PRINCIPLES OF MANAGEMENT OF ORAL VIRAL INFECTIONS

CONTENTS

INTRODUCTION

Viruses contain only one type of nucleic acid, either DNA or RNA. They are reproduced solely from their nucleic acid, i.e., a virus never arises directly from a pre-existing virus.

Viruses are not self-reproducing. They need the presence of another organism or host to reproduce or replicate. Viral infections of the oral mucosa are frequently encountered in general practice. The clinical diagnosis of these lesions can sometimes be confusing due to similar clinical presentations. Diagnostic virology has now entered the mainstream of medical practice. Multiple methods are used for the laboratory diagnosis of viral infections, including viral culture, antigen detection, nucleic acid detection, and serology. The clinical presentation of common oral viral infections encountered in the dental practice are discussed

below along with the diagnosis, principles of management and pharmacological agents available for the treatment of oral viral infections

MAJOR VIRAL FAMILIES IN THE HUMAN ORAL CAVITY[1]

- HERPES VIRUSES
- ENTERO VIRUS
- PAPILLOMA VIRUS
- PARAMYXOVIRUS
- RETRO VIRUS (HIV)

HERPETO VIRIDAE

Herpesvirus virions vary in size from 120 to 250 nm and consist of a double-stranded linear DNA molecule surrounded by an icosahedral capsid, a proteinaceous tegument and a lipid-containing envelope with embedded viral glycoproteins. Herpesviruses infect most animal species, and almost 300 different types of herpesvirus have been identified to date. Eight human herpesvirus species with distinct biological and clinical characteristics have been described:[2]

The Herpesviridae family consists of:

alpha subfamily	herpes simplex virus-1 (oral-facial type),
	herpes simplex virus-2 (genital type),
	varicella–zoster virus
beta subfamily	human cytomegalovirus,
	human herpesvirus-6
	human herpesvirus-7)
Gamma subfamily	Epstein–Barr virus and human herpesvirus-8

General properties of Herpes group of viruses:

Alpha herpes viruses	Relatively short reproductive cycle[2]
	Rapid lysis of infected cells
	Latency in sensory ganglia.
Beta herpes viruses	Long reproductive cycle
	Slowly progressing infection
	Wide tissue tropism
Gamma herpes viruses	Specific for B and T lymphocytes and
	Typical lymphoid tissue latency

Human Herpes Virus (HHV)		**Common associated disesase[3]**
Herpes simplex, type 1 (HSV-1)	-	Oral Herpes lesions
Herpes simplex, type 2 (HSV-2)	-	Genital Herpes

Varicella zoster virus (VZV)	-	Chicken pox, Shingles
Epstein-Barr virus (EBV)	-	Infectious mononucleosis
Cytomegalovirus (CMV)	-	CMV mononucleosis
Human herpes virus 6 (HHV-6)	-	Roseola, mononucleosis syndromes
Human herpes virus 7 (HHV-7)	-	Currently, no human disease definitely linked
Human herpes virus 8 (HHV-8)	-	Suspected association with Kaposi's sarcoma

Epidemiology

HSV-1 and HSV-2 occur worldwide and have no seasonal variation. HSV infection is rarely fatal. Most human beings have been infected and harbour latent virus that can reactivate; hence there is a vast HSV reservoir for transmission to susceptible individuals.

Demographic factors affect acquisition of HSV-1 infection. In less developed countries seroconversion happens early in life – at 5 years in around a third of children and in 70-80% by adolescence. In comparison, individuals in more developed countries become infected later on – seroconversion occurs in about 20% of children younger than 5 years; then no substantial rise in frequency happens until an increase to 40-60% at age 20-40 years

Latency:

Each herpesvirus subfamily maintains latent infection in specific cell population(s)[2]

Latency occurs in - trigeminal, cervical or lumbosacral ganglia

In contrast to a chronic infection, latency is not associated with infectious virions. A single individual can simultaneously show herpesvirus latent infection in some cells and active viral infection in other cells.

Herpesviruses express proteins during the normal lytic and latent viral life cycle that can interfere with activities of the innate and adaptive immune systems and alter the cellular environment. The alteration of the host defense ensures a lifelong persistence of the viruses in the infected host and can contribute to disease development. Herpesvirus active infections can remain asymptomatic but still give rise to viral shedding, or can cause illness ranging from classic infectious diseases to benign and malignant tumors, especially in immunocompromised hosts.

HERPES SIMPLEX VIRUS

PRIMARY HERPETIC GINGIVOSTOMATITIS[1]

The first episode of HSV infection in humans who have not previously been exposed to HSV-1 and HSV-2 is called the primar infection .

Mode of Spread [3]

- Skin-to-skin contact with an infected individual
- Infected saliva
- Semen
- Vaginal fluid
- Fluid from herpetic blisters

Incubation period – 3- 9 days

The infection that accompanies primary herpetic gingivostomatitis is usually subclinical in early childhood and only a small percentage of patients develop an acute primary infection. This usually occurs in older children and consists of fever, malaise, headache, cervical lymphadenopathy and a vesiculo-ulcerative eruption on the peri-oral skin, vermilion or any intra-oral mucosal surface.1 The vesicles, which are 2 to 3 mm in dia-meter, rupture, leaving painful ulcers that heal without scarring after seven to ten days. The gingiva is swollen and reddish due to a general inflammation. The virus then migrates to the trigeminal ganglion, where it remains latent.

