a hostile environment for this bacterium.  
Shallow, irregular painful ulcers. Edema with scattered pustules.
- **Diagnosis:** gram stain shows gram negative diplococci (within neutrophils).

**Treatment:**

- Cephalosporins (ceftriaxone) and doxycycline.

# FUNGAL INFECTIONS

- Fungi are eukaryotes, which have thick cell walls and ergosterol-containing cell membranes.
- Grow as budding yeasts or as slender filamentous hyphae.
- Fungi may cause superficial or deep infections.
- Superficial infections involve skin, mucosa, hair, nails.
- Deep fungal infections spread systemically and invade tissue, destroying vital organs in immunocompromised hosts, but heal in otherwise normal hosts.

## CANDIDIASIS (CANDIDOSIS; MONILIASIS)

### Etiology:

- *Candida albicans*.
- Most common oral fungal infection in humans.
- Common commensal 30 -50% of people.
- Spores are non-pathogenic; hyphae are pathogenic.
- 3 general factors determine whether clinical evidence of infections exists:
  - Immune status of the host.
  - Oral mucosal environment.
  - The strain of *Candida albicans*.

### Clinical types of Candidiasis

#### 1. Pseudomembranous candidiasis (Thrush).

- Occurs in:
  - Infants who acquire infection at birth.
  - Adults using long-term broad spectrum antibiotics.
  - Diabetics.
  - Immune dysfunction: leukemia, HIV positive patients.
  - Chemotherapy and radiation treated patients.
- Mucosa covered by white coating (pseudomembrane) resembling cottage cheese or curdled milk.
- Pseudomembrane can be scraped off, leaving red area.
- Occurs on buccal mucosa, palate, tongue.
- Smear with PAS stain reveals *Candida* hyphae.

#### 2. Erythematous (atrophic) candidiasis.

- a. Acute atrophic candidiasis.
  - Red bald tongue.
  - Follows course of broad spectrum antibiotics.
- b. Central papillary atrophy of the tongue (Median rhomboid glossitis).
  - Well demarcated red zone in midline posterior tongue due to loss of filiform papillae.
  - May be associated with Candidal infection at other sites in the mouth: termed Chronic multifocal candidiasis.
- c. Angular cheilitis (perlèche).
  - Erythema, fissuring and scaling at commissures of mouth.
  - Causes: 20% *Candida albicans* alone.

60% *C. albicans* and *Staphylococcus aureus*.  
20% *S. aureus* alone.

- Predisposing factors include iron deficiency anaemia, vitamin (riboflavin deficiency), over-closed vertical dimension, immunosuppression.
- d. Denture stomatitis (chronic atrophic candidiasis).
- Erythema, sometimes with petechiae, on denture bearing surfaces of maxilla.
  - Asymptomatic; patient wears denture continuously.
  - Smears with PAS stain usually reveals *Candida* hyphae.

**3. Chronic hyperplastic candidiasis.**

- White patch that cannot be removed by scraping.
- Usually on anterior buccal mucosa.
- Histology: Hyperparakeratosis, acanthosis of the epithelium; fungal hyphae and neutrophil micro-abscesses (Munro abscesses) in superficial epithelium; chronic inflammatory cell infiltrate in superficial connective tissue.
- Diagnosis: presence of *C. albicans* hyphae in lesion, and resolution of the lesion after antifungal therapy.

**4. Mucocutaneous candidiasis.**

- Group of sporadic or inherited immune deficiency disorders which result in candidiasis of the skin and mucous membranes.
- Oral lesions appear as chronic hyperplastic candidiasis.

**Treatment of candidiasis.**

- Nystatin (Mycostatin):
  - Effective and safe, but bitter taste may affect patient compliance.
- Ketoconazole ((Nizoral):
  - Effective but can cause liver damage, therefore liver enzymes should be monitored during treatment. Use minimal effective dose, since in large doses it can also cause adrenal suppression and male hypogonadism.
- Fluconazole (Diflucan):
  - More effective than ketoconazole, well absorbed, requires only once daily dosing.
  - Disadvantage: interaction with other drugs such as phenytoin (Dilantin), oral hypoglycaemics and warfarin compounds.

**MUCORMYCOSIS (ZYGOMYCOSIS; PHYCOMYCOSIS).**

- An opportunistic fungal infection occurring in debilitated patients, especially diabetics, patients on chemotherapy, patients on steroids.
- Etiology: Organisms of the class Zygomycetes, including *Mucor* and *Rhizopus*.
- Organism exhibits large, non-septate hyphae which branch at obtuse angles.

**Clinical features:**

- Affects various sites, but the rhinocerebral form is most relevant to the oral health care provider.
- Occurs mainly in diabetics with maxillary “sinusitis”.
- May present as a hemorrhagic ulcer or maxillary alveolar ridge, as a result of extension from the antrum.

**Histology:**

- Necrotic tissue caused by vascular thrombosis; organisms tend to invade blood vessels.

- Organisms are present in superficial tissues or within sinus.
- Chronic inflammatory cell infiltrate.

**Treatment:**

- Control primary underlying disease (diabetics).
- Surgically remove the necrotic tissue.
- Amphotericin B.

## **OTHER ORAL FUNGAL DISEASES IN ONTARIO**

- Histoplasmosis - occasionally
- Cryptococcosis - rarely
- Coccidioidomycosis - rarely
- Paracoccidioidomycosis - rarely
- Blastomycosis - rarely
- Aspergillosis - occasionally
- Mucormycosis (Zygomycosis) - occasionally