In more affluent countries with better living conditions and less overcrowding, many young adults do not acquire the infection during childhood. They are at risk of developing a symptomatic infection as an adult, usually presenting as a pharyngotonsillitis, with constitutional symptoms of fever, malaise and headaches. In the case of cervical lymphadenopathy, the vesicles and ulcers on the tonsils and posterior pharynx can resemble infectious mo-nonucleosis or a streptococcal sore throat infection. Primary infection in an immunocompromised adult can be life threatening, with disseminated disease, or it may present with extensive non-healing oral ulceration.

Secondary Herpes Infection

RECURRENT HERPES LABIALIS (RHL)

(cold sore, fever blister)

Around 15 to 30% of the community is affected by episodes of secondary herpes simplex lesions (herpes labialis). Common colds, influenza, fever, UV exposure, menstruation, emotional upset, stress and anxiety predispose the patient to recurrent infection, as these cause reactivation of the virus, which subsequently migrates along one of the sensory divisions of the trigeminal nerve. The lesions are most often seen at the mucocutaneous junction of the lip or peri-oral skin. A burning sensation usually precedes the development of a small cluster of vesicles. These vesicles enlarge, coalesce, ulcerate and become crusted before healing within 10 days.

RECURRENT INTRA ORAL HERPES SIMPLEX INFECTION (RIH)

In oral cavity, secondary herpes manifestations are seen as cluster of small vesicles which rapidly rupture to form ulcers. Lesions are seen on keratinized mucosa – gingiva, hard palate and alveolar mucosa.

HERPES GLADIATORUM

In old days when gloves were not used routinely contact sports such as wrestling, rugby, and football(soccer) sometimes acquire a condition caused by HSV-1 known as herpes gladiatorum, ***scrumpox, wrestler's herpes.***

Aetiopathogenesis

Herpesviruses have two biologic properties: the ability to invade and replicate in the host nervous system and the ability to establish a site of latent infection. The neurovirulent properties of herpes simplex virus (HSV) enable the virus to cause a disease primarily of the sensory nervous system rather than of the skin. The ability of HSV to infect and cause lyses of cells of the central nervous system (CNS) is illustrated by sporadic cases of potentially fatal HSV encephalitis. In more usual circumstances, however, the main target of the virus is the peripheral nervous system. During primary infection, virus is transported via sensory ganglia to establish a chronic latent infection, most commonly in the trigeminal, cervical or lumbosacral ganglia. Retrograde transport of HSV along nerves and the establishment of latency are not dependent on viral replication in the skin or neurons therefore neurons can be infected in the absence of symptoms. Periodically HSV may reactivate from its latent state and virus particles then travel along sensory neurons to the skin and other mucosal sites to

cause recurrent disease episodes. Recurrent mucocutaneous shedding of HSV can be associated with lesions or asymptomatic shedding and in either scenario is allied with a period when virus can be transmitted to a new host.

Complications

- Keratoconjunctivitis
- Eczema herpeticum (auto-innoculation from oro-labial herpes)
- Mononucleosis-like syndrome
- Encephalitis
- Neonatal infections
- Erythema multiforme and Stevens-Johnson syndrome (trigger)

Diagnosis [4]

Although acute herpetic gingivostomatitis and recurrent labial and intraoral herpes simplex infection are diagnosed by the clinical history and signs several laboratory techniques may assist in the diagnosis of the difficult case. These include:

Morphologic studies (Tzanck test) – smear taken from an intact vesicle

Viral culture, antigen or DNA studies (Immunomorphologic, immunovirologic, molecular virologic methods)

Serologic – a rising titre of serum antibodies is confirmatory, but gives the diagnosis retrospectively. It is not helpful in primary infection.

Polymerase chain reaction: Enzyme-linked immunosorbent assay (PCR-ELISA) - HSV encephalitis

Cytology:

Cytopathic effects – multinucleated giant cells, syncytium, ballooning degeneration of nucleus

Tzanck cells - marginated nuclear chromatin (“ground-glass” nuclei)

Eosinophilic intranuclear inclusions (Cowdry type A)

Management [5]

Primary Gingivo-Stomatitis

I. Supportive Treatment

- Adequate fluid intake and soft,bland diet
- Ice chips
- Antipyretic/analgesic agents
    - Paracetamol (acetoaminophen) - pain and fever
- Benzydamine hydrochloride 0.15% mouthwash/spray or
- Lidocaine hydrochloride 1% gel - local pain control or
- 2% viscous lidocaine 5ml(swish and spit 4-5 times/d)
- 0.2% aqueous Chlorhexidine mouthwash or
- Tetracycline mouthwash (contents of 250mg capsule of Tetracycline or doxycycline dissolved in 15ml warm water and held for 2-3 minutes and expectorated four times daily) wil provide resolution of painful ulceration by decreasing secondary bacterial infection

Definitive Management

A. Topical medication - not highly effective[3]

- Acyclovir (Zovirax) – 5% cream/ointment qid - 4 days
- Pencyclovir (Denavir) – 1% cream qid - 4 days
- Docosanol (Abreva) – 10% cream qid until healed

B. Oral antiviral agenst: Limited evidence from RCTs suggests that prophylactic oral antiviral agents may reduce the frequency and severity of attacks compared with placebo, but the optimal timing and duration of treatment is uncertain. Long term prophylaxis should be reserved for those subjects who suffer regular severe attacks

Acyclovir

- Mechanism of action necessitates early administration (within the first 3 days of disease onset)
- Bioavailability : iv (10-fold higher) > oral administration
- Adverse effects : Nausea, vomiting, rash and headache

  Rare: Lethargy, seizures , delirium
- Shortens duration of all clinical manifestations
- Adult dosage : 400 mg qid for 7-14 days
- To prevent HSV induced Erythema multiforme and Stevens-Johnson syndrome[6]

  - 600 mg twice daily for 6 months

Recurrent herpes labialis [7]

Prevention: Early treatment of recurrent HSV infection will decrease the size and duration of lesions

a. Oral antiviral agents :

Long term prophylaxis - subjects with regular severe attacks can be given

Acyclovir - 400 mg QID 5 days

Famciclovir (Famvir) : 250 mg TDS - 5 days (decreased mean lesion surface area by > 50 % + accelerated healing time)

Valacyclovir (Valtrex) for RHL : 2gm BD (12h) -1 day

Topical antivirals: Ayclovir 5%

Pencyclovir (Denavir) – 1% cream qid - 4 days

Docosanol (Abreva) – 10% cream qid until healed

HSV in Immunocompromised patients

- Acyclovir - 800 mg 5times daily

- Famcyclovir - 125mg bid - 5days(recurrent HSV)
- FOSCARNET

  Indication : Acyclovir resistant HSV
- HIV-exposed and HIV-infected infants and children:

  40 mg/kg IV (minimum 2 hour infusion) 3 times a day or 60 mg/kg IV (minimum 2 hour infusion) 2 times a day
- Adolescents:

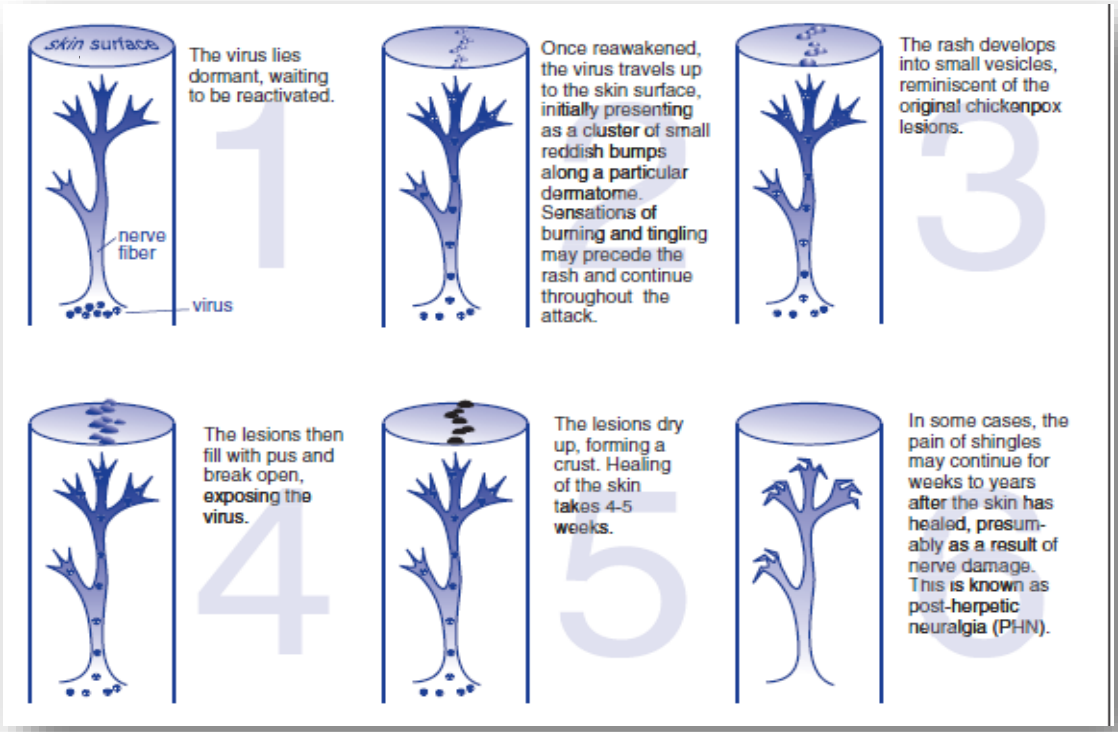
  40 mg/kg IV (minimum 1 hour infusion) every 8 or 12 hours until clinical response

VARICELLA ZOSTER VIRUS

- Primary infection: **CHICKEN POX**
- Prodromal illness with oral vesicles and ulcers typically on the palate
- Skin - pruritic, papular and pustular rashes with vesicules - often occur on the trunk
- Self-limiting, lasting 5-10 days, contracted by direct contact
- Incubation period: Usually 14-16 days (10-21 days) .
- In Children who received zoster immune globulin (VZIG), incubation period = 28 days

- Prodromal period – 2-4 days
- Isolate child from other immune compromised children during the incubation period
- Source of infection - Respiratory system
- Replicates at an undefined site (presumably nasopharynx)
- Infiltrates the reticuloendothelial system and enters bloodstream. Evidence of viremia includes scattered nature of skin lesions.

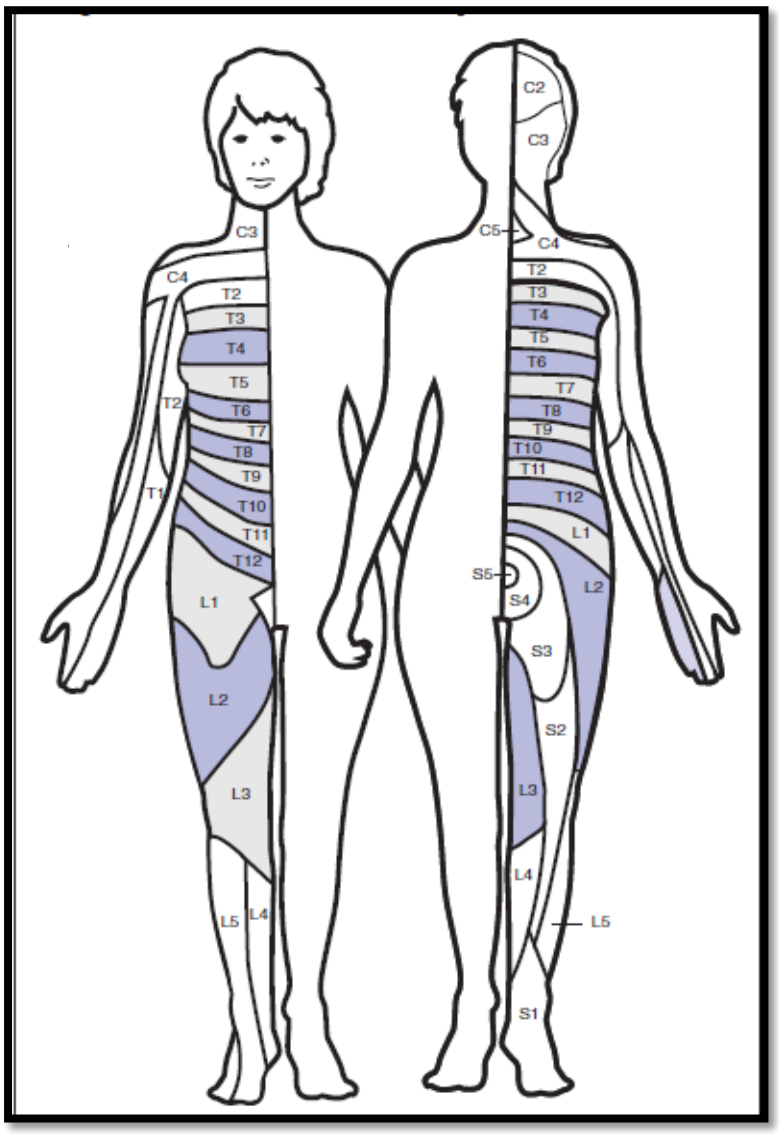
PROGRESSION OF VARICELLA



Herpes Zoster Reactivation[8]

Dermatomes involved in Herpes Zoster is shown in the figure below.The virus cases lesions along -

- T3 – L3
- Cranial nerves – V, VII, VIII
- Generalized lesions are seen in immundysfunction and underlying malignancies



Dermatomes involved in Herpes Zoster reactivation

Secondary Infection - SHINGLES

- viral reactivation in middle to late life
- unilateral, linear & clustered vesicular lesions
- dermatomal distribution on the thoracic/lumbar area followed by craniofacial area
- localized pain or paresthesia ±
- Nerves commonly affected – C3,T5,L1,L2, 1ST div of trigeminal nerve
- Heals with scarring

RAMSAY HUNT SYNDROME [9]

- Reactivation in geniculate ganglion (chorda tympani nerve)
- Vesicles and ulcers of the external ear (otitis externa),soft palate
- Loss of Taste sensation -anterior 2⁄3 of tongue
- Facial palsy (rarely bilateral)

Infection involving Auditory Nerve (cranial nerve VIII) presents with

- Pain and lesions in external auditory canal
- Vertigo, tinnitus,ipsilateral hearing loss

HERPES ZOSTER OPHTHALMICUS[8]

- Recurrent HZV infection of V1 (10- 25% of HZ cases)
- Conjunctivitis
- Corneal ulcers
- Complication : acute retinal necrosis, blindness

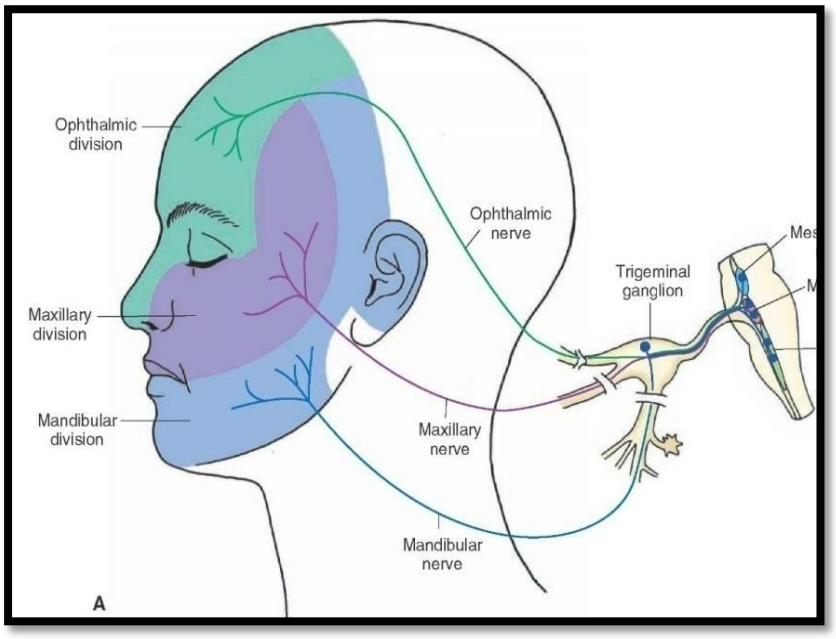


Fig- 2 Areas of distribution of reactive virus from trigeminal ganglion

Oral Manifestations (V2)

- Unilateral vesicles and ulcers
- Pain , burning and tenderness palate (Unilateral distribution)

Painful clustered vesicles which progresses to1- 5mm ulcers

ZOSTER SINE HERPETE[10]

Dermatomal distribution pain in the absence of an antecedent rash

Misdiagnosed as Appendicitis, myocardial infarct, renal colic, cholelithiasis, or colitis, depending on its intensity and location of the affected nerve.

Common differential diagnoses: Trigeminal neuralgia

Bell's palsy

POST HERPETIC NEURALGIA

Defn: Pain that lingers for 30 days or 120 days after the onset of acute rash.

A residual complication of herpes zoster is post-herpetic neuralgia. It occurs in 10% of patients with herpes zoster and affects the trigeminal nerve, most commonly the ophthalmic division. There is persistent, unilateral pain in the affected area. A history of previous skin lesions and possible scarring may aid in the diagnosis. The pain is not paroxysmal, as is seen in trigeminal neuralgia, although it may be just as severe.

Predisposing factors :

- Gender
- Older age
- Prodromal pain
- Severe clinical disease during the acute rash phase

Pathogenesis:

Injury to peripheral nerve by the virus attack leads to demyelination, Wallerian degeneration, sclerosis along with CNS manifestations such as atrophy of dorsal horn cells in

spinal cord which leads to spontaneous discharge of neurons & exaggerated painful response to non-painful stimuli.

Clinical features:

- Burning, lancinating pain
- Persistent pain, paresthesia, hyperesthesia, allodynia - months to yrs after zoster lesions
- Pain in response to non-noxious stimuli (slightest pressure from clothing, bedsheets or wind may elicit pain)

Other complications

- Encephalitis
- Meningitis
- Myelitis
- Disseminated cutaneous and visceral disease in with severe immunosuppression

Diagnostic Testing for Herpes Zoster[11]

Test	*Sensitivity (%)*	*Specificity (%)*
• Polymerase chain reaction	95	99
• Direct immunofluorescent antigen staining	82	76
• Virus culture	20	99

Histologically, HZV, HSV are similar - Intranuclear eosinophilic inclusions and ground-glass nuclear changes

Immunohistochemical stain (diaminobenzidine/hematoxylin counterstain) - reactivity for the viral capsid antigen

Prevention of Varicella Zoster infection[12]

- Since the infection is highly contagious, avoid contact
- Increase school awareness
- Transmission modes: air or droplet , direct contact
- Infectious for 24-48 hours prior to onset of rash and until the last vesicle is scabbed over
- Most contagious phase - during the development of vesicles

General Management:

- Local control measures: cut finger nails short, keep nails clean
- Calamine and/or Benadryl - for itchiness
- Cool baths soothe
- Discourage breakage of blisters.
- Encourage oral intake with clear fluids.
- Monitor fever, appetite, fluid intake and appearance of lesions.
- Isolate child in hospital with airborne precautions.
- Notify infection control.

Varicella Vaccination (VARIVAX)

- Efficacy - approximately 95% in normal hosts
- Varivax II - 0.5 ml subcutaneously (subQ) x 1 dose for ages 1 -12 years
- Varivax II - 0.5 ml subcutaneously (subQ) x 2 doses 4-8 weeks apart for
- ages ≥13 years

Definitive treatment:

Oral antiviral drugs:

- ACV : 800mg q4h - 7-10 days (poor bioavailability)
- Valacyclovir : 1gm tid -7 days
- Famciclovir : 500mg tid – 7 days

Analgesics

Ibuprofen:

Avoid Aspirin or any product containing acetylsalicylic acid (risk of Reye's syndrome)

For children ≥ 1 year of age, use acyclovir 1500 mg/m^2/day IV in 3 divided doses for 7-10 days.

For children < 1 year of age, use acyclovir 30 mg/kg/day IV in 3 divided doses for 7-10 days

HZV in Immunocompromised patients/disseminated lesions [13]

- High risk lesions – eye, tip of nose
- Age > 50 yrs
- Severe pain at presentation

Management : Acyclovir : 10mg/kg iv 8h until resolution of cutaneous /visceral lesions

HIV-exposed and HIV-infected infants and children not responding to acyclovir:

FOSCARNET (Foscavir)

40 to 60 mg/kg IV (minimum 2 hour infusion) 3 times a day for 7 to 10 days Adolescents: 90 mg/kg IV (90 to 120 minute infusion) every 12 hours

Treatment for Post-Herpetic Neuralgia

Topical agents:

- Capsaicin cream (Zostrix) - apply to affected area 3 to 5 times daily (.075% cream)
- Lidocaine 5%(Xylocaine) patch - every 4 to 12 hours as needed

Tricyclic antidepressants

Amitriptyline (Elavil) - 10 to 25 mg orally at bedtime;

increase dosage by 25 mg every 2 to 4 weeks until response is adequate or

maximum dosage of 150 mg per day

Opioid analgesics:[14]

- Tramadol : 5- 10 mg on day1

Increase every 3 day to maximum 200mg/day

- Oxycodone: 5mg every 4-6h on day 1

increase by 5-10 mg increments as needed to 40 mg/day

Corticosteroids [14]

Prednisone: 60 mg orally for 7 d, taper for next 2 wk

Reduce the severity and duration of acute symptoms.

Indication: older patients and/or those with severe pain (Significant adverse effects)

Anticonvulsants

Phenytoin (Dilantin), carbamazepine (Tegretol) and gabapentin (Neurontin) - control neuropathic pain

Gabapentin

Day 1 – 300 mg

Day 2 -300 mg BD

Day 3 -300 mg TDS

Maximum dosage -1800 mg /d in 3 divided doses

Taper gradually over 1 wk

Pregabalin - 75mg at bedtime

Increase by 75mg every 5 days to maximum 300mg BD

CYTOMEGALOVIRUS[3]

Infects mainly T lymphocytes and macrophages. The gB protein in the virion envelope participates in the virus–cell interaction and is a major target of the immune response. Herpes simplex virus and cytomegalovirus are potential pathogens of Behcet's syndrome ulcerations

Transmission occurs through

- Intimate contact
- Direct transfer of infected blood/blood products

Virus can be isolated from saliva, urine, breast milk, blood & feces.

Cytomegalovirus can cause serious infections in immunologically immature hosts (e.g. those with congenital infection) and in immune-compromised hosts [e.g. patients with acquired immunodeficiency syndrome (AIDS) and organ transplant recipients]. Severe cytomegalovirus infections may be more common than previously thought.
Oral lesions in immunocompromised patients present as persistent large necrotic ulcer with pain. The virus infects salivary glands and thus provide a source of constant viral shedding.

Disease association of CMV virus includes:

- Preterm birth
- Transplant rejection
- Hemorrhagic retinal necrosis (HIV patients)
- Gastrointestinal disease
- Pneumonia
- Encephalitis
- Retinitis

Epstein–Barr virus and cytomegalovirus have been associated with multiple chronic "autoimmune diseases, including systemic lupus erythematosus, antiphospholipid syndrome, rheumatoid arthritis, multiple sclerosis, pemphigus vulgaris, Sjogren's syndrome, giant cell arthritis, Wegener's granulomatosis and polyarteritis nodosa.

CMV- **"ONCOVIRUS [2]**

Malignancies associated with CMV includes that of brain, breast, lung, colon, and prostate and salivary gland neoplasms - Mucoepidermoid tumor.[15] Protein markers for active hCMV are present in 97% of MEC.hCMV correlates and colocalizes with an upregulation and activation of an established oncogenic signaling pathway

Diagnosis:

- Biopsy: Enlarged cells within the vascular endothelial cells in the connective tissue with intranuclear inclusions - "owl's eye"
- Immuohistochemistry for CMV antigens
- Antibody /antigen testing
- Blood culture using Shell vial assay
- Qualitative and quantitative PCR

Treatment:[16]

To prevent CMV infection in solid organ transplant (SOT), hematopoietic stem cell transplant (HSCT) recipients, disseminated infection in HIV

Ganciclovir : iv 6 mg/kg every 12 hours

Valganciclovir : 16 mg/kg every 12 hours

Cidofovir : 5 mg/kg of body weight, once weekly for 2 weeks and then once every other week

Foscarnet (CMV Retinitis): IV 60mg/kg q8h x 2 weeks followed by maintenance therapy with 90mg/kg/day

Follow-up: to assess for healing of oral lesions.

EPSTEINBAR VIRUS (HHV4)

Identified initially in 1964 from African Burkitt lymphoma. The virus infects epithelial cells with a cytolytic infection and B lymphocytes with a latent infection and hence also called as B-cell Lymphotropic virus.

Replicates within oropharyngeal epithelial cells

Latency in B- cells, salivary glands and oropharyngeal lymphoid tissues

Viral transmission occurs through constant shedding in saliva during latency. Also through blood transfusion/organ transplantation.

Initial infection - mild , non-specific, occurs during childhood

In adolescence associated diseases includes:[17]

- Infectious mononucleosis
- Hairy leukoplakia of the tongue
- Burkitt lymphoma
- B lymphoproliferative disease
- Hodgkin's lymphoma
- X-linked lymphoproliferative disease
- nasal T-cell lymphoma
- nasopharyngeal carcinoma
- gastric carcinoma, parotid carcinoma and leiomyosarcoma

INFECTIOUS MONONUCLEOSIS (Kissing disease)

Long incubation period – 35 +days

Prodromal symptoms: Malaise, arthralgia , myalgia

Clinical features:

Acute onset of sore throat + fever 100^0F to 103^0 F

Pharyngitis

Submandibular/ Cervical lymphadenopathy (anterior & posterior)

Tonsillitis- Cheesy yellow exudate in tonsillar crypts

Transient oral ulcerations & petechiae (24-48 hrs) during acute phase

Acute symptoms: 2 wks

Viral shedding occurs upto 18 mnths

Infection occurs with increased intensity in immunosuppressed pts Eg: HIV pts

Complications: Neurologic – transitory paralysis

Ruptured spleen

Mononuclear hepatitis

Hemolytic anemia

Thrombocytopenia

Fatalities (.01%) occurs due to respiratory paralysis (lymphocytic infiltration of respiratory centre)

Diagnostic aids:

(a) Lymphocytosis

(b) Atypical lymphocytes on peripheral smear

(c) Positive EBV serology: Mono- spot test

(d) PCR for EBV associated lymphoproliferative disorder

Management

Most cases resolves in 4 – 6 wks

I. Supportive therapy

II. In life threatening cases of (massive lymphadenopathy, tonsillar hyperplasia, oro pharyngeal edema) :

- Corticosteroids (cautious)

- Tonsillectomy and tracheostomy

Possible medications for symptomatic treatment of Infectious mononucleosis

Corticosteroids[18]

Prednisone - 60 mg po daily followed by 10 day taper

Prednisolone - 0.7 mg/kg po 4 days , followed by tapered dose

Dexamethasone - 0.3mg/kg 1 dose

Antiviral drugs[19]

Acyclovir - 600- 800 mg po 5 times/day × 7-10 days

10 mg/kg iv q8h × 7 days

Valacyclovir - 3g/day × 14 dyas

20mg/kg tid × 14 dys

Management of Oral hairy leukoplakia

No malignant potential

Treatment instituted mainly for cosmetic reasons

- Topical retinoic acid (Tretinoin cream 0.05%)

Recurrence occurs after treatment is discontinued.

ENTEROVIRUS

Picornaviridae (small RNA virus) family

COX-SACKIE VIRUS - A (serotype10 and 16)

Diseases caused: Herpangina

Hand foot mouth disease

Acute lymphonodular pharyngitis

COX-SACKIE VIRUS - B

Myocarditis

Infectious Type 1 Diabetes

Atherosclerosis

HERPANGINA "vesicular eruption –inflammation of throat"

An epidemic in childhood (3-10yrs)

CV serotypes : 1,10,16,22

Clinical features:

- Fever, headache , myalgia
- Sore throat, dysphagia
- Erythema followed by vesicles which developes into ulce
- Common sites: Tonsillar pillars, soft palate, oropharynx

Differentiating from primary HSV:

1. Epidemic pattern

2. Milder symptoms

3. Site: Posterior oral mucosa

HSV – Anterior portion – gingiva

4. Absence of generalized acute gingivitis

5. Size of lesion : smaller in Herpangina

6. Histopathology : absence of ballooning degeneration

ACUTE LYMPHONODULAR PHARYNGITIS

Virus: Causative Coxsackie A 10

Variant of Herpangina

Yellowish- white nodules – *do not* progress to vesicles/ulcers

Self-limiting

HAND FOOT AND MOUTH DISEASE

Epidemic in summer among schoolchildren

High transmission rate

Clinical features:

- Oral lesions without prodromal symptoms

- Sore mouth and throat
- Small vesicles – Buccal , labial mucosa, tongue
    - Palmar surfaces of hands and plantar surfaces of feet

Alert Dentists: In patients with acute stomatitis & fever, examine hands & feet for maculopapular/ vesicular lesions.

Diagnosis:

1. Based on Clinical features

2. Culture (from throat or feces)

3. Biopsy findings: intra-epidermal vesicles

dermal edema

eosinophilic nuclear inclusions

intracytoplasmic virus particles

In case of Lymphonodular pharyngitis – hyperplastic lymphatic nodules will be seen

4. PCR

Management :

Self-limiting condition (1 week)

Supportive treatment to be provided:

Hydration & Soft diet

- cold milk, ice cream
- avoid hot beverages & citrus fruits, spicy, fried, or hot foods.

gargle with cool water or try eating popsicles

Limit contact

Pain management :

- Acetaminophen 500 MG

- Ibuprofen 400 mg TDS
- Topical anaesthetic: lidocaine 2%

HUMANPAPILLOMA VIRUS (HPV)

Small, epitheliotropic, nonenveloped, icosahedral, doublestranded, circular DNA viruses

Infection presentation: Epithelial cell proliferation with specificity principally in

- ano-genital area
- larynx–tracheo–bronchial mucosa
- oral mucosa
- skin

Benign lesions of

- skin - WARTS
- mucous membranes - CONDYLOMAS

Oral, cervical and anogenital cancers

Condylomata acuminatum (sexually transmitted diease)

Recurrent respiratory papillomatosis

HPV Induced lesions of oral mucosa

- Squamous cell papilloma
- Condyloma
- Verruca vulgaris
- Focal epithelial hyperplasia (FEH)
- Pre-malignant and malignant oral lesions – OSMF, Lichen Planus

SQUAMOUS CELL PAPILLOMA

A benign soft tissue lesion with finger-like projections and Cauliflower-like verrucous surface

FOCAL EPITHELIAL HYPERPLASIA[1]

- Multiple multiple, soft, flat/rounded nodular elevations of oral mucosa
- Pale to normal appearance
- Commonly seen in American Indians
- Asymptomatic lesion
- Spontaneous regression

HPV with Oncogenic Risk:

- High - HPV 16, 18, 31
- Low - HPV 6, 11, 42, 36
- Type 16 - Oropharyngeal squamous cell CA (30%) , CA tonsils
- HPV related head and neck cancers – high mortality rates

PARAMYXOVIRUS (Morbillivirus)

Associated disease: **RUBEOLA(MEASLES)**

- Incubation period - 10 -12 days
- Transmission – respiratory droplets
- Associated with lymphoid hyperplasia – tonsils, adenoids, Peyer's patch
- Serous exudation and proliferation of endothelial cells around the capillaries

Nine day measles

- 1-3 day : Coryza, Cough, Conjunctivitis, KOPLIK'S SPOTS
- 4-6 day: Maculopapular, erythematous skin rash

- 6-9 day: Fever subsides Desquamation followed by pigmentation of skin lesions

Oral manifestations:

- Candidiasis
- NUG
- Necrotizing stomatitis
- Enlargement of lymphoid tissue – lingual and pharyngeal tonsils
- Severe measles during early childhood affects odontogenesis

eg: pitted enamel hypoplasia of developing permanent teeth

Diagnosis:

- Virus isolation from a clinical specimen(nasopharynx, urine)
- Multinucleated giant cells in smears of nasal mucosa - WARTHIN-FINKEHELDEY GIANT CELLS
- Positive serological test for IgM antibody
- Immunoflourosence detects measles antigen
- Measles encephalitis - raised proteins and lymphocytes in CSF

PREVENTION

- Infants protected for 6 months after birth due to immunity passed on from mothers
- Vaccine - measles-mumps-rubella immunization (MMR) or
- measles-mumps-rubella-varicella immunization (MMRV)

1. 12 to 15 months
2. 4 to 6 years of age
3. Pregnant women – vaccine may offer some protection if given within 72 hours of measles exposure

MANAGEMENT

- Diet
- Rest
- Non-aspirin fever medications
- Closely watch for other complications, such as otitis media, croup, diarrhea, pneumonia, and encephalitis, which may require antibiotics or hospitalization

TOGA VIRUS (RUBIVIRUS) – CONGENITAL RUBELLA SYNDROME[1]

RUBELLA (GERMAN MEASLES)

- Symptoms often last three to seven days. They may include:
- Mild fever
- Coryza
- Headache
- Muscle pain
- Inflamed or red eyes (may develop into conjunctivitis)
- Swollen lymph nodes (suboccipital, post-auricular,cervical)
- Exanthematous rash that starts on the face and spreads downward

O**RAL MANIFESTATIONS**

- Forchheimer's Sign – Papular lesions on soft palate – hard palate, simultaneously with skin rash
- Lasts for 12- 14 hrs
- Palatal petechiae

PARAMYXOVIRUS (RUBULAVIRUS)

Infection caused: MUMPS (epidemic parotitis)

- Salivary glands (parotid) , (pancreas, choroid plexus, mature ovaries and testes)
- Incubation period = 2- 4wks
- Infectious – day 1 to 14 days after clinical presentation
- Transmission- saliva, respiratory droplets

Clinical Features:

- Discomfort, pain, swelling surrounding lower half of external ear
- Chewing, salivary stimulation - pain
- Post-pubertal
- Males - Epididymoorchitis

  Females - Oophoritis, mastitis

  Pregnancy - spontaneous abortion

Oral Manifestations: Redness and enlargement of salivary gland ductal openings

Diagnosis:

- Based on clinical presentation
- Viral isolation from salivary swabs
- Confirmatory tests: Mumps- specific IgM
- Convalescent sera – Mumps specific IgG titres

Prevention: MMR Vaccine

Management:

- Conservative, supportive medical care
- A self-limited disease - No antiviral agent indicated for viral illness
- Maintenance of adequate hydration and alimentation of patients
- Refrain from acidic foods and sour foods

- Analgesics (acetaminophen, ibuprofen) for severe headaches or discomfort due to parotitis
- Patients with orchitis should be adviced bed rest.

ORAL DISEASES WITH A VIRAL COMPONENT

- Recurrent aphthous stomatitis - HCMV, HSV-1, EBV, VZV, HHV-8, HPV (inconclusive relationships - Lin et al, Pedersen & Hornsleth ,Sun et al.)
- Acute necrotizing ulcerative gingivitis -
- Behcet's syndrome - HSV, HCMV
- Oral pemphigus vulgaris - HSV, HCMV
- Erythema multiforme - HSV, EBV, HCMV
- Adult herpetic gingivostomatitis - HSV
- Herpangina - Coxsackie virus A (enteroviruses)
- Hand, foot and mouth disease - Enterovirus-71 and Coxsackie virus A16
- Uvulo-palatoglossal junctional ulcers - HHV-6
- Unspecified oral ulcers - HPV
- HIV/AIDS-related oral ulcers - HSV/HCMV
- Pure red cell aplasia/systemic lupus erythematosus - Human parvovirus B19

ORAL TUMORS RELATED TO VIRUSES[2]

- Cyclosporine-steroid associated lymphoproliferative disorder - HCMV (Tonsillar involvement)
- Benign infantile hemangioendothelioma - HCMV (Parotic gland involvement)
- Kaposi's sarcoma - HIV/HHV-8/HCMV

- Focal epithelial hyperplasia,squamous cell carcinoma／verrucous carcinoma- HPV

Tumours associated with Epstein Bar Virus:

LYMPHOID-TYPE EBV TUMORS

- Burkitt’s lymphoma
- Hodgkin!s lymphoma
- T-cell／natural killer cell lymphoma
- Follicular lymphoid hyperplasia

EPITHELIAL TYPE EBV TUMORS

- Oral squamous cell carcinoma
- Tonsillar carcinoma
- Warthin’s tumor
- Lymphoepitheliomalike CA
- Oral hairy leukoplakia(HIV)

SUMMARY AND CONCLUSION

Human viruses are involved in the development of various types of oral ulcers, oral tumors, classical oral infectious diseases and periodontitis. Herpes simplex virus-1 and cytomegalovirus are linked to oral ulcers; Epstein–Barr virus, herpesvirus-8 and papillomaviruses to oral tumors; Epstein–Barr virus and cytomegalovirus to aggressive periodontitis. Principles of management of viral infections includes confirming the diagnosis following which medical considerations (B12/folate/iron deficiency, diabetes, medication, immune deficiency) should be assessed, ensure adequate hydration, provide symptomatic and specific treatment and prevent secondary infection. When a patient exhibits severe lesions with dehydration, any evidence of ocular or other extra-oral involvement or when they are immunocompromised, they should be referred to a specialist in oral medicine.

